INFECTIVE HEPATITIS AND ASSOCIATED MALADIES

BEING AN ANSWER TO

" AN APPEAL "

AS MADE BY W. N. PICKLES M.D.

IN HIS

"EPIDEMIOLOGY IN COUNTRY PRACTICE"

(Bristol 1939)

Entia non multiplicanda praeter necessitatem

SUBMITTED AS A THESIS FOR THE

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BY

A. K. MacRae M. B., Ch.B.

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PART I

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I N T R O D U C T I O N

INTRODUCTION.

In the spring of 1944 Professor J. W. McNee addressed a meeting of Medical Practitioners in Newcastle on the subject of Infective Hepatitis.

He dealt mainly with the symptomatology, the revised conceptions of the pathology and the problems of aetiology and epidemiology. Also, he discussed the occurrence of Homologous Serum Jaundice and Post Arsphenamine Jaundice and the views on their relation to Infective Hepatitis.

The writer, who had the privilege of being present at the address, was the more interested as there had been a small epidemic in his practice in 1941. Further, the speaker had emphasized the gaps which existed in the knowledge of the aetiology and epidemiology of the disease in spite of the large amount of painstaking study which had been devoted to their elucidation. To the listener these confessions of our ignorance of such important aspects of the disease seemed like a challenge. Were we just listeners, anxious, no doubt, to acquire such hard-won knowledge? Or could we carry on the story?

The presence of Dr. W. N. Pickles at the meeting, and his interest in, and knowledge of, the disease, made one realise that it might be possible for a busy general practitioner to glean some information about the very points which were in dispute.

This was a possibility which I was later to find stressed

by Pickles [1] himself, and also by Witts[2] . The former emphasizes the peculiar advantages enjoyed by the general practitioner in determining the natural history of this complaint: the latter states that "the analysis of concrete situations is the proper method of approach."

At this time there were two cases of infective hepatitis in the writer's practice. They had occurred in a small compact community at Cold Hesledon, numbering about 600. Within a mile, there was a large colliery village of Murton, with a population of some 9,000.

It was anticipated that the numbers involved in the early months of the epidemic might be small (especially if the epidemic remained confined to the smaller community), in which case the analysis might be the more intimate. Further, the experience gained in this early stage, might, it was hoped, be of great assistance in the attempt to follow the incidence and spread of the disease in the larger community.

As events proved, the epidemic did smoulder in the small community for several months, when it spread to Murton. I was thus fortunate in those respects.

Here was an opportunity to attempt to emulate others in, say, the field of epidemiology. With a due humility for the many shortcomings in my knowledge, I felt that the possibilities of solving some of the problems of this disease depended, not entirely on knowledge and ability, but on the product of ability (including knowledge), application, and opportunity.

Opportunity afforded; on application I resolved; ---- and the product ? I hoped it might be helpful.

Reference.

1. Pickles, W. N. Epidem in Country Practice. Bristol 1939.

2. Witts, L. J. B.M.J. 3 / 6 / 44 p741. Vol I.

THE CONTENTS OF THIS WORK AND THE MANNER OF PRESENTATION.

The work can be devided, rather obviously, into original and non-original sections.

The original work is contained in the second portion of this thesis, and it consists of an account of the epidemic referred to in the introduction, and a discussion of the findings. It will, therefore, be dealt with later.

In view of the vastness of the subject and of the recently published literature, the selection of the contents of the first portion of this work has obviously called for considerable discernment and a nicety of selection. A fully comprehensive survey would be beyond my reach, especially as I desire to emphasize my original observations as the main feature of the study.

I feel that I must crave the indulgence of the reader if I briefly state my reasons in justification of the selection and inclusion of the various components of the non-original section of the work.

I have included mention of such facts as would be useful, and in fact necessary, to allow the student of infective Hepatitis to observe intelligently, the characters and progress of an epidemic of the disease; such facts as would also enable him, further, to assess and analyse the observations

which he was so enabled to make.

A knowledge of the anatomy and physiology of the liver is obviously essential for such a study.

In no other instance is the term "an introduction to the study of medicine" more applicable to pathology than in Infective Hepatitis.

It soon became obvious that a study of the work of others would depend in many instances on an understanding of, or familiarity with, the numerous tests for liver function.

It is commonly accepted that the casual agent of Infective Hepatitis is a virus.

When I qualified in 1923, my knowledge of viruses and virus diseases was scant. In order to attempt to understand the problems of Infective Hepatitis, it appeared to me that I must become familiar with the present day views on virus diseases in man. Having confessed to this original defect in my armament, I have felt it necessary, in order to retain the confidence of my reader, to show that I have in some measure remedied it. I therefore include a section on Viruses and their Role in disease.

These sections of the work are preceded by an historical review, which can so often be not only interesting but also instructive; especially as the unconfirmed views or "suspicions" of earlier writers quite frequently receive support from more recent investigations and knowledge, and thereby assume a fresh significance.

Possibly the most difficult question to decide is the form in which to present the recent views on the disease in question. A vast literature has to be considered in view of the revival of interest in this disease, and it is felt that to attempt to review it in any detail would throw the intended study completely out of the intended balance. If I deal rather briefly with this section of the work, at this stage, it is nevertheless hoped that a consideration of the thesis as a whole may point to my being not unduly unfamiliar with such recent study and thought.

For such reasons then, have I included such work as now follows, and in the order already given in the "table of contents."

THE CIRCUMSTANCES UNDER WHICH THE INVESTIGATIONS WERE CARRIED OUT.

Murton is a colliery village in the County of Durham. The present investigations were conducted from March, 1944, to March, 1945, whilst I was engaged in general practice there. In the winter months, when the majority of the recorded illnesses occurred, it was necessary to visit 25 to 40 people daily and to consult with at least twice as many.

This is mentioned not in any spirit of excusing the quality of the case records, etc., but it may explain many omissions, e.g. serum protein estimations, van den Bergh tests, etc.

I can only offer such information as may be acquired by a general practitioner in his round of visits, and have attempted to add to this such additional academic data as time and opportunity afforded.

THE GENERAL APPROACH TO THE PROBLEMS.

At the risk of anticipating the findings of this work, it might still be helpful to the reader if certain principles adopted in the investigation were now mentioned.

The obvious method would appear to be, to become acquainted with the symptomatology of the disease in so far as personal experience and study of the literature would allow, to seek out the patients who had these symptoms, and to base one's findings on such cases.

But I soon began to doubt the soundness of this procedure.

Others, more able, had toiled at the problem in this manner, and its complete solution had evaded them.

I considered that this orthodox method of approach could be critized for the following reasons:

1. Few could claim to be completely familiar with the symptomatology, in its entirety, according to the published accounts: nor was I one of the few.

Whilst there was considerable uniformity in the descriptions, there were noticeable variations in the symptoms, and their relative frequency, in many of the epidemics.

2. As regards my personal experience, whilst I had been relatively fortunate in having observed the epidemic of 1941, I hoped to greatly enlarge it during the 1944 epidemic.

3. To adopt the so-called orthodox method of study and recording, would imply that my observations would be limited to the acceptance of the previously recorded symptomatology as complete, in so far as I would not include the considerations of illnesses which did not correspond to the descriptions published by others.

The last enumerated reason seemed the more relevant in that this was a disease where our knowledge was, admittedly, very incomplete. It seemed reasonable to assume that our knowledge of the symptomatology of Infective Hepatitis might be incomplete.

Looked at from this angle, it appeared to me that a more laborious method of investigating the epidemic was indicated,

differing from what I have called the orthodox in certain respects, which I will now mention.

Whenever I encountered a case of Infective Hepatitis I noted the usual data of name, age, occupation, and address. I further took similar note of all contacts, both with regard to the source of the patient's infection and the role of the patient in the further spread of the disease.

Next I ascertained where the child sat in his classroom at school, and had diagrams made showing the seats occupied by every child in the school: noting the distance between seats.

It will be remembered that the epidemic occurred in the small community of 600 people at Cold Hesledon. I had intimate knowledge of the friendships, customs, hygiene, habits, etc., of the villagers (who were almost embarrassingly co-operative) as I had practised there for over 20 years.

I watched closely, shamelessly copying Pickles, the local dances and socials, etc., either by personal observation or inquiry; water and milk supplies, including those to the village school, were investigated. The drainage system was considered re the course and efficiency. The local reservoirs and stagnant pools, including even the A. R. P. water storage tanks, were scrutinized, partly in view of insect vectors having been previously considered, especially in the Middle East.

The records of absenteeism at the local works, e.g. the colliery, the larger business premises, including, especially,

a very large bakery, the 'bus garage staff, etc., were inspected to see if periodicity in absenteeism occurred. Teachers, the Attendance Officer, and works managers --- they all co-operated.

This, I am afraid, may be boring in the recital, but it was essential and it was orthodox.

Now, for some time the epidemic ran true to type, and jaundice led to jaundice in the contacts.

Later some of the contacts did not develop jaundice. This I had anticipated from the literature --- in fact it had been stressed by Ford[1] in relation to Wembley epidemic.

And now I decided to break away from the orthodox.

Suppose a contact took ill after the anticipated, say, 30 days. Further, suppose he was not jaundiced. Again let us assume that he did not develop an illness which seemed to fall within the limits of what was commonly termed "infective hepatitis without jaundice". Must we exclude this patient's illness from our consideration of illnesses related to infective hepatitis or even illnesses caused by the agent responsible for infective hepatitis ?

Of course, it might well be by chance that he had developed an illness entirely unrelated to infective hepatitis on that particular date.

If, however, 20 or 30 or more developed a similar illness at an approximately similar interval of time after contact with cases of infective hepatitis, the aetiological relation-

ship, it seemed to me, would constitute a probability rather than a possibility.

Therefore, agreeing with the dictum that "knowledge is dull" and that the greater pleasure lies in the pursuit of knowledge, I decided upon a more laborious method: the more laborious in that much of the work involved could not be expected to show any return.

The plan adopted, therefore, was to watch all the contacts of a case of jaundice from the 14th to the 35th day after contact: to record, preferably verbatim, every complaint made by such contacts, no matter, within reason, how irrelevant it appeared to be, together with any physical findings, and, later, to study the recorded histories.

To be consistent it was necessary to make similar records of people who had been in contact with such contacts, whether the latter had been jaundiced, or had had an illness accepted as indicating "Infective Hepatitis without Jaundice", or an illness falling within neither of those classifications.

This was a policy of the ideal, impossible of complete fulfilment. I, personally, attend professionally upon some 75 per cent. of the small population (600) at Cold Hesledon, but at the larger village of Murton (9,000 population), the proportion does not exceed 40 per cent.

My partner and my other professional colleague, who practice in the area, offered generously to help me. This

offer I could not accept, and for at least two reasons: first, the inquiry had to be my own unaided work: and secondly, time did not permit.

It only remains to add that some of the cases which I originally considered to be so atypical as to be without the accepted bounds of "Infective Hepatitis without Jaundice" were discovered on more intimate acquaintance with the literature to fall within these bounds:-- thus justifying, if on the grounds of my original partial ignorance, my procedure..

Reference.

1. Ford J. C. Infective Hepatitis. Lancet Vol 1, p 675 29/5/1943.

A REVIEW OF THE HISTORY OF INFECTIVE HEPATITIS.

According to Ford[1], "Jaundice of epidemic type is mentioned in De interms affectionibus, often ascribed to Hippocrates and quoted by Cockayne (1912)" Ford also states that correspondence between Pope Zaccharias and Saint Boniface in the eight century A.D. reveals that it was then regarded as contagious.

In July, 1745, an outbreak of epidemic jaundice occurred in Minorca[2]. It is referred to by Hirsch, who, in the same book, discusses the outbreak of jaundice in a Bremen shipyard in 1885. This incident was of great interest in that the 191 cases of jaundice followed the vaccination of 1,280 workers with glycerinated humanised lymph. The cases occurred over a period of several weeks. Additional significance attaches to the further fact[3] that of two other groups of workers in the same yard, one group of 87 men, the other of 500, who were vaccinated with different lymphs, not one developed jaundice. Hirsch attributed the epidemic to the vaccination. He also supposed that some epidemics of the disease were of a dietetic kind. As the Lancet[4] remarks in a leading article on Diet and Hepatitis: "To-day the first of these premises finds immediate acceptance, while a variety of exact observations focusses attention on the second."

But prior to Hirsch's work, Bright and Addison in 1836 in their "Practice of Medicine" expressed the view that "many cases of simple jaundice were expressions of mild forms of subacute

Hepatic necrosis. Thus, in discussing subacute inflammation of the liver, they observed that [5] cases of the less acute kind --- generally yield to treatment --- and they form a large proportion of the cases of simple jaundice which present themselves in practice."

The first epidemic to be recorded in England is said by Lisney [2] quoting Hirsch, to have occurred in Birmingham in 1852.

A few years after Hirsch wrote, Weil described the disease which now bears his name, and in 1912 Cockayne was the first in this country, at least, to differentiate "epidemic catarrhal jaundice" from Weil's disease. It was not until 1916 that Inada et al set the seal on Weil's earlier work by the discovery of the leptospira icterohaemorrhaegiae.

Progress in the knowledge of catarrhal jaundice was impeded by "one of Virchow's less fortunate contributions to pathology." Such was the eminence and authority of this observer that his conception of the pathology of the disease held the field for over sixty years. Virchow held that there occurred a catarrh of the duodenum which involved the ampulla of Vater. The oedema of the mucosa at this site, or the presence of a mucous plug, was held to lead to obstruction of the common bile duct. This pathology fitted in "beautifully" with the symptomatology of the disease, as it was then understood. It now appears that Virchow based his report on the observation of, to put it mildly, an insufficient number of cases.

Many clinicians had suspected, like Bright and Addison, that the jaundice was due to a Hepatitis and that, in the rare fatal cases, the liver cells had undergone necrosis. During the War of 1914-18, Eppinger reported on the post mortem findings in the liver in the case of three soldiers who had been killed whilst suffering from jaundice. He stated that there was no distension of the bile ducts and described the liver as showing "acute yellow atrophy in little."

In 1929 Roholm and Iverson confirmed this view, and, in 1943, Dible, McMichael, and Sherlock's liver biopsy studies [6] further confirmed and extended this knowledge.

Until a very recent date there were many eminent clinicians, who, with the late Sir Arthur Hurst, thought that whilst some cases of the disease were due to Hepatitis, there were still many which were due to the duodenitis aforementioned.

It can now be said that few clinicians still uphold this view, and the occurrence of Hepatitis is almost universally accepted as the cause of the jaundice, and indeed much of the symptomatology in every case.

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In the midst of this account of the work of such a galaxy of talent, it is, with considerable trepidation that I venture to interpolate a personal opinion.

But, if it took 60 years of clinical observation to undo the error of Virchow, we must be careful that the brilliant

work of Eppinger; Roholm and Iverson; Dible, McMichael and Sherlock, and others does not lead us to "rest on our clinical oars."

In a leading article[7] The Lancet refers to the importance of epidemiological studies --- "Snow, Budd and Panum had by keen observation and logical deduction --- revealed the essential epidemiology of cholera and typhoid and measles before the bacteriological era." It also refers to the work of Pickles of Aysgarth in infective hepatitis etc.

Many have a part to play in increasing our knowledge of infective hepatitis.

As Witts[8] says: "Obviously, infective hepatitis is not a disease one would chose to study if one was out for quick results."

From those possibly apparently disconnected remarks, I would state that, in my opinion, clinical observation should be guided by pathological findings and opinions, and not led by them.

McMichael and his colleagues have proved much, and helped much, in the study of infective hepatitis. But I feel that the clinician must not accept even such really beautiful work as being final and total.

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Although special mention of Pickles has been made, this is partly to be ascribed to the writer being similarly engaged in "general practice" and due credit must be given to others. At

this stage a mere enumeration appears to be indicated.

Among these are Ford, who described the Wembley epidemic of 1943; Evans[9] reported 65 cases in an institutional outbreak; Edwards gave an account of 64 cases -- the patients being mainly school children.

Cookson[10] described an epidemic in Gloucester during 1943, and Damodaran and Hartfall[11] reported on the disease as encountered in the garrison at Malta.

Cameron's report of infective hepatitis affecting military personnel in Palestine in 1940 included accounts of the 342 cases encountered: and his discussion on, and interpretation of, the circumstances of the outbreak bear the mark of the expert, with negative findings as significant as the positive.

But with all this work, and that of others, the problems of the disease were to a large extent unsolved, and in 1944 it was still termed "the medical problem of the year."

How large that problem was, and is, I feel we have not hitherto fully recognised. As will be seen later, I think that the question of the non- jaundiced patients is a much larger one than the rather brief mention made to them in the published work, might lead us to suppose.

It would here appear relevant to refer to the occurrence of Homologous Serum Jaundice and Post Arsenical Jaundice, although the nature of the 'original' observations of the writer which follow later, might 'indicate' a comparatively brief resumé as adequate, at least for the present.

The occurrence of jaundice after vaccination with glycerinated humanised lymph in Bremen in 1885 has already been noted. In 1937, of 100 persons who received measles convalescent serum no fewer than 41 developed jaundice and 6 died. The incident occurred in the South of England.[12]

Findlay and McCallum,[12] who have both contributed much to the literature, reported similarly in 1937; the causal agent in this instance being Yellow Fever Vaccine. This again was the agent implicated in Brazil[12] in 1939, where an attack rate of 27% occurred. On both occasions the Vaccine contained human serum.

The matter assumed serious proportions in 1942, when about 30,000 cases with 62 deaths followed the vaccination with Yellow Fever Vaccine of troops of the American Army.[12] In March of that year no fewer than 86 British soldiers became jaundiced following the administration of less than 14 c.cm. of Seitz filtered pooled mumps convalescent serum.

Suffice it for the present to say that, although definite differences in the incubation period of the illnesses as compared with Infective Hepatitis were encountered, and other differences were also remarked, many considered that the similarities far exceeded the differences, and seriously considered whether the diseases might be due to a common agent. This was a view which the similarity of the pathological changes in the liver, as previously referred to,

showed to be a distinct possibility.

Jaundice occurring in the course of the treatment of Syphilis by the organic arsenicals is frequently referred to as Post Arsphenamine Jaundice. Many hold the view that it is caused by the virus of Infective Hepatitis acting on a liver already subjected to the "insult" of two potentially hepatotoxic agents in the form of the initial disease --- syphilis -- and the therapeutic agent --- arsenic. This brief reference, which will later be supplemented in this work, will serve the purpose of showing that the considerable recent increase in the numbers of cases of Homologous Serum Jaundice and of Post Arsphenamine Jaundice have added to the complexities of the understanding of the aetiology and epidemiology of Infective Hepatitis. On the other hand I feel that any such problem may well be brought nearer to an ultimate solution by the acquisition of more knowledge, however puzzling it may be immediately.

Recent investigations and experiments such as that of Himsworth and Glynn on Trophopathic and Toxipathic Hepatitis[13] focus attention, inter alia, on the possible influence of diet on the occurrence, location, nature, and extent of liver damage and the possible influence of such (Trophopathic) dietetic factors on the course of a case of Infective Hepatitis. .....

It is hoped that the above resume will serve to show the trend of thought and the evolution of the methods of approach

to the understanding of this disease.

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THE ANATOMY OF THE LIVER.

The Finer Anatomy of the Lobule.

In the study of hepatitis it is essential to have a knowledge of the finer anatomy of the liver lobule. Many authors provide schematic diagrams, which are helpful particularly with regard to the occurrence of jaundice and the classification of the varieties of jaundice. In Beaumont's Medicine the author employs a diagram modified from Rich. Rolleston and McNee in their Diseases of the Liver,[1] base their description on a schematic diagram, and from this description I propose to quote freely.

Each lobule comprises a series of tubular glands shaped like a test tube, the closed ends being situated centrally. The walls of each test tube are taken to represent a basement membrane, which membrane is lined by the glandular cells of the liver. These glandular cells are polygonal. The bile capillary situated in the centre of the test tube is thus completely surrounded by the glandular polygonal cells. The centre of the lobule is occupied by a branch of the hepatic vein. The wide portal vascular capillaries pass between the tubular glands described, to join this branch of the hepatic vein.

The star cells, now termed Kupffer cells after van Kupffer who described them in 1876, lie along the walls of these

portal capillaries. They were later recognised as belonging to the Reticulo Endothelial System to which further reference will be made.

Passing between the glandular cells to form a very fine fibrous mesh work is the so called liver reticulum. The preservation of this reticulum is an important feature in the extraordinary repair processes which frequently follow even severe hepatic injury.

McNee[1] found no evidence of different types of glandular cells within the same lobule.

THE BLOOD SUPPLY.

This is derived from the Portal vein and the Hepatic artery.

Formed by the union of the splenic and superior mesenteric veins, the portal vein carries by far the largest amount of blood through the lobules. It is interesting and important to note that the left branch courses from the large bowel, whereas the right branch derives its blood from the small intestine. In this way the right lobe receives blood rich in protein derivatives thus contrasting with the blood supply to the left lobe.

The blood in the portal vein has already passed through one set of capillaries in the intestine.

The splanchnic plexus provides the nerve supply to the portal vein and its tributaries -- stimulation of the splanchnic area causes active contraction of the portal venous system.

The hepatic artery is surrounded by a dense sheath of sympathetic nerve fibres as it enters the liver. It provides a considerable proportion of the oxygen supply to the glandular cells and supporting tissues. The capillaries eventually drain into the central branches of the hepatic vein.

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THE PHYSIOLOGY OF THE LIVER.

A knowledge of the physiology of the liver is an obvious essential to the study of infective Hepatitus. It is certainly obvious from recent studies that in many cases, if indeed not in all, the initial lesions occur in the glandular cells of the liver and in the portal tracts, and certainly the liver is the organ most prominently affected when the disease has become established.

The functions of the liver are so many and varied and also so vital to life that their study is complex and a really prodigious task.

In the following chapter I have included such knowledge as I have considered essential to the present study, and I have dealt with the following and in this order.

Bile. 1. Bile Salts. Composition.
Functions.
The cycle of the bile salts.

2. Cholesterol Action of liver on.
Effect of diet on.

3. Bile pigment. The cyle of bilirubin.
Urobilinuria and the significance thereof.

The Liver and Carbohydrate metabolism
and Fat metabolism
and Protein metabolism
as a blood forming organ

The Liver in relation to Haemopoietic Factors.

in relation to Blood Coagulation.

Toxiphylactic function of

As an excretory organ.

Bile. The main constituents of bile are

1. Bile salts.
2. Cholesterol and lechithin
3. Bile pigment.

1. The bile salts are dextrarotatory sodium salts of mixtures of the complex acids -- glycocholic acid and taurocholic acid. In human bile, glycocholic acid predominates, there being about three times as much of it as of taurocholic acid.

On hydrolysis they yield a cholic acid, and glycine or taurine respectively.

Starling[2] states that taurine is probably derived in the body from the metabolism of cystine.

The bile salts are believed to be produced in the liver. They are the substances which are mainly responsible for the unique functions of bile in digestion and absorption, especially of fats.

(a) Hydrotropic action of the Bile salts.

Hydrotropic substances have the power of making water insoluble substances, water soluble. The bile salts have this power, forming hydrotropic compounds with a

number of substances; these compounds so formed, are diffusible through membranes. One of the cholic acids, desoxycholic acid, is especially active in this (hydrotropic) respect. The resulting compound are called choleic acids.

By such combinations insoluble fatty acids, cholesterol, fat soluble vitamins, drugs (e.g. alkaloids) are rendered soluble and diffusible and can be absorbed.

It is interesting to note that when gall stones containing cholesterol are present, the bile acid: cholesterol ratio is usually less than 8:1. This is a lower ratio than the normal.

(b). Effect on Surface Tension.

The bile salts lower surface tension. They lower the surface tension between the watery and oily fluids in the intestine and allows of perfect emulsification.

(c) Effects on the action of Lipase.

When fats are acted upon in the intestine by steapsin, the lipase of pancreatic juice, they are hydrolised. It should be stated that fats are the fatty acid esters of the trihydric alcohol, glycerol: the chief fatty acids being palmitic, stearic and oleic acids. The products of this lipolytic action are thus readily understood to be:-

1. Glycerol.
2. Fatty acids.
3. Soaps.

Glycerol is soluble in water. Fatty acids are soluble in

bile acids, as mentioned.

The alkaline soaps are soluble in water.

The soaps of magnesium and calcium are soluble in bile.

In this way, the fats are reduced to substances which are soluble in the intestinal contents whatever their reaction.

Now, in pure pancreatic juice, steapsin is relatively inactive, but it is activated by bile (or calcium salts).

Furthermore, the actions referred to under (a) and (b) facilitate the action of the lipase.

(d) Cholagogue action.

Bile salts are reabsorbed from the intestine and are returned to the liver. They stimulate the production of bile and, incidentally, economise in the amount of bile acids which the liver must synthesize.

(e) Buffer action.

As a large amount of the base in bile is combined with weak acid, bile can buffer hydrochloric acid. Thus it can neutralise the hydrochloric acid of the gastric contents.

(f) The Absorption of Fatty Acids.

It was formerly considered probable that minute particles of fat passed through the cell walls of the intestinal epithelium. It is now thought, on convincing experimental evidence, that most of the fat is completely hydrolysed before absorption. Fat can be demonstrated in the epithelial cells and the explanation now offered is as follows.

Hydrolysis 'reduces' the fat to glycerol and fatty acid. The glycerol is soluble and passes into the epithelium. The fatty acids (see Section (a)), are acted upon by the hydrotropic bile acids and a soluble loose compound, choleic acid is formed which is diffusible even at pH 6.0. After diffusion of the glycerol and fatty acids, resynthesis to fat occurs.

It should be remarked that if bile does not enter the intestine - as in obstruction of the bile duct - the absorption of fats is practically nil. Obstruction of the pancreatic duct does not have a similar result, as the presence of lipases in the succus entericus may allow of the absorption of 50% of ingested fat; the failure to completely absorb the fat being in fact mainly due to delayed digestion as evidenced by the fact that the faecal fat is hydrolysed or "split".

(g). The amylolytic power of a pancreatic extract is doubled by the addition of bile or bile acids.

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THE CYCLE OF THE BILE SALTS.

The bile salts produced in the liver and excreted in the bile pass into the intestine. The work of Whipple[3] points to their source being body protein or food protein. There is no appreciable loss of bile salts in the urine and faeces as none can be detected in either excretion. They are re-absorbed

rapidly by the intestine, 'picked out' by the liver and re-excreted in the bile; thus they complete a cycle. In starvation they are still produced for a considerable time, and they are present in small amount in the peripheral blood, in health. They must therefore be 'threshold' substances.[3]

In the early stages of obstruction to the bile passages, the amount of bile salts in the blood increases above this threshold, and they are found in the urine. Later, they disappear to reappear frequently for a short time after relief of the obstruction.[3]

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2. Cholesterol.

It will be remembered that the cholesterol content of the blood in health ranges from 150 to 200 mgm per 100 c.c. Of this amount some 50% to 80% is bound as cholesterol-ester of higher fatty acids.[4]

The cholesterol in the bile is free cholesterol.

The glandular cells of the liver, therefore, act on the cholesterol ester, de-esterizing it and not merely excreting it unaltered.

There is an interesting parallel in the supposed alteration of bilirubin in its excretion by the liver to which reference will later be made.

The effect of diet on the concentration of cholesterol in blood and bile.

Nancy Gough[5] reported in The British Medical Journal the effect on the blood cholesterol produced by feeding hospital patients whose metabolism was supposedly normal, on diets low in cholesterol (about 300 mg daily), and later the comparable results of a diet rich in cholesterol (1,100 to 2,170 mg daily). She concluded that the blood cholesterol did not rise in direct proportion to the cholesterol content of the diet. By further experiments in patients with biliary fistulae, and in a dog, she concluded that the cholesterol content of the bile was not affected to any permanent appreciable extent by a greatly increased intake of cholesterol in the diet, even when combined with an increase in the dietetic fat content.

Her findings inclined her to the view that in patients suffering from Cholelithiasis, a low fat, low cholesterol diet was probably of no benefit; in fact, it was unphysiological as being low in fat soluble vitamins, and because fat is a natural stimulant to biliary contraction and drainage.

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3. <u>The Bile Pigment.</u>

<u>The Cycle of Bilirubin and the occurrence of Urobilinuria.</u>

Red blood cells probably become effete after they have been present in the circulation for some two to three weeks. They then become engulfed by the phagocytic cells of the reticulo endothelial system and are disintegrated.

The cells of the reticulo endothelial system are widely distributed throughout the body especially in the connective

and perivascular tissues. The stellate cells of the liver, previously referred to as being present in the wide portal venous capillaries, are termed Kupffer cells after van Kupffer, who described them in 1876. It is now realised that these Kupffer cells represent a very small proportion indeed of the whole reticulo endothelial system, the cells of which are particularly numerous in the spleen, the bone marrow and the lymph glands, and are also present in connective tissues; for example, the microglial cells (del Rio Hortega) of the interstitial tissue of the central nervous system, and the phagocytes which engulf the silica in the lung in cases of Silicosis.

When the red blood corpuscles are engulfed the haemoglobin is broken down into a compound containing iron, which is used by the bone marrow for the building up of new red cells; and the iron-free compound, bilirubin. The bilirubin is conveyed in the blood stream to the liver, and it passes through, and is excreted by, the polygonal glandular cells of the liver in the bile, Thus bilirubin is to a very large extent produced 'outside' the liver which simply excretes it and does not secrete it, as was formerly believed. This fact has been convincingly demonstrated for example by animal experiments where the formation of bile pigments has been demonstrated after the extirpation of the liver.

However, it is generally thought that the liver modifies bilirubin as it passes through the liver cells; and the terms

haemobilirubin or indirect bilirubin, and cholebilirubin or direct bilirubin are employed to denote the two slightly different types.

The bile passes from the liver to the gall bladder where the bilirubin, in common with other constituents of the bile, is concentrated and thence it passes to the duodenum. In the large intestine the bilirubin is reduced by bacterial action, to stercobilinogen which is a colourless chromogen. The stercobilinogen is partly converted into the brown pigment stercobilin which colours the faeces. But a lesser part of the stercobilinogen is absorbed into the blood stream from the large bowel. The bulk of this absorbed pigment, which is now referred to as urobilinogen, is returned to the liver which re-excretes it as such, or oxidises it back to bilirubin before excreting it in the bile. A very small amount of the absorbed urobiliogen escapes the liver and, entering the general circulation, is excreted by the kidneys. Thus the urine normally contains a slight trace of urobilinogen.

.....

It is probable that fresh normal urine contains only the chromogen, urobilinogen, and that urobilin is not present. In pathological conditions the amount of urobilinogen exceeds that of urobilin but the term urobilinuria is, nevertheless, usually employed to denote the presence of the pigment or the chromogen.

The occurrence of urobilinuria may signify either disease

of the liver or excessive haemolysis. But the clinical value of this test is robbed of part of its specificity by the fact that an excess of urobilinogen occurs in other widely different affections of the body. For instance, constipation admits of an increased absorption from the stercobilinogen of the intestine; and an increase of urobilinogen in the urine is described as occurring in many specific fevers. Again, it is often present after the absorption of large extravasations of blood.

Nevertheless, urobilinuria is of value as a diagnostic aid, bearing in mind those limitations, in the consideration of cases where liver damage is suspected.

THE LIVER AND CARBOHYDRATE METABOLISM.

The carbohydrates in the diets are converted into monosaccharides in the small intestine. They are absorbed and reach the liver in the portal blood stream. For our present purpose it will be simpler and sufficiently accurate to consider the fate of the glucose.

The original conception was that enough glucose passed through the liver to meet the immediate requirements of the body and to maintain the blood sugar at a constant level. The remainder, it was thought, was stored in the liver in the form of glycogen. To this conversion of glucose to glycogen the term "Glycogenesis" was applied.

But this simple conception proved to be both incomplete and otherwise inaccurate.

In the first place it was found that the blood sugar level did not remain accurately stabilized especially after the ingestion or injection of carbohydrates or glucose.

Again it was found that the liver continued to contain glycogen in animals which were suffering from starvation. The diet of Eskimos, which is very low in carbohydrate content did not lead to hypoglycaemia.[6] The blood in the hepatic veins was frequently found, especially in starving animals, to have a higher glucose content than the blood in the portal veins. In this, and many other ways, which space does not permit of even the mere enumeration, it became

known that glycogen can be formed from many non carbohydrate substances.

To this process Starling applies the term"Glyconeogenesis."[7] We, therefore, now believe that the liver cells are continually manufacturing glycogen from a variety of materials. Thorpe states that these materials include galactose, mannose, fructose pyruvic acid, glycerol and several amino acids, e.g. alanine, glutamic acid and glycine.

As regards the conversion of fats to glycogen, Rolleston and McNee[8] stated that this is "not yet agreed upon" (1929). Starling[9] assumes that such a conversion does occur, and Thorpe[10], speaking of the fatty acids, states "Only those with an odd number of carbon atoms like propionic acid form glycogen in the liver."

When the glycogen in the liver is given out to the blood, we refer to the process as "glycogenolysis." This process is continually in operation although not always proceeding at the same rate.The conversion from glycogen to glucose takes place under the influence of an enzyme glycogenase. Incidentally, glycogenolysis is stimulated by adrenaline and inhibited by insulin: these occurrences are instanced by the occurrence of hypoglycaemic coma and its treatment. Thus glycogen storage and glycogenolysis proceed in the liver concurrently.

It must not be assumed that all the blood glucose is derived from glycogen. Some of the glucose in the portal

circulation derived from carbohydrate metabolism passes through the liver unaltered to the general circulation and is ready for immediate utilization.

The presence of an adequate carbohydrate intake in the food renders it unnecessary for the liver to utilize protein as a source of glucose.

This is referred to as the Protein sparing action of carbohydrate. It was clearly demonstrated in the experiments of E. P. Cathcart.[11]

THE LIVER AND FAT METABOLISM.

The action of the bile acids and the emulsification and absorption of fats has already been referred to.

It is believed that the liver plays an important part in the further metabolism of fat.

The fat content of the liver is relatively low. It contains 3% phosphatide and 1% glyceride. The phosphatide is mainly lecithin. The iodine value of the fat content is high, 115 to 135. "During starvation the percentage of true fat rises, while the iodine value falls, indicating that the liver is being flooded with neutral fat, of iodine value 35-65. This increase is transitory..." (Thorpe.)[12]

A similar increase in liver fat occurs in such conditions as poisoning by alcohol, chlorofrom or phosphorus: in diabetes and pernicious anaemia; and in experimental feeding with "high fat" diets.

Experiments on animals employing labelled fats show that the store fats or depot fats are transferred to the liver, possibly in the form of lipomicrons.[13]

It has also been proved that ketone bodies are produced in the liver. A bare enumeration of these facts is all that can be included in this paper, but as the result of this work and other interesting investigations it is now generally concluded that the fats are desaturated in the liver, being converted into phosphatide by replacement of one of the fatty acids by a phosphoric acid complex (e.g. phosphoric acid -- choline).

The extent to which further oxidation occurs in the liver is not yet definitely known. In his short book "The Diabetic Life", Lawrence states that after some 36 hours starvation in normal men "the body turns to the utilization of fat for energy requirements. Fat is withdrawn from the body depots and carried in the blood to the liver --- in the liver the fat is broken down into ketone bodies and these are circulated to the muscles for burning, it having been recently proved that both diabetic and normal muscles use them readily as fuel"[14]

This extract is quoted to make the point that many now consider that ketosis is simply an exaggeration of a normal process. When carbohydrate metabolism is proceeding normally, the need for such excessive fat metabolism does not arise, and so harmful ketosis does not occur.

LIPOTROPIC ACTION OF CHOLINE.

Best[15] discovered that on diets which are free from choline large amounts of fat appear in the liver, whereas a diet containing choline prevented this deposition of fat. Choline therefore controls the 'liver fat'. If choline is administered to an animal with a fatty liver the fat is removed. This control of liver fat by choline is known as the lipotropic action of choline.

The Liver and Protein Metabolism.

As the result of gastric and intestinal digestion the protein in the diet is reduced (largely) to amino acids. These amino acids are absorbed by the capillaries of the villi to enter the portal vein. They are thus conveyed to the liver where they are readily 'taken up', but they are also distributed to other tissues. The amino acids serve two main purposes. The first function is to maintain the protein of the body protoplasm. The second function is to provide energy. The needs of the body for the repair of tissue waste are modest, and the amount of nitrogen available in the amino acids is far in excess of such requirements. The nitrogen is eliminated as of no further use, by a process of deamination (or deaminisation). In this process the protein molecule is not completely disintegrated, the nitrogen portion is, as it were, simply thrown off. The first step is the formation of ammonia, which probably occurs chiefly

in the liver and to a less extent in the muscles. The ammonia is in turn converted to urea and this process occurs probably exclusively in the liver. Many believe that this chemical change is the explanation of the so called specific dynamic action of protein: a belief which appears to be supported by the experimental finding that ammonium salts are converted into urea in the liver, with the production of heat.

The molecule remaining after removal of the amino group is probably an α ketonic acid which may be converted into a fatty acid. These fatty acids are ultimately oxidised to $C\ O_2$ and water: their more immediate metabolism varies. Some form glucose, some form aceto-acetic acid, some form neither, as an intermediate stage in their metabolism. Amino acids which form aceto-acetic acid at a stage in their metabolism are termed 'ketogenic.' Those which form glucose are said to be antiketogenic.[16]

The sulphur providing proteins in the diet contain the amino acids, cystine, cysteine or methionine. Food proteins contain on an average 1% of sulphur.
The sulphur is excreted in the bile in the taurine of taurocholic acid, some is utilized in the body, e.g. for the formation of keratin, and some is excreted in the urine.

Sulphur occurs in the urine as inorganic sulphates, ethereal sulphates or unoxidised as 'neutral' sulphur.

The rate of excretion of the inorganic sulphates corresponds so closely with the rate of urea excretion under average

conditions that we believe that the sulphur containing part of the protein molecule is thrown off in the process of deamination in the liver. Like urea excretion, the excretion of inorganic sulphates can be regarded as reflecting exogenous protein metabolism.

Neutral sulphur excretion, in the form of cystine and thiocyanates does not decrease in starvation. It may be regarded as an indicator of endogenous metabolism.

Vitamin A. The liver is the site of storage of the bulk of the Vitamin A in the body.

THE LIVER AS A BLOOD FORMING ORGAN.

Early in foetal life the liver, with the spleen, begins to form blood. The red cells are formed from the endothelial linings of the blood channels; the leucocytes are formed extravascularly, from reticulum cells.[17] At about the fifth month of foetal life the bone marrow begins to form blood and from this time it rapidly and progressively becomes the main blood forming organ.

Although the liver ceases to take any active part in haemopoiesis in the adult, in times of stress it can and does resume this function, in common with the spleen, the renal pelvis, and the lymph glands.

In this way we can understand the myeloid metaplasia seen in the liver when the bone marrow is invaded by e.g. carcinoma, when the erythropoietic activity is hampered as in some forms of leukaemia, in many types of anaemia, and after a large blood loss.

THE LIVER IN RELATION TO HAEMOPOIETIC FACTORS.

When it is considered that the chief materials essential for erythropoiesis are "iron, traces of copper etc., the haemopoietic principle, pigments, vitamins and internal secretions we[18] can not fail to remark the important role of the liver in the production of normal red cells.

IRON. The liver has a great capacity for iron storage. The iron which is absorbed from the duodenum and jejunum is transported

in the plasma, and excess iron is stored in the liver. When iron is administered therapeutically it is believed that this iron reserve in the liver is replenished (when the plasma iron has reached its physiological level), before the bone marrow can receive any of the ingested iron. We have already referred to the phagocytosis of the red cells (page 30).

The iron portion of the haemoglobin molecule provides the liver with haemosiderin, a pigment believed to be mainly ferric hydroxide in organic combination.[19]

COPPER.

The liver contains a small quantity of copper.

Copper does not cure anaemia but it probably acts as a catalyst.

If pure iron is administered medicinally the liver reserve of iron is increased, but this hepatic iron may not be adequately utilized until copper is also given.

THE HAEMOPOIETIC PRINCIPLE.

The haemopoietic principle is formed by the interaction of the dietetic extrinsic factor and the intrinsic factor of the gastric juice. After absorption it is stored in the liver.

THE LIVER IN RELATION TO BLOOD COAGULATION.

It is commonly accepted that blood clotting occurs in this manner. (Whitby and Britton quoting Morawitz).[20]

A blood clot is essentially composed of fibrin.

This fibrin is formed by the action of thrombin on the

soluble fibrinogen of the plasma.

The circulating blood does not contain thrombin but an inactive precursor named "prothrombin."

When blood is shed the prothrombin is converted into thrombin, and this conversion is effected by thrombokinase or cephaline. This thrombokinase is a substance liberated by the blood platelets which disintegrate when they come in to contact with a water-wettable surface: it is also formed by damaged tissue cells. The presence of free calcium ions is also essential for the conversion of prothrombin to thrombin.

How does the activity of the liver affect this process ?

In the first place Vitamin K is essential to the manufacture of prothrombin. Like Vitamins A, D, and E, it is a fat soluble vitamin. The action of the bile salts in the absorption of fats has been considered (see page 27), and it is obvious that an absence or deficiency of bile salts will reduce the absorption of Vitamin K.

Further, prothrombin is synthesized in the liver, and disease of the liver may lead to reduced manufacture of prothrombin: this even in the presence of normal absorption of Vitamin K, or, indeed,when it is absorbed in excess of the normal in attempts at therapy.

Yet again, in severe liver damage, plasma fibrinogen may be reduced.[21] Forster and Whipple consider that the liver is the main, if not the only, source of fibrinogen. 22

THE TOXIPHYLACTIC FUNCTION OF THE LIVER.

As described in the anatomical section, the liver has a blood supply from the hepatic artery as well as its major supply from the portal vein. Any noxious substance present in the systemic circulation can therefore gain access to the liver, as well as any similar 'poison' absorbed from the intestinal tract.

The liver may thus be damaged in any systemic or generalised disease, as for example in acute specific fevers or syphilis.

The portal vein may convey to the liver certain drugs, inorganic poisons or bacterial toxins absorbed from the intestines.

In dealing with these many and varied 'poisons', the liver not only protects itself but in many cases acts as an important line of defence against attack on the body generally. The liver may be damaged by the action of the poisons, in which case we refer to the resulting pathological condition of the liver as 'hepatitis."

The harmful substances may be dealt with either by oxidation, reduction or conjugation: the two principle methods of conjugation being with sulphates, and with glycuronates. They may be destroyed or they may be arrested and stored in the liver cells.

When the liver is damaged there are two facts which

influence the immediate and remote effects of the lesion.

First, the liver may function perfectly for some considerable time when a large portion of it is destroyed. There is a very large 'reserve' as in the kidney.

Second: the liver has truly amazing powers of regeneration and repair after injury. This will be referred to in the section on pathology (see page 83).

THE LIVER AS AN EXCRETORY ORGAN.

Just as the kidney serves for excretion from the systemic circulation, so does the liver provide the excreting path for the portal circulation. In addition to its normal ingredients which we have previously considered, the bile may serve as a vehicle for the excretion of drugs, organisms -- as in typhoid fever -- and other poisons. The bile is the chief medium for the removal of fat soluble dyes such as Sudan III and certain water soluble dyes are excreted by it, mainly, or even entirely.

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JAUNDICE.

When the bilirubin content of the blood is in excess of the normal, this may be evidenced by the visible staining of the skin, mucosae and conjunctivae. To this visible yellow staining we apply the term "Jaundice."

It is noteworthy that there is no fixed level of hyperbilirubinaemia at which jaundice can be said to occur. It may be evident in a patient whose blood bilirubin level is lower than that of a patient who is, nevertheless, not jaundiced. In some conditions e.g. acholuric jaundice, jaundice may be absent in spite of there being well-marked hyperbilirubinaemia.

How does this hyperbilirubinaemia occur ?

A consideration of the source and cycle of bilirubin as given on Page 30 of this study, is helpful, and from it, it will be evident that bilirubinaemia may occur in several ways.

I propose to classify jaundice as being of three types.

1. Haemolytic Jaundice.
2. Obstructive Hepatic Jaundice.
3. Toxic or Infective Hepatic Jaundice.

1. Haemolytic Jaundice.

When excessive haemolysis occurs, we have increased production of bilirubin. The liver cells excrete it but they may be unable to cope with the increased load, and so bilirubin is retained and jaundice occurs. It would seem to be an unnecessary complication to postulate a decreased functional activity on the part of the liver cells in all these cases,

as does Rich, according to Beaumont.[1] It will be noted that in haemolytic jaundice only bilirubin is retained in the blood.

Acholuric Jaundice "a chronic familial disease characterised by crises of excessive blood destruction"....."but with no bilirubin in the urine" may be taken to typify this class of Jaundice.[2]

The absence of bilirubinuria in the presence of bilirubinaemia will be remarked. This finding is not confined to acholuric jaundice but is typical of Haemolytic jaundice in general.

As to the site of the haemolysis, Fairley's view is that methaemalbuminaemia indicates intravascular haemolysis, whereas bilirubinaemia without methaemalbuminaemia denotes that haemolysis has been affected by the cells of the reticuloendothelial system.[3]

2. OSTRUCTIVE HEPATIC JAUNDICE.

If the flow of the bile to the intestine is arrested by pressure on the bile duct, there is a rise of pressure in the bile in the bile ducts and, as a result, bile is absorbed into the blood stream.

Obstruction to the bile duct may occur by the blockage of the lumen of the duct, by swelling of the duct walls, or from pressure from surrounding structures. Gall stones, carcinoma of the duct, careinoma of the pancreas, enlarged glands in the portal fissure, chronic pancreatitis, atresia following operation -- such are typical causes.

The obstruction may be partial or complete and it may be intermittent, the latter as for example in the case of obstruction by a gall stone, in the ampulla of Vater.

3. TOXIC OR INFECTIVE JAUNDICE.

In this type, jaundice is produced in the absence of haemolysis or biliary obstruction, and is caused by the "sickness" (as Boyd[4] so tritely puts it) of the glandular cells of the liver.

These cells are damaged in such conditions as poisoning by e.g. arsenic, chloroform arseniuretted hydrogen, phosphorus, and T. N. T., and similar benzene derivatives. They are similarly affected in such illnesses as pneumonia, typhoid, and typhus fever.

Most important from our present point of view, they are the site of extensive damage in infective Hepatitis.

In fact the substitution of the term "Infective Hepatitis" for the previously employed "Catarrhal Jaundice" is due to the recognition that in this disease the essential pathology is this liver cell damage.

The extent of this damage is probably far in excess of that estimated even by those who were the first to entertain the "hepatic" theory of the pathogenesis of jaundice. Thus McNee and Smith[5] state Cartarrhal Jaundice "is essentially a toxic or infective hepatitis, generally of fairly mild degree, and due to an unknown cause." Reference to Page 97 of this

study would suggest that this, then progressive, view is probably a marked understatement.

I propose to defer the discussion of the mechanism of the production of the jaundice in such cases to a later stage, as it entails a knowledge of the recent pathological findings. But at this stage it may be stated that some incline to the view that not only do the liver cells fail to excrete in normal amount the bilirubin from the blood into the bile canaliculi, but that some of the bilirubin, which they do succeed in excreting, is absorbed from the canaliculi owing to interference with the flow of the bile in these very fine channels.

BILIRUBINAEMIA AND THE VAN DEN BERGH TEST.

The estimation of the bilirubin in the blood is the more important in that we can not estimate the bile acids which the blood contains. Bilirubin is a normal constituent of the blood, normal serum containing from one part in 1,000,000 to one part in 250,000. Whitby and Britton[6] give the normal range as 0.31 ± 0.03 mgm per cent. in the serum but admit that higher readings do normally occur. It is commonly believed that the liver modifies the bilirubin in its passage through the glandular cells, although some (cf Harrison)[7] do not accept this view as proved. Some explain the difference between bilirubin in the blood stream, which has not passed through the liver cells — (haemobilirubin) and bilirubin which has

entered the blood stream after passing through the liver cells (Cholebilirubin) in the following way. It is assumed that the haemolilirubin is adsorbed to the plasma proteins, whereas, when cholebilirubin is present, the bile salts absorbed into the blood stream with the cholebilirubin prevent this adsorption.

The van den Bergh test was introduced in an attempt to distinguish between the two varieties of bilirubin, and, from this differentiation, it was hoped that we would be able to deduce the exact pathology operating in any given case exhibiting jaundice. It enables us to estimate the amount of bilirubin present in the blood. Although brilliantly conceived, it fell short of expectations in some respects.

As a quantitative test it has proved invaluable. As a qualitative test, it was least helpful in the very cases in which we had hoped it would supplement our scant knowledge of the pathology.

The test owes its name to Hijmans van den Bergh of Utrecht who found that hyperbilirubinaemia could be demonstrated by the occurrence of a colour reaction, employing as a reagent Ehrlich's diazo solution. The solution contains p - sulpho-phenyl-diazonium chloride in acid solution.

There are two distinct processes in the test, one being termed "the direct reaction", the other, "the indirect reaction".

In the direct reaction, the diazo solution is added directly to serum or plasma, and we note any colour change and the time

taken for its development. The colour change is effected by the formation of azobilirubin.

If the maximum colour change occurs within 30 seconds, the direct reaction is referred to as "prompt."

If the colour change occurs in 1 to 15 minutes, we term it a "Delayed" direct reaction.

The colour change may occur in part as a "prompt" direct reaction, to be followed by a further deepening of the colour later, as in the "delayed" direct reaction, and this we refer to as a "biphasic" reaction.

Finally, no colour change may occur, this obviously constituting a "negative" direct reaction.

In the indirect reaction the proteins of the plasma are precipitated with alcohol prior to the addition of the diazo solution. The alcohol also extracts the azobilirubin. In this test the colour change occurs immediately. A quantitative estimation of the bilirubin can be made by comparison with a standard. The 'standards' usually used are solutions of anhydrous cobaltous sulphate or coloured glasses made by Messrs. The Tintometer Ltd. for use with the Lovibond comparator.[8] Whitby and Britton[9] employ a standard of ferric thiocyanate dissolved in ether. Bile pigment giving the direct reaction will invariably give an indirect reaction.

INTERPRETATION OF THE RESULTS OF THE VAN DEN BERGH TEST.

From a consideration of the foregoing paragraphs, and taking the majority view of this much debated question, it would seem to be fair to summarise our interpretation of the van den Bergh test results as follows:

"The character of the bilirubin in the blood in all probability depends on the integrity of the liver cells, so that at one end of the scale, as in pure haemolytic jaundice, the van den Bergh test shows a completely negative "direct" reaction, and at the other extreme, as in typical obstructive jaundice, the "direct" reaction is always obtained: while, in between, a "biphasic" reaction is taken to mean that some form of liver damage is present."[10] The direct result is negative, delayed, or biphasic, according to Price's Medicine,[11] when the jaundice is due to inability of the liver cells to excrete bilirubin.

The "indirect" reaction is invaluable in the detection of latent jaundice.

Bilirubin is a "threshold" substance, and the kidney does not excrete it until the plasma level is about 4 (van den Bergh) units (one van den Bergh unit = 1 in 200,000). The "indirect" test is the best way in which this "latent" jaundice can be detected. This hyperbilirubinaemia may reach 18 units in the plasma, in the haemolytic types of jaundice, and there may still be no bilirubin in the urine. This may be explained by

the haemobilirubin being adsorbed to the protein molecule, and so having a raised renal threshold. Here again the "indirect" test uncovers the "latent" jaundice.

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LIVER FUNCTION TESTS.

The present would seem to be the logical stage at which to consider the tests employed in the evaluation of hepatic efficiency. It must, at once, be admitted that such tests as we have evolved are, on the whole, disappointing in the help they afford, not only as indications of the presence and degree of hepatic dysfunction, but also as a means of differentiating between the site of the lesion in the liver or bile passages. (But see later comment.)

Like the kidney, the functions of the liver are many and varied. They are not all, as we have seen, excretory functions, nor is the bile (the liver excretion) readily available for examination, unlike the renal excretion (the urine).

Not only has the liver a large functional reserve, but it has remarkable regenerative powers, as will be noted in the section on pathology, and, thus, apparently normal functional activity may be preserved in the face of considerable damage even to its glandular cells.

Many tests have been evolved from time to time, and at this stage I propose to refer only to such tests as are considered to be of clinical value. Among the tests which I do not propose to discuss further are those depending on the analysis of the duodenal juice, obtained by duodenal intubation, and

the estimation of the concentration and amount of stercobilin plus stercobilinogen in the faeces. The results of the former give very limited help, and the latter test gave results which were of limited value owing to the wide physiological variations --- the estimations varied widely as between healthy individuals and even in any one person from day to day.

This direct approach, in an attempt to evaluate the bile excretion, being largely unsuccessful, we have had to employ less direct methods mainly based on examination of the urine and the blood.

As the various liver functions are frequently not affected to the same degree in any particular patient, the employment of several tests becomes essential in each case.

By the correlation of the results of various tests, and after allowing for the activity of, especially, the pancreas, it would be fair to state that recent progress, in the face of the great difficulties already mentioned, has been encouraging.

Reference will be made in the following survey to recent evaluations of some of the tests.

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The tests are dealt with in the undermentioned order.

1. Fat in the faeces. The colour of the faeces.
2. Examination of the urine for (a) bilirubin; (b) urobilin and urobilinogen, and (c) bile salts.
3. Examination of the Blood Serum.

(a) The van den Bergh test.

(b) The icterus index.

(c) Klein's Intradermal Histamin Test

4. The Laevulose Tolerance Test.
5. The Galactose Tolerance Test.
6. Dye Tests.
7. Hippuric Acid Tests.
8. Plasma Phosphatase Determination.
9. Bilirubin Excretion Tests.
10. Estimation of Plasma Proteins.
11. Flocculation Tests.
12. Serum Choline Esterase Test.
13. Vitamin K Administration and Prothrombin response.
14. Dextrarotatory Sod. Lactate Test (considered at this stage as it is so recent).
15. Recent References to Liver Efficiency Tests.

1. Fat in Faeces. The colour of the Faeces.

In obstructive jaundice, the bile salts fail to reach the intestine and the absorption of fats is grossly defective. But the pancreatic lipase splits the fats in a normal manner. We have therefore an increase in the total fat but the proportion of split fat is normal --- in the faeces.

Normally the fat content in the dried faeces is not more than 25 % and of this proportion not more than 25% is unsplit

neutral fat. When there is biliary obstruction fat may comprise 50% or more of the dried faeces but the proportion of unsplit fat is usually unaltered.

The pale stool in obstructive jaundice is partly due to this high fat content, but also partly owing to the decreased excretion of bilirubin. The failure of the intestine to absorb the fat causes an increase in the bulk of the stool.

In haemolytic jaundice the fat content is unaltered, but excess of stercobilinogen leads to the stools being dark.

2 (a). Examination of the Urine for Bilirubin.

Normally there is no bilirubin in the urine.

Urine containing bile pigment is greenish or brownish yellow in colour. It is more viscid than normal and after it has been shaken the froth, which is coloured, usually yellowish or greenish, persists if bile salts are present.

The following are simple tests for the presence of bilirubin in the urine. They are the tests which I found it feasible to employ.

IODINE TEST.

Tincture of Iodine, diluted with an equal quantity of distilled water, is floated on the surface of the urine, in a test tube. This is a ring test and the presence of a green ring indicates bilirubin.

Formula for the Tincture of Iodine (Harrison).[1]

Iodine 2.5. Potass. Iodid. 2.5 Aq Dest. 2.5. alcohol to 100 parts.

Hutchinson and Hunter advise 10% alcohol solution of iodine.[2]

Gmelin's Test. On 3 c.c. of concentrated nitric acid in a test tube superimpose 3 c.c. of urine.

A green or blue ring indicates bilirubin.

This test is not very delicate and I employed the following improved modification:-[2]

The urine is filtered repeatedly through an ordinary filter paper. A drop of yellow nitric acid is then placed on the impregnated paper. Urobilin in the urine is revealed by a play of colours ---yellowish red, red, violet and greenish.

2 (b). UROBILIN AND UROBILINOGEN IN THE URINE.

This question has already been referred to on Page 30.

A recent comment of the significance of excess urobilinogen in the urine is that of Gordon. [3]

In assessing its value as a diagnostic aid in the pre-icteric stage, he says:

"Excess urobilinogen is (also) found at this stage, but its presence must be accepted with caution, since it occurs in the urine..... indeed where pyrexia is high from any cause. Excess urobilinogen in the urine of afebrile cases is of much more diagnostic value."

The following tests were used as a routine in my cases, the latter, however, was not employed where the former was negative.

Schlesinger's Test.[4] To about 10 c.c. of urine in a test tube add 6 drops of the tincture of iodine as employed in the iodine test for bilirubin. In another tube place 10 c.c. of absolute alcohol and 1 gm. of finely powdered zinc acetate and shake thoroughly. Pour the contents of one tube into the other and repeat this decanting until the zinc acetate has mostly gone into solution. Filter and then examine the filtrate directly by transmitted light, and secondly by transmitted light with your back to the window.

A positive result is indicated by a green fluorescence.

This should be confirmed spectroscopically --- there

is a characteristic band at the junction of the green and blue. (I was quite unable to purchase a spectroscope for the confirmation advised.

Bogomolow's Test.[5] Add 10 drops of 20 per cent. copper sulphate to half a test tube full of urine. Add 3 or 4 c. c. of chloroform.

Place the thumb on top of the test tube and invert ten times, without shaking.

Urobilin is present if the chloroform is coloured pink or yellow.

Here again spectroscopic confirmation is indicated.

Bilirubin may colour the chloroform greenish yellow, but it gives no absorption band although it may cause a general absorption of the blue end of the spectrum.

3 (a). The van den Bergh Test.

I have referred to this test at some length on Page 50.

It may here be added that Aitken[6] postulates the presence of bilirubin in the blood in a colloid form and its conversion by the liver cells to a soluble form, probably a bilirubinate. He further summarises the uses of the reaction, as we have already also mentioned, as:-

(i) To detect the presence of bilirubin in the plasma or serum i.e. in the absence of clinical jaundice or bilirubinuria.

(ii) To distinguish the colloidal from the soluble form.

(iii) To measure its amount.

3 (b). The Icterus Index.

This test attempts to estimate the degree of bilirubinaemia by a determination of the yellowness of the blood serum by a comparison with a solution of potassium dichromate. The index is the ratio of the intensity of the colour in the serum to that of the standard potassium dichromate solution (1 in 10,000).

I find that different authorities give varying values for the normal range but the normal limits are exceeded when six units are present. Between 4 and 6 units is accepted as a normal index.[7] Some (e.g. Bernheim)[8] regard any reading below 4 units as constituting hypobilirubinaemia, although more workers regard the lowest normal range as extending to as low as 1 unit.

Forster[8] gives the normal range as 0.24 to 0.97 mgm per 100 cc of urine corresponding to an index of 1 to 5.

Latent jaundice gives an index of 6 to 15 at which higher figure jaundice becomes visible, usually.

The test has largely been supplanted by that of van den Bergh. The main use now made of it, is in the investigation of carotinaemia, where in conjunction with the van den Bergh reaction it yields helpful information.

The reading does not always vary directly with the degree

of bilirubinaemia and the results are not accepted as very accurate.

5 (c). Klein's Intradermal Histamine Test.

This test is also attributed to Brodribb and Cullinan.

As I will state later in my summary and conclusions, I think it is really disappointing as a pre-icteric aid to diagnosis. This view is also expressed by Gordon.[5] Professor McNee referred to the test in his address at Newcastle.

The test consists of the intradermal injection of ½ cc of histamin hydrochloride . A positive result is evidenced by the edge of the wheal becoming yellow in 90 seconds; presently the yellow colour is evident throughout the intradermal wheal.

4. The Laevulose Tolerance Test.

The liver "takes up" nearly all ingested laevulose from the blood and converts it into glycogen. Next to none of the laevulose is utilised by the tissues. It has been assumed that rapid glycogenesis prevents a rise in blood sugar. The test is performed exactly as we perform the glucose tolerance test. The patient takes 50 grams of pure laevulose, fasting, and the blood sugar level is estimated before the test, and ½, 1, 1½, and 2 hours after the administration of the laevulose. Urine examinations are not an essential part of this test (cf glucose tolerance test) as laevulose is a non threshold substance.[9]

Usually the blood sugar level is very little raised, the curve being very flat, or almost a straight line. If the blood sugar level rises to 30 mgm, or more, beyond the pre-test level, it is indicative of disordered hepatic function.

A very high rise, and a late peak in the curve indicate proportionately, severer degrees of liver dysfunction.

However, the test may fail to give a positive result even in the presence of marked disease of the liver --- the remaining liver cells being sufficient to deal with the laevulose.

The part played, if any, by pancreatic disease is uncertain. The test is positive in diabetes mellitus.

A negative result is therefore of no value.[9]

The test is of use mainly in following the course of a liver disease where a flattening curve of increasingly shorter duration would indicate recovery and vice versa. It has been used in an attempt to assess the probable risk of e.g. salvarsan treatment.

This test has been to a large extent superseded by the Galactose Test which is incidentally simpler.

b. The Galactose Tolerance Test.

Galactose is not so readily converted into glycogen by the liver as are glucose and laevulose. The test essentially consists in the ability of the liver to carry out this conversion. If the liver fails to carry out this glycogenesis

efficiently, the galactose passes out into the general circulation. It is utilised to a really very slight extent only by the tissues, and it is excreted by the kidney as a "no threshold" substance.

The maximum dose with which the liver can deal in health appears to be about 40 grams , and this is the test dose employed. In health, not more than 3 grams are excreted in the urine in the five hours following the ingestion of this test dose.[7] The range is from nil to 5 grams.

The test may be of value, unlike the laevulose Tolerance test, even in diabetics because the glucose in the urine can be removed by fermentation as a preliminary to the estimation of galactose.

Aitken[7] states that the main value of this test (and the preceeding test too) is in the diagnosis between jaundice due to acute liver disease and jaundice caused by obstruction of the bile ducts. Broadly speaking, performed in the early weeks of the jaundice, the test gives abnormal results in the former condition and normal results in the latter condition.[7]

5 (a). Galactose Index.[10]

Maclagan defines the galactose index as the sum of the four blood galactose values at ½, 1, 1½, and 2 hours after the oral administration of 40 g. of galactose. He considers a normal result in health to be 0 to 160.

He gives an evaluation of the test in 145 cases and states that the index is almost invariably raised in toxic and infective cases, but is frequently normal in obstructive cases. A raised index can, however, occur in obstructive cases, especially after the first three weeks, and in febrile and cachectic patients.

He further states that a normal result in an elderly jaundiced patient has so far only occurred in obstructive cases and is of high diagnostic significance.

It is interesting to note that this test gives raised values in most cases of hyperthyroidism.

6. DYE TESTS.

These tests have fallen into comparative disuse owing to the fact that while they are possibly rather more helpful than the laevulose and galactose tests in the assessing of the presence and degree of liver damage, they are of no help in the determination of the type of jaundice.

They frequently simply corroborate more obvious evidences of disease, and they may, indeed, increase the existing liver damage (but see later). [11]

The dyes employed are foreign substances excreted by the liver into the bile and not by the kidneys into the urine. There is a parallelism between the biliary excretion of the naturally occurring pigment bilirubin and those foreign dyes.

Obviously the abnormal results depend on either liver cell damage, or mechanical obstruction to the bile excretion via the bile ducts; thus explaining the failure to aid differentiation in this respect.

Harrison discusses the use of Phenoltetrachlorphenolphthalein and Bromsulphalein and states that the latter is non-toxic and non-irritant. Rose bengal was formerly employed.

In the case of the latter dye there is, at most, a mere trace of the dye in the blood stream half an hour after the intravenous injection of a dose equivalent to 2 mgm. of the dye per Kgm body weight.

The test may show up to 5% dye retention in "non hepatic" diseases.

In liver disease the value may actually reach 100 %.

7. Hippuric Acid Test.

This test was devised by Quick in 1936. It is considered to be a gauge of the "Conjugating and detoxicating" powers of the liver, and is based on the relative ability of the liver to convert benzoic acid to hippuric acid.

This conversion depends on the fact that glycine required for conjugation with benzoic acid to form hippuric acid, is produced by the liver.

In the original test 6 g. of benzoic acid was administered orally and the total urinary output for the following four

hours was tested for its excretion, in the form of hippuric acid.

A normal excretion in health was 3 g. with extremes of 2.6 to 3.3.

Gordon's report in the British Medical Journal[5] claims that the test is reasonably accurate and satisfactory. Quick's original test has been modified by some workers in two respects. e.g. Freda K. Herbert (Biochemist Royal Victoria Infirmary Newcastle) employs a dose of 4 g. benzoic acid, and I have had access to some 'cases' in this institution where the test has given support to 'clinical suspicions' of hepatic disease.

Again Lipschutz has administered the test dose intravenously --- 20 c.cm. of a 10 per cent. solution (2g) of sodium benzoate.

To refer to Gordon's article again, his results showed a very slow return to normal hepatic efficiency in many of his cases of infective hepatitis --- which findings confirmed the suspicions of slow regaining of full function arrived at by the author on clinical grounds.

H. B. Cates[12] showed that only 18 out of 32 patients who were proved to be suffering from cirrhosis, by biopsy through a peritoneoscope, synthesized a subnormal amount of hippuric acid as compared with 22 out of 28 showing retention of bromsulphalein. Other workers, however, have more favourably

compared the test with the dye test mentioned.

8. Plasma Phosphatase Determination.

The enzyme phosphatase which is normally present in small amount in the plasma is excreted, by the liver cells, in the bile where it is present in large amount. Obstruction of the bile ducts would therefore be expected to lead to retention in the blood, with raised phosphatase content. In haemolytic jaundice we should expect no increase, and in infective hepatitis we should be prepared to find a moderate rise. The raised levels in bone diseases etc (the recent work on prostatic carcinoma and secondary bone growths comes readily to mind) must be remembered.

Maclagan[10], however, states that the estimation of serum alkaline phosphatase "does not test any known function of the liver." He employed the method of King and Armstrong (this is mentioned owing to the different "units" referred to in different methods).

As a general rule, cases of hepatitis gave values below 25 units and 'obstructive' cases showed values of usually over 35 units.

Doubtful results (25 to 35 units) occurred, and exceptions to the above generalisation were remarked.

Aitken[13] in an editorial commentary on the Liver Function Tests, states that the higher values found in obstructive jaundice (as compared with the lower values found in disease

of the liver parenchyma) are considered by Kennie "as merely reflecting the absence of bile from the intestine."

9. Bilirubin Excretion Tests.

This test is based on the fact that only the liver and the kidney can excrete bilirubin from the blood. If renal excretion of bilirubin is avoided, and we inject a known quantity of bilirubin into a vein, it follows that the speed with which this bilirubin is removed from the blood depends on the efficiency of the liver as a bilirubin excreting organ.

The technique is exacting and difficult and it receives little mention in the latest reviews (1944).

10. Estimation of the Plasma Proteins.

There is a relation between albumin deficiency and liver deficiency. In a recent contribution to the British medical Journal, Higgins, O'Brien, Stewart and Witts[14] state that changes in the plasma protein in diseases of the liver are of great significance. They found that the changes were not at all marked in acute hepatitis but that they are of great significance in subacute and chronic cases especially from the point of view of prognosis.

If the albumin-globin ratio remains disturbed for a long time, the liver is probably permanently damaged.

So long as the albumin keeps above 3.5 g. per cent. in chronic hepatitis, the liver may continue to function adequately: below this content, the outlook becomes rapidly worse, and below 2.0 g. it is grave.

Similarly, in subacute hepatitis with progressive disease of the liver, they found that an increase in the plasma albumin accompanied temporary improvement in the remissions.

While the albumin diminishes the globulin increases: an extremely high globulin level was reached in many of the subacute cases which eventually proved fatal. So much so, that it more than compensated for the reduced albumin content of the plasma and in several instances there was marked hyperproteinaemia (up to 9.8 g per cent.)

In carcinoma of the liver the globulin was not usually increased and in no case did it exceed 3 g per cent.

11. Flocculation Tests.

(a). Serum Colloidal Gold Reaction.

(b). The Takata Ara Reaction.

(c). The Cephalin Cholesterol Reaction.

These tests are thought to be dependent upon an increase in the gamma globulin content of the serum. It has not been proved that this protein is metabolised in the liver, but positive results in those tests occurs principally in diseases of the liver.

(a) Maclagan[10] selects the serum colloidal gold reaction,

as modified from Gray's original method described in 1940, as the best of the tests for the purpose of differential diagnosis of the types of liver damage. The excess of serum gamma globulin is not directly dependent upon the total serum globulin, nor upon the albumin globulin ratio. In Maclagan's report he demonstrates this by the fact that half of his series of cases which yielded strongly positive reactions had normal globulin figures. A further important observation was that the 'inverted' albumin-globulin ratio in cases of nephritis did not lead to positive test results.

The test yielded, in a large series of cases, the following results:

Infective hepatitis: 93 per cent. positive.

Jaundice due to biliary obstruction: 93 per cent.negative.

Another important diagnostic aid lies in the fact that increasing liver damage in cases of obstructive jaundice usually yielded a negative result. Here the test is an improvement on the galactose test where differentiation is not possible.

Further, in infective hepatitis the test, strongly positive at the onset of the jaundice, became increasingly weaker, becoming negative in 3 to 6 or more weeks; whereas, in cirrhosis there was little change from month to month.

Maclagan remarks on the fact that negative results in post arsphenamine jaundice may suggest a different actiology from that of infective hepatitis where, as mentioned above, positive results are the rule.

12. Serum Choline Esterase Test.

In disease of the liver there is a diminution of the serum choline esterase, which is an enzyme whose action is to destroy acetylcholine with the formation of choline and acetic acid.[15]

If acetylcholine is added to a mixture of the blood serum and Ringer's solution, the amount of acetic acid formed (as estimated by the amount of CO_2 produced) reveals the choline esterase content of the tested serum.

In a review of the results of the test, Schifrin Tuchman and Antopol[13] conclude that values over 40 are against cirrhosis and values of over 50 practically exclude it: values under 40 are "against obstruction", if metastases and cholangitis can be excluded. As the values in "catarrhal" and toxic jaundice ranged from 28 to 100 and were rather more frequently over, than below, 50, it will be seem that the test is of limited value in the study of this group of cases.

13. Vitamin K. Administration.

Prothrombin Response.

In "extra-hepatic" (obstructive) jaundice, the blood prothrombin level is reduced. This is due to the fact that Vitamin K is fat soluble and its absorption is thus diminished in such cases. If Vitamin K is administered and its absorption is assured, the prothrombin level rises quickly and markedly.

But in cases of "intrahepatic" jaundice where the liver cells are damaged they are unable to manufacture a normal quantity of prothrombin from the Vitamin K supplied to them -- even when the supply is in excess of normal.

Briefly, the fault in obstructive cases lies in the absorption of the Vitamin K: whereas in cases of hepatitis the fault lies in the inability to synthesize the prothrombin from Vitamin K.

In performing the test we assure the absorption of the Vitamin by administering it hypodermically (10 mgm daily is the dose employed by Allan and Julian)[16] or by administering it orally,with bile salts.(Allan and Julian's oral dose was 8 mgm Vitamin K with 2.5 gramms bile salts, daily).

It follows from a consideration of the above and reference to Page 42, (The Liver in relation to blood coagulation) that the test dose would be expected to restore the prothrombin level to normal in obstructive cases, and to have little similar effect in "intrahepatic" cases. And such

is the case.

Similarly we can understand how the recovery of the glandular cells of the liver can be gauged by a rising response to Vitamin K administration.

14. Dextrarotatory Sodium Lactate Test (Cohn).

Cohn claims that this test gives more reliable results in the recognition of jaundice as being due to diffuse liver damage or extrahepatic biliary obstruction, than any of the following-- the sodium benzoate test (benzoic acid test) the galactose tolerance test and the ratio of total to esterified cholesterol.

Normal liver cells convert the test substance into glycogen.

As the test is a new one it may be worthy of brief, cryptic description. [13]

Patient in bed fasts for 12 hours.

Blood sample taken before test. Lactic acid content estimated.

Inject d sodium lactate. Dose 75 mgm. per kilo body weight (in 14 per cent. solution), intravenously.

Blood sample lactic acid content estimated 30 minutes after the test.

A retention equivalent to 5 mgm or more per 100 cc of the total dose indicates liver damage.

ADDENDUM.

15. Recent references to Liver Efficiency Tests.

Maclagan[10] classifies the tests as follows:

Class 1. Testing known or accepted functions of the liver.

(a) Serum bilirubin estimations.

(b) Galactose and Laevulose Tolerance Tests.

(c) Serum protein tests.

(d) Urinary urobilin estimations.

(e) Hippuric acid test.

Class 2. "Empirical procedures which do not test known functions but which are obviously correlated either with certain types of liver damage or with certain diseases in which liver damage is prominent."

(a) Estimation of the serum alkaline phosphatase.

(b) Choline esterase test.

(c) Flocculation tests (i) Takata ara reaction.

(ii) Serum colloidal gold reaction

(iii) Cephalin cholesterol test.

Class 2 tests are said to show more striking differences in different types of liver damage and are therefore considered to be, in this respect, the more promising.

He mentions positive results from the newer more sensitive tests in pneumonia, hyperthyroidism, rheumatoid arthritis, scarlet fever, diphtheria and tuberculous meningitis.

In an attempt to obtain the greatest differentiation possible between cases of toxic jaundice and of obstructive jaundice he selects a Flocculation test ---the serum colloidal gold reaction; --- an enzyme test -- serum alkaline phosphatase estimation: -- and a purely functional test -- the galactose index.

He summarises his findings by stating that:--

1. A jaundiced patient with a negative colloidal gold reaction and'a phosphatase' above 35 King Armstrong units probably has biliary obstruction.
2. A jaundiced patient with a positive colloidal gold reaction and a 'phosphatase' below 25 units probably has not biliary obstruction.
3. A strongly positive gold reaction (4 or 5) is against biliary obstruction whatever the phosphatase level.
4. The galactose index is helpful as a confirmatory test and to assess the degree of any liver damage present.

.....

A leading article in "The Medical Journal of Australia" [17] stresses the importance of the speed factor in the evaluation of liver function tests. In relation to the Hippuric Acid Test it advises that the test should be conducted by giving the equivalent of 1.5 gramms benzoic acid (1.77 gramms of Sodium Benzoate) intravenously. "Readings" are taken in 1 hour. The normal value is equivalent to from 0.70 to

0.95 grammms of benzoic acid.

It advises the serial bromsulphalein test.

It stresses the fact that a damaged liver may give normal test results if given time, but that the deficiency is more likely to be revealed in its inability to perform its functions as speedily as the healthy organ.

Aitken[15] sees most promise in the (intravenous administration) galacose test in differentiating between obstructive jaundice, and/ jaundice due to diseases of the liver perenchyma, and welcomes the new and promising sodium d lactate tolerance test of Conn.

A. Dick[18] reports on the cephalin cholesterol flocculation reaction. The test introduced in 1939, by Hanger, depends on the degree of flocculation produced by the patient's serum acting on a cephalin-cholesterol emulsion. Readings are taken in 24 hours and described as "zero" to 4 plus. It is an extremely sensitive test in the early detection of hepatic insufficiency. Positive flocculation occurs in the presence of parenchymatous disease of the liver, and the degree of flocculation is found to correspond to the extent of the damage. Dick reports that the test was positive in all cases of infective Hepatitis, being 4 plus in severe cases.

Clinical improvement was attended by a lowering degree of flocculation and conversely the persistence of positive results was of unfavourable prognostic significance.

The test is of great value in differentiating between

obstructive jaundice and jaundice due to parenchymatous damage, but of comparitively little help in determining whether cirrhosis or carcinoma are present.

It is interesting to note that Dick found the test positive in only 7 patients suffering from post arsenical jaundice, and in view of the fact that the author is a pathologist, it is particularly important that he does not accept the view that the jaundice in such cases is always due to parenchymatous liver damage (hepatitis) "but may be caused by an obstructive process within the billiary passages."

The test is negative in normal healthy individuals. It is positive in a small number of patients suffering from disease not known to effect the liver. In such cases the use of other hepatic function tests usually gives negative results.

.....

The **Erythrocyte Sedimentation Rate.**

In a recent contribution to the British medical Journal [19] Paul Wood stresses the value of the E. S. R. in the early diagnosis of infective hepatitis, especially in its differentiation from clinical malaria: such differentiation is naturally of greatest importance in e.g. the Mediterranean area, where both conditions are prevalent.

He concludes that in the first 10 days of infective hepatitis about 85% of cases have an E. S. R. below 10 m.m. in an hour, using Wintrobe's method. Conversely, in the first 10 days of malaria about 85% of cases have an E. S. R. above 10 m.m.

A result exceeding 20 m.m. in one hour during the first week of the "P.U.O." is said practically to exclude infective hepatitis, whereas in malaria he found such a reading in two-thirds of his cases during the first week.

Robinson[20] confirms the above and extends the period of observation of the E. S. R. The mean value in the first 12 days was about 4 m.m. Between the 12th and 30th days the range was from 3 m.m. to 29 m.m. in a series of 63 cases. The mean value was 10 m.m. and the standard variation 5.89.

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THE PATHOLOGY OF INFECTIVE HEPATITIS.

Reference has already been made in the "Historical Review" to the theory expressed by some clinicians that in infective jaundice the main pathological changes consisted of a degree of hepatitis. This was believed by those observers to be usually of a mild degree, and fatal cases of acute yellow atrophy were considered to represent extreme degrees of the same pathological process.

Logical as this deduction seemed to be, its further consideration was largely neglected in face of the "verdict" of Virchow which few appeared to question or, might we say, dared to question openly.

The firm foundation on which the modern conception of the pathology of the disease is based, lies in the work of Eppinger.[1] During the War of 1914-18 Eppinger examined the livers of three soldiers who had been killed in action while suffering from jaundice. He found no evidence of any obstruction to the bile ducts, but he described a condition of hepatitis which he stated was "an acute atrophy in little."

Biopsy studies conducted by Roholm and Iversen and reported in 1929 did more than confirm this work. They showed that similar damage to the liver occurred not only in infective hepatitis but also in hepatitis occurring in patients under treatment with organic arsenicals.

In 1943 Dible, McMichael and Sherloch[2] published their brilliant work which confirmed the above-mentioned findings, and further extended them.

They employed the method of "punch" biopsy.

The technique employed was to pass a 2 mm canula transpleurally into the right lobe of the liver and to thus obtain a small cylinder of liver tissue.

The fact that the authors found it impossible to make a differentiation based on the histological findings between the cases of infective hepatitis, post arsenotherapy jaundice and serum jaundice will bear the emphasises of repetition.

They describe the changes encountered in the following words ---"Broadly speaking, the picture is one of hepatic cell necrosis and autolysis associated with leucocytic and histiocytic reaction and infiltration."

It was found that the cellular necrosis and autolysis were most marked around the hepatic vein in the centre of the lobules and that, if the process spread, it did so outwards or centrifugally.

The infiltration on the other hand was most marked in the portal tracts whence the spread was towards the centre of the lubule, i.e. centripetal.

In severe cases the early changes were described as of the Diffuse type, and in these the liver cell degeneration

was most marked and the histiocytic and leucocytic infiltration invaded the lobule in a widespread manner.

In contrast to this diffuse type was the Zonal Type of change. This was found to occur in the milder cases, or in cases which had reached a favourable stage in their recovery; and in those the picture was dominated by the periportal cell accumulations --- centrilobular necrosis and autolysis being relatively inconspicuous.

The distinction between the 2 types was frequently definite and decided, but they recognised the occurrence of an intermediate picture where a 'mixed' lesion occurred.

The original article demonstrated the Diffuse, Zonal, and Mixed Diffuse and Zonal lesions, by reference to microphotographs and it is a model of conciseness allied to clear and masterly description. In fact it is difficult to condense the article and the vital knowledge which it conveys, and no apology is offered for the length of the following summary.

Starting with the Diffuse lesions, they give two illustrative instances each of slightly differing type.

Type 1. 1 (a) Severe Acute Hepatitis (Diffuse lesion).

The general histological appearance is chaotic when compared with the regular pattern of the healthy liver. The whole architecture appears to be disorganised. Thus the lobular pattern of the liver is largely lost and the usually orderly columnar arrangement of the liver cells is equally interfered with.

Many of the glandular cells have undergone necrosis and autolysis and have been replaced by a tissue composed of collapsed sinusoids with their Kupffer cells and reticular framework. Other glandular cells are seen to be undergoing necrosis and yet others have two nuclei. The process of regeneration is occurring pari passu with that of destruction. Complete recovery from this condition can and does occur.

1 (b). Severe Acute Hepatitis.

The case illustrated (a post arsenotherapy hepatitis) demonstrated the conditions as in 1 with an associated marked periportal leucocytic and histiocytic infiltration.

We are told that in this case recovery was delayed by the persistence of jaundice and ascites.

The authors add that while complete clinical recovery occurred it may not have been accompanied by complete structural recovery and may subsequently show marked nodular hyperplasia and a true cirrhosis.

Next they deal with the mixed type of lesion, and give a demonstration of biopsy liver material from a case illustrating

Type 2. Moderate Acute Hepatitis with mixed diffuse and Zonal lesions.

In this instance the destruction of the liver lobule is less marked and there is more marked infiltration in the portal tracts. The disturbance of both the lobular arrangement of the liver and the regular architecture of the liver columns is still considerable.

The liver cells in the central region of the lobule are found to be reduced in number, and many of the surviving cells are undergoing necrosis and autolysis.

Not only is there an infiltration with small inflammatory cells in the portal zone, but the whole of the liver lobule shows leucocytic infiltration. The Kupffer cells are increased in number.

Type 3. They next proceed to the study of cases where the lseion is predominently Zonal.

This picture, they state, is seen in two circumstances.

(a). In cases of a mild type it is present from the beginning.

(b). In recovering cases of hepatitis where it may be associated with other, chronic, changes.

(a) The striking feature in this type is the cellular infiltration of the portal tracts by histiocytes, polymorphonuclear leucocytes and a relatively few eosinophils. In contrast to the changes in Type 1 and Type 2 the normal liver structure and architecture is usually unaffected, but there is usually relatively trifling or slight evidence of autolysis of the glandular cells around the hepatic central vein; slight proliferation of the Kupffer cells of the sinusoids, and glandular cell multiplication.

The normal cells stain well with Best's stain --proving that they contain a normal amount of glycogen.

(b) The retrogressive zonal lesion.

The authors give the following clinical data to illustrate the periods at which the two illustrative biopsis were taken.

A man aged 32 years suffered from infective hepatitis. He developed jaundice, which cleared up in 8 days. Jaundice recurred 15 days later. After it had continued for 7 days he was admitted to hospital. The serum bilirubin was then 6.4 m gm. per 100 cc.

1st Biopsy. On admission.

It shows a wide zone of periportal cellular connective tissue with numerous new bile ducts. The lobule also shows some inflammatory change becoming more intense towards the centre.

2nd Biopsy.

8 weeks later. i.e. 12 weeks after the initial attack of jaundice.

The serum bilirubin was now 0.6 m gm per 100 cc. and clinical recovery appeared complete.

This biopsy shows a narrower periportal fibrotic zone and less numerous bile ducts.

The inflammatory changes in the lobule have subsided.

The authors believe that, whilst perilobular fibrosis, or scarring, is quite frequently to be observed in the biopsy specimens obtained at a considerable period of time after clinical recovery appears complete, such fibrosis may ultimately disappear altogether: this in view of the extreme rarity of such perilobular fibrosis in "routine" autopsies.

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Pathological Lesion in Relation to the Duration of the Disease.

Bearing in mind that the biopsies were carried out in 14 cases of Epidemic Hepatitis, 35 cases of Arsenotherapy Jaundice and 7 casesof serum jaundice, it is instructive to note that "jaundice persisting over 2 weeks is more likely to be due to a zonal lesion."

I reproduce the authors' table which is self explanatory.

Type of Lesion	Duration in Weeks.		
	Under 1.	1 to 2.	Over 2.
Diffuse.....	12	2	1.
Mixed Diffuse and Zonal	7	4	3.
Zonal.....	9	3	9.

END RESULTS OF HEPATITIS.

There are 4 possible end results.

A. Recovery.

This is the rule. It is obvious from an examination of the photographs that the degree of necrosis present is frequently greatly in excess of that which the clinical picture would have led us to anticipate. And, further, the presence of marked peri-portal cellular infiltration is present to a surprising extent even in ambulant cases.

Nevertheless a complete recovery (restitutio ad intergrum) structurally and functionally, is probably the rule. The preservation of the reticulin framework as a scaffolding for subsequent orderly regeneration and repair is here of prime importance.

B. Death.

The death rate is low. Fatal cases proceed to acute hepatic necrosis by an extension and exaggeration of the diffuse or mixed diffuse and zonal lesions previously described. The fatal outcome may be delayed when the condition progresses with remissions, with more gradual destruction of the liver cells, in subacute hepatic necrosis.

C. A classical Cirrhosis may be the outcome when the disease is prolonged.

The liver cells become broken up into islets. These islets "assume the circular adenomatous character of

cirrhosis or nodular hyperplasia."

They are surrounded by bands of collagenous fibrous tissue and outgrowths of new bile ducts. "The essence of the condition is the destruction of hepatic cells and their replacement by fibrous tissue."

D. Mild Residual Cirrhosis.

It is considered probable that, although the mild residual fibrosis consequent on the zonal type of hepatitis may persist for some time ultimate complete recovery is likely. This the authors compare with a reversible fibrosis, which they quote as having been described by Cameron (1936) who demonstrated the condition produced by experiments on animals.

HISTOLOGICAL DETAIL OF THE LIVER BIOPSY SPECIMENS.

Before discussing the mechanism by which jaundice is produced, it would be helpful to summarise the histological detail as revealed by the liver biopsies. At the same time we can summarise the findings mentioned in the immediately preceding pages, grouping them as they occur in each part of the liver lobule.

1. Hepatic Lobules.

In the severe cases, including all those showing "diffuse" lesions, disorganization of the hepatic lobule architecture is observed. The regular pattern of the columns of polygonal glandular cells is disturbed, the columns being broken up and the individual cells separated. Many of the cells are seen to be swollen and they may contain a large nucleus or more or more than one nucleus. Other cells are seen to be devoid of a nucleus and such cells frequently become converted into eosinophilic masses.

The changes are less marked in the "mixed" lesions and still less marked in the zonal lesions. In the latter the changes are present mainly in the cells surrounding the central vein, where swelling and autolysis are observed frequently to a minimal degree. Dual nuclei are often observed. Periportal infiltration is thought to lead to loss of polygonal cells in the periphery of the lobule.

2. Central Zones.

Owing to the destruction of the liver cells in this area rarefaction is usually marked. The cells which survive in the centre of the lobule are often swollen, their nuclei being swollen and the cytoplasm shows rarefaction. The sinusoids entering the central vein are dilated, and this vein frequently shows hyaline thickening.

3. Portal Zones.

Cellular infiltration is especially marked here. The cells are mainly small mononuclears of the histiocyte class, a much smaller number of polymorphs and a relatively few eosinophils. Besides spreading from portal tract to portal tract, these cells infiltrate centripetally into the lobules. This lobular infiltration is probably in part a simple infiltration, in part a replacement of necrosed liver cells. This latter assumption is based on the fact that these cells infiltrate into areas where the condensation of the reticulum appears to signify the prior destruction of cells of the liver parenchyma. If the proliferation persists fibrosis occurs.

4. Sinusoids.

Polymorph. leucocytes and eosinophils are frequently visible within the sinusoids. The endothelial cells of the sinusoids are enlarged and increased in number.

5. Glycogen.

The surviving liver cells have a normal glycogen

content. As autolysis proceeds the glycogen content is lost.

6. Fat.

In contrast to the findings at autopsy, the cells obtained by biopsy show no evidence of fatty change.

7. Reticulin.

Several of the microphotographs demonstrated the remarkable preservation of the reticulin framework in the presence of even marked cellular necrosis. The preservation of the framework is essential to the restoration of the normal liver architecture which so often follows even such marked injury. The peripheral condensation has been remarked above, but more striking and important is the condensation of the reticulin which follows really severe injury in the central zones: in which case scarring is permanent.

8. There was no evidence of haemorrhages and the iron content of the liver was not increased.

9. Bile Ducts and Bile Pigment. THIS IS IMPORTANT

Proliferation of the bile ducts is more noticeable in the severe types -- mixed and diffuse lesions.

Some bile staining occurred in the central cells of the lobules, many of which it will be remembered are undergoing necrosis. Kupffer cells in the central zone were similarly stained.

"Bile thrombi were frequently seen: occasionally they were prominent. The distribution of the thrombi was chiefly in

the mid-zones of the lobules; the larger interlobular ducts appeared normal."

THE MECHANISM OF THE PRODUCTION OF JAUNDICE.

As a result of the biopsy findings referred to above we are enabled to form a fairly accurate opinion as to how jaundice occurs in (most cases of) infective hepatitis, post arsephenamine and homologous serum jaundice.

The findings of Dible, McMichael and Sherlock agree with the earlier findings of Eppinger, the biopsy studies of Roholn and Iverson, and the recent observations of Cameron. Very recently Lucke has produced a very valuable paper, confirming, and in some respects, augmenting, the work which I have just detailed. He based his observations on 125 fatalities from over 52,000 cases of the disease in the U. S. Army in 1942.

A. NEGATIVE FINDINGS AND INFERENCES THEREFROM.

The first observation I would make is that none of those workers found any evidence of disease of the ampulla of Vater or of any obstruction either at that site, or in the main bile ducts. (The absence of the alleged plugging of the Ampulla of Vater had also been recorded in 1942 by van Rooyen and Gordon after observations employing duodenal intubation.)

Further there was evidence that the larger interlobular bile channels were not obstructed: nor was there evidence of any degree of ascending cholangitis.

B. POSITIVE FINDINGS AND CONCLUSIONS THEREFROM.

The most striking finding was that of hepatitis. This we might term the essential lesion, in such cases. From the detailed account of the condition it seems reasonable to infer that jaundice can be produced in the following ways:-

The degree of liver cell damage in some cases may be such that the remaining liver cells are "quantitatively inadequate" to excrete all the bile pigment brought to them in the blood stream. It must be observed that the percentage of the liver cells which are severely damaged is almost invariably in marked excess of the number which we would anticipate ~~in~~ FROM the clinical findings.

The disruption of the liver cell columns, leading to consequent rupture of the intercellular bile canaliculi may result in interference with the flow of bile. Cells which become isolated may, similarly, excrete bile into tissue spaces.

Particularly important is the presence of thrombi which occur in the finest ~~intra~~ ER cellular canaliculi.

The thrombi consist of bile which has failed to escape.

The presence of pigmented cells in the central areas of the lobules, which has been mentioned, calls for a word of explanation. Many of these cells are dead and the affinity of dead tissue for bile, which is well known, explains their

pigmentation. Other cells in this area have lost their glycogen and it is thought that they are unable to excrete the bile which they contain.

Thus, liver cell damage and intralobular or intercellular obstruction both contribute to the production of jaundice. The reabsorption of bile "spilled" into the pericellular tissue spaces is probably a contributory factor.

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DIET AND HEPATITIS.

With reference to the more recent views on the effect of diet on the causation and course of the disease: and some observations on dietetic experiments in man.

DIET AND HEPATITIS.

It has long been believed that if the liver cells were well filled with glycogen they were better able to withstand the action of hapatotoxic agents. The use of a high carbohydrate diet in cases of hepatitis, and the preoperative administration of glucose to protect against the possible hepatotoxic effect of the anaesthetic, have been common practice.

Recent experimental work has shown that the provision of a high carbohydrate diet is, in itself, inadequate to ensure that the liver glycogen content is maintained at a high level: the diet had to be generous, in other words of high caloric value. As regard the composition of the diet, the importance of its protein content has recently been stressed. In an article on the Prevention of Liver Damage[1], The Lancet refers to the work of Whipple.

He showed that when the plasma protein level was low, dogs became increasingly susceptible to poisoning by chloroform and that the sulphur containing amino-acid "Methionine" protected them from such hepatic injury. The methionine afforded protection even when it was administered up to 4 hours after the chlorofrom.[2] Miller and Whipple found that the N/S ratio in dogs with depleted plasma proteins was nigher than normal and they believed that this was due to a greater reduction in the S

in the liver than of the N. By the administration of methionine the Sulphur (S) was increased, the N/S ratio was restored to normal and the liver was again protected.

Anderson of Copenhagen found that he could transmit infective hepatitis to pigs, and from pig to pig, but that only the undernourished pigs became ill[3]. This was a significant observation.

Other workers found that the susceptibility of the liver to injury produced by adminstration of arsphenoxide to dogs fed on a protein deficient diet, could be reduced by giving the dogs methionine.

This protection might be, in part, explained by the fact that cysteine and methionine can combine with and detoxicate many organic arsenical compounds. These sulphur containing amino acids might be "used up" in detoxicating the arsenicals, and the liver would then be deprived of their continued protection.

The protection of the liver by proteins in infective hepatitis, if it was so protected, could not admit of such a simple explanation; we would have to assume that the guarding of the liver cells by the proteins was , as it were, of a more direct nature.

The Lancet[3] states that Kosterlitz was able to show that a low protein diet led to diminution in the liver cell cytoplasm. An earlier issue of the same journal[4] referred to

the work of Gyorgy and Goldblatt who produced acute necrosis of the liver in rats by feeding them on a diet deficient in caseine. This effect they were able to counteract by administering methionine alone, or cystine and cholin in combination.

In 1944, Himsworth and Glynn published their article on Toxipathic and Trophopathic Hepatitis [5].

It had the effect of stimulating interest in the possible effects of diet on the occurrence of hepatitis, and on the course of the disease. The Lancet immediately devoted an editorial article to the subject of Diet and Hepatitis [4], and writers [6.7.] who reviewed the year's work on Infective Hepatitis gave prominence to the views of Himsworth and Glynn: not that those views were accepted as being proved, but they were generally considered to be worthy of close consideration.

The authors based their views on the results of animal experiments, they employed rats, and compared their findings in these experiments with the types of hepatic injury known to occur in man.

They found that by feeding rats on diets deficient in protein they were able to produce severe liver damage. Not only could they assure the production of this damage in 100% of the rats, but they could modify the time of its onset

and the severity of the lesions by varying the protein content of the diet.

The type of liver damage produced in such experiments was consistently uniform and the authors termed it a "massive necrosis."

After a latent period of several weeks the animals became ill, be it noted, suddenly. During this latent period the liver showed no evidence of disease. Coincident with the onset of the illness, the liver showed evidence of injury. The early microscopic appearance was that of acute yellow atrophy and this was followed by subacute red atrophy, and finally nodular hyperplasia. Thus, in the early stages, there were large areas of coagulative necrosis alternating with areas in which the liver cells remained intact. Later, the diseased cells were removed and diluted sinusoids took their place.

Ultimately the picture was that of areas of normal liver tissue, separated by broad bands of scar tissue, within which could be seen islets of regenerating parenchymal liver cells.

The histological picture as portrayed above is quite distinct from that of the true portal cirrhosis, which can be produced by quite different dietetic means, in rats. This portal cirrhosis begins as a fine generalized peri-lobular fibrosis which later invades the liver lobule.

The progress of this type of cirrhosis is gradual and hepatic necrosis does not accompany it if the protein intake is adequate.

When the diet was very deficient in protein, those changes were present throughout the whole organ. A lesser degree of protein deficiency led to similar changes affecting only the left lobe of the liver.

This was a particularly interesting observation as we know that the left branch of the portal vein, which supplies the left lobe of the liver, contains blood which courses from the large intestine and the spleen; whereas the right lobe of the liver is supplied by the right branch of the portal vein which contains blood from the small intestine, and in this way it receives blood which is much richer in the products of protein digestion.

This type of liver damage, produced by protein dietetic deprivation, the authors designated "Protopathic Hepatitis." Protection against the onset of such massive necrosis was afforded by caseine or methionine, a sulphur containing amino acid in which caseine is rich.

Contrasting with the Protopathic Hepatitis is the Toxipathic Hepatitis which the authors describe as resulting in their experiments from the use of chemicals, such as phosphorus, chloroform and carbon tetrachloride, and a

bacterial toxin, the endotoxin of B. Proteus. Those liver poisons produced their effect rapidly, usually in a few hours. The resulting hepatitis took the form of either a periportal, zonal, necrosis (Phosphorus and endotoxin of B. Proteus) or a centrilobular, zonal, necrosis ($CH\ Cl_3$ and $C\ Cl_4$) Always the changes were uniform in nature and degree in all the liver lobules.

The illness was fully developed in some 48 hours, and, usually, within 14 days, the dead cells had been removed, and the liver presented a normal microscopic appearance.

Such was the effect of a single dose of the poison, but repeated doses were followed by the development of a typical portal cirrhosis.

How could those findings be correlated with the types of hepatitis which were known to occur in man?

Himsworthy and Glynn thought that the Toxipathic Hepatitis which occurred in their rats was exactly copied in cases of poisoning by Phosphorus, chloroform and carbon tetrachloride in man.

More closely pertinent to our present study, the histological picture of the liver in Infective Hepatitis was usually of this zonal type. Here again we had the, frequently, acute onset, the disease rapidly reached its height usually in a few days, and recovery was the rule.

The delay in the onset of the symptoms they ascribed to the "incubation of the infecting agent;" the resulting damage was similar to that produced by a single dose of the chemical poisons already mentioned; complete restitution to health similarly occurred, in most cases.

Now we have previously seen, in our consideration of the pathology of Infective Hepatitis, that the lesion is not always of this transient zonal type. In fact, examples have been given of the hepatitis featuring the massive necrosis, leading up to scarring and nodular hyperplasia (which we have described as characteristic of Trophopathic Hepatitis) occurring as a result of Infective Hepatitis.

Those workers thought that the development of such massive necrosis was to be ascribed not to a prolonged or very severe action of the causal agent of infective hepatitis, but to the occurrence in the course of the attack of infective hepatitis of a deficiency of the supply of protein to the liver: it was not due to severe toxipathic action but to trophopathic influences.

If trophopathic influences caused the massive necrosis which sometimes occurred in casesof infective hepatitis, how could we understand or explain the mechanism of their production?

The supply of the protective protein factors to the liver via the blood stream would obviously depend on the amount of

such factors present in the blood, and on the quantity of blood supplied to the liver. If either of the above were reduced, the liver would be less efficiently protected and the damage to the liver might be anticipated to be proportional to the reduction in the product of thosr two controlling factors, and to the duration of such a reduction.

In infective hepatitis the liver is enlarged, the swelling leads to increased tension, and this, in turn, must lead to the circulation being impeded. Such circulatory restriction would inevitably reduce the amount of protective protein factors supplied to the liver. In this way, Himsworthy and Glynn state, there occurs in infective hepatitis a "conditioned protein deficiency."

We have already remarked that, normally, the left lobe of the liver is supplied by blood poorer in protein factors than is the right lobe. If the blood supply to the liver is restricted the left lobe would receive a supply of protein protective factors which would fall below the "critical" level necessary for the maintenance of its integrity, whilst the right lobe's supply continued to be adequate for its protection. This agrees with the finding that massive necrosis tends to "Pick on" the left lobe of the liver.

In the experimental Trophopathic hepatitis, we have observed that there was a long latent period, during which the "protein" content of the blood gradually diminished

until it reached a level where hepatitis, quite suddenly, occurred. But in man, as Dible, McMichael and Sherlock have proved, "massive necrosis" occurred early in the course of some cases of infective hepatitis. This could be understood if we accept the theory that in infective hepatitis the portal circulation is restricted, as it is obvious that such a mechanism would operate rapidly as compared with the deficiency consequent on gradual depletion of the protein protective factors produced by dietetic measures.

Was there any other evidence to support this theory of the trophopathic hepatitis in man? There was no certain evidence[4]. The high incidence of cirrhosis of the liver in the poor natives of the Punjab and the Rand might be so explained. Their diets were very low in protein.

The incidence of cirrhosis is very high in the poorly nourished classes of Egypt, Bengal and China.[6]

Further by feeding rats on a diet similar to that of the native workers in the South African mines Gillman[7] produced hepatic cirrhosis.

A proportion of people who have been poisoned by T.N.T. or by Cincophen develop a "massive necrosis" of the liver, and at autopsy typical changes, scarring, nodular hyperphasia etc. are evident. Frequently a long latent interval intervenes between exposure, or continued exposure, to those poisons and

the onset of the consequent illnesses. It may well be that this latent period is the time required for the production of a protein deficiency. In the case of T. N. T. poisoning the deficiency could be caused not by circulatory restriction in the substance of the liver, but probably by an increased nutabolic rate and protein utilization induced by the drug, which may also reduce the amount of the circulating amino acids by combining with them.

This hypothesis is in line with their finding that if they fed rats on diets low in protein and high in fat, but short of causing a trophopathic hepatitis, they could then produce such a change by administering T. N. T. after a latent period of a week or two.

In pregnant woman such influences as anorexia, vomiting, dietary defects, malabsorption, the possibility that the foetus may have first call on certain nutriment, and the predisposition of the pregnant female to deficiency state may lead to deficiency of the protective protein factors. In such a way might we explain the reputed affect of pregnancy on the course of Infective Hepatitis in pregnant woman as commented on by Cockayne, by Ballot in the epidemic in St. Peirre in the island of Martinique and by Bardinet (instances quoted in Himsworthy and Glynn's article).

Thus in Infective Hepatitis, poisoning and pregnancy the course of the hepatitis might be influenced, and massive

necrosis be produced not by separate factors but by the common factor of reduction of the sulphur containing amino acids essential for the protection of the liver or the maintenance of the organ in a healthy state: such reduction below a critical level would lead to trophopathic hepatitis.

In support of such a theory as the above was the observation of German clinicians that the remarkable frequency of massive necrosis in Central Europe which followed the war of 1914-1918 occurred at a time when the inhabitants had existed on diets low in protein. The astonishing increase in such cases was not thought to be, at least entirely, due to the prevalence of infective hepatitis.

.....

This ingenious, interesting and attractive study was however in its entirety barely consistent with the views expressed as a result of biopsy study combined with clinical observation. Nevertheless it led many to hope that at least the more serious forms of hepatitis, where scarring and nodular hyperplasia developed, might be influenced or even prevented by dietary measures: such measures would include the use of methionine.

A consideration of the results obtained by the employment of this, extremely expensive, amino-acid can, I fear, only be considered very disappointing.

Thus McMichael[6] states "Benefit has not resulted from the treatment of acute hepatitis with large doses of amino acids

or with a high protein diet."

Beattie and Marshall[8] found that amino acids, especially methionine, did not reduce the "overall incidence" of liver damage in syphilitis under treatment with neoarsphenamine. They stated that certain of them were markedly effective in " (a) shifting the time of peak incidence of liver damage towards the end of the 2nd course of antisyphilitic treatment or later,
(b) moderating the severity of the liver damage when it did occur."

Later Beattie[5] again reported further favourable results in the course of infective hepatitis and postarsphenamine jaundice when a diet containing 150 grammes of protein daily was employed.

Other workers, e.g. Peters (I have not read the original report of his investigation) thought that cysteine and methionine had a "significant but not remarkable effect on the, postarsphenamine, jaundice."[3]

Certainly with regard to the treatment of infective hepatitis, the most recent contributions to the literature, 1945, make it clear that neither the use of methionine nor the provision of a diet high in protein have proved of benefit. Wilson, Pollock and Harris[9] found that the administration of 5 grammes of Methionine daily, by mouth, to

100 patients suffering from infective hepatitis was not attended by any benefit judging by the severity of the attack, its duration and the incidences of relapses.

Higgins, O'Brian, Peters, Stewart and Witts[10] treated two groups each of 18 patients suffering from infective hepatitis. The control group was given a low fat high protein diet with vitamin supplements. The other group received an exactly similar diet with the addition of a daily dose of 5 grammes Methionine. "Treatment with Methionine did not significantly affect the clinical course of the illness, the anorexia or the average duration of bilirubinuria or of bilirubinaemia.

As recently as June of this year, 1945, Darmady[11] discussed the effect of "protein diet" on infective hepatitis.

In view of the fact that yeast was thought to contain a liver protecting factor[6], it was added to the diet, which then consisted of:-

1.	Carbohydrate	370 G.	
	Protein	154 G.	
	Fat	108 G.	
	Bakers' Yeast	30 G.	All the above daily.
	Anahaemin	2 cc.	
	Thiamine Hyd.	5 mg.	Each twice weekly subcutaneously.

The Control diet was a classical low fat diet.

2. Carbohydrate 320 G.
   Protein 70 to 90 G.
   Fats. 60 G. All the above daily.

No improved response to diet 1 was observed.

In spite of this adverse finding, Darmady, with commendable restraint, does not condemn the views on which the trial of this diet was based. Rather does he appear to credit that the findings of Himsworthy and Glynn are applicable to hepatitis in man, in some aspects. He points out that the patients in his series of cases were R. A. F. personnel, whose diet, prior to their illness, was above what is estimated to be adequate as regard protein requirements.

At present, the findings, he states, are consistent with the effect of protein being maximal as a "protective but not as a restorative measure." As no harm resulted from the use of the high protein diet, this contributor is now undertaking further experiments with widely divergent protein intakes.

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POST ARSENICAL and HOMOLOGOUS SERUM JAUNDICE.

(a). Post Arsenical Jaundice.

I have previously referred to the occurrence of jaundice in the course of the treatment of Syphilis by the injection of organic arsenicals and also to its similar occurrence after the injection of sera or vaccines containing even minute quantities of human serum. We have further seen that the histological detail of the liver in both of those conditions and in infective Hepatitis has been described as being identical.

This latter observation naturally led many to question whether all three diseases were in fact simply instances of one disease process caused by a common agent.

The subject of Post Arsphenamine Jaundice was reviewed by Beattie and Marshall in the British Medical Journal[1] and the latter discussed the question at a meeting of the Section of Experimental Medicine and Therapeutics of the Royal Society of Medicine.[2] Jaundice tends to occur most frequently at certain periods in the arsenical treatment of syphilis.

In the early stages of treatment, e.g. from the 6th to the 21st day, hepatitis is regarded as a "true toxic arsenical reaction", the hepatitis and resulting jaundice being considered as part of a "general toxico dermal reaction" (Millian). About 100 days after the start of treatment a larger number of cases occur, and it is this group with such delayed hepatitis, with which we are at the moment concerned.

The authors quote the biopsy observations of Gutman and Hanger, and of Naunyn, stating that bile thrombi and cholangiolitis are present in the early class of cases; the late group of cases is characterised by the picture of hepatitis as described by Dibble, McMichael and Sherlock (to which I have previously referred.)

To what agent, or agents, are we to ascribe this delayed jaundice ?

Earlier workers thought that it might be due to "one or a combination of the following factors -- the drug, syphilis itself, or intercurrent infection. The evidence is convincing that many cases represent attacks of non specific catarrhal jaundice occurring in patients whose livers are subjected to the added insults of syphilis and an arsenical." (The quotation is from the writings of Goodman and Gilman).

In 1943 Mitchell suggested that the jaundice was due to "the association of two hepatotoxic agents -- the arsenic and the agent of infective hepatitis."

These opinions (prior to the date of Beattie and Marshall's writings) implied that the agent of the "infective Hepatitis" recently so prevalent in the general population was responsible for the marked increase in the incidence of jaundice in V. D. clinics.

To consider seriatim the 3 likely factors in Post arsphenamine jaundice, syphilis, arsenic and "non specific

catarrhal jaundice" let us first deal with the influence of Syphilis.

Millian advanced the view that the jaundice might be due to a hepato-recurrence of syphilis. This theory is discounted by the fact that in such "late jaundice" there is no evidence of simultaneous relapse apart from the liver; the occurrence of jaundice as described seems, similarly, to have no bearing on the prognosis of the syphilitic disease.

Again when arsenicals were administered throughout the period of this "delayed jaundice" the results definitely suggested that this was a dangerous procedure:. In fact it "produced alarming evidence of increased liver damage."

Dible, McMichael and Sherlock[3] stated that there was no evidence to support the view that this late hepatitis was due to syphilis.

Arsenic.

Whilst arsenic has undoubtedly some part in the aetiology of post arsphenamine jaundice, "it is not the prime factor."[2] In clinics employing the same arsenicals, from the same batch supplied by the same manufacturing chemists, the incidence of the occurrence of "late jaundice" varied significantly, in different areas. If the drug employed was the sole cause of the incidence of the jaundice it would be anticipated that the attack rate would have remained fairly constant. This was not found to be the case. An incidence of 2% in the cases treated before 1941 rose until at one clinic it actually reached the

peak of 46%. This in spite of similar dosage and scheme of treatment and the use of the same arsenical throughout.

Nevertheless, it is generally believed that the incidence of jaundice may be modified by the dose of the arsenical. Curtis reported that, in 1942, an increase in arsphenamine dosage from 7.5 G. to 13 G. in a course extending over 13 weeks was attended by an increase in the incidence of jaundice from 7 or 8% to 25 to 30%, in the Whitechapel Clinic. In the British Army a reduction from 6 G. to 4 G. (for each 10 weeks course) yielded no significant reduction in the number of cases of delayed jaundice.

In a clinic where the same dosage, the same course of treatment employing one drug throughout, had been employed, it was obvious that some other variant must be involved. The most probable variant might be an infection by

The Virus of Infective Hepatitis

or a similar icterogenic agent.

Many observers have commented on the fact that the rate of incidence of post arsphenamine jaundice varies directly with the prevalence of infective Hepatitis in the community. Ruge's report on this parallelism is frequently quoted: it has frequently been confirmed. I may add that in Murton this increase in post arsphenamine jaundice has been very marked, although my figures would be, fortunately might I say, small. (Of 6 people treated by arsenicals in the past

four years, in this practice, 3 have had post arsphenamine jaundice, one has had the early stage jaundice -- he has only had 3 weeks treatment to date -- and one has had no jaundice so far after 8 weeks treatment. The 6th patient is a female who I am not convinced is suffering from syphilis. In the preceding 17 years I saw only one case of " Post arsphenamine jaundice" in some 25 to 30 treated cases.

It was noted that the delayed jaundice usually occurred at a period of some 12 to 17 weeks after the commencement of the treatment by arsenic. This and a general consideration of the attendant circumstances led Bigger[4] to suggest that the infection might be being spread as the result of imperfect sterilization of the syringes and needles. It was easy to visualize how small quantities of "infective material" could enter the needle (and syringe) and be in turn injected into the next patient: especially when a rinse in water and immersion in spirit was often regarded as "sterilization."

Beattie and Marshall tested this theory by allotting to each patient his own syringe to be used throughout his course of treatment. The syringe and needles were new and previously unused in each case and were boiled before and after each injection. Thus it was argued that the transference of infection should be eliminated. The results of the experiment were as anticipated. Nine of the ten patients so treated did not become jaundiced within the 120 days during which they were 'observed'. The tenth patient did become jaundiced at

a later date after 2 injections at another clinic which used the water and spirit process of sterilization. The dates given are interesting

1. Date of 1st injection at B. and M's Clinic May 26, 1940
2. " " " " at 2nd Clinic. Sept. 2, 1940
3. " " 2nd " at 2nd Clinic Sept. 8, 1940
4. " " 1st symptom of liver damage Nov 24, 1940
5. " " icterus Nov 27, 1940

interval 1 to 4 = 83 days.

These authors suggest that the incubation period of post arsphenamine jaundice in this case wasprobably therefor 12 weeks. They further express the view that their findings are consistent with this being the usual incubation period, longer periods between injection and illness being accounted for by the fact that not all patients could be expected to be infected at the first injection.

Lissieux[5] and Biggar's experience supported the theory of such a transmission of the infective agent, and Salaman's [6] observations further substantiated it. The last named employed a careful aseptic technique and autoclaved his syringes and needles. He thus "reduced the incidence of jaundice to negligible proportions in a venereal disease clinic in which the incidence in control cases was very great." [7]

Thus the commonly accepted view at present is that Post Arsphenamine Jaundice "is due to the transmission of small amounts of serum from patient to patient in imperfectly sterilized syringes."

Some believe that a diet deficient in protein favours the onset of the jaundice, or expressed rather differently, that a diet rich in protein probably has a tendency to protect against the onset of jaundice and may at least delay the time of its occurrence.[2] The liver protecting factor in the protein is thought to be methionine, a sulphur containing aemino - acid. It is allowed that the arsenical employed probably lowers the resistance of the liver to the infective agent.

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HOMOLOGOUS SERUM JAUNDICE.

This is not a purely introductory section and although based on the observations of others, it is intimately related, in parts, to my own observations which follow in part 2. It includes several comments on the published work of others.

(b) HOMOLOGOUS SERUM JAUNDICE.

Having already referred in the historical review to the occurrence of homologous serum jaundice I now propose to confine my remarks in this section to the more recent views on its aetiology and its relation to infective hepatitis.

In a series of contributions to The Lancet, Findlay, Martin and Mitchell [1,2,3.] record, analyse and discuss their observations in relation to hepatitis occurring after yellow fever inoculations. As such jaundice can be regarded as typical of homologous serum jaundice, and as the article deals with those matters in which I have been most interested, close consideration of the authors' views would appear to me to be the most profitable way in which to deal with this matter, within the relatively short compass which can be here allotted to it.

In 1934 it was remarked that jaundice occurred in many patients who had been inoculated with yellow fever vaccine, but it was thought that those patients had fortuitiously contracted infective hepatitis which was a common disease in the area concerned -- Africa. By 1937 it was realised that this explanation was quite inadequate, as the incidence of jaundice after the inoculation was so strikingly high, and the interval intervening between the inoculation and the occurrence of jaundice was in many cases fairly uniform. Further, it was soon found that jaundice occurred in a very

high proportion of the patients inoculated with some batches of the vaccine: in short, certain batches were proved to be markedly icterogenic. At this time prophylactic inoculation against yellow fever consisted of the injection of human yellow fever immune serum and a vaccine; human serum was, further, employed in the preparation of the vaccine.

Careful investigation showed that the human serum was the agent responsible for the hepatitis which ensued: this finding applied to the vaccine. Presently it became established that jaundice similarly followed the use of measles immune serum, mumps immune serum, and plasma, serum and, probably, whole blood.

Thus it became known that human serum in many instances contained an icterogenic agent.

What was the symptomatology of this post inoculation jaundice?

It is most important to this study that we should consider it in close detail. Findlay, Martin and Mitchell have described the symptoms which occurred in their cases exhaustively and in detail. They deal not only with leading symptoms but with the less prominent symptoms also.

Now, while many diseases mimic each other closely in regard to the leading or presenting symptoms, in very few diseases are the less prominent and less frequently occurring symptoms identical. Lest this remark be criticised as a platitude, I would say that, in practice, diseases are

commonly compared and contrasted with relation to the main symptoms.

I am convinced that the comparison of, what I might term, the "minutiae" of the symptomatology of similar diseases is the most likely method by which we may decide as to whether those diseases are closely related or identical.

A chief aim of my study has been to compare closely, similar diseases, with a view to establishing (or at least suggesting the possibility of) their identity.

For those reasons I now refer to the symptoms of the illnesses recorded by Findlay and his colleagues[1]. I will first reproduce two tables. Table 1 gives the presenting symptoms and signs in their large series of 432 cases. Table 2 gives the aggregate symptoms in the same series. The inclusion of those two tables is necessary for later references to their contents. They are very slightly modified from the originals.

Table 1. Presenting Symptoms and Signs in 432 patients.
In order of frequency.

Key No.	SYMPTOM or SIGN	Percentage of Cases.
1.	Loss of appetite	= 56%
2.	Nausea	= 49%
3.	Lassitude	= 23%
4.	Epigastric pain	= 21%
5.	Bad taste in mouth	= 20%
6.	Constipation	= 16%
7.	Vomiting and retching	= 14%
8.	Headache	= 13%
9.	Diarrhoea	= 6%
10.	Upper abdominal pain	= 5%
11.	Flatulence	= 4%
12.	Giddiness	= 4%
13.	Fever	= 4%
14.	Backache	= 3%
15.	Joint pains	= 2%
16.	Mental Depression	= 1%
17.	Pruritus	Less than 1
18.	Sore Throat	" " "
19.	Insomnia	" " "
20.	Heartburn	" " "
21.	Pain at back of the neck	" " "
22.	"Blackout"	" " "
23.	Palpitations	" " "
24.	Muscle Pains	" " "
25.	Blurred Vision	" " "
26.	Hiccough	" " "
27.	Dysphagia	" " "

1.	Liver enlarged	36
2.	Bile in urine	32
3.	Jaundice	13
4.	Spleen enlarged	12
5.	Light stools	4
6.	Skin rashes	2

TABLE 2. Aggregate Symptoms and Signs in 432 Patients.

In Order of Frequency.

KEY NO.	SYMPTOMS OR SIGN.	PERCENTAGE OF CASES IN WHICH PRESENT.
1.	Anorexia	73
2.	Nausea	66
3.	Epigastric pain	34
5.	Bad taste in mouth	32
7.	Vomiting or Retching	32
3.	Lassitude	30
6.	Constipation	29
8.	Headache	23
10.	Upper Abdominal pain	11
9.	Diarrhoea	10
11.	Flatulence	10
12.	Giddiness	7
14.	Backache	6
15.	Joint Pains	5
19.	Insomnia	5
13.	Fever	5
17.	Pruritus	4
20.	Heartburn	3
16.	Mental Depression	3
18.	Sore Throat	3
	Pain in back	1
26.	Hiccough	1
24.	Muscle pains	1
23.	Palpitations	Less than 1%
25.	Blurred Vision	" " "
27.	Dysphagia	" " "
	Biliary Colic	" " "
21.	Pain at back of neck	" " "
22.	Blackout	" " "
28.29.	Dysuria. Urinary incontinence	" " "
30.31.	Deafness. Profuse sweats	" " "
32.	Extreme restlessness	" " "

There are a few features of the symptomatology to which the authors refer, after mentioning the main symptoms, and which peculiarly interest me in the light of my findings in the Murton epidemics.

5.5 % of the patients complained of joint pains in the absence of any swelling of the joints. The joints usually involved were the shoulders, knees and hips.

Dizziness, insomnia, blurred vision, conjunctivitis and dysphagia occurring early in the illness are remarked on by the authors, as is marked loss of weight.

All of those less common symptoms are later reported in my own observations, as is the frequent occurrence of a bad taste in the mouth.

The importance and significance of those "minor" symptoms in the comparison of otherwise similar illnesses I shall discuss in the "Summary" to Part 2 of this work.

Finally in relation to the symptomatology I would mention that skin rashes were described in 5.5% of the cases. They took the form of urticaria in the majority of cases, but purpuric, erythematous and maculopapular eruptions also occurred. The time of the onset of the skin rashes was commonly a few days prior to the onset of jaundice, but they were noted in an occasional case as early as 25 days before jaundice occurred, and as late as 32 days after the patient became jaundiced.

Haemorrhages were uncommon: occurring in 2.5% of the series; haematuria, haematemesis, epistaxis, bleeding gums and subconjunctival haemorrhages were reported.

The Leucocyte Count and the Differential Leucocyte Count.

As I later devote a section of my observations to this matter, I would briefly remark that the typical findings were a fairly low total leucocyte count, 6000 or under. The low count was due to a neutropenia. There was commonly a relatively small lymphocytosis, occasionally a slight absolute lymphocytosis, and in a few cases the large mononuclears were slightly increased. Atypical monocytosis was only rarely detected.

.....

The report on the occurrence of cases not featuring jaundice is again pertinent to this enquiry. The authors describe cases attended by definite jaundice, others where bile was present in the urine but jaundice did not occur, and yet others where neither bile in the urine nor jaundice occurred.

The diagnosis of this last group of cases rested on the occurrence of illnesses exhibiting relatively mild and vague symptoms, (such as nausea, anorexia, abdominal pain, diarrhoea

or constipation, headache, bad taste in the mouth, flatulence and tiredness or listlessness) in association with the simultaneous occurrence of the definite "epidemic" illnesses. Such relatively vague illnesses occurred after a latent period, following the inoculation, of some 72 to 99 days. The use of the icterus index and the van den Bergh test helped to establish the diagnosis.

Incubation Period. Relation to Infective Hepatitis.

The only point of clinical difference between this post inoculation jaundice and infective hepatitis, observed by those workers, is that, in the former, the incubation period averages 100 days, whilst, in the latter, the incubation period is believed to be from 20 to 40 days.

In view of the identity in the clinical and pathological findings, it is suggested that the diseases may be due to a common agent, the difference in the incubation periods being then ascribed to the virus being introduced into the body by different routes in each instance.

I consider that this was indeed a very reasonable hypothesis and I might here state that I believe that the truth in this matter lies concealed in this assumption.

Cameron's work suggests that the incubation period in infective hepatitis is from 1 to 6 months when the infection is transmitted by subcutaneous injection.

Conversely, Findlay and Martin[4], showed that the incubation

period of post inoculation hepatitis is only 28 to 50 days when this disease is transmitted by intranasal instillation.

Post Inoculation Jaundice. Spread to Contacts.

In 1938, Propert[5] thought that children who had suffered from hepatitis following the injection of measles immune serum had spread the disease to contacts. The fact that Findlay and Martin were able to transmit the disease --- post inoculation hepatitis -- by the instillation of nasal washings, made it appear that spread by contact was likely to occur. They present evidence[3] which supports the view that such a spread does indeed occur from patient to contacts. Thus 5 officers, out of a total of 6 who had not been injected by icterogenic serum, developed "infective hepatitis" in circumstances which suggested that the only possible source of infection was the post inoculation jaundice present in their units.

Again the authors showed that cases of infective hepatitis which were notified to them, "came almost without exception from units where hepatitis following inoculation was rife."

Of particular interest to us in relation to the two epidemic illnesses in Murton is the authors' further observation that, in the area considered in their work, the increase in the incidence of infective hepatitis varied directly with the incidence of post inoculation hepatitis, suggesting that spread by contact in the latter condition

might explain the increased number of cases of "infective hepatitis."

Although more recent work may throw doubt on the likelihood of the occurrence of droplet spread in infective hepatitis, this does not invalidate much of the evidence ~~addressed~~ advanced by Findlay et al).

The Nature of the Icterogenic Agent. Series of Findlay et al[3]

What was the nature of the icterogenic agent which caused this post inoculation jaundice? How did it gain entrance to the blood?

These were the questions which Findlay and his co-workers had to consider.

And the answer to those problems would hold the key, I felt, to the solution of the problems connected with the epidemic illnesses prevalent in the area of my medical practice in Murton in 1944.

Here might I explain that I have only recently, 30/6/44, carefully studied the discussion of this matter by Findlay et al, whereas my own thoughts in relation to the Murton epidemics, as expressed in the text of part 2 of this work, were recorded at the times of their occurrence.

I am painfully aware of the laboured and rather unscientific manner in which I have attempted to express my thoughts and suspicions as regards the nature of the icterogenic agents, especially when I compare the writings of those gifted investigators.

And yet I feel that the reader will later find, or sense, that my conception of "infective hepatitis and its allied diseases" bears a fairly close resemblance to the views of Findlay et al, referred to below. My remarks, of course, apply only to (2) below.

(1) <u>As regard the nature of the icterogenic agent</u>.

It is probably a virus: this is suggested by the facts that

(a) Persons who have suffered from jaundice after injection of yellow fever vaccine showed no symptoms on re-inoculation with known icterogenic serum. This experiment was conducted to refute the suggestion that hepatitis in post inoculation cases was an allergic phenomenon.

(b) No visible organisms have been demonstrated in these cases. The pathogenic agent increases in media which are usually suitable for virus growth: it is filtrable through Seitz filters; it resists freezing and drying for long periods; it resists strong concentrations of phenol. It can be transmitted to man by subcutaneous and intranasal inoculation. (And I would, now, add, by ingestion of faecal matter.)

(c) The latent period is 28 to 50 days. (Introduced intranasally or, later, by ingestion.)

The latent period is 26 to 239 days (subcutaneous inoculation.)

2. And this is the important section for our present consideration.

How did the icterogenic agent gain access to the blood?

The obvious question was whether the icterogenic agent was none other than the virus of infective hepatitis. It would be redundant at this stage to enumerate the more obvious reasons for the suspicion that this was the case. The authors observe that the spread of infective hepatitis depends on close contact, and they believe that a similar spread by contact occurs in post inoculation or homologous serum jaundice.

As second attacks of infective hepatitis are rare, it is inferred that a considerable degree of immunity is conferred by an attack. Now the authors show, that while persons who have suffered from an attack of infective hepatitis may later be affected by homologous serum hepatitis following inoculation, the attack rate is much lower than the rate obtaining among persons who have not had an attack of infective hepatitis. In other words, they claim to have demonstrated that an attack of infective hepatitis confers a marked degree of immunity, which is not absolute, to homologous serum jaundice: or as it might better be expressed, to the agent present in icterogenic sera.

Although it is outwith the scope of my comparable observations it should be noted that an antigen made from

the livers of patients dying with infective hepatitis fixes complement with the sera of patients who have recovered from infective hepatitis and from post inoculation (homologous serum) jaundice.

Thus the authors conclude that the two diseases, if in fact they can be considered to be 2 diseases, homologous serum jaundice and infective hepatitis are due to an identical agent, namely a virus: or alternatively that the causal agents are very closely related indeed.

Thus post inoculation jaundice would be due to the introduction of serum from a patient with the virus of "the infective hepatitis group" in his blood. The virus would be present in this patient's blood because he was suffering from, or in the incubation stage of, infective hepatitis. Finally:-

A further possibility is postulated.

I think it is a suggestion of the greatest importance and I believe I have evidence to support it in my own experiences as later recorded.

"The virus of infective hepatitis" possibly "appears occasionally in the blood of an immune person."

It is believed that in many virus infections the virus continues to be present in the tissues. The liberation of small amounts of the virus, occurring at intervals, is believed to lead to the co-incident formation of fresh

amounts of antibody; and in this way immunity to the virus continues.

With this last paragraph I would couple the observation that many have commented that the serum of a person who has not suffered from a known attack of infective hepatitis has at times proved to be interogenic; and the further fact that infective hepatitis, like homologous serum jaundice, is well known to occur in formes frustes.

.....

Whilst I have based this section on the findings and observations of Findlay, Martin and Mitchell, I have done so because the nature and methods of their enquiries have impressed me and I am inclined to think that they are probably nearer to the true interpretation in these matters than any other observers.

I must, however, point out that their views are not by any means universally accepted.

McFarlane and Chesney[6] had in January 1944 published an article on hepatitis following injections of mumps convalescent serum. They expressed the view that the agent responsible for the hepatitis was <u>not</u> the virus of infective hepatitis.

They were unable to trace any possible way by which the virus of infective hepatitis could have gained entry to the

serum. There was no reason to suspect that the virus could have been introduced in the processing of the serum. Neither could they find any evidence of any of the donors of the serum having suffered from either "jaundice" or symptoms suggestive of a subicteric attack.

To this I would comment that it would be obviously impossible to state that none of the donors had ever suffered from a subicteric attack and that we must not rule out the possibility of the icterogenic agent (or virus) appearing from time to time in the blood stream of a patient long after, even possibly years after he had suffered from such an attack.

These authors then question the identity of the aetiological agent in infective hepatitis and homologous serum jaundice on the grounds of the greatly increased incubation period in the latter disease. They add the following remark:-

> "It is unlikely that the intravenous injection of a hepatotoxic agent would result in a longer incubation period than infection by the respiratory tract."

I might, in the light of more recent findings re the possible sources of entry of the virus, be allowed to add to this quotation....."or alimentary tract."

I would like to comment on this observation, as this difference in the relative incubation periods has so frequently been stressed as evidence against the identity of the two types of hepatitis.

The observation is based on the assumption that the icterogenic agent present in the blood would be expected to be identical with the agent present in the "droplet" (if the spread of infective hepatitis is by droplet) or the faeces (if spread occurred by faecal contamination in infective hepatitis.)

I think that we are quite unjustified in making such an assumption.

If infective hepatitis is due to a virus and that virus gains entry to the alimentary tract (e.g.) and thence enters the blood stream should we expect it to be found quite unaltered in the blood stream?

There is a long incubation period of some 30 days. We know that there are marked changes in the leucocyte count, both total and differential. Other more subtle changes may occur.

And yet we find eminent investigators assuming that the virus in the bowel and faeces is certain to be in a state identical to the virus present in the blood.

I believe that the answer to the difference in the incubation periods in the two diseases may depend on an alteration in the state of the virus after it has entered the blood stream.

McFarlan and Chesney appear to make one point however in that they describe the occurrence of jaundice following inoculation in 8 out of 11 men who had suffered from "jaundice" in infancy which gave a higher attack rate than that obtaining in those men who had not so suffered in infancy or childhood viz. 77 out of 160 men. Those authors did not think that post inoculation cases were infectious to others.

They further claim that the symptoms were slightly but definitely different in homologous serum jaundice and infective hepatitis. They found a greater lag in reporting ill, a lower incidence of vomiting and a higher incidence of severe arthralgias and rashes in the serum hepatitis cases. Even if such findings were substantiated consistently by other works, which they are not, I think that they do not suggest that the agent in serum jaundice is necessarily essentially different from the agent responsible for infective hepatitis: and a comparatively slight alteration in the same agent could explain such minor differences.

.....

With regard to the low infectivity of homologous serum jaundice (assuming that it is infectious) Findlay made the interesting suggestion that "where whole populations or military units are inoculated with icterogenic serum it is possible that those who do not develop jaundice may nevertheless receive an immunising injection."

.....

The minute quantity of serum required to cause jaundice is illustrated in the writings of Bradley, Loutit and Maunsell.[7 and 8.] The severity of the resulting hepatitis was not related to the quantity of serum given or to the route of its administration --- intradermal or intravenous. The range of doses given in this series of cases was from 0 • 1 c.cm. to 1200 c.cm.

As it has been suggested that allergy played a part in the occurrence of hepatitis in serum cases it is noteworthy that the patients in whom this investigation was conducted had various intradermal skin tests and were divided into allergic subjects and normal controls: the incidence of jaundice was not higher in the allergic group.

EXPERIMENTAL TRANSMISSION OF HOMOLOGOUS SERUM JAUNDICE.

As it was undecided whether patients suffering from homologous serum jaundice did infect others, certain workers attempted to find out whether the disease could in fact be experimentally transferred from a patient suffering from it, to others: and if so, by what route and in what dosage etc.

As a preliminary measure, adopted for obvious reasons, experimental transmission to animals was attempted. Findlay and Martin in West Africa, MacCallum and Bauer in England, and Fox et al in Brazil, failed to transmit the disease to numerous animals, although they employed serum, bile -- stained duodenal juice, blood, blood serum, urine, liver, spleen and icterogenic yellow-fever vaccine in their attempts.[8]

In 1943 Findlay and Martin[9] succeeded in transmitting this disease to human volunteers by the intranasal insufflation of nasopharyngeal washings obtained from 4 officers of the British Army who were suffering from post inoculation serum jaundice. Three of the volunteers became jaundiced, the incubation period being 28 days, 30 days and 50 days. The presence of an interogenic agent in the nasal secretions of sufferers from serum jaundice was thus clearly demon-- strated.

It is interesting to note that in 1942, Voegt (Germany)

had transmitted infective hepatitis to volunteers who ingested 5 cc. of duodenal juice obtained from patients in the preicteric stage of the disease, and here again the shortest incubation period had been 28 days.

Although the presence of an icterogenic agent in the nasal secretions of sufferers did not prove that they did spread the disease, the experiment did lend support to Propert's view that a spread to contacts did occur.

Different but in some respects comparable were the human transmission experiments of MacCallum and Bauer.[10]

They demonstrated that serum from a case of homologous serum jaundice was icterogenic on the 7th day after the onset of jaundice but not 59 to 134 days later.

The disease was successfully transmitted by both the subcutaneous (.5 c.c.) and intranasal routes (1 c.c.) and the incubation period was much the same in both instances.

The case V.6. described by the writers bears a very close resemblance to the illness of one of my patients, Dorothy B. Elliott as a reference to page 670 of this work will demonstrate.

This patient was an "intranasal volunteer." He developed jaundice on the 39th day, the serum bilirubin being 1.5 mg. per 100 cc. After his apparent recovery the serum bilirubin level rose slowly and after being free from symptoms for

nearly a month "he suddenly developed a severe attack of the disease on the 82nd day, the serum bilirubin rising to 17 mg. per 100 cc."

Relative to my reference to page 670 I would remark that jaundice might well not have been evident with a serum bilirubin level of 1.5 mg. per 100 cc. as this level is frequently exceeded in the absence of clinical jaundice.

.....

Although not comparable with the above-mentioned work, the experiments conducted in America by Oliphant, Gilliam and Larson[8] merit a brief word of reference. They employed icterogenic yellow fever vaccine and by human transmission they showed that the icterogenic agent was not destroyed by heating at 56°C for 30 minutes but that it was destroyed by irradiation by ultra violet lights for one hour: it was filterable: the agent was present in the circulating blood before jaundice appeared but not 10 weeks after the disappearance of the jaundice: it survived drying at 4 °C. for long periods.

Definitely it had no relation to the virus of yellow fever, and it was almost certainly contained in the human serum diluent of the vaccine.

Space will allow of only mention of a special article by the Medical Officers of the Ministry of Health, on the subject of Homologous Serum Jaundice to which I have previously referred.[11]

They suggested that in one outbreak, which was closely investigated and which followed the use of measles convalescent serum in England in 1937, the only symptoms which were encountered in the whole outbreak and which did not occur in infective hepatitis were:- "the mention of irritability, restlessness, intractability, screaming and delirium; and the occurrence of urticaria and extensor plantar reflexes.

To-day, June 1945, there are several accounts of such nervous manifestations occurring in association with Infective Hepatitis, (e.g. reference 12) and urticaria also occurs in this disease.

It should further be remarked that "detailed investigations were directed towards the suspected measles serum without profit, and re-survey of the donors afforded no clue."[13]

Thus again there is the suspicion that people who have not suffered from a known attack of infective hepatitis may have an icterogenic agent in their serum.

In an editorial article The Lancet[14] tentatively offered the following as being "appparent possibilities" in an attempt to explain the relation between the agents responsible for Infective Hepatitis, Homologous Serum Jaundice, (and Post Arsphenamine Jaundice.)

1.

These three conditions are due to infection with one and the same virus.

The immunity of the usual childhood infection is usually permanent but is capable of being overcome by the direct inoculation of the causative agent in the presence of certain other unknown factors.

2.

There are different agents producing the same clinical picture but not mutually protective.

For instance this is true of Influenza viruses A and B.

3.

There are different strains of the same virus antigenetically related.

Infection by one of them does not necessarily give complete protection against others.

Hepatitis may therefore develop if resistence is lowered e.g. by deficiency of an essential cell metabolite or injection of a toxin.

.....

Just as I had completed this section of this work the British Medical Journal published an editorial entitled "Syringes, Serum and Jaundice" which incorporated the up-to-date views on those matters.

Yellow-fever-vaccine jaundice and post arsphenamine jaundice the editor regards as examples of homologous serum jaundice. "The common factor is the contamination of the inoculation with small quantities of human plasma or serum which contains an icterogenic virus." Pointing out that "jaundice" is now a disease not only of campaigns but also of clinics, the writer refers to outbreaks of "jaundice" in diabetic clinics, rheumatism clinics and sanatoria.

The estimation of blood sugar, or of the blood sedimentation rate or any intravenous therapy or estimations requiring the withdrawal of venous blood, are all possible modes of spread of such infection.

Homologous serum jaundice has occurred after transfusion of blood plus plasma, and serum.

It is still obviously not known whether homologous serum jaundice and infective hepatitis are due to two separate varieties of the same species of virus though, the article continues "it may prove that they are different phases of the same virus."

With this underlined phrase, I will conclude this section.

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V I R U S E S.

Many consider that Infective Hepatitis is probably caused by a virus. It appears apt, therefore, at this stage, briefly to summarise some of the views on the nature of viruses and their role in disease.

I. GENERAL HISTORICAL.

Pasteur considered that rabies was probably caused by an organism so small as to be invisible to microscopic examination. It was later found that the pathogenic agent responsible for the mosaic disease of the tobacco plant was not arrested by the standard earthenware filters employed. A similar finding in the foot and mouth disease of cattle was followed by Reed, Carroll, and others demonstrating in 1901, that Yellow Fever was caused by an organism which also passed the filter. The standard filters them employed arrested all particles exceeding 0.2 μ in diameter. The possibility of a contagium fluidum was later discounted by the use of the graded collodion membranes of Elford which proved that the pathogenic agent was particulate, and more accurately assessed the size of the viruses; a proof which was corroborated by Schlesinger's technique of high speed centrifugation of the filtrates.

With improved optical methods and improved microscopes and methods of staining (the use of e.g. green light, U.V.Light, dark ground illumination, oblique illumination, Nelson's extinction method, special mordants, and the magnetic electron

microscope may be mentioned), many of the formerly so-termed "ultramicroscopic viruses became visible.

Again the term "filtrable" viruses was not sufficiently accurate as factors other than particulate size affect filtration. Small bacteria, such as the Bact Pneumonitis, were found to be filter passing, and some large viruses passed the filter with difficulty.

Allowing for these and other fallacies it may yet be accepted as a broad generalisation useful as a working hypothesis that viruses are pathogenic agents measuring under 0.2 μ which is taken as the border line dividing them from the accepted bacterial forms.

.....

2. THE NATURE OF VIRUSES.

(a) Most generally accepted is the view that viruses are minute animate organisms.

(b) Some have sought to prove that certain viruses represent a phase in the life cycle of well-defined bacterial species.

(c) The viruses are regarded as non-organismal chemical substances mainly of protein composition.

(d) Green and Laidlaw attempt to reconcile (a) and (c).

(e) A recent view is the conception of spontaneous generation of the viruses in the affected cells.

.....

(a) The spread of virus diseases in man and the serial experimental transmission of these diseases in animals corresponded with the similar occurrences in bacterial diseases. Furthermore the viruses appeared to propogate and multiply in the host exactly as did bacteria.

A further resemblance was the fact that attacks of Smallpox, Yellow Fever, Measles, and Poliomyelitis all seemed to lead to a lasting (natural) immunity: and that the use of attenuated viruses gave an artificial immunity as illustrated by Pasteur's method against rabies.

Although differences did occur, the viruses were affected by such agents as heat, ultra violet light, and certain chemicals in a manner resembling the corresponding effects on bacteria.

The viruses can act as antigens, and antibodies are produced which are specific as in the case of bacteria. The phenomena of precipitation and complement fixation can be demonstrated; and the serum containing the antibody can inactivate the virus, if mixed with it.

When a suspension of the elementary bodies of a virus disease is acted on by the appropriate antiserum, agglutination of the elementary bodies occurs.

Striking and suggestive as are the similarities when we compare the bacteria and the viruses they do not prove that viruses are the "midgets of the microbial world."

A highly important distinction between the bacteria and the viruses is that the latter can not be cultured in inanimate media: a substrate of living cells is essential

"It must be emphasised that the mechanism and phenomena of immunity to various antigenic agents whether micro-organisms, cells derived from the animal body, or protein substances are all fundamentally similar.

The contents of this section of the work are based on a study of:—

VIRUS DISEASES IN MAN.
van Rooyan C. E. and Rhodes A. J.
London 1940.

(b) This hypothesis receives little general support.

(c) The study of plant diseases especially the mosaic disease of the tobacco plant has stimulated the chemical theory.

From the tobacco mosaic disease crystals of an infective protein have been isolated, which appear to contain the actual virus.

It is believed by the supporters of this theory that the viruses are all chemical substances which interfere with the vital functions of the cell, which they attack in such a way as to lead to the further production of the virus chemical.

In this way increase in the amount of the chemical would simulate and be mistaken for reproduction.

Laidlaw (1938) does not consider that this theory is convincing as an opponent of the organismal theory.

We do not know whether elementary bodies are proteins or "even approximate to proteins", and various workers have noted that they give reactions for fats, carbohydrates and calcium.

(d) Green, and later and independently, Laidlaw expounded an interesting theory which offered a means of reconciling the apparently irreconcilable views mentioned in Sections (a) and (c). The viruses require an intracellular habitat. Granted this habitat they show the reproductive property considered typical of life. Apart from the living cells they appear to be inanimate, there being no evidence of the existence of free living viruses. Green points out that the evolution

of parasitic organisms can be traced to free living forms. The free living forms produce everything necessary for their own growth and reproduction. As the organism becomes more parasitic it ceases to produce such substances as are readily available in its environment, produced, as it were, "ready made" by the tissues of the host.

Laidlaw argues that the viruses represent the most extreme example of parasitic evolution. "The largest viruses are simply bacteria or other micro-organisms which can not synthesize one or more factors (e.g. an enzyme or co-enzyme) necessary for their growth, but obtain these readily within the protoplasm of the living tissue cells." As we descend the scale of the viruses, as the viruses become progressively smaller, it might be postulated that they would lose progressively more growth factors until the smallest viruses become devoid of all enzyme systems and autosynthetic activity.

Thus we envisage a biological entity which is "truly animate in its intracellular habitat, utilising the necessary enzyme systems of the cellular protoplasm" -- but which, apart from these cells, is in a state of suspended animation. Apart from the cells, it will retain the chemical composition which determines the maintenance of its species: which composition may be that of a heavy protein similar to the heavy protein of plant virus diseases.

VIRUS INCLUSION BODIES.

In 1886 J. G. Buist, of Edinburgh, described 'elementary bodies' in Vaccinia and variola, and in 1894 Guarnieri described the "inclusion bodies" of vaccinia. These inclusion bodies are abnormal intracellular structures present in the lesions of virus diseases. They are present within the cytoplasm of the cell or in some cases within the nucleus of the cell. They are usually more or less rounded bodies and they vary in their affinities to stains, being variously eosinophilic or basophilic.

In several diseases of virus aetiology it has been demonstrated that the inclusion bodies represent an accumulation of elementary bodies, the latter being regarded as virus units.

Some think that the inclusion body may represent a phase in the life cycle of the virus --- during which phase these relatively large intracellular structures are formed and contain within them the elementary filterable forms

(A fairly recent publication by van Rooyen and Rhodes gives really beautiful illustrations of the Guarniere bodies, the Negri inclusion bodies of hydrophobia and different morpho logical growth phases of psittacosis virus.)

PATHOGENIC MECHANISM OF VIRUSES.

Our knowledge in this matter is scanty and incomplete.

Necrosis of tissue cells has been emphasized as a frequent pathogenic effect of the viruses, but we do not know whether this is brought about by the virus multiplying within the tissue cells and thus interfering with the normal cellular metabolism --- or as a result of the action of toxins produced by the virus and causing a toxaemia similar to the toxaemia produced by bacterial infections.

Indeed we have not proved that virus toxins are produced-- they have never been demonstrated.

Whilst in many of the diseases caused by viruses the symptomatology and pathology is to be understood by an attack on certain selected tissues ---"tropism" --- (for instance, the brain in encephalitis, the liver in yellow fever and hepatitis, the spinal cord in poliomyelitis) --- many more generalised symptoms are frequently present. It is to account for such generalised symptoms that we have inclined to assume that they are due to a virus toxaemia.

As I mention later, C. H. Browning has recently told that recent work leads to the belief that viruses are frequently more widespread in their distribution in the body than we have previously thought --- and their activity probably continues for a longer time than has been heretofore thought.

T R O P I S M

Certain viruses show a tendency to attack particular tissues. This is strikingly exemplified by the viruses which attack the nervous system and are termed "Neurotropic", e.g. rabies, poliomyelitis, and encephalitis.

The viruses which cause smallpox, chicken pox, and herpes febrilis are similarly termed dermotropic.

We know that the virus of chickenpox may acquire neurotropism after cerebral passage. It must be constantly remembered that these terms are simply convenient labels and nothing more.

In measles, although we find a characteristic skin eruption, we know that the main attack is on the lungs. Again, in herpes zoster we find that the attack is made on the posterior root ganglia and the posterior cornua of the cord.

.....

I, personally, find great interest in the views of Levaditi on the group which he terms "Herpetico encephalatic", when discussing the relation of the virus of herpes febrilis to that of epidemic encephalitis.

They suggest that at one extreme are neurotropic strains, at the other are dermotropic strains. Intermediate strains are, of course, encountered. The neurotropic strains, granted a suitable host, may cause encephalitis, while the dermotropic strains are possessed of no neurotropic properties.

EPIDEMIOLOGY.

In the "historical review" I have referred to many of the workers who have studied the problems of infective hepatitis. This I do not propose here to repeat. Rather do I desire to state the views on the epidemiology of infective hepatitis prevailing prior to and during the period of my own attempts at similar observations. Thus I propose to refer only to recent contributions to the literature.

In an excerpt reprinted from The Lancet of 15 April 1939, which Dr. Pickles courteously forwarded to me, that author states:-

"Epidemiological studies suggest that the disease is transmitted by direct contact, probably by droplet infection; that the incubation period is probably about a month: and that there is some evidence of a short period of infectivity".

Ford's report of the Wembley epidemic published in 1943[1] was in agreement with the above. He quoted instances of the parallel infections but stated that the "serial" incidence noted by Pickles was also well marked. Close contact was said to be necessary and he considered that the spread was probably by droplet, adding, however, the possibility of spread by faecal contamination of the fingers. Like Pickles, Ford considered that the spread was not due to water, milk or foodstuffs: nor did he think that the spread could possibly have occurred by rodents.

In February 1944 the report of the Proceedings of the Royal Society of medicine[2] revealed the varying views of the mode of transmission. Thus Lisney concluded "infection is spread by close personal contact, probably by means of droplet infection....There is no evidence that infection is spread by means of milk, water, food or vermin."

At the same meeting of the society Spooner supported the opposite view: at least he advanced evidence "which cast some doubt on the hypothesis of droplet infection."

One such observation was that "in units which lived by vehicle crews there did not seem any special tendency for more than one case to occur in the crew of one vehicle." "The other observation which seems inconsistent with a droplet spread, was that the disease showed curiously little tendency to spread from prisoners of war--- among whom jaundice was rife-to others who shared the same camps etc."

In June 1944, Witts[3] reviewed the question of the epidemiology. He stated that to his mind the "orthodox hypothesis of droplet infection was quite adequate." However, with commendable impartiality he gave due prominence to the theory of excretal spread. I would like to make a point of one of his remarks, or observations. He wrote "The place localization and the seasonal incidence may be more suggestive of transmission by excreta, and it has been stated that on taking up position on a clean site there is no jaundice and on a dirty

site there is jaundice, though little ~~inc~~evidence is advanced for this statement." He does not peremptorily dismiss this "suspicion" because of the insufficient evidence but later adds:- "There is no conclusive evidence that insects or excreta spread infective hepatitis, but there is enough to make experimental work in this connection desirable, and indeed rather urgent."

(Here I would make bold to remark that if the busy general practitioner is to be encouraged to play his potentially important role in the field of epidemiology, he must not be intimidated by being told he must conclusively prove his suspicions, or impressions in such matters. Pickles tells us that his senior partner knew of the occurrence of epidemics of catarrhal jaundice not referred to in the then current medical literature.)

Early in 1945, Kirk[4] published his paper on the spread of infective hepatitis among New Zealand soldiers at Alamein in 1942.

The article as published is a model of brevity allied to clear exposition and it is based on careful analysis of a concrete situation as advocated by Witts.

He attempted to prove that the disease was spread in this instance, by flies carrying the infection from human excreta.

In a leading article, The Lancet[5] accepted Lieut. Colonel Raymond Kirk's evidence.

It is interesting and instructive to observe that in 1915 it was thought that the epidemic jaundice, then so prevalent in the Mediterranean Expeditionary Force, was a "product of the insanitary conditions associated with the campaign."[5]

Very recently, definite proof that the virus is present in the urine and the faeces has been provided by experimental work on human volunteers. A leading article in the Lancet[6] refers to the work of MacCallum and Bradley. Those workers found that spraying the throat with nasopharyngeal washings obtained from early cases of infective hepatitis led to a "subicteric condition" and that frank jaundice occurred when faeces were spread into the throat. A preliminary communication by Findlay and Wilcox[7] in the same issue of this journal reported the experimental transmission of the disease by faeces and urine: a Seitz filtrate of the stools was potent. Oral administration was employed.

Havers, Paul and van Rooyen[8] transmitted the disease to volunteers by the oral route. They transmitted the disease by spraying faecal material into the nasopharynx and also "by feeding such material in capsules." (They also found that if icterogenic serum was administered in gelatin capsule, by mouth, jaundice occurred: of 3 patients to so become jaundiced, 2 contracted hepatitis in 30 days and a third after a longer incubation period of 84 days. These figures I shall refer to later in this work.)

Thus during the early stages of my observations it was generally accepted that Infective Hepatitis was spread by droplet. Later in this period the tendency was to emphasize the possibility of spread by faecal contamination either by spread from the soiled hands or by the agency of flies.

To this matter I devoted some considerable attention and at a later stage the reader will have the opportunity of considering my impressions.

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1. Inf. Hep. 25/5/43. p 675 Lancet Vol I.

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3. B. M. J. Vol 1. p 739. Some Problems of Inf. Hep.

4. Lancet. Jan 20, 1945. Spread of Inf. Hep. Lieut. Col. R. Kirk.

5. Lancet L. A. Autology of Inf. Hep. Feb 17,1945. p 213.

6. Lancet. L. A. AET. of Inf. Hep. 17/2/45.

7. Findlay G.M. and Wilcox R.R. Lancet p 212 15/2/45.

8. Havers W.P. Paul J.R. and C. E. van Rooyen Human Transmission of Inf. Hepatitis by the Oral Route.

PART TWO.

This section comprises that part of the work which is based on the 'original' observations of the writer.

In it he attempts to relate and comment upon an epidemic, which began in March, 1944, and which was still continuing one year later.

On the surface, there appeared to be two very similar epidemics, one attended by jaundice, and the other not so attended but presenting similar or comparable features re the apparent mode of spread, incubation period and symptomatology.

The writer suggests and attempts to demonstrate that there were not two separate and distinct epidemic illnesses occurring concurrently, but one only.

During the period in question over 600 case histories were recorded --- by far the greatest number were recorded in four winter months. It is not proposed to incorporate all those records in this section, but I feel that I must tax the patience of the reader by including a number such as is usually considered rather many for a work of this nature, and for the following reasons:--

1. To establish the fact that an epidemic did occur, and to illustrate the nature, and prove the identity, of the disease initially encountered --'infective hepatitis with jaundice.'

2. To similarly illustrate the identity and features of the second type of illness, where jaundice was not a feature.
3. To attempt to demonstrate the similarity of the two illnesses and to show any links between them.

.....

As to the nature of the observations made:--

The problem was to select the clinical features which could be recorded in the available time. I estimate the incidence of this disease in this community (some 10,000 population) at not less than 10% (1,000 cases).

It had to be a 'mass' observation as no evidence could be ignored lest it might later prove to be of significance: and colliery practice is ordinarily exacting.

In what way could I best contribute to the problem? What observations was I best equipped to make?

I decided not to devote my studies primarily to an attempt to emulate e.g. the pathologist, the haemotologist of the biochemist: important as they all are.

The main contribution which I could make was from the approach as a general practitioner:-- to listen, to look, to note, and to think:-- for example, by careful consideration of the history of the illnesses and the attendant circumstances, the complete symptomatology and by such observations as are ordinarily made by such a practitioner at the bedside or in his consulting room.

Ophthalmoscopic and laryngoscopic examinations could readily be performed in the time available: to take a blood film was usually practicable: a fairly complete urinalysis is a routine. Klein's Test could readily be carried out.

But to make total white cell counts was seldom feasible as it necessitated almost immediate performance. I regret that I was not familiar with the simple procedure advised by Strong. More 'ambitious' tests or observations were impracticable.

I attempted to formulate an opinion as to the mode of spread and the incubation period in the summer months if possible. The cases were then few and my work was lighter then, and, consequently, I could give more time to the study of the circumstances attendant upon each case. Also the problem could only become more involved as more cases occurred. What was true in 10 cases must be <u>at least part</u> of the truth in say 1,000 cases. Particularly did I wish to form an opinion before the children were moved from one class to another in September.

.....

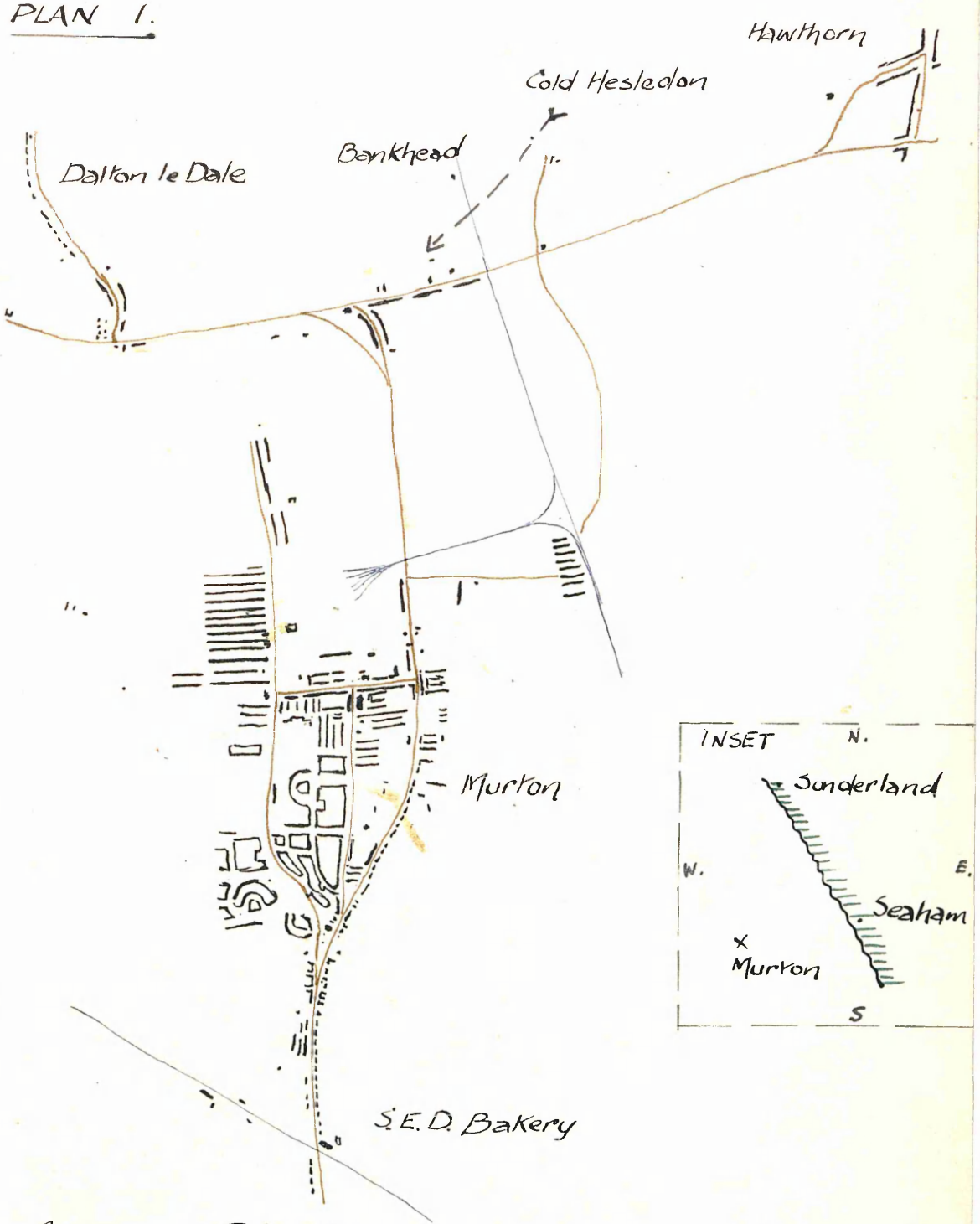
Whilst trying to avoid any slackness in the style of presentation, I have taken the liberty of including in a few of the case histories one or two of the expressions used by the patients, when they have appeared to me to be particularly expressive. They are sometimes terms employed

possibly only locally and they are included in the hope that the reader may understand some of them, in which case they may assist in the understanding of the conditions described. If they fail to do so, I crave the reader's indulgence.

THE EPIDEMIC AT COLD HESLEDON AND DALTON LE DALE

G R O U P 1.

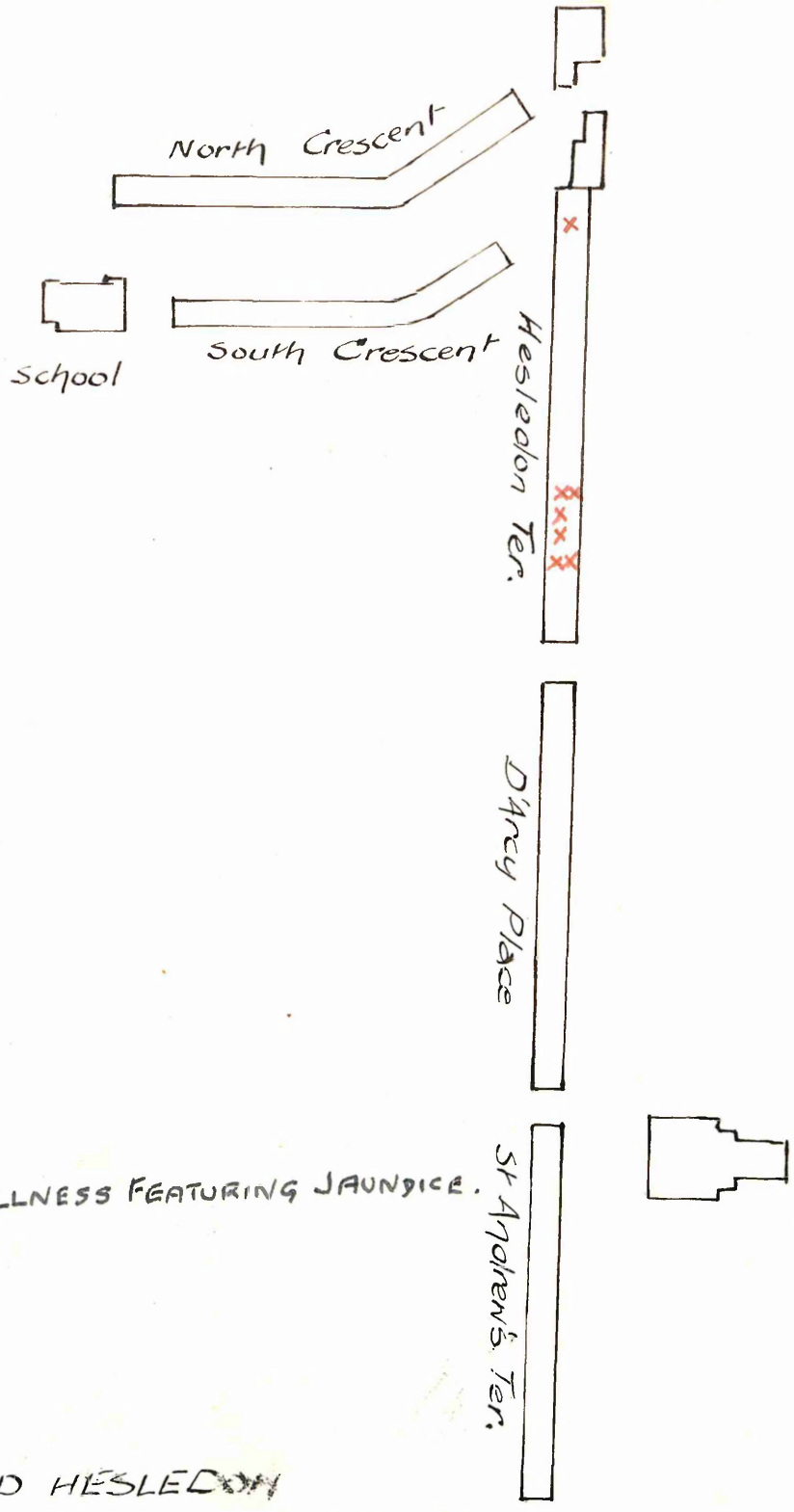
PLAN 1.



Murton & District.

Scale - 3 Inches = 1 Mile

PLAN 2.



x DENOTES ILLNESS FEATURING JAUNDICE.

COLD HESLEDON

THE EPIDEMIC AT COLD HESLEDON AND DALTON LE DALE.

Foreward.

Cold Hesledon is a small village within a mile of Murton, and Dalton le Dale is still smaller and lies a further ¾ mile away, north of Cold Hesledon.

Most of the children in both of these small villages attend the school at Cold Hesledon. The school is attended by 100 children, a number which is well below its capacity.

Sporadic cases of jaundice have occurred from time to time in the 21 years during which I have practised in those villages, but they were both practically untouched in the epidemic of 1941.

The Outbreak.

The last case encountered in Cold Hesledon had occurred in May, 1943, when a young married woman, Mrs. Brown, sent for me on 20th February, 1944. Mrs. Brown was then three months advanced in her second pregnancy. She suffered from an attack of what I considered to be infective Hepatitis. The leading symptom was vomiting; this was accompanied by a dull heavy frontal headache, epigastric discomfort and subjective vertigo, all of which preceded the onset of jaundice by about one week. Although I did not make a written record of her case at the time, I clearly recollect

that the urine did not contain albumin, that the blood pressure readings were below 120 mm Hg. (systolic) and 80 mm. Hg. (diastolic) and that she did not appear to be seriously ill. Epigastric pain was more in the nature of a marked discomfort and she was tender in that region. The most exhaustive inquiry failed to reveal the source of the infection. Her husband, recently returned from the Mediterranean battle zone, was considered as a possible source of infection (from various aspects which I will not here discuss) but I could not attribute the infection to him. I suspected him as he arrived here on 18th January, 1944, and the date of onset of Mrs. Brown's vomiting was not too definite as she considered it was "just pregnancy sickness," at first. There being no preceding case of jaundice in the area, to my knowledge, and believing the incubation period to be about a month, it was logical, I thought, to 'suspect' the husband. This the more especially as Mrs. Brown lives in an isolated cottage five-eighths of a mile from the village of Cold Hesledon and she had not recently 'been about' very much.

The next patient to become jaundiced in the locality was Audrey Branthwaite, a child living at 5 Hesledon Terrace, Cold Hesledon. She developed a marked jaundice and the features of the illness were consistent with a diagnosis of infective Hepatitis. I regret that I can not give the exact date of the occurrence of the jaundice, an omission

which may be atoned for by subsequent careful recording, but it was in the neighbourhood of the middle of April.

On the 24th May, 1944, Audrey's sister, Lorna Branthwaite, became ill (need I say at the same address) and on Whit Monday, 29th May, 1944, she was deeply jaundiced.

It was now anticipated that an epidemic was likely to occur.

On 20th June, 1944, Elizabeth Jackson, a schoolgirl, took ill at 8 Hesledon Terrace, Cold Hesledon. She vomited several times on rising and is said not to have appeared 'febrile.' The mother stated that Elizabeth had a 'lazy, helpless' look, and lolled about all day or rested on the couch. After 3 days illness she returned to school apparently recovered. On 27th June the symptoms recurred "exactly as before," I am told, and I first saw her on 28th June, 1944. Abdominal pain and tenderness were severe and definite, and I considered that she might have appendicitis. A fuller history of her illness is appended, and I will simply state now that she showed very markedly positive reactionsto Schlesinger's and Bogolomow's tests for urobilinuria on 28th June, 1944, and that bile appeared in the urine and she became jaundiced on 29th June, 1944.

The next patient, Jean Armstrong, lives at 7 Hesledon Terrace, Cold Hesledon, and she had an illness very closely copying that of Elizabeth Jackson, just described. Abdominal

pain was again present, but it was comparatively slight. She took ill on the 10th July, 1944, again beginning with early morning vomiting, and on the 17th July, 1944, she was jaundiced.

One day after Jean Armstrong's illness commenced, i.e. on 11th July, 1944, her friend and playmate, Iris Etherington, 32 Hesledon Terrace, Cold Hesledon, took ill and she likewise showed jaundice on 17th July, 1944. Iris had vomited on rising on 11th July, 1944, had kept lying about saying that she felt tired, and had complained of peri-umbilical discomfort and eaten very little food prior to the appearance of jaundice on, or before, 17th July, 1944, when I visited her. (It should here be mentioned that she had an illness lasting four weeks, commencing on 15th May, 1944. I could not then arrive at a diagnosis. I have made fuller reference to it in her case record.)

The next girl to develop jaundice was Brenda Robinson, 10 Hesledon Terrace, Cold Hesledon. A reference to her case record will show that this normally healthy girl had been noticed by her mother to have been obviously "off colour and not herself" for about a month. The girl herself gave a history of an illness commencing on 7th August, 1944. The early symptoms were, according to Brenda: a feeling that she was not very well, headache, dizziness, a sensation of swelling of the throat, chilliness; all culminating in

abdominal pain of an intermittent dull colic nature, vomiting and jaundice.

Jaundice was obvious on 15th August, 1944, but the diagnosis was obvious on the 14th August, 1944, when I first visited her.

(Here I mention that she had a severe and, in some ways, vague illness later, commencing on 30th October, 1944).

Brian Robinson, Brenda's brother, who like her became jaundiced on the 15th August, 1944, did not resemble the other cases so far encountered as the prodromal stage of his illness was very brief and jaundice was marked within 24 hours of the onset.

(Again, however, we have the puzzling second illness, this time again a severe illness ---- it began on 19th December, 1944.)

Catherine Robinson, the oldest child in the family, was ill for a few days. I have no doubt but that she had been infected too, as she had been listless and out of sorts for a few days prior to 15th August, 1944, when she vomited so urgently that she could not reach the lavatory at school 'in time'.

In every case so far encountered the mother had administered a purgative -- either a saline or the locally popular proprietary brand of syrup Ficorum --- in the prodromal phase of the illness, and Mrs. Robinson had thought that Catherine

was on the verge of a bilious attack and she had given the usual purgative.

(Catherine had no second illness, however, to date, 17th March, 1945).

Having mentioned Brenda Robinson, Brian Robinson, and Catherine Robinson, let me here refer to the only remaining child of the family, the nine years old son, Douglas Robinson.

Had he escaped the infection ?

I did not attend him, but I am convinced that he did not escape the infection.

It will be noticed that Mrs. Robinson did not send for me until Brenda had been ill for a week. The main reason which made her decide to 'call me in' was that Brenda's urine was very dark yellow and her motions were very pale, just like clay.

Now she had noted that some weeks before, when Douglas had been ill, his urine and faeces were similarly altered in colour. It was indeed this striking similarity which aroused her curiosity and suspicion and made her seek medical aid. But there is further suggestive evidence.

Douglas was absent from school on the morning of the 10th July, 1944. He attended in the afternoon of the 10th and all day on the 11th July, only to be absent again on the 12th, 13th, and 14th July.

(I confirmed these dates in the school register.)

Now his illness was exactly like that of the other Robinson children, being characterised by headache, giddiness, repeated vomiting, abdominal pain sufficiently severe to make him weep, and he "could not be bothered with anything and would not go out to play but just lay about" ---- this last symptom continuing after he returned to school. I further checked this history by interviewing Douglas and his mother separately, and there was convincing and complete uniformity in their stories. The mother especially remarked the peculiarly listless and sickly facies and the limp posture so alike in all the childfens' illnesses.

At this early stage of the outbreak I tried to take stock of the incubation period and to consider the probable mode of spread.

I do not include consideration of the illnesses of Mrs. Brown and Audrey Branthwaite because I felt that my judgment should be based on accurately recorded facts and at this period I had no reason to assume that an epidemic was impending and I did not record such data.

Lorna Branthwaite was in contact with Elizabeth Jackson on 26th May, 1944, and as the latter became jaundiced on 29th June, 1944, the interval was 34 days.

Elizabeth Jackson was at home, absent from school, on Tuesday, 20th June, until Friday, 23rd, attended school on Monday 26th June, and was off school ill thereafter.

The next two patients, Jean Armstrong and Iris Etherington, may have been infected on or before 19th June or on 26th June. (I do not think they visited Elizabeth Jackson between those dates, but I could not be definitely certain). As they both became jaundiced on 17th July, the interval between infection and the occurrence of jaundice would thus be 28 (or more) days, or 21 days, in each instance.

If we include Douglas Robinson, as I feel that we are justified in doing, the same dates and intervals would apply to him.

Brenda Robinson, Brian Robinson, and I should include Catherine Robinson, could have been infected either by their brother Douglas Robinson: or by Jean Armstrong or Iris Etherington.

The probable date of their being infected may have been on or before Monday, 10th July, when Jean Armstrong attended school: on or before Tuesday, 11th July, when Iris Etherington last attended school; or before, on, or after 10th July, 1944, as will be apparent on referring to Douglas Robinson's case record.

To summarize therefore: and calculating from the probable date of infection to the appearance of jaundice the data suggest intervals of :-----

1. Audrey Branthwaite to Lorna Branthwaite - more than a month
2. Lorna Branthwaite to Elizabeth Jackson - 34 days.
3. Elizabeth Jackson to Jean Armstrong - 28 days or 21 days.
   Elizabeth Jackson to Iris Etherington -28 days or 21 days.
   (Elizabeth Jackson to Douglas Robinson -28 days or 21 days).
4. A member of Group 3 to Brenda Robinson - 35 days.
   to Brian Robinson - 35 days.
   (to Catherine Robinson) 35 days.

The incubation periods thus seem to be at least 21 days and at most 35 days.

.....

I have underlined "seem".

As to the mode of spread.

I decided to ignore the possible mode of spread from Mrs Brown to Audrey Branthwaite on the grounds of the enquiries being retrospective, among other reasons, and to consider the spread from Audrey Branthwaite onwards.

The next patient was Lorna Branthwaite, also of 5 Hesledon Terrace, and here close 'contact' was obviously present in the home.

Let us consider the possible mode of spread in respect of:

1. The patient's home address.
2. The patient's class room and her position in the class room.
3. The patient's playmates.

1. The cases so far considered had occurred in Hesledon Terrace alone, namely at

Numbers 5; 7; 32; 10 Hesledon Terrace,

or considering each case

Numbers 5, 5; 7; 32; 10, 10, 10, 10.

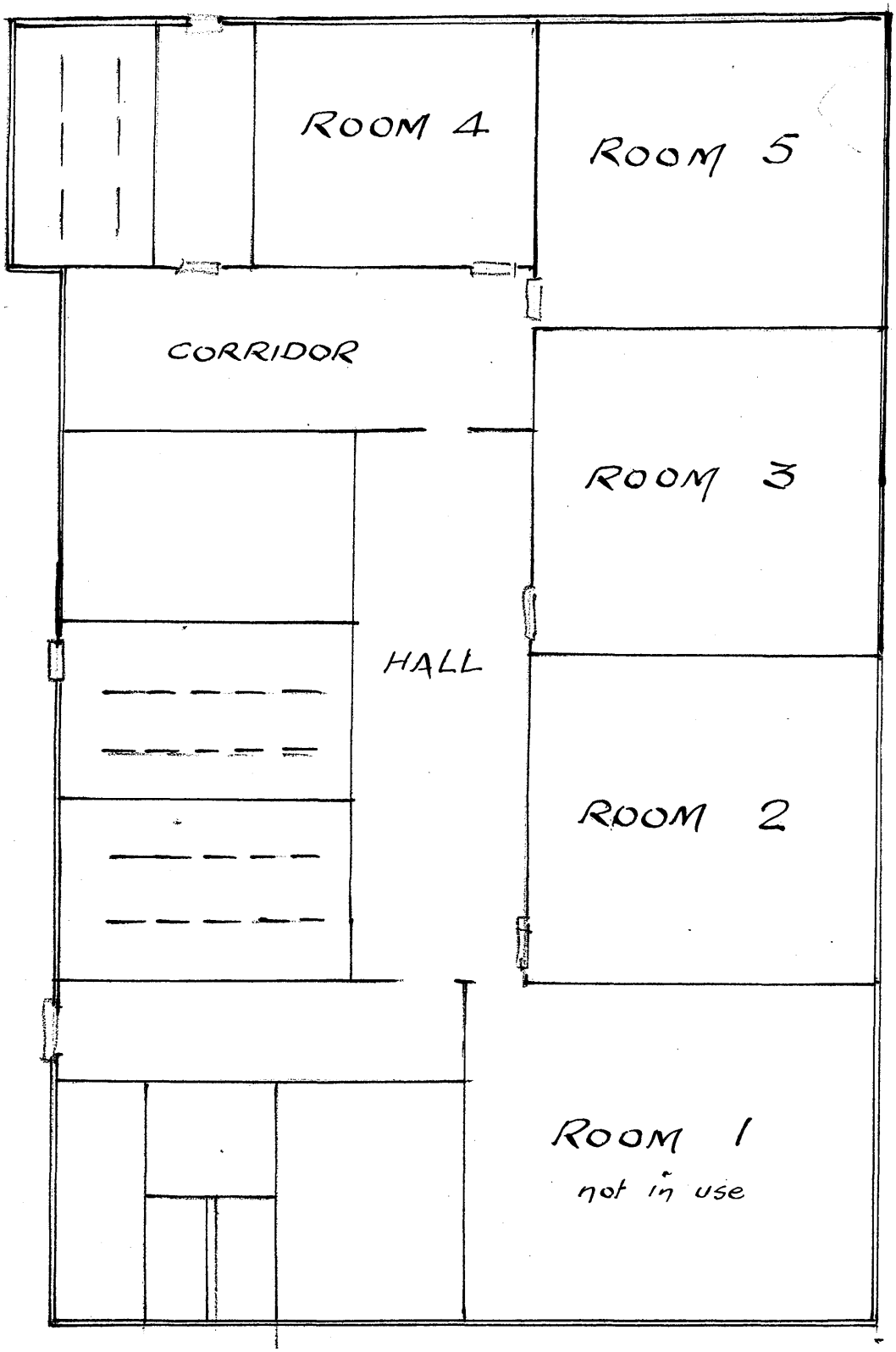
The first question was whether there was anything to suggest that Hesledon Terrace was 'picked out' from the other streets because of any local factor or peculiarity. This was especially queried as I noted that Ford[1] had reported that one school was especially heavily attacked in the Wembley epidemic.

The Following Plans, 3, 4, 5, 6, and 7 are copies of those prepared for me by the Headmaster of Cold Hesledon School.

They illustrate the general lay out of the school and the seating of the scholars.

The names of pupils who suffered from illnesses featuring Jaundice are underlined in red.

PLAN 3 HESLEDON SCHOOL



PLAN 4.

ROOM 2

A. SMITH.	NORMA COLLINS.	JOYCE REED	BET. GEE.	EDGAR WARIN.
C. RICHARDSON.	MARY SHORT.	LILIAN PURVIS	SHIELA LAWSON.	WILF ROBINSON.
T. GEE.	JEAN ETHERINGTON	MARY COLLINS	STOREY WALTON	EDW. ATKINSON.
S. HUDSON.	BETTY BERRY.	LILN. ANDERSON.	C. ETHERINGTON.	FLOR CLARK.
R. KING.	LEWIS RICHARDSON	BET McNALLY.	BRENDA. ROBINSON.	Wm. PICKERING.
J. HILL.	JEAN HUNTER.	ELLEN SHORT.	Wm VICKERS.	MARY GALLON.

PLAN 5.

ROOM. 3.

AUD GRAHAM.	EVE POW.	JEN TURNER.	CATH. SCOT.	ARTHUR LYALL
JOAN CUMMINGS	ALAN CLEMENTSON	IVAN WAY.	PAUL PICKERING.	WM. WALTON.
MAVIS RUTTER.	BET HARRISON. FREDA. COLLINS.	IRIS ETHERINGTON	IVY GEE	JAS. HARRISON.
DAN WEBT.	ELS ATKINSON.	JOHN MCKEON.	ALICE SOPPITT.	JOE HUDSON.
ARTHUR DEAN	DOR. ARMSTRONG	BET JACKSON.	JUNE LAWSON.	JOHN ATKINSON.
CON HILL	BET NEWTON.	JEAN ARMSTRONG.	RON BARTRAM.	JEAN BARTRAM.

PLAN 6.

ROOM. 4.


STAN WILSON
DOUG. ROBINSON
H. MULLEN.
MAL RICHARDSON
HARRY McNALLY
MARGt HOY.
HAZEL HUDSON.
GEO PURVIS
ROSE PICKERING.
JOHN THYNNE.
RALPH ELLIOTT
JOHN COOK.
OSWALD BLENKINSOPP
ALB. SHORT.
DEREK JACKSON.
CATH ROBINSON.
LOR. BRANTHWAITE
ANNE MILLER.
EVE TREWEEKE.
Wm. PARKER.
JANE HILL
ALAN. GRAHAM.
VIN ELWICK.
FLOR WITHINGTON.
JANE THUBRON

PLAN 7.

ROOM. 5.

		JOE THOMPSON. BRIAN ROBINSON	TOM COLLINS. RICH° ORAM.	
	PETER BARTRAM.	DAV. PEGMAN. JOE TURNBULL	DEREK RACE AUD REED	
	JOHN KING. ROB^t AVERY.	MARTHA KING. AUD BRANTHWAITE	ANNE WALKER MIR SHORT.	
	ALAN PURT. DAV. LINCOLN.	KEN SOPPITT	JOHN MILLER	
	CON. WALTON TOM. MASON.	JIM. GOLIGHTLY.	JIM BOWATER. ROB^T BURNS.	

The water supply was exactly the same to all the streets. The only possible difference was that the drains from No. 5 Hesledon Terrace down to No. 12 Hesledon Terrace were the subject of complaint on the grounds of being very foul-smelling on occasion. It may be here noted that the later observations did not appear to support the association of possibly defective drainage with the spread in other areas--cases occurring in many instances after 'contact' at work, in travel or at play in people who lived in widely separated localities.

But the fact was noted, and kept in mind.

2. I then inspected the school at Cold Hesledon.

The Headmaster assisted me by preparing a plan of the school. He prepared seating diagrams which showed the seat occupied in each class room by each pupil.

If a child became jaundiced I had only to refer to the diagrams to see who were her immediate neighbours in the class and who were the remaining pupils in the same class room. (See diagram provided.)

To consider the cases seriatim, and assuming, as I then did, that the incubation period did not exceed 40 days.

In case she might have conveyed the infection to the school, although she herself was not ill, I referred to the position in class of Joyce Reed, the sister of Mrs Brown, our first case in the epidemic. She sat in class room 2. No (further) case occurred in this class room within the

time stipulated.

Audrey Branthwaite's case could not apply as she had been absent ill, before her 'jaundiced' illness.

The first really reliable finding therefore was in reference to Lorna Branthwaite, who attended school until the day when she took ill with infective Hepatitis --- in fact she attended school during the stage of her prodromal illness. She sat in class room 4.

I noted that not only that she apparently failed to infect any member of her class room but that she was one of the few children who shared a desk with another pupil. In spite of this close proximity, transference of the infection had apparently not occurred.

Elizabeth Jackson was in yet a different class room --3. Now in this instance we find that the next two children to become jaundiced --- Jean Armstrong and Iris Etherington -- were in the same class room.

No other member of the class appeared to have been infected, and I should state that Douglas Robinson was not a member of this class. He was in class room 4.

The next two children who became jaundiced, it will be remembered, were Brian Robinson and Brenda Robinson.

Brian Robinson's class room was again different -- it was No. 5. Brenda also sat in a different class room --No.2.

To summarise:- the evidence did not support the view that

the infection was being spread from pupil to pupil as they sat in their class rooms at school. The only case where this spread might appear to have occurred was in the "relay" from Elizabeth Jackson to Jean Armstrong and Iris Etherington.

Now, considering this "relay" further.

5. I had observed that the children, E. Jackson, I. Etherington (and Brenda Robinson) were close friends ---they seemed to come home from school together and play with each other, etc. --- and the schoolmaster said that this was an understatement -- they were inseparable. Lorna Branthwaite, a more recent arrival in the village, was an occasional playmate.

.....

I therefore formed the opinion that the spread was occurring outside the class rooms, either in the patient's home or in the close association with her friends.

Why was the disease not spreading in the class rooms ?

If it was an air borne infection I should have expected such a spread to have occurred. It was not until 20th of January, 1945, that Mitman[2] contributed his article on "Aerial Infection" in the British Medical Journal, but I was interested to observe then, that he believes that the great majority of such infections occur indoors.

Even allowing for the fact that the class rooms at Cold Hesledon are large and that in many cases each pupil had a desk designed for two pupils --- and further allowing for the fact that an upper respiratory catarrh was not a feature in those cases of infective Hepatitis, it was 'peculiar' that an infection commonly supposed to be spread by droplet did not spread (more obviously) in the class rooms.

If one was trying to support the theory of aerial droplet spread, it could be stated that conversation is louder and that the children come into closer 'contact' out of doors.

But on the whole, to say the least, the cases gave little support to the theory of droplet spread.

As regards the possibility of spread by actual contact, I thought the series gave more support in this direction.

The well spaced seating was against ready spread in the class rooms, where actual contact would occur less fre - quently than at play out of doors.

If actual contact led to infection I thought the most likely mechanism of the introduction of the infective agent into the body would be a spread from the hands to the mouth.

Ford[1] considered that the spread was probably by droplet or possibly by faecal contamination spread by the fingers.

<u>The latter seemed to be the more likely of the two suggested modes of spread in the few cases with which we have dealt</u>.

Finally I should state that the school water supply is the same as that to the rest of the village.

The only food supplied at the school was pasteurised milk, which was drunk directly from the milk bottles. It was obtained from the same source as the milk supplied to Murton School, with its 1400 to 1500 children, where no jaundice had occurred.

On Monday, 14th August, 1944, the day on which I visited the Robinson children, I was called to see William Collings, a four years old boy at 28 Hesledon Terrace, Cold Hesledon.

It is important to state that this boy spent most of his time at 3 Hesledon Terrace, with a Mr and Mrs Walshaw, who had no children and who had all but adopted him.

Now the child's illness was strikingly similar to the preceding cases of infective Hepatitis, and I felt convinced that it was in fact the same illness. Here again we had the initial illness, the interval of apparent recovery and the second phase of the illness. The initial illness was characterised by diarrhoea and vomiting and it occurred on 3rd. of August, 1944. This was followed by an "exactly similar" attack on 12th August, 1944, which however did not clear up rapidly and led on to the fully developed picture which I found on the visit of 14th August. I feel that this was no 'ordinary' gastro intestinal upset. The appearance of the boy sitting limply in his chair, apparently scarcely able to support his head, the extremely fatigued appearance of the face with the complete absence of change of expression and the 'drooping' eyelids made up a picture which I began to regard as distinctive. There seemed to be not only physical weariness but mental apathy and lethargy also. I thought that he would probably become jaundiced but he did not. Meanwhile I examined the urine and found it to be

(When I wrote this I was not on the staff of Sunderland Royal Infirmary) →

normal, except in one respect: it contained no albumin or bile, but it showed a definite urobilinuria. Unfortunately I was not at this date conversant with the white cell changes in infective Hepatitis, and the histamin which I ordered for a Klein's intradermal test, arrived too late to be of use --- if indeed it would have been helpful.

The importance of William Collings's illness lies in the possible relation to the illness of T. Walshaw, 3 Hesledon Terrace, mentioned above. I have recorded the fatal illness of this 53 years old fitter at some length. It may be considered a rather homely narrative but that is the way in which the case presented itself to me as a general practitioner. The reader, whose everyday work may lie in a more academic approach to the problems of such an illness, will find very essential data for criticism and consideration in the findings of the examination of the blood, the cerebro spinal fluid, the urine and the sputum.

Clinically, the illness gave the impression of an atypical pneumonia with an encephalomyelitis, both being conditions commonly caused by a virus infection.

During this winter, 1944 -- 1945 I encountered several cases of atypical pneumonia and one fatal case of ascending myelitis[3] where contact with patients suffering from the epidemic illness had occurred.

I think it fair that one should consider the possibility

of a virus which is obviously present in the community being the aetiological agent in such cases, before postulating the presence of a further virus.

Walshaw's illness bore a resemblance to the fatal case of "atypical pneumonia with encephalitis" reported in the British Medical Journal by Perrone and Wright.[4]

The presence of cold agglutinins in the blood will be remarked: as will be the absence of lymphocytosis. The blood was sterile on culture.

The cerebro spinal fluid showed a complete absence of polymorphonuclear leucocytes.

The pathological report appended illustrates those and other features.

On reading over this section of the account of the epidemic, I have decided to reproduce the table on page 195 to enable the reader to follow the "chronological" order of the illnesses described.

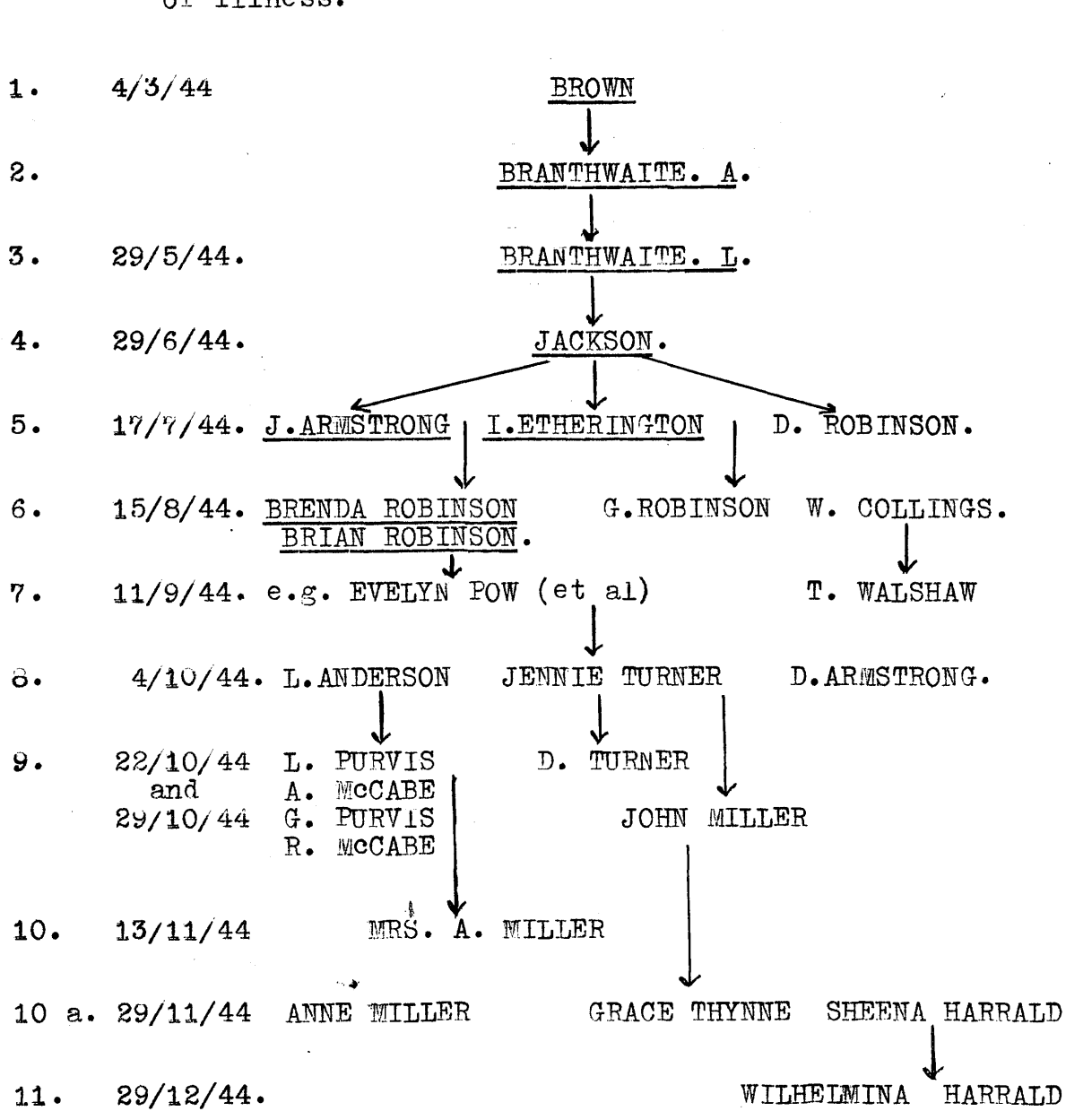


DIAGRAM TO ILLUSTRATE THE POSSIBLE ORDER OF SPREAD

UNDERLINING OF NAMES DENOTES CLINICAL JAUNDICE.

To resume the narrative of the epidemic.

The occurrences of the 14th August, just referred to, led me to expect that a fresh group of cases would occur at any date after, say, 7th September.

I called regularly to consult with the so-co-operative headmaster, and soon afterwards I received the following information from him and from the parents of the children named. It points to a heavy incidence of sickness absenteeism on 11th, 12th, and 13th September, 1944. The date is significant and the fact that vomiting occurred in several instances is of added significance. Several of the cases do not further interest us in this account, and the reader is requested to scan those rapidly for one reason only --- that is to note that the sick children were distributed in different classrooms at school and that they lived in "well-separated" houses.

Case 6 is vital to the inquiry.

1. Jane Hill. Class room 2. 9 St.Andrew's Terrace, Cold Hesledon. Sick in school on 12th and 13th September,1944.
2. Miriam Short. Class room 5. 20 St. Andrew's Terrace, Cold Hesledon. Vomited frequently in school 11 Sept,1944.
3. Henry McNally. Class room 4. 10 D'Arcy Place, Cold Hesledon. Common cold, anorexia and nausea for 4 days from 13th September, 1944.
4. Evelyn Pow. Class room 3. 20 Hesledon Terrace, Cold Hesledon. 1st September, 1944. She was listless and

sat or lay down all day "absolutely lifeless." Anorexia for one week.

11th September, 1944. She appeared to be feverish, complained of a frontal headache, had a profuse urticarial rash and could not attend school.

5. Jane Lawson. Class room 3. Hesledon Terrace, Cold Hesledon.

Was absent from school on Tuesday 12th September, 1944. (Not my patient).

6. Jennie Turner. Class room 3. 9 Dunelm Terrace, Dalton-le-Dale.

She vomited in school on 11th September, 1944.

The subsequent history is recorded as Case Record No. 11.

A study of her illness, as related, will show that it presented many features in common with the illnesses which we have so far considered. But it differed from several in that jaundice did not occur and from others in that it could not be considered a fleeting and abortive attack. Points of resemblance were evidenced by the initial vomiting, the temporary recovery leading to the second phase of the commonly bi-phasic illness, the anorexia, the nausea, the strikingly fatigued facies and appearance, and the epigastric discomfort and tenderness. Further we have the same type of headache, the giddiness and the urobilinuria. I further noticed the

'unwillingness to complain' on the part of the patient who was at first content to state, again typically, only that she " did not feel well."

I thought that a white cell count would be helpful. The results were:--

Differential White Cell Count. 8th October, 1944.

Neutrophil Polymorphs.	21
E o s Polymorphs.	1
Lymphocytes.	72
Monocytes	6

Total White Cell Count. 4,200 per c. cm.

Now this appeared to me to be a finding indistinguishable from the findings in accepted cases of infective Hepatitis.

To check this result a differential white cell count was made in the case of Lilian Anderson (Case Record 12).

This girl's story and her condition on examination contrasted markedly in many respects with the illness of Jennie Turner, her leading symptom being an unexplained diarrhoea.

Differantial white cell count. 5th October, 1944.

Neutrophil Polymorphs	34
E o s i n o Polymorphs	5
Large Lymphocytes	7
Small Lymphocytes	50
Monocytes	4

At this time I attended Doreen M. Armstrong (Case Record 13) another pupil at Cold Hesledon School. Her initial illness, 6th October, 1944, was typical of the epidemic but milder than some. The interesting feature to me was the occurrence of a second illness for which I attended her on 30th October, with complaints including paraesthesia and little darting pains in the fingers --- aching and stiffness in the thighs, proximally and anteriorly I noted, and bitemporal, 'non pulsing',headache. Again there was a marked relative lymphocytosis --57.5 % of the total white cell count.

.....

Another word about the incubation period, before proceeding.

I thought that the children, or some of the children who were sick on 11th, 12th, and 13th September had been affected by the children who were ill around 14th August, 1944: this was consistent with an incubation period of one month.

We must next consider the case of Jennie Turner, Lilian Anderson, and Doreen Armstrong just mentioned.

Jennie Turner was sick in school , in common with others who we will assume suffered from abortive attacks, on 11th September, 1944. We have either to assume that this vomiting was an initial illness and the illness of around 30th September, 1944, was a second illness. Or we

may consider that the vomiting of 11th September, 1944, was an invasion symptom and the subsequent illness marked the end of the incubation period. As I consider that both suppositions are tenable, I would not base my calculation of the incubation period upon such controversial evidence.

Similarly, a consideration of Lilian Anderson's history presents the difficuly of knowing where incubational symptoms end and the 'disease proper' commences.

Doreen Armstrong's illness commenced on 4th October, and if we presume that she was infected on or about 6th of September (a Friday) the incubation period could be 26 days. Although her second illness on 30th October, 1944, again complicates the picture, I do not consider that it confuses it sufficiently to strongly contest the validity of this assumption.

To continue the observation of this illness now occurring at Dalton le Dale, and which appears to have been the direct descendant of the infective Hepatitis at Cold Hesledon.

We have encountered the gastro intestinal symptoms, the listlessness, the giddiness, urticaria, urobilinuria (in some cases) and the very suggestive white blood cell findings: also the complaint of dysphagia with little visible local cause, and in one case paraesthesiae etc.

The next similar case at Dalton le Dale occurred at 5 St. Andrew's Terrace, where I visited Lilian Purvis and her mother, Agnes McCabe, on 24th October, 1944, and Robert McCabe and his son, George McCabe, on 29th October, 1944.

In this case the infection was almost certainly introduced by Lilian Anderson (previously mentioned) who visited this house frequently, and had visited this family several times between 21st September and (certianly not later than) 4th October.

The onset of the illness was 22nd to 25th October in the case of the female patients and 29th October, 1944, in the case of the males. It is easy to understand how the males may have been infected later than the females as Lilian Anderson called to talk to the females. Reference to Lilian Anderson's history would suggest that she may have been infectious from 21st September onwards. An incubation period of up to 31 days is therefore possible, in this 'relation'.

It will be noticed that in the case of Lilian Purvis the lymphocytes numbered 46% of the total white cell count. Her stepfather showed a percentage of 59.5. But the mother, who was pregnant had only 16% lymphocytes in her differential count. The mother, Mrs. McCabe, was at no time confined to bed and she was clinically a mild case. I record her count

for two reasons. First it may illustrate an altered response to the infection in a pregnant woman. Secondly it may illustrate an error in diagnosis. In either case the figure is instructive and interesting.

.....

I will later comment on the leucocyte count, especially the differential count, in many other cases which occurred in the Murton area, at the same time, or just after the illnesses which we are now considering.

They serve the illustrate that a relative lymphocytosis was an almost constant feature in cases which I considered to be of a similar type.

.....

At this stage a diagram (Page 195) to illustrate how the infection may have spread will probably enable the reader to follow the narrative more easily. Beginning with Mrs. Brown as Stage 1, although we have no proof that she was the source of the origin of the epidemic, it will be seen that we have now considered no fewer than 8 relays of the disease, and that the illnesses of the McCabe (and Purvis) family represents Stage 9.

Also in Stage 9 we find the illness of David Turner, who consulted me on 1st November, 1944. The features of the

illness were the occurrence of a head cold, nausea, and quite disproportionate weakness and lethargy. An interesting feature was the marked visual disturbance as mentioned in the case history. David Turner is the father of Jennie Turner. His illness inclined me to the view that Jennie Turner's "illness proper" probably dated from 2nd October and not from 11th September, 1944 (refer to her history).

Included in Stage 9 we have the illness of the 6 years old John Miller, commencing on 5th November (with one week later the very severe illness of his mother, Anne Miller.) see below.

The boy showed the following symptoms --- headache, intense giddiness and listlessness and the facies and appearance of physical exhaustion. Anorexia was marked and persistent and there was moderate pyrexia.

The mother's case presented those and additional important features. Minor additional points were

1. Conjunctivitis.
2. Dysphagia at the thyrohyoid level -- a feature which I later found to be common.
3. A most unpleasant breath of which she was aware.

More important or significant features, as they occurred to me, were:

1. Apparent recovery in 4 days followed by the second more serious phase of the illness. This was strikingly

similar to the early cases where jaundice was prominent.

2. The peculiar urticarial eruption.

3. Symptoms highly suggestive of an atypical pneumonia (but) with little respiratory embarrassment.

4. Nocturnal insomnia associated with daytime drowsiness— "disturbance of the sleep rhythm."

As regards the source of the infection in those 2 cases.

My considered opinion is that John did not infect his mother which would mean an incubation period of some 7 days. The inhabitants of this very small village are very unlike those of Cold Hesledon in that infectious disease arouses curiosity more than respect, and sick visiting at such times is at its peak. I considered that John Miller had been infected from the Stage 8 patients, with whom he travelled to school. The incubation period would thus be just over one month: and that Mrs Miller had been infected at her next door neighbour's (McCabe— Purvis) around 22nd October,1944.

.....

This brings us to the final stages in our present consideration of the outbreak.

Anne Miller (see Stage 10) the sister of John Miller, vomited on 28th November, 1944. Her brief case history illustrates a very typical, well defined but mild attack: the prodromal symptoms included such utter weariness that she all but fell asleep on the desk at school.

The other members of Stage 10 were Grace M. Thynne and Sheena Harrald. Their illnesses dated from 25th and 27th November, 1944. In the case of the former, aged 12 years, an interesting feature was the complaint of indistinct vision. Otherwise the illness was true to type. The younger child, Sheena Harrald, showed evidence of bronchitis and had two nose bleeds. The facies, etc., in both cases was striking and immediately commented upon by everyone who saw the patients.

.....

The mother of the last-named child consulted me on 29th December, 1944. I regarded her symptoms as being highly suspicious, but the reader may consider that they are not conclusive.

In the latter part of the outbreak I could not possibly find time to make blood films to discover whether the relative lymphocytosis was persisting. I was convinced that I had at least to my own satisfaction established the identity of this outbreak and I was by now investigating the extension of the disease in other areas.

.....

There now follows a diagram to illustrate the suggested order of the spread of the infection and the case histories. The case histories include one not so far mentioned. Cyril Ellis, a coal miner, aged 21 years, who showed a 10%

monocytosis and a 48% lymphocytosis in his relative white cell count.

He lives next door to Lilian Anderson, who may have infected him. A feature in this case was the complaint, later, of weakness in the shoulder girdle muscles.

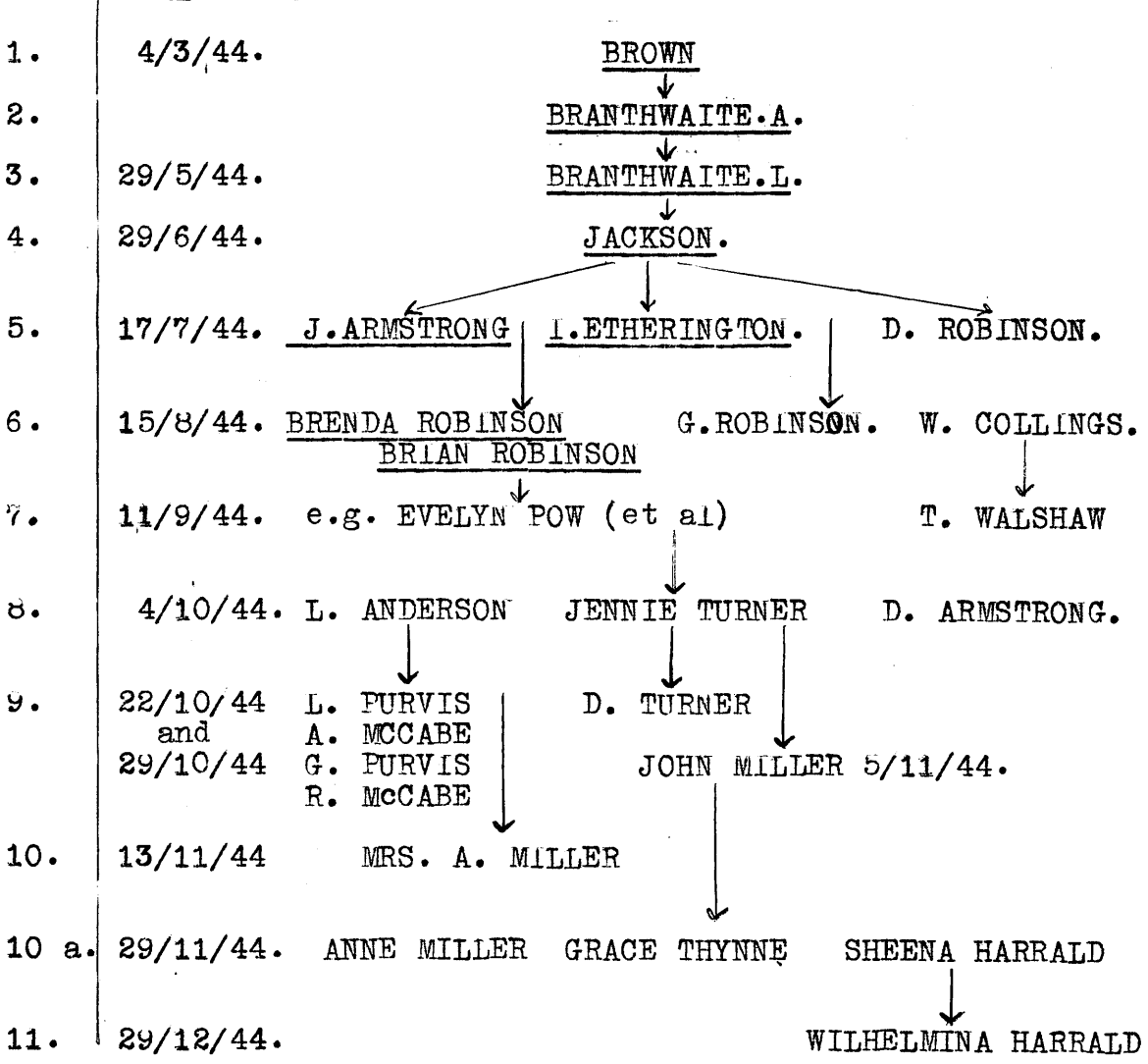


DIAGRAM TO ILLUSTRATE THE POSSIBLE ORDER OF SPREAD.

UNDERLINING OF NAMES DENOTES CLINICAL JAUNDICE.

Where jaundice occurred the date of its occurrence is given as the date of the illness.

CASE HISTORIES AND ATTENDANT CIRCUMSTANCES.

In order to avoid confusing interruption of the preceding narrative, the reference to several of the cases has been kept very brief. So much so, that many important features of the epidemic have received only scant mention.

The section which follows on the next 53 pages is not, therefore, simply an elaboration of the preceding account, and, in many respects, it is much more vital to our study than the brief chronological review just concluded.

If I therefore appeal to the reader to resist the 'temptation' to neglect this section, even temporarily, as being a mere elaboration of the first section, I trust that on completing his study of it, he will consider its interest to be commensurate with the effort entailed.

LORNA BRANTHWAITE, Age 7 years. Case 1

5 Hesledon Terrace, Cold Hesledon.

Attending Cold Hesledon School. Class Room 4.

Retrospective History.

She had obviously been 'off colour', the mother states, from Wednesday, 24th May, 1944: she "had no life" about her and was disinclined to eat or play, and kept on saying that she was tired.

On Friday, 26th May, 1944, she returned from a film show, obviously very much worse --- she seemed to be exhausted. Over the week end she seemed feverish, she complained of frontal headache and abdominal pain and she vomited several times. On the Monday, 29th May, 1944, her mother took her out walking and she seemed to be recovering, but at night all the symptoms returned "exactly as before":-- the vomiting, headache and abdominal pain. The mother then noticed the jaundice.

The urine contained bile. The faeces were pale.

Recovery was rapid.

ELIZABETH JACKSON. Age 11 years. Case 2.

8 Hesledon Terrace, Cold Hesledon.

Attending Cold Hesledon School. Class Room 3.

Visit

Wednesday 28th June, 1944.

The history given is that on Tuesday, 20th June, 1944, she was ill. She vomited several times on rising but she did not appear febrile. She had a "lazy helpless" look and she sat about, lolling in a chair or resting on the couch until the afternoon, when she went to bed. Wednesday she was still listless and "lifeless" but she gradually brightened up, and on Thursday she returned to school. On Friday, Saturday, Sunday and Monday she appeared to be well, but on Tuesday, 27th June, she again vomited on rising and said that she felt ill --- exactly as on Tuesday 20th June: and again she sat apathetic all day, and she had abdominal pain.

When I visited her for the first time on Wednesday, 28th June, 1944, I found her complaining of obviously severe abdominal pain --- a constant dull pain with acute exacerbations. The abdomen was tender --- there was no rigidity. The tenderness was most marked over the right side of the abdomen and extended from the epigastrium and the right subcostal margin to McBurney's point. The tongue was slightly coated and moist. Pulse rate was 80 and

temperature 99.2 ^{o} F.

The urine contained no pus, albumin or bile, but gave a definite positive result to Schlesinger's urobilinogen test --- and also to Bogolomow's test. Later bile appeared in the urine. On

Thursday, 29th June, 1944

She became jaundiced, the jaundice appearing in the usual manner in the conjunctiva then spreading to the face and neck and becoming generalised.

Recovery was gradual and apparently complete.

JEAN ARMSTRONG. Age 11 years. Case 3.

7 Hesledon Terrace, Cold Hesledon.

Attends Cold Hesledon School. Class Room 3.

This case was a replica of the preceding one (Elizabeth Jackson), and I shall not repeat it in detail therefore.

The initial phase occurred on 10th July, 1944, when early morning vomiting occurred.

She appeared to improve temporarily, but the vomiting recurred on 17th July, 1944, and jaundice was then evident. Again the stools were clay coloured and the urine dark. Recovery was gradual, the jaundice cleared within a fortnight

Second illness. It is considered as 'a relapse.'

She had avoided excess of fats in the diet until 22nd August, 1944, when she ate some suet pudding. That night she was ill. She had a dull ache in the epigastrium with colic exacerbations. She vomited frequently and had profuse watery diarrhoea, the stools being very pale (? undigested fat). I called in to see her (inquiry call, I had not been sent for) on 25th August, 1944.

The temperature was 101°F. Pulse was 100 per minute. She complained of headache, but she did not look so ill as during the first illness.

I was surprised to find acute tenderness on pressure under the right subcostal margin.

Recovery was rapid.

IRIS ETHERINGTON. Age 11 years. Case 4

32 Hesledon Terrace, Cold Hesledon.

Attends Cold Hesledon School. Class Room 3.

Monday, 17 July, 1944. Visited.

History: She took ill on Tuesday, 11 July, 1944, when she vomited on rising. She 'lay about' all day saying that she felt tired. She had a frontal headache and complained of peri-umbilical pain, and her head felt giddy and, as she terms it, 'swimmy'.

The mother gave her a proprietary laxative -- this was the domestic remedy invariably used by the mothers during the outbreak -- but Iris continued to be listless, to refuse all food, and the peri-umbilical pain persisted until 17 July, 1944, when I visited her. She was then obviously jaundiced. The liver was palpable and tender.

Temperature 99°F. Pulse 60.

She looked sickly, tired, listless and apathetic.

The stools were pale -- clay coloured, and the urine contained bile.

Recovery was uneventful.

.....

Subsequent illness.

She was ill again on Wednesday, 6 September, 1944.

At 5 a.m. she came downstairs saying that she felt sick, and she 'tried' to vomit. She had abdominal pain.

Presently she vomited a little. At teatime she again felt sick and vomited.

Her appetite continued to be poor for a few days.

However she is said to have had similar attacks before.

Vague illness prior to the Jaundice illness.

Retrospective History in Part.

Some 8 weeks prior to the illness described above, she had an illness attended by a pyrexia up to 100.5°F. (15/5/1944 -- 13/6/1944). I could find no obvious cause for the rise of temperature, which persisted for 16 or 17 days. The child complained very little indeed. She did complain of vague pains in the limbs, but apart from that she simply said that she did not feel well. The urine was normal on examination for gravity, reaction, albumin, pus, blood and sugar --- the ears were healthy and so was the throat. She looked poorly and rather apathetic rather than very ill, and her condition did not alarm her (observant) mother, apart from the fact of the prolonged pyrexia.

There were a few physical signs in the chest. A few fine moist rhales were evident especially in the inter-scapular region -- right side. At one time I thought there was a slight dulness and "feeling of resistance"

on percussion and I arranged to have the chest X Rayed when Iris was able to travel.

She had a cough -- it was not very troublesome or marked-- and she had no respiratory embarrassment. The pulse respiration ratio was normal throughout.

.....

Through an unfortunate error I did not receive the written reports until 28 March, 1945. (It was not the fault of the Tuberculosis M.O., who is always most helpful).

.....* X Ray photographs are available.

The first X Ray, on 19 June, 1944, showed evidence of a recent inflammatory lesion in the right mid zone.

It was considered probable that the shadow resulted from a "simple" inflammatory pneumonitis, but a 'serial' X Ray was considered advisable to exclude the possibility of a primary tuberculous lesion. Accordingly a second X Ray was taken four months later, on 13 October, 1944.

It showed that the condition had cleared up and that there was no evidence of calcification.

.....

I think therefore that the child had suffered from an atypical pneumonia

.....

Note. She has 4 playmates. Three of them are:-

1. Elizabeth Kackson. q.v.
2. Jean Armstrong. q.v.
3. Joyce Reed, a sister of Mrs Brown, the first person referred to in this epidemic

She also visits "Bankhead" the home of Joyce Reed and Mrs. Brown.

BRENDA ROBINSON. Age 12 years. Case 5.

10 Hesledon Terrace, Cold Hesledon.

Attends Cold Hesledon School. Class Room 2.

Visited.

Monday, 14 August, 1944.

She states: "All last week I was not feeling very well. I had a headache and I felt dizzy. I was in the house most of the week (the school was on holiday) as I did not feel like going out to play much. I was not out at all on Friday (11/8/44) but I went out on Saturday. When I came in I felt that my throat was swelling" (she pointed to the thyrohyoid level) "my head felt dizzy again, only worse, and I felt shivery. I did not want to eat anything all week"

The mother stated that Brenda vomited frequently on Saturday, Sunday, and this morning. Brenda then had epigastric and generalised abdominal pain of an intermittent dull colic nature. She also had a slightly troublesome cough.

This girl is usually the 'picture of health' but she is said to have appeared 'off colour' for the past 3 or 4 weeks.

On examination. The face is expressionless, practically masklike, and she appears weary, languid and apathetic. She is tender in the epigastrium and under the right costal margin, but the liver is not palpable, neither is the

spleen. The temperature is 99.2°F. Pulse is 70 per minute.

There is urobilinogen and bile in the urine. The faeces are clay coloured. Jaundice appeared on 15 August.

The recovery was rapid and uneventful. The jaundice cleared up in 14 days.

The second illness.

Visited

Monday, 30 October, 1944.

She then complained of a 'sore throat' and of headache. There was nothing of note beyond a slightly inflamed throat, temperature 99 and pulse 84.

Through an unfortunate error she was not visited again until Friday.

I was told that on Tuesday she was very dizzy, on Wednesday she had more severe frontal headache, and that on Thursday she had had a very heavy nose bleed. "All the time" she had felt chilly.

Friday, 3 November, 1944.

There is obvious conjunctival injection — her eyes are smarting and irritable, and she complains of photophobia. She is eating fairly well. The pulse is 116 per minute. The temperature is 101.5°F. Examination gives entirely negative results. There is no albumin, pus, blood, sugar, acetone, bile or urobilin in the urine.

Saturday, 4 November, 1944.

She had another nose bleed this morning. She has a profuse watery nasal discharge. The temperature is again 101.5°F. The pulse is 100. The bowels are acting normally, and regularly. There is a little patch of exudate on the right tonsil.

Monday, 6 November, 1944.

To-day she appeared to be a little better. As before she made very little complaint. For these reasons neither she nor the parents are greatly concerned about her condition. She complains however that she has a headache if she stands up (e.g. prior to attending to her toilet) and that her knees are painful and have a peculiar stiff feeling. She has no abdominal pain. She points to the thigh just above the knees.

I was surprised to find the temperature 103°F but the pulse at only 100 per minute.

With some hesitation I decided to try the effect of Sulphapyridine.

Tuesday, 7 November, 1944.

Markedly improved. Pulse 90. Temperature 99.4°F.

Face pale but cheeks red. Costive motion to-day.

Wednesday, 8 November, 1944. P.m. She is said to have eaten well yesterday and slept well last night but to-day she is not so well. Headache has returned: it is a frontal

headache and severe. Pulse 120. Temperature 101. She again feels chilly.

After my visit she vomited frequently.

Saturday, 11 November, 1944. Pulse 100. Temperature 101.

Sunday, 12 November,1944. Pulse 80. Temperature 98. (Looks better).

Monday, 13 November, 1944. Pulse 66. Temperature 98.

Saturday, 25 November, 1944.Pulse 66. Temperature 98.

The tongue is moist and it looks raw --- moist raw beef tongue with prominent papillae.

On this date and for some 2 weeks thereafter she was very easily fatigued and kept sitting up only to return to bed after a few minutes.

At no time did I find any physical signs of pneumonia and the pulse respiration ratio was never suggestively disturbed.

.....

SUMMARY OF SYMPTOMS. First Illness.

1. Malaise.
2. Giddiness.
3. Headache.
4. Lethargy.
5. Throat discomfort at Thyrohyoid Level.
6. Aggravation of Vertigo.
7. Chilliness.
8. Loss of appetite.
9. Vomiting.
10. Abdominal pain.
11. Cough.
12. Mask like facies.
13. Tenderness in epigastrium and under right subcostal margin.
14. Slight elevation of temperature: pulse normal or slow
15. Bile and urobilin in the urine.
16. Jaundice.

SUMMARY OF SYMPTOMS. Second Illness.

1. Feeling of sore throat with little to see on examination.
2. Vertigo.
3. Frontal headache.
4. Epistaxis.
5. Chilliness.
6. Conjunctivitis.
7. Sharp rise in temperature and pulse rate (101.5°F. 116 per minute).
8. Lack of complaint by an obviously ill patient
9. Lack of appreciation of severity of the illness by intelligent parents.
10. Headache aggravated by standing.
11. Repetion of epistaxis.
12. Painful stiffness above patellae.
13. Lack of physical (abnormal) signs in the presence of a temperature of 103°F.
14. Pulse now however only 100 per minute.
15. Apparent initial response to Sulphapyridine.
16. Pale face with red daubed cheeks.
17. Pulse became 120 per minute with temperature only 101°F. (cf 7, 13, and 14).
18. Vomiting again.
19. Very slow convalescence.
20. I am convinced that now, 17 March, 1945, she 'is not the girl she was.'

BRIAN ROBINSON 6 years. Case 6

10 Hesledon Terrace.

Attending Cold Hesledon School. Class Room 5.

Visited

Monday, 14 August, 1944.

Yesterday he complained of a heavy frontal headache -- he vomited frequently, and he suffered from a dull aching pain inthe region of the umbilicus and above it. He shows some degree of bronchial spasm --- he is subject to occasional mild attacks of bronchial spasm. The stools are 'almost white'.

The urine contains bile.

He was markedly jaundiced on the 15 August.

Recovery was uneventful and fairly speedy.

SECOND ILLNESS.

Tuesday, 19 Deeember, 1944.

He vomited frequently all yesterday and last night. He complains mainly of photophobia and he has a headache. The bowels have not acted for 48 hours. He does not mind being examined, nor is he interested (as he usually is) in his examination. He appears entirely disinterested and obviously just wants to lie and be left alone. The temperature to my surprise is 103.5 and the pulse 120. He makes very little complaint, saying that he just "does not feel well." He has a slight cough which is not troubling him and there is evidence of only a slight

generalised bronchitis.

Wednesday, 20 December, 1944.

He has severe frontal headache. A little sputum is being expectorated; it is mucous and it is streaked with 'threads' of bright red blood. Photophobia is marked. Absolutely nothing abnormal on examination of urine, ears, abdomen or chest.

Temperature 101.5. Pulse 108.

The temperature remained normal until Saturday.

He continued to have no desire for food and remained listless and apathetic. He continued to say that he did not feel well.

Saturday, 23 December, 1944.

The temperature is 98.2° F., and the pulse 66.

He began to eat, and thereafter he improved steadily.

CATHERINE ROBINSON. Case 7

10 Hesledon Terrace.

Attending Cold Hesledon School. Class Room 4.

She was not attended. The history is to be relied upon.

Tuesday, 15 August, 1944.

She felt very sickly and told her teacher so. She vomited before she reached the lavatory.

For 3 or 4 days prior to this she had been very listless, and as expressively stated locally, she had looked "washy"[x], and her mother had given her a purgative on the 13 August as she thought Catherine looked 'bilious'.

When I examined her on Wednesday, 16 August, she said that she felt quite better.

She continued at school.

x. A local term denoting listlessness and limpness.

DOUGLAS ROBINSON. 9 years. Case 8.

10 Hesledon Terrace.

Attending Cold Hesledon School. Class Room 4.

School attendances.

On referring to the register I find that he was absent on the forenoon of Monday, 10 July, 1944. He returned in the afternoon and attended on 11 July, 1944. He was absent again on the 12th, 13th, and 14th July, 1944, thereafter attending regularly.

.....

His mother, who is an intelligent and reliable witness states that on the above dates (confirmed as above) Douglas had an illness which was similar in every respect to that of Brenda and Brian. The urine and the stools were remarked on when Douglas was ill and that was why she decided to send for me for the illnesses of the other two children without trying 'domestic' treatment first.

He had 'stomach pain' which made him weep. He vomited, had a headache and felt giddy. He 'sat about' after school hours, was markedly listless, and 'couldn't be bothered with anything', refusing to go out to play.

WILLIAM COLLINGS. 4 7/12 years. Case 9

28 Hesledon Terrace, Cold Hesledon.

He does not attend school.

Visited

Monday, 14 August, 1944.

History:-- On Thursday, 3 August, 1944, he suffered from diarrhoea and he vomited several times. He had very little pain which was a little accentuated prior to each action of the bowel. He was thirsty. He spent half of the day saying "Oh, I want to be sick, oh, I want to go to the lavatory!" The vomiting was precipitate. Later he slept for two hours and was apparently quite better.

Nothing abnormal was noted until Saturday 12 August, 1944, when exactly the same symptoms occurred, with the same history of recovery after sleep, and in the evening he was well enough to go for a walk. (cf. biphasic illness with e.g. Elizabetn Jackson).

But that night he slept little, being restless, and coughing. He is inclined to have attacks of bronchitis occasionally, and his mother says that he was "chesty".

On Sunday, 13 August, 1944, he lay about all day, languid, listless, and obviously out of sorts. He had no appetite. He would fancy certain foods, but when they were given to him he toyed with them and then pushed them aside.

To-day, Monday, 14 August, 1944, he vomited several times. His diet to-day has been a spoonful of rice. He looks sleepy, languid, weary and apathetic. He is sitting limply in his chair as if he can scarcely support his head. During the 20 minutes visit his features never altered. The complexion is dull and pale: the eyelids droop and he looks as if he had been kept awake for 48 hours.

The faeces are very pale. The bowel action has been undisturbed, and the motion is of normal consistency.

The urine is acid. The specific gravity is 1018. There is no bile, no sugar, no albumin: and it is normal on microscopic examination.

When shaken the urinary froth is not white but a creamy brown tint.

Urobilinogen is present in marked amount.

His subsequent recovery is that of an uneventful recovery.

Unfortunately I was not then conversant with the white cell count in infective Hepatitis.

I obtained supplies of Histamin too late for an intradermal test.

Subsequent history.

On the night of 5 and 6 September, 1944, he vomited several times and suffered from diarrhoea.

He recovered rapidly and uneventfully.

TOM WALSHAW. Age 53 years. Case 10

3 Hesledon Terrace, Cold Hesledon.

COLLIERY FITTER. (Underground).

Visit.

Wednesday 6 September, 1944.

His wife said that her husband had eaten very little on Tuesday, 5 September, 1944. At teatime he flatly refused to try to eat anything, and he retired early to bed, (9.30 pm), intending to rise at 3.30 a.m. to go to work. He was too poorly to get out of bed, and at 7 a.m. he awoke his wife and complained of pain in the shoulders, elbows and knees. He seemed feverish, but he said he felt 'chilly' inside. He complained of headache.

However, when I saw Walshaw upstairs, he said it was 'just a bit of cold', to give him his certificate of incapacity and not trouble to call again. He made light of his illness, mentioning only a headache and generalised aches. The temperature was 99.5 ^{o} F, the pulse rate 90 per minute, and I accepted his diagnosis.

I did not call on Thursday, 7 September, 1944.

Friday, 8 September, 1944.

He was much worse.

I append the history as given, first by his wife, who says that he has had two very disturbed nights. Last night, or rather this morning, she awoke at 6.45 a.m. to find that

Walshaw was not in bed. She found him muddled and confused, with no idea where he was, downstairs 'having a drink of water' behind the blackout curtains, where, of course, there was no water. She coaxed him back to bed. He had complained of epigastric pain on Tuesday, Wednesday, and Thursday, and although the bowels had acted regularly, as is his habit, she gave him a saline purgative at 8 a.m. When he had a watery motion he soiled the bedlinen.

He became very muddled at intervals. Whilst talking to Mr Collings, father of William Collings referred to, his voice 'trailed away' into an incoherent mumble, and he fell asleep.

Shortly he awoke, spoke clearly and sensibly for a little, and then talked at random before again falling asleep.

Tom Walshaw gives his own history as follows: it is practically verbatim, and the wording is his. "He felt off colour on Monday, as if he had a severe loss of strength. He had pain in the pit of the stamach and on both sides round the lower ribs. He had a headache just above the eyes --- he points to the lateral aspect of the forehead just above the lateral half of the eyebrows. He had a 'job to keep warm' on Tuesday night. The alarm clock awoke him at 3.30 a.m. on Wednesday, 6 September, 1944. He felt weak and listless and "all in." More worrying, he

felt muddled and dazed just like a drunken man, and he could not imagine where the electric light switch was. He had severe pains around his shoulders, knees and elbows. He could drink water but everything else made him feel very sick.

He says that to-day he feels terribly drowsy and can't keep alert or awake. He tried to read the newspaper but the words became indistinct and danced about. He dozed off to sleep. Later, when reminded, he could not recollect that he had seen the paper. Still later he remembered what had happened.

He has a supraorbital headache. His chest feels "tight and sore."

Visit a.m. Pulse 84 Temperature 99.2°F.

p.m. Pulse 90 Temperature 101.2°F. The tongue is very dry.

The urine is acid and deep orange in colour.

There is no bile.

Moderate Urobilinogen Reaction.

A trace of albumin.

Saturday, 9 September, 1944.

He is obviously more seriously ill. The facies is ominous. The eyes look dull and resemble those of a person recently dead. He has thus a 'vacant' look. He converses intelligently and alertly for a minute of two, then falls asleep only to awaken with a start and an

apology. "How rude, doctor, letting you down like that when you are trying to help me! I hope you do not think I am lead-swinging." His head and his extremities give frequent involuntary jerks. The tongue is dry and coated--a yellow brown coating almost crusted in spite of attention.

In the morning the temperature is 99°F., and the pulse 90 per minute. The breathing is easy at 22 per minute. He complains of pain in the left subcostal region. He is not tender there but he is acutely tender in the right subcostal region, where the liver is palpable.

The urine contains no albumin to-day, there is a marked positive reaction to Schlesinger's Urobilin Test, there is no bile. He coughs a little and produces a little thick yellowish sputum.

There is a slightly impaired note at the left base and I think some consolidation as evidenced by a suspicion of increased vocal fremitus and tubular breathing. Examination was difficult, and had to be rapid to avoid upsetting the very sick patient.

At 4 p.m. the temperature was 100, and when I visited him again at 11 p.m. the temperature was 99°F, the pulse 90 per minute, and he was breathing with no noticeable difficulty.

Abdominal distension was now a feature and he had retention of urine, with a full bladder.

Sunday, 10 September, 1944.

He says he "does not care if he dies." He is dying. In spite of an extension of the dulness on percussion of his chest his breathing is not rapid or embarrassed. The legs are not being moved and although he retains a little sensation in them, they are almost completely paralysed. I could obtain no knee jerk, no ankle jerk, and the feeblest response to Babinski's test --- the big toe did not move and the others only a trifle. He took a little rice to-day --- nothing else. The eyes are almost closed. The head is tremulous, as are the arms where the movements verge on being athetoid.

Most of the time he is delirious --- a low muttering delirium with moaning and groaning. For a brief interval he becomes lucid; but the lucid intervals are becoming more infrequent and of shorter duration. The temperature is 99.4°F., the pulse 98 per minute.

In the evening the temperature was 100°F., the pulse 100 per minute.

He is said to have had a terminal black vomit which however was not retained for my inspection.

Report by Dr. Cookson. Pathologist, Sunderland Royal Infirmary.

Blood Culture. Sterile after 5 days.

Cold Agglutinins. The blood contains cold agglutinins.

White Cell Count. Total 15,000.

Polymorph.Leucocytes	86%
Lymphocytes	11%
Monocytes	3%

Sputum. (Very little and difficult to handle).

Obtained by tickling the throat, during patient's delirium.

Not rusty. No blood.

Type II Pneumococcus. Direct method.

Cerebrospinal Fluid.

Clear fluid with a minute clot.

Faint globulin ring.

Protein. 55 mgm.

Sugar. Unfortunately not estimated exactly but said "not to have been below normal."

Chlorides. .65

Cells. 35 per c.mm.

The cells are chiefly lymphocytes with large mononuclear cells and endothelial cells.

No polymorphs. seen at all.

Urine. Febrile Type.

Albumin present in very small amount.

Urates ∓

A few red blood cells.

Numerous granular hyaline casts and an occasional epithelial cast.

Urea (for what it is worth) .3 %

Pathologist suggests:

Encephalomyelitis: Atypical Pneumonia.

It should be noted that Dr. Cookson[x] visited Walshaw, and discussed his illness with me.

x. Cookson H. A. Hon. Pathologist. Sunderland Royal Infirmary.

JENNIE TURNER, Age 10 years. Case 11

6 Dunelm Terrace, Dalton le Dale.

Attends Cold Hesledon School.

History.

She was sick in school and complained of 'stomach' pains on Monday, 11 September, 1944 (the day when 6 other children 'fell' absent as related on Page 184).

She was absent from school on Tuesday, 12 September, 1944, but returned next day.

On Wednesday, 27 September, 1944, she was again absent from school. She felt sick and she ate nothing --- she felt sick at "the sight or the thought of food."

Again she attended school on the Thursday and Friday, 28th and 29th of September, 1944, but next day she felt, as she puts it, "all out of it", and her mother says that she had "a pale drawn look about the face." The father states that then "she looked awful. She looked helpless. Her eyes looked heavy, and she had dark rings under them. She looked as if she was exhausted and had not a spark of energy."

She went to bed early as she felt so tired and exhausted, but she had a very restless night. She 'tossed and turned' all night, and her parents thought that she was feverish. She got out of bed on the Sunday, 1 October, 1944, and was seen to be red and swollen -- puffy -- above and round her eyes. She lay about 'helpless' on the couch all day, refused

all food and complained that her throat was sore. The mother gave a laxative -- Castor Oil -- the result was the 'normal'.

Monday, 2 October, 1944. Visited.

The facies was striking. Expressionless except for an appearance of the most extreme fatigue, apathy and weariness. The eyes were not jaundiced but they had a flat, dull look, and the conjunctivae looked dirty. The 'posture' was in keeping with the facies -- limp and relaxed. The temperature was 98°F: the pulse 90 per minute. There was a small herpetic patch on the upper lip.

Tuesday, 3 October, 1944.

Morning: Pulse 100. Temperature 99° F.

Night : Pulse 120. Temperature 99.4 ° F.

Urticarial rash (erythema multiforme) marked on trunk, especially posteriorly. Moderate conjunctival injection.

Her breath was particularly offensive and could be noticed at 2 yards range. The tongue was moist and clean. She looked really very ill.

She was very tender over the liver which was just palpable on deep inspiration and she was likewise tender on palpation under the left subcostal region but the spleen was not palpable.

She complains of a sore throat but there is nothing to account for it on inspection, and there is no cervical glandular swelling or tenderness. She is only 'slightly

giddy' when she is lying down, but this is at once greatly aggravated if she sits up.

Wednesday, 4 October, 1944.

Pulse 96 per minute. Temperature 100.5°F.

She had a very restless night, tossing and turning and asking for (and drinking) water freely.

The itching of the skin rash is easing.

The facies of the child is made the more striking if one manages to elicit a hard-won smile. The urine to-day is much darker -- the urinary foam is coloured a very slight pink brown and it shows a definite green fluorescence on Schlesinger's test and a weaker but definite positive Bogomolow's test reaction.

Thursday, 5 October, 1944.

Pulse 96 per minute. Temperature 98.0°F.

She has had a good night's rest and she has improved markedly. The facies is much brighter. The herpes aborted, on the upper lip, and is rapidly subsiding -- it was a very small lesion.

Thereafter convalescence was steady but weakness and the appearance of extreme weakness were slow to clear up.

Jennie Turner (continued).

A. Blood Film 8 October, 1944.

Neutro. Polymorphs	21
Eosino. Polymorphs.	1
Small Lymphocytes	72
Monocytes.	6

B. White Cell Count. 8 October, 1944.

4,200 per c. mm.

C. No abnormality in red cells.

Monday, 30 October, 1944. Visit.

She is again ill. For the past week she has had a very poor appetite. She has cried on the slightest provocation ---"if spoken to."

People again remarked how poorly she looked.

She has herpetic lesions on her lips and looks pale and weary again. She has a troublesome cough and a mild bronchitis.

She gradually recovered her normal health.

LILIAN ANDERSON. Age 13 years. Case 12.
4 St. Cuthbert's Terrace, Dalton le Dale.
Attending Cold Hesledon School.

On Tuesday, 3 October, 1944, the headmaster reported to me that Lilian Anderson had been sickly and had vomited on 2 or 3 occasions recently. She attended school on 3 October, 1944, and I visited her.

Tuesday, 3 October, 1944. 9 p.m. Inquiry visit.

History. On Thursday, 21 September, 1944, she was ill in school. She felt sick and was allowed out but she did not vomit. She remained at home in the afternoon and by 5 p.m. she felt better and had a little tea. She attended school on Friday, 22nd, and remained well on Saturday and Sunday.

On Monday, 25 September, 1944, on rising to go to school she was again ill--- she felt sick and then vomited repeatedly all forenoon. But she recovered to attend school on Tuesday, Wednesday, and Thursday.

On Friday, 29 September, 1944, she was again at home, ill. She again vomited frequently on rising and on this occasion she had pain across the epigastrium and on both sides at the lower rib level.

To-night, Tuesday, 3 October, 1944, she felt perfectly well. Her eyes looked dull, which may have been due to the lateness of the evening. She told me, however, that she had had diarrhoea at 5 a.m. to-day, 4 loose, almost watery

stools, within two hours.

Thursday, 5 November, 1944. Visit (I was this time 'called in').

The diarrhoea of 3rd October, 1944, has been repeated on 4th and 5th October, but occurred only during the night. It is profuse and watery -- "just like a tap." The odour was not very offensive, I am told.

She has the upper abdominal pain, as before.

She had a frontal headache, and she feels very tired and listless. The tongue is clean. The conjunctival vessels are definitely but only slightly injected. The temperature is 98.2 ^{o} F. The pulse is 120 per minute.

Recovery was rapid and complete. In 48 hours she felt quite well.

Blood Test. Differential White Cell Count.

Neutro. Polymorphs.	34 %
Eosino. Polymorphs.	5 %
Large Lymphocytes.	7 %
Small Lymphocytes.	50 %
Monocytes.	4 %

DOREEN MARY ARMSTRONG. Age 11 years. Case 13.

4 Dunelm Terrace, Dalton le Dale.

Attending Cold Hesledon School.

FIRST ILLNESS.

Friday, 6 October, 1944.

History: She had a frontal headache in school on Tuesday. On Wednesday, 4/10/44, she states: "My stomach went wrong. I did not feel very well. I couldn't eat anything. I felt 'all egg shells.' "

She had aching across the abdomen at the umbilical level. She was given a saline and it acted normally. On Thursday her condition remained the same, but she felt repeatedly that she was going to vomit.

To-day, Friday, 6 October, 1944, I visited her .

She looks very pale, much paler than usual, and her eyes are heavy. But she has eaten a little to-day. She has played outside a little but is evidently soon exhausted as she soon returns to lie down. She says "she does not like to play too much as it brings on the pain" at the umbilicus. The temperature and pulse were undisturbed and she made a steady and fairly rapid apparently full recovery.

.....

SECOND ILLNESS.

I was recalled to see her on

Monday, 30 October, 1944.

History. She had been well until Thursday, 26/10/1944,

when she developed a 'head cold', sneezing and coughing, and her nostrils became excoriated with the watery nasal discharge. She has felt chilly at times ever since and she has had

1. "Pins and needles" in her fingers.
2. Little pains keep darting or shooting to her finger tips.
3. Aching and stiffness and a feeling of weakness in the proximal part of her thighs anterolaterally.
4. Bitemporal headache.

She has a tongue like the Scarlet Fever strawberry tongue but the 'fur' is much less marked and salivation is very free.

Pulse 108 per minute. Temperature 101 ^{o} F.

Recovery was gradual and steady. The temperature settled in 5 days.

Differential White Cell Count. 30 October, 1944.

Polymorph Leuc.	37
Eosino. Leuc.	2.5
Lymphocytes	57.5
Monocytes.	3

LILIAN PURVIS, Age 13 years. Case 14.
5 St. Andrew's Terrace, Dalton le Dale.
Attending Seaham Intermediate School.

Tuesday, 24 October, 1944. Visited.

History. On Sunday, 22 October, 1944, she felt dizzy (at tea time) and she felt that she was going to vomit. She tried to vomit but she was not sick until some 2 hours later when she vomited urgently. Since then she has felt intensely nauseated and she has vomited frequently. If she lies still she does not feel so sickly but immediately she raises her head from the pillow she feels giddy and she vomits. It is not an effortless vomiting --far from it.

On the occasions when she feels more sickly she has an exacerbation of the dull frontal headache, which she says she has all the time, but which she describes as being not really very bad; and right-sided only. She is said to have been delirious during the past two nights.

On examination, she looks strikingly tired and 'helpless', and the facies is typical. The breath is particularly foul resembling a B. Coli odour. She is not at all tender over the epigastrium or anywhere else in the abdomen.

There is a slight trace of albumin in the urine, which contains a particularly large amount of Urobilin.

The pulse is 90 per minute.The temperature is not elevated.

Differential White Cell Count.

Neutro. Polymorphs	50
Eosino. Polymorphs.	2
Lymphocytes	46
Monocytes.	2

She continued to vomit on Wednesday and Thursday. Thereafter she continued to have no desire for food, felt lazy and was intensely giddy if she got out of bed e.g. for micturition or defaecation.

Tuesday, 31 October, 1944.

She had extensive herpes labialis. She was now improving, but went pale and felt giddy and sickly if she tried to stand.

Thereafter she gradually improved but remained very weak for several days longer.

Robert McCabe. Age 44 years. Case 15.
5 St. Andrew's Terrace, Dalton le Dale.
Coal Miner.

On Sunday, 29 October,1944, his head felt slightly "swimmy" and this sensation recurred at intervals until Tuesday, 31/10/1944, when he felt intensely giddy and vomited twice, very suddenly. He went to bed as he felt so weak and tired. During the night he sweated heavily.

Wednesday, 1 November, 1944. Visited.

His appearance to-day is striking. He looks pale,drawn and worn-out: the face is pinched and the eyes look dull. He says he feels exhausted and he certainly looks it.

White Blood Cell Count.

Polymorph. Leuc.	55.5
Eosinophil Leuc.	1
Lymphocytes	39.5
Monocytes	4.

Saturday, 4 November, 1944. Improved but looks weak and feels weak. The tongue is coated but the edge is raw. Anorexia is marked.

Tuesday, 7 November, 1944. Little change. His main complaint is of insomnia.

He resumed work,obviously far from well,on 15/11/1944.

? Relapse.

Monday, 20 November,1944. He worked three days. Again he is very giddy and weak, and has complete loss of appetite. Now complains of low back ache and pains in front of the knees and above. Recovery was slow.

Mrs. Agnes McCabe. Age 36 years Case 16.

5 St. Andrew's Terrace, Dalton le Dale.

25 October, 1944. Visited.

For the past 10 days she has repeatedly felt that she was going to be sick. She has felt very giddy and at times "everything seemed to be going round." She now feels tired, listless and irritable, and her legs and arms feel heavy. The urobilin tests are very strongly positive. There is a trace of albumin in the urine (not a catheter specimen). The blood pressure readings are normal.

Differential White Cell Count.

Polymorph Leucocytes	82.
Lymphocytes.	16
Eosinophil.	2

A week later she complained of extreme fatigue. In another 10 days she was back to her normal health.

It should be noted that she was five months advanced in her pregnancy.

George Purvis. Age 9 years. Case 17

5 St. Andrew's Terrace, Dalton le Dale.

Monday, 30 October, 1944.

Yesterday he would not go out of doors. He was listless. To-day he got out of bed and was immediately giddy, and intensely nauseated. He suffered from bitemporal headache. Later he vomited urgently and frequently. (At night he was delirious).

He was very tender over the epigastrium where he had a constant dull pain which became worse if he tried to sit up. The facies was exactly like his father's. Thereafter his illness presented no striking features. There was the usual anorexia lasting for 5 or 6 days and extreme weakness marked his convalescence.

Cyril Ellis. Age 21 years. Case 18.

5 St. Andrew's Terrace, Dalton le Dale.

Coal miner. I have underlined this to avoid confusion, as the other patients were schoolchildren.

Friday, 13 October, 1944.

History. When he arose yesterday he vomited. Since then he has lost all desire for food. He feels extremely giddy and he feels that "he wants to vomit but he can't." He looks 'sleepy', the tongue is clean and moist, and the temperature and pulse show no abnormality. He complains that he feels very tired and "just can't be bothered with anything."

I rather doubted his story for various reasons and made the following tests.

Differential White Cell Count.

Polymorph Leucocytes	40
Eosinophil Leucocytes	2
Lymphocytes	48
Monocytes.	10.

He improved gradually with slight return of appetite, decreasing and less frequent attacks of nausea and less marked lethargy until 19 October, 1944, when he felt more sickly and generally out of sorts an on 20 October, 1944 he vomited twice. By 4 November, 1944 he felt sufficiently recovered to resume

work.

He had obviously lost weight.

.....

Saturday, 16 November, 1944. Consultation.

He complains of pain above the left scapula extending into the neck. His left arm felt powerless if he attempted to raise it. He attributed the loss of power to the pain mentioned.

David Turner. Age 54 years. **Case 19.**

6 Dunelm Terrace, Dalton le Dale.

He is the father of Jennie Turner (q.v.)

Wednesday, 1 November, 1944. Consultation.

Verbatim history.

"Last Wednesday, 25 October, 1944, I felt sickly, weak and useless. I had a head cold, my nose watered and I was sneezing a lot.

Since then I have been useless. I work a little and then I have to rest quite a long time. If I try to do any more work the same thing happens again. I can't understand it because I am eating quite well".....

"On Monday, (30/10/44) my eyes went queer --- everything seemed indistinct and muddled and misty --- I thought I must be going squint eyed. My head went funny as if it was full of water when I moved it."

"I have been having heavy sweats, and I am always cold and clammy with them."

.....

He presented an appearance in keeping with his symptoms--- he looked weak, and had a tired and confused appearance exactly comparable to someone who has been awakended, unwillingly, from a deep sleep. The eyes looked heavy lidded. He admitted to no abdominal pain and he had no gastro-intestinal symptoms whatever. The tongue was clean. The temperature and pulse were normal -- pulse 72 per minute.

John Miller. Age 6 years. Case 20

8 St. Andrew's Terrace, Dalton le Dale.

Attending Cold Hesledon School.

Wednesday, 8 November, 1944. Visited.

History. On Monday he complained of headache, the pain being present in the forehead and suboccipitally. He felt very giddy and he was listless and just 'lay about' all day. On the night of 5th-6th November, he lay awake all night, complaining of pain in the abdomen and of feeling sick.

To-day, Wednesday, 8/11/44, he is lying in bed, the picture of lethargy and 'lifelessness'. He has no desire for food which he immediately refuses if it is offered, or suggested. The breath is foul and he is conscious of the bad odour. The tongue is clean in front but has a slight white-yellowish fur posteriorly. Bowel action is regular. No pulse or temperature disturbance.

Friday, 10 November, 1944.

To see a 6 years old normally mischievous boy lying so quite and utterly listless is striking. I can not get a word of complaint from him, but he is obviously more ill. He just says wearily that he is "not well." The tongue is peeling anteriorly, the edge and tip are raw and in places slightly ulcerated -- clean base -- as if peeling had gone 'too deep.'

John Miller (continued).

Pulse 108 per minute. Temperature 100°F.

Saturday, 12 November, 1944.

Still listless and apathetic. Thick yellow coating of tongue centrally and posteriorly. The edge and tip are like raw beef. He is eating a very little.

Temperature 99.4°F.

Recovery was gradual, weakness and loss of weight were striking features.

Anne Miller. Age 54 years. Case 21

8 St. Andrew's Terrace, Dalton le Dale.

She is the mother of John Miller (last case) and Anne Miller (next case).

On Sunday, 12 November, 1944 she had little appetite for her dinner and afterwards she felt sickly and wanted to go to sleep. She could not combat this drowsiness and she had to go to bed with her sick son.

Monday, 13 November, 1944. Visited.

She has a headache affecting the occiput and the nape of the neck. Although she frequently suffers from headache, this headache is usually situated on the vertex.

Her appetite has failed completely, in fact, she "can not look at food." She has a feeling that she wants to belch flatus. When she did try to eat, the food "seemed to stick in her throat and she could not get it down."

The taste in her mouth was horrible and like that of a bad egg. She is extremely giddy and dare not lift her head from the pillow. At times she feels heated and at times chilly. She looks dull and apathetic and sickly, and her eyes are bloodshot and dull.

The bowel action is undisturbed.

Temperature is 100 ^{o} F. The pulse is 84 per minute.

I was unable to visit her daily.

Thursday, 16 Nov. 1944. Until to-day she has continued to feel sickly and wanted to vomit, but she could not be sick.

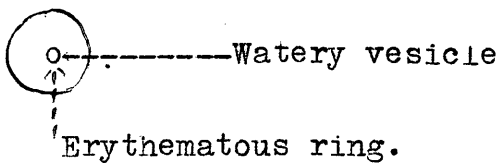
To-day her temperature is normal and she feels much better.

Saturday, 18 November, 1944.

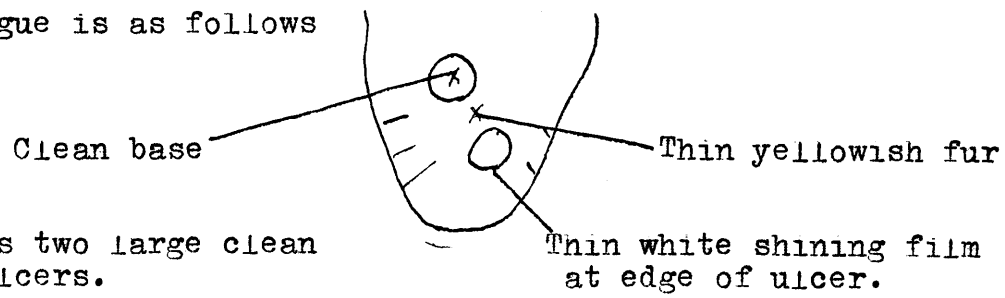
She is much worse to-day. She feels exhausted and depressed and very ill, and that is how she appears. The breath is foul and she is painfully aware of it.

Temperature 102°F. Pulse 120 per minute.

She has a rash on the face. There are only 5 lesions and they are distributed: 2 on the forehead, 1 on the side of the nose, 2 on the chin.

They are this size 

I presume they represent an urticaria verging on vesicle formation.

The tongue is as follows 

it shows two large clean based ulcers.

Monday, 20 November, 1944.

Temperature 102°F. Pulse 100 per minute.

Respirations 28 per minute.

Suboccipital headache.

Vomiting all solids but retaining all drinks.

She has a short cough: it seems rather restrained.

The urine contains no bile or urobilin.

She is very tender over the right subcostal region. There are a few râles in the chest and a suspicion of more than the normal dulness over the right lower lobe.

Tuesday, 21 November, 1944.

Temperature 101.5°F. Pulse 132 per minute.

Respirations 52.

Diarrhoea occurred to-day -- 3 loose stools in the morning. This was so urgent and she felt so weak that she soiled the bedlinen. Suboccipital headache is severe. She is sleepless. The cough is troublesome, especially at night.

Thursday, 23 November, 1944.

Diarrhoea continues: it is profuse and watery. She now vomits everything, even a teaspoonful of water, and she has marked discomfort in the epigastrium and continues to belch wind (aerophagy).

On Friday, 24 November, 1944, the temperature returned to normal. The pulse was 100 per minute. She is sleepless.

Monday, 27 November, 1944. Marked urobilinuria.

Convalescence was slow. At no time were the physical signs typical of a lobar pneumonia. I am aware that this does, often, occur in ~~the~~ lobar pneumonia, but the absence of such signs persisted throughout the illness and convalescence.

The picture was dominated by the non-pulmonary symptoms.

Anne Miller. Age 8 years. Case 22

8 St. Andrew's Terrace, Dalton le Dale.

Attending Cold Hesledon School.

Wednesday, 29 Nov, 1944.

History. On Sunday, 26 November, 1944, she was listless to a degree and just sat in the chair all day. She would do nothing, not even talk, unless forced to answer. She ate an orange and nothing else all day.

Next day she went to school. On returning home she sat in the chair until 5.30 pm., and then went to bed.

Thursday, 28/11/44, she felt so tired that she lay forward on the desk as she felt too tired and weak to sit properly. The teacher sent her home saying that she was annoyed at Anne coming to school "in that condition."

When she came home she ate no dinner and later she began to complain of epigastric pain. She vomited twice or thrice through the night.

She now complains of epigastric pain. The cheeks are flushed. The pulse is 108 per minute. Temperature is normal. She is said to have had a 'dry' cough for 2 or 3 weeks.

Now she presents the appearance which I have already described and shall here omit.

She can not be bothered with anything and lies quite apathetically passive and disinterested in my examination and questions! She resents pressure over the epigastrium and the right subcostal region.

She complained of frontal headache and of feeling "dizzy."

Anorexia continued for 4 or 5 days: therefater she recovered gradually.

Grace Mary Thynne. Age 12 years. Case 23
6 St. Andrew's Terrace, Dalton le Dale.
Attends Cold Hesledon School.

Monday, 27 Nov. 1944.

History:-- On Saturday, 25/11/44, shecomplained of peri-umbilical pain. Since then there has been complete anorexia. Frontal headache has been complained of, and she says that her head feels 'thick' and muddled. If she tries to stand she has to grasp rapidly at anything handy for support as she is quite unable to balance owing to vertigo. Even raising her head leads to immediate giddiness. The eyes are bloodshot and she says that she can not see distinctly or clearly. Everything seems misty and when she shifts her gaze she has to look at the 'new' object for quite a time before it is at all well defined.

She is very tender over the epigastrium, where pressure leads to immediate nausea.

The temperature is normal. The pulse is 90 per minute.

The facies was typical. She lay in bed as if she was quite incapable of making anything but the slightest movement --- not only incapable of the physical effort but apparently too apathetic to make thementa1 effort required.

Her condition varied little for 5 or 6 days when she began to eat a little. Thereafter gradual and uneventful recovery occurred.

It should be remarked that ophthalmoscopic examination revealed no local cause for the visual disturbance.

Sheena Harrald. Age 3 years. Case 24
1 Dunelm Terrace, Dalton le Dale.

Monday, 27 Nov. 1944. Visited.

She has had a restless night and now she just wants to lie on the couch or to be nursed. She is quite 'lifeless' and limp and her head lolls against her mother's shoulder as she is obviously unable to hold it erect. She is not interested in anything or anyone. The face bears an expression of extreme fatigue and 'helplessness.' She complains of a frontal headache and says that "her tummy hurts", pointing to the epigastrium. She refuses all food as if she is upset at the sight of it. She is drinking water freely. The temperature is 99.5 ^{o} F.

Wednesday, 29 Nov. 1944.

She has a troublesome cough and there is evidence of bronchitis: there is a slight expiratory wheeze. She is afraid because "she is falling." Lassitude is grossly marked and quite disproportionate to the respiratory disturbance. The breathing is not rapid. Temperature 99.4^{o}F.

Friday, 1 Dec., 1944. Her nose bled twice yesterday. The slight bronchitis and respiratory 'wheeze' are clearing. But the appearance of the child is quite unlike anything that I have encountered outwith this epidemic. She seems too tired to alter her expression and there was not a vestige of a change of expression during my visit. The eyes look dull, the upper eyelids seem to be too heavy to be kept

open. She appears to be depressed as well as lethargic, as I can not amuse her, or interest her, by any subterfuge.

The condition was quite unlike the illnesses which we frequently encounter in our practice here, where a temporary bronchial spasm is associated with acute gastro-intestinal symptoms: the condition occurring in young children.

In addition to the above symptoms she co
of a low backache.

She speaks in a 'forced whisper' and says
[illegible] been weak for 14 days. However she
[illegible] hysterical) aphonia in her manner. It
is dyspnoeic and has stridor.

On laryngoscopy the condition is seen to
[illegible] bilateral paralysis.

Her cough and insomnia began to improve
[illegible] Her improvement was steady.

Wilhelmina Harrald. Age 27 years. Case 25.
1 Dunelm Terrace, Dalton le Dale.

She is the mother of Sheena Harrald (the preceding case)

Friday, 29 December, 1944. Consultation.

She complains that she is listless, completely lacking in energy, and that she finds her housework a great trouble. She feels drowsy all day and her one desire is to sleep. But she can not sleep at night. She feels as if she is dull mentally and incapable of clear thinking. This sensation is referred to the frontal area where she has a dull heavy headache.

In addition to the above symptoms she complains of a low backache.

She speaks in a 'forced whisper' and says that her voice has been weak for 14 days. However she had a similar (? hysterical) aphasia in the summer. There is no dyspnoea and no stridor.

On laryngoscopy the condition is seen to be a bilateral adductor paralysis.

The lethargy and insomnia began to improve in about a week, whence improvement was steady.

DISCUSSION OF THE SYMPTOMATOLOGY.

Discussion of the Symptomatology.

AT this stage an enumeration and consideration of the symptoms, so far encountered, may serve to give a picture or impression of the epidemic in the small area of Cold Kesledon and Dalton le Dale.

The majority of the patients were children attending the local school. I found no reason to suspect that any of the illnesses had originated from an 'outside' source and believed that the outbreak represented a series of relays of the original infection.

If that was a correct assumption a study of the symptomatology might yield information regarding the effect of 'passage' on the infecting agent.

The cases so far encountered fall obviously into 2 groups; those in which jaundice occurred, and those in which it did not occur.

Relapses occurred in both groups.

Two of the jaundiced children had well-defined illnesses which I would not classify as relapses, but which were apparently related to the jaundice illness, and I propose to call them "2nd. illnesses."

One of the non jaundiced children similarly had a 2nd illness.

Relapses especially in the jaundiced group presented

TABLE 2.

	Group 1	2	3	4
	Brown	Branthwaite A.	Branthwaite L.	Jackson E.
Headache	+	+	+	+
Vomiting	+	+	+	+
Nausea	+	+	+	+
Anorexia	+	+	+	+
Vertigo	+	+	+	+
Abdominal Pain	+	+	+	+
Diarrhoea	+	+	+	+
Lethargy	+	+	+	+
Pains in Limbs	+	+	+	+
Paresthesia	+	+	+	+
Bronchitis	+	+	?	+
Atypical Pneu'ia				
Conjunctivitis	+	+	+	+
Hoistaxis	+	+	+	+
Feeling of chill	+	+	+	+
Dysphagia	+	+	+	+
Rhinorrhoea	+		+	+
Visual Disturb.			+	+
Bimnasic Illness	+	+	+	+
Typical Facies	+	+	+	+
Temperature	+	+	+	+
Urobilinuria	+	+	+	+
Rel. Lymphocytosis.	JAUNDICED 2nd Illness ↗	NON JAUNDICED 2nd Illness		

HISTORY ONLY

	Group 1	2	3	4
	Robinson Brenda	Robinson Brian	Robinson Brenda	Robinson Brian
Headache	+	+	+	+
Vomiting	+	+	+	+
Nausea	+	+	+	+
Anorexia	+	+	+	+
Vertigo	+	+	+	+
Abdominal Pain	+	+	+	+
Diarrhoea	+	+	+	+
Lethargy	+	+	+	+
Pains in Limbs	+	+	+	+
Paresthesia	+	+	+	+
Bronchitis	+	+	+	+
Atypical Pneu'ia				
Conjunctivitis	+	+	+	+
Hoistaxis	+	+	+	+
Feeling of chill	+	+	+	+
Dysphagia	+	+	+	+
Rhinorrhoea	+	+	+	+
Visual Disturb.	+	+	+	+
Bimnasic Illness	+	+	+	+
Typical Facies	+	+	+	+
Temperature	+	+	+	+
Urobilinuria	+	+	+	+
Rel. Lymphocytosis.	NON JAUNDICED 2nd Illness			

	Group 1	2	3	4
	Robinson Cath.	Robinson Douglas	Collings William	Turner, J.
Headache	+	+	+	+
Vomiting	+	+	+	+
Nausea	+	+	+	+
Anorexia	+	+	+	+
Vertigo	+	+	+	+
Abdominal Pain	+	+	+	+
Diarrhoea	+	+	+	+
Lethargy	+	+	+	+
Pains in Limbs	+	+	+	+
Paresthesia	+	+	+	+
Bronchitis	+	+	+	+
Atypical Pneu'ia				
Conjunctivitis	+	+	+	+
Hoistaxis	+	+	+	+
Feeling of chill	+	+	+	+
Dysphagia	+	+	+	+
Rhinorrhoea	+	+	+	+
Visual Disturb.	+	+	+	+
Bimnasic Illness	+	+	+	+
Typical Facies	+	+	+	+
Temperature	+	+	+	+
Urobilinuria	+	+	+	+
Rel. Lymphocytosis.	NON JAUNDICED 2nd Illness			

	Group 1	2	3	4
	Anderson L.	Armstrong D.	Purvis L.	McCabe R.
Headache	+	+	+	+
Vomiting	+	+	+	+
Nausea	+	+	+	+
Anorexia	+	+	+	+
Vertigo	+	+	+	+
Abdominal Pain	+	+	+	+
Diarrhoea	+	+	+	+
Lethargy	+	+	+	+
Pains in Limbs	+	+	+	+
Paresthesia	+	+	+	+
Bronchitis	+	+	+	+
Atypical Pneu'ia				
Conjunctivitis	+	+	+	+
Hoistaxis	+	+	+	+
Feeling of chill	+	+	+	+
Dysphagia	+	+	+	+
Rhinorrhoea	+	+	+	+
Visual Disturb.	+	+	+	+
Bimnasic Illness	+	+	+	+
Typical Facies	+	+	+	+
Temperature	+	+	+	+
Urobilinuria	+	+	+	+
Rel. Lymphocytosis.	NON JAUNDICED 2nd Illness			

	Group 1	2	3	4
	Purvis G.	Ellis C.	Turner D.	Miller J.
Headache	+	+	+	+
Vomiting	+	+	+	+
Nausea	+	+	+	+
Anorexia	+	+	+	+
Vertigo	+	+	+	+
Abdominal Pain	+	+	+	+
Diarrhoea	+	+	+	+
Lethargy	+	+	+	+
Pains in Limbs	+	+	+	+
Paresthesia	+	+	+	+
Bronchitis	+	+	+	+
Atypical Pneu'ia				
Conjunctivitis	+	+	+	+
Hoistaxis	+	+	+	+
Feeling of chill	+	+	+	+
Dysphagia	+	+	+	+
Rhinorrhoea	+	+	+	+
Visual Disturb.	+	+	+	+
Bimnasic Illness	+	+	+	+
Typical Facies	+	+	+	+
Temperature	+	+	+	+
Urobilinuria	+	+	+	+
Rel. Lymphocytosis.	NON JAUNDICED 2nd Illness			

	Group 1	2	3	4
	Miller A. (Mrs).	Miller A.	Thynne G.M.	Harrald, Sheena	Armstrong D.
Headache	+	+	+	+	+
Vomiting	+	+	+	+	+
Nausea	+	+	+	+	+
Anorexia	+	+	+	+	+
Vertigo	+	+	+	+	+
Abdominal Pain	+	+	+	+	+
Diarrhoea	+	+	+	+	+
Lethargy	+	+	+	+	+
Pains in Limbs	+	+	+	+	+
Paresthesia	+	+	+	+	+
Bronchitis	+	+	+	+	+
Atypical Pneu'ia					
Conjunctivitis	+	+	+	+	+
Hoistaxis	+	+	+	+	+
Feeling of chill	+	+	+	+	+
Dysphagia	+	+	+	+	+
Rhinorrhoea	+	+	+	+	+
Visual Disturb.	+	+	+	+	+
Bimnasic Illness	+	+	+	+	+
Typical Facies	+	+	+	+	+
Temperature	+	+	+	+	+
Urobilinuria	+	+	+	+	+
Rel. Lymphocytosis.	NON JAUNDICED 2nd Illness				

few features of note, and I propose to classify the cases for purposes of comparison as:--

Group 1. Cases attended by Jaundice.

Group 2. 2nd Illnesses after Jaundice.

Group 3. Cases not attended by Jaundice.

Group 4. 2nd Illnesses after Group 3.

Table 2 (Page 251) gives a summary of the symptoms in each of the groups. It is not quite complete either as regards the number of patients or the range of symptoms but it is representative.

It should also be noted that I did not include a symptom if it was not specifically mentioned by the patient. Leading questions were carefully avoided. The question the table and the histories previously recorded attempt to answer is not so much "What symptoms has the patient?" as "Of what does the patient complain?"

I feel that the distinction is important.

A reference to the table or the case histories will serve to show what I previously have tried to stress, namely, that there were two features which dominated the picture throughout the whole epidemic. They were:--

1. <u>A feeling of extreme listlessness and fatigue</u>.

Practically every patient made this complaint. It was obviously the complaint which they worried about most, or which impressed them most strongly. The majority of them seemed to be puzzled as to why they should feel so

lacking in energy, so disinterested in everything, and so overpoweringly fatigued and weary. Very frequently they stated that they "just could not be bothered with anything"; that "they felt useless" or that "they had not list to do anything." Not only was the complaint almost uniform, but the puzzled air with which the patient told of it was also equally striking.

In the jaundiced patients the complaint was not so marked, possibly because the observer anticipated it being made, nor was the patient so mystified about it, probably accepting it as a symptom of the jaundiced condition.

It impressed one most strikingly in the case of the ambulant non-jaundiced patient, and especially when it occurred as a prodromal symptom or even the first prodromal symptom in such cases it was so prominent as to be almost diagnostic of the illness.

2. An appearance of extreme weariness and fatigue.

Here again I have never seen a disease, other than the few cases of Encephalitis Lethargica encountered in 1924, where the facies, demeanour and appearance was so uniformly suggestive of the diagnosis.

The appearance occurred in ambulant cases, where it was no less marked than in the patients who were confined to bed. Once one had seen and appreciated the picture several times, its identity became so impressed mentally, that if a patient

presented the typical appearance, one felt that it was only a matter of waiting for the other symptoms to be complained of, if they did not then present.

What then constitutes such a typical picture?

Let us consider an ambulant patient with few other striking symptoms, who has called to see his doctor (cf McCabe R., Ellis C., Turner D.)

His appearance suggests the diagnosis.

He walks forward in a limp and 'toneless' manner, as if he had arrived exhausted after a long walk after having had no sleep. His slouching posture suggests that he is incapable of even attempting to assume an orthodox carriage, the features never change from a fixed expression of extreme lethargy, the eyes look heavy and sleepy with their drooping lids. When he is asked to state his complaints, he appears puzzled and bewildered and at a loss what to say. Then he says: "I don't know what is the matter with me, I feel useless and I just can't be bothered with anything" --- probably adding "I feel awful."

In the patients who were confined to bed, the appearance was similar and distinctive and arresting. In the case of the children the appearance, combined with the child's inactivity and complaint of weakness, impressed and worried the parents.

It formed a triad of symptoms with which they, and

for that matter, I, too, were not familiar. It is a commonplace to see children who are ill and consequently weak; it is uncommon for it to so dominate the picture, and seldom have I heard children say: "Oh, I do feel weak."

I could not make a reliable estimate and comparison of this appearance, etc., as between the jaundiced and the non-jaundiced groups, because so frequently I did not observe the prodromal period of illness prior to the onset of the jaundice. But I formed the opinion that it was at least as marked in the children who did not become jaundiced.

.....

Headache, vertigo, nausea, anorexia and vomiting, and abdominal pain were the most commonly encountered symptoms, in addition to the two already mentioned.

Headache. Most patients complained of headache, but they usually qualified their complaint by saying that it was not so much a pain as a dull ache. Or they combined their complaint of it with another, for instance, by saying that the head delt "fuzzy" or "dull" or "thick"--meaning to suggest that it was a dull ache combined with a feeling of slight mental dulness.

Others combined the complaint of headache with that of feeling giddy.

The commonest site was the supraorbital and frontal area. Suboccipital and temporal headaches were noted only

in the cases where jaundice did not occur.

Vomiting. This was present in every case of 'jaundice' but in only just over half of the non-jaundiced patients.

The commonest time of onset was on rising in the morning, when the patient complained of giddiness and then vomited.

In some cases the patient had nausea and felt as if about to vomit, but this cleared a little, and when vomiting did occur, it was urgent.

Abdominal Pain.

A constant symptom where jaundice developed, this symptom was complained of in about half of the remaining cases.

In one case, Elizabeth Jackson, it was so severe, and the abdominal tenderness so marked, that the appearance of urobilin and then bile in the urine leading to the onset of jaundice relieved me of considerable anxiety. In the absence of the previous cases the decision that the condition was not appendicitis would have been more difficult.

I encountered no other case in this series where the abdominal pain led to any similar doubt --- but I may add that very acute abdominal pain was later met with in such cases.

On the whole, however, the abdominal pain was not usually acute. More often it was a dull ache, with occasional superadded "dull colic" exacerbations.

Vertigo. This symptom was common to both groups -- jaundiced and non-jaundiced. It was most marked in a non-jaundiced

case --- Grace M. Thynne, where it was present to a gross degree, the patient being quite unable to balance when she attempted to stand.

More frequently it was complained of as a fleeting feeling of "swimming" in the head. Sometimes it was so transient that the patient "thought he must have imagined it, but it kept coming back."

Biphasic illness.

An interesting feature was the occurrence of a short illness, followed by a period of apparent more or less complete recovery, prior to the onset of the 'illness proper.' Four of the eight jaundiced patients showed this feature. I would stress that the two phases were apparently identical in their subjective symptomatology --- it was not the same as I have heard by colleagues where the initial phase was marked by an upper respiratory infection and the later phase, only, showed the characteristic symptoms of the 'jaundice' illness.

A similar biphasic illness occurred in 5 of the patients who did not show jaundice, and in 3 especially the feature exactly corresponded with the occurrence in the jaundiced group.

Relative Lymphocytosis.

Whilst recognising and admitting that the differential white cell count may vary or fluctuate markedly in health,

I felt that the occurence of a relative lymphocytosis (with perhaps a tendency to a high monocyte count in one or two cases) was a valuable finding. I am indebted to Dr. Pickles, of Aysgarth, who mentioned the matter as one which he would have liked to have persued further in cases of infective Hepatitis (personal communication). He referred, I assumed, to jaundiced cases, and it ocurred to me that such a finding in non-jaundiced cases of a similar type might help to substantiate my conviction that the diseases were closely allied and in some respects identical.

I will late show that a relative lymphocytosis was a practically constant feature in all the blood films examined during the epidemic in its entirety.

A low total white cell count was found when this examination was made. Unfortunately, as this test has to be performed practically at once, I found it practically impossible to fit it into my day's work, a fact which I greatly regret. See page 261.

As explained previously, I did not make differential white cell counts in the earlier, jaundiced, cases, but it will be later seen that I did so in subsequent jaundiced patients.

The results of the test in the non-jaundiced cases were in general indistinguishable from the results where jaundice was present.

To conclude, let me briefly complete the symptomatology of the local outbreak.

Epistaxis occurred in one case in group 2 and one in group 3.

Visual disturbance -- an inability to see clearly, especially after looking in an altered direction, was noted in two cases. Ophthalmoscopic examination revealed normal media and an apparently normal fundus in both. Both cases occurred in group 3, and in both the appearance of drooping of the eyelids was also very marked.

Paresthesia in the hands, associated with little darting 'needle like' pains in the fingers, were described in one case only, in group 4.

(The last two symptoms will be observed as occurring in the Bakery Epidemic also where they are identically noted).

The skin eruptions in the case of Jennie Turner and Mrs. Miller will be noted. In the case of the former it took the form of a giant urticaria, in the latter case, as detailed, there was an attempt at vesicle formation.

In a few cases the patient complained of some form of discomfort in the throat. My experience has been that it is not infrequent in general practice to encounter throat discomfort with little local evident cause. At first I thought the complaint in the patients whom we are now

considering was of this type. As the complaint was made more frequently I began to think the explanation was not so simple. Commonly the patient said he had a sensation as if the throat was swollen -- at the thyrohyoid level-- and it required an effort to swallow. Laryngoscopy gave negative findings.

In this outbreak and later cases I tried the effect of repeated swallowing. The act frequently required an obvious effort especially after repetition.

Several of the patients in group 3 (non-jaundiced) felt drowsy all day and kept falling asleep, but at night they just could not go to sleep: a disturbance of the sleep rhythm constituting a further resemblance to Encephalitis Lethargica.

The condition of the tongue varied, but it was never dry. Indeed, moistness of the tongue and mouth was frequently marked, although thirst was a common complaint, and the patient sometimes complained that the mouth felt dry or "clammy".

The tongue was frequently clean but in some cases it will be noted that a moderate yellowish fur was present, with the papillae appearing hyperaemic and prominent. The appearance in those cases was similar to that seen in Scarlet Fever -- a very close resemblance indeed. The fur seemed to 'peel' from the edges and tip. The final condition

of the tongue when this process was marked was what I would term "A wet raw beef tongue."

I encountered it frequently later.

LEUCOCYTE COUNT. I did not become familiar with the convenient Strong's method until later.

2nd Illnesses.

I attach great importance to the occurrence of a secondary illness as described in the cases of Brenda and Brian Robinson. They had both been attended in August,1944, when they were ill together, and were jaundiced on 15 August.

Brenda had a second illness on 30 October, 1944, and Brian began a second illness on 19 December, 1944.

The reader is requested to refer to the account of those illnesses.

What were the illnesses ?

Were they related to the original attacks of infective Hepatitis?

How did they compare with the cases of infective Hepatitis with Jaundice, and the patients who had no jaundice but such strikingly similar symptoms otherwise ?

To enumerate the symptoms for convenience, they were, in order as they occurred.

Brenda.	Brian.
1. "Sore throat." (little to see)	1. Vomiting.
2. Vertigo	
3. Frontal headache	5. Frontal headache
4. Epistaxis	
5. Feeling of 'chill'.	
6. Conjunctivitis. Photophobia.	2. Conjunctivitis. Photophobia. The latter the chief complaint.
7. Sharp rise of temperature and pulse (101.5°F. 116 per. min)	3. Temp 103.5°F. (Pulse 120)
8. Lack of complaint.	4. Lack of complaint.
9. Lack of appreciation of severity of illness by intelligent parents	6. Blood streaked sputum.
10. Headache aggravated by standing.	
11. Repetition of epistaxis	7. See 9 opposite.
12. Painful stiffness above patellae	
13. Lack of 'physical signs' with temperature of 103°F. Pulse 100.	8. See 13 opposite.
14. Apparent initial response to Sulpha pyridine	
15. Pale face with red daubed cheeks	
16. Pulse rose to 120 p.min. with temperature now only 101°F (cf. 7--13).	
17. Recurrence of vomiting.	
18. Protracted convalescence.	9. More rapid convalescence.

The two illnesses had several features in common, possibly more than the histories and the tables suggest. Brian was'un-co-operative'. He obviously could not be troubled to talk to me. He was content to say"he did not feel well", whereas Brenda is older, a brighter child, and more helpful.

I could not have the children X Rayed in their home, but I do think it possible that an atypical pneumonia may have been present in the case of Brenda. If Brian was similarly affected it must have aborted. But that is conjecture.

The facts were that they both had similarly high temperatures, that I could find no cause for the pyrexia and that photophobia and conjunctivitis was a common feature.

Now if the reader will refer to the table on Page 251, he will note, as I did, that those 2nd illnesses presented several features which were present in the non-jaundiced cases previously described.

For instance conjunctivitis is noted as a feature in the cases of Turner,J; Anderson L; Miller A.(Mrs); and Thynne G. M; it was not however noted as a feature in the jaundiced cases.

Again a rise of temperature was noted in only one jaundiced patient, namely Brenda Robinson herself. It was a fairly common feature in the non-jaundiced series. In

nearly every case where the temperature was raised there was either pulmonary involvement or a suspicion thereof.

Stiffness or aching in the limbs was not a feature of the jaundiced cases, but it did occur in two patients not jaundiced.

A profuse watery rhinorrhoea present in the case of Brenda Robinson was also noted in two other non-jaundiced cases.

It would be fair to state that in all cases of "jaundice so far seen at Cold Hesledon the symptoms were comparatively few --- Headache, Vomiting (nausea and anorexia), Vertigo, abdominal pain, Lethargy and a similarly lethargic appearance: also to state that the non-jaundiced patients had frequently all these symptoms with other additional symptoms and finally to conclude that the two "2nd illnesses" bore more striking resemblance to the non-jaundiced illnesses than to the disease attended by jaundice.

The Vague Illness Prior to the Jaundiced Illness.

Particularly thought provoking was the illness described under the above heading in the case of Iris Etherington, to which the reader is requested to refer.

It will be noted that the X Ray findings taken in conjunction with the history of an illness characterised by few symptoms or complaints on the part of the patient, pointed very strongly to the illness having been an atypical pneumonia.

I should here add that Audrey Branthwaite's attack of Hepatitis was proceeded by a long period of very puzzling malaise, with, at one stage, a fairly marked, but fairly quickly resolving, cervical adenitis. It should be noted however that such adenitis or indeed any glandular adenitis (apart from Mumps) was "conspicuous by its absence" in the remainder of the epidemic in its entirety.

Uncommon Illnesses. (P. U. O. etc.)

It struck me as very suggestive that during the period of this inquiry I could honestly state that in only 5 children at Cold Hesledon was I at a loss to account for the occurrence of a pyrexia lasting more than a day. They were to me cases of pyrexia of unknown origin --- to use the convenient label to denote my ignorance.

Now all of these children suffered from infective Hepatitis attended by Jaundice. Two -- the Robinsons-- had the 'jaundice illness' first: one, Iris Etherington, had the vague illness first and the 'jaundice illness' later.

The interval between the infective Hepatitis illness and the P. U. O. in the first mentioned cases was:--

77 days in the case of Brenda Robinson.

127 days in the case of Brian Robinson.

The interval between the atypical pneumonia (as I assume the diagnosis to be) and the onset of infective Hepatitis in the case of Iris Etherington was:--

63 Days.

I am convinced that the two sets of illnesses stood in aetiological relationship. Either the one illness rendered the patient susceptible to the other, or the two illnesses represented a sequence in the activity of one common agent, probably a virus. My impression was that the second was the correct or more likely assumption.

A study of the literature regarding Atypical Pneumonia, including the report of a meeting of the Royal Society of Medicine, led me to believe that all three children named had indeed suffered from attacks of atypical pneumonia.

Further, such a condition was believed to be caused by a virus, not yet identified in many cases.

Might not the unidentified virus of Infective Hepatitis be capable of producing an atypical pneumonia.[5]

The illness of Tom Walshaw, which has been described at some length and which had a fatal termination, resembled what Capt. John W. Brown[6] termed "atypically atypical pneumonias" and (as stated before) the fatal case reported by Peronne and Wright.

An atypical pneumonia was here associated with an encephalomyelitis.

In this case infection by the virus of Infective Hepatitis was a distinct possibility, the source of infection most probably being William Collings as previously stated.

The illness of Mrs. Anne Miller, which I have already commented upon (Page 191) was also a very unusual one with its peculiar rash, conjunctivitis and, I think, atypical pneumonia, in addition to the dysphagia and the 'biphasic' course of the illness.

Argument and interpretation.

Please refer, at this point, to the last paragraphs on Page 275.

The reader, it is hoped, will now have a general impression of the illnesses which had occurred in the small area in question from March until the end of the year 1944.

How could I sort out, correlate, and interpret the occurrences ? With what impressions had they left me ?

My initial reaction was to agree that the epidemic "fitted in" with the records and views of previous workers—Pickles, Ford, Cameron, etc.

The disease was evidently an infectious one, with an incubation period of some three to five weeks. The spread occurred after close association, I should prefer the term 'intimate association' or actual contact.

It had been stated that non-jaundiced cases did occur and were probably important factors in the spread of the disease.

We had, therefore, to date, the fairly simple conception that a jaundiced patient could infect another person, who might similarly become jaundiced, or who might suffer from an attack not characterised by the occurrence of clinical jaundice. In either case the second patient could transmit

the infection to others.

It must be added that the continued occurrence by relay, as it were, of non-jaundiced cases had not been remarked (as far as I could find in the literature).

The spread has been said to occur either, thus:—

1. Jaundice patient
   ↓
   Jaundiced patient
   ↓
   Jaundiced patient and so on,

or:- 2. Jaundiced patient
   ↓
   Jaundiced patient
   ↓
   Non-Jaundiced patient
   ↓
   Jaundiced patient.

My later reaction was to definitely question the accuracy and more especially the completeness of this simple conception.

A. In the first place, I believed from my observations that an illness similar to Infective Hepatitis but without the occurrence of jaundice did occur, as had been stated, but that it was not necessarily, as in 2 above, simply 'interpolated' as an occasional happening.

I believed that this similar illness not attended by jaundice could be relayed and transmitted, the fresh cases occurring to a fairly regular or well defined symptomatological pattern, none of the patients being jaundiced.

The spread might then be represented as occurring thus:-

3. Jaundiced Patient
↓
Jaundiced Patient
↓
Non-Jaundiced Patient
↓
Non-Jaundiced Patient
↓
Non-Jaundiced Patient. and so on.

B. I now began to question another previously held conception. It seemed to be generally accepted that if a person was infected by the virus of Hepatitis, what happened was as follows:--

The liver parenchyma was damaged and in some 4 weeks the patient took ill. He remained ill for some, say, 2 or 3 weeks, and then began to improve as the liver damage was repaired.

In particular the antecedent illness of Iris Etherington and the subsequent illnesses (2nd illnesses) of the Robinson children made me wonder whether this again was a too simple and incomplete conception.

My view was that Iris Etherington had probably harboured the virus for a few weeks, taken ill on 15 May, 1944 (Atypical Pneumonia) and that the virus had given evidence of its renewed activity on 11 July, 1944, when she began her second illness, which we term infective Hepatitis.

Similarly, reviewing the cases of the two Robinson children, I held the view that the sequence of events was exactly reversed. After an incubation period of 5 weeks the children became jaundiced on 15 August, 1944. Their second illnesses I was persuaded marked the renewed activity of the virus which had originally caused the infective Hepatitis.

In short, I thought that the original view might be the correct one, as applied to many of the cases, but that it was incomplete and did not cover the whole range of the activities of the virus.

As a working hypothesis I postulated the following theory:—

The virus of infective hepatitis commonly attacks the liver and leads to hepatitis. Thereupon, or thereafter, its activity may terminate. It may, however, later, show renewed activity in the form of an illness bearing some resemblance to the original illness, but with more generalised symptoms such as conjunctivitis, aches and pain in the limbs and possibly atypical pneumonia.

Alternatively the virus may <u>initially</u> cause a 'vague' illness such as an atypical pneumonia, and <u>later</u> show renewed activity by attacking the liver, such hepatotoxic action being evidenced by the onset of "infective Hapatitis

I fully realised that my 'amateur' theorizing in the field of epidemiology might well meet with criticism and I was pleased to find anything to support me to have the 'courage of my convictions'.

I found such support in Professor C. H. Browning's article on "Bacteriology" in "Medical Progress 1944."[7] He writes: "Further evidence has been contributed, by laboratory investigations, that various specific infective organisms have a much wider distribution and persist for a longer time in the body than would be expected from the clinical observations made."

That was exactly what I was convinced could and did frequently occur in infection by the virus of Infective Hepatitis. Let me repeat:--

1. The virus persisted longer in the body than could be expected from the clinical observations made.

2. The virus had a wider distribution in the body than could be expected from the clinical observations made.

A further fact which encouraged me was that there was a very close resemblance and, <u>some</u> thought, an aetiological identity in the hepatitis following the injection of organic arsenicals (post arsphenamine jaundice), homologous serum jaundice and infective hepatitis but there was a wide <u>discrepancy in the incubation period</u> of the last type as compared with the first two.

If the virus did persist longer in the body than we had previously thought, if indeed, in some cases, as in the case of Iris Etherington, the incubation period in infective hepatitis was some 3 months, the study of such cases might throw light on the discrepancy in the incubation periods, referred to above.

Did the answer to those problems lie, I wondered, in the route of entry and attack of the virus ? If the virus entered the portal circulation and attacked the liver, as appeared to be the commonest happening, we had a consequent hepatitis after an incubation period of some 4 weeks.

If the virus did not enter into and attack via the portal circulation it might cause more generalised symptoms as described in the non-jaundiced series of cases: with possibly a delayed, or secondary, attack on the liver.

If such a distinction could be proved or deduced in naturally occurring illnesses it might give an obvious lead to the understanding of the mechanism of the occurrence of hepatitis after therapeutic injections: by mechanism I mean not only the information to be gained by a study of the histological detail of the liver pathology but, and more especially, the "life cycle" or fate of the virus in the body.

I felt that differences in the nature and course of the illness caused by the virus of hepatitis might be dependant

on two main factors.

1. The virus might enter and attack by different routes and primarily affect different tissues.

or 2. The virus might have been altered by passage, and thereby alter its 'tropism' or predilliction to attack certain tissues.

Finally 1 and 2 might be combined with varying result.

Such then was the impression generally, and in such ways did I attempt to reason and debate the significance of this series of illnesses:- the cases of obvious infective hepatitis; the cases which I thought were indicative of non-jaundiced hepatitis; the preceding illness; the subsequent illnesses and possibly the case of Tom Walshaw.

I may appear to have attempted to make too many bricks with too little straw. But by this time I had a great deal of evidence in the cases of illness observed in other parts of the colliery practice. I had taken, or presently I had taken, records of some 600 cases which I considered to relate to this problem.

They appeared to support the views which I had been forming, and I now propose to extract and present such evidence as, I trust the reader may agree, at least tends to corroborate the views expressed in this section.

L A T E R.

On reviewing this section of the work at a later date, just prior to the presentation of this thesis, I find much which might be altered: this in the light of the knowledge which I have acquired in the interval.

I have decided not to amend the section, however, in any way, even when an opinion expressed in it now seems incorrect.

In this way the reader will be able more "truthfully" to follow the manner in which the happenings in this epidemic impressed me at the time of their occurrence.

Naturally, I shall not include such views as I now realise to be inaccurate, in my Summary and Conclusions of the completed work.

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5. Fleming J. Lindeck E.W. Evans I.H. B. M. J. 1945. Vol 1. Page 689.

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7. Browning C.H., B.E.M.P. Med. Progress 1944. p 39.

ILLNESSES AT HAWTHORN.

G R O U P 2.

~~I do not regard this as a particularly convincing or vital part of the work.~~

GROUP 2 H A W T H O R N.

This group was of particular interest to me as it provided a confirmation of the statement which has been made that many outbreaks of infectious disease occurring in an area do not represent a simple sequence of illnesses derived from one source, but that the local epidemic frequently represents the sum of several lesser epidemics, each one having its separate source. There were several other points of interest but it is illogical to state one's conclusions before reciting the findings, so I will proceed to the history of this little outbreak.

Hawthorn is situated two miles from Murton and it is a country village with no industries.

The first patient whom I attended was Alice Mary Fry.

Her history is recorded as (Case History 1).

It will there be seen that she had been feeling "run down and out of sorts, listless and tired" at her home near Kidderminster and that she had to come North to Hawthorn for a 'change' and a holiday. She later became ill and the features of her illness suggested that she was suffering from hepatitis. The main features of her illness as they occurred were:

1. The initial period of "just not feeling well" as referred to above.

2. An attack of severe, acute diarrhoea.

3. A phase of nausea.

4. An attack of bronchitis.

5. Intense nausea if she attempted to eat. Intense giddiness.

6. Mild degree of mental confusion.

7. Epistaxis.

8. Liver tender and palpable.

I found that she had a marked relative lymphocytosis --- her differential white count was Polymorphoneclear leucocytes 50, lymphocytes 46.5. monocytes 3.5. and her total white cell count was 5,200 per c. cm.

At no time had she bile in the urine but urobilin was present on several occasions on testing by Schlesinger's and Bogomolow's methods; it was at no time marked.

I had little doubt from my clinical experience of the Cold Hesledon and Murton cases that she was suffering from an attack of non jaundiced infective Hepatitis.

I wondered whether she could have been in contact with anyone suffering from jaundice. She had been. The son of Mrs. Fry's 'domestic help' ran errands for Mrs. Fry, and he had recently suffered from jaundice. Further, the boy's attack had ben shortly followed by Mrs. Fry's malaise which culminated in her present illness.

Dr. Wilkins, of Highley, near Kidderminster, courteously supplied me with the following information, and I think that

it is so suggestive in several respects that in view of its brevity it merits quotation:--

"During August and September we had quite a small epidemic of what I took to be catarrhal jaundice ..... could you tell me the cause of your cases of infective Hepatitis ? We had a number of cases here of gastroenteritis, which have been subject to relapse, associated with a slightly raised temperature for two or three days. Recovery has been complete without apparent physical signs, during the period of illness. Mrs Fry has suffered from a chronic dyspepsia for some years, and I have long suspected a chronic cholecystitis. She has never, however, had a frank attack of gall stone colic, or been jaundiced,at any time. "

Every statement in this letter seemed to me to call for careful analysis.

First of all it demonstrated that in the Kidderminster practice an epidemic of jaundice had been followed by an outbreak of gastro enteritis. I felt that Dr. Wilkins had been unable to detect the cause of this outbreak. In my letter to him, I had mentioned about the cases here, and he had apparently considered that they were similar to the illnesses of his patients. The mention of relapses tallied with my own observations as did, broadly speaking, the absence of "apparent physical signs", and the complete recovery

Mrs Fry's previous history was also thought-provoking in relation to her illness. Subsequent illnesses in the house in which she was residing pointed to the fact that not all her symptoms were due to her possible or probable chronic cholecystitis. Mrs Fry's illness was very unusually protracted as compared with that of my other patients. I consider that Dr. Wilkins's information gives the explanation. In chronic cholecystitis we find that the liver function is disturbed --- this fact has been mentioned in the section on Liver Function Tests. Might we not therefore expect that a superadded acute illness attacking the liver would yield either more severe symptoms or that the resulting illness would be of longer duration:- the already damaged liver might be expected to be longer in recovering from this freshly - inflicted damage. Therefore, in fact, I considered that Mrs Fry's long illness supported my suspicion that her illness and those which I had found at Cold Hesledon and Murton were indeed due to a hepatitis.

The history records 1 and 2 show that Mrs Fry slept with her sister, Mrs Widdas, on 29 September, 1944. The latter had a "throat cold" on the 13th October, and she felt listless and generally out of sorts until 17th October, when she vomited violently and repeatedly all day. Abdominal pain was so intense that she "had to go on the floor resting on her hands and knees." She made a quite rapid recovery from the

acute stage of this illness, but she lost her appetite and felt sickly at the mere smell of coffee or tea and remained weak and listless. Mrs Widdas had never been sick in her life, and she had eaten nothing except the food consumed by the other members of the household.

The period between probable infection and the onset of really acute symptoms would here be 18 days.

Mrs Widdas's last complaint was that on the 21st October she had to go to the local post office, and she felt ashamed because she had felt that she was walking like a "drunk"--- she literally swayed about, requiring most of the footpath, and equally important to our inquiry, she there conversed over the usual shop counter with the postmistress, Miss Haythorn. Also she would probably hand her a letter.

.....

Now when Mrs Fry arrived at Hawthorn she lived with the Rector (Mr. Widdas) and Mrs Widdas. They have recently resided, not at the rectory, but in one half of a large house, the other half being occupied by Mr and Mrs Hunt and their child Avis. Mrs Hunt acted in part as a landlady and was in intimate contact with Mrs Widdas, who assisted in the 'common' kitchen.

So Mrs. Widdas's contacts were:

Miss Haythorn (on 21st October, 1944) and Mrs Hunt and Avis Hunt continuously.

To return to Miss Haythorn, whom, we shall take it, was exposed to infection on the 21st October. She had to jump out of bed at 4 a.m. on Friday, 17th November, 1944, as she had diarrhoea and later urgent vomiting. Then she improved apart from extreme lassitude, which is in contrast to her normally active habit, only to have a return to the symptoms on the 23rd November: and again, like Mrs Widdas, she took a violent dislike to tea, to which she is very partial. Her case record (No. 5) which confirms and amplifies these symptoms is of interest in several respects. First, it suggests an incubation period of 26 days (or 32 days counting to the'relapse') and secondly it illustrates the biphasic nature of the illness:- this as mentioned by Dr. Wilkins and as noted by me in the cases at Cold Hesledon (e.g. Case records 1, 2, and 3).

But,also, it illustrates the fact which I have so frequently noted that the onset of the really acute symptoms,especially urgent vomiting, commonly occurs in the early morning, from 3.30 a.m. onwards. And this time of onset must, I feel, be of significance when we try to reason out its cause.

Mrs Hunt, the landlady, was intensely sickly on Monday and Tuesday, the 20th and 21st November, 1944, and she had epigastric pain. She did not vomit, although she wished to, as she felt this might lead to relief. She was awakened, again in the early hours, by an acute attack of diarrhoea.

After this she improved, complaining only of a horrible taste in the mouth and a persistent headache, both of which were found to be very common symptoms in the epidemic.

Avis Hunt, a 14 years old schoolgirl, first complained on Wednesday, 22nd November, 1944, when she felt a "tightness behind" the lower half of her sternum all day, and she vomited frequently and distressingly all through that night, until at least about 4 a.m., when she fell asleep, and again vomited on getting out of bed at 8 a.m. The 8 a.m. vomiting on rising was a very marked feature of the jaundiced Hepatitis cases at Cold Hesledon, but there it was an initial vomiting.

In the case of Mrs Hunt and her daughter Avis, the incubation period could not be so definitely assessed as in the case of the postmistress, but the interval between Mrs Widdas's vomiting and their attacks of vomiting etc., was 34 days in the case of Mrs Hunt and 36 days in the case of Avis Hunt.

But Avis Hunt did not come into contact with Mrs Widdas unless in the kitchen, and in that case Mrs Widdas might not have given her the infection until the 20th October, when the interval for Avis would be reduced to 34 days.

On the 18th December, 1944, I was consulted by R. H. Turner (Case 6) a man aged 41 years, who resides at the Post Office, Hawthorn, with Miss Haythorn and others.

He stated that he had had a severe head cold for the past two weeks, accompanied by attacks of sneezing, which were sufficiently marked, to call for special mention. The head cold cleared a little, but his headache did not improve: and now it was accompanied by a numb, "fuzzy" feeling. It was not a severe pain really, but he said he had a muddled feeling as if he could not think clearly. I subsequently noted that a frontal headache of this type was very frequently encountered. Turner had the usual loss of appetite and listlessness.

I would place the incubation period in this instance at about a calandar month.

ALICE MAY FRY. Age 67 years. Case 1
C/O Widdas and Hunt, Laburnum House, Hawthorn.

Explanatory.

This woman stated that she had been feeling vaguely out of sorts and her doctor advised her to have a holiday. She left Highley, Kidderminster, Worcestershire, on Friday, 29/9/1944, and journeyed to relations at Bishop Auckland, County Durham, that day. There she met her sister, Mrs. Widdas, Hawthorn, with whom she slept. On Sunday, 1/10/1944, at 4 a.m. she was awakened sudden epigastric and subcostal pain and she had to rush to the lavatory, where she was 'doubled up' with cramp, and had frequently repeated profuse watery diarrhoea.

She improved on the 2nd and 3rd of October, and on Wednesday, 4/10/1944, she travelled to Hawthorn,Co. Durham.

On Thursday, 5 October, 1944, she was visited by a colleague --- she complained of a sickly feeling. He attended her again on Thursday, 12 October, and Sunday, 15 October, 1944, when she had a definite bronchitis.
I attended her

Wednesday, 18 October, 1944. Visited.

She gives the further history that she has not felt well since she arrived at Hawthorn on 4 October, 1944. She has had a very poor appetite. If she went for a short walk she returned tired and exhausted and had to lie down. She had a horrible taste in her mouth, which she can only compare to a faecal smell.

On Wednesday, 10 October, 1944, she felt violently sick but did not vomit. She was very thirsty. The nausea and feeling that she was actually going to vomit continued until yesterday, 17/10/44, when she did vomit. If she lay flat she could keep the nausea partially controlled, but the slightest raising of her head immediately made her feel violently sick.

Her condition to-day, 18/10/1944, is as just mentioned.

The cough is productive and, she states, easier.

She is lying with no bolster or pillow, which I at once noticed, in view of the history of bronchitis.

The temperature is 98°F. Pulse is 70 per minute.

She is immediately very giddy if she raises her head, when she has an aggravation of her constant dull frontal headache, as well as feeling intensely nauseated. No Urobilinuria.

Differential White Cell Count.

Polymorph Leucocytes	50
L y m p h o c y t e s	46.5
M o n o c y t e s	3.5

She tells me that her domestic help in Highley has a son aged 7 years who had jaundice a few weeks ago. Mrs Fry employed this boy to run her errands.

See letter from Dr. Wilkins, Page 279.

Until Tuesday, 24 October, 1944,

The condition altered very little. The pulse rate rose to 96 per minute. Vertigo is still marked if she raises her head. She feels hungry, but her appetite vanishes when she eats a 'trifle'. She then feels very uneasy in the epigastrium and wishes she had not eaten. She complains of drenching sweats. At times she feels "chilly".

Saturday, 28/10/1944.

She feels sickly but hungry, and wishes she could eat. Pulse to-day 72 per minute.

She has improved.

Monday, 30/10/1944.

Rise of temperature to 100°F. Pulse 84 per minute. The skin is not and dry to-day. She complains of insomnia, at night. Through the day time she feels mentally confused, especially if she falls "half asleep" when she has the "silliest ideas" which she has difficulty in dispelling.

Tuesday, 31/10/1944. Temperature was 101.4°F. Wednesday 100.2

Thursday, 2/11/1944. Epistaxis occurred to-day. She continued to feel very muddled and confused, at intervals.

Sunday, 5/11/44. The temperature has settled, to normal. The pulse is normal. 72 per minute. The liver is tender and palpable. She still complains of the vertigo, but it is

decreasing.

Occasionally she feels sickly.

There is now more than a trace of urobilin in the urine. Her head is still "not clear" and she has a dull frontal headache ---- the pain is not severe. Insomnia persists.

Thereafter recovery wasgradual, and on

Sunday, 12 November, 1944,

The urine was again free from urobilin. She is convalescent.

Mrs. Widdas. Age 63 years. Case 2.
Laburnam House, Hawthorn.

She is Mrs. Fry's sister.

She slept with Mrs Fry from 29/9/44 until 3/10/44 at Bishop Auckland, and since then at Hawthorn. On Friday, 13/10/44, she had what she terms a "throat cold". Since then she has felt listless and "off colour" until

Tuesday, 17/10/44,

when she vomited repeatedly all day. She does not remember having ever vomited 'in her life'. She had severe abdominal pain and she got on to the floor on her hands and knees in her agony.

Wednesday, 18/10/44.

She can give no dietetic cause for the vomiting, especially as for three of four days she had a very poor appetite. To-day she feels better except for, understandable, weakness; at times she has attacks of nausea.

The smell of tea or coffee immediately leads to violent nausea. The abdominal pain has not recurred.

Saturday, 21/10/44.

Being markedly improved, she went to the Post Office to-day. She felt like someone drunk as she could not keep to a straight course and "swayed all over the pavement."

Recovery was rapid and complete.

Margaret Hunt. Age 54 years. Case 3
Laburnam House, Hawthorn.

Landlady to Mrs. Widdas and Mrs. Fry.

Thursday, 23/11/44. Consultation.

On Monday, 20/11/44 and Tuesday she felt sickly and several times she seemed to be about to vomit. But she did not vomit. She had a dull epigastric pain. Diarrhoea commenced at night and continued until the next morning: she had several profuse watery motions. During this period she had a dull, heavy frontal headache.

To-day she is markedly improved (she travelled 2 miles, by 'bus, to the surgery). The headache is still present, but much less marked, and her chief complaint is that she has a "horrible" taste in her mouth and a 'soreness' in the epigastrium. She feels weak.

Avis Hunt. Age 14 years. Case 4

Laburnam House, Hawthorn.

Attending Seaham Secondary School. Form III.

Friday, 24 November, 1944. Visited.

On Wednesday, 22 November, 1944, she complained of a tightness behind the lower half of her sternum. At night she vomited --- frequent and violent, distressing vomiting continued until 3 a.m. She vomited again on rising at 8 a.m. but she went to school. She was sent home from school at noon as she looked so pale and ill.

She vomited twice to-day, 24/11/44. The facies is striking --- she looks weary, exhausted, pale and languid. She admits to only slight epigastric discomfort.

Recovery was rapid and uneventful.

Miss Anne Elizabeth Haythorn. Age 55 years. Case 5.

Post Office, Hawthorn.

Tuesday 21/11/1944. Visited.

History:-- On Thursday, 16 November, 1944, she felt as if she had eaten far too much for her supper. She had had a particularly light supper, but she felt distended and uncomfortable in the epigastrium.

At 4 a.m. (17/11/44) she had to jump out of bed as diarrhoea threatened and as soon as she got out of bed she vomited. The vomiting was repeated several times and she had 4 or5 watery motions. Her head became dull, heavy, and "fuzzy" and she continues like that to-day. There is an associated frontal headache. She has no desire for food, and the little she has eaten has tasted oily and greasy. Lethargy is extreme. She is an exceptionally alert and active woman, but she states that she can scarcely fight against her drowsiness. At night she is restless.

The face is set in an expression of extreme drowsiness--- the eyes are heavy lidded and she presents a picture,entirely alien to her, of extreme weariness and exhaustion.

Thursday, 23/11/44. She again vomited violently -=- the vomitus contained'streaks or threads' of blood which she attributed to the violent retching. After the vomiting had apparently ceased, she found that it immediately recurred if she moved "an inch" in bed. She 'settled down' by keeping absolutely still. At no time did I find the pulse raised above 80 per minute. Temperature was 98° F.

Convalescence was gradual, and marked by nausea at the smell of tea, to which she took an intense dislike.

Robert H. Turner. Age 41 years. Case 6.

Post Office, Hawthorn.

18 December, 1944. Consultation.

For the past two weeks he has suffered from a "head cold". He has had a profuse watery rhinorrhoea and has had frequent attacks of sneezing. He has had a supraorbital headache. It is a peculiar headache, he says, not a severe pain but accompanied by a numb "fuzzy" feeling; this gives him a sense of being muddled and not clear mentally. His appetite is poor. He feels chilly at times and he is weak and listless. Everything has been a trouble to him for over a week. The two mile walk home from work has seemed endless. He has gone to work, rested at home and returned to work --- that was all.

22 December, 1944.

He complains of pain in the occiput, the nape of the neck, and on to his shoulders. He looks sleepy and tired, and says that he feels limp and useless. "It is not like an ordinary cold, my headache and pain in the neck are no better after the nasal discharge and I feel worse than ever."

26 December, 1944.

He can not sleep at nights -- he is then extremely restless. This surprises him as he feels so sleepy through the day. He now complains of pain just below the scapulae and pain high in the epigastrium--'it is hard to know whether the pain is in his stomach or his chest.' There was no nausea, vomiting or diarrhoea, only lack of appetite.

He resumed work on 16 January, 1945.

SUMMARY AND COMMENTS.

Whilst the number of patients included in this account is very small, it did seem to suggest the following points.

1. The disease was introduced by a visitor.
2. The visitor had been in contact with cases of typical infective hepatitis featuring jaundice.
3 (a) The visitor's illness resembled infective hepatitis with jaundice and cases which I had considered to represent infective hepatitis without jaundice.
   (b) Her illness may have been protracted owing to her chronic cholecystitis.
4. Her sister, a contact, took ill in 18 days.
5. The sister appeared to have conveyed the infection to 3 other people in 26 to 32, 34 and 32 days.
6. A further possible relay case occurred in 31 days.
7. Diarrhoea usually occurred or was worse at night.
8. Acute onset on vomiting and diarrhoea usually occurred at about 4 a.m.
9. The Leucocyte count in Mrs. Fry's case was low -- a leucopenia with a marked relative lymphocytosis.
10. The occurrence of the so-called fuzzy headache and of slight mental confusion is remarked.
11. Mention is made of diurnal lethargy and sleepiness with nocturnal sleeplessness.
12. Heavy night sweats and epistaxis both occurred.

The history of Turner's illness with predominatingly nervous symptoms was at the time not at all convincing to me and I greatly doubted if it was related to the preceding illnesses: in fact I still doubt this.

Nevertheless in view of subsequent happenings in the area, the reader may, with me, wonder whether this man's illness signified an 'alteration' in the virus in its 'passage' through several patients.

GROUP 3.

THE OUTBREAK AT THE BAKERY.

GENERAL REVIEW.

This is an important section of the work.

THE EMPLOYEES OF THE SOUTH EAST DURHAM CO-OPERATIVE BAKERY.

The outbreak began in the packing department at the bakery, where the goods are assembled and made ready for dispatch by motor van.

Stage 1. On the 30th August, 1944, I attended Elsie Nichols, who was employed in this department. Her symptoms were strongly suggestive of an attack of hepatitis as the following account may illustrate. For a few nights she had had cramp like pains in her legs, when on 27th August, 1944, she vomited several times. When I visited her on 30th Aug., she complained of marked nausea, frontal headache and giddiness --- the giddiness was very severe. She also complained of feeling tired and sleepy and she had pain across the upper abdomen. But most striking of all was her appearance. A patient who is nauseated would be expected to have a dull sickly facies, but this girl's facies was arresting. The eyes looked dull and sleepy with a heavy lidded appearance as if she could not prevent the upper lids from drooping. The face was devoid of expression and during my interrogation and examination this normally vivacious girl did not alter her expression. It seemed as if her lethargy was such that she was not inclined to make the essential effort entailed in altering her expression. Her general bearing seemed to support this supposition. She had been lying down on the couch all day as "if she could not hold up" as her mother stated.

Now as I spoke to her she sat limply in her chair with a posture of extreme fatigue --- her shoulders drooped as if dragged down by the weight of her limp arms and her head moved uneasily at times as if she was scarcely able to support it.

She had, further, drenching sweats --- cold sweats. Stage 0. Very suggestive was the history of her younger sister's illness. She, Sheila, was still attending school. On the 4th August she commenced an illness which, I was told, (I did not attend the child) was exactly similar to Elsie's present illness: except that she did not complain of cramp pains in the legs: vomiting, headaches, dizziness, and epigastric pain were complained of --- the vomiting had been repeated and urgent, and she had been listless and weak. She had wept, and when asked why she did so, replied that she could not help it as she felt so weak. In my experience in general practice, now over a score of years, I have seldom heard a child say she was crying because she felt "so weak", and later I came to regard this as a symptom of high diagnostic significance.

I assumed that Sheila had probably infected Elsie, and I decided to investigate any further cases at the Bakery to test the validity of this assumption.

Before proceeding to the subsequent illnesses among Elsie's workmates, I should state that she returned to work on 6th September, 1944, and that she realised that she

should not have done so, as in the hot atmosphere at work she continued to feel very 'sickly.'

Stage 2. The number of employees in the packing department at the Bakery is not large, and when three of those packers fell ill and were attended, from 7th October, 1944, to 11th October, 1944, for illnesses attended by symptoms almost identical to those described by Elsie Nichols, it was considered probable that the illness was an infectious one with an incubation period of some four weeks.

The three girls were Rita Gordon, Hilda Richardson, and Margaret Browell, and they had been especially mentioned to me by Elsie Nichols as being her intimate friends. Their case histories are appended.

To add to my suspicions three male workers who were in close contact with Elsie Nichols also took ill with similar symptoms on the 6th and 9th of October. The men were John T. Brewster, A. F. M. Russell, and A. Watson, and their case histories are also appended.

At about this time I had written a brief note to Professor J. W. McNee, who had not only replied but had put me in touch with Dr. Bradley, of the Ministry of Health, and Dr. Pickles, of Aysgarth.

A remark in the letter, which the last-named so encouragingly addressed to me, concerning the white cell counts in cases of epidemic jaundice, made me decide to investigate the

white cell counts in the commencing epidemic. I felt that this might help me to decide whether this infectious illness bore this further resemblance to infective Hepatitis.

I did not examine Watson's blood. He is not my patient, and I am indebted to my local colleague, Dr. R. Mackinnon, for the retrospective history which I later give. But the three girls and two remaining men are attended by me. The differential white cell counts showed a definite lymphocytosis. Not only that, but the count was indeed very similar to that subsequently found in the case of the two girls, L. Anderson and J. Turner, and one youth, Cyril Ellis (see Group 1), who developed what were almost certainly attacks of non-jaundiced infective hepatitis in the 'jaundice' epidemic as described in Group 1: and again very similar to the count in the case of Mrs Fry (Group 2) who was almost certainly a "1st relay" (if I may be excused the use of such a handy term) non-jaundiced infective hepatitis, having been infected by a patient actually jaundiced.

I feel that the importance of the similarity in all those blood counts may be such that the reader should be spared the necessity of referring to them, and for the purpose of ready comparison, I give below the 9 counts referred to:

Date of Test.	Name	"Epidemic" Group.	Polymorph Leucocytes	Lymph-ocytes	Mono-cytes
13/11/44	Rita Gordon	This 2	53.	43	4
9/11/44	H. Richardson	2	59.5	35.5	3.5 Eo. & Bas .5
16/11/44	Margaret Browell	2	50.	45	3. Eos .2.
16/11/44	J. T. Brewster	2	48.	48.	1.5 Eos2.5
16/11/44	A.F.M.Russell	2	53.5	39.5	2.0 Eos4.5 Bas .5
8/11/44	L. Anderson	1	34	57	4.0 Eos 5.
8/11/44	J. Turner	1	22	72	6.0
13/11/44	C. Ellis	1	40	48	10.0 Eos 2.
18/11/44	Mrs. Fry	3	50	46.5	3.5

I have included the last four tests at this stage although they did not occur among the Bakery employees for the reason stated --- to show the similarity of the counts in illnesses where a definite relation to jaundiced cases had been noted, and those at the Bakery where I had no case of illness accompanied by jaundice.

But also I have included it here in order that the reader may more readily grasp the relation in time between the cases occurring in Group 1 at Cold Hesledon and Dalton-le-Dale : Group 2 occurring at Hawthorn, and Group 3 occurring at the Bakery.

It is hoped that the reader can therefore follow the chronological order in which the separate components of the epidemic revealed themselves to me. They were all 'running' concurrently, and while I have described them in groups it will be realised that this is a division made for convenience of description. To me the groups really presented a wide composite picture as I felt convinced "sets of illnesses" so similar in symptomatology, incubation period and blood picture, and withal occurring at the same time were almost certainly closely related aetiologically. More than that: the similarity in symptomatology was more striking than can be conveyed by the written word. Time and again the same expressions were used by the patients in each group to describe their complaints. The facies and posture: the whole impression conveyed by an inspection of the patient, they were also apparently identical in each group.

It seemed an incredible coincidence that 2 epidemics should be so similar and be unrelated in one community at one time.

It now appeared that this Bakery outbreak, similar in many respects to that described by Bradley as Epidemic Nausea and Vomiting was characterised by

1. Symptoms similar to those of Infective Hepatitis.
2. An incubation period of similar duration, about a month.
3. A similar differential white blood cell count, but with no consistent high degree of relative monocytosis.

Before continuing further with the narrative of this outbreak as I observed it, I would state that Dr. Mackinnon's patient, Watson, apparently infected his child Michael and his wife Ann. The incubation period in the case of the child was probably some 22 days: in the case of the mother 27 days: their illnesses commencing on 30th October and 5th November, 1944, respectively.

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Particularly interesting to me was the fact that in the case of Margaret Browell I examined the patient's blood because I heard that she had vomited at work nearly a week before, and had then complained of headache. I awaited her return from work, when she said she was perfectly well, but submitted to the test being performed. Although she was forced to stay at home 48 hours later owing to a very definite attack of the prevailing illness it is obvious that she was probably infective for eight days prior to so doing. This would appear to illustrate that a considerable latitude is indicated in the estimation of the incubation period.

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As regards the incubation period in the 6 cases mentioned, I consider that Elsie Nichols may have infected them on or about 29th August, 1944, or possibly on her return to work on 6th September, 1944.

To consider the 6 people mentioned: incubation periods would thus appear to be:

Rita Gordon	Took ill	11	October	1944	--35 or 43 days.
H.Richardson	" "	8	"	"	--32 or 40 days.
Margaret Browell	" "	9	"	"	--33 or 41 days.
J. T. Brewster	" "	9	"	"	--33 or 41 days.
A.F.M. Russell	" "	7	"	"	--31 or 39 days.
A. Watson	" "	6	"	"	--32 or 40 days.

It will be noted that the periods were (e.g.)32 or 40 days; not 32 to 40 days.

.....

Before proceeding to the further discussion of the epidemic I have decided to include a table to illustrate the apparent stages of the infection, as it appeared to have spread in this bakery.

As Sheila Nichols did not work at the bakery, although I considered that she was the source of the infection, I have included her illness as stage 0.

Elsie Nichols would then be Stage 1, and the 6 illnesses described above would be considered as Stage 2.

The Stages in the Epidemic.

Name	Date of illness		Stage.
Sheila Nichols	4 Aug., 1944.	C.	0
Elsie Nichols	27 Aug., 1944.	C.	1
Returned to work, ill 6 Sept. 1944			
Rita Gordon	11 Oct 1944	C.	2
H. Richardson	8 " "	C.	2
Mgt. Browell	9 " "	C.	2
J. T. Brewster	9 " "	C.	2
A. F. M. Russell	7 " "	C.	2
A. Watson	8 " "	C.	2
Jean Taylor	29 Oct 1944	C	3
S. N. Curry	29 " "	C	3
A. Hall	29 " "	C	3
J. G. Burn	6 Nov 1944	C	3
W. Palmer	30 Oct 1944	C	3
Mary E Gurkin	? 23 Nov 1944(Doubtful)	?	4
James E Hocking	30 " "	C	4
Mary Charlton	27 " "	=	4
Eliz. A. Johnson	27 " "	C	4
A. Price	27 Dec 1944	C	5
Continued ar work until 3/1/1945 (again acutely ill)			
Mgt. Reekie	22 Dec 1944.	=	5
Mary McEwan	31 Jan 1945	=	6.

C denotes that the patient was in intimate contact at work with other patients in this group.

The reader will notice that I have not included all the cases in the preceding table. The following cases have been omitted.

Name	Date of my 1st Attendance.	
Jennie Balls	18 Oct 1944	C.
Jean Trewhitt	20 Oct 1944	C.
M. Fraser	21 Oct 1944	Doubtful
and Mary E. Gurkin	15 (and 23) Nov.1944	is included as doubtful in Stage 4

Again C denotes intimate contact with the infected group.

As it may appear that I have omitted those cases from the table to avoid upsetting the orderly arrangement of the epidemic into stages, I must briefly give evidence to refute any such suggestion.

Jennie Balls.

On the 18th October, 1944, when I first attended Jennie Balls, I also visited her sister Sheila Balls. The child's illness was similar to that of her sister, in that she had a heavy frontal headache, epigastric pain, giddiness, and that she vomited violently and urgently. It thus appeared that the two sisters had been infected at, about, the same time, presumably from a common source. As Sheila is only 7 years old, the source of her infection could not have been the bakery.

Jean Trewhitt and M. Fraser.

In both instances the onset was so insidious that it was patently impossible to state when the illnesses commenced.

Further evidence pointed to Mrs Fraser having been infected from her husband, who had had a very typical attack.

Mary E. Gurkin.

Included as doubtful in Stage 4 as explained later

Stage 3.

Jean Taylor, S. N. Curry and Arthur Hall all commenced their illnesses on the morning of 29 October, 1944.

I assumed that they had all been infected not earlier than, say, the 2nd October, and not later than the 8th October, from the people mentioned above, which would give an incubation period of from 27 to 21 days.

This assumption was supported by the fact that the last mentioned of the people in "Stage 2" evidently infected his infant son, who became ill on the 30th October; and his wife, who became ill on the 5th November, 1944.

The illnesses in this stage 3 group were clinically almost identical with those of stage 2.

Again the differential white blood cell counts afforded supporting evidence. I give them below:--

Name	Polymorph Leuc.	Lymphocytes	Monocytes.
Jean Taylor	54	42	4.
S. N. Curry	56.5	41.5	2. Eos.1.
A. Hall	48	50	2.

I would also include as belonging to this stage the illnesses of J. G. Burn and W. Palmer. The former dated

his illness from the 6th November, 1944, and the latter gave an interesting story with symptoms dating from the 30th October.

As I intend to devote a section of this work to a survey and discussion of the symptomatology of the outbreak, I will simply state that it appeared obvious that Burns's and Palmer's illnesses were typical of the outbreak, and the differential white cell count showed:

Name.	Polymorph Leuc.	Lymphocytes.	Monocytes.
J. G. Burn	49	47.5	3.5
W. Palmer	54	44	1.5 Eos .5

In the last two cases the incubation period was probably around 28 days.

Stage 4.

The next batch of cases recurred as follows:--

James E. Hocking visited 30th November, 1944.
Mary Charlton consulted 27th November, 1944.
Eliz. A. Johnson, consulted 27th November, 1944.
Mary E. Gurkin, visited 15th November, 1944
and 23rd November, 1944.

I regard the case of J. E. Hocking as of importance in the assessing of the incubation period.

This 14 years old lad started work at the bakery on the 4th November, 1944. Being a beginner, he was in intimate contact with the foreman, W. Palmer, who was at that time a

sick man, although attempting to carry on at work, as his case history shows. After some prodromal symptoms on 23 Nov, 1944, Hocking became acutely ill at 6 a.m. on Thursday, the 30th November, 1944.

This would place the incubation period at 26 days.

In relation to Hocking's illness it was interesting to note that Martha Curnow, a 5 months old infant living in the same rooms at the same address as Hocking, took ill on the 29th December, 1944. Her symptoms were initial vomiting and a mild bronchitis. She had three or four loose motions daily, not watery. The mother aptly referred to it as "not quite diarrhoea." The infant vomited after even the slightest little cough. I frequently observed such illnesses and witnessed the so easily induced vomiting in infants in several homes where cases of Hocking's type had occurred. It thus seemed reasonable to suspect that they represented instances of the present infection, in which case the incubation period would here be 29 days.

The illness of Eliz. A. Johnson seemed typical, with the lethargy so similar to that encountered in cases of infective hepatitis featuring jaundice.

Mary Charlton's history and illness was unmistakably typical of the outbreak, and it featured a relapse. Her differential white cell count read:

Polymorph Leuc.	Lymphocytes	Monocytes.	Eosin.
56	37.5	2.5	4

Mary E. Gurkin.

As I have previously remarked, I thought that this was a stage 4 illness but I could not be certain. I visited her on 15 Nov, 1944, but I then considered that her symptoms were probably prodromal, occurring in the incubation period. She improved, but only temporarily, as I was recalled to see her on 23 Nov 1944. She then has the typical expressionless facies and "dead tired" look, with marked conjunctivitis, frontal headache and giddiness; and I then considered that the illness proper had begun. This was a great difficulty in some of the cases now occurring. Whereas earlier cases had frequently had an acute onset I was now finding, in some cases, a very long prodromal period and the transition to the "actual illness" was so insidious that it was difficult or impossible to state where the prodromal period ended and the post-incubational symptoms began.

However, subsequent illnesses in M. E. Gurkin's home, and in the home of her next door neighbours, who visit daily, seemed to point to her having conveyed the infection to others at those addresses.

Malcolm John Gurkin, age 1 year. Same address as M.E.Gurkin.

Initial vomit. Two weeks' malaise. Then, on 20 Dec., 1944, repeated and violent vomiting, with severe attack of diarrhoea.

Edna Mary Gurkin. Age 43 years. Same address.

Severe "fuzzy or muddled" headache, followed by diarrhoea on 20th December, 1944.

Evelyn Gurkin Age 23 years. Same address.

22 December, 1944. Diarrhoea. Severe nausea caused her to rush to vomit on two or three occasions. But she did not vomit. This fruitless rush was subsequently frequently encountered in the epidemic.

Ernest Harper. Age 10 months. Lives next door to M.E.Gurkin.

17 December, 1944. Vomiting: repeated and violent. Next day he suffered from a sharp attack of diarrhoea.

James Harper. (father of Ernest Harper).

18 and 19 December, 1944. He suffered from diarrhoea and from severe epigastric and upper abdominal pain -- he had no colic. The last two patients are attended by my colleague in the village.

It seemed likely that Mary E. Gurkin had introduced the infection. If so, the incubation period would again be about one month.

Incubation period in Stage 4.

I regard the patients Hocking, Charlton, Johnson, and Gurkin, in this group, as having been infected by the stage 3 group on, or just before, 28 October, 1944. Thus, again, the incubation period approximated to a month. The relays in the homes, if acceptable to the reader, lead to a similar conclusion.

Stage 5.

Margaret Reekie and Alice Price were the next two employees to consult me. In the case of Margaret Reekie

I would be disposed to believe that the illness began on 21/12/1944.

Alice Price had a biphasic illness, so commonly encountered, as mentioned in other groups. She was ill with urgent vomiting and diarrhoea on the early morning of 27 December, 1944.

An interval of almost normal health intervened until 3/1/45, when she had typical symptoms, feeling giddy, limp and listless and showing the typical facies and posture.

Assuming that these two girls had been infected from the members of stage 4, infection might have occurred at any date from 21 November to 30 November, 1944: this would be consistent with an incubation period of one month.

Stage 6.

Mary McEwan fell ill on 31 January, 1945.

The onset of the illness was intense nausea, giddiness, dull frontal headache combined with a feeling of mental dullness, and something just short of frank diarrhoea was as frequently encountered in the epidemic generally. Bradycardia in the presence of pyrexia and marked urobilinuria supported the diagnosis: there was no bilirubinaria. The conjunctivae were slightly jaundiced.

Again, the incubation period appears to have been about a month. However, I could not trace the source of her infection accurately.

Subsequent Course.

I decided to close the record of this outbreak in the

bakery packing department at this stage, as the evidence appeared to suffice for our present study. I thought indeed that the observations of Stages 1, 2, 3, and 4 were ample to illustrate the spread, and the picture would become too involved and difficult especially as I did not attend all the employees. Further cases did occur -- 3 or 4 -- and they gave as their complaint "I work in the packing room. You will know what is the matter with me!" The monthly incubation period continued to apply.

Symptomatology.

In the twenty two cases occurring in the bakery employees only, apart from the patients infected by them, the symptoms encountered were.

1. A relative lymphocytosis occurred in all 15 patients whose differential white cell count was estimated.

	Cases.
2. Headache	16
3. Nausea	16
4. Giddiness	15
5. Abdominal pain (a) (Majority were tender)	13
6. Vomiting	12
7. Lethargy	12
8. Marked Anorexia	11
9. Diarrhoea	9
10. Pains in the limbs	9
11. Marked feeling of weakness	8
12. Heavy sweating	7
13. Rhinorrhoea (mainly in relapses or recurrences)	6
14. Conjunctivitis	5
15. "Ptosis"	5
16. Bronchitis	5
17. Distinct from 15. Tightness round the chest: a sense of restriction or constriction	5
18. Marked mental dulness, complaint of	5
19. The facies of the disease	Very frequently typical.

ADDITIONAL. Insomnia. Paraesthesiae. Cramps. 'Bad taste.' Visual disturbance. Transient deafness. Nocturnal enuresis. Menstrual disturbance. Feeling of 'chill.' Urobilinuria, itch.

The onset frequently occurred at certain times of day.

Relapse occurred in 5 cases.

Recurrence occurred in 3 cases.

Differential White Cell Counts.

Case	Neutrophil Poly.	Lymphs.	Mono.	Eos.	Bas.
1. (Relapse)	57.	36.	3.	4.	—
2.	53.	43.	4.	—	—
3.	59.5	35.5	3.5	1.0	0.5
4.	50.	45.	3.	2.	—
5.	48.	48.	1.5	2.5	—
6.	53.5	39.5	2.0	4.5	0.5
8.	56.5	39.5	2.5	1.5	—
9.	57.5	40.5	2.0	1.0	—
10.	48.	50.	2.0	—	—
11.	49.	49.	2.0	—	—
12.	58.	40.	1.0	1.0	—
13.	57.	37.5	1.5	4.0	—
14.	53.	41.	5.	1.0	—
15.	53.	46.	1.	—	—
17.	56.	37.5	2.5	4.0	—
Approximate Average.	53.5%	42%	2.5%	2%	—

2. Headache.

The headache occurred in one or more of 3 sites. (a) The commonest site was across the brow, especially marked just above the eyes. Although the pain was occasionally severe it was more typically described as being a dull heavy ache and it was frequently associated with a feeling of being 'fuzzy' in the head, the patient feeling muddled or confused or rather stupid, and incapable of clear thinking. In many cases the headache was aggravated when the patient assumed the erect posture, or even raised the head from the pillow.

Occasionally this headache was associated with (b) Suboccipital headache.

This was less frequent than (a). It sometimes occurred in a recurrence when it was absent in the first illness. When associated with (a) the pain was said to encircle the level of the base of the skull being worse at sites (a) and (b).

(c) Headache situated between the eye and the ear was encountered. It was either bilateral or unilateral.

3. Nausea.

This occurred as an initial symptom but also after vomiting had already occurred; occasionally it was not a feature until one or two days after a definite acute onset of the illness. I have only included it as a feature in this section if it was a marked feature in the case. In patients who were confined to bed it was severe and aggravated immediately by raising the head.

4. Giddiness.

This was frequently an early symptom. The patients frequently complained of it but often said that it only occurred on stooping, when they felt like falling forward; or if it occurred at other times it was often fleeting but definite and disturbing. In patients who were confined to bed the vertigo was usually subjective, but objective vertigo also occurred.

Again in patients confined to bed it was acutely and immediately aggravated by raising the head.

5. Abdominal pain.

This was not characteristically very severe, although severe abdominal pain was encountered.

The commonest descriptions referred to a dull ache with a heavy feeling extending right across the abdomen usually at the epigastric level, compared with the discomfort and fulness experienced after a generous meal. One patient graphically described his sensations "as if he had a balloon half full of water dangling in his stomach" --- this was accompanied by nausea. Acute exacerbations of a dull heavy ache was sometimes complained of: in these the additional pain was of a cramp or colic nature and definite nausea accompanied it.

The nature of the abdominal pain when diarrhoea was a feature was interesting and striking. Even when severe purging diarrhoea occurred intestinal colic was not conspic-

uous. More frequently the pain was identical to that in cases having no diarrhoea. Any intestinal colic was not severe and even more severe generalised abdominal pain occurred in the cases with no diarrhoea

5 (a) Abdominal tenderness.

The great majority of the patients were tender to light pressure over the epigastrium and nearly always as marked on similar pressure under the right subcostal margin. Tenderness localised or most marked over the gall bladder was not encountered in this group. The palpation was frequently resented not only on account of the discomfort but because it evoked nausea.

6. Vomiting.

This was frequently preceded by nausea sometimes of up to a week's duration. But a striking feature was that although the patient had been so nauseated in several instances that he (or she) had actually rushed to be sick, or had attempted to make himself vomit, vomiting had not occurred then. And when it did occur it was very precipitate and gave no immediate warning so that the patient vomited at his work or in his bedroom. The vomiting was frequently violent and distressing on this account and because of its frequent repetition. It frequently occurred when the stomach was empty and the vomitus consisted of mucus only.

7. Lethargy.

This was frequently very striking, and was reflected in the facies and appearance of the patient. So much so that the 'slogan' of the disease might be summed up in the expression almost invariably employed by the sufferers --- "I just can't be bothered." I feel that I can not overstress this symptom and I have not laboured thepoint in the case records to avoid monotony. It was a marked prodromal feature , the patient sat in the chair all night after returning from work, just wanting to do nothing but sit. He had no interest in anything or anyone and could not be troubled to do anything of think of anything. The sensation was overpowering. Longer hours of rest in bed did not seem to combat it, but it should be noted that insomnia, at night, was frequently associated--- a combination reminiscent of the cases of Eucephalitis Lethargica which I attended in 1924.

I have not previously mentioned it, but it was sometimes stated to be accompanied by irritability of temper.

8. Marked Anorexia.

Anorexia was almost invariably encountered at some stage of the illness. Surprisingly, in this group as in others, it was sometimes absent even in the presence of vomiting and epigastric discomfort, but this occurred more especially in the early stages of the illness. It was sometimes a prodromal symptom.

9. Diarrhoea.

This was usually preceded by nausea or vomiting or both. In some cases the motions were frequent and soft and the patient described the condition as "not quite diarrhoea," --- more frequently it was frank diarrhoea with profuse watery motions. Acute and severe abdominal pain was not a feature (see 5).

10. Pains in the limbs.

In this group pains in the upper extremity were an inconspicuous feature. Pains in the lower extremities were common. (I would here suggest that this distribution is explained by the fact that these workers are standing or walking all day. The coal miners complained more frequently of shoulder girdle and upper arm pains. Many of them work on their knees, and nearly all use their 'arms' more than their legs as evidenced by their build.)

The lower limb pains were situated usually in one of two positions. Either stiffness and aching occurred in the anterior aspect of the proximal part of the thighs or pain of an aching nature was present in front of the knees and more especially above the patellae.

11. Marked feeling of weakness.

This was frequently a prominent feature. Even allowing for the weakness to be expected from nausea,

anorexia, vomiting and diarrhoea when they occurred, it was frequently striking. In some cases increasing weakness was a prodromal symptom, and it was a feature in cases where convalescence was protracted.

It was reflected in the posture of the ambulant cases.

12. Heavy Sweatings.

The initial nausea was accompanied by sweating as a rule. But apart from this initial sweating, several patients complained of drenching sweats. An elevation of temperature was not a feature in this series and sweats were described as being cold drenching sweats.

13. Rhinorrhoea.

A profuse watery nasal discharge, usually accompanied by bouts of sneezing, was uncommon as an initial symptom. It occurred more often later in the attack or most frequently during a relapse or recurrence.

I thought that this sequence might be of significance.

14. Conjunctivitis.

This occurred independently of symptom 13, and in theabsence of any evidence of respiratory catarrh. In one case smarting in the eyes preceded any evidence of conjunctivitis even on examination with a lens.

In only one case was circumcorneal injection associated with it.

15. "Ptosis."

Many of the patients who were lethargic felt "sleepy eyed."

I have used the term "ptosis" in inverted commas in order to convey the impression that it was not a true complete paralytic ptosis, and to denote however that it was a specially remarked complaint of several of the patients. They said that their (top) eyelids felt heavy and that it required a frequent effort to keep them up, and their eyes open. In one case it affected one side only.

16. Bronchitis.

This was never severe but occasionally it was associated with a mild degree of bronchial spasm.

17. Tightness round the chest.

Several of the patients had a feeling of constriction of the lower half of the thorax. They felt that their breathing was thereby restricted and this led to a sence of dyspnoea.

At times this symptom was associated with the upper abdominal discomfort so that the patient said "he did not know whether to complain of his stomach or his chest" (This was a more prominent feature in cases occurring outwith this series.)

18. Marked Mental Dulness.

The frontal headache was commonly associated with a slightly muddled feeling. In no case did I consider the patient to be noticeably dull mentally --- it was a purely subjective symptom. In several cases it rendered the patient incapable of clear thinking to carry out his duties at work, before he had to absent himself.

19. The Facies of the Disease. (This applies to other series too.)

In this, as in other series, the facies of the patient suggested the diagnosis. This is the more important in the recognition of the disease in the early stages, especially in the prodromal stage as it is then frequently the most definite symptom. Not only are the early symptoms frequently vague but the patient realises this. He probably feels very 'poorly' but he feels that he has nothing to show in the way of feverishness, etc., and can only state, probably, that he feels tired, listless, has admittedly trifling and fleeting giddiness, and that his appetite is poor. Now unfortunately the seriousness of absenteeism during the war, and the great care called for in certification has tended to make the patient feel that he has to prove that he is ill. In other instances, e.g. the mother has told me that "she (the patient) would not come to see you --- she said "the doctor will just laugh at me." Thus in most cases the

ambulant patient's approach to the doctor in consultation is characteristic. A glance suffices for the recognition that the patient is not well. The posture is poor and 'limp' all attempt at 'correct' carriage being abandoned. The face is expressionless or rather it has one set and fixed expression suggestive of apathy, weariness and possibly a hint of nausea. The eyes look dull, the opposite of bright and clear, and the top lids seem to droop. When asked what they feel the matter, they say "Oh, I don't feel well. I just can't be bothered with anything." -- as much as to say that they really are ill.

It is only when one appears to credit and understand their sometimes vague and frequently apparently unrelated symptoms that they reveal the complete symptomatology. Without the recognition of the facies and sympathetic credence, the symptoms would probably not be related by the patient.

Insomnia.

This was sometimes complained of and contrasted with the day time languor.

Paraesthesia.

Pins and needles in the hands occurred in two cases. In one case it was the first and presenting symptom.

Cramps.

In one case cramp occurred in the forearms and hands. In one other case the legs and feet were affected.

'Bad' Taste.

I omitted to note this in the case histories, but it was a very common complaint. The taste was variously described. Sometimes I could get no further than the term 'bad'; more often it was described as a 'stale fat' taste; occasionally as a sour sickly taste; and once as a taste like ink.

Visual Disturbances.

In one case --- in which dimness of vision was remarked there was marked fine circumcorneal injection. The fundus oculi was normal on ophthalmoscopic examination. Visual disturbances were noted in cases not included in this series.

Nocturnal Enuresis.

A return of this complaint after several years of freedom from it was noted in one case. (This complaint was made by Raymond Elliott. Case 10 group. 4.(a jaundiced patient.)

Feeling of Chill.

Some patients felt 'chilly' or "hot outside and cold inside."

Urobilinuria.

This was marked in only 3 cases.

Second Attack.

I have referred in some detail to a 2nd attack of the illness in the case of Elsie Nichols.

The reader is referred to the histories of the two attacks which follow presently --- Case 1.

The interval was some two months from the first to the second attack.

This occurrence is suggestive of a continued presence of the virus (if this epidemic at the bakery was due to a virus) in the body: a matter to which I later refer and discuss.

THE OUTBREAK AT THE BAKERY.

THE MODE OF SPREAD.

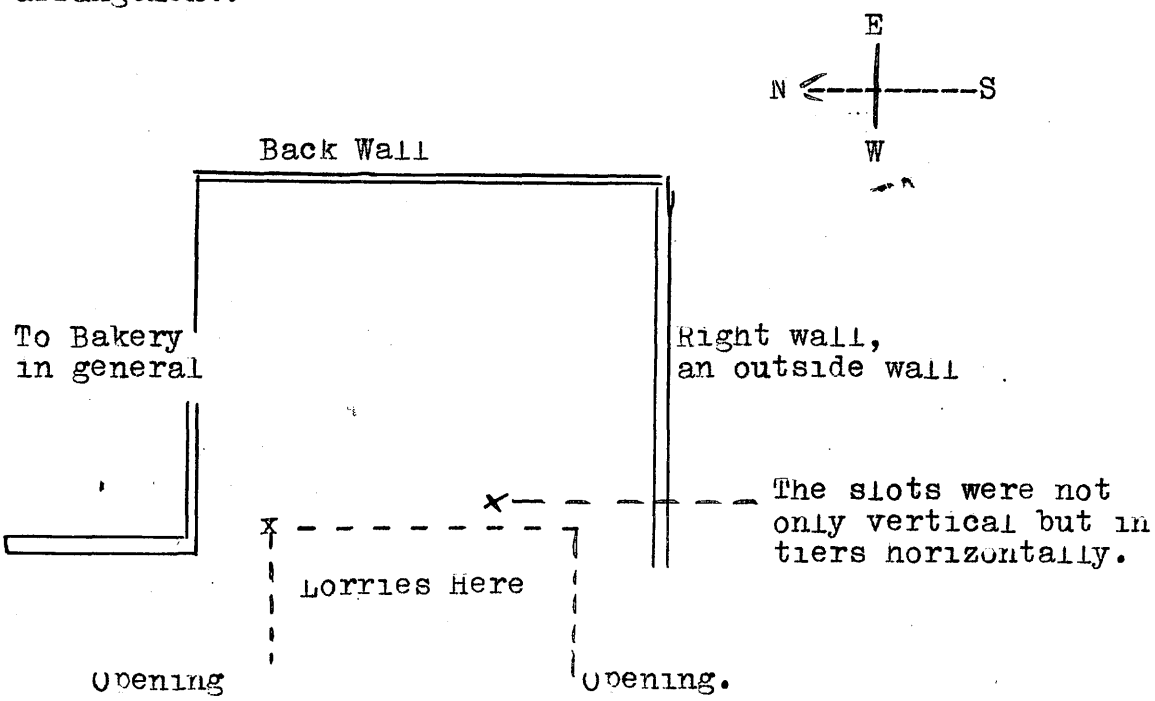
AS HAS BEEN STATED, the outbreak commenced in the packing-room. It did not extend to the bakery in general, in spite of the fact that it persisted in the packing-room from late August until, I believe, March 1945. A very occasional case did occur outside of the packing department, or outwith the people in intimate contact with it, but my generalization holds; 18 of the patients were in close contact with or actually employed in the packing-room: 5 were not.

It was not until May, 1945, that, with the necessary permission, I closely inspected the bakery premises. Not that the necessary permission was so long withheld, but because I had relied on descriptions of the premises. In case the reader may at some time have a similar problem, I would state that I learned more in one hour of inspection than in weeks of deduction based on verbal descriptions of that packing-room, and its surroundings, etc. It is vital to this discussion that the packing-room's construction should be understood.

The first thing I noted was that the packing room was hardly a room, in the accepted sense of the word, at all. It was not a completely enclosed space. The wall facing you as you entered, was a complete wall. On your right was another complete wall. On the left there was a generous

opening in the wall leading into the manufacturing part of the bakery --- it was a large opening, not a door. The front of the "room" was not a wall at all. There were two very generous openings to the right and the left, and between these the front wall simply acted as a scaffolding to lend support to numerous "slots" through which the produce of the bakery was passed, via racks, on large trays, to the lorries assembled for dispatch.

A simple line diagram may serve to illustrate the arrangement.



THE PACKING ROOM.

I at once noted that the packing room, or space, was very well "ventilated." The prevailing wind, partly owing to local causes, is from the South West and it circulated freely in

in this space. Birds flew in and out. The slotted west wall (see diagram) created a series of draughts far in excess of what prevailed in the yard outside. I was told that an airy and cool packing room was to be desired, but the manager added that this packing room exceeded all necessary requirements, indeed to the point of discomfort.

In fact, therefore, a less likely place for the aerial spread of a disease could not be imagined.

This was the conclusion which the manager and the foreman had reached also.

The bakery employes over 300 hands, and there are 16 girls and a few men employed in the packing room. I had attended 8 of those girls and it was believed that altogether 12 out of the 16, at least, had suffered from this same disease. The result was chaos in the dispatch of produce from the bakery. Thus the foreman and manager had given the matter serious consideration, and I was not above considering their observations.

In the large room to the left or north of the packing room, the atmosphere is warm and comparatively still and is, of course, continuous with that of the packing room. The conditions are much more favourable here for the aerial spread of an infection. But no one in this adjacent room was infected

Who were the people not employed in the packing room who became infected ?

Let us simplify the matter by considering the first twelve people to be infected in the bakery i.e. Stages 1, 2, and 3.

The following people were employed in the packing "room".

Elsie Nichols	Rita Gordon	H. Richardson
Margaret Browell	Jean Taylor	S. N. Curry
J. G. Burn	W. Palmer	

The remaining four not engaged in this "room" were:-

J. T. Brewster, A. F. M. Russell, A.Watson, A. Hall.

What did they do and in what way did they come into contact with the packing room ?

Brewster and Watson are bakers. They each produce special products. At times, when the vans call to collect such special goods there may happen to be a temporary shortage in the packing room. On such occasions one of the packing room girls goes to Brewster or Watson and asks for an immediate supply of the desired article. It is then the custom for Brewster or Watson to carry the boards or trays, which the girls have previously been handling, with the help of the girls, out to the waiting delivery vans. Thus contact, indirect contact, could occur.

Russell and Hall are van drivers. They assist the girls to carry the trays or boards to the vans. In this way they are similarly exposed to an "indirect contact" infection.

Now the girls in the packing department are not entirely segregated from the remainder of the employees, outside of

working hours. They travel to and from the bakery with the other workers. Evidently the infection did not spread in this way: e.g. in 'buses.

The determining factor in the spread of the infection was apparently not mere proximity. Aerial spread seemed to be definitely contra-indicated. The essential in the spread was contact.

The spread appeared to copy exactly the serial spread described by Pickles asoccurring in familiesor households in infective Hepatitis and the incubation period was also similar.

If the spread was by such indirect contact, i.e. by contact with a common object, it followed that the infection was conveyed by the hands: in which case faecal contamination of the hands seemed the most likely way in which the object would become contaminated.

Such faecal contamination appeared to me to be a very real possibility, in fact when diarrhoea occurred it was a probability almost to a point of certainty.

It has to be remembered that diarrhoea was frequently most severe in the night hours. The war-time "blackout" was in operation. Picture the weak and limp patient suffering from diarrhoea under such conditions, and it is not difficult to conceive of faecal contamination of the hands. I am loathe to comment adversely on my patients'habits, but it must be admitted in some instances such matters of personal hygiene

leave something to be desired. In some instances the toilet of the hands does not follow the act of defaecation; in others the finger nails are more cared for as regards their fashionable shaping than as regards the possibility of the harbouring of infection beneath their protruding redundancy.

The spread of the threadworm infections in children is a reminder of the potency of such a method of spread.

Finally let me say that the product of "Toilet Facilities" available and "use of such facilities" at the bakery, was less than ideal.

Possibly the above remarks, stated without undue elaboration, will suffice to indicate the very real possibility of faecal contamination by the hands.

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The above is my conception and interpretation of the bakery outbreak. Might I briefly refer to an attractive alternative theory, on, albeit, similar lines, which I considered but rejected ? This in order to demonstrate the lines of my enquiry.

As the packing department staff supplied and loaded the vans, they came into contact with people, van drivers and their friends, from a widespread area: up to 50 miles range. No other people in the bakery did so. The possibility of such an extraneous source of infection had obviously to be con - sidered.

Among the vans coming to Murton Bakery was one from a military camp some 50 miles distant. The packing room girls packed this van. It was not packed by trays; the girls packed the bread, loaf by loaf and layer by layer from the floor upwards. To start the loading they smoothed out a canvas matting on the floor of the van, with their hands. I learned that there were cases of infective Hepatitis (with jaundice) at this camp, where the bread was similarly unloaded. The possibility of infection from this source is obvious, and appeared, dare I say, "attractive."

Further enquiry re dates of delivery, etc., conducted with considerable care and attention to detail, showed that this was not the source, or a source, of infection.

Elsie Nichols.

The fact that this girl had two very similar illnesses, both of which I have recorded, appeared important. The 2nd illness began some 8 weeks after the first. In the interval I did not visit or attend this girl, but I am told, by the patient herself and by her mother, that she was not really well after her return to work on the first occasion. The bakery foreman, an intelligent and 'sensible' observer, had noticed that Elsie was then far from well. From observations in similar cases, to which I later refer, I am disposed to the view that the 2nd illness did not signify a re-infection but, rather, that it was caused by the renewed activity of the virus which had remained in the patient's body.

Case O.

Sheila Isobel Nichols. Age 14 years.
48 Gray Avenue, Marton.
Schoolgirl.

The history is reconstructed from the mother's and child's story, as I did not attend her.

Friday, 4th August, 1944.

She commenced an illness which was the same in every respect to that described in Case 1. -- her sister Elsie. The only difference noted was that while Sheila's legs and thighs ached, she had no cramps.

She vomited very violently and repeatedly --- this was said to be more distressing than in the case of her sister. She had headache, felt giddy and had pain "in her stomach."

She went "because she felt so weak." She had complete loss of appetite.

However she apparently recovered rapidly and returned to school within one week.

BAKERY.

Case 1.

Elsie Nichols. Age 16 years.
48 Gray Avenue, Murton Co. Durham.

This history although retrospective is based on my memory of the case aided by the patient.

For a few nights prior to August 27th, 1944, she had 'cramps' in her legs. On 27th August, 1944, a Sunday, she vomited and and lay on the settee all day. She complained of upper abdominal pain.

Monday, 28th August, 1944.

She vomited at work. She had cramps in her legs. She felt giddy --- intensely giddy. Severe frontal headache.

Tuesday, 29th August, 1944.

Vomited and refused all food.

Wednesday, 30th August, 1944. Visited.

Off work. Feels sick and giddy, especially if she sits up. Complete anorexia. Could not take tea, to which she is partial. She lay on the couch prostrated, 'lifeless'. Very heavy night sweats. 'Stomach' pain.

She improved gradually and resumed work on:

Wednesday, 6th September, 1944.

Still far from feeling well and feels sickly in any warm atmosphere at work.

She works in close association with Rita Gordon (q.v) Hilda Richardson (q.v.) Margaret Browell (q.v.)

Described as Stage 1. Summary of Symptoms.

28 August, 1944

1. Cramps in legs.
2. Vomiting.
3. Giddiness.
4. Frontal headache.
5. Giddiness and nausea increased by sitting up.
6. Anorexia.
7. Heavy sweating attacks.
8. Listlessness.

Case 1.

Second Attack.

Elsie Nichols.

Sunday, 22nd October, 1944.

Epigastric pain. Vomited twice.

Monday, 23rd October, 1944.

Off work. Giddy. Headache extending from the suboccipital region to above the eyes.

Tuesday, 24th October, 1944.

At work but feeling very sickly.

Wednesday, 25th October, 1944.

At work but feeling very sickly all day and vomited.

Thursday, 26th October, 1944.

At work but feeling very sickly all day and vomited.

Friday, 27th October, 1944. Visited.

At work but vomited and had to come home as she was so weak.

She looked exactly as during the first attack.

She appeared to be feverish, owing to a dull red suffused flush on the cheeks --- very similar to that seen in many jaundiced patients but the temperature was not elevated.

There was no urobilinogenuria.

Wednesday, 1st November, 1944.

Feels tired and listless.

Watery nasal discharge. Sneezing frequently.

Upper respiratory catarrh with cough.

Blood Test. 27th October, 1944.

Poly. Leuc.	-- 57
Lymphocytes	-- 36
Monocytes	-- 3
Eos.	-- 4

.....

Summary of Symptoms. Second Attack.

1. Epigastric pain.
2. Vomiting.
3. Giddiness
4. Headache -- frontal and suboccipital.
5. Flushed cheeks but afebrile.
6. Tiredness. Lethargy.
7. Watery rhinorrhoea, and sneezing developed later
8. Relative lymphocytosis.

Case 2.

Rita Gordon, Age 17 years.
14 Toft Crescent, Murton.

Wednesday, 11th October, 1944. Consultation.

She has been feeling sickly for about a week, and at times she has felt chilly.

She went to work at 7 a.m., and at 8.30 a.m. she had her breakfast (at work). After that she felt ill- her meal seemed to "just lie uneasily" in her stomach and she wished she could vomit, but she could not vomit. She developed a severe frontal headache and she had a "muddled feeling". Later she did vomit. She has had heavy drenching sweats.

Friday, 13th October, 1944. Visited.

She has had two very restless nights, tossing and turning and her legs aching. She is normally a very sound sleeper. Her eyes smart and she has a mild degree of conjunctivitis. She feels very lethargic. Pulse 82. Temperature normal.

Klein Test. --- ve result.

No Urobilinuria.

Differential White Cell Count.

Poly. Leuc.	53
Lymphocytes	43
Monocytes	4

Monday, 16th October, 1944.

Conjunctivitis and blepharitis present.

She is eating a little but she still has a fleeting sickliness at times. Feels very weary and tired.

Gradual recovery marked by lassitude and by her being very easily fatigued for next three weeks.

.....

COMMENTS.

1. Onset at 8.30 a.m.
2. Muddled feeling with headache.
3. Conjunctivitis --- Blepharitis.
4. Daytime lethargy. Night time insomnia.
5. Klein Test -- ve.
6. No Urobilinuria.
7. Relative Lymphocytosis.

Case 5.

Hilda Richardson. Age 16 years.
38 Watkin Crescent, Murton.

Sunday, 8th October, 1944 (History).

She had upper abdominal pain while at work. Suddenly, with no preceding nausea, she vomited, and this was frequently and violently repeated.

Monday, 9th October, 1944. Consultation.

She has a dull heavy frontal headache. She has sweated freely and she feels that she is "going hot and cold." The appetite is poor to moderate. The toungue is clean and moist. The bowels acted normally. Pulse 96. Temperature normal. She is tender over the epigastrium and below the right costal margin.

She improved uneventfully until:

Sunday, 15th October, 1944.

Headache and epigastric pain returned with pain over the right lower ribs (over the liver), and she felt tired, 'useless', disinterested in everything and extremely weak

Differential White Cell Count. 9th October, 1944.

Polymorphs.	59.5
Lymphocytes	35.5
Monocytes	3.5
Eos.	1.0
Basophil	.5

Relapse.

Wednesday, 6th November, 1944. Consultation.

For the past 48 hours she has had umbilical pain.

The pain is said to fluctuate but is not of a colic nature. It is described as a severe dull ache with exacerbations.

She feels sickly but states that her appetite is not affected :

She has profuse watery rhinorrhoea and frequent bouts of sneezing.

Again gradual recovery occurred.

Recurrence.

Saturday, 30th December, 1944. Consultation.

She vomited urgently last night. The vomiting was repeated at short intervals all through the night. She again had the dull 'muddled' frontal headache.

Again a gradual recovery ensued.

Case 4.

Margaret A. Browell. Age 15 years.

6 Murton Street, Murton.

Monday, 16th October, 1944. Inquiry Visit.

I called to see her as I heard that she had been ill at work on Monday, 9th October. She said that she had had a frontal headache and vomited on the 9th October, but that she had felt quite well since then. I obtained a blood film --- she had just returned from work.

Differential White Cell Count.

Polymorph.	50
Lymphocytes.	45
Monocytes.	5
Eosinophils.	2

.....

Wednesday, 18th October, 1944. Visit.

She is ill to-day. Last night she began to suffer from a bitemporal headache: mainly accurately localised to from above the outer third of the supraorbital ridge and the ear. She had an aching across the abdomen -- over the epigastrium and the hypochondrium on both sides. At intervals there was a superadded cramp pain and she felt she was going to vomit. Diarrhoea occurred. She was thirsty. This morning (Wednesday, 18th October), she awoke after a sound sleep, and arose at 6 a.m. to go to work. She

immediately felt intensely giddy, had a return to headache as described, upper abdominal pain, and profuse diarrhoea. The vertigo was objective ---"everything seemed to spin round." She did not vomit.

She feels less giddy lying down but if she attempts to sit up all her symptoms (I do not include diarrhoea) return.

The tongue is clean. It is dry.

She complains of pains in the legs -- below the knees.

Case 5.

John T. Brewster, Age 31 years.
9. Station Road, Murton.

Monday, 9th October, 1944.

He felt giddy at 7 a.m. when he set out for work. He vomited twice at work. He had a marked but dull pain extending right across the upper abdomen, and a dull heavy frontal headache. He thought that the vomit looked like 'altered' blood. (I did not see it). He came home at noon, and I saw him at 1 p.m. The pulse was 60 per minute. The temperature was 98.2°F. He was tender in the epigastrium (but in view of the ? haematemesis, I did not palpate much).

He felt sickly and thought he would vomit again at 10 p.m: but he did not.

Tuesday and Wednesday, 10th and 11th October.

Complete lack of appetite. Feels very sickly especially in the morning. Headache persists.

Recovered gradually and by Monday, 16th October, resumed work.

Differential White Cell Count.

Polymorph	48
Lymphocytes	48
Monocytes	1.5
Eosinophils	2.5

Case 6.

Alfred F. M. Russell. Age 27 years.
11 Doxford Terrace, Murton.
Van Driver.

History.

He was discharged from the army suffering from a duodenal ulcer.

Saturday, 7th October, 1944.

He had a heavy feeling in the epigastrium. He felt giddy and had a dull 'muddled' frontal headache. He vomited. The appetite was very poor and he felt intensely 'sickly' after every bite of food.

Since then he has felt extremely listless, and unless forced he sat motionless in his chair caring neither to think, take an interest in anything, nor do anything.

Every morning he felt as if he could vomit in his first journey -- 7.30 a.m. to 8.30 a.m.

Saturday, 14th October, 1944.

Lethargy became extreme. He only carried on at work as it was a half holiday.

Sunday, 15th October, 1944.

He continued to eat but he felt he was going to vomit. He had a feeling of fulness and tightness across the abdomen at and above the umbilicus: it was "as if he had a balloon half full of water dangling in his stomach."

Monday, 16th October, 1944. Visited.

He vomited several times through the night and this morning. Heavy cold sweating occurred during the night and he felt extremely restless even when he was not vomiting. His pulse was 62. Temperature was 98.0 ^{o} F.

He is tender in the epigastrium and over the right subcostal region arteriorly. The liver is not palpable.

Differential White Cell Count.

Polymorph.	53.5
Lymphocytes.	39.5
Monocytes.	2.0
Eos.	4.5
Basophil.	.5

On Tuesday, 17th October, 1944.

He felt much better.

Wednesday, 18th October, 1944.

Severe epigastric pain accompanied by marked tenderness began in the afternoon and was followed by a sharp bout of profuse watery diarrhoea. The pain then eased considerably.

Saturday, 21st October, 1944.

He is up and about. Marked loss of weight has occurred. The pulse is 100 per minute. He is very tender over the liver which is just palpable. He says he "could hardly say he has a headache, it is a dull

muddled sensation in the brow --- a heavy feeling and a sort of 'depression' above the eyes."

Convalescence was slow, subject to fluctuation and weakness, and lethargy persisted after his return to work.

Case. 7

Mr. A. Watson. Age 39 years.
Cairns Buildings, East Murton.

Histories obtained from Dr. R. Mackinnon.

6th October, 1944.

He could not eat his lunch. He had no appetite and he felt that he was going to vomit. Later he suffered from a dull frontal headache and pain across the trunk anteriorly at the level of the epigastrium. Presently he vomited and had diarrhoea, both of which continued all through the night.

Recovery was rapid and complete.

Michael D. Watson. Age 1 6/12 years.

30th October, 1944.

He looked pale and exhausted, was completely 'lifeless' and uneasy. He refused all food --- he would not attempt to eat at all. Next day diarrhoea commenced and continued for 48 hours. At night he was very restless and disturbed and he slept very little. He did not regain his appetite until 5th November, whereafter he recovered gradually.

On the 9th December he suffered from a right sided parotitis: the left gland was involved later.

Ann Watson. Age 36 years.

5th November, 1944.

She felt tired and completely lacking in energy and suffered from a unilateral temporal headache. She had pains in her fingers, her thighs and legs, described as being "like stabs of a needle." Also she had a 'pins and needles' sensation in her fingers and hands.

On the 6th November she had pain in the epigastrium, she vomited frequently and violently all day. After two or three days complete anorexia she began a gradual convalescence.

Case 8.

Jean Taylor. Age 18 years.
44 Gray Avenue, Murton.

Sunday, 29th October, 1944.

Loss of appetite. Brow headache.

Monday, 30th October, 1944. Consulted.

This morning she felt very sick and this has continued all day. She is very dizzy. There is a complete loss of appetite.

She has a lifeless pale expression and looks sickly.

The tongue is very clean and watering freely.

Pulse 84. Temperature 98.

Absolutely no other symptoms.

Urine. Nil abnormal detected on testing for Specific Gravity colour, albumin, sugar, bile, urobilin.

Blood.		
	Polymorph. Leuc.	56.5
	Lymphocytes	39.5
	Monocytes	2.5
	Eosinophils.	1.5

1st November, 1944.

Feels poorly. Pulse 120. Frontal headache.

Temperature normal.

She just wants to sit and do nothing. She has no desire for food. She has night sweats.

Case 9.

S. N. Curry. Age 25 years.
54 Calvert Terrace, Murton.

Sunday, 29th October, 1944. History.

At 11 a.m. he bent down to fasten his bootlaces and he felt very dizzy. He felt very sickly and tried to induce vomiting but failed. An hour later he was violently sick. The vomiting when it did occur was very precipitate. He continued to feel giddy and he had a heavy suboccipital headache. Profuse sweats occurred -- cold sweats.

Monday, 30th October, 1944.

He went to work and "it all started again", vomiting followed the drinking of a cup of tea which was instantly rejected. He vomited repeatedly after that, the vomited matter being said to resemble rice. Later nothing was vomited although violent retching continued. He continued at work.

Tuesday, 31st October, 1944. Consultation.

Again this morning the vomiting and retching recurred. "He can't keep his eyes open, the lids feel so heavy, and he keeps blinking as he can't see clearly at times. If he looks at e.g. a row of houses they seem to fluctuate in size, at first becoming smaller and smaller."

He feels listless and lethargic to a degree. He has a dull,'dazed', frontal headache and he complains of

aching and sharp pains in his thighs.

The temperature is 98.° F. Pulse is 70 per minute.

The skin is moist and clammy.

Differential White Cell Count.

Polymorph. 57.5

Lymphocytes. 40.5

Monocytes. 2.0

Eosinophil. 1.0

Friday, 3 November, 1944.

He complains that he cannot see clearly. "He tries looking at things but he does not see them properly." The conjunctival vessels are injected --- a coarse peripheral injection with a very fine circumcorneal injection: and the eyes look 'dirty'.

Loss of appetite continues to be marked.

He has a headache extending from above the eyes to the suboccipital region. Also complains of aching in the thighs anteriorly and proximally and just above the patellae. Rather atypically he states that he feels well in the morning, poorly by tea time and brighter again at night.

The pulse rate rises markedly when he stands up,-- jumping from 60 to 100 per minute.

Case 10.

Arthur Hall. Age 27 years.
5 Cedar Crescent, Murton.
Van Driver.

Tuesday, 31 October, 1944. History.

He states that on Sunday, 29 October, 1944, at 7 p.m. he felt sickly. He had 4 profuse watery stools. Thereafter he vomited precipitately and violently, and he was purged every 20 minutes until 5 a.m. He had pain all over the abdomen but mainly in the upper abdomen. It was not of a severe colic nature. He had no headache or giddiness, in fact there was no other symptom apart from weakness as would be anticipated.

Monday, 30 October, 1944.

He stayed at home. He felt sickly all the day, and vomited 4 or 5 times --- not forcibly. He had 4 or 5 loose motions.

Tuesday, 31 October, 1944. Consultation.

His 'leading' symptom to-day is that he feels tight round the chest --- he points to the lower half of his thorax --- and that he keeps sighing as his breathing feels tight and restricted. He continues to feel rather sickly, weak and generally off colour. The facies is striking: an expressionless mask depicting extreme fatigue and nausea. The upper lids droop as if he was with difficulty keeping them open at all. The pulse is 58 per minute. The temperature is normal.

The skin is moist. The tongue is clean and moist. He says that he sweats heavily.

Differential White Cell Count.

Polymorph. 48

Lymphocytes. 50

Monocytes. 2

Saturday, 4 November, 1944.

He looks weak and sickly but states that he is all right now, and he resumed work.

Relapse.

On the night of 9th to 10th November, 1944.

Recurrence of diarrhoea. He had 7 or 8 loose motions. He felt very distended in the abdomen.

Recurrence.

Friday, 12 January, 1945.

He has had diarrhoea from 11 p.m. Wednesday.

No sickness this time. On this occasion he does complain of a slight dull frontal headache, and he says that his head feels "thick and muddled". He remarks that the abdominal pain is not at all colic like: it is a steady pain as if due to "wind" on the stomach."

Tea or food causes diarrhoea to recur.

Case 11.

John G. Burn, Age 37 years.
9 Webb Avenue, Murton.

Thursday, 9 November, 1944. Consultation.

History. On Monday, 6 November, 1944, he felt extremely weak and he felt sickly. The latter symptom was not continuous or very marked. He had a severe headache extending from the suboccipital region to above the eyes. He felt slightly muddled --"his head was not clear."

His thighs felt stiff and weak and they ached, especially anteriorly and proximally.

On Wednesday, 8 November, at work he did nothing at all practically. He felt useless mentally and physically. He had "no energy, enterprise, or initiative, in fact he felt unable to walk about from sheer lack of power."

To-day, Thursday. 9 November, 1944.

He has diarrhoea. It is quite painless and the motions are watery and profuse. The facies is again striking and alone suggests the diagnosis as in Cases 1 and 10. He has no desire to eat. The temperature is normal. The pulse is 78 per minute. He is tender in the epigastrium and on pressure over the right subcostal margin and such pressure makes him intensely nauseated.

Differential White Cell Count.
Ploymorph. 49, Lymp. 49. Monocytes 2.
Subsequent gradual and uneventful recovery.

Case 12.

William Palmer, age 45 years.
4 Coronoation Street, Murton.
Foreman. Packing Department.

Thursday, 2 November, 1944. History.

He felt exactly as one does after a too generous meal -- blown up and uncomfortable. He vomited and was better for a time, but the distension and discomfort recurred, localized to the epigastrium, and he was very giddy.

By Sunday, 5 November, 1944, he felt much better but was very thirsty and drank water freely.

Monday, 6 November, 1944. Consultation.

To-day he again feels 'poorly and out of sorts.' He has a complete lack of appetite and thw abdominal fulness is more marked than ever. His mouth feels "claggy" (a Scot's Term) and his head feels swollen and "thick" (not clear). He is giddy, at times very giddy. The facies is typical -- dull and weary, and he looks 'sleepy eyed.' The eyes are very markedly bloodshot and the conjunctivae look jaundiced, but I think it is not a genuine jaundice.

Since 2 November, 1944, he has attended at the bakery. He says that he has been unable to think clearly and had to relegate his duties to others. Prior to this, on Tuesday, 30 October, he was deaf, but after 48 hours

his hearing returned to normal. He has no cerumen in the meatus, the tympanum of each ear is healthy and he did not describe any naso pharyngeal catarrh.

Friday, 10th November, 1944. Consultation.

He complains of intolerable itching all over his body. Conjunctival injection is gross -- it is peripheral and centripetal. His eyes feel, he says, as if they were full of hot sand. He has no diarrhoea but the past two mornings he has had one watery motion, "just as if he had taken a strong morning saline."

He is tender over the epigastrium and in the right subcostal region and palpation evokes marked nausea.

He remarks that although he feels sleepy during the day, he is restless and sleeps hardly at all, at night.

Differential White Cell Count.

Polymorph	58
Lymphocytes	40
Monocytes	1
Eosinophils	1

By the 18th November, 1944, the itching and conjunctivitis and all other symptoms had cleared up and he started work next day.

Case 13.

Jennie Balls. Age 16 years.
9 Watkin Crescent, Murton.

Wednesday, 18 October, 1944. Consultation.

History:— She states that for two or three weeks she has had a headache, especially on the right side where it is accurately localized to the area between the lateral extremity of the eyebrow and the pinna. Her right eye lid has seemed to sroop and she has constantly to be raising it. She has felt giddy but only if she has stooped e.g. to fasten her shoe-laces.

Yesterday she had severe cramp pain in the epigastrium extending down to the umbilicus and across the lower ribs.

Neither her appetite nor her bowel action is disturbed. She has a weal feeling, with stiffness and aching in the thighs, but this occurs only on standing.

The temperature and pulse are not affected.

98 ^{o} F and 78 per minute.

Defferential White Cell Count.

Polymorphs	57
Lymphocytes	37.5
Monocytes	1.5
Eosinophils	4.0

Thursday, 19 October, 1944.

At 10 p.m. she had a very severe attack of peri-umbilical and epigastric pain lasting for 2 hours.

She has eaten nothing all day -- complete loss of appetite.

Saturday, 21 October, 1944.

She complains of severe headache -- "in the mornings it is dreadful." The tongue is clean and moist. She has had no further abdominal pain. To-day she mentioned that for the past two weeks she has had pains in her wrists and "pins and needles" in her fingers and hands.

Tuesday, 24 October, 1944.

Headache continues.

Pain marked under right lower ribs.

She feels weak and tired and she still feels that she is far from well.

Relapse.

Saturday, 28 October, 1944.

The abdominal pain returned again to-day, and the headache became worse after having considerably improved. She has a profuse watery rhinorrhoea and is sneezing frequently. She complains of chilly sensations.

Wednesday, 8 November, 1944.

She still has abdominal pain, "off and on", at intervals.

She resumed work on 13 November, 1944.

Case 14.

Jean Trewhitt, Age 19 years.
45 Calvert Terrace, Murton.

Friday, 20 October, 1944. Consultation.

She stated that she had been menstruating for 14 days. Her periods are usually of five days duration.

Further, the period began one week before it was due. She is of very regular menstrual habit, normally. She went to work to-day but she had to return home as she felt sickly. He head was aching, and she felt lazy and sleepy at work. She could not think about what she was doing and felt "dazed and stupid." Consequently she did little work. Her thighs are stiff and they ache above the patellae and in the "thick of the thighs" anteriorly especially if she stands. She looks dazed, dull, and stupid.

In view of the similarity of her appearance and features in her symptomatology to similar features in the epidemic, I made a blood film. The result was:—

Differential White Cell Count.

Polymorph.	53
Lymphocytes	41
Monocytes	5
Eosinophil	1

She made a gradual recovery but loss of appetite and lethargy persisted for over a week.

Case 15.

May Fraser, age 59 years.
1 Turnbull Crescent, Murton.

Saturday, 21 October, 1944. Consultation.

She complained that she has had pains in the knees and small of the back for over a fortnight. The pains are worse if she is going up, or down, stairs.

She is particularly worried about her hands. In the morning when she awakes her hands are burning and "all in pins and needles" up to her elbows and down to her finger tips.

She 'rings' and rubs her hands and forearms and eventually has to have someone else to do so before she obtains relief. In view of Jennie Balls's complaint of paresthesia and May Fraser's association with her, I took a blood film, although I considered that Mrs. Fraser was of a neurotic type.

Differential White Cell Count.

Polymorph	53
Lymphocytes	46
Monocytes	1

Tuesday, 24 October, 1944.

The burning and pins and needles are accompanied by 'cramps' in the fingers, hands and forearms.

She enjoyed her breakfast to-day but soon afterwards she felt very giddy and sickly. She rushed to vomit but she did not vomit. The tongue is clean and

moist. Pulse ~~if~~ is 72 per minute and temperature is normal.

After this her appetite became very poor and she continued to have attacks of feeling sick and giddy. She felt sleepy by day and sleepless by night. She developed bitemperal headache. She complained that her mouth had a taste like ink.

By Saturday, 11 November, 1944

She had improved but her appetite was very moderate and she felt "run down" and weak.

She resumed work on 19 November, 1944.

Case 16.

James E. Hocking. Age 14 years.
67 Calvert Terrace, Murton.

Tuesday, 30 November, 1944. Visit.

History:— This youth started work at the bakery — in the vicinity of many of the preceding patients — on Saturday, 4 November, 1944.

On Thursday, 23 November, 1944, he states he had a heavy frontal headache and epigastric pain, and he felt very weak. But within 24 hours he felt fully recovered.

At 6 a.m. to-day, 30 November, 1944, the headache recurred and he says he "felt as if something was pulling his stomach out." The pain was acute and he vomited violently several times. After that he felt absolutely 'useless',weak, lifeless and drowsy. If he lies flat he does not feel quite so bad apart from being weak and drowsy but as soon as he lifts his head from the pillow the epigastric pain returns, he feels giddy and thinks the room is going round and the headache is aggravated. The facies was exactly as described in Case 1.

For a few days he had complete lack of appetite but all the symptoms gradually cleared up without any relapse.

Case 16 a.

Martha Curnow, age 5½ months.
67 Calvert Terrace, Murton.

She lives in the house of J. E. Hocking (Case 16).

Wednesday, 3 January, 1945 Visited.

History. On Friday, 29 December, 1944, she appeared to lie taking no interest in any one. She appeared to be "lifeless" and she refused most of her feeds. She vomited several times. The very slightest cough led to immediate vomiting. Very often the attempts to vomit, retching, leads to no vomit except a little mucus. To-day she resents pressure on the upper abdomen and appears to be tender.

She has a mild 'medium tube' bronchitis.

The temperature is 100 ^{o} F.

She improved a little until my visit of Saturday, 6 January, 1945.

when she took ½ to ¾ of each feed. Since Wednesday she has had what the mother terms "not quite diarrhoea" --- the motions being much softer than usual and more frequent (4 motions instead of her usual one or two).

The temperature was normal.

Recovery was steady and no relapse occurred.

Case 17.

Mary Charlton. Age 17 years.
2 Toft Crescent, Murton.

Monday, 27 November, 1944. Consultation.

History. For the past few weeks she has not felt well. Her eyes smarted and watered and she felt that "she had no strength." She had pain in the epigastrium and she felt that she was "not able to get her breath" owing to a tightness round the lower ribs.

To-day, 27 November, 1944, she feels very giddy and this is noticeably more marked after she eats a meal. She complains of pains -- aching -- if front of, and just above, her knees. The tongue is clean and moist. She fainted as she spoke to me. I noted that the face did not go pale when she fainted. The temperature was normal.

Differential White Cell Count.

Polymorph	56.0
Lymphocytes	37.5
Monocytes	2.5
Eosinophil	4.0

Monday, 4 December, 1944.

Epiggstric pain continues and she has pain between the scapulae. She complains of a'bad' taste in her mouth. Again she fainted. (Nervousness ?).

She returned to work on 15 December, 1944.

Relapse.

Saturday, 6 January, 1945. Visited.

She now states that she was not well after she started work. She had no desire for food and she 'never' went out at night after work.

On Sunday, 31 December, 1944, she did go out, but on her return she was exhausted. She just lay on the couch and could not be bothered with anything or anyone.

Since Thursday, 4 January, 1945, she has had a severe suboccipital headache, complete anorexia and epigastric fulness and discomfort.

She presents a picture of extreme fatigue and exhaustion. The skin is very moist and clammy. She complains of drenching cold sweats.

Recovery was uneventful. Complete rest in bed was the main treatment.

Case 18.

Elizabeth A. Johnson. Age 18 years.
8 Landsbury Drive, Murton.

Monday, 11 December, 1944. Consultation.

She had been off work ill since:

27 November, 1944.

Her leading symptom was "overpowering sleepiness." Every night she had gone to bed at 6 p.m. to be ready for work in the morning, at 7 a.m. In spite of this, she felt very tired on rising and as she graphically expressed it, she felt that she could "sleep her head off." During this period of time she has felt sickly and thought frequently that she was going to vomit and she has taken purgatives to see if that would relieve her of the nausea.

When she had been one week off work she developed a 'head cold' with profuse watery rhinorrhoea and she sneezed a great deal. She has felt giddy especially if she stoops or stands up after sitting.

The facies is typical --- expressionless, as a mask: heavy lidded, sleepy looking and apathetic.

I did not take a blood film. I thought she was somobviously suffering from the epidemic illness and time was not available.

Case 19.

Mary E. Gurkin. Age 19 years.
19 Turnbull Crescent, Murton.

Wednesday, 15 November, 1944. Visit.

For the past week she has felt weak, lacking in energy and generally out of sorts. She is listless and has no interest in anything — she says she just cannot be bothered with anything. She has had a 'catarrhal cold' with nasal discharge and a "throat" cough.

To-day she complains of a crushing sensation in the epigastrium and right across the 'lower chest.' She feels chilly at times and she is very tired, and she looks it.

This normally vivacious girl is lying in bed with no rise in temperature and a pulse of 84.

She did not complain of headache or loss of appetite.

She improved gradually.

Thursday, 23 November, 1944.

The symptoms are now more typical of the epidemic. She is again weary, tired and listless. She has complete loss of appetite and feels sick at the mention of food. She has the dull heavy frontal headache extending to the suboccipital region which we have previously encountered. If she sits up she immediately feels giddy, has upper abdominal discomfort and is nauseated. The conjunctival vessels are grossly injected and her eyes

smart. The cough continues troublesome and she has some large tube bronchitis.

Cases 19 a, b, c, d, and e.

(a) Malcolm John Gurkin. Age 1 year.
19 Watkin Crescent, Murton.

Thursday, 21 December, 1944. Visited.

He has been obviously poorly for the past two weeks, having no life about him. He has taken little interest in his parents and appeared to be quite apathetic. At the beginning of this period he vomited once or twice -- the first day only.

Yesterday he vomited violently and repeatedly. The vomiting is described as alarming in its violence. He had diarrhoea. To-day 21 December, 1944, he has vomited twice but not violently and the diarrhoea continues. The temperature is 99.2 ^{o} F.

(b) Evelyn M. Gurkin, the infant's mother. Age 23 years.

She is suffering from diarrhoea, pain is not marked, and she feels intensely sick. She has rushed to vomit several times but she could not vomit.

(c) Eda Emma Gurkin, the grandmother, Age 43 years.

On Wednesday, 20 December, 1944.

She suffered from diarrhoea and for 72 hours she had a severe dull frontal headache accompanied by a "fuzzy" muddled feeling in the head.

Case. 19.

(d). James Harper. Age 35 years.

On Monday, 18 December, 1944, and Tuesday he suffered from diarrhoea.

(e). Ernest Harper. Age 10 months.

On Sunday 17 Deember, 1944, he vomited 2 or 3 times and on the Monday he suffered from diarrhoea.

Case 20.

Margaret Reekie. Age 21 years.
12 Talbot Street, Murton.

Friday, 22 Deeember, 1944. Consultation.

Yesterday she had periumbilical and epigastric pain. She compares the pain to the discomfort she has at her menstrual periods -- a dull severe ache with a feeling of fulness. Diarrhoea began yesterday in the morning and continues. She feels shaky and weak but makes no other complaint. She looks waery and dispirited. Pulse 88. Temperature 98 ^{o} F.

The diarrhoea continued until 27 December, 1944.

She then felt sickly after meals. She has a dull heavy supraorbitral headache.

Friday, 29 Deeember, 1944.

She sits down to eat anticipating that she will take a good meal, but whenever she starts to eat her appetite invariably fails at once.

Friday, 5 January, 1945.

She feels sickly and the headache continues -- a dull, heavy, frontal ache. Her "head does not feel clear." She now has a copious watery nasal discharge and a troublesome cough: also frequent attacks of sneezing.

Case 21.

Alice Price, Age 37 years.
7 Aged Miners' Homes.
Bakery cleaner.

Wednesday 3 January, 1945. Consultation.

On Wednesday, 27 December, 1944, she vomited 3 times on rising at 7 a.m. The vomiting was urgent and severe and recurred 2 or 3 times until 5 p.m. She had one or two watery stools.

On Thursday, 28 December, she again vomited, at 8 a.m., diarrhoea again occurred and lasted all day. But on Friday, 29 December, she felt better, having no vomiting and no diarrhoea.

This (3/1/45) morning she felt very dizzy on rising and she now feels limp, listless, lazy, lifeless — she finds every little thing a trouble and had to force herself to come to the surgery to-night.

She is nervous and the pulse rate is 120. There are numerous extrasystoles.

Sunday, 14 January, 1945.

She had another 12 hour attack of diarrhoea and vomiting accompanied by epigastric pain.

Case 22.

Mary McEwan. Age 14 years.
22 Pilgrim Street, Murton.

Wednesday, 31 January, 1945. Consultation.

She started work at 6.45 a.m. At 10.30 a.m. she felt intensely nauseated. She tried to vomit,(including using hot tap water as a possible emetic) but she could not be sick. Then she felt chilly and she has since had very troublesome frequency of micturition.

Her eyelids feel heavy and it is "an effort to keep her eyes open." She complained of a heavy, dull "fuzzy" frontal headache and if she stoops she has to hold on to anything handy in case she falls forward as she is then very dizzy.

The bowels have acted 4 times in the past 10 hours and the motions are not formed.

Friday, 2 February, 1945. Visit.

I received the information that she 'wet the bed' on Sunday night. Also that on 1 February, 1945, she was ill, suffering from shivering, giddiness -- vomiting for one day only.

To-day she is in bed. She has a cough with evidence of bronchitis attended by a slight degree of bronchial spasm. The face is flushed -- a dull

red daubing of the cheeks. The conjunctivae are slightly jaundiced. She complains of dizziness which is marked if she sits up. She has a frontal headache. The temperature is 100.2 ^{o} F. The pulse is only 84 per minute.

The urine is pale and contains no and no albumin or sugar, but there is a moderate amount of urobilinogen present.

She made a steady uneventful recovery.

INFECTIVE HEPATITIS AND ASSOCIATED MALADIES

BEING AN ANSWER TO

" AN APPEAL "

AS MADE BY W. N. PICKLES M.D.

IN HIS

"EPIDEMIOLOGY IN COUNTRY PRACTICE"

(Bristol 1939)

Entia non multiplicanda praeter necessitatem

SUBMITTED AS A THESIS FOR THE

M.D. DEGREE OF GLASGOW UNIVERSITY

BY

A. K. MacRae, M.B.,Ch.B.

INFECTIVE HEPATITIS IN MURTON.

The following section deals mainly with those illnesses in which jaundice was present.

It refers to 39 such illnesses, not including the illnesses previously described, which occurred at Cold Hesledon.

The sources and the mode of spread of the epidemic are discussed.

The incubation period is considered.

(A detailed review of the symptomatology of the outbreak is provided in the next section.)

In discussing the mode of spread reference is made to several illnesses in which jaundice was not a feature.

Case Histories of all the illnesses to which I refer are provided.

Illnesses attended by Clinical Jaundice.

In the following table there will be found, numbered 1 to 39, those cases which I attended in Murton between June 1944 and April 1945, in which clinical jaundice was a feature.

Five patients who were attended by Dr. R. Mackinnon are included in the list. I attended three of these patients only. To distinguish Dr. Mackinnon's patients I have numbefed them A. B. C. D. and E. A and B were not seen by me.

To complete the series of illnesses attended by jaundice I have 'headed the table' with particulars of the 8 patients who were jaundiced, in the Cold Hesledon outbreak. It is not proposed to make any further reference to them in this section.

Name.	Address	Age	Date	No.
Mrs. Brown	Bankhead	26	4.3.44	C
Branthwaite A.	5 Hesledon Ter.	5	April	O
Branthwaite L.	5 " "	7	29.5.44	L
Jackson E.	6 " "	11	29.6.44	D
Armstrong J.	8 " "	11	17.7.44	
Etherington I.	32 " "	11	17.7.44	H
Robinson Brian	10 " "	6	15.8.44	E
Robinson Brenda	10 " "	12	15.8.44	S
				L
				E
				D
				O
				N
Painter	25 Williams Road	58	19.6.44	1
Hollingsworth R.	Hill Crescent	7	Aug. 44	A
Hollingsworth A.R.	" "	10	Aug. 44	B
Marriott J. H.	7 Oak Terrace	3	9.9.44	2
Border J.	7 Gray Avenue.	11	28.9.44	C
Clews J.	27 Ripon Terrace	2	1.10.44	3
Forster G. W.	29 Alfred Street	3	6.10.44	4
Sheach A. W.	Montana	20	6.10.44	5
Young A. I.	93 Calvert Terrace	11	9.10.44	6
Lumsden E.	14 New Pilgrim Street	7	12.10.44	D.
Griffiths H.	45 Silver Street	20	17.10.44	7
Oliver D.	Montana	3	18.10.44	8
Smith J.	10 No. Cres. Cd.Hes.	11	10.10.44	9
Elliott R.	25 Ripon Terrace	12	20.10.44	10
Morris H.	1 Beech Terrace	7	20.10.44	E.
Marr T.	44 Albion Street	47	22.10.44	11
Warin H.	19 Ash Terrace	7	30.10.44	12
Lavery A.E.	23 Wetherburn Avenue	8	30.10.44	13
Hunter A.	69 Princess Street	5	1.11.44	14
Bond R.	22 Brooklyn Terrace	3	3.11.44	15
Turner M.	50 Windsor Terrace	8	14.11.44	16
Barksby T.	13 New Pilgrim Street	11	15.11.44	17
Scothern M.	12 Oak Terrace	6	23.11.44	18
McQuilliam Y.	2 Adelaide Terrace	5	27.11.44	19
Vest R.	7 Pilgrim Street	11	2.12.44	20
Walker A.W.	4 No. Doxford Ter.	19	5.12.44	21
Applegarth E.	34 Hawkins Road	6	11.12.44	22
Turner A.	30 Windsor Terrace	11	15.12.44	23
Elliott J.R.	35 Shinwell Terrace	13	20.12.44	24
Bridges A.	Welfare Park House	13	2. 1.45	25
Johnson A.T.	29 Albion Street	5	31.12.44	26
Pow R.	15 Hawkins Road	18	10. 1.45	27
Wearmouth P.	Baysdale	8	19. 1.45	28
Elliott Dorothy	25 Shinwell Terrace	10	23. 1.45	29
Sugden M.	7 Stephenson Street	6	27.1. 45	30

Name		Address	Age	Date	No.
King	R.	21 D'Arcy Pl. Cd. Hes.	15	30. 1.45	31
Forster	M.	5 Stephenson Street	10	26. 2.45	32
Sugden	W.	7 Stephenson Street	10	1. 3.45	33
Robinson	A.E.	Murton Moor Farm	7	1. 3.45	34
Hough	A.	91 Princess Street	6	5. 3.45	35
Newton	E.	4 Stephenson Street	4	9. 3.45	36
Davison	E.	5 Ash Terrace	10	20. 3.45	37
Gannon	J.	3 Hawkins Road	4	21. 3.45	38
Southgate	A.	4 Forster Avenue	7	2. 4.45	39

The Mode of Spread and the Incubation Period.

The sources of the Epidemic.

In the first place there was evidence that the epidemic did not represent an outbreak derived from only one source. It could not be considered to be entirely endemic. In two instances the evidence in support of this view could not be contested.

Hannah Griffiths, Case 7, had obviously been infected at Witten le Wear. She had been in very close contact with the jaundiced girl from whom I presumed she had derived her infection, sharing the same dormitory, eating with her, and working with her. The incubation period was a month.

I thought it improbable that this girl caused a further spread in Murton as she was ill when she arrived and was isolated for a fairly long period.

Dr. Mackinnon's patient, Rhoderick Hollingsworth, like Hannah Griffiths, became jaundiced a few days after he arrived at Murton, and obviously he had been infected before

he arrived here. In this instance we have two facts to determine the incubation period. R. A. Hollingsworth, who was Rhoderick's cousin and had only just arrived on holiday from Dover, was in the company of Rhoderick Hollingsworth for 3 to 5 days before the latter became jaundiced. R. A. Hollingsworth became jaundiced 21 days after his cousin. (Dr. Mackinnon had taken particular notice of this interval). The incubation period could not have exceeded 26 days.

Here again contact was very intimate, theboys being strangers to this village, spent all their time togetner, and several modes of infection was therefore possible.

A. W. Sheach (case 5) was almost certainly infected in Elgin where he spent the week end of 1st to 4th September,1944. He took ill on 29 Sept. 1944 and was jaundiced on 7th Oct,1944. One week later he was again in Elgin and there he found that his brother, with whom he had spent the week end of 1st to 4th September, had been ill suffering from infective hepatitis and had been jaundiced. Sheach was particularly impressed by the fact that tney had both been jaundiced at exactly the same time and they had both been confined to bed for the same period. Neither my patient nor his brother knew of any person who had been suffering from an illness diagnosed as infective hepatitis. The incubation period in this instance would be from 28 to 24 days counting to the onset of the (1st stage of) illness; and the interval until jaundice occurred would be from 36 to 32 days.

These 3 examples therefore point to incubation periods of about a month, 24 to 26 days and 24 to 28 days. They do not help us, however, to determine whether the infection was being spread by droplet or otherwise. In the first two examples very intimate contact was obviously present. In the third example it was evident that the brothers had been infected from a common source, the nature of which, of course, I could not profitably investigate. The negative finding that it was not known to be from a person who had infective hepatitis was interesting -- nothing more.

A. W. Walker (case 21) may also have been infected outside Murton. But in the great majority of the remainder of the cases, I had no reason to doubt that the infection had been contracted locally.

What facts did I have regarding the spread in Murton?

There were a few cases where the spread from patient to patient appeared to be obvious.

In 3 houses a second patient became jaundiced some time after the initial case of jaundice had occurred.

Example 1. A. W. Sheach and D. Oliver (Cases 5 and 6).

We have noted that Sheach took ill on the 29th September, and became jaundiced on the 7th October, 1944. During the interval between these dates his urine had probably been bile stained (vide case history 5).

Dorothy Oliver became jaundiced on 18th October, 1944. We have either to assume that Sheach was infective before 29th September, 1944, or that the incubation period in this case was some 18 days. Sheach played with and nursed Dorothy and I think it almost certain that he was the source of her infection. If so, we here again have intimate contact.

Example 2. M. Turner and A. Turner (cases 16 and 23).

Here the interval between the children becoming jaundiced was 31 days.

Example 3. J. R. Elliott and D. Elliott.

The sequence of events in this household was so interesting and possibly important to our study, that I have devoted a short section to it (pages 670 to 678).

The conclusions I came to there are:-

In the case of the boy, the incubation period was one month, but in the illness of Dorothy, his sister, the incubation period may have been 3 months.

Example 4. M. Sugden and W. Sugden. (cases 30-33 page 378)

The interval between the occurrence of jaundice in each case was 36 days.

Having considered the spread from 'outside' sources and the spread in the homes, it might now be well to consider the spread in the schools.

The first pupil attending Murton Council School to become

PLAN 8.

CLASS I SENIOR GIRLS SCHOOL.

EVELYN. McROY. MARG. MORDUE.	LOUISA FORSTER BEBE HUDSON.	GLADYS. STEPHENS. ELLEN TAYLOR.	VERA. BLYTHE. MAURINE CARDY.	LORNA. TAYLOR. MARG. DIXON.
JOAN ALLISON. ELSIE PURVIS.	BETTY ANDREWS. BETTY EMERY.	BETTY BOUSFIELD ANN COATES.	EDNA MALPASS. DOREEN DAVISON	IRENE GRAY. JEAN RUTHERFORD.
JOAN. BALLS. JEAN FRANKS.	MAUD REDHEAD. ANN ELLIOTT.	ELIZA GRAY.	ANN YOUNG. BERYL DORMAND	MARG. ARTHUR. MARJORIE POTTS.
MARY STRUTHERS	MARG. DIXON.	MURIEL LOWES. ENID McGINN.	MAY CARABINE.	MARIE THOMPSON. NELLIE OLDMAN.
	ANNIE CRUMBIE	BLANCHE MOSLEY JOAN REAY.	ENA HUTCHINSON. LILY ELLIOTT.	OLIVE BROWN. JEAN LOWERSON.

Although no more cases of 'Jaundice' occurred in this class room, I reproduce this seating diagram as prepared by the teacher.

I believe that such diagrams may be helpful in trying to trace the spread of an infectious disease.

To precede p 383.

jaundiced was Anne S. Young, an 11 years old girl. She became jaundiced on 9 Oct. 1944, Her case history shows that Anne had been ill for some 14 days before she was absent from school and became jaundiced. The headmistress co-operated by having a diagram made showing the seat occupied by Anne and each other member of the class. Ann had become acutely ill at her cookery class, and I therefore made a record of all girls who attended this class -- the "Monday Class" as it so happened.

The class rooms at Murton contrast with those at Cold Hesledon. Each desk has its two pupils, the desks are placed more closely together, in fact the rooms are packed almost to capacity. Now in spite of this close proximity, which continued throughout the prodromal stage of Anne Young's illness, not one of the other 43 children in that class developed jaundice.

The cookery class comprised 18 children and was exclusively drawn from the 44 children in the class we are considering. In this way some of the 17 children who were in Anne's cookery class would be handling objects and utensils which she handled They would therefore be exposed to infection whether it was an airborne infection or was an infection which could be contracted by manual contamination, although in this connection it should be noted that Anne Young is a child of very cleanly habits. Six months later not one of the children in this class had become jaundiced.

I should further add that although I was particularly well acquainted with the movements, friends and acquaintances of Annie Young, I could not trace any contact between her and a person who had been jaundiced.

Nor could I trace any case of jaundice as having its origin in the patient's contact with Anne Young. (Of course, it had to be admitted that Anne Young went to the local cinema, and might have contracted or spread the infection that way. However if Anne Young had been infected at the picture hall, the only person who was jaundiced at a time which would fit in with theory was J. H. Marriott (jaundiced 9/9/1944.) This child attended the Saturday matinee only, which Anne Young did not attend.

To consider further the question of spread in the class rooms at Murton Council School:- I found it impossible to make a daily inquiry visit at this large school, even if I had received the requisite permission. I therefore recorded, as the reader may note, in each case the name of the child's school teacher. It was appreciated that the results would need to be carefully assessed. It was realised that children who are in the same class are frequently playmates both in and out of school hours, and that some who are exposed to aerial infection are also exposed to infection by actual contact. In no fewer than 12 class rooms a single case of illness attended by jaundice had occurred -- there being no repeat cases.

In four class rooms more than one case of infective Hepatitis attended by Jaundice had occurred.

In case the reader may wish to confirm the facts, or otherwise further consider them, I append a table to illustrate.

Teacher	Patient.	Date of Jaundice.
Miss Anderson	A. Hunter	1 Nov. 1944
	M. Scothern	23 Nov. 1944
Mr. Porter	M. Turner	14 Nov. 1944
	P. Wearmouth	19 Jan. 1945
Miss Robson	E. Applegarth	11 Dec. 1944
	A. Hough	5 Mar. 1945
Miss Redfern	D. B. Elliott	23 Jan. 1945
	M. Forster	26 Feb. 1945
	E. Davison	20 Mar. 1945

The following children became jaundiced. Each was the only child in his or her class room to become jaundiced.

Anne S. Young	9 Oct. 1944	A. T. Johnson	31 Dec.1944
Emily Lumsden	12 Oct. 1944	A. E. Robinson	1 Mar.1945
Raymond Elliott	20 Oct. 1944	J. R. Elliott	20 Dec.1944
H. Warin	30 Oct. 1944	M. Sugden	27 Jan.1945
A. Turner	15 Dec. 1944	W. Sugden	1 Marc1945
A. Bridges	2 Jan. 1945	A. Southgate	2 Apr.1945

.....

A consideration of the facts set out in the table above impressed me more by the apparent failure to spread in the class rooms, than by the few illustrations it afforded of

instances where spread in the rooms might have occurred.

The only striking sequence was provided in Miss Redfern's class, where three children became jaundiced at intervals which would be compatible with a spread from one to another.

In this case, however, there were features in the case history of Moira Forster's illness which made it appear doubtful if she had indeed been infected by D. Elliott. My opinion was that she had probably not been so infected. (see page 679 et seq.)

To sum up, I did not think that the facts suggested that the disease was being spread by aerial droplet infection among the children as they sat in their seats at school. In fact they seemed very definitely to suggest that such a spread did not occur, in the class rooms.

To approach the problem from a different angle let us enumerate the cases of Infective Hepatitis as they occurred in this school, in chronological order.

Name	Age									Date			
	5	6	7	8	9	10	11	12	13				
Young A. S.							11			9	Oct.	1944	
Lumsden E.			7							12	Oct.	1944	
Elliott R.								12		20	Oct.	1944	
Warin H.			7							30	Oct.	1944	
Hunter A.	5									1	Nov.	1944	
Turner M.				8						14	Nov.	1944	X
Scothern M.		6								23	Nov.	1944	
Applegarth E.		6								11	Dec.	1944	
Turner A.							11			15	Dec.	1944	X
Elliott J. R.									13	20	"	"	X
Jonnson A. T.	5									31	"	"	
Bridges A.									13	2	Jan.	1945	
Wearmouth P.				8						19	"	"	
Elliott D.						10				23	"	"	X
Sugden M.		6								27	"	"	X
Forster M.						10				26	Feb.	1945	
Sugden W.						10				1	Mar.	1945	X
Robinson A. E.			7							1	"	"	
Hough A.		6								5	Mar.	"	
Davison E.						10				20	"	"	
Southgate A.			7							2	Apr.	"	

X Denotes brotners and sisters.

In the above table it will be seen that we have the brothers and sisters Turner, Elliott, and Sugden. If we exclude these six children we are left with a distribution out of which I could make no possible arrangement which would be consistent with a spread of the disease at school. We have established the fact that, in most cases at least, the incubation period was about 28 days. Considering only the first five cases, the dates when jaundice occurred, Oct 9, 12, 20, 30, and Nov 1., suggest that these illnesses were certainly not related. Further the ages of the children and other circumstances such as their home adresses pointed to their illnesses not having been derived from a common source.

From my knowledge of the childrens' friendships (this was of course much less complete at Murton than it was at Cold Hesledon) from inquiry to supplement that knowledge, and allowing for the likelihood that children at school would sort themselves out roughly according to their age groups, I deduced that in only one age group was there any semblance to a possible spread at school.

As can be seen by referring to the table, that was in the age 10 years group, and we have discussed the occurrence before, as the children were all in the one class room -- Miss Redfern's.

.....

The reader may think I must have been very unobservant when I state that it was only later, when I analysed the data which I had accumulated, that I realised that 5 cases of jaundice, all of which I was entirely unable to relate with one another, occurred in this school between Oct 9th and Nov. 1st. It must be remembered that at this time I was attempting to investigate and record the outbreaks of illness at the Bakery, Cold Hesledon, Dalton le Dale, and Hawthorn, and that an epidemic illness was beginning to show itself in the practice generally.

From our consideration of the cases of hepatitis encountered at Murton Council School we at once see that the sequence of the cases was entirely different from that obtaining at Cold Hesledon School (q.v.)

At Cold Hesledon School we found the interval between cases to be about a month. Here, there was no such order. Here also, at Murton, unlike the experience at Cold Hesledon, the disease seemed to have been introduced from several different sources: in no way could the first 5 cases be related one to another, or as regards their respective origins.

And yet the "jaundiced illnesses" appeared to be practically identical in the patients at both schools. They further seemed to be identical in that the incubation period where a second illness occurred in a home, was from 18 to 35 days.

On Page 177 of the section dealing with the spread at

Cold Hesledon (jaundiced patients only) I wrote:-

"I therefore formed the opinion that the spread was occurring outside the class rooms either in the patient's home or in her close association with her friends."

The findings in Murton seemed to me to support this view, to the extent that

(a) The spread was not occurring in the class rooms.

(b) There were illustrations of the disease spreading in the homes -- examples were Turners, Elliotts, and Sugdens.

(c) As in B, we had the spread from Hollingsworth to his cousin, from Sheach to Oliver, and from a fellow workman to H. Griffiths: and the evidence of Sheach's brother.

But the striking features at Murton Council School were

1. The low attack rate. 21 cases in 1,400 children in 6 months.
2. The apparent impossibility of tracing the illness of one jaundiced patient to its source in the illness of any other person who had also been jaundiced (except in patients from one house).
3. The lack of evidence of spread of the "jaundice" occurring from jaundiced children to other children (except in patients from one house).

Jaundice is a symptom that attracts attention, and the overwhelming majority of cases in Murton would certainly be reported and come to my notice. I knew therefore that many of the patients had not been in contact with people in Murton who were jaundiced.

It might be said that they had acquired the infection outside the boundaries of Murton. I could not deny the possibility of this having occurred in an odd case, but I do not credit that it had occurred in the majority of the cases.

I formed the definite opinion that many of the children had not been infected by a person suffering from infective hepatitis accompanied by jaundice.

Further, it appeared in this series that if a person was jaundiced, the chance of anyone else becoming infected from him and becoming jaundiced was slight at school, but at his home the spread was much more likely to occur.

Apart from the cases where spread had apparently occurred in the home, the jaundiced patient seemed to have acquired his jaundice from no one and he seemed to pass it on, in the main, to no one.

(I am aware that jaundice is a symptom and that it is diseases which are passed on, not symptoms. Nevertheless I think the wording above is excusable.

.....

St. Joseph's Roman Catholic School in Murton has some 120 pupils, comparing with the 100 at Cold Hesledon School and 1,400 at Murton Council School. Four children attending St. Joseph's became jaundiced. They were:--

Joan Smith	Age 8 years	Jaundiced on	18 Oct. 1944
Henry Morris	7 years	" "	20 " "
Eileen A Lavery	8 years	" "	30 " "
Y. McQuilliam	5 years	" "	27 Nov. "

There were one or two circumstances which made me seriously consider whether a separate spread of the illness was occurring at St. Joseph's R. C. School.

It did appear remarkable that 3 Roman Catholic school children should have become jaundiced within 12 days and the fourth practically one month later; and yet no Roman Catholic school child was jaundiced before or after this period. (The 3 years old J. H. Marriott who was jaundiced on 9 Sept. 1944 is however a Roman Catholic.)

Further, the illness of Laura Collett occurred at the same time, 18 Oct, 1944, as the illness of J. Smith, 18 Oct,1944 and Henry Morris, 20 Oct. 1944, and although she did not become jaundiced it appeared to me that her illness was definitely indicative of a subicteric attack of infective Hepatitis. She suffered from diarrhoea, sickness, vertigo, pains around the elbows and lethargy -- the last-named being so very marked that it was the feature which occasioned most

anxiety on the part of her observant parents.

The differential white cell count showed

Polymorph Leuco.	23
Lymphocytes	69
Monocytes	4
Eosino	4

There were further illnesses affecting the Roman Catholic School children which demonstrated that an infection was spreading among them. I think that if I limit my reference to these illnesses to two further illnesses it will suffice to illustrate my point. They can be taken as representative of the type of illness, which, it could readily be confirmed, affected this group of children. The two illnesses which I give as examples are those of Dorothy James and Anne Moira Penman, and I enclose a record of the illnesses of both of those children and also that of Laura Collett. Dorothy James was ill from 17 Nov. 1944. Although she vomited, suffered from epigastric pain and tenderness and was very constipated and presented symptoms and signs which were very suggestive of a non jaundiced hepatitis, the arresting feature of her appearance and illness was undoubtedly the impression that the nervous system was attacked. As the mother truly remarked she looked "awful" --- the appearance of lethargy and exhaustion was very striking and at once compelled attention. The child said that she "wanted to go to sleep all day."

Also she complained of always feeling dizzy, and two weeks after she took ill she complained of pains in the upper part of her thighs and told me that "she often had a feeling that she had no legs on."

The interesting features in the illness of Anne Moira Penman, who first took ill on 20 Nov. 1944, were the overpowering laziness and drowsiness ---"She could not be bothered with anything" --- and the visual disturbance. The latter was so marked that (like one of the children who was jaundiced and who attended Murton Council School) she could not see to thread her needles, and her teacher had arranged for Anne to have her eyes examined. It was not until 6 Dec. 1944 that abdominal symptoms became marked.

I think that a study of the 5 illnesses as recorded will convince the reader that they were probably all due to the same agent, and that the jaundiced and non-jaundiced children alike were suffering from the same infection.

Was that infection spreading from child to child as they sat in their class rooms? Again the answer appeared to be "NO".

Was the infection occurring or spreading at the school, for instance in the playtime periods?

I eventually realised that I could not form any reliable opinion as to whether the infection was being spread at school or elsewhere. Careful, painstaking and exhaustive inquiries revealed to me a condition such as I had not

imagined to exist in the Roman Catholic community. The Roman Catholic children, I found, constituted in effect what amounted to practically a large family. They visited each others homes much more frequently and in larger numbers than did the Protestant children. A birthday party was attended by 30 or even 40 of the total of 120 children, and there contact would be intimate and all would partake of the same foodstuffs.

I have no desire to tax the patience or, indeed, the endurance of the reader, so I will simply state that the result of my inquiries led me to suspect that the spread did not occur mainly at the school, but predominantly at the homes of the Catholic children.

In several instances I found that there were antecedent cases of illness in the housesof the children, pointing to the home as the source of the infection.

I would merely state in order to illustrate how I formed this opinion, that in the case of Anne Moira Penman, to whom I have referred above, I had attended Angus McAulay, a "Bevin Boy" lodging at her home, for an illness which presented symptoms suggesting that he had contracted the prevalent infection, on 18 Nov. 1944. He was giddy and he was worried, as, for no obvious reason, he was suffering from an overpowering lethargy. Later he complained of tingling - "pins and needles" - in the hands and forearms.

The subsequent illnesses of Mary Penman and Margaret Penman, who are aged 24 years and 27 years respectively, who live at the same address, pointed to the spread of the infection in this house.

Definitely the disease did not spread in the Roman Catholic School from child to child as they sat in adjoining seats in their class rooms. Here again, as at Cold Hesledon, the disease seemed to spread from friend to friend and seemed to depend on intimate social association.

(I should point out, in order to avoid confusion, as the reader will no doubt have observed, that in this section dealing with the Roman Catholic children, I have discussed the question of spread, taking into consideration the non-icteric illnesses.)

.....

There were two further points which the outbreak at the Roman Catholic School seemed to illustrate.

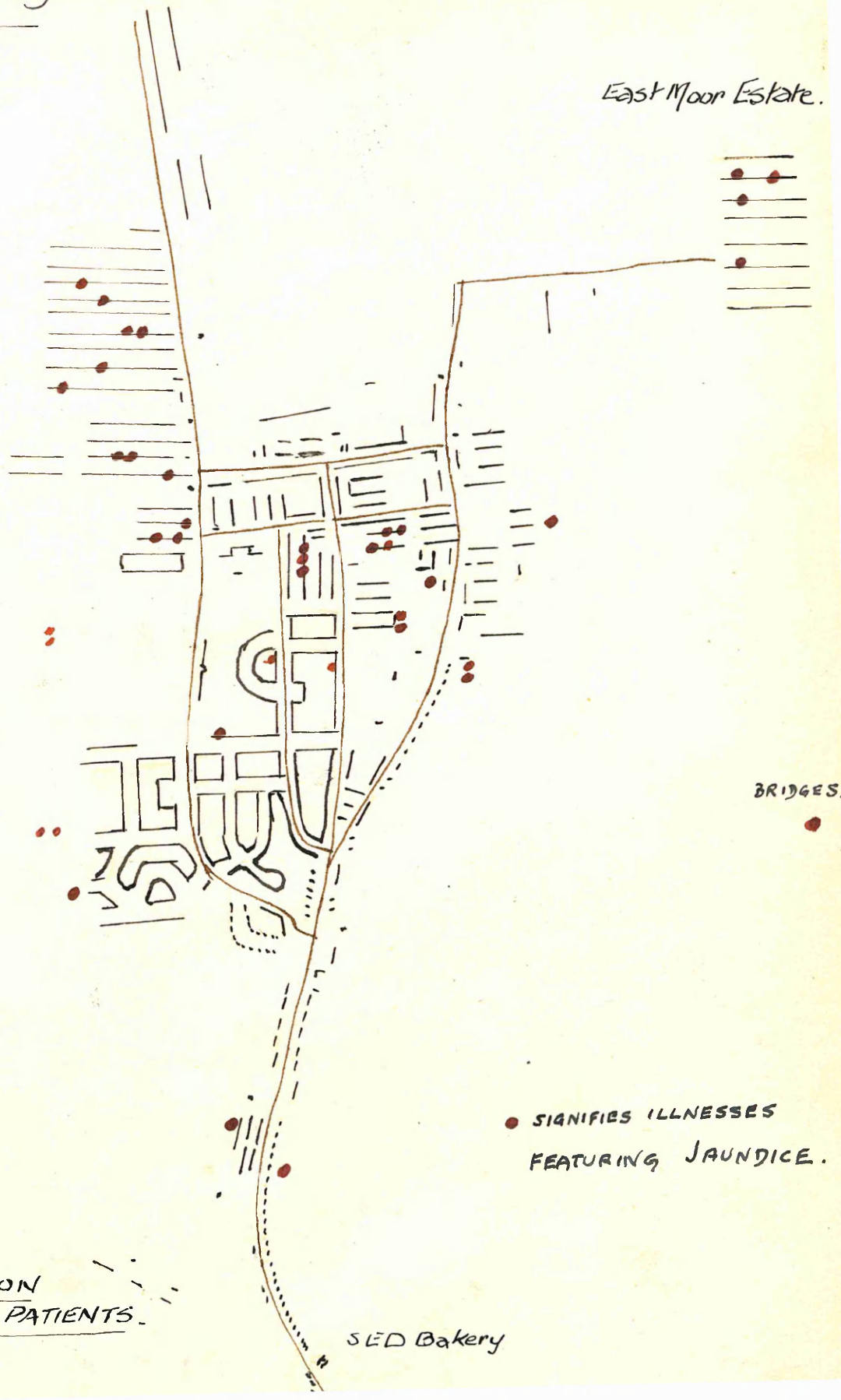
Joan Smith lived at Cold Hesledon. There it will be remembered several children (attending Cold Hesledon School) became jaundiced between April and August, 1944. Joan Smith's illness accompanied by jaundice, on 18 October, 1944, therefore seemed definitely to have depended not on where she lived but on her attendance at the Roman Catholic School and her aasociation with the R. C. children, Her illness therefore appeared to argue against locality and was in favour of human contacts as the determining factor.

I considered that the timing of the attack on the R. C. schoolchildren as described -- 3 children jaundiced in 12 days and the fourth one month later -- with no casesof jaundice before or after that period --- was significant. If the water supply, the milk supply or any article of food which was regularly supplied all over the area, such as the bread supplied by the local bakery, had been conveying the infection throughout the epidemic, I would not have expected this sudden incidence in the Catholic School: it will be seen that there were only 3 cases among the "non R.C." children, who numbered 1,400 to the 120 Catholics, in the same 12 days.

But <u>again</u> I could not find any evidence of the jaundiced R. C. children having been in contact with a person who was jaundiced. To the best of their knowledge they had not been in contact with any of the previously jaundiced patients.

In what way, I wondered, would the likely sources of infection vary as between the R. C. and the Protestant children. An obvious difference lay in the people with whom they associated. As I have already remarked, I was amazed to observe how the R. C. children comprised an almost separate social community. If the common origin of the R. C. childrens' illnesses lay in the illness of another (probably R. C.) child, then I felt that child had not been jaundiced.

PLAN 9



MURTON

EWING DISTRIBUTION
THE JAUNDICED PATIENTS.

THE FOLLOWING SECTION IS OFFERED AS AN

IMPORTANT FEATURE OF THIS WORK.

A Summary of the Findings.

The present seems to be a suitable stage of the work at which to review the findings in the various phases of the epidemic as I have detailed them.

(a) Among the scholars at Cold Hesledon School.

(b) Regarding casesimported from outside areas, as it were.

(c) Cases where spread occurred in the home.

(d) Cases occurring among the scholars at Murton Council School.

(e) Cases occurring among the scholars at St. Joseph's Roman Catholic School

In every instance where I could 'prove' case-to-case spread (and I am only considering at the moment cases where clinical jaundice occurred) the patients were living in the same house or they were on intimate terms and visited at each others homes. My experience in this epidemic offered no support to the view that the disease was spread by aerial droplet, droplet nuclei etc., in the class rooms at school. I could quote no instance where I was convinced that such a spread had occurred in a class room.

The emphasis apparently lay not in mere proximity: it appeared to depend on intimate association.

It may be commented that the number of children who became jaundiced comprised a very small proportion of the total attending the schools, and would not average out at more than one child per class room. If however aerial droplet infection

in the class room was the mode of spread then I contend that such an "averaging out" would not occur.

In view of the opinion prevalent during the greater part of the period of my investigations that infective Hepatitis was probably transmitted by droplet, I was greatly impressed by the fact that no child sitting next to a child who presently became jaundiced, became, in turn, jaundiced.

I appreciated that this was a matter quite outside the scope of my normal work, previous experience, or, indeed, special study.

A tendency to jump to the conclusion that the spread was certainly not due to aerial droplet infection was rather countered by the accounts of the findings in measles, and the experts' interpretation of such findings.

Van Rooyan and Rhodes[1] state that the experience of London epidemics proved that most intimate contact definitely occurred in the home and not at school: and it is definitely accepted that, in the vast majority of cases, measles is spread by droplet.

Nevertheless it did seem remarkable that, if this infection was indeed spread by droplet, the spread between home contacts should so very markedly predominate. A study of Mitman's article on "Aerial Droplet Infection"[2] a comment on the article by Hare of Toronto[3] and comparisons of Gunn's views on such modes of infection as expressed by him in 1938[4] and

1943[5] showed that there was considerable controversy concerning the frequency of direct droplet infection in infectious diseases. Some considered that the direct inhalation of droplets which had recently been 'sprayed' was relatively uncommon compared with "an alternative mechanism of infection namely, atmospheric contamination."

Hare's view that many air borne infections are transmitted by an indirect route is very interesting in this relation. He does not subscribe to Mitman's theory that the "so called droplet nuclei are the chief factors in the spread of intramural infection." He enunciated the theory that this type of infection is transmitted by an indirect route "the organism being expelled by the 'donor' when speaking, coughing, snoring etc, inside heavy droplets, which fall on to whatever is below the level of his mouth(clothes, desk, table, sheets, pillow case etc.) quickly dry thereon and are subsequently released into the atmosphere on dried particles of dust, fluff etc. when the surface is disturbed."

This theory (I do not think that Hare could regard it as entirely original or exclusively his own) if it were the more correct would allow of a more ready interpretation of the occurrences in the Murton epidemic again assuming that we were attempting to support the possibility of aerial infecting occurring. Big kitchen fires in the colliery district cause dust. There are no coal fires in school. Cleaning of the

school is carried out after the children have left for home.

In fact in a colliery village the schools, built to a much higher ideal and with an attempt to limit the spread of such infections as we are now considering, expose the still very low hygenic standard of the living conditions in many of the homes; a low standard consequent upon overcrowding and generally cheap building.

It seemed to me from a careful review of this epidemic, after trying to allow for variations in immunity in the children, that if the disease was spread by any form of aerial infection then it was not a spread occurring directly from person to person by means of germ charged droplets, or droplet nuclie, as surely/if such a mode of spread was to be of much significance it could bridge the gap, if such it could be called, between two children sitting on a common seat in a school class room.

Atmospheric contamination must be the determining factor in the spread, if aerial infection did occur.

Mitman stresses the view that most air borne infections (whether this is a direct or indirect process) take place indoors. If aerial infection did occur in infective Hepatitis the epidemic in Murton pointed to the home as the source of such infection as opposed to the class room. This seemed to be a likely state of affairs as the living room in most colliery houses is usually overcrowded and ill ventilated,

and the "black out" curtains etc., which further restricted such ventilation as was indulged in, in the home, were seldom in use at school.

I have said it before, and I repeat that I did not consider that all the patients who became jaundiced had been in contact with another person who suffered from a recognized attack of infective hepatitis with jaundice. My inquiries led me to believe that frequently such contact had very definitely not occurred. Nevertheless, I do not think that this statement invalidates the remarks which I have made above. Time after time I received the names of the children who were 'ringed around' a child who became jaundiced at school, and I made enquiry calls to learn of any "subclinical" attack.

My observations and enquiries failed to show or suggest that such "neighbouring" children suffered from even mild non jaundiced attacks of infective hepatitis.

The cases so far considered therefore pointed to the possibility of aerial infection as it is stated to occur, according to Hare's view, by aerial contamination, but not to direct aerial infection by droplet nuclei as described (in other diseases) by Mitman.

As it appeared to me that the weight of expert opinion favoured the importance of direct infection from person to person by the projection of droplets from infector to infectee,

my findings disposed me to doubt whether infective hepatitis was indeed spread by any form of aerial infection.

Further the findings did not seem to support the view that any article of food which was universally distributed throughout the area during the whole period of the epidemic was the cause of the spread.

In spite of the fact that in the early stages the epidemic confined itself to Hesledon Terrace, Cold Hesledon, the subsequent spread suggested that locality per se was not the main factor. Generally speaking the cases were apparently indiscriminately distributed throughout the area; where several cases occurred in one area the concentration seemed to depend on the intimate association of "neighbours" rather than on the site.

.....

How did the findings support or negative the theory that Infective Hepatitis is caused by the ingestion of infected food or otherwise introduced via the alimentary tract?

I have stressed that intimacy and not mere proximity appeared to be a very important factor in the spread of this disease. In the first few pagesof this section I have noted how Hannah Griffiths was in intimate contact with her Land Army girl friend. The cousins Hollingsworth were in the most intimate association. Sheach and his brother, who both became jaundiced, had been closely associated during the week end

when they both became infected. Then we have the four examplesof spread in the home, which I have enumerated earlier. Those children attending Cold Hesledon School who became jaundiced were very intimate friends and were frequently in and out of one another's homes. Similarly the illnesses among the Sugdens, Forsters, and Newtons, to which I have referred, pages 679 to 701 suggest that intimate contact and social intercourse are important factors in the spread: A similar impression remained after a consideration of the illnesses among the Roman Catholic children.

There were several ways in which we might attempt to account for the effect of intimate association on the spread of the disease. In several instances the patients would obviously have partaken of the same food, but it will be noted that only in one instance did two children in one home become ill with infective Hepatitis at the same time: the children were Brenda and Brian Robinson, and I believed that Catherine Robinson at the same time suffered from a subicteric attack. In the case of the Robinsons the spread was of what Pickles terms the 'serial' type consequent upon the illness of the older son Douglas (see page 213). So it appeared likely that if contaminated food was the cause of the illness of Brenda, Brian and Catherine, the food had been contaminated by Douglas. This seems a much more likely explanation than

to assume that any food so contaminated had been purchased already contaminated, as then we would be compelled to assume that such food had been eaten by Douglas and that a month later the other children had partaken of the same or further similarly contaminated food.

A second instance of a possible simultaneous infection by ingestion of contaminated food is provided by the interesting story of the brothers Sheach, one becoming jaundiced in ELGIN the other in MURTON. I had no proof that the children who became ill within a few days of each other at the Catholic School had consumed a common aliment. I regarded it as possible. But I would base no argument, or indeed definite opinion, upon the possibility.

But in the great majority of casesit was obvious that any spread which occurred was of the serial type. How can we reconcile such a spread with the theory of infection via the alimentary tract ?

Surely it may be complained, if the food is infected and several children consume it, more than one child will ordinarily be infected: this especially when it is remembered that the children not then affected are obviously not immune to the infection, as commonly they become ill a month later.

I think that all the circumstances of this epidemic, and indeed of other epidemics to which I have referred in this work, can be best understood if we imagine the spread to be due in many cases to faecal contamination of the fingers,

and all which that implies.

We could readily understand how several people might be infected simultaneously by eating food which had been handled and contaminated by a person whose fingers conveyed the infection to such food, by reason (I will avoid the word virtue!) of faecal contamination. In this way we could understand the occurrence of an explosive outbreak such as that described by Cookson[6] as occurring in Gloucestershire during 1943 among the children in 2 residential nurseries. Cookson concluded that the infection of the children in the nurseries had in each school, a common source. In the nursery he thought that the common source was probably a visitor recently convalescent from infective hepatitis. In the other nursery he thought it possible that the infection had been water borne, although he advances this supposition with considerable caution and reserve.

Whilst the quality of Cookson's observations at once commend admiration and respect, I could not help but wonder, with all due humility, whether he had devoted sufficient attention to the possibility of the infection having had as its source a non icteric attack of hepatitis ---this the more so, as I believed that such an attack might take a form not commonly believed to represent such an attack. Again it might be that he had indeed considered it possible that such a source had existed but did not think it wise to advance such a necessarily unsubstantiated view in a contribution to a

scientific medical journal. It is indeed emphasized that all such epidemiological studies should be based on facts, and it appeared likely that such a course would be adhered to by Cookson, he being, I note, a barrister-at-Law.

Whilst the necessity of such an injunction is apparent I would still question the wisdom of rigidly and exclusively adhering to it. Many people who assert and emphasize that jaundice is a symptom and not a disease, and who remark and enlarge upon the occurrence of hepatitis without jaundice, appear to require the firm factual evidence of the presence of a jaundiced patient as the origin of an outbreak.

It would appear to me to be a very interesting exercise to obtain details of all the illnesses which preceded a local outbreak of Infective Hepatitis, for instance in a boarding school or institution, whether they appeared to comply with our accepted views of the symptomatology of infective hepatitis or not. Comparisons of all such preceding illnesses might reveal a similarity of symptoms which might in turn point to their being of importance epidemiologically. To attempt to argue always from facts to theory must stifle imagination. I feel that in such studies we ought to attempt to form theories on the basis of the facts in our possession, and put these theories to the test by such mass observations as I have suggested. There seemed no need to apologise for such a method of arguing from theory to fact, as I have indicated.

Having made this long, and I trust pardonable, digression, I would return to the immediate discussion of the mode of spread by stating that a serial spread seemed the more common in the outbreak at Murton. Here this compares with the spread as described by Ford in the Wembley Epidemic[7] and again by Cookson in the elementary schools in Gloucestershire. Such a spread could be explained, as Ford believed possible, by faecal contamination of the fingers. In the Murton epidemic the importance of intimate contact and social intercourse appeared evident and here I considered that it probably operated in several ways. A child might touch the hands of another, or he might convey the infection to another by means of fomites, or he might infect the foodstuffs of others by handling.

War time conditions would greatly favour such a spread as the last named. For instance bread and other articles of diet were brought home carried unwrapped in the hands. A consideration of the circumstances in the various groups of cases in Murton supported the possibility of this mode of spread.

The spread in the patients' homes, or in the homes of intimate friends, where even in war time the children will presumably eat together on occasion, would allow of one contaminating the food of others, whilst obviously actual contact with one another would commonly occur in such intimate friends or relations.

In the great majority of cases it seemed unlikely that, if an article of diet was the vehicle for the infection, such an article, solid or liquid, had been contaminated when it had been purchased or, as a rule, delivered. In such a way a serial spread could be understood in the absence of an explosive outbreak. One might understand in fact a retail as opposed to a wholesale spread -- a spread in the home as opposed to an explosive spread in the community.

I think it fair to state that the average person and indeed the average medical practitioner is more inclined to visualize the spread of an infection as occurring by aerial means than by the method of faecal contamination. This tendency is readily corrected by the consideration of the mode of infection in such a prevalent condition as infection by oxyuris vermicularis.

.....

Such a study of the epidemic in Murton led me to favour the view that infection in infective Hepatitis was spread by reason of faecal contamination of the hands, not by direct aerial droplet (nuclei) spread. As regards aerial spread of a more indirect type as supported by Hare, I could not deny the possibility of its occurrence.

We have still advanced no evidence as to how many of the jaundiced patients became infected. I have stated that I am firmly convinced that many of them did not acquire their

infection from a patient who was jaundiced. The cases occurring in the early stages of the epidemic obviously allow of less margin of error in considering possible sources of infection than do the cases which occurred later. Let us refer to one or two of the early cases. The cases are numbered on Page 378.

Mrs. Painter, Case 1, and Anne S. Young, Case 6, had not been in contact with any person in Murton who subsequently became jaundiced.

It appears fair to comment that both of these patients visit regularly at Cold Hesledon, where Infective Hepatitis was, or had been, prevalent, where they have relations. None of those relations had been jaundiced nor do I know of them having been ill, although I only attend professionally on one of the families. In the first 9 cases which I enumerate in the table as Cases 1, A, B, 2, C, 3, 4, 5, and 6, it will have been noted that cases A. and B. originated outside Murton, as did case 5. Thus two jaundiced patients, out of a total of 6 remaining, had frequent and intimate contacts at Cold Hesledon: the total may be considered as 5 when we learn that patients C and 4 were cousins and I believe that their infections were related. The number of people in Murton who visit regularly at Cold Hesledon is surprisingly small. Murton is the shopping centre, it contains all the three picture halls and the numbers of people who travel

from Cold Hesledon to Murton is therefore very much in excess of the number who travel in the reverse direction.

I would doubt whether it was worthy of recording that 2 people out of the first five infections in Murton had very intimate social contacts at Cold Hesledon except for one striking fact. That is, that although all the children who were jaundiced at Cold Hesledon attended the Murton picture halls with varying regularity, and that some had been at these halls just prior to their attacks of infective Hepatitis the facts did not suggest that they had infected any one at the picture halls. I considered this in fact to be a point strongly opposing the conception of aerial infection of any type in the spread of the disease. Any environment calculated to encourage the spread of an infectious illness so communicable it would be difficult to imagine, than that prevailing in a childrens' matinee in a colliery picture theatre: this the more especially in a cold and bleak East Coast colliery village built on a moor, with restrictions in heating compensated for by ~~compensatory~~ reduction of such ventilation as is ordinarily available.

Both Mrs. Painter and Anne Young had meals at Cold Hesledon; the latter had dinner there every Sunday. I can only state that Anne Young knows all the children of her own age at Cold Hesledon and had been in the company of many of them before she became ill. I thought it possible that Cold Hesledon was

a likely place for her to have been infected by any child who might well have had a subclinical infection.

I have recorded this relation more because I think that it would be unfair to omit it, than in an attempt to form any opinion based on what may only be a co-incidence.

.....

If it were true, as I believed, that many of the children did not become jaundiced by contact with a person who later did become jaundiced, how had they become infected ?

There appear to be several ways in which we could attempt to explain such infections.

(1) The patient might become infected by eating food which had been touched by a "jaundiced" patient, or he might acquire the infection by handling fomites, similarly handled by such a person. An analysis of the situation made it appear unlikely, I think, to the point of certainty, that this was the explanation which we seek. The incidence of the disease did not so fall on e.g. shopkeepers as to suggest that this was a possibility. Further I was sufficiently well acquainted with the inhabitants as to know which people were likely to consume food handled by jaundiced patients. (I will use the term "jaundiced" to avoid constant repetition of the phrase " a patient who presently became jaundiced.")

(2) The patient might have handled fomites which had been contaminated by a jaundiced patient. Similar considerations

to those in (1) made me discount this theory.

(3) The patient might have in some way become infected by or from a person who was not jaundiced.

This I thought was a likely explanation.

I have instanced several cases where there could be no reasonable doubt that a patient was suffering from infective Hepatitis without clinical jaundice. For instance, Case 3 on page 378 referring to Judy Clews (recorded in detail on page 483) shows that she had gross bilirubinuria with symptoms of infective hepatitis but was not jaundiced. Undoubtedly she would be a possible source of infection.

Recent articles dealing with the epidemiology of infectious diseases stress the frequently large numbers of people who became infected in an epidemic and fail to develop a typical attack of the disease which is prevalent. The clinical evidence of the disease produced varies in all degrees from severe, to mild, to trifling, to no evidence at all; except e.g. evidence of serological response to the infection. Cruickshank[8] in discussing "Some Problems in the Control of Infectious Diseases" states "Influenza is due to a number of viruses, of which two varieties have already been isolated and labelled influenza virus A and B. After a clinical attack, specific antibody, which can be readily detected by a simple test, develops to these viruses; many individuals during an epidemic develop antibody <u>without being clinically affected</u>.

I am aware that some eminent authorities do not agree with the orthodox views on infectious mononucleosis but the report on an outbreak of this infection by Halcrow[9] is interesting in that the author describes severe, moderate, mild and latent cases. These he describes as "cases with a relative or an absolute mononucleosis with abnormal lymphocytes present and a positive Paul-Bunnell reaction, but in which there were no symptoms or signs of the disease. Again recent studies regarding the epidemiology of measles point to the probability that many people become infected without showing any clinical evidence of the infection.[10]

It might truly be stated that such observations have led to the view that very mild infections in many infectious illnesses are not only more frequent than we have heretofore thought, but that the clinical evidence of infection may be trifling or indeed, apart from serological tests, absent.

Here it is necessary to remember that C. H. Browning[11] has advised "Caution in the acceptance for all conditions of purely serological criteria as evidence of present or past infection."

Thus I thought that while a patient such as (No. 5) Judy Clews, who was obviously suffering from infective hepatitis without jaundice, could be a source of infection, it was possible that many others who presented symptoms which were less typical could similarly infect others.

It seemed to me probable that we might be taking a too narrow view of what constituted a typical attack of "infective hepatitis". In other sections of this report I have discussed the occurrence of very many illnesses which I am convinced stand in close aetiological relation to infective hepatitis and it is my belief that they may have been factors in the spread of infective hepatitis as it occurred in Murton in 1944--1945.

If this was a correct assumption it would explain my failure to trace the source of the infection in many instances where I was so favourably situated and informed, that a spread from a person who was jaundiced, or who indeed had an illness patently indicative of infective hepatitis without jaundice, should not have escaped my vigilance.

Previous observers have stated that subclinical or mild cases might play, or probably played, an important part in the spread of an epidemic. It appeared that in the epidemic which occurred locally this was probably true.

Was there any evidence that subclinical or atypical cases were spreading the infection ?

I would request the reader to consider at this stage the very interesting sequence of events in the 2 children Elliott (pages 670 to 678). It appeared that Dorothy, who had an attack of non jaundiced hepatitis, had infected her brother, who became jaundiced one month later. In yet another month Dorothy became jaundiced. As I have mentioned before it might be considered that Dorothy's first illness was quite unconnected with either of the "jaundiced illnesses" and that all that had happened was that Joseph R. Elliott had become jaundiced and infected his sister who in turn became jaundiced 4 weeks later. To me that would be a view which discounted evidence overwhelmingly against its acceptance. Dorothy's first illness so accurately resembled her second illness and the symptom complex, if such I may term it, of the first illness was so distinctive and unlike any such combination of symptoms which I have previously encountered, that I would emphasize that I considered her first and second illnesses to be closely related or indeed one. Even the slight differences between the two illnesses seemed to illustrate that they were related, as I trust the reader will now agree.

A similar occurrence is suggested by the 2 illnesses of Moira Forster (page 683) who became jaundiced in a second illness which closely resembled an illness from which she had

suffered 112 days later. I have related the illnesses which occurred in her immediate and extremely intimate neighbours during this period, and, as I have already suggested, I consider that all those illnesses were related.

I feel compelled to pause for a moment, at this stage, to remark that the illnesses of Dorothy Elliott (I mention it first as it appears to me to be the most certain or reliable and also the 'simplest' example) and Moira Forster compare with the illnesses of Iris Etherington and Brenda Robinson and Brian Robinson which occurred in the Cold Hesledon Group and all suggest the prolonged action of the virus.

Moira Forster's first illness occurred on 6 November, 1944, and on that very date her friend Mary Newton, who lives next door, the families were so intimate that they could be regarded for our present purpose as one, took ill with an illness which appeared to be identical. I mention this to remark further that Mary Newton did not subsequently become jaundiced. In this Mary Newton resembled the great majority of the patients who developed what I would prefer to call "the epidemic illness not featuring jaundice."

Arguing from Dorothy Elliott's illness and bearing in mind the similarity of the illnesses of Moira Forster and Iris Etherington, I offer the following suggestions in explanation of these occurrences, and as being at the same time, consistent with and deducable from the general picture of the outbreak.

SUGGESTED MODES OF SPREAD OF THE INFECTION.

1. A person who was jaundiced could infect another person who, in turn, in about a month, would become jaundiced.

2. A jaundiced person could infect another person who might develop an illness so closely resembling a fully developed picture of infective hepatitis that the only difference was that jaundice did not occur.

3. A jaundiced person could infect another person who might develop an illness less closely simulating a "fully developed infective hepatitis" than did 2: frequently the difference between 2 and 3 lay in the relative prominence of "nervous" symptoms and the less prominent "gastrointestinal" symptoms in the latter group.

4. A person who contracted an infection leading (as in 2) to an illness simulating infective hepatitis but without jaundice might continue to harbour that infection and subsequently, 2 or 3 months later, become jaundiced: the virus at this late stage exerting its full hepatotropic, or as I would prefer to term it, hepatotoxic action.

5. A patient such as Dorothy Elliott, 4, could, in the early stage of his or her initial illness, infect others: and such others might become jaundiced.

It seemed from 4 and 5 that the virus which had attacked 4 had definite hepatoxic properties. In 4 this hepatoxic effect was delayed, or, at least, it was delayed in exerting its full hepatoxic action or effect. In 5 no such delay in attacking the liver occurred.

This might be explained by assuming that 5 had little or no immunity to the virus: and, conversely, by assuming that 4 had an immunity which had been acquired in earlier childhood but which had ultimately broken down under the continued action of the virus.

It occurred to me that such a "relation" as the above might help in the solution of the problems connected with homologous serum jaundice and post arsephenamic jaundice. If the views which I have expressed are accepted it will be at once apparent that if serum had been taken from a patient as in 4, such serum (I underline the word as it is vitally important) would possess hepatoxic properties and anyone who received such serum might well become jaundiced.

Now when would we expect that they would become jaundiced?

Well, Dorothy Elliott became jaundiced 60 days later, I mean 60 days after her initial illness, not her initial infection: Moira Forster 112 days later; Iris Etherington 63 days later.

I would therefore answer that I would expect any person who received serum from one of those children to develop jaundice in 2 or 3 months time (ignoring, for the moment,

possible variations according to the recipient etc.)

How could I justify such a view ?

I thought it likely that if the virus of infective hepatitis had attacked Dorothy Elliott (quoting her case for 'simplicity') and she had not become jaundiced she had probably not become jaundiced as she had in some way altered that virus by virtue of an immunological reaction on the part ultimately of her blood.

If her blood was then given to another patient that patient would receive not blood, or serum, containing the virus of hepatitis but blood containing an altered virus.

This altered virus, so transferred to the recipient's blood stream, could then attack his liver just as later it attacked the liver of Dorothy Elliott.

Many factors, and I do not profess to a very intimate knowledge of such factors, might then influence the action, or the time of the full action, of such an altered virus. It might depend on the time of the withdrawal of the blood from the so infected donor as presumably the virus would vary in the degree of its alteration with the passage of time. It would undoubtedly vary with the degree of immunity of the recipient, who might indeed even fail to become clinically affected.

It might be protested against the acceptance of my theory that local defence mechanisms against the action of the virus

might be the reason why Dorothy Elliott was so long in becoming jaundiced. If the virus entered the portal circulation, to attack the liver, by penetrating the defensive barriers present in the intestinal villi, then variations in such local defences might be offered as an explanation of such delayed attack. I thought that such an explanation was untenable in view of the free anastomosis between the portal and systemic circulations, the blood supply of the liver derived from both the systemic and portal circulation and the free intermingling of portal and systemic blood streams in the liver.

We could readily understand, of course, why Joseph R.Elliott the brother, became jaundiced in one month. He had been infected by reason of contact, and the virus which Dorothy Elliott had altered in her bloodstream would of course be quite unaltered in her faeces -- for it is by faecal contamination, as I have attempted to demonstrate, that the infection was probably ordinarily transferred.

The above discussion might be of much wider significance than would at first appear likely, at first sight. If people did harbour such a virus for such a time, and many considered that such frequently was the case, we must believe that in many instances it still did not later cause jaundice as in the case of Dorothy Elliott. Just as some people did not become jaundiced after receiving serum which proved to be icterogenic to others, so many people would resist their own potentially

icterogenic virus -- they presumably were able to counter its hepatoxic properties and such immunity, albeit late in its full development, apparently continued permanently.

We might consider that for a time in such cases the question of whether the liver would be attacked was in the balance. Thus we could understand the condition prevailing in Dorothy Elliott's blood between her two illnesses. Later the balance was weighed down and jaundice occurred, or the reverse happened and immunity resulted.

If, however, such potentially icterogenic serum were transferred to another person he might not be able to resist its hepatotoxic action.

Therefore serum from a person who had in fact at no time been jaundiced might still be hepatotoxic and thus icterogenic.

Initial illnesses like that of Dorothy Elliott varied from illnesses so closely resembling infective hepatitis as to compel the acceptance of their being identical to it, to no doubt apparently trifling gastro intestinal upsets.

In this way we could readily understand the difficulty, nay the practical impossibility of tracing the source of the icterogenic serum ~~inducted~~ INCLUDED in many batches of serum which subsequently led to outbreaks of post homologons serum jaundice.

6. A person such as 2 or 3, who suffered from the epidemic illness might convey the infection to others. Such others would in most instances suffer from an illness of the type described under 2 or 5, but in the case of 2 certainly,

and in the case of 3 possibly, and I thought only occasionally, such others might become jaundiced.

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Of the 6 suggestions which I have made above, I consider that no further evidence is required, in substantiation, in respect of numbers 1. Spread from jaundiced patient to jaundiced patient and 4 and 5 which I have dealt with in some detail.

It now remains for me to give such evidence as gives support to my suggestions numbered

2,
3,
and 6,

and this I propose to do as briefly as is compatible with their adequate demonstration.

2. Infective Hepatitis without Jaundice. Cases illustrating the spread from a Jaundiced Patient to patients who did not become jaundiced.

I will begin by relating 3 illnesses occurring in one family. The three case histories relating to the children Lavery demonstrate this spread, and I therefore produce them now for the reader's consideration. (at page 534.)

Eileen Anne Lavery, an 8 years old girl attending the Roman Catholic School, became jaundiced on the 30th October, 1944. Prodromal symptoms, it will be noted, had been marked for a week prior to this date, and they would suggest that Eileen

might have been infective from 23rd October, 1944.

When I visited Eileen on 17 Nov 1944, I found her brothers Henry, aged 3 years, and William, aged 13 years, both ill. There seemed to be no possible source of infection for Henry's illness other than his sister's illness, and as William took ill at the same time it appears reasonable to assume that his illness had a similar origin.

The salient features in Henry's illness were:

1. He had been off colour for a week or more. His paleness and the facies had suggested to his mother an oncoming illness.
2. Vomiting: including precipitate vomiting at 3 a.m. after being awakened by epigastric pain.
3. Loss of appetite. Constipation -- diarrhoea later.
4. Tenderness in right subcostal margin.
5. Child lying "lifeless" in his pram.

Similar features in William's illness were:

1. Biphasic illness.
2. Headaches.
3. Conjunctivitis.
4. Vertigo. (fleeting).
5. Anorexia. Nausea.
6. Pain over the liver.
7. Erythema.
8. "Pins and needles" --"his legs felt like electricity."
9. Tongue simulating streptococcal tongue.
10. Occasional sudden loss of voice.

The similarity in the appearance of the patients and in the symptomatology was such that I have no doubt that the same pathogenic agent was at work, and that Eileen had infected her brothers. Their illnesses represented infective Hepatitis without Jaundice.

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Next I will refer to an illness which appeared to demonstrate the occurrence of subicteric hepatitis as the result of infection from a patient who became jaundiced: and in this instance the spread did not occur in the home but probably by actual contact at play.

The jaundiced patient was Raymond Elliott (case No 10 page378and page 497) and his friend was George Parker. Raymond Elliott was jaundiced on 20 October, 1944. Parker consulted me a month later, but he had been ill for 2 or 3 weeks prior to this date. I considered Parker's illness to be indicative of subicteric hepatitis of a type intermediate between the type presenting marked gastro intestinal symptoms and nervous symptoms . As his brief, but I trust adequately illustrative, history reproduced at page538 will show the onset occurred,as it so often did,when he arose in the morning. He tha felt sick and giddy, and, which was unusual, he actually fainted. An attack of vomiting was followed by an apparent, if partial, recovery and he returned to school. Five days later we have the occurrence of diarrhoea to

illustrate the commonly biphasic nature of the illness, which I have emphasized especially as occurring in the children who were jaundiced at Cold Hesledon. Preceding and continuing throughout the whole illness, we have the lethargy which occasioned more anxiety to the observant mother than any of the other symptoms: beginning in the usual way "he would not go out to play with his friends" and complained of by the boy in his simple and convincing way - "he just wanted to keep on taking rests."

.....

It is natural, if not indeed essential, in illustrating a spread as I am attempting to do, that I should have selected cases which leave little room for doubt as to the identity of the 2nd illness, but I feel that it is a point which is worth making that all such subsequent or 2nd illnesses as may have occurred as the result of a spread from a jaundiced patient would not, as it were, be so obligingly typical. They could not be expected to represent, what an investigator might term (to himself possibly) "good cases."

A possible instance of a purely gastro intestinal type of the prevalent illness is provided by Richard Bond, the father of the 3 years old Richard Bond, who took ill on 29 Oct, 1944 and was jaundiced on 3 Nov, 1944.

Richard Bond Senior awoke at 3 a.m. on 20 Nov, 1944, with severe upper abdominal pain, and he vomited urgently and violently. He was immediately purged and both diarrhoea and

vomiting were repeated four or five times. The motions were described as being like water. He remarked on the fact that the pain was not at all like colic, it was severe but it was dull, although it did ~~not~~ vary in intensity. Neither the temperature nor the pulse was disturbed. The tongue was lightly furred, the papillae rather prominent, and the top and edges were clean, inclined to be raw.

I decided to include this case not because it proves anything by itself. But all through the winter, October to April, we had many such cases. It appeared noteworthy that for 21 years there had been no such incidence of winter diarrhoea in Murton --- nothing approaching the proportions of this epidemic of diarrhoea. Some cases, as I have related elsewhere, seemed to simulate subicteric hepatitis. Richard Bond's illness frankly did not do so apart from the absence of colic and possibly the changes in the tongue.

Further the medical Press contained many references to an enteritis which was apparently widespread in the country and for which no organisms could be proved to be responsible. Dr. Wilkins, of Kidderminster, as I have stated on page 279 referred to the similar occurrences in his practice after an epidemic of catarrhal jaundice.

A boy under my care was so ill with such an acute enteritis that I transferred him to an isolation hospital. He was almost comatose and I made an incorrect tentative diagnosis, but the

cause of his diarrhoea was not ascertained in spite of exhaustive investigations. This occurred in a house where the inmates had suffered from the Bakery illness (son of A. F. M. Russell, see page 346)

I will not burden the reader with details of this case history, as I include this section more in the spirit of provoking thought on the matter, than of proof which I cannot supply.

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Having provided examples where I should say it was certain that a jaundiced patient had infected others, (Lavery) where it was highly probable (Elliott - Parker) and possible Bond - Bond, I propose to refer to 2 instances where a child was jaundiced and the brother or sister suffered from an illness which was obviously similar, except for jaundice, at the same time.

Catherine Robinson (page 212) was not jaundiced but it certainly appeared that she suffered from the same infection as her brother Brian and her sister Brenda who were jaundiced and at the same time.

George Warwick Forster's illness is described on page 485

He was jaundiced. In this case it can be ragarded as almost certain (I would say certain) that his sister Elizabeth, whose history is given on page 559, was suffering from subicteric infective hepatitis, again at the same time.

In both of the above instances it appeared that the jaundiced and non jaundiced patients had been infected from a common source.

The above cases make it appear that the occurrence of jaundice or the non occurrence of jaundice did not entirely depend on, or was not entirely determined by, the strain of the virus or the properties of the virus.

5. Demonstrating the Occurrence of an illness which was probably due to infection from a case of infective Hepatitis accompanied by jaundice, in which the symptoms were predominantly nervous, the gastro intestinal symptoms being relatively less conspicuous.

Maureen Turner became jaundiced on 14 Nov, 1944, and her brother Alan was jaundiced on 15 December, 1944. In both cases the prodromal period was well marked, particularly I would refer the reader to the mention (pages 506 and 516) of well marked "nervous symptoms" in each case. Maureen had been listless, and her mother said, "just hanging about the house" for 2 or 3 weeks. Further she complained persistently of pains in her thighs, which were dismissed as "just rheumatism". Alan, to quote the same observant authority "had had no life about him for a fortnight."

In view of these "nervous" symptoms the illness of the father, David Turner, assumes an added interest. His only gastro intestinal symptom was loss of appetite but it was not

simply a loss of appetite. He remarked that he was eating less and less. Yet he sat down each meal with the anticipation that he would enjoy his food. But after one or two bites -- the amount gradually decreased -- his appetite failed and then he became mauseated. (How similar to the story of Raymond Pow, who became jaundiced! see page 520). His nervous symptoms comprised a concomitant progressive weakness, tiredness and weariness. He said that he had been "too listless to bother with anything"-- this was a complaint which was typical of so many of the prevalent illnesses. Further Turner showed a moderate amount of urobilin. From these remarks and the history on page 539, the reader will remark how similar Turner's illness was to very many which I have recounted. I do not wish to emphasize it ad nauseam but Turner's illness definitely suggested the action of a neurotropic virus: the increasing languor and exhaustion, the overpowering "laziness" and the unmistakable and distinctive facies.

I attempted to reason out why the father should be so affected, and I offer the following suggestion, as it has occurred to me.

The virus which had attacked both of the children possessed I assumed, both hepatotoxic and neurotropic properties. The children had no immunity against this virus, and so they suffered from symptoms due to both of those actions.

Here, as in so many other instances, the neurotropic action showed first, in the lethargy and "rheumatism" of the prodromal stages of the illnesses. Later the virus caused the actual hepatitis, hence the onset of jaundice.

Now it was obvious that most of the parents must have possessed an immunity to the virus of infective hepatitis, as otherwise the incidence of the disease would not have fallen so largely upon the child population only. However, as regard the "nervous" type of illness there was quite a high incidence in the adult population.

The explanation might be that whilst the adult population had, sometime, acquired an immunity to a virus which was no doubt closely allied to the present virus in its hepatotoxic properties, they had not acquired an immunity to the neurotropic properties possessed by the present virus. The virus which was at present active in the community would, thus, be assumed to possess neurotropic properties such as had not been possessed by any virus which this community had previously encountered.

In the case of David Turner it appeared that his immunity to the hepatotoxic action of the virus was not absolute as witnessed by the intensity and suggestive type of his loss of appetite and the occurrence (for what it may be considered worth) of his urobilinuria. As regards its neurotropic action he appeared to possess no immunity, or at least no higher degree of immunity than his children.

I know of nothing in the present state of our knowledge which would definitely rule out the possibility of the theory which I have advanced above. If the reader is possessed of such knowledge, I trust he will bear with me in my attempt to explore these fields of knowledge ---immunology and the study of virus diseases --- with which he may be more familiar and in which I am humbly if ambitiously inexperienced.

.....

6. It remains for me to now consider the spread of the disease from people who were not jaundiced: as in 2 and 3.

As I have stated it appeared obvious that such patients could infect others, who then, in about a month's time, developed illnesses similar to that of the infector. But more striking and important would appear to be any evidence suggesting the spread from such a person who was not jaundiced and which resulted in the illness of a patient who did not become jaundiced.

In the first instance I would refer the reader to the illnesses which occurred in the Robinson family at Cold Hesledon. Here we have as described on page 213 the history of the illness of Douglas Robinson. I did not attend the boy but there can be no reasonable doubt that he had suffered from subicteric infective hepatitis. This is as nearly proved as such evidence would admit, by the fact that the mother had

noted his dark orange yellow urine and his clay coloured stools especially as she is a very sensible woman. When the other 3 children became ill a month later, Mrs. Robinson at once remarked on the colour of the urine and faeces and sent for me on that account, mainly. Of these three children, two became jaundiced --- Brian and Brenda -- and Catherine did not become jaundiced. In the section of this work entitled "Cold Hesledon" I stated that I considered that the 3 children might have been infected either by Iris Etherington or Jean Armstrong, both of whom had been jaundiced; or by Douglas.

Now I have no bias in favour of the view that Douglas was the infector, I only seek the truth. But on more mature consideration at this distance of time * I certainly do consider that it was much more likely that Douglas conveyed the infection to the other members of the family. Douglas, like the two girls I have mentioned who were jaundiced, took ill on 10th July, 1944. Now all the three remaining Robinson children took ill on 14 August, 1944: I would deduce that they were probably all infected at the same time. If the spread was conveyed as I have suggested by contact or similar method it wasobvious that Douglas had every opportunity to act as the infector. Every day before, during, and after his illness there would be that intimacy which is so understandable in the house; an intimacy which investigations into the epidemiology of measles, as I have previously remarked, is more

* Written on 11 June, 1945.

potent in the matter of infection than any other. Further, either of the 2 jaundiced girl friends of the family would be much less likely to infect 3 members or varying age and sex in the one family, especially at one time. Such friends would certainly be inclined to select a member of the family, or very likely 2 members as Catherine and Brenda are of similar age, to the exclusion of the 6 years old Brian in their social activities. Douglas they had always with them, when he was out of sorts, really ill and afterwards.

Especially if the disease was not spread by aerial infection, was it likely that Douglas caused the spread, as here again he would have more, and more frequent, opportunities of so doing.

.....

I think that the sequence of events in the case of David Clews and his daughter Judy is suggestive, and I trust of some interest, in this connection.

I must preface the report by stating that Judy did not become jaundiced: she did, however, have gross bilirubinaria for several days accompanied by almost white stools, and I think and submit that the distinction is not vitally material to out present study.

David Clews' history is given in narrative form on page 563 and Judy Clews' illness is reviewed on page 483 . Might I ask the reader to refer to them for a moment?

Without further elaboration I would leave the reader to decide whether he agrees with me that the symptoms are very similar, and that the circumstances, and the time relation of their occurrence, suggest that the father may have infected the child; assuming the incubation period to be in the neighbourhood of a month. The father was ill from about 5 Sept.1944: his daughter Judy had gross bilirubinuria for several days dating from 2 October, 1944. The significance of Clews' story did not occur to me until I noted later, in common with my partner, that such a story was becoming common.

I consider this to be a <u>really definite</u> instance of infection, as suggested.

The third and last example which I will submit in support of the spread in the home, from a patient not jaundiced to another who became jaundiced is in respect of the family Bridge.

The first member of the family to consult me was the father, Edward Bridge, and his illness is recorded on page 668, which I must ask the reader to consult. The main features were the initial "head cold" with profuse watery rhinorrhoea with pains in the neck extending on to the shoulders. This was followed by pain on coughing, the pain being felt anteriorly over the region of the liver and in the epigastrium. Next we note the pains in the left leg which would arouse suspicion of early tabes, but I encountered such pains in several cases, children and adults alike, and I have reasons for believing that Bridge has not suffered from syphilis.

Bridge began his illness some ten days before he consulted me on 10 Dec 1944, and his son A. Bridge became jaundiced on 2 Jan 1945.

.....

In each of the preceding three "relations" the people affected lived together.

It would obviously be much more difficult to trace the spread if it occurred outside of the home. I submit the following as a possible instance of such a spread.

When Raymond Pow (page 520) became jaundiced I was very keen to attempt to trace the source of his infection: this the more so, as he told me that he had no friends now, they having seriation forsaken him for members of the gentler sex. Thus Pow had spent all his leisure time in domestic hobbies, his days being fully occupied by his pit work and such work at home. He knew of no one who had been jaundiced.

Pow is employed as a "dish lad" down the mine: his duties were to manoeuvre the tubs to and from the onsetter. The onsetter is engaged in loading full tubs into the upgoing cages, and, conversely, unloading the returning or downcoming empty tubs. Thus the onsetter and the dish lad are in the closest proximity and they handle the same objects.

Pow told me that his onsetter had been ill. The onsetter was named Bertie Wood.

On the 16 January 1945 I was called to attend James W.Wood, the 19 years old son of the said Bertie Wood.

The boy's illness was very suggestive of a mild infection of the type prevalent in Murton. The pulse was slow --50 per minute -- he looked weary to the point of exhaustion, and it seemed such a trouble for him to answer questions that one might have considered him almost insolently disrespectful: which indeed is quite unlike the lad's normal behaviour. A most peculiar coincidence was that he complained about his voice sounding strange to himself, a symptom of which Pow complained also. The way in which Pow and he described this symptom varied, as reference to Wood's history (page 540) will demonstrate. (Incidentally no one else made exactly this complaint to me throughout the epidemic.)

But of more immediate importance is the history of the father, Bertie Wood. This particularly well preserved and robust man of 62 years gave me a history (page 541) which I thought typical of the nervous group of illnesses in the epidemic. The weakness, tiredness and reduction of his leisure activities, all of them progressive, for a fortnight before he was forced to stay from work; the aches in the shoulders; the use of the very words which were, one might say, the slogan of the epidemic - "I can't be bothered"; the thick and muddled headache of frontal and suboccipital distribution and the peculiar dysphagia --- they were all characteristic. My partner, who had attended Bertie Wood, confirmed the history.

Thus it seemed possible that Bertie Wood had infected Pow.

There was another occurrence which strengthened my belief in the relation between the illnesses.

Mrs. Wood (Bertie Wood's wife) suffered from an attack typical of the gastro intestinal form of the epidemic illness on 28 November 1944. The main features of her illness were precipitate vomiting, vertigo and dull frontal headache, with a degree of pyrexia and a relatively slow pulse. Her history is not retrospective: it is one of several hundreds which I recorded, in order to attempt to trace the spread of the infection, at the time of my attendance. It is reproduced on page 542.

It thus seemed likely that Mrs. Wood had infected her husband and that he had, in turn, infected his son James and, possibly R. Pow, who alone became jaundiced.

Finally in this relation, it should not go unnoticed that A. T. Johnson, a boy who lived next door to the Wood family, took ill on 20 December 1944 and became jaundiced on the 1st January 1945.

The dates of the illnesses referred to are:--

Mrs. Wood.		28 Nov 1944
Bertie Wood	off work	18 Dec 1944 to 8 Jan 1945.
Raymond Pow		11 Jan 1945
James W. Wood		16 Jan 1945.

The history will supplement these data.

I suspected that J. H. Marriott's illness (page 480)--- he was jaundiced on 5 September 1944 --- was not unconnected with the previous illnesses which had, recently, occurred in his home.

His infant sister died on 11 August 1944, after an acute attack of, clinically, gastro-enteritis. She was ill for 36 hours but the mother thought the diarrhoea and vomiting "were just due to teething" and did not seek medical aid until the child became convulsed (the infant was dead when I arrived). The child was very devoted to his sister, uncommonly so: he would nurse her for hours and frequently awoke her from sleep by kissing her.

Significant I thought was the further fact that an older sister, Isobel Marriott, had been ill, again a month earlier. She attended school on 10th July, 1944, but seemed "queer, generally out of sorts and listless," and she thereafter remained at home all that week. She is said to have "sat about the house" refusing to go out to play, etc.

She improved and returned to school on Monday 17 July 1944, only to come home obviously worse than ever. She said that she felt sick and that she wished that she could vomit: she did not vomit. She has a severe epistaxis and it was on this account that a doctor was called in. The temperature was found to be 101° F. The nose bleedings were severe and were repeated several times during the next seven days. I subsequently discussed the child's illness with the doctor who attended her.

He told me that he had feared that Isobel might be developing a lobar pneumonia, but that, frankly, the evidence was very doubtful. After some hesitation he put her on a course of sulphapyridine. No evidence of consolidation following, he was left undecided as to whether he had acted correctly or incorrectly. It is unnecessary to elaborate on the situation, which the reader will readily appreciate.

I should add that Isobel Marriott attended St. Joseph's Roman Catholic School to which I elsewhere refer.

The nature of the illnesses and the time intervals of their occurrence may justify the inclusion of this reference.

To complete this section, 6, I have to illustrate the case to case spread where jaundice was not a feature of the illness of the infector or theinfectee. In order to prevent the work from being too bulky, I have included in the case histories, which I have previously offered as illustrating the epidemic illnesses in which jaundice was not a feature, a considerable number which will serve to demonstrate the spread.

I have indeed included such "runs" of the infection for another reason also. I realise that it would be possible to extract several cases which I have included in the previous section referred to, and to maintain that when they are examined individually the picture is not pathognomaric of any specific illness. Within limits, however, I feel that such a procedure might well be unfair. To extract a sentence from

its related context is at times most unfair and misleading: to consider a symptom apart from the complete history of an illness can be equally misleading, as for instance Walshe insists when he states that "physical examination can be fully interpreted only in its context of history." (e.g. retrobulbar neuritis in relation to disseminated selerosis).[12]

By relating several sequences of illness among people who were in intimate association, and by virtue of the fact that these illnesses bear a resemblance which is at times very close and at all times suggestive, I seek to convince the reader that they ~~cultivate~~ CONSTITUTE examples of the spread of the epidemic illness.

The epidemic at the bakery, which is described at some length is the most obvious example in this work, but it has already been discussed and I desire to refer to other examples more fully at this stage.

Let us consider Cases 37, 38, and 39 on pages 655 and 656.

When the 15 years old Thomas Holmes sent for us on 11 Oct 1944 he complained of difficulty and discomfort in swallowing. There was absolutely nothing abnormal to be seen on examination of his throat and his temperature and pulse were normal. The discomfort was said to be situated at the thyrohyoid level. We arrived at no definite diagnosis and in fact departed more in sympathy with our own unnecessary work than with Holmes' alleged discomfort.

As so often follows upon such a hasty and unusually unsympathetic impression, we were soon proved wrong.

The next day the lad was so giddy that he could not stand, and after being intensely nauseated he vomited violently and repeatedly. He had no pain whatever. (I later found such thyrohyoid discomfort to be a symptom frequently encountered in the epidemic).

The vertigo persisted for 4 or 5 days.

Exactly 4 weeks after her son's illness, Margaret Holmes became ill. Again the initial symptoms were referred to the throat, but this time we were not consulted until the following day when she vomited so violently and so frequently that she became alarmed. The "vomitus" consisted of "just a little froth." Again the vomiting was unaccompanied by pain although it led to soreness from the violent, muscular, exertion.

That the two preceding attacks were related seemed certain, because, on the day following the onset of Mrs. Holmes' illness, I was called upon to visit her sister, Mrs. Bowater, who resides at over a mile distant. This illness was similar to the other two but it was distinguished by several interesting features.

The initial symptoms were that she felt cold and had severe frontal headache. She had severe epigastric pain and pains shot up her back -- like arrows darting or a

knife stabbing, was the description. To complete a now familiar syndrome, she felt overpoweringly tired and weary and this was indeed patent at a glance. Anorexia was complete and she felt ill at the thought of food. She was puzzled and worried because she felt "light headed" by which she meant "stupid", incapable of clear thinking "as if her brain was clouded or dazed."

It should be stated that Mrs. Bowwater visited the Holmes household when Thomas was ill and that she had a meal during her stay.

Another simple sequence of infection appears to be illustrated by cases 43 and 44 (pages 661 and 662).

The former patient, Mary Ruby Askew, consulted me on 11 December 1944. It will be seen that she had an upper respiratory catarrh for a fortnight prior to that date, and she felt 'tight' in her breathing especially in the mornings. Her other symptoms were not at first at all distinctive, but she began to worry about feeling listless, out of proportion to what she would have expected with such "a cold." She used the usual expression -- she "could not be bothered with anything." Further she had fleeting giddiness and pains in front of the knees -- both common complaints in the epidemic. When she consulted me she complained of pain in the epigastrium and over the right lower ribs in front. Later she complained of pains in the

thighs and shoulder girdles and especially in the left upper arm, where the pain was said to be accompanied by a sensation of powerlessness.

The illness of her mother, Emma Johnson, began with a similar upper respiratory catarrh and culminated in an attack of vomiting, faceache, headache and intense vertigo on 11 January 1945. The nature of the onset of the vomiting was of interest. It was preceded by a "turning-over sensation or commotion in her stomach"; an alarming sensation which was exactly copied in many cases of the illness and is reported in the case of, for instance, Mrs. Wilson, described as Case 12, page 625.

I feel compelled to substantiate the claim that this type of illness had an incubation period closely comparable, or identical, to that of infective hepatitis by giving yet further sequences of the infection, in case my previous evidence may be considered insufficient, and to be explained on the grounds of coincidence.

The next group of cases will be readily referred to as they are described together (pages 663 to 667.) as cases 45, 46, 47, 48. The reader is requested to read them in the order 48, 47, 46, 45, this giving the chronological order. The patients are closely related and they visited almost daily at one another's houses, being on the most intimate terms.

The first patient was Joseph McNally. I suggest that he infectd his sister Joan Smith: that she in turn infected George W. Richardson, her sister's husband; and that the last-named infected Leslie Smith -- Mrs. Smith's son.

Some of the illnesses present features which in the light of my previous recordings may serve to establish the identity of the illnesses. The first illness, that of Joseph McNally, commenced on 8 November 1944.

The leading symptoms were diarrhoea and vomiting. Recovery was protracted, especially so, in view of the patient's exceptional physique and, generally fit condition. Twice after attempting to resume work he had to absent himself as he was weak and dyspnoeic:this last being a common and interesting symptom.

The second patient, Joan Smith, could not see to thread a needle or do any close work. This was again an interesting symptom frequently encountered. The visual disturbance was, of course, fleeting, else I should not have remarked on it. It was preceded by pain in the occiput,neck and shoulders. Later she had gastric symptoms and the overpowering listlessness so typical of the illness. A peculiar feature of her description was that if she rested, leaning her head back in the chair, it required a great mental effort to sit forward from that position. Several patients made this same, uncommon, complaint. Further she mentioned that she had to

keep raising her eyelids as they seemed to be too heavy to remain open -- exactly as complained of by the Bakery patients q.v.

The third patient, George D. Richardson, had a most peculiar illness, featuring headache, profuse sweatings, and a bradycardia remarkable in relation to the degree of pyrexia. To complete this rather remarkable story, I would point out that he felt ill only from 3 a.m. to 9 a.m. daily.

Finally in this group is the illness of Leslie Smith. It was indeed typical and distinctive. Pains in the thighs just above the patella were as commonly encountered. Next was the familiar combination of aching and a feeling of powerlessness in the shoulder region. Giddiness was marked and alarmed him. The appearance and complaint of extreme lethargy and the rushing to vomit, but not doing so, complete the distinctive symptomatology.

The onset of the case of Joan Smith was vague and ill-defined, probably 1st December would be approximately correct. The sequence was therefore:

Jos. McNally	Case 48	8 Nov 1944
Joan Smith	Case 47	1 Dec 1944
Geo. D.Richardson	Case 46	23 Dec 1944
Leslie Smith	Case 45	22 Jan 1945.

.....

I thought that the illnesses of John W. Bate and his stepson, Peter Laws, as described, (cases 36 and 35) were probably related. Very briefly, the father's illness featured diarrhoea, vomiting, and disproportionate lethargy. The precipitate vomiting all over the bedclothes, which occurred later, is noteworthy. The stepson's illness beginning insiduously incapacitated him by 29 December 1944. An obviously genuine fatigue was the presenting symptom. The facies was striking --- I have already referred to the typical appearance.

.....

A further group of 5 illnesses appear to illustrate the spread, and I propose to conclude this section by referring to them.

The patients concerned in this group are Jane A. Bell, George Bell (Cases 10 and 9, pages 570, 569 Frank Penman, William Brown, Mrs. Edna Brown (cases 40, 41, 42 pages 657, 658 and 659.

I will leave it to the reader to observe the nature of each illness, but I must mention how the patients were in intimate contact.

Frank Penman lives with Mr. and Mrs. Bell (Mrs. Bell is his sister). He visits regularly at Mr and Mrs. Brown's (Mrs. Brown is also his sister) where he frequently helps

with the domestic work --- washing dishes etc, and being a bachelor he spends much of his time there.

The sequence of the illnesses was as follows:

Name	Date of illness.
Mrs. Bell	29 Sept 1944
George Bell	18 Oct. 1944
Frank Penman	13 Nov. 1944
Mr. Brown	6 Dec. 1944
Mrs. Brown (18 Dec) and	1 Jan. 1945

Mrs Bell's symptoms were gastro intestinal followed by persisting lethargy.

Mr. Bell's symptoms were gastro intestinal.

Mr. Penman's symptoms were mainly "nervous" - lethargy, giddiness and a muddled feeling.

Mr. Brown's chief complaint was his inability to think clearly.

Mrs. Brown's illness presented gastro intestinal and nervous symptoms. I was interested in her description of feeling that "her brain had lost the power to command the body." It compared with Hunter's story (Case 28, page 645).

THE SPREAD OF THE INFECTION.

THE EPIDEMIC.

"Genesis", Course and "Exodus."

Some Thoughts and Impressions.

THE SPREAD OF THE INFECTION.

Having thus attempted to justify the 6 suggestions which I made earlier, I think it would be well to repeat them in full for the convenience of the reader: with certain additions.

1. A person who was jaundiced could infect another person, who, in turn, in about a month would become jaundiced.
2. A person who was jaundiced could infect another person who might develop an illness so closely resembling a fully developed picture of infective hepatitis that the only difference was that jaundice did not occur.
3. A jaundiced person could infect another person who might develop an illness less closely simulating "a fully - developed infective hepatitis" than did 2: frequently the difference between 2 and 3 lay in the relative prominence of "nervous" symptoms and the less prominent gastro-intestinal symptoms both in the latter group.
4. A person who contracted an infection leading (as in 2) to an illness simulating infective hepatitis but without jaundice might continue to harbour that infection and subsequently, two or three months later, become jaundiced; the virus at this late stage exerting is full hepatotoxic action.
5. A person such as Dorothy Elliott, group 4 immediately above, could in the early stages of her initial illness,

infect others and such others might become jaundiced.

6. A person such as 2 or 3 immediately above, who suffered from the epidemic illness might convey the infection to others. Such others would in most instances suffer from an illness of the type described under 2 or 3, but in the case of 2 certainly and in the case of 3 possibly, and I thought only occasionally, such others might become jaundiced.

I would here add that consideration of 4 and 5 appeared to offer an explanation of the prolonged incubation period in homologous serum jaundice, as I have previously remarked.

Further it appeared likely that, in respect of 4 and 5 above, the so called initial illness might not always be so well defined as that of either Moira Forster or Dorothy Elliott. Now, if such an illness was ill defined, it might be "missed" as it were, and in that case we would have a long interval before jaundice occurred. In the case of the 2 following children they became jaundiced after there had been illnesses of the, non-jaundiced, epidemic type in their homes; 106 days and 82 days previously.

Edith Davison.

This girl was jaundiced 20 March, 1945.

I had made a note of the illnesses of her mother, father and brother just over 100 days previously.

The notes, I must emphasize, were, as usual, taken down at the time of my visit. I remember that the thing that made

me record the illnesses in early December was not so much the symptoms of any one of the patients but the picture presented by the whole three when considered together.

I include the brief records which I made of the 3 illnesses.

The mother/had/gastro intestinal type of symptoms:— nausea, vomiting and diarrhoea, with the typical upper thigh aches and frontal headache. The pulse was slow. The facies was suggestive of the prevalent infection.

The husband had few symptoms, but they were suggestive; like his wife, he had pains in the upper part of the thighs in the exact position which I have elsewhere noted, and he complained bitterly of dysphagia. "Everything seemed too big or too dry so that it just would not go down." Davison is a very steady worker and certainly not of a neurotic type. Incidentally I have many recorded cases, which cannot be included for reasons of space, of such dysphagia in addition to those included in this work.

A few days prior to the illnesses of the parents, the son, Brian Davison, began to feel sleepy, later had diarrhoea, and then with no warning he had vomited several times.

Harriott Gormen.

This child was jaundiced on 21 March 1945. The illness was typical of infective hepatitis and the mother noted the jaundice on 16 March 1945.

I append, at the end of this section of the work, the

record of the mother's illness on 29 Dec 1944. It was suggestive of the prevalent illness which did not feature jaundice. To support this opinion I should state that another child in this home had suffered from a similar illness featuring, nausea, headache and vomiting with marked lethargy and exhibiting a biphasic course 25 days before the mother was ill.

I agree, or rather, indeed, would I point out, that owing to the prevalence of the illnesses described in which jaundice was not a feature, it might be anticipated on the grounds of coincidence that cases of "jaundice" would be expected to follow in some of the homes.

Nevertheless, and especially in view of the evidence of other sections of this work, the interval 106 days and 82 days between the illnesses seemed significant.

I have therefore included these two cases and their associated circumstances in the hope that they may provoke thought.

Further a true record of an epidemic should include not only "the truth and nothing but the truth" but also the whole truth, lest data which appeared unimportant should later prove of moment.

THE EPIDEMIC.

"Genesis", Course and "Exodus."

Some Thoughts and Impressions.

It was just over one year from the appearance of "jaundice" in the community that the last case of illness featuring jaundice occurred. The period concerned was from 4 March 1944 when Mrs. Brown took ill, until 2nd April 1945, when the last patient, Audrey Southgate, became ill and was jaundiced. To date, 16th June, 1945, there have been no further cases featuring jaundice.

Just over a year ago I should have simply recorded that Murton was visited by an epidemic of Infective Hepatitis which began on 4 March 1944 and finished on 2nd April, 1945.

To-day that is not my conception of the events.

From an early stage in the epidemic it became evident that cases not accompanied by jaundice were occurring. Nor did those cases in which jaundice did not occur, keep to a fixed or uniform pattern. The symptoms in a case of infective hepatitis accompanied by jaundice could be grouped into two main classes: those which might be termed gastro-intestinal and those of a nervous type. I group those symptoms as viewed from a clinical viewpoint. In some of the jaundiced patients both groups of symptoms were well marked but they varied in their relative prominence from case to case. Similarly in

those patients who were not jaundiced the symptoms were mainly of gastro-intestinal and nervous types. Here again in many cases both groups of symptoms were marked; and again the relative prominence of the groups of symptoms varied from case to case. But among the patients who were not jaundiced it appeared that there were many whose symptoms were simply frankly gastro-intestinal and yet others whose symptoms were almost entirely "nervous." Nevertheless there was usually some gastro-intestinal upset, albeit of a relatively inauspicuous nature in the "nervous" group. Further the simultaneous occurrence of gastro intestinal illnesses and "nervous" illnesses in the one household, as in the one community, at the same time, was one factor which suggested their being related. Again in many but not all of the apparently purely gastro intestinal types of non jaundiced illnesses there were less conspicuous "nervous" symptoms.

As I have already stressed the nervous symptoms were of a type and pattern distinctive to the present epidemic, as I would like to think I have succeeded in demonstrating to the reader.

Therefore, if we picture jaundice as the central feature of the illness, we can imagine the epidemic keeping in its early stages to this central feature. Gradually an occasional case breaks away from the centre and we have a case of infective hepatitis not featuring jaundice. We might term this a "centrifugal" tendency.

Such a case leads to others: many of those resulting cases copy exactly the original centrifugal case, we might visualize them as staying at the same distance from the centre; an occasional case leads to the occurrence of clinical jaundice in a contact, and this we could visualize therefore as a centripetal tendency; yet others lead to cases which depart more from the typical picture of infective hepatitis, a further centrifugal tendency. The last cases referred to are represented by those cases which present either exclusively gastro intestinal symptoms and exclusively nervous symptoms.

After such a manner did it appear to me that in the very early stages there was a rough uniformity in the symptomatology, and gradually cases occurred strikingly similar but different in detail. Progressively the tendency to depart from a uniform pattern became stronger, although the similar features were still recognisable.

Ultimately the resemblance to the original central cases became less and less distinct. Thus it is that now, 16 June, 1945, I could not give accounts of illnesses occurring in this area which bear a convincing resemblance to the illnesses of the "original" infective hepatitis illnesses.

When one has formulated such a theory it is difficult to weigh the balance between bias and unbiased judgment. I can only state that we still continue at this date to have large numbers of cases of gastro-enteritis for which we can find

no obvious cause, and we still encounter fairly large numbers of patients with rather trifling upper respiratory catarrh and peculiarly disproportionate lethargy and fatigue.

But even ignoring those last two remarks, it seemed obvious to me that if the epidemic did begin with a case of "jaundice" it did not terminate suddenly. It was not cut off, rather did it fade out.

Thus I now believe that a well defined clinical entity in the form of infective hepatitis, maintained that identity for some time, before gradually and progressively losing it, and thus tapering off and fading into a background of ill-defined illnesses.

Was it possible that in this way it might linger on in the community, the cases becoming less numerous and more vague until such time as circumstances exerted a "centripetal" influence ?

Was this a possible explanation of the inter-epidemic (or endemic) existence of the virus ?

Andrews, Smith and Laidlaw[13] leading research workers in the epidemiological problems of epidemic Influenza, have postulated as a working hypothesis the existence of an inter-epidemic, non-virulent basic virus, "harboured by a number of individuals, especially during periods when winter colds and febrile catarrhs are prevalent." "These two affections have been observed to precede outbreaks of influenza and it

is probable that by the medium of repeated human passage a non virulent virus may be raised to the virulence of virus A."

I had no evidence to present of the illnesses which preceded the Murton epidemic. But my observations of its course and "disappearance" from the community suggested that after a time the virus had probably become altered by repeated passage. It had, I presumed, become less specific till at the end it might be compared with the hypothetical non-virulent basic virus of Andrews, Smith and Laidlaw.

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SYMPTOMATOLOGY.

The symptomatology in the case of the Cold Hesledon patients who were jaundiced has already been discussed.

The cases[x] numbered A, B, C, D, and E were attended by Dr. Mackinnon. At no time did I attend the first two, A and B. In the case of C, D, and E, Dr. Mackinnon very kindly suggested that I should make inquiry visits. I have included a brief record of each of these cases.

Cases 1 to 39 occurred in the practice of my partner and myself. I attended some two-thirds of these patients throughout their illnesses, the remainder after my partner had referred them to me.

I now propose to present a summary of the main symptoms encountered with special reference to their relative frequency; and to consider each symptom, where this appears to be indicated, in some detail.

Every effort was made to avoid the use of leading questions, and the symptoms as they are now given are the symptoms of which the patient actually complained.

x. References are to the table on Page 378.

SYMPTOMS.

Total number of patients in group.....44

Excluding Cases A and B.....42

Jaundice.....41

Bile in urine but no jaundice...1

Jaundice but no bile in urine...1

Vomiting	30
Abdominal Pain	29
Anorexia	27
Marked Lethargy	27
Headache	18
Vertigo	14
Skin eruptions	8
Liver Palpable	7
Upper Respiratory Catarrh	7
Itchiness of skin	7
Conjunctivitis	6
Diarrhoea	4
Marked constipation	3
Association with Parotitis	2
Hiccough	2
Herpes Simplex	1

A relative lymphocytosis was present in all, 8 cases, in which the examination was conducted.

Also noted. Pains in the limbs.

Pins and needles sensation.

Visual disturbances.

Disturbance of hearing.

Disturbance of voice.

Disturbance of micturition.

Noteworthy was the condition of the tongue.

Differential White Cell Count.

Case No.	Poly. Leuco.	Eosino Leuc.	Baso. Leuc.	Lympho	Mono.	Intensity of Jaundice.
4.	29.0	3.5	--	66.5	1.0	Moderate to deep
5.	28.0	1.0	1.0	48.0	12.0	Moderate to deep
6.	45.5	1.5	--	49.0	4.0	Deep.
7.	34.5	2.0	--	60.5	3.0	Moderate.
9.	54.0	3.5	--	37.5	5.0	Slight to moderate.
10.	48.0	2.0	--	49.0	1.0	Moderate.
11.	34.0	2.0	--	62.0	2.0	Very slight.
14.	47.0	1.5	--	49.5	2.0	Moderate.

The main feature of the counts is obviously the marked relative lymphoocytosis.

The degree of lymphocytosis bore no relation to the intensity of the jaundice.

Jaundice.

The jaundice was usually of the type which is described as "obstructive" in many (not all) textbooks.

In 3 cases (8, 11, and 26) the jaundice nowever was of a pale lemon tint, and much more marked on the face and neck than in the conjunctivae. One patient had bile in the urine for several days but did not become jaundiced, and another, on the contrary, was jaundiced but did not have bile in the urine.

Vomiting.

This was the most frequently encountered symptom but 12 of the patients did not vomit. Three of those 12 "wanted to be sick" but could not vomit. (Cases 7, 9, and 38).

The time of onset -- the time of day and the time in relation to other symptoms -- of vomiting varied considerably. In 2 cases (C and E) vomiting occurred on three consecutive forenoons, but the boys ate normally in the afternoons, before they both became incapacitated next day: a condition rather resembling the morning sickness of pregnancy.

In the majority of cases the onset of vomiting was proceeded by several days malaise but it was the initial symptom in 6 cases (Cases 8, 15, 22, 30, 31, 32). In 2 instances the patient awoke in the night to vomit. Although I have not especially remarked on it in many case histories, I should here state that vomiting seemed to be less marked if the patient lay still and was immediately aggravated if he raised his head. Vertigo and abdominal pain if present were similarly and concomitantly aggravated by such change of posture.

Even when the patient had been nauseated the onset of vomiting, when it did occur, was frequently abrupt, and the patient was unable to restrain the vomiting till e.g. a suitable receiver was to hand.

Roseby Vest (Case 20) was so frequently and urgently sick

that his condition appeared alarming. (He later developed parotitis).

Equally worrying was the vomiting in Case 53, W. Sugden. It lasted 5 days and was associated with severe abdominal pain mimicking rather closely appendicitis.

The most prolonged period of vomiting was met with in Case 19. This girl developed mumps. Three weeks later she became jaundiced and during this interval she vomited almost "every day", sometimes twice, sometimes oftener.

Only in one case did vomiting persist for any time after the onset of jaundice (Case 2) and here it might well have been expected. On the third day of his illness I did not see him as he was dining at the British Restaurant !

In one third of the cases in which it occurred vomiting could be termed "rather severe", using this term to include vomiting which continued all through the night, and all more marked vomiting.

Abdominal Pain.

Abdominal pain was complained of in 29 instances. In the case of the remaining 14 patients they either had no pain or it was not sufficiently severe to be the cause of complaint. In a few instances the presence of any abdominal pain was denied, even mild discomfort and uneasiness being absent.

On the other hand the pain was severe in ten cases, and in two instances it was sufficiently severe and prolonged to cause anxiety until bile appeared in the urine to support the diagno-

sis. The presence or absence of pain, and the degree of pain when present, bore no relation to the depth of the jaundice, icterus being very marked in the absence of pain in a few cases.

The pain was usually described as a dull ache and even when it was severe it was described as a very severe dull ache, possibly with exacerbations, but even one patient who said that she had been doubled up with the pain, did not consider that the term 'colic' was correctly descriptive of it.

Nevertheless, from my previous experience of infective hepatitis, I suspect that acute colic pain does occur at times. In any case, if I had a patient who was doubled up with abdominal pain, I should certainly not rely on a distinction between a "very severe dull ache with exacerbations" and a "colic pain" as a diagnostic aid.

Having emphasized this point in case anyone may misconstrue my generalisation, I repeat that in the great majority of cases the pain is a dull pain.

The location of the pain varied, but my experience was that it was always definitely most severe above the umbilicus, and in most instances it was definitely confined to the upper half of the abdomen. The commonest situation was around the level of the transpyloric plane, extending from the midline bilaterally for a varying distance, sometimes more marked to the right One intelligent patient, Case 5, described his sensations thus:

"A tightness and discomfort in the lower part of the chest and the pit of the stomach." He stated that this was accompanied by a feeling of constriction which seemed to prevent easy and full breathing. I attach great importance to this symptom which I later encountered frequently in patients who were not jaundiced but were suffering from the epidemic illness.

In 4 instances the patient placed his hand accurately over the liver in front to denote the area where he had the pain.

Pain occurred as an initial symptom in several of the illnesses. But more commonly it followed a phase of malaise, lethargy and listlessness and with other acute symptoms it heralded the onset of the more severe phase of the disease. If pain was not present at this stage it was seldom a feature later. In fact there was only one instance in this series where severe pain began 48 hours after the onset of urgent and repeated vomiting.

Apart from pain a patient occasionally referred to a sensation of weakness, of powerlessness, or of chill in the epigastrium.

Anorexia.

Loss of appetite was a marked feature in 27 cases. In many cases it was noticed in the prodromal stage of the illness, when it was associated with languor and general malaise. Sometimes it followed the onset of the acute stage of the illness, only.

A rather remarkable illustration of a gradual loss of appetite is seen in the case 27, Raymond Pow. For three weeks this boy's "bait" (as the midshift snack is termed in colliery villages) became progressively less before he became jaundiced. Incidentally such an occurrence as this is a very good lead to the incubation period of the hepatitis.

Particularly striking when it occurred was the continued hearty appetite of the jaundiced patient. Two of my patients enjoyed every meal throughout the illness (Cases 10 and 36), and had no gastro intestinal symptoms whatever.

Some patients had no warning of having lost their appetites until they were confronted by their meals: they then felt that they could not eat anything --- to use their expressive colloquialism, they "felt full up."

Listlessness. (Lethargy).

In 27 cases listlessness was a marked feature and it very frequently was the first indication of the patient's illness. The history given by the patient or the patient's parent was the more interesting in that the same phrases were used in the descriptions time and again. A mother would tell me that she was worried as the boy ""won't go out and play with the other bairns." Or else she would say that the child just "lay about" and would not even talk or be interested in anything. Or the child just seemed to "hang about."

Another parent would say the boy seemed to have no life

about him, being listless and weary.

Energetic children would play a little out of doors or indoors and then lie on the couch, the playtime becoming progressively less and the rests correspondingly longer. The most common complaint which was frequently made was that the child would not go out to play with his friends. The mother might remonstrate with the child for not going out to play, or not talking or taking an interest in anything. If so, the child was said to cry ("she cries if spoken to" the mother would tell me) and to say simply that she "couldn't help it."

The reader may think I have rather over-elaborated this section. If so, I have done so to draw a parallel between the symptom in those cases attended by jaundice and the remainder of the cases in the prevailing epidemic to which I shall later refer.

Headache.

18 patients complained of headache. It was occasionally the initial symptom. In one instance where the illness was of a biphasic type, headache was a feature in the first part of the illness, but did not occur in the 2nd or jaundiced stage of the illness. The location of the headache varied: most frequently it was a frontal headache, less frequently it was bitemporal midway between the eye and the ear, and suboccipital headache was also encountered. In one case the patient complained of pain at the root of the nose and across the forehead immediately above the eyes.

The pain was described as a heavy, dull ache ---- no 'pulsing' was described. Frequently the patient said it was more a "fuzziness" or "thickness" rather than a real pain.

Skin Eruptions.

The frequency of skin eruptions was higher than I anticipated from my knowledge of the literature --8 cases. By far the most marked eruption occurred in the case of A. W. Walker (Case 21). He had a profuse erythematous rash of a rather widespread distribution, affecting mainly and almost exclusively the front of the chest and the abdomen. There was no punctate element. A reference to his case record will show that there was a definite if superficial resemblance to scarlet fever in this illness.

The remaining eruptions were in comparison rather trivial. Let me briefly refer to them. The terminology is intended to be descriptive rather than dermatologically accurate.

Case 6. On 7th day of illness slightly elevated urticarial rash on palms of hands and volar aspect of forearms.

Large erythematous patches on medial aspect of thigh. Punctate haemorrhagic rash -- 3 spots -- root of nose, right cheek and chin.

Case 9. Rapidly fluctuating erythemato urticarial rash on volar aspect of the forearm.

Case 18. Showed a blotchy erytnema of the left cheek1st day

Case 20. On 7th day showed urticaria on trunk -- 3 lesions on back, 3 on abdomen.

Case 29. Large erythemato urticarial patch on left buttock.

Case 34. Large areas of erythema on face and neck, the nip regions and the back (4 areas). As they cleared up the skin was left very rough and intense itching was experienced in those areas. Appeared on 4th day.

Case 35. Rash not seen. Said to have been present on abdomen and back and apparently was erythematous.

Vertigo.

The patient complained of giddiness or dizziness in 14 instances. In 3 cases it was very marked and was the first indication to the patient of his illness.

One, a 10 years old girl, had to return to bed as she could not balance, being quite incapable of standing when she tried to get out of bed. The other patient had much more alarming vertigo. "Suddenly he had to grasp at anything handy to maintain his balance, his legs went all wobbly as if he would fall and he felt exactly like one drunk."

The vertigo was usually subjective, but in the three severe examples it was described as being both subjective and objective. Some of the patients did not complain of vertigo but in reply to leading questions said that they had been giddy. They are not included in the total given -- 14. They described fleeting attacks of vertigo--they would have "thought is was imagination but it kept coming on again."

Liver palpable. With remarks on palpation.

The liver was palpable in 7 of the patients but (as mentioned in the case record 32) in one instance this may not have been entirely attributable to the hepatitis.

In one other case where the illness had simulated lobar pneumonia the liver was markedly swollen, but in all other cases it was just palpable.

Tenderness under the right subcostal margin lateral to the midclavicular line was occasionally noted although the liver could not be palpated.

Most of the patients onjected to even fairly light pressure in the epigastrium --- it evoked nausea.

It was however striking to note that in such an obviously ill patient as Vest (Case 20) who promptly rejected a teaspoonful of water, there was a complete absence of tenderness and no aggravation of the nausea on even firm pressure over the epigastrium or under the right subcostal margin.

Itching.

Apart from itching of the skin localised to the area of an erythematous rash, which occurred in one case, seven patients complained of itching of the skin.

In one case the itching was localised to the forearms and it was complained of on the third day of the illness.

The itching was generalised in the 6 remaining instances. In no case did it persist longer than 3 or 4 days. The time of

onset of the itching varied. One boy complained of this symptom for 2 or 3 days prior to the occurrence of jaundice; with the advent of jaundice the itchiness ceased.

In 3 cases the itching was complained of on the 3rd day of the illness. In the remaining 3 cases there was one instance of itching being complained of on the 2nd day of the illness, the 4th day, and the 5th day respectively.

Diarrhoea.

This was a feature in 4 of the illnesses. In one case, following mumps, it was said to have continued for 21 days before the onset of jaundice. It never became sufficiently severe to occasion anxiety.

Conjunctivitis.

This occurred in 6 of the patients. The occurrence of jaundice and conjunctivitis combined to give the eyes an extremely distinctive appearance. In only one case was there an associated blepharitis.

> Might I ask the indulgent reader to refer to Case History 24 ?

It will here be noted that I have referred to a dirty discolouration of the conjunctivae in association with the conjunctivitis. (It was recognised that conjunctivitis per se does tend to detract from the clean appearance of the sclerotic).

"The conjunctival vessels were injected, giving the

eyes a markedly bloodshot appearance. But the appearance is not adequately described by calling it a conjunctivitis; there was a dirty discolouration of the conjunctivae which I have frequently observed in these cases."

The description of the conjunctivae in the above case was I then thought typical of many I had seen in patients suffering from the prevalent illness, where jaundice did not develop. It will be noted (see Group 7) that Elliott's sister had suffered from a typical non-jaundiced attack a month previously and I had anticipated Elliott's illness would copy hers.

48 hours after I selected Elliott's conjunctivae as being typical of the appearance frequently seen in non jaundiced patients, Elliott became markedly jaundiced.

I had tried to avoid any bias in my view that the jaundiced patients constituted a small percentage of those affected in the prevailing epidemic. I had avoided the use of the word subicteric.

This incident showed that the words "preicteric" or "subicteric" would certainly have been suitable, and strengthened my belief in the aetiological identity of the 2 groups of illnesses.

Upper Respiratory Catarrh.

A well marked upper respiratory catarrh was a feature in 7 cases. In 6 cases it was an early symptom and it preceded the more severe stage of the illness by anything up to 3 weeks.

A profuse watery nasal discharge was typical. In one case it occurred 3 weeks after jaundice and may have been unrelated. In some cases it persisted throughout the prodromal phase of the illness.

In one case the child had a severe respiratory infection suggestive of pneumonia before he became jaundiced.

I was unable to find any other difference in the symptomatology of cases attended by such "upper respiratory catarrhs" and those not so attended.

I took particular note of this point as I wondered whether the infection might possibly occur via either the upper respiratory passages or the alimentary tract.

Constipation.

This was a marked feature in 3 cases. As in 2 of these cases it was remarked that the patient was usually of particularly regular habit, and the third patient never needed a laxative it seemed that they were picked out for this symptom.

Hiccough. Complained of by two patients.

Parotitis.

One patient developed parotitis on the fifth day of his illness. Another became jaundiced 21 days after she had mumps.

Herpes Lubialis. I mention that this occurred in one case as I believe that it is sometimes said that it does not occur in infective hepatitis.

Pains in the Limbs.

One patient complained of pain in the thighs --- it was her chief complaint --- for 2 or 3 weeks before she became acutely ill. The pains were present just above the knees, anteriorly, and also anteriorly in the "thick of the thighs." (Page 506). The distribution interested me in relation to other prevalent illnesses.

Another patient (Case 6) had pains in her ankles. I think the pains were chiefly located in the peri-articular structures, in this case.
Two youths complained of low lumbar backache.

"Pins and Needles."

In one case the patient complained of this sensation in the fingers and hands. It was evidently very marked but did not persist for more than 48 hours. Another patient complained of such tingling in one hand only --- here again it cleared up quickly -- 2 or 3 days.

Visual Disturbances.

The onset of visual disturbance was very acute in one instance. The patient dreaded facing the light (I ought to state that he was not suffering from miners' Nystagmus) and he had the impression that he was going blind.

Very interesting was the story of M. Forster (Case 33) who could not see to thread a needle at school: the very same story as I received from a non jaundiced child (page 394).

Disturbance of Micturition.

One boy had marked nocturnal frequency of micturition as one of the earliest symptoms. Another boy had a return of nocturnal enuresis from which he had been clear for over a year.

The Voice and Hearing.

One child had some disturbance of voice production, during her convalescence. Her voice seemed to leave her suddenly and then, after a short interval, to return just as suddenly.

In the case of Raymond Pow I was particularly interested in his complaint --- he complained that his hearing was affected. His voice did not sound the same to him. He could hear it, in fact it appeared to be louder than normal, but it appeared strange.

I refer to this later in the section of the work beginning on page 590 dealing with non jaundiced illnesses.

The Tongue.

The state of the tongue has possibly not received sufficient attention in the case records appended. It should be stated that whilst the state of the tongue varied from case to case there appeared to be no doubt that there was a degree of uniformity in the changes which occurred. I mean as regards

the course of their occurence.

When I first saw the patient it was the exception to find the tongue very thickly coated, but when the fur cleared, it did so in a very uniform manner --- first of all the tip and the edges became red and occasionally looked quite raw, more centrally the papillae stood out prominently against the furred background. The tongue became clean from the tip and edges and from before backwards. When all the coating had cleared up the tongue looked "unnaturally" clean and as it was then also noticeably moist it gave the impression of what I might term "a moist raw beef tongue."

When the tongue was clean on my first visit to the patient it frequently appeared as if it nadgone through the change described -- it was not just a clean tongue, it frequently appeared like "moist raw beef."

Some of the mothers had given purgatives to the children in the prodromal stage of their illnesses "as the tongue was so coated". In such cases I frequently found, later, of course, that the child had a strikingly clean tongue. Furtner, on no occasion did I observe such a tongue to become furred later in the illness.

Like all the other symptoms and signs in this epidemic the degree to which the tongue was affected varied markedly. But a consideration of the findings makes me believe that the tongue very frequently desquamates. In a few cases the physician will see this occurring from day to day.

More frequently, and especially in the milder cases where the physician is not consulted in the prodromal stage, the tongue will be seen to be either strikingly clean, clean to the extent of looking as if scraped clean, or present the appearance of "moist raw beef." In cases when there is a very slight fur to be seen on the initial visit, the desquamation is probably equally mild and the tongue subsequently appears simply to be very clean.

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I think that a careful study of the case histories alone, would lead to the belief that the incubation period in this disease is a long one. The prodromal phase of the illness in several instances was definitely of 2 or 3 weeks' duration.

CASE HISTORIES.

"JAUNDICED" CASES AT MURTON.

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Dr. Mackinnon's Patients.

Rhoderick Hollingsworth. Age 7 years. Case A.
He lives at Seaham Harbour.
While he was on holiday at Hayden Bridge he felt out of sorts and returned to his parents at Seaham.

After a few days he felt better and came to Murton for a holiday, but he had been here only a further few days ---- a typical two stage or bi-phasic onset ---- when he became jaundiced (approximate date 7 Aug., 1944).

At Murton he was constantly in the company of
Arthur Rd. Hollingsworth, age 8 years, Case B.
his cousin, a visitor from Dover.

This boy became jaundiced exactly 21 days after his cousin. The two boys would be together, they were inseparable, for 24 to, at most, 26 days, before Arthur Rd. became jaundiced, (approximate date 28 Aug., 1944).

Mrs. Painter age 58 years. Case 1

23 Williams Road, Murton.

History from recollection.

19 June, 1944.

After dinner she had a headache. Presently she suffered from severe epigastric pain and a short time afterwards she vomited. Thereafter she had complete loss of appetite, this giving place to anorexia and nausea provoked especially by cooking. The smell or the sight of food made her feel intensely sickly.

Next day she had attacks of vertigo, and otherwise her condition remained unaltered. She thought that she was going to develop jaundice.

Next day she was jaundiced.

[illegible] for time. Of course,

[illegible] convalescence was obstructed by lack

[illegible] was not confined to bed, or even indo

[illegible]lish Restaurant and Picture Houses.

Case 2

John Hughes Marriott. Age 3½ years.

7 Oak Terrace, Murton.

Saturday 9/9/44. Consultation.

His mother brought him to me as he had vomited in the local picture hall at 2 p.m. He has been obviously out of sorts for a few days and has kept lying down apparently exhausted. He complained of pain over the liver in front. The facies was so striking in conjunction with the story that I thought he had hepatitis and promised to call to see him on the Monday.

Sunday, 10/9/44. Visited.

The mother brought his urine for examination as she saw it was deeply bile stained. He is tender over the liver, in the epigastrium and under the right costal margin. He ate a "good" dinner but has vomited several times since. Bowel action is regular. The stool is clay coloured.

Monday, 11/9/44.

Deeply jaundiced. Very irritable, "cross" and miserable. Not eating now.

Bile rapidly disappeared from the urine, being present no longer than 48 hours.

Convalescence was protracted by lack of parental control. He was not confined to bed, or even indoors, and attended the British Restaurant and Picture Houses.

Later:— He developed Mumps on 9 November, 1944.

Additional Notes. Carole Marriott, age 4 months died on

11 August, 1944. She had suffered from diarrhoea and sickness for 36 hours before she died in a convulsion. She was not medically attended.

ISOBEL MARRIOTT. Age 7 years.

History:-- She attended school on Monday, 10 July, 1944, but seemed generally out of sorts and listless and remained off school all the week. She improved gradually and returned to school on Monday, 17 July, 1944, only to come home obviously worse than ever. She said that she felt sick and that she wished she could vomit but she could not. The doctor was called in on account of severe epistaxis, and found that she had a marked pyrexia, 102°F or so. Nose bleedings were severe and recurred several times during the next seven days. No definite diagnosis was made. At that time the doctor in attendance thought Isobel might be developing a lobar pneumonia, and she was treated with sulphapyridine.

Dr. Mackinnon's patient. Case C.

John Border Age 11 years.
7 Gray Avenue, Murton.

Attending Ryhope Secondary School (cf. R. Vest).

The history is retrospective, being obtained on Sunday 15/10/44

History:-- He "vomited all day" on Monday, 4 September. Little notice was taken as he has "often done this." However, this attack appeared to be rather different as John remained very listless. He was disinclined to do anything and seemed content to lie about. He did not look well, seeming very debilitated. He continued at school.

On Saturday, 23 September, 1944, it was obvious that he was ill he "never moved from the couch" on Saturday and Sunday, and he ate practically nothing.

Monday, 25/9/44, Tuesday, and Wednesday he attended school in spite of vomiting on each of those mornings and eating little, if anything. He had some epigastric discomfort and on Thursday he complained of a frontal headache. The parents noted the dark urine and Dr. Mackinnon observed the jaundice, which gradually deepened, and diagnosed Infective Hepatitis---

Thursday, 28 September, 1944.

He returned to school on 10th October, 1944.

Judy Clews. Age 2 years. Case 3
27 Ripon Terrace, Murton.

Sunday, 1 October, 1944. Consultation 9 a.m.

The mother states: "She is normally an active child 'full of life' and never still. For 5 or 6 days she has not been her normal self. She has not wanted to go out to play and she has not sat up at table at meal times but rested her head on the arm of the chair; and although she has eaten she has done so with less enthusiasm than usual.

On Wednesday Judy seemed to be feverish. On Thursday she was very persistently naughty and was smacked and sent to bed. To-day for the first time she has left part of her morning meal.

Mrs. Clews is an excellent mother, and she realises that her child is probably in the prodromal stage of an illness. I asked her to let me have a specimen of the child's urine, and she remarked that that was one thing she had intended to tell me -- how dark the urine was. The child had a heavy eyed appearance and looked listless.

Sunday, 16/10/44. Visited 7.30 p.m.

Vomited violently after lunch, and seemed brighter and asked for tea. Motion very pale, like clay. Urine contained bile --- very foul smelling. The froth is a very deep yellow. No jaundice

Mon. 2 Oct., 1944.

Vomited again last night. Playful to-day.

Tues. 3 Oct., 1944.

Stools are still clay coloured. Urine is loaded with bile.

She is not jaundiced. She vomited last night. Her vomiting is entirely confined to the evening.

Thereafter recovery was rapid and complete, and by Sunday, 8 October, 1944, the urine and stools had almost regained their normal colour.

[illegible] no is markedly jaundiced [illegible]
[illegible]ctal lighting. No complaints of hea[illegible]
[illegible]bdominal pain. Otherwise a happy child, h[illegible]
[illegible]. The liver is readily palpable [illegible]
[illegible]per's breadth.

[illegible], 8 Oct., 1944.

[illegible]ibosis marked, jaundice deeper. C[illegible]
[illegible]ouched. Still has very disturbed stoo[illegible]

[illegible]ential White Cell Count. 8 October,

Polymorph Neutrophil	29.0
Eosinophil. Poly.	2.5
Large Lymphocytes.	7.0
Small Lymphocytes.	59.5
Monocytes.	1.0

[illegible]ed cells appeared normal in the fi[illegible]

George Warwick Forster. Age 5 years. Case 4
29 Alfred Street, Murton.

Fri. 6 Oct. 1944. Consultation.

History:- Last Saturday, 30 September, 1944, he wastaken to a football match and he fell asleep, very abnormal for him as he is a very alert young man. He has refused to eat since and has been lying about the house "with no life about him." Last night his sleep was very disturbed -- he kept shouting out. He vomited before he went to bed at 6 p.m.

To-night he is markedly jaundiced --- easily visible in the artificial lighting. He complains of headache and upper abdominal pain. Usually a plump child, he has obviously lost weight. The liver is readily palpable -- the edge is down 2 finger's breadth.

Sunday, 8 Oct., 1944.

Halitosis marked. Jaundice deeper. Cries if his belly is touched. Still has very disturbed sleep-- shouting out,etc.

Differential White Cell Count. 8 October, 1944.

Polymorph Neutrophil	29.0
Eosinophil. Poly.	3.5
Large Lymphocytes.	7.0
Small Lymphocytes.	59.5
Monocytes.	1.0

The red cells appeared normal in the film.

There was some toxic granulation of the polymorphs.

16 October, 1944.

He cries with headache at night. He cannot "stand" the wireless. The mother complained, I had already remarked it, that the child's abdomen was 'swollen' --- it was markedly distended. There was no rigidity and no sign of ascites.

24 October, 1944.

Still far from well. Still irritable and listless.

The appetite is still very poor.

Later. Friday, 29 December, 1944. Consultation.

He is said not to have been really well since he was jaundiced.

On Wednesday, 27 Dec., 1944, he suffered from epigastric pain, and vomited and retched repeatedly and violently.

He had a widespread erythematous rash --- it is now subsiding but still evident. The rash was said to have resembled a scarlet fever rash, involving the whole body, including the face, but not present around the eyes and mouth.

Alex Webster Sheach. Age 20 years. Case 5.
Montana, Murton.

"Bevin Boy. - Miner."

Fri. 6 Oct. 1944. Visited.

History:- He consulted my partner on Friday, 29 Sept.1944. He "was pained by wind in the stomach and he had a sore back and felt very much off colour." When he tried to stand up straight, especially if he tried to "brace his back", the tension made the backache worse. He was sitting over a big fire all day, shivering. He could not get warm.

Gradually he lost his appetite, lost all desire to smoke, and became thirsty. However he was absent from work only on Friday and Saturday and has worked all this week.

2nd Phase.

He says he became definitely worse yesterday, Thurs.28/9/44.

He felt as if he had no energy and as if he had lost all his strength. He suffered from a tightness and discomfort over the lower half of his chest and the pit of the stomach. This led to a feeling of constriction which prevented easy and full breathing. He kept "belching wind" and at such times he felt that he was likely to be sick. Although he had the impression, especially then, that he would be sick, he could not say that he felt sickly.

Today, 1 p.m. Friday, 6 Oct. 1944.

No itching. No joint pains. Loss of appetite marked. Pulse 64 per minute. Temperature 97.8°F.

The urine contains bile.

He tells me that the urine has been this colour for a week, and that his motions have been "white grey like cement" during the same period. He has absolutely no headache --- he had one on Friday, 29/9/44 only.

In the evening the pulse dropped to 52 per minute.

Saturday, 7/10/44.

Jaundice noted at 3.30 p.m. Pulse remained slow, 52 per min. for several days. Appetite gradually improved. Painless diarrhoea to-day.

Thereafter recovery was rapid and uneventful.

Differential White Cell Count. 8 Oct., 1944 (3rd day of jaundice).

Polymorph Neutro.	38
Polymorph Eosino.	1
Polymorph baso.	1
Small Lymphocytes.	48
Monocytes.	12

No abnormality in reds.

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Additional notes. Movements.

Fri. 1/9/1944 to Mon 4/9/44. Home in Elgin.

Sat. 9/9/44. Newcastle (theatre).

Sun.10/9/44. Local picture hall.

Sat.16/9/44. Sunderland picture hall.

Sat.23/9/44. At South Shields.

Anne S. Young. Age 11 years. Case 6
93 Calvert Terrace, Murton.

Attending Murton Council School. Teacher, Miss Pine.

Tuesday, 10 October, 1944. Visited.

History:-- She says that she has not felt well for 14 days. She has felt weak and tired and has had frontal headaches. On Friday, 6/10/44, she was listless and on Saturday this was even more marked and obvious. Her mother then gave her "Syrup of Figs", She seemed better on Sunday morning but ate a very poor dinner. She attended Dalton-le-Dale Church but had to leave owing to vomiting which was frequently repeated.

On Monday, 9/10/44, she went to school, but in the cookery class she felt sick, and she had to go out to vomit repeatedly. Each vomiting "bout" had an urgent onset. Later "her legs were shaking", she had pains in her ankles, and her hands kept going into "pins and needles" she said.

10 October, 1944. Pulse 98 per min. Temperature 98.2°F. Vomiting persists and she feels giddy. She is jaundiced. Later in the day she suffered from severe abdominal pain, and the vomiting became more distressing.

Wed. 11/10/44. Pulse 60 per minute. She feels sickly but vomiting has ceased. The bowels acted normally --- the motion was said to be like "putty". Urine. Bile +++ Phosphates +++

Differential White Cell Count.

Polymorph Leuc.	45.5
Lymphocytes.	49.0
Monocytes.	4.0
Eosinophils.	1.5

By Monday, 16/10/44, she was really intensely jaundiced.

There was marked conjunctivitis and this with the deep jaundice made the appearance of the eyes striking.

There was marked malar redness contrasting with the deep jaundice present on the brow, chin, etc. The rest of the body was deeply jaundiced. The liver was palpable but only slightly tender. Loss of weight was marked. No nausea. She indeed fancies food but she looses the desire after a bite or two.

Pulse 60. Temperature 99 ^{o} F.

She is extremely drowsy and is sleeping "all day long."

Tues. 17/10/44.

Very slightly elevated urticaria on palms and on the volar aspect of the forearms. Large erythematous areas on medial aspect of thighs. Punctate purpuric rash - 3 spots - root of nose, right cheek and chin.

Improving. Pulse 70. Temp. 99 ^{o} F.

She has been having heavy sweats.

Friday, 20/10/44.

Since Tuesday she has had severe generalised itching.

Saturday 28/10/44.

Jaundice still marked. It began to clear noticeably thereafter, and cleared up after being present for 5 weeks.

NOTES.

1. Chief playmate who also sits next to her at school: "M.P." did not become ill.

2. Every Sunday she goes to Cold Hesledon for dinner.

Dr. Mackinnon's patient. Case D.

Emily Lumsden age 7 years.
14 New Pilgrim Street, Murton (grandparents).

Home address: 8 Windsor Terrace, Murton.

Attends Murton Council School. Teacher: Mrs. Sheppard.

History. Sunday 8 Oct., 1944.

She returned from Sunday School and vomited. The vomiting was repeated frequently throughout the night, and she complained of abdominal pain in the pit of the stomach and extending as low as the umbilicus.

Thereafter she was very listless and "just lay about the house" not seeming to take an interest in anything, completely disinterested and apathetic.

Jaundice was noticed on Thursday, 13 October, 1944. The grandmother noticed it in the scalp.

When I called to see her on Sunday, 15/10/44, she was still definitely jaundiced. The urine was still bile stained and the motions were still very grey.

NOTES.

She has 3 intimate friends. None of them took ill or had been ill.

Only once at "the shows" ---22/9/1944.

Hannah Griffiths. Age 20 years. Case 7
45 Silver Street, Murton.
Land Army at Witton le Wear, Co. Durham.

History. Sat. 14 Oct., 1944.

She came home for a week end. She had a headache "as if someone was cutting her head open" she had no appetite and she felt dizzy.

On Sunday she was "doubled with pain in the pit of the stomach", she felt she wanted to be sick but she could not vomit. The headache and vertigo continued.

Monday she had still no appetite but the epigastric pain was easier. She felt lazy and listless and had to keep lying down on the settee.

Tues. 17 Oct. 1944. Visited.

The headache and abdominal pain eased. She became jaundiced. Pulse 64 per minute. Temperature 98.4°F. She is in the Land Army stationed at Witton le Wear. She sleeps in a hostel with other 33 girls. One of them had been ill and about one month ago she became jaundiced, and then, and then only, she went home to Yorkshire.

She is tender in the epigastrium and under the right costal margin but the liver edge is not palpable. There is bile in the urine.

Differential White Cell Count. 17 Oct., 1944.

Polymorph Leuc.	34.5
Lymphocytes.	60.5
Monocytes.	3.0
Eosinophil.	2.0

Friday, 20 October, 1944.

Not in bed. She is very sleepy and listless, and if she tries to knit she can only manage a few lines.

She made a very slow recovery and a month later she still had occasional sickly feelings and felt very listless.

Dorothy Oliver, Age 5 years. Case 6

Montana, Murton.

This child is the daughter of the landlady of A.W.SHEACH(qv).

History. Sunday, 15/10/1944.

Wakened up at 5 a.m., and vomited. Cried with abdominal pain. Later had diarrhoea.

Monday, 16/10/1944. Seemed better in the morning.

Again 2 a.m. diarrhoea -- vomiting.

Tuesday, 17/10/1944. Vomited 4 p.m. Dairrhoea recurred and continues on

Wednesday, 18/10/1944. Visit. Pulse 108. Temperature 98°F.

No appetite since onset of illness. She is irritable. Her face is exactly like that of A. S. Young. (q.v.)

Red cheeks like a crudely painted doll: with yellow (jaundiced) neck, face, etc.

Very little jaundice in conjunctivae. Not in bed.

Runs around but soon tires and keeps lying down.

Friday, 20/10/1944.

Improved. Eating well. Facial and bodily wasting, however, are very marked.

Joan Smith. Age 11 years. Case 9
8 North Crescent, Cold Hesledon.

This is the only child residing in Cold Hesledon who attends St. Joseph's Roman Catholic School at Murton.

History:- She has not been well for 3 weeks, and has been definitely ill since.

Tuesday, 10/10/44. She was chilly, had a headache and felt poorly. She felt that she was going to vomit but she did not vomit. She has eaten practically nothing since. On Friday she was unable to return to school after lunch because she felt so helpless and tired. She lay on the couch all day.

Wednesday 18 Oct. 1944. Consultation.

She has a pale, sickly and exhausted appearance. "Everyone" has been remarking on her appearance -"How pale you look" etc. She complains of feeling sickly and of being giddy: also of headache of frontal and suboccipital distribution. Mermother says that Joan "cries if spoken to". She has been obstinately constipated.

Differential White Cell Count. 18 Oct.1944 (One day previous to onset of jaundice.)

Polymorph Leuc.	54
Lymphocytes.	37.5
Monocytes.	5
Eos.	3.5

Thursday, 19/10/44.

Jaundice became evident. Urine contained bile. A widespread erythematous rash, which fluctuated markedly, is most marked on the flexor surface of the forearms.

Monday 23/10/44. Still dizzy and sickly and "no appetite." Rash fading.

Gradual fairly rapid recovery followed.

Raymond Elliott. Age 12 years. Case 10
25 Ripon Terrace, Murton.

Friday, 20/10/44. Visit.

He has not been well since Sunday, 8/10/44. He has not gone out to play with his friends and has been "lying about the house" as if he was lazy, or tired. His appetite has remained good until to-day 20/10/44, when he consulted me. But his mother says that he has lost weight and examination gives that impression.

He has a bilateral headache between the eyes and the ears and he is irritable and can't stand the noise of the wireless. The urine contains bile and the stools are putty coloured.

The facies is characteristic. Normally a rosy cheeked boy with a 'round' face, he is now pale, dark under the eyes, his face looks long and thin and the expression is flat, almost like the "Dead pan" of the Americans with no change in the features occurring during a 20 minutes' conversation. Temperature is normal, but he feels chilly: at other times he says he has felt hot. An interesting feature is that he has began to bedwet after a year's freedom from this complaint and further that he fainted when I took a blood film. During this faint he voided urine and on recovering he vomited violently for some 15 minutes.

Differential White Cell Count.

Polymorph.	48
Lymphocytes	49
Monocytes.	1
Eos.	2

Sat.28/10/44. Still jaundiced. Recovery was gradual.

Henry Morris. Age 7 years.
1 Beech Terrace, Murton. Case E.

Attending St. Joseph's Roman Catholic School.
Teacher: Miss Daley.

This boy has "bilious" attacks about every nine months. He has obviously been 'not himself' for about 2 weeks, not ill enough to be off school.

He is usually a big eater, but recently he has eaten little; furthermore he has been lying down resting instead of playing as is his normal.

On Tuesday and Wednesday, 17 and 18 October, 1944, vomiting occurred each forenoon but he ate his food in the afternoons. But on Thursday, 19 Oct., 1944, he came downstairs and said "I can't eat anything", and promptly vomited a glass of water which he drank.

Friday, 20 October, 1944.

He looks haggard, pinched and pale. The eyes are jaundiced and there is marked conjunctivitis. There is no abdominal tenderness. The urine contained bile. The faeces are pale. No headache.

Pulse 70. Temperature 98 ^{o} F.

Thomas Marr. Age 47 years. Case 11
44 Albion Street, Murton.

Coal Miner.

My partner referred this case to me on 22 October, 1944.

Sunday, 22 October, 1944. Visited.

History:— He went to his workmen's club on Friday at 5.30 pm and he felt quite in his normal good health then. Suddenly at 7 pm he became dizzy and he had to hold on to neighbouring objects to maintain his balance. His legs went 'wobbly' as if he was sure to fall. In fact he felt exactly as if he was drunk.

With assistance he managed home. He dreaded facing any light on the way home — his eyes felt most peculiar — his sight being so disturbed that he felt he was going blind. His head began to ache — the pain fluctuated markedly, at times clearing entirely. He felt sick. Later he vomited. Mrs Marr says that Marr looked pale and was absolutely helpless. All night in bed he was uneasy, restless, and he sweated profusely. On Saturday morning he got out of bed and felt fair, but on Saturday night the headache and vomiting recurred.

To-day, 22 Oct. 1944, he is jaundiced. It is a pale lemon tint and scarcely noticeable in the conjunctivae but quite marked on the face and neck. There is no bile in the urine. There is a positive result on testing for urobilin. The temperature is normal. Pulse to-day is 48 per minute.

I detected no abnormality in the circulatory system and careful examination showed no other abnormal signs than very slight tenderness in the epigastrium.

The response to Klein's intradermal Test in this case was very interesting --- the pale lemon tint present on the skin of the face was markedly accentuated in the wheal.

Differential White Cell Count.

Polymorph. Leuc.	34
Lymphocytes.	62
Monocytes.	2
Eosinophil.	2

There was nothing of note in the subsequent course of the illness, and he resumed work on the 17 November, 1944. The optic disc, fundi and media were normal on ophthalmoscopic examination.

Hannah Warin. Age 7 11/12 years. Case 12
19 Ash Terrace, Murton.

Attending Murton Council School. Teacher: Miss Gorman.
The child is rather 'mentally backward' and a poor witness.

Tuesday, 31 October, 1944. Visited.

On Thursday, 26/10/44, she arose, made no attempt to dress herself, but sat limply in the chair. Presently she asked if she could go back to bed. She appeared to be feverish and she felt sick and complained of a frontal headache. Since then she has eaten practically nothing. On Friday she vomited after every drink and she was sick several times apart from this. Abdominal pain was not a symptom. She has continued to be extremely listless until today. Yesterday my partner visited her and noticed that she was jaundiced. Today the jaundice is of slight to moderate degree, most intense in the conjunctivae. The urine contains bile. The motions are said to be like cement, in colour. She looks weary and exhausted. The tongue is clean.

Friday, 3 November, 1944.

She is still extremely listless, but she has begun to eat. She is obviously very weak and has lost weight --- the mother says markedly.

Thereafter her recovery was uneventful.

Eileen Ann Lavery. Age 8 years. Case 13
23 Wetherburn Avenue, Murton.

Attending St. Joseph's Roman Catholic School.
Teacher: Miss Maddigan.

Mon, 30 Oct.1944. Visited.

On Monday 23 October she was very listless all day and she had no appetite for her supper. Her mother had noticed that Eileen had appeared out of sorts for 2 or 3 weeks. On Tuesday, 24/10/44 she complained of feeling sick and giddy and she vomited several times. On Wednesday she looked and felt better and seemed to have recovered, but next morning she was ill again. She looked tired and pale and had no appetite. All day long she sat in the chair, not even talking, and she seemed to have no desire to do anything. She had no headache, nor did she again complain of giddiness, but, she says, she had a peculiar 'cold numb' feeling all over her body, but especially in her back. She had been obstinately constipated during this period. This is said to be very 'unusual for her'.

At this stage of the illness the mother observed the tongue to be covered with a thick yellow fur, and gave Eileen an ounce of Castor Oil. The condition remained as described until Sunday, 29 Oct., when she vomited several times.

To-day, 30 Oct., 1944, she is jaundiced. She is not tender abdominally. The tongue is very clean at the edges and tip

but otherwise slightly coated.

Temperature 98.0 ° F. Pulse 78 perminute.

Urine is intensely bile stained.

Differential White Cell Count.

Polymorph Leuco.	47
Eosino. Leuco.	1.5
Basophil. Leuco.	0.5
Lymphocytes.	48.5
Monocytes.	2.5

Wed. 1/11/44.

She is very deeply jaundiced. The cheeks are dull red. These combine to give a peculiar appearance. It looks as if the cheeks had been painted a bright red and then the colour had been toned down with face powder.

Temperature 99 ° F. Pulse 78 per minute.

She says she feels itchy -- her forearms.

She improved steadily and by the 16 November, 1944, the jaundice was definitely clearing.

On Friday, 23 November, 1944, she developed a severe common cold, nasal catarrh being marked.

Audrey Hunter. Age 5 years. Case 14
89 Princess Street, Murton.

Attends Murton Council School. Teacher, Miss Anderson.

Friday, 3 Nov., 1944. Visited.

She has been ill since Sunday, 29 October, when she was listless and sleepy and vomited several times. She improved a little on Monday but on Tuesday she vomited repeatedly and urgently and she had profuse watery diarrhoea. Jaundice was first noticed on Wednesday since when it has become rapidly more intense.

To-day the jaundice is intense, being deepest in the conjunctivae.

Pulse 100 per minute. Temperature 99 ^{o} F.

The tip and edge of the tongue appear raw but moist --- the remainder strikingly resembles the early peeling stage in scarlet fever.

The urine is bile stained. The motions are "like clay."

Monday, 6 Nov., 1944.

She is eating ravenously although she is intensely jaundiced.

Recovery was uneventful.

Richard Bond. Age 5 years. Case 15

22 Brooklyn Terrace, Murton.

Thursday, 2 November, 1944.

He had been quite well until Sunday, 29/10/44, when he vomited in the evening. Next day he had apparently recovered but on Tuesday and Wednesday he appeared to be feverish, and he vomited several times and refused his meals.

To-day he is rather inactive but he is not markedly listless, nor does he appear very ill. The urine contained bile. The tongue was very slightly coated except for the edge which gave the appearance of peeling. He objected to pressure on the epigastrium but the liver was not palpable.

Fri. 3 Nov., 1944.

He was jaundiced.

He immediately began to improve and by Monday he appeared to be perfectly well although his jaundice persisted for another week.

Note.

He plays with Lawson's child, 21 Fife Street.

They visit each other's houses.

See Page 505 a overleaf.

Georgina Lawson. Age 2½ years.

21 Fife Street, Murton.

This child is the inseparable playmate of Richard Bond (previous page).

She was not jaundiced.

Saturday 7 Oct. 1944. Complained of epigastric pain. Went as usual to the picture show - 8 pm to 11 pm !

Sunday 8 Oct. 1944. At picture show again, but she had diarrhoea and she "twisted and kicked" and wanted to go home. At 11 pm she vomited.

Monday 9 Oct. 1944. Complained of headache. "Heavy about the eyes." Wanted to be nursed. Diarrhoea continued.

Tues 10 Oct 1944. Brighter.

Visit Wednesday 11 Oct 1944

Lay helpless and "lifeless" in her mother's arms -- "as if she was sickening for something." Thirsty. Still diarrhoea. Not eating. Brightened up and seemed well for a short time after sleeps which were frequent and easily induced by nursing.

Till Saturday 14 Oct 1944 diarrhoea continued until to-day. Restless at night when she sweated heavily.

Maureen Turner Age 8 years. Case 16
50 Windsor Terrace, Murton.

Attends Murton Council School. Teacher: Mr. B. Porter.

Tuesday, 14 Nov.1944. Visited.

For 2 or 3 weeks she has obviously been out of sorts. She has been listless and she has "just been hanging about the house." She complained of pains in her thighs during this period, but her mother dismissed them as "just growing pains."

On Tuesday, 7 Nov, she appeared to have a 'head cold' --- she had a frontal headache, her eyes watered freely and she was put to bed where she remained until Friday, when she was allowed up. But she became very giddy and had to return to bed. Her appetite had been poor but it now failed her entirely and she began to feel sickly.

Today her conjunctivae are jaundiced.

Pulse 84 per minute. Temperature is normal. There is bile in the urine and the motions are pale.

The jaundice became gradually deeper and by

Monday, 20 November, 1944

she was intensely jaundiced. The liver was tender and the edge was down over one finger's breadth. Pulse 72 per minute. Temperature 99.2°F.

Monday 27 Nov. 1944.

Jaundice beginning to fade.

Tom Barksby. Age 11 years. Case 17
13 New Pilgrim Street, Murton.

Attends Seaham Intermediate School.

Fri. 17 Nov. 1944 Visited.

The history is that he ate his usual breakfast on monday, 13th, but he felt ill in school in the afternoon. He felt sickly and he had pain in the epigastrium and to the right--- he points to the region of his liver. He did not have a headache. When he came home he could not eat tea or supper.

On Tuesday nausea was more marked and the pain continued. He had complete loss of appetite. The urine was noted to be deep orange coloured and the motions to be very pale – cream coloured.

He became jaundiced on Wednesday, 15/11/44, when my partner visited him.

To-day he does not look very upset. Temperature is normal and pulse is 64 per minute. The tongue is clean and the papillae prominent -- it resembled the peeled tongue of scarlet fever.

His mother suffered from infective Hepatitis 3 months before I did not then attach any significance to this fact.

Note.

He travels to school with Arthur Dean and J. McKeon.

Maureen Scothern. Age 6 years. Case 18
12 Oak Terrace, Murton.

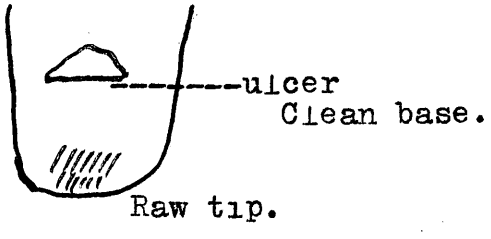
Attends Murton Council School. Teacher: Miss Anderson.

Tuesday, 21 Nov. 1944 Visited.

For the past fortnight she has complained of headache and the mother noticed that she was listless and "hanging about the house." She is usually a bright child, active and full of life, but now she will not go out to play with her friends.

Yesterday she came home from school looking exhausted. She refused her tea and complained of pain in the 'stomach'. At 10 pm. she vomited and she continued to vomit at frequent intervals all through the night.

To-day the temperature and pulse are undisturbed. She looks rather sickly and is obviously quite content to lie in bed. There is a blotchy erythema on the left cheek. The tongue looks raw and sore at the tip and there is a superficial triangular shaped ulcer in the centre of the tongue. The base is clean. It looks as if it had simply been denuded of epithelium



The urine gives a very marked positive result on testing for urobilin, but there is no bile.

Wednesday, 22/11/1944.

Bile in the urine - large amount. She slept most of the day and could only be roused with difficulty. Her cheeks are flushed "like a painted doll." The stools are "putty coloured."

Thurs. 23/11/44.

Jaundice appeared. Quite definite in the conjunctivae but slight elsewhere.

Friday, 24/11/44. Jaundice generalised.

Monday, 11/12/44.

She is said to have been very poorly ever since she had jaundice. The mother has been particularly worried about Maureen's voice - when she was speaking "it seemed to leave her suddenly and then to return just as suddenly."

She developed a cervical adenitis which went on to abscess formation.

Yvonne McQuilliam. Age 5 years. Case 19
2 Adelaide Terrace, Murton.

Attends St. Joseph's Roman Catholic School. Teacher: Miss Gallacher.

Monday, 27 Nov. 1944. Visited.

She had mumps 3 weeks ago - both parotid glands were affected, in turn.

Since then she has vomited practically every day, sometimes twice and occasionally more than twice. She has also suffered from diarrhoea which however has been neither frequent nor watery and profuse. She ate very little and generally (as can be well imagined) "she did not seem to pick up" and appeared to have "no life about her." At intervals she complained of a heavy frontal headache and she has been very "cross" and difficult to deal with. Abdominal pain has not been a marked feature - she appears to have had only slight pain. Yesterday she became jaundiced and since then she has appeared to become much better. There is now no sickness, no diarrnoea, and she is brighter.

The temperature is normal. Pulse 90 per minute.

She is tender in the epigastrium and in the right subcostal margin.

The urine is deeply bile stained.

Notes.

Absent from school - mumps - 6th to 20th November.

Attended school 20th to 25th November.

Roseby Vest. Age 11 years. Case 20
7 Pilgrim Street, Murton.

Attends Ryhope Secondary School.

Sat. 2 Dec. 1944. Visited.

History. Some 3 weeks ago, Thursday, 9/11/44 until Monday, 13/11/44, he had a frontal headache and a 'cold' and he then also felt sick but he could not be sick. Since then, he has not been really well, appearing to have no "life about him" and being listless and weary especially after school hours. He has become thinner, he has definitely lost weight, and at times his complexion has been "like wax."

On Thursday last, 30/11/44, he felt very poorly. He had epigastric pain and again he felt very sickly and wanted to vomit but could not do so. Yesterday, Friday, he felt better until the afternoon and since then he has vomited practically incessantly. Even a teaspoonful of water is promptly vomited.

He looks rather 'worryingly ill' to-day. He is tossing about in bed, very restless and distressed - uneasy to the point of appearing miserable. The pulse is 92 per minute. Temperature 99.2°F. Strikingly, he is not at all tender anywhere in the abdomen.

The urine contains urobilin -- a very marked + result.

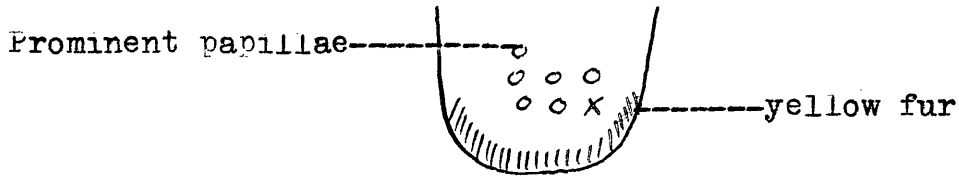
Sunday, 3 Dec. 1944.

Through the night he vomited incessantly. He is intensely giddy. His appearance leads to some anxiety - he looks exhausted and on the verge of collapse. He has no headache.

The tongue is coated and he complains of a sour taste in the mouth. He is very itchy all over the body. In the evening bile appeared in the urine and he vomited only after drinks.

Monday, 4 Dec. 1944

Jaundiced, the eyes intensely so. There is a dull red flush on the face, the distribution is uncommon and covers the beard area. The tongue is now clearing, or peeling.



Tues. 5 Dec. 1944.

He developed a right sided parotitis, the gland was very swollen. He is now really intensely jaundiced all over his body. Still no appetite.

Thurs. 7 Dec. 1944.

Urticaria on trunk. Very few lesions. 3 on the back and 3 on the abdomen.

Sat. 9 Dec. 1944.

Pulse 60 per minute. Very markedly improved. Eating a little. Bowels are acting normally now, the motions are clay coloured. He made a steady uneventful recovery.

Notes. A friend, Pawsey, at school was absent from 30 Oct. to 20 Nov. (Jaundice). J.Border, also a class mate, attended school although ill on 25,26,27 Sept. before being absent owing to jaundice (Case C). He returned to school on 10/10/44.

Allan Wilfred Walker. Age 19 years. Case 21
4 No. Doxford Terrace, East Murton.

Apprentice Surveyor.

Sunday, 3 December, 1944.

History:— He slept poorly on Thursday night, his throat feeling painful and dry, and he had headache, localised in the frontal area and just above it. When he rose on Friday morning to go to work he was intensely giddy and he had to return to bed. Since then he has had no desire for food and has eaten practically nothing.

To-day he has all the above symptoms, and has a rather widespread erythematous rash - it affects almost exclusively the front of the chest and the abdomen. The rash has a superficial resemblance to a scarlet fever rash, but there is no punctate element and of course the distribution is quite atypical. The tongue is slightly furred, the fauces are swollen and inflamed -- the redness is very dull, with a suspicion of a dusky blue tint. The palate is normal. Temperature is 100 ^{o} F. Pulse 90 per minute.

Tues. 5 Dec. 1944.

The tongue is normal in appearance. The throat is easier and has almost regained a normal appearance.

He is intensely itchy all over - not only in the area affected by the transient erythema (this lasted 24 to 36 hours only). He is jaundiced, the staining being deepest in the conjunctivae.

The jaundice deepened but he made a rapid recovery.

.....

Notes.

He works in an office with 4 other men.
None of them had been ill so far as I know.
None of them became ill within five months.

He travels to night classes at Sunderland by train. Three or four weeks ago one of the three youths who travel with him took ill with urgent vomiting.

Enid Applegarth. Age 6 years. Case 22
34 Hawkins Road, Murton.

Attends Murton Council School. Teacher: Miss Robson.

Sunday, 10 Dec. 1944 Visited.

On Tues. 5/12/44 she vomited and complained of giddiness. She improved until Friday, 8/12/44, when she looked sickly, lost all desire for food and was very listless. She just sat in a chair all day as if she had not even the energy to talk.

To-day she complains of upper abdominal pain and she is vomiting everything including even sips of water. She is obstinately constipated in spite of aperients. This is a most unusual state of affairs for her as she is of regular habit and never constipated.

The facies is interesting and I think highly suggestive, or characteristic, of incipient jaundice. She does not look haggard: just a little dull, and the play of her features when she is engaged in conversation is less marked than usual; as if she was conservative in the use of her expressions and also as if there was a time lag in their appearance; a little reminiscent of the smile of the post encephalitic patient but much less marked.

The complexion is also characteristic, a dull suffused blush of the cheeks serves to accentuate the pallor of the rest of the face. It is not a simple pallor, there is a dull creamy tint suggestive of incipient jaundice. Temp. 99.8°F. Pulse 120 per minute. Urine contained bile and urobilin.

Mon. 11 Dec.44. Slight epigastric pain. Temp 98 Pulse 96 p.m. She is jaundiced, but the malar flush persists. She has a herpes of the upper lip and on the chin.

Alan Turner. Age 11 years. Case 23
50 Windsor Terrace, Murton.

Attends Murton Council School. Teacher: Mr. J. Hume.

Visited Thursday 14/12/44.

During the past two weeks he has made frequent complaint of abdominal pain, and he has had a very poor appetite. He has had "no life about him."

To-day he is vomiting very frequently, immediately rejecting even sips of water. He has no headache. He liesin bed looking very seedy and disinterested in anything but his vomiting. He has very little pain.

Temperature 98 ^{o} F. Pulse 72

Conjunctivae are very injected.

Fri. 15/12/44.

He is jaundiced -- deeply in the eyes -- very slightly on the face. He has no malar flush.

No bowel action for past 48 hours. He has vomited all night.

Pulse 104. Temperature 98 ^{o} F.

He feels intensely giddy and has had several drenching sweats. No headache.

Tues. 19 Dec. 1944. Pain right chest over liver.

Very deep jaundice.

Bile in urine +++

Pulse 72.

Joseph R. Elliott. Age 13 years. Case 24
25 Shinwell Terrace, Murton.

Attends Murton Council School. Teacher: Mrs Flynn.

Mon. 18/12/44. Visited.

In bed. Had a heavy dull and sickly appearance, and his expression altered very little during my visit. For a few days he had felt sickly and faint at times, and yesterday he vomited several times. He complained of a sensation just like a heavy ball in the epigastrium.

He admitted to absolutely no headache.

Temperature was 98, and the pulse slow, 66 per minute.

The conjunctival vessels were injected, giving the eyes a markedly bloodshot appearance. But the appearance is not adequately described by calling it a conjunctivitis; there was a dirty discolouration of the conjunctivae which I have frequently observed in these cases (when jaundice did not later occur).

By Wednesday the eyes were markedly jaundiced and by Thursday the skin was noticeably yellow.

The urine contained urobilin and bile on Thursday 21/12/44, when the pulse was 60.

He complained then of nothing except loss of appetite.

Arthur Bridges. Age 13 years. Case 25
Welfare Park House.

Attends Marton Council School. Teacher: Mr. Gardiner.

Sun. 31/12/44 Visited.

Three weeks ago he developed a head cold - watery nasal discharge and very slight frontal headache. He was out of sorts and remained at home, absent from school, all the week. He improved but since Tuesday, 26 December, he has had a slight return of the nasal cold, this time accompanied by epigastric pain. He vomited last night.

To-day he ate a hearty dinner but vomited soon afterwards. He has had frequent hiccough. The appearance is fairly typical --- pale, apathetic and listless --- 'seedy' looking.

He is definitely tender in the right hypochondrium subcostally and in the epigastrium he resents even slight pressure. Pulse 72. Temperature normal.

Tues. 2 Jan. 1945. There is a definite lemon tinting of the skin of the face excepting on the cheeks where there is a dull red flush. The colour is much more marked on the face and neck than in the conjunctivae where it is so slight that I should not have recorded it if the definite lemon tint of the skin had not been present. He feels sickly after food. He looks sickly but says that he feels fairly well but listless. The urine contains a very marked amount of urobilin and a trace of bile. The mother remarked the colour of the skin yesterday when she says the urine was darker.

Anthony Thomas Johnson. Age 5 years. Case 26
29 Albion Street, Murton.

Attends Murton Council School. Teacher: Miss Thompson.

My partner attended him from Wed. 20/12/44 until Wed. 3/1/45.

History.

He was very listless and looked weary and heavy eyed on Wednesday, 20 December. He would not play but wanted to be nursed in his mother's arms like a baby, which was most unlike him. By evening he was feverish and was noticed to be breathing rapidly and using his alae nasi vigourously. Dr. McIntyre thought the symptoms suggestive of/ an incipient lobar pneumonia and he prescribed sulphapyridine. The child rapidly improved, and by Sunday, 24 December, he appeared to be almost better. The sulphapyridine was stopped. The temperature remained normal thereafter and no physical signs developed in the chest.

However, the boy did not seem to continue to improve and again became listless and refused to eat. On Saturday, 30/12/44 he vomited twice, and on Sunday the urine was first noted to be deep yellow. Jaundice was present on 1 Jan. 1945.

I saw him on Wednesday, 3 Jan 1945, when he was fairly deeply jaundiced. He complained of generalised itching and has done so since Sunday. The urine contains bile and urobilin

The liver is palpable over 2 finger's breadth below the costal margin and it is tender. I could not palpate the spleen.

Recovery was gradual and progressive.

Raymond Pow. Age 18 years. Case 27

15 Hawkins Road, Murton.

Coal Miner.

Thursday 11 Jan. 1945. Visited.

He consulted me some ten days before as he felt out of sorts ---"he did not know what was the matter with him" --- and nervous. I attributed his condition to his having witnessed a particularly gruesome fatal accident at his work on 28 Dec., 1944. His mother had noted that the mid-shift meal, which he carried to and consumed at work had been getting smaller and smaller as far as 3 weeks before. Gradually he dropped from 7 sandwiches to 6, to 5, and then to 4. Recently he has brought some sandwiches home, and for the past three days he had not touched them at work.

On Wednesday, 3 January, 1945, he felt really ill at work. He had a queer sensation in the epigastrium --- a weak, powerless sensation not adequately described as a sinking feeling. He longed for the shift to get over, and he has been off work since. He complains of a horrible breath. For the past three or four days he has had a lumbro-sacral aching which was worse when he straightened up, after stooping (cf Sheach, Case 5). He has not left the house as he felt he could not trouble to do anything recently.

He complains that his hearing is affected. His own voice does not sound the same to him. He can hear it all right, in

fact, it appears to be louder than usual, but it sounds strange, and "not like his voice."

He became jaundiced yesterday and he noticed the deep yellow urine, which is to-day very marked.

To-day jaundice is moderately deep, most marked in the conjunctivae. The tongue is coated.

Pulse 72 per minute, and temperature is normal.

He is tender in the epigastrium and the right subcostal region.

Mon. 15 Jan. 1945

He complains of itching of the skin. Jaundice is now intense. The faeces are almost white. He is now eating a little.

Notes.

1. He is termed a 'dish lad' at work.

   He is in intimate contact with Bertie Wood, an 'onsetter'.

2. His brother, Harry Pow, suffered from post arsphenamine jaundice in November, 1943.

Paul Wearmouth. Age 7 11/12 years. Case 28
Baysdale, East Murton.

Attends Murton Council School. Teacher: Mr B Porter.

Sunday, 21 Jan. 1945 Visited.

History:-- The illness evidently began on Sat. 13/1/45. He did not want to go to the seaside because he had a headache and when he got there he refused his 'favourite' tea. He said that his stomach felt shivery but that he did not feel cold. During the night he had marked frequency of micturition. On Monday, the 15th, he did not want to go to school as he had a frontal headache. His story was discredited ! He improved and made no further complaint until Wednesday, 17th, when epigastric pain and headache were complained of, this time at piano practice time.

But on Thursday he was obviously genuinely ill. He was listless, seemed weary and exhausted and soon tired of playing with his toys etc. He had epigastric pain at intervals. On Friday his urine was seen to be very dark and he had four soft stools "not quite diarrhoea."

Sat. 20 Jan. 1945, the urine was sent to me for examination. The result was: Acid urine S.G. 1020. No albumin, no sugar.

Bile and urobilin present.

To-day, 21 Jan,1945, he has vomited everything for the past 24 hours. The pulse was 90 per minute. Temperature 98. He is jaundiced. He was tender in the epigastrium and right hypochondrium and pressure evoked nausea.

NOTE. His sister, Rosalind, aged 5 years, suffered from what I considered to be a mild attack of hepatitis not attended by jaundice, her illness commencing 13/12/44.

Dorothy B. Elliott. Age 10 years. Case 29

25 Shinwell Terrace, Murton.

Attends Murton Council School. Teacher Miss Redfern.

SECOND ILLNESS. See Page 670.

Tuesday, 16 January, 1945.

Pain in the epigastrium. No appetite. Suboccipital headache. Dizzy. Tender right costal margin.

At times epigastric pain, headache and dizziness coincide. Hiccough daily. Goes pale at times. Continued thus until Tues, 23 Jan, 1945, she vomited all last night. Everything she took was promptly returned. She cried with epigastric pain and she had a frontal headache. Her breath is very offensive. She is markedly jaundiced. The urine is loaded with bile and urobilin (and phosphates). Urticaria left buttock since Sunday, 21 Jan, 1945.

Pulse 84. Temperature normal. She is said to have been poorly 'off and on' since 25/11/44: to have complained of dyspnoea --- couldn't keep up with other children, and tea makes her feel very sick.

Mary Sugden Age 6 years. Case 30

7 Stephenson Street, Murton.

Attends Murton Council School. Teacher: Miss Penk.

Saturday, 27/1/1945. Visited.

She had no sooner got out of bed to-day than she started to vomit. Even sips of water have been promptly rejected.

She is definitely jaundiced. She complains of pain over the liver anteriorly but of absolutely nothing else. She is tender on pressure over the right subcostal margin but I could not palpate the liver.

Temperature is 99°F. Pulse 100.

Tues. 30/1/45.

She is more deeply jaundiced, but her condition is improved in so far as the vomiting has ceased and she is beginning to eat a little.

The urine is acid. S. G. 1020. Bile is present in moderate amount.

Urobilin is present. There is no albumin, nor is there any other abnormality.

Robert King. Age 15 years. Case 31
21 D'Arcy Place, Cold Hesledon.

Tuesday, 30 Jan. 1945. Visit.

He has had a head cold for the past 10 to 14 days, but he felt otherwise well. On Friday, 26/1/45, he awoke at 4 a m and immediately vomited. The vomiting was frequently repeated but the vomitus consisted of 'only a little water'. He was doubled up with upper abdominal pain, a constant severe but dull ache. The pain continued for 5 days, becoming progressively less severe, until by Monday evening it passed off.

To-day he feels giddy at times. He has no desire for food, and he feels very listless. His thighs ache just above and behind the knees. The tongue is moderately coated.

The pulse is 56 per minute, the temperature 99.2°F.

He is markedly jaundiced.

The stools are said to be clay coloured. The urine contains bile in large amount, very little urobilin, is acid and the gravity is 1018. Itching of the skin is not now present, but was complained of on Thursday, Friday, 25th and 26th Jan.

Thurs. 1 Feb. 1945.

The liver edge is readily palpable 2 finger's breadth below the right costal margin. It is not very markedly tender. The patient has a deformed chest which may account in part for this finding. The spleen can not be palpated.

His only complaints are that he feels rather tired and that he has a heaviness in the epigastrium.

Moira Forster. Age 10 years. Case 32
5 Stephenson Street, Murton.

Attends Murton Council School. Teacher: Miss Redfern.

Wed. 8 Nov. 1944. Visited.

On Monday she vomited urgently in school, and was intensely giddy. The giddiness persisted and she suffered from frontal headache and epigastric and periumbilical pain. She looks dull, 'lifeless', apathetic and weak. Her mother says that Moira cries 'if she is spoken to.'
The pulse is 96 per minute. Temperature is normal. The tongue is raw on the tip and edges, elsewhere the papillae are prominent and there is a thin yellow fur as a background. She has lost her appetite and complains that she keeps feeling sickly. At school she has not been able to thread her needle as she could not see clearly.

2nd Attack.

I was unable to attend her throughout her next illness on 26 Feb. 1945.

The symptoms above repeated themselves almost exactly. She suffered from vertigo, abdominal pain, epigastric and umbilical, she had severe dull frontal headache. Nausea and anorexia also recurred. This time she had fairly sharp diarrhoea and she became deeply jaundiced. The faeces and urine were typically altered in colour.

Walter Sugden. Age 10 years. Case 33
7 Stephenson Street, Murton.

Attends Murton Council School. Teacher: Mr. W. Brown.

Thurs. 1 March, 1945

His sister was jaundiced on 27 Jan. 1945.

Walter complained of epigastric pain and of feeling sick at that time, but he did not vomit.

A week ago he complained of abdominal pain and wanted to vomit, but he could not be sick. He was very listless. He began to vomit on Sat., 24 Feb, 1945, and continued to suffer from acute abdominal pain and vomiting until early to-day. Dr. McIntyre, who was attending him, was relieved to find Walter jaundiced to-day, "fearing appendicitis."

To-day the liver is palpable and tender.

Pulse 96 per minute. Temperature 98° F.

He says he feels "top heavy"-- very giddy, especially if he sits up. The urine contained urobilin and bile.

The faeces were clay coloured.

Albert Eric Robinson. Age 7 years. Case 34
Murton Moor Farm.

Attends Murton Council School. Teacher: Miss Wootton.

Thursday, 1 March, 1945.

He came home from school yesterday complaining of a frontal headache. He was so tired and weak that he sat on a chair and could not undress to go to bed. He vomited several times.

To-day he is jaundiced. The urine is deeply bile stained. He feels very giddy at times and says his head feels ever so big and seems to be floating. He has pain above the umbilicus and is so tender that examination is difficult.

He continued to vomit for the next three days and refused all food. He felt sickly at the sight of food. The jaundice became very deep. The faeces were pale. The urine contained bile.

Mon. 5/3/45.

He had large patches of erythema on the face and neck. Later they appeared on the "mid region" and on the back. He complains of troublesome 'tingling' in his right hand --- "pins and needles."

Thurs. 8/3/45.

Marked loss of weight. Appetite still very poor.

In the areas where he had the erythematous rash the skin looks and feels rough and it is said to be 'intolerably' itchy.

Alan Hough. Age 6 years. Case 35

91 Princess Street, Murton.

Attends Murton Council School. Teacher: Miss Robson.

Dr. McIntyre informed me of this case.

Wed. 7 March, 1945.

History. On Thursday, 1/3/45 he had a head cold and remained in bed. But he was much better next day, continued so, and returned to school on Monday, 5 March. He did not feel well at school, being sickly and being troubled with epigastric and umbilical pain. There was a suspicion of jaundice on Monday evening.

On Tuesday he vomited several times, and he had an erythematous rash on the abdomen and on the back.

He became definitely jaundiced.

To-day Wednesday, 7 March, he complains little. The urine is bile stained and the stools are pale. He is not markedly tender on abdominal palpation.

Edna Newton. Age 4 years. Case 36

4 Stephenson Street, Murton.

This child became jaundiced on 9 March, 1945.

For a week she had been lazy and sleepy. The appetite remained fairly good throughout the illness.

The urine was bile stained, the faeces were pale.

She complained of her eyes being irritable -- she had some conjunctivitis and blepharitis. The liver was palpable and tender.

She remained in bed, eating nothing all day and slept. She got up and about and felt a little better. On Monday, however, she complained of high pabilical and epigastric pain. She had no desire to eat and at times was sick. The mother noticed that Edith was extremely lash... could not be bothered with anything. The urin... to be dark and the motions were almost white.

Her mother, father and brother suffered f... recently a severe illness (no jaundice) on 5 De...

Edith Davison. Age 10 years. Case 37
5 Ash Terrace, Murton.

Attends Murton Council School. Teacher: Miss Redfearn.

Tues. 20 March, 1945.

She is jaundiced; it is really quite marked but evidently had escaped notice. The temperature and pulse are unaffected. The tongue is clean and moist. The facies is striking -- a heavy dull weary expression with a dull malar flush, and the child looks sickly. She is tender to pressure over the epigastrium and right hypochondrium subcostally. The urine contained bile. The history was:--

On Friday, 16/3/45, she felt sickly when she rose in the morning. She could not stand as she felt so giddy, and she therefore remained in bed, eating nothing all day. Saturday and Sunday she was up and about and felt a little shaky but otherwise almost better. On Monday, however, she was ill again complaining of high umbilical and epigastric pain.

She had no desire to eat and at times she felt nauseated. The mother noticed that Edith was extremely listless and "could not be bothered with anything." The urine was noted to be dark and the motions were almost white.

NOTES.

Her mother, father and brother suffered from the prevalent epidemic illness (no jaundice) on 5 Dec, 1944.

Interval 106 days.

Josephine Gannon. Age 4 years. Case 58

3 Hawkins Road, Murton.

Not yet attending school.

History.

This child has been ill since Monday, 12/3/45, when she complained of upper abdominal pain. She has felt sickly and several times she has tried to vomit but has not done so. All the week she 'lay about' listless, and she would not go out to play. The mother noticed that Josephine was yellow on Friday, 16/3/1945, and gave her a purgative 'to clear it'. The motions were very pale --- said to be a "dirty white". Vomiting occurred on Sunday, 18/3/45. Visited Wed. 21/3/45.

The child is jaundiced -- moderately. She does not look very ill. The mother says she did not send for me as the child's condition varied so greatly: at times she brightened up ("picked up") and then she would fall asleep for an hour or two. The urine is dark and bile stained.

There seemed to be no possible contact with any patient suffering from clinical jaundice.

Note. The mother suffered from the epidemic illness on Friday, 29 December, 1944.

Audrey Southgate. Age 7½ years. Case 39.
4 Forster Avenue, Murton.

Attending Murton Council School. Teacher: Miss Agar.

Sat. 31/3/45. Visited by my partner.

History:-- She has not been well since Monday. She has complained of pain across the root of the nose and supraorbitally. At times she has been active and playful only to in turn become listless, when she has had to lie down. Her appetite was poor. On Saturday morning she vomited repeatedly and violently on rising -- the vomitus was very foul smelling. The tongue was moderately furred. She had severe epigastric pain. The vomiting was repeated on Saturday night.

On Sunday the urine was noted to be of a deep orange colour and the faeces were clay coloured. Jaundice was marked on Monday 2 April, when she was otherwise much better.

Tues. 3/4/45.

Moderate degree of jaundice. Most marked in the conjunctivae where it is deep. The cheeks are a healthy red and indeed she looks well and not at all fatigued.

She has now no pain or tenderness in the epigastrium or anywhere in the abdomen. Temperature is normal. Pulse is 76 per minute. The liver is not palpable.

NOTE. Her father suffered from the epidemic illness on 7/11/1944. 145 days interval.

ADDITIONAL CASE HISTORIES.

The following Case Histories refer to Illnesses discussed in the preceding Chapter.

They are mainly cases in which jaundice was not a feature.

Eileen Ann Lavery. Age 8 years.
25 Wetherburn Avenue, Murton.

Attending St. Joseph's Roman Catholic School.
Teacher: Miss Maddigan.

Monday 30 Oct 1944 Visited.

On Monday 23 October she was very listless all day and she had no appetite for her supper. Her mother had noticed that Eileen had appeared out of sorts for 2 or 3 weeks. On Tuesday 24/10/44 she complained of feeling sick and giddy and she vomited several times. On Wednesday she looked and felt better and seemed to have recovered, but next morning she was ill again. She looked tired and pale and had no appetite. All day long she sat in the chair, not even talking, and she seemed to have no desire to do anything. She had no headache, nor did she complain of giddiness again, but, she says, she had a peculiar 'cold numb' feeling all over her body, but especially in her back. She had been obstinately constipated during this period. This is said to be very 'unusual for her.'

At this stage of the illness the mother observed the tongue to be covered with a thick yellow fur, and gave Eileen an ounce of Castor Oil. The condition remained as described until Sunday, 29 October, when she vomited several times.

To-day, 30 Oct 1944 she is jaundiced. She is not tender abdominally. The tongue is very clean at the edges and tip

but otherwise slightly coated.

Temperature 98.0 °F. Pulse 78 per minute.

Urine is intensely bile stained.

Differential White Cell Count.

Polymorph Leuco.	47
Eosino. Leuco.	1.5
Basophil. Leuco.	0.5
Lymphocytes	48.5
Monocytes.	2.5

Wed. 1/11/44.

She is very deeply jaundiced. The cheeks are dull red. These combine to give a peculiar appearance. It looks as if the cheeks had been painted a bright red and then the colour had been toned down with face powder.

Temperature 99°F. Pulse 78 per minute.

She says she feels itchy --- her forearms.

She improved steadily and by the 16 November, 1944, the jaundice was definitely clearing.

On Friday, 23rd November, 1944, she developed a severe common cold, nasal catarrh being marked.

William Lavery 13 years.
23 Wetherburn Av. Murton.

Attending St. Joseph's R C School. Teacher Miss Gallagher.

Visit Thursday 17/11/44.

States: Last Wednesday he had abdominal pain, it was coming and going and "not all that bad." His mother noted that he was puffy round the eyes which thus appeared to be smaller than usual. They were blood shot. He has had a headache off and on ever since and at times had a fleeting giddy sensation.

He took really ill yesterday, 16th. He had a pain - he places his hand over his liver -- a much higher situation than during last week. He had no appetite and felt sick-- particularly sick and dizzy if he stood up.

Rash. Last week he had "heat spots" which were very itchy -- he describes a small blotchy erythema.

Temperature normal. Pulse 60 (age 13 years).

On Mon 20/11/44 his legs felt like "electricity" --- he compares it with a home made "shock set" -- both legs.

Tongue. Tip red and looks raw. The rest of the tongue has a moderate coating - yellow and white and the papillae stands out prominetly - red.

Sat. 19/11/44. Complained of pain below his heart. Eyes are'smarting'. His eyes and complexion are what I would term "just short of jaundiced."

Monday 20/11/44. "Heat spots round waist and knees. Very itchy.

Fri 24/11/44. A little bronchitis. Looks listless.

Occasional sudden loss of voice. It just seems to go off and return just as suddenly.

Henry Lavery. Age 3 years.
23 Wetherburn Av. Murton.

Visit Fri 17/11/44.

The intelligent mother has noticed that the child has been off colour for a week or more.

He has looked "very pale above the cheeks" and his facies suggested an oncoming illness, to his mother. He has vomited through last night, several times, and again this morning. He was awakened by epigastric pain at 3 a.m. and was sick precipitately shortly afterwards. The vomited material amounted to extremely little compared with his efforts.

To-day he has lain in his pram "dead felled" (lifeless). He is costive and constipated and has no desire for food. He is exquisitely tender "over the liver." (right subcoatal)
Blood. Friday 17/11/44.
Friday 24/11/44. For the past 3 nights diarrhoea at night and kept awake by abdominal pain (? around umbilicus).

George Parker Age 11 years.

11 Forster Av. Murton.

Attends Murton Council School. Teacher: Mr. Hume.

He is the close friend and class mate of Raymond Elliott who was jaundiced on 20 October, 1944.

Tuesday, 21/11/44. Consultation.

On Monday 13/11/44 he got out of bed and immediately felt giddy, he went very pale and then fainted. He vomited once. He stayed in bed that day but returned to school on the 14th November, and has attended ever since. He improved, but on Saturday and Sunday, 18th and 19th, he had a severe attack of diarrhoea --- the motions being watery and frequent.

The diarrhoea has cleared to-day 21/11/44, but his mother brought him to see me as she says that for the past 2 or 3 weeks he has gradually become more listless, refuses to go out to play and is entirely disinterested in everything. He looks seedy, pale, haggard and exhausted.

The temperature and pulse are undisturbed. The tongue is clean — it looks too clean. He says that he just wants to keep on taking rests.

David Turner Age 35 years.

50 Windsor Terrace, Murton.

Coal Miner.

Thursday, 4 Jan 1945. Visit.

For the past 2 or 3 weeks he has been becoming progressively weaker. He has felt very tired and weary and recently he has been "too listless to bother with anything." During the past few days he has felt dizzy. Last night he felt definitely worse. He felt chilly and, later, he sweated freely. He has a suboccipital headache and low backache. During the past week he has eaten progressively less. He sits down to eat anticipating that he will enjoy his meal, but after one or two bites his appetite goes and he feels nauseated.

He is in bed to-day. Temperature 98.4°F. Pulse 90 per min.

He looks heavy lidded and weary. This man seldom loses work. I asked him why he could not sit up in the chair when he had no rise in temperature or other apparent sign of illness (a question which may appear unkind and provoking in the telling) and he replied that he felt too weak and indeed too lazy to sit up.

I noted that his urine contained a moderate amount of urobilin.

He continued to look extremely exhausted for about a week, thereafter he steadily improved.

Jas. W. Wood Age 19 years.

28 Albion Street, Murton.

Tuesday 16 Jan 1945. Visit.

He is lying in bed. The temperature is 98°F. Pulse 50. Yesterday he complained of heavy frontal headache — more heaviness than ache. He felt dreary. Later he went out. He says that "he must have been mad to go out the way he felt." "He did not know what he felt like. He just felt awful."

To-day he could not get out of bed, he felt so dull, heavy and listless. His throat feels queer and he feels that he is not speaking normally. He feels that his voice is not being produced in the ordinary way and it sounds queer to him.

The calves of his legs are aching. He feels chilly.

It seems remarkable for a usually active lad to lie in bed with such little, almost no, evidence of illness apart from a very sleepy appearance. He converses as if it was the greatest trouble to talk.

Recovery was gradual.

WOOD. Bertie. 62 years.

28 Albion Street, Murton.

Onsetter.

Enquiry Visit.

Friday 12 Jan 1945.

Off work from Mon 18 Dec until resumed on Mon 8 Jan 1945.

He states that for over 2 weeks before he fell off work he had found his work a trouble. His thighs ached and his arms, especially towards the shoulders, felt very tired and lacking in strength. At night he did not go out. He felt too weary to want to do anything. He refused to get in coals or water for his wife -- he usually does this; telling her: "Oh, do it yourself, I can't be bothered."

From the root of the nose to the suboccipital region his head ached, and felt thick and muddled. Especially he noticed that he had trouble in swallowing -- as if his throat would not "work properly."

To-day he says that he still feels very listless and is trying to carry on by lying in bed 14 hours daily to get ready for work.

Mrs. Wood. 64 years.

28 Albion Street, Murton.

Visit Wed 29/11/44.

Yesterday she was suddenyl seized with vomiting and giddiness. There was absolutely no warning, she just vomited where she stood, and the giddiness was so intense that it was with difficulty that she struggled to lie down in bed. Prior to this she had a dull frontal headache.

To-day the vomiting has quietened down. Her eyes are bloodshot and there is evidence of conjunctivitis.

Temperature 99.4°F. Pulse 70 per minute.

She is still very giddy if she raises her head.

She has never previously had an attack at all like this. On examination there is nothing e.g. in the cardiovascular or nervous system to suggest that the illness is ~~just~~ OTHER THAN indicative of the prevalent epidemic.

Tues 5 Dec 1944.

Got up but felt sickly and giddy. She is obstinately constipated. Normally she is inclined to have rather loose bowel action. The taste in her mouth, she hesitantly states, is like the smell in an unhygienic dry closet.

(It will be noted that the taste had been said by Mrs Fry --- see Hawthorn Group -- to compare with a faecal odour.)

Raymond Pow Age 18 years.

15 Hawkins Road, Murton.

Coal Miner.

Thurs. 11 Jan 1945. Visited.

He consulted me some ten days before as he felt out of sorts --"he did not know what was the matter with him" -- and nervous. I attributed his condition to his having witnessed a particularly gruesome fatal accident at his work on 28 Dec, 1944. His mother had noted that the mid-shift meal, which he carried to and consumed at work had been getting smaller and smaller as far as 3 weeks before. Gradually he dropped from 7 sandwiches to 6, to 5, and then to 4. Recently he has brought some sandwiches home, and for the past three days he had not touched them at work.

On Wednesday, 3 Jan 1945, he felt really ill at work. He had a queer sensation in the epigastrium -- a weak, powerless sensation not adequately described as a sinking feeling. He longed for the shift to get over,and he has been off work since. He complains of a horrible breath. For the past three or four days he has had a lumbro-sacral aching which was worse when he straightened up, after stooping (cf Sheach, Case 5). He has not left the house as he felt he could not trouble to do anything recently.

He complains that his hearing is affected. His own voice does not sound the same to him. He can hear it all right, in

fact, it appears to be louder than usual, but it sounds strange, and "not like his voice."

He became jaundiced yesterday and he noticed the deep yellow urine, which is to-day very marked.

To-day jaundice is moderately deep, most marked in the conjunctivae. The tongue is coated.

Pulse 72 per minute, and temperature is normal.

He is tender in the epigastrium and the right subcostal region.

Mon. 15 Jan 1945.

He complains of itching of the skin. Jaundice is now intense. The faeces are almost white. He is now eating a little.

Notes.

1. He is termed a 'dish lad' at work.
   He is in intimate contact with Bertie Wood, an 'onsetter.'
2. His brother, Harry Pow, suffered from jaundice in November, 1943.

POSTARSPHENAMINE

Edith Davison Age 10 years.

5 Ash Terrace, Murton.

Murton Council School. Teacher: Miss Redfern.

History.

Fri 16/3/45.

She felt sickly when she got out of bed in the morning. She said that she could not stand as she was so giddy. She remained in bed all day and did not eat.

On Saturday she got out of bed and she was out and about on Sunday feeling practically normal.

On Monday, however, she was ill again. She had complete anorexia and complained of umbilical and epigastric pain and nausea. She was obviously listless and could not be bothered with anything.

The urine was noted to be dark and the motions were pale—clay coloured or the colour of concrete.

Tues 20/3/45. Consultation.

She is jaundiced.

Eliz. Davson 35 years.
5 Ash Terrace.

Visit Tues 5 Dec 1944.

On Sat 2/12/44 she felt sick and dizzy when she arose. She had frontal headache and aching in the buttocks and the upper part of the thighs. Presently sharp diarrhoea occurred accompanied by pain below and to the left of the umbilicus: a constant pain with superadded colic excerbations.
Today the pulse is 60. Temperature no elevation.
The tongue is dry and brown.

Geo. R. Davison 35 Years. 5 Ash Terrace.

Visit Tues, 5 Dec 1944.

He lost his voice on Saturday. He has had dull frontal headache. He is not dizzy and he has no abdominal symptoms. He has pains in his thighs exactly like his wife's.
He complains now of difficulty and discomfort in swallowing—everything seeming to be too big and too dry so that "it just can't go down."

Brian Davison 6 years. 5 Ash Terrace.

Attending Murton Council School. Teacher, Miss Wotton.

30 Nov. 1944. He seemed quite well when he went to school but at the lunch hour he looked tired and said he was sleepy and had a headache. He went to school after lunch but he was up all that night with diarrhoea which occurred every half hour. He has vomited several times since (written 5/12/44). He seems to get no warning at all before he vomits, having to rush precipitately in an effort to reach e.g. the lavatory.

Josephine Gannon age 4 years.

3 Hawkins Road, Murton.

Not yet attending school.

History.

This child has been ill since Monday 12/3/1945, when she complained of upper abdominal pain. She has felt sickly and several times she has tried to vomit but has not done so. All the week she "lay about" listless, and she would not go out to play. The mother noticed that Josephine was yellow on Friday 16/3/45 and gave her a purgative "to clear it." The motions were very pale - said to be a "dirty white." Vomiting occurred on Sun 18/3/45.

Visited Wednesday 21/3/45.

The child is jaundiced -- moderately. She does not look very ill. The mother says she did not send as the child's condition varied so greatly: at times she brightened up ("picked up") and then she would fall asleep for an hour or two. The urine is dark and bile stained.

There seemed to be no possible contact with any patient suffering from clinical jaundice.

Interval = 82 days.
Interval = 82 days.

Harriett Gannon. Age 40 yrs.
Fri 29 Dec. 1944 Visited. GIDDY; She awoke and, suddenly, ay.
Last night - dull frontal headache, & vomiting occured at 4 am. today. ely
- urgent, repeated and violent. Upper abdominal pain. Vomit extremely scant. Feels chilly at times. Today, even a sip of water is rejected.
Another daughter had a very typical attack on 4 Dec. 1944.
After gradually improving, Mrs Gannon had a repeat attack —
similar but milder — one week later.

G R O U P 5

ANOTHER EPIDEMIC AT MURTON

(With reference to

the

Differential Leucocyte Count.)

The Differential White Cell Count.

Non Jaundiced Patients at Murton

I now wish the reader to consider another group of cases, which occurred in Murton in 1944.

It would be about the end of August that my partner and I began to think that an epidemic was beginning. And a most uncommon type of epidemic it seemed to us: quite unlike anything of which we had had experience ~~of~~ in general practice.

An increasing number of patients began to consult us, complaining of symptoms which were vague and indefinite. In the year 1944, the Essential Works' Order, etc., did not offer any inducement to the doctor employed in colliery practice to allow coal miners to absent themselves from work on trivial, or indeed too ill-defined grounds.

The increasing number of patients with such vague symptoms was then the cause of considerable anxiety on our part, and we no doubt partly on this account, began to interview such patients with possibly added care and attention to detail.

The first point which I noted was that there could be no doubt of the genuine nature of the complaints. Included in the numbers were men who I knew were very keen workers, and never absented themselves from work unless absolutely forced to do so.

What then were the symptoms of this illness ?
(They bore a close relationship to the symptoms as described on Page 250 et seq. of the Cold Hesledon Epidemic).

The patient looked tired and exhausted as he entered the consulting room. This impression was conveyed not only by the facial expression, which seemed fixed with the eyelids appearing to droop, but by the limpness of the posture. When he was asked to describe his illness the patient frequently seemed at a loss to do so. Most frequently he said that he felt useless, or that he seemed to have a "severe loss of strength" --- as many peculiarly expressed themselves. Very often the story was that this gradually increasing weakness had occurred over a period of 2 or 3 weeks. Accompanying the weakness was a feeling of increasing 'laziness'. The patient found that he could not be bothered with anything. Gradually his hobbies became neglected. He would not go to the club at night. Or the little bit of 'joinering' he was attempting as part of some domestic alteration remained unfinished. He just sat in his chair at night after work, went to bed and then to work.

In some cases the time in the chair got less and the time in bed more, until there were patients who went to bed on returning from work to get ready for the next day, eventually only absenting themselves from work when even all this rest still found them too weak and listless to carry on.

It will be appreciated that such a degree of lethargy, weakness and listlessness, as I have indicated, was not met with in all cases. It varied in degree. Sometimes the patient's

appearance enabled one to correctly anticipate what the patient would say of his condition and even the hesitant manner in which the patient would say it. The patients were at a loss to explain their symptoms and were obviously puzzled or bewildered at their condition. In an effort to give his illness a label the patient frequently said "I don't know what is the matter with me. I think I must have the 'flu' (influenza)".

If I asked if he had ever suffered from influenza and if he replied in the affirmative, I then asked him if his present illness resembled his influenza attack. Invariably he said that it did not. Frequently he said rather inconsequently that it was "not at all like that."

Another thing of which I soon became aware was that not only did the patient fail to understand his illness, but he gave the impression that he did not expect his doctor to understand it either. Time and again I found that the patient did not consult me sooner because, as he said to his wife, "the doctor would think there is nothing the matter with me."

This frequently repeated remark is an illuminating one. It shows that the patient realises how little he has to 'show' compared with the condition in which he feels himself to be. No obvious rise in temperature, no fevered pulse, often no striking 'leading' symptom, he feels there is nothing to substantiate his story of increasing weakness and lassitude.

often the patient seemed loathe to tell his complete story until an obvious interest in and acceptance of his narration led to a realization that "the doctor" had an idea how he, the patient, was feeling, and what ailed him: in this illness which was so unlike anything he had ever experienced.

I may appear to have dealt with the appearance, approach, demeanour, and the behavious of the patient, and with his 'leading' complaint, at unnecessary length. I feel that they all combine to present a picture and create an atmosphere which was characteristic of this epidemic.

Now this weakness and lethargy was very like the condition observed in the epidemic at Cold Hesledon, the Bakery, and in the illnesses of the patients at Murton who became jaundiced. Very soon it was found that practically every symptom which had been found in each of these outbreaks was encountered in this outbreak.

Headache, vertigo, nausea, anorexia, vomiting, abdominal pain and diarrhoea were common complaints. It was not simply that headache occurred in this group of cases as in the others, it was the same type of headache and it was commonest in the same locations. The vomiting occurred under similar circumstances, and so on.

The close resemblance between the less commonly complained of symptoms was also striking. For instance, the persistent "pins and needles" sensation in the fingers and hands: or the child who could not see to thread a needle at school, and the

pains in the limbs occurring in e.g. the same part of the thighs. In some cases the gastro intestinal symptoms dominated the picture so that one wondered whether there must be an epidemic of e.g. a salmonella type of gastro enteritis. In others the lethargy was the dominant or sole feature making one wonder if the dreaded encephalitis of 1923 - 1924 was returning --- especially as disturbed sleep rhythm was not uncommonly noted.

In yet others there was a combination of both these sets of symptoms.

It appeared to me, therefore, that all the patients in this group were probably suffering from the one infectious disease. Further, it seemed that this infectious disease bore a striking resemblance to the disease at the Bakery and many of the illnesses at Cold Hesledon.

In the preceding sections of this account I have referred to the differential white cell count in patients suffering from infective Hepatitis and the other so similar and concomitant epidemic. The occurrence of a high relative lymphocyte count led me to wonder whether this finding might be constant throughout all the groups of illness. Whilst I decided to check the count in cases attended by clinical jaundice, I could not help but think that others (for instance in the services) would have ample material and opportunity forsuch an investigation, and that my contribution to this aspect of the problem could be at most a

relatively trifling one.

On the other hand I felt that such an enquiry in the case of some of the large number of patients who were not jaundiced might lead to a genuine contribution to medical knowledge.

By this time there appeared to be little doubt that some uncommon infectious disease was prevalent in the area. Neighbouring practitioners told me of similar occurrences of 'gastric influenza', 'gastro enteritis', 'vertigo' and so on, with features similar to the epidemic in this area. The lay press had occasional reference to a new type of influenza. More suggestive still was the fact that I had several war workers under my care who had returned from different parts of the country as they were ill. Although they were not jaundiced they had been diagnosed as suffering from infective hepatitis. Their stories were frequently of outbreaks in which the non jaundiced cases seemed to outnumber the cases attended by jaundice. Dr. Wilkin's letter (Hawthorn Group) pointing to an outbreak of gastro enteritis following upon his jaundice epidemic was, as it were, emphasized by increasing references to similar outbreaks in England and Scotland in the medical press (ref. page 554) where no organism had been identified in spite of careful investigation.

In brief, I concluded that the epidemic which had occurred in the Murton area was of very widespread - probably country-

wide --- destribution.

I therefore decided to determine the differential white cell count in say the next 20 to 30 cases where I thought the patients might be suffering from the epidemic illness.

The cases were not specially selected. I naturally at first selected such cases as were to hand which appeared undoubtedly to offer very suggestive symptom complexes.

But, later, I applied the test to patients whose symptoms seemed less in number or less strikingly distinctive.

The following table shows the result of the differential leucocyte count.

Reference from preceding page.

British Medical Journal 1945. Vol 1. page 577.

"(Any questions?)" See also Pages 789 to 792.

Differential White Cell Count.

No.			POLY.	LYMPH.	MONO.	EOS.	BAS etc.
1.	Forster	E.	50	46	-	2.5	1.5
2.	Harrison	L.	58	34	7	1	
3.	Burdess	M.	57	40	0.5	2.5	
4.	Clews	D.	49	51	-	-	
5.	Hunter	M.	58.5	35.5	4.5	1	.5
6.	Ridley	T.	49.5	42.5	4.5	3.5	
7.	Ridley	S.	53	45	1.5	0.5	
8.	Elliott	M.	48.5	43	3.5	4.0	1.0
9.	Bell	G.	58	40	2		
10.	Bell	Mrs G.	42	54	-	4.0	
11.	Collett	L.	23	69	4.0	4.0	
12.	Beer	Mrs A.	76	24	-	-	
13.	Beer	A.	49	49	2	-	
14.	Sugden	W.	54	40	-	6	
15.	Forster	Mrs E.	45	50	2	3	
16.	Newton	M.	63	36	-	1	
17.	Hallimond	T.	40	58	-	2	
18.	Davison	W.	58	44	-	2	
19.	Jobey	M.E.	52	46	-	2	
20.	Blackmore	E.	58	40	2	-	
21.	Lashley	R.	62	38	-	-	
22.	Mordue	T.	55	45	-	-	
23.	Skinner	J.	48	40	2	2	
24.	Emery	A.	58	40	2	-	
25.	Kebell	H.	63	31	3	2	1.0
26.	Muncaster	Wm.	64	22	2	2	
27.	Penman	Terence	78	18	-	4	

Comment on the Differential White Cell Count.

The great majority of the cases showed a well marked relative lymphocytosis.

Exceptions were (a) Mrs Beer, who showed 24% lymphocytosis
(b) Case 26. Muncaster. He is a heavy drinker and I was really doubtful about him.
(c) Case 27. Penman. His story did not seem suggestive in the presence of an epidemic

I have excluded Cases 26 and 27 from the summary of symptoms in which I therefore only include Cases 1 to 25.

Number of Illnesses. 25.

Average Lymphocyte Count 44 %

Listlessness.	Lethargy	21
	Headache	17
	Vomiting	15
Lower Thoracic-Abdominal	Pain	14
	Vertigo	13
	Anorexia	12
	"Aches and Pains"	5
	"Pins and Needles"	4
	Diarrhoea	4
	Visual Disturbance	3
	"Joint" Pains	4

Also noted.

Relapse.	Urticaria.
Epistaxis.	"Shooting" Pains.
Menstrual Disturbance.	Conjunctivitis.

The 25 cases which I have just mentioned are reported (Case histories 1-25). They represent a very small proportion only of the cases occurring in the epidemic and I have therefore included a further 50 case reports. (Case histories p.613)

As I intend to give a rather detailed analysis of the 50 cases, more especially in respect of the symptomatology, I think it would be easier for me and more acceptable to the reader if I did not similarly analyse the 25 cases separately but refer to them later as indicated.

There are, however, one or two points to which reference appears to be indicated, at this stage.

Relation to Cases showing Clinical Jaundice.

Case 1. Elizabeth Forster. Her brother was jaundiced.

Case 4. David Clews. His daughter became jaundiced.

Cases 9 and 10. Bell. Granddaughter had been jaundiced three months before.

Cases 14, 15, and 16. Newton; Forster; Sugden. Cases of jaundice occurred later in each house.

.....

Secondly I would state that the relative frequency of the symptoms is probably more fairly portrayed in these 25 cases than in the further group of 50, some of which have been selected to illustrate special features in the symptomatology.

I now propose to consider the symptomatology in the 50 further cases mentioned: where it may be desirable to compare

with cases in this group of 25, I shall do so.

The 75 cases, in all represented illnesses, occurring in Murton, which I thought were due to a prevalent infectious disease.

.....

It is realised that some may think I should have analysed the symptoms in the 25 cases in which the differential leucocyte count was estimated, in preference to analysing the symptoms in a further 50 cases. I see the point of their argument, but I would state that the 50 cases are picked as more representative of the epidemic as I could select them from over 500 cases recorded: further they illustrate or emphasize some point which I wished to stress and finally, having demonstrated that a relative lymphocytosis was certainly prevalent I still did not think that elaboration on such a finding was the chief aim of my work.

Meantime I would add that the reader should defer judgement as to whether the cases recorded were instances of a 'common' infectious illness until the end of this, complete, section of the work.

Case 1.

Elizabeth Forster. Age 10 years.
29 Alfred Street.

Attending Murton Council School.

Her brother, G. W. Forster, was ill for one week before becoming jaundiced on 6 Oct., 1944.

Her cousin, John Border, became jaundiced on 28 Sept. 1944.

Tues. 10/10/44. Visit.

For the past 10 days the child has been obviously listless, disinclined to play and depressed. She seemed most listless in the morning after school. For the past two days she has had frontal headaches -- "she keeps getting them." She has complained of pain across the shoulders and around the shoulders. She blames the aching on someone who is "always leaning on her" (I mention this to illustrate the type of pain).

Last night she vomited urgently, violently, and repeatedly. The mother says that Elizabeth cries "if you speak to her" and is sitting about sleepy all day. The child did not look sleepy to me.

Differential White Cell Count.

Polymorph. Leuco.	50
Lymphocytes.	46
Eosinoph.	2.5
Bas.	1.5

Wed. 11/10/44. To-day her appearance has altered. She appears tired and sleepy to a degree. There is marked conjunctivitis, the conjunctivae look very dull and dirty and the eyes are "heavy lidded." She complains of epigastric pain and she is tender in the epigastrium and under the right costal margin,

Case 1 (Continued).

but not the left. She says that she cries readily because she feels so weak and useless. Complete anorexia. Nausea continues.

.....

Subsequent History.

She seemed to have recovered completely within a week. But thereafter she had a recurrence of all the above symptoms but she did not vomit.

Case 2.

Louisa Harrison. Age 17 years.
14 Watt Street, Murton.

Visit Sat. 14/10/44.

Last night she felt sick and giddy. She wanted to be sick, but she could not vomit. She slept very poorly, feeling sick all night, and the room seemed to be going round if she opened her eyes. This morning she vomited frequently with distressing violence. She has slight frontal headache: and anorexia. Pulse 72. Temperature 98.

Sund. 15/10/44. She now has pain -- Umbilical pain. She has had one action of the bowels to-day, a very pale stool. She felt sickly all day and tired, and tried to vomit. She vomited twice in the evening, precipitately it should be noted. Pulse 80. Temperature 98. Differential White Cell Count showed lymphocytes 54% and monocytes 7%.

Mon. 16/10/44. Has been sickly and vomited all night. She feels worse and she looks worse. She continues to suffer from vertigo. She has pain (slightly colic-like at times) across the abdomen at the level of the umbilicas. She is not pained in the epigastrium or hypochondrium on either side. There is no abdominal tenderness. Firm palpation of the abdomen does not evoke nausea.

Tuesday 17/10/44.

She began to improve. Nausea persisted for a few days, lack of appetite for almost another week. Continued to feel dizzy if she sat up and for over a week her gait was unsteady-- she felt as if she was 'walking on air'. Pulse remained slow 54 per minute at times during convalescence.

Margaret Burdess. Age 11 years.
23 W. Coronation St. Murton.

Attending Seaham Intermediate School.

History.

Monday, 9 Oct. 1944. Returned from school feeling sick and out of sorts. Would not eat anything.

Tues. 10 Oct., 1944. Exactly the same events occurred.

Wed. 11 Oct., 1944. To-day she again returned home ill. She had been weeping in the classroom on account of upper abdominal pain.

Tues. 12 Oct, 1944. Consultation. The child told me she "feels useless" and sleepy. She felt that her chest (she pointed to the lower third of the sternum) was 'burning and crushed', and that she was going to be sick. There was no vomiting, however. Complete loss of appetite. "Heavy" frontal headache -- the pain was slight, the "heaviness" more marked. She looked peculiarly exhausted. The facies and posture were typical of those I have elsewhere frequently described.

Until Monday, 16 Oct. 1944, Felt listless and looked lazy and apathetic -- strikingly so, as she is usually very active and bright. Complete lack of appetite - distaste for food too. Lay apathetically on the couch all this time.

Differential White Cell Count No 12 shows Lymphocytes 40% .

Fri. 20 Oct. Appetite very poor. Looks somewhat brighter.
Wed. 25 Oct. Same.
Sat. 4 Nov. Appetite returning. Marked loss of weight. She now has a watery rhinorrhea, sneezing frequently.

At no time was there pyrexia. Appeared to be really quite ill during the 4 weeks. The dominent feature of the illness was lethargy and striking appearance of apathy and physical and mental fatigue.

Case 4.

David Clews. Age 31 years.
27 Ripon Terrace, Murton.

'Bus driver. Northern General Transport.

He suffered from Cerebrospinal meningitis in 1941.

This man consulted me on the 15 September, 1944.
He felt weak and was diagnosed as suffering from fatigue due to long and irregular hours of work.
On 17 Oct., 1944 I called to see him on an'enquiry'call and he gave this history, which is reported almost verbatim.

For about a week to ten days before he consulted me on 15 September 1944 (i.e. 5 to 8 Sept 1944) he felt tired, weak, and weary, and went, straight from his work, to bed. He did not get up until he had to go to work again. He felt that he was trailing about and no more: that he could scarcely carry his body, and his neck and arms were aching and heavy. He was continually feeling that he wanted to be sick and he had complete loss of appetite. He lived on cups of tea and thin wafer biscuits. (As stated above he consulted me on 15/9/1944, but I could find nothing of note on fairly full examination).

He, correctly, felt that I did not understand his condition and decided not to consult me further in the matter.

For the next five weeks to date (17/10/44) he has continued as above -- no appetite, weak, tired and irritable: and constipated, as is his habit. He began to vomit frequently, having at times to stop the 'bus and get out, to vomit. He had a horrible taste in his mouth and a peculiar feeling in the stomach and throat.

Case 4 (Continued).

His daughter, Judy Clews, Case 3[x], was jaundiced 2 Oct 44. To-day, 17/10/44. He is tender in the epigastrium. The liver is just palpable and it is tender. He feels sick on such palpation. Vomited twice to-day. Remarks that he does not feel sickly when lying down, but immediately he sits up he feels sick and giddy. There has been marked loss of weight since he consulted me five weeks ago.

Differential White Cell Count showed

Poly. Leucocytes 51 % Lymphocytes 49 %

(it was an unsatisfactory film and monocytes may have been missed).

Subsequent progress was gradual.

A feeling of upper abdominal 'fulness' with associated nausea persisted for 5 or 6 days. Thereafter the appetite began to return and vertigo was less readily provoked.

He resumed workon the 30 October, 1944.

.....

NOTE. I think it very likely that David Clews may have infected Judy Clews.

David Clews ill from 5 to 8 Sep.1944 (Approx. date).

Judy Clews "Bile in urine" 2 Oct.1944 (exact date).

x See Table Page 578

Margaret A. Hunter. Age 10 years.
30 Gray Avenue, Murton.

Attends Murton Council Schools.

Mon. 9 Oct. 1944. Consultation.

Ill since Wed, 27/9/44. Has been listless and complained of diarrhoea ever since, having five stools daily, soft not watery. No colic pain, just discomfort. Appetite has been poor. She has been absent from school from Monday 2 Oct, 1944.

To-day she presents a picture of weariness, weakness, and exhaustion. The mother says she "lies about the house, refusing to go out and play."

"Perhaps she does a little writing or painting, but she rapidly tires of it, and lies down." Sometimes she complains of feeling cold. She says her head feels fuzzy and muddled, and at times it seems to be "floating."

Differential White Cell Count.

Polymorph. Leuco.	58.5	
Lymphocytes.	35.5	* 1 plasma cell in 200 cells.
Monocytes.	4.5	
Eosino.	1.0	

Case 6.

Theresa Ridley. Age 12 years.

27 Calvert Terrace, Murton.

Attends Murton Council School.

She is a friend of M. Hunter (previous case).

Tues 10 Oct. 1944.

She has felt vaguely out of sorts for the past 2 weeks. She "could not be bothered with anything" and she has felt sickly. Yesterday she had severe upper abdominal pain and she vomited several times. She has been very giddy for the past 24 hours, and she complained of frontal headache.

On 16, 17, 18, 19, and 20 October she had nosebleeds.

This is the first time she has suffered from epistaxis. She still has frontal headaches. Since her 'illness' she has been very sonstipated: this is unusual for her.

Differential White Cell Count.

Polymorph. Leuc.	49.5
Lymphocytes.	42.5
Monocytes.	4.5
Eosino.	3.5

Case 7.

Sylvia Ridley. Age 17 years.

27 Calvert Terrace, Murton.

Colliery Canteen Employee.

This girl, who is of regular menstrual habit, commenced a 'period' three weeks ago. Since then the loss has continued, irregularly.

She feels tired all the time and she wants to sit down and do nothing.

Thurs, 20 Oct. 1944 This morning she went to the canteen but immediately felt chilly, had a heavy frontal headache, felt giddy and sick, and she vomited.

For a few days she suffered from loss of appetite and headache. She looks tired and exhausted.

Differential White Cell Count.

Polymorph. Leuco.	53
Lymphocytes.	45
Monocytes.	1.5
Eosino.	.5

Muriel Elliott Age 23 years.
95 Calvert Ter. Murton.
Conductress, Northern General Transport.

Foreword. cf D. Clews.

This girl consulted me on Friday, 1 Sept., 1944.

She had been well until the beginning of this week but since then began to feel increasingly tired and lazy. She was overpowered by this lethargy and could sleep all the time. It was an effort to combat the drowsiness. She also suffered from loss of appetite and vomited once or twice, this being preceded by epigastric and umbilical pain which doubled her up.

Unfortunately I did not then appreciate the significance of the symptoms. I made an enquiry call on Friday, 20 Oct, 1944. I remembered her illness and I had then realised that it was typical of what was becoming an epidemic.

Fri. 20 Oct. She further tells me that when she was ill she felt very depressed and irritable, and frequently sat down and cried. She felt so weak and powerless that she thought she was 'pining away.' She felt sickly and "just could not face her food." Normally she is a conscientious, industrious, and happy worker.

Differential White Cell Count.

Polymorph.	48.5
Lympho.	43
Mono	3.5
Eosin.	4
Bas.	1

She recovered and felt active, fit and well until
2nd ILLNESS, 27 Nov., 1944. Again felt sick but did not vomit. Loses all desire for food "at sight of it." Tired and sleepy and goes to bed at 7 p.m. to be ready for work next day, but she sleeps poorly. The tongue is clean and moist.

George Bell Age 53 years.
15 Dobson Ter. Murton.
COAL MINER.

History. He states that on Monday, 26 Sept. 1944 he was off work for one day only, complaining of frontal headache, pains in the lumbar region and weakness in the legs. But he felt well until Wednesday, 18 Oct. 1944.

He was ready to go to work when he was seized with violent upper abdominal pain. He had a headache and vomited. Vomiting was so urgent and severe that he became alarmed. This attack abated and he gained relief, but soon he had a sickly sensation. He wished to vomit but could not. In the evening the vomiting returned urgent and violent again.

He felt very giddy and had a "floating or swimming sensation". Thirst was marked and he had a sense of great weakness.

Thurs. 19 Oct 1944.

Improved. Loss of appetite continued. Very weak.

Friday, 20 Oct. 1944. Visited.

He is lying in bed but there is nothing of note in his appearance or on examination. He rarely loses any time off work. Pulse 62 per minute. Temperature 97.6 ^{o} F.

Slight return of appetite. The tongue is clean and moist, the edges are almost raw.

Differential White Cell Count.

Polymorph. Leuc. 58. Lymphocytes 40. Monocytes 2 %

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Elizabeth Jackson (Cold Hesledon Group) calls here frequently.

Jane A. Bell. Age 58 years.
15 Dobson Ter. Murton.

Wife of George A. Bell (preceding case).

I saw her on my visit to George A Bell on Fri. 20 Oct., 1944. She gave me this history.

On 29 Sept. she was suddenly seized with violent vomiting, which continued from midnight until 2.30 a.m. She had a dull frontal headache which is persisting. Since then she has felt extremely weak and tired. She cannot be bothered with anything. Usually an energetic and industrious woman, she is now inclined to sit about or lie down when her domestic duties do not compel her to work. She feels dull and muddled -- in fact at times she has felt quite stupid.

Abdominal pain is not complained of, but she feels 'uneasy and uncomfortable' in the upper abdomen. This uneasiness is associated with a 'sickly' sensation.

Differential White Cell Count.

Polymorph. 42

Lymphocytes. 54

Eosinophil. 4

Laura Collett Age 6 years.
57 Williams Road, Murton.
Attending St. Joseph's R. C. School. Teacher Miss Riley.

Wednesday, 18 Oct. 1944. Visited.

Yesterday she suffered from diarrhoea and vomiting: both were severe and each was repeated 6 or 7 times. Through the night and to-day the diarrhoea has continued. She has no headache but she is at once giddy if she stands up.

Pulse 114 per minute. Temperature 98 ^{o} F.

Fri. 20 Oct. 1944.

Her appearance is not adequately accounted for by the diarrhoea and sickness, dibilitating as they are. The mother is alarmed at the child's apathy and listlessness. "She won't even bother to talk." She feels utterly tired and listless and complains that her elbows are paining. The elbows are not tender.

Differential White Cell Count.

Polymorph.	23
Lymphocytes	69
Monocytes.	4
Eosin.	4

The appetite remained very poor for several days.

Note.

There was evidence of the spread of an infection in the children
R. C. School/at this time, one child being jaundiced on the 16th and one on the 20th October.

Case 12.

Mrs. A. Beer Age 36 years.
2 Faraday St. Murton.
House duties.

History. Thurs 19 Oct. 1944. She suffered from generalised aches and pains. Her fingers ached and tingled -- very marked 'pins and needles' sensation. She vomited several times and after fainting, she went to bed, where she again vomited. For the rest of the day she felt chilly, had a severe frontal headache and wanted to vomit but could not do so.

Fri. 20 Oct. 1944. Visted.

She is prostrated. Intense nausea and complete anorexia are complained of. The skin is moist and she complains of heavy drenching sweats. Dull heavy frontal headache is associated with vertigo. No disturbance of pulse or temperature --- 84 per minute and 98°F.

Pins and needles sensation is still marked in the fingers. Differential White Cell Count showed lymphocytes only 24 %

Sat. 21 Oct 1944.

Frequent profuse watery stools to-day but anorexia is not so marked. She is tender and complains of pain over the right lower ribs and down almost to the umbilicus from the middle line to the mid clavicular line.

Mon 30 Oct 1944. She was still very weak and sweated freely on slight exertion. Her legs ached and she lay in bed. She said that she felt useless, listless, and could not be bothered with anything.

Subsequent recovery was slow but uneventful.

Case 12 (continued).

With reference to the illnesses of Mr and Mrs. A. Beer it should be observed that their son, Alfred Beer, aged 7 years, was absent from school on Monday, 2 Oct, 1944. He had abdominal pain and felt he was going to vomit — he did not vomit. Frontal headache was complained of. He 'lay about' for a few days and was disinclined to play and disinterested in everything. He is said to have appeared lazy, pale and "drawn" and he would not eat.

Further, Mrs. E. J. Beer, Age 62 years
29 Dene Terrace, Murton.

She is a widow and spends much of her time at 2 Faraday Street, the home of her son, Alfred Beer. She gave this history.

22 Oct. 1944.

Her feet and toes felt "stiff, numb, and tingling."

She had a heavy dull frontal headache, had epigastric pain, and felt sick.

Later she vomited precipitately and violently. She was intensely giddy. In a few days she began to improve, but she was still weak 2 weeks later.

Mr. Alfred Beer Age 37 years.
2 Faraday St. Murton.
COAL MINER.

Mon 16 Oct. 1944.

He had to leave his work owing to the sudden onset of acute epigastric pain. The pain eased off in an hour or two but since then he has felt that it 'has left him very weak'. He had an urgent duty (bereavement) 4 miles away, and there he felt so weak and exhausted that he had to go to bed for two hours before he could return by bus. Tues and Wed. worked at the pit. Thurs 19 Oct 1944. Went to work but was useless and did no work. He had pain above his knees and in the "small of the back" and sharp shooting pains in the forearms with tingling in his fingers. He had to open and close his fists vigorously to combat this tingling sensation. He felt chilly.
Visited 20 Oct 1944. He feels very weak and listless. He looks to be exhausted. He has a mild, dull frontal headache. Tongue is clean.Loss of appetite continues. Pulse 80. Temperature 98.

Mild conjunctival injection present (more than would be accounted for by his occupation).

Blood Test 20 Oct 1944.

Polymorph.	49
Lymphocytes	49
Monocytes.	2

Sat. 21/10/44. Apparently recovering."Simply weak and no stamina"
Mon. 30/10/44. Still feels weak. Exhausted and sweats freely if he has the slightest exertion. He cannot understand his continued weakness and lethargy.

Gradual recovery.

Walter Sugden. Age 35 years.
7 Stephenson Street, Murton.

History. Consulted me on Monday, 30 October, 1944.

For about three weeks he has felt weak, tired and listless. He has gone to work, and sat 'in the house' doing nothing, and not desiring to bother with anything.

For the past 4 days he has had pain in the small of the back and across the shoulders -- at the back, and the tired feeling has become almost overpowering.

His appetite has become progressively poorer in the past week, especially in the mornings: and the last 2 days he has felt very giddy, especially on rising. He has then also felt sickly but he has <u>not</u> vomited.

<u>30/10/44.</u> (Monday).Typical dead tired facies.Pulse 72.Temp.Nor.

" " Differential White Cell Count.

Polymorph	54
Lymphocytes	40
Eosin.	6

Resumed work 6 November, 1944.

.....

Monday, 25 December, 1944.

Diarrhoea. Very Little pain.

Not profuse nor very frequent.

Elizabeth Forster Age 39 years.
5 Stephenson Street.

Visited Tuesday 31 Oct. 1944.

History. "On Sunday, 29th, when I got up out of bed I felt dizzy and had to sit down. I felt that my head was floating. I then vomited. My forearms felt weak and useless."

This floating feeling and dizziness goes off and she feels fairly well, but it returns, and again she feels 'powerless.'

She is sitting with her legs up on two chairs, and is tired and weak and powerless, and just wants to sleep. She asks:"Doesit affect your eyes? Now and then things go misty as if I were going blind, and I find myself blinking to take it away."

Pulse 72. Temperature normal.Bowel action normal,regular.

Severe supraorbital headache. Cold clammy skin.

Differential White Cell Count.

Polymorph Leuc.	45
Lymphocytes	50
Monocytes.	2
Eosin.	3

3/11/44. Feels much better.

NOTE. She did not maintain this improvement.

Tues. 7/11/44. She vomited in a 'bus -- she vomited only froth and felt very dizzy, sickly and fuzzy-headed all that day. She felt chilly. She sweated profusely and frequently.

Recovery was protracted.

Mrs. Mina Newton. Age 38 years.
4 Stephenson Street, Murton.

Sunday, 22 Oct. 1944. Visited.

History. About a month ago she took ill. She vomited, felt giddy and had a severe frontal and suboccipital headache. At times she 'went blind.' In two or three days she felt better and she dismissed the episode as being due to an acute gastric upset. No sooner did she feel almost better than she had a relapse. She now wanted to vomit but she could not do so. The intervals of the "blindness" became worse, and she consulted a colleague who was then assisting us, and who reassured her. Since this consultation she has had frequent attacks of giddiness, complete anorexia, and she feels limp, listless and useless. Her sight continues to vary.

She complains bitterly of pins and needles in the hands and feet. This sensation is accompanied by a feeling that the hands are swollen. She obtains relief by vigorous rubbing, especially the first thing in the morning when the sensation is most troublesome. At times she wondered whether she might be pregnant as the nausea resembled nausea during pregnancy.

She has aching above the knees, around her wrists, and in her fingers.

On examination. The pulse is 52 per minute. The tongue is clean. She is not tender over the liver. Systolic apical murmur. There is marked urobilinuria.

The Klein's intradermal Test gives a + ve result, the wheal is of a dirty creamy yellow colour resembling the patient's complexion, which might be described as subicteric.

Differential White Cell Count.

Polymorph Leuc.	63
Lymphocytes.	36
Eosin.	1

Tues. 31 Oct. 1944.

Gradual improvement with rest. Supraorbital headache persists. She describes both subjective and objective vertigo as having occurred previously --- " at times the bed was going round with me."

Tues, Wed, Thurs. 31 Oct., 1 Nov., 2 Nov., 1944.

She had completed her normal menstruation on 24/10/1944. She now had a slight return of the flow. She is normally of very regular menstrual habit.

Sat. 4 Nov. 1944.

I was called to see her at 10.30 p.m.

She was seized with epigastric pain, she felt very sick and retched repeatedly, but only a little 'water' was vomited. In the end she dropped to the floor, "her legs gave way and she felt powerless."

After this attack recovery was uneventful.

The Apical systolic murmur "cleared up."

Thompson Hallimond. Age 63 years.
23 Albion Street, Murton.

Coal Miner.

Sunday 22 Oct. 1944

For the past 3 weeks he has felt himself becoming progressively more and more tired. Gradually he has stopped going out at night, and during the past week he has returned from work, had a meal and gone to bed "dead tired." But he could not sleep. Usually he is a very sound sleeper. When he sat at home he would not talk and his wife made him go out on Sat. He had begun to lose his appetite, and on Saturday he had to leave his beer unfinished and go home. Did not sleep at night.

To-day he looks exhausted and limp. The tongue is clean at the tip and edges, slightly furred elsewhere. The complexion is very dull and muddy.

There is no urobilinuria.

The Klein intradermal Test is negative.

Differential White Cell Count.

Polymorph. Leuc.	40
Lymphocytes.	58
Eosino.	2

He improved gradually and by Saturday, 11 Nov 1944 he looked entirely different. His colour was good, his complexion bright and alert. He feels as "full of life" as he previously felt devoid of it.

Wilfred Davison. Age 46 years.
5 No. Western Ter. Murton.

Thurs. 26 Oct. 1944.

On Monday, 23 Oct 1944 he had dinner and went to bed at 1 p.m. At 3 p.m. he felt giddy in bed. He arose at 5 p.m. but he could not 'face' his tea. He felt as if "all his strength had left him: powerless," and he slumped in his chair. On returning to bed he was suddenly violently sick all over the bed, and he continued to vomit and retch for some time. He had a dull frontal headache. On Tuesday he felt better and went to work. As he changed into his pit clothes at the pit-head baths he suddenly became giddy again, and he had to return home. Since then he has felt weak.

To-day, 26 Oct. 1944 he just "feels weak and powerless."

Pulse 60 per minute. Temperature 98.4 ^{o} F.

Differential White Cell Count.

Polymorph Leuc.	54
Lymphocytes.	44
Eosinophil.	2

There is no urobilinuria.

He improved until

Mon, 6 Nov. 1944.

He vomited twice yesterday. He had little warning --- a return of the giddiness coincided with a wave of nausea and then he vomited.

Jobey, Mary A. Age 20 years.

6 Matthews Road, Murton.

Wednesday 25 Oct. 1944. Consultation.

This woman has had an erythemato - urticarial rash on the face and forearms, with one or two lesions only on the legs. The lesions are to-day fading. She complains that she has complete lack of appetite, that she has a dull heavy frontal headache extending round to the suboccipital region and that she is "useless, lowerless and lazy." She is normally a particularly robust and vivacious young woman.

She just wants to lie down and do nothing. The facies is arresting --- dull, tired and otherwise expressionless.

Pulse 72 per minute. Temperature normal.

Differential White Cell Count.

Polymorph.	52
Lymphocytes.	46
Eosin.	2

Her husband felt faint and vomited on 7. 10. 1944. Her son, Kenneth Jobey, aged 7 months, was then also ill, with sickness and diarrhoea.

Case 20.

Edward Blackmore. Age 22 years
11 Dobson Ter. Murton.
Coal Miner.

Mon. 23 Oct 1944. Consultation.

History. He states "On Friday, 20 Oct., 1944, I felt queer at work. I could not change the wheels properly and seemed unable to get ahead with my work. I felt tired and weak, but it was more than just that. I came home, ate very little, and went straight to bed. I slept well. On Sunday my hands were trembling. Headache kept going off and on, and I felt very poorly. On Sunday I felt better."

To-day he looks tired. The expression is fixed -- pale, drawn, dismal to expressionless. Complains that he feels he is losing his sight at times. His vision fluctuates, at times going very dim. This is said to be aggravated if he stoops, or if he is jolted, e.g. by stepping off the pavement.

He complains of headache, situated in the nape of the neck and the frontal area.

Wed. 25 Oct. 1944.

He feels better in that he is not so "dazed", but he now complains of discomfort to pain in the epigastrium. He feels, and looks, very weak.

Pulse 84 per minute. Temperature normal. Tongue is clean.

Differential White Cell Count.

Polymorph.	58
Lymphocytes	40
Monocytes.	2

Robert Lashley Age 54 years.
24 Pilgrim St. Murton.

Coal miner.

Thurs. 26 Oct. 1944.

On Tues 24 Oct 1944 he had pain over the region of the liver in front - under the lower ribs - and just medial to the right shoulder joint just above the clavicle. At times the pain was like a knife stab.

There is little to find on examination. The tongue is slightly coated. He feels extremely weak and he has lost his appetite.

Sat. 28 Oct 1944.

The severe pain has gone but he feels weak, listless and 'useless' and he cannot be bothefed with anything. He is not sure of his balance when he is walking, especially if he is walking upstairs.

Differential White Cell Count showed lymphocytes 38 %

Case 22.

Thomas Mordue. Age 17 years.

74 Toft Crescent, Murton.

Tues. 24 Oct. 1944.

For over a week his mother has been telling him to visit the doctor, as she noticed that he was eating very little and was not looking well. He first felt really ill on Sunday 22 October, when he began to have fleeting attacks of giddiness and a dull frontal headache. He has been gradually feeling more and more tired. He feels he just wants to go on sleeping. "It is not just as if he was tired in his body, he just can't be bothered with anything." This morning he felt extremely tired. A walk in the fresh air dispelled this overpowering drowsy sensation for only a short spell and then he began to feel very dizzy.

This boy visited Anderson's, 4 St. Cuthberts Terrace, Dalton le Dale daily (L. Anderson, Cold Hesledon Group). Differential White Cell Count.

Polymorph Leuc.	55
Lymphocytes.	45

Case 23.

John Skinner. Age 52 years.

31 Watkin Cres. Murton.

Tues. 24 Oct. 1944.

When he arose yesterday morning he felt very sickly. He wished he could vomit. Eventually he vomited several times. He had pain in the epigastrium and felt a tightness round the lower half of his chest. He had a frontal headache.

Differential White Cell Count.

Polymorph. Leuc.	48
Lymphocytes.	40
Monocytes.	2
Eosinophils.	2

Friday, 27 Oct, 1944.

He has still very little appetite. He feels very listless and says that he just wants to sit down or lie down and take no notice of anything.

Arthur Emery. Age 21 years.

30 North Street, Murton.

Tues. 24 Oct. 1944.

He felt very sickly but did not vomit. He had a dull heavy frontal headache. Later diarrhoea commenced and he had severe upper abdominal pain. He did not feel giddy.

The tongue is clean.

Diarrhoea persisted for 72 hours. It was not profuse or watery.

Differential White Cell Count.

Polymorph. Leuc.	58
Lymphocytes	40
Monocytes.	2

Harold Kebell Age 43 years.
5 Model Street, Murton.
S. E. D. Bakery.

History. On Saturday, 14 Oct, 1944, he went to bed at 11 pm. He had had some beer but there was no suggestion that the amount was at all excessive.

At about 4 am on Sunday he awoke and was urgently and violently sick. He felt "swimmy and giddy, and his feet were floating about." He was not fevered and he had no headache.

At 9 am he was again sick on rising. He went out for a walk to "try the affect of fresh air" and he had to steady himself with a walking stick, as he still had this "terrible floating sensation." In the evening he went for a walk and again required the aid of a stick -- he was reeling about like a drunken man.

Mon 16 Oct 1944

He went to work. He ate and enjoyed a very big lunch.

At 6.30 pm when I called to see him his pulse was 60 per minute. Temperature 98°F. He still felt weak and listless.

Differential White Cell Count.

Polymorph. Leuc.	63
Lymphocytes.	31
Monocytes	3
Eosin.	2

Case 26.

Wm. Muncaster Age 47 years.
17 Luke Cres. Murton.

Coal miner.

Wed. 25 Oct 1944. Visited.

On Monday, 23 Oct., he could not eat his 'snack' half way through his shift at work. He had a "sickly feeling rising into his throat." He wanted to vomit but could not do so. He actually tried to induce vomiting by 'putting his finger down his throat": to no effect.

To-day he has a sensation in his chest just above the epigastrium which he describes as follows: it is partly a soreness as if he had been kicked and partly as if he had been scalded. He appears to be suffering severe pain.

He is very dizzy especially if he tries to sit up.

Pulse 96 per minute.

Temperature 98 ^{o} F.

Differential White Cell Count.

Polymorph. Leuc.	64
Lymphocytes.	22
Monocytes.	2
Eosin.	2

I noted that the illness began on a Monday.

Muncaster drinks rather heavily, especially on Sundays.

Case 27.

Terrence Penman Age 16 years.

36 Albion Street, Murton.

Tues. 24 Oct. 1944. Consultation.

For the past 2 or 3 weeks he has felt out of sorts. He has pain across the epigastrium extending into the right and left hypochondria. Usually a big eater, he has gradually lost his appetite. He has felt sickly several times, more especially on rising in the morning, and he has had occasional dull frontal headache. The bowels are acting normally.

He is very tender in the epigastrium and under the right subcostal margin. His mother's statement is:

"His eyes seem to have sunk into his head. He has dark rings under the eyes. He is very pale." (this is 'fair comment'.) "He lies about and has no energy, looking lifeless and dull. He is very irritable."

Differential White Cell Count.

Polymorph Leuc.	78
Lymphocytes.	18
Eosino.	4

He recovered gradually and resumed work 6 Nov. 1944.

(I have always regarded Mr Penman as an "alarmist", but I believed that the youth's story was genuine.

GROUP 6.

NON JAUNDICED PATIENTS AT MURTON.

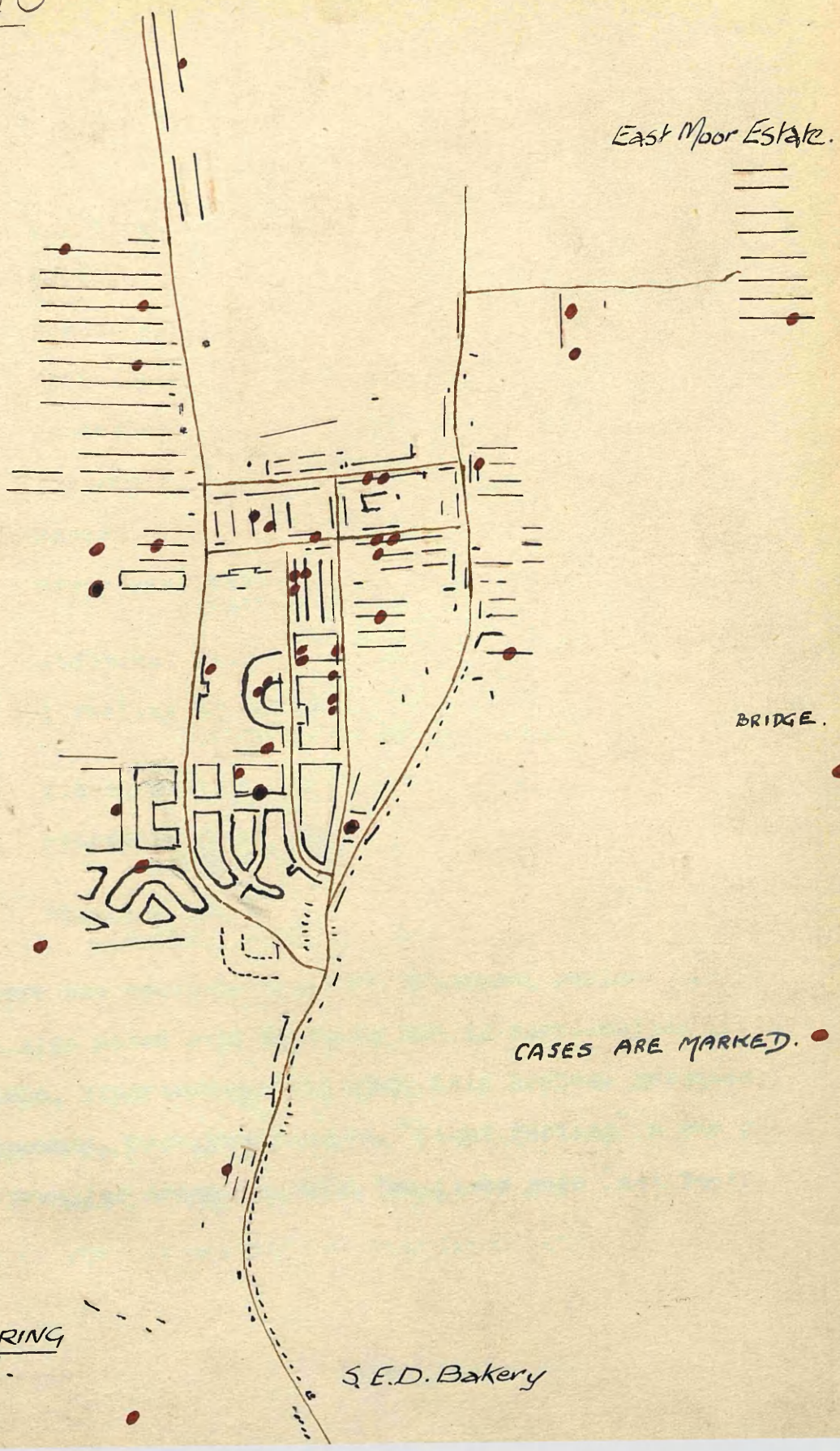
From the large number of illnesses and case histories thereof, I have selected the following 50 to describe the epidemic. Although I intend at once to draw up a table of symptoms it must be remembered that this is not strictly to be compared with such a table as applied to the patients who became jaundiced. I have included all patients who were jaundiced in my report whereas I can only select a modest proportion for consideration from the large number of patients who had illnesses not accompanied by jaundice.

Nevertheless I believe that the main symptoms, by which I mean to convey, the symptoms most frequently encountered, will still be presented without much loss of proportion, as it were.

Plan 10 overleaf, shows the distribution of the 50 cases referred to in this group of illnesses, Group 6.

It must be pointed out that it can not strictly be compared with the plan, 9, on Page 398, showing the distribution of the illnesses featuring Jaundice; as all of the latter group of cases is there included: Plan 10 deals with only a fraction of the total cases which I recorded,-- viz. 50 out of 600 cases.

PLAN 10



URTON

WING DISTRIBUTION
CASES NOT FEATURING
INICAL JAUNDICE.

NUMBER OF CASES DESCRIBED. 50.

Vomiting	30
Vertigo	25
Headache	25
Lethargy	24
Anorexia	21
Diarrhoea	18
Nausea	16
Upper Respiratory Catarrh	14
Abdominal Pain	13
A Feeling of Mental Dullness	15
Visual Disturbances	11
Sensation of choking Dysphagia etc.	6
Stabbing Pains (darts, needles)	5

There was commonly a marked prodromal period. 15.

Also noted were Weakness and in-coordination in the limbs, Bradycardia, Relapses, Skin Rashes, Dyspnoea, Insomnia, Urobilinoginuria, "Tight feeling" in the chest, a peculiar sensation that the limbs were "not there."

VOMITING.

This varied in many ways from case to case. Whereas one patient was awake all night trying to vomit before he eventually succeeded (Case 33) others vomited very precipitately, receiving no immediate warning (Cases 14, 18, 40).

It was occasionally an initial symptom, more frequently there had been prodromal symptoms. It occurred on the 3rd day and 6th day of my attendance in 2 cases (40 and 22) respectively. More often during the early stages of the illness the patient had not consulted me. But there seemed to be no reason to doubt that in several instances the period had been from 1 to 2 or 3 weeks (Cases 3, 6, 10).

One man, R. W. Wood, Case 32, was repeatedly and violently sick. He was very little disturbed by the vomiting which he explained was quite effortless and caused only slight discomfort: no pain. The same history was obtained in the case of a woman, Margaret Holmes, who became alarmed at the violence and frequency of her vomiting but who had not the slightest pain. (Case 38).

In one case after an initial day of vomiting and diarrhoea the patient did not again vomit until the 6th and 7th day of his illness, and on each of these days he vomited once only and at the same time, 10.30 a.m. each day. A week later he again felt sickly and went to bed. Then suddenly with no immediate warning he vomited over the bed. (Case 36).

VERTIGO.

The degree of vertigo varied markedly. Being noted as a symptom in 25 cases (50 per cent.) it could be said to be really marked in 10 cases.

One boy (case 27) was terrified in case he was made to sit up: several were afraid to stand up, but I did not witness this. One youth said he reeled about (case 45) and I witnessed this occur in a woman who consulted me at my rooms (case 21).

In all the casesmentioned the giddiness was relieved by sitting down, but in cases 1 and 7 it will be observed that movement of the head as the patient lay in bed caused intense vertigo.

In the group of cases where differential white cell counts were made vertigo was very marked in one woman, Case 2, and one man (case 18). In both cases it was present as the patient lay in bed. It was much more marked and persistent, several days, in the case of the woman.

HEADACHE.

The importance, or rather let me say, the prominence, of headache as a symptom would be grossly exaggerated if it was assessed only by the frequency of its occurrence. It was frequently mentioned by the patient as being accompanied by a muddled, or as locally expressed, "fuzzy", feeling in the brow. Again it was almost always said to be a dull heavy ache.

Most frequently occurring supraorbitally or in the frontal region, it sometimes was present in the suboccipital region: occasionally in both areas. When suboccipital headache was a feature the pain often spread on to the shoulders and it was occasionally accompanied by a "numb feeling."

LETHARGY.

In direct contrast to what I have said concerning "headache" as a symptom, "lethargy or listlessness" was prominent to a far greater degree than would be suggested by a table of symptoms.

I do not wish to over-elaborate the point, but I fell that in a very marked case occurring in this epidemic the appearance is almost unmistakable. It was possibly most striking in the ambulant patient, a few of whom really looked as if they were walking about half asleep. Two of the patients in this epidemic (one was case ≠5) the other a police constable --case not recorded -- said "I have a stupid look; I know I have a stupid look." This was certainly a symptom entirely new to me.

The appearance of lethargy and the patient's emphasis of this complaint was frequently disproportionate to the patient's other symptoms and complaints. Very often the patient was puzzled as to why he should be so overpoweringly tired, weak and useless as the result of e.g. an ordinary 'cold.'

ANOREXIA.

Occasionally there was a fairly prolonged prodromal period of anorexia, at times marked by a distaste for a favourite drink, tea (Cases 1, 24, 25).

Anorexia was often a very difficult symptom to assess when not an initial symptom especially e.g. when the patient had vomited or was giddy.

The appetite usually failed gradually when anorexia was an initial symptom.

The history in the case of Margaret Burdess (Case 3 in the preceding group) was typical of many: anorexia, lethargy and abdominal pain gradually leading to extreme weakness.

DIARRHOEA.

I was interested in this symptom especially in respect of the day of the illness on which it occurred. When it occurred as an initial symptom or the first symptom it was of course possible that some article of food recently consumed had caused it. But in several cases the patient had been ill for some time before diarrhoea occurred, and I think that several

of the illnesses merit close consideration to demonstrate this fact.

Alexander Hewitt's Case record (No. 23) makes the point very clearly. This youth had felt sleepy, had frontal headache and epigastric pain before I was called to see him on 12 Nov 1944. I attended him for a week, and I considered his condition to be definitely indicative of the epidemic illness. His appearance was typical, he ate practically nothing, and, most interesting, he told me that his right hand felt stiff and did not move easily. I think he meant to convey that the movements of the hand were clumsy.

This last was a symptom not <u>frequently</u> encountered. It was not until 20 Nov. 1944, that diarrhoea occurred, and I think it is fair to assume from the case history that this diarrhoea was not due to a separate illness but represented a symptom in a continuing illness.

John Bate (case 36) suffered from diarrhoea on 7 Dec,1944. He remained ill until 19 December, but he had no diarrhoea until 19th December, when it recurred. Here again was the exhausted facies and appearance and the marked weariness and fatigue continuing throughout the illness.

One patient who appeared to be very ill was at first constipated, which was a very unusual happening for him, before severe diarrhoea began on the 3rd day of his illness.

Case 3 shows a prodromal period of 6 days before the onset of diarrhoea. The story of the prodromal symptoms seemed the

more convincing to me as it was obviously not overstressed or exaggerated, and the fluctuation in the symptoms which this woman described was typical of the prevailing illness.

Robert Inman's story also appeared to show that the onset of diarrhoea was frequently the sequal to an illness lasting several weeks (case 14). He told me that he had had a 'head cold' for a fortnight and that he had felt unable to do any work at above shoulder-level as his arms then ached and felt useless. Now, I considered this, the latter, symptom to be very significant (weakness of the upper arm in 'arm workers'; weakness of the upper thigh in 'lower limb workers'). A more concrete symptom was that on Saturday 16 December, 1944, he was suddenly and violently sick -- not the slightest warning. It was not until 23 December 1944 that diarrhoea became a symptom, and when it did occur it was of a type frequently noted in the epidemic: the stools being described as like those which result from taking e.g. Magnesium Sulphate and occurring 3 or 4 times (only) each day.

Case 12 gives the history of a nervous woman, in whom the prodromal phase was doubtless rendered unusually dramatic by reason of such 'nervousness.' In this case after 3 days malaise the patient became aware of loud borborygmi and the onset of gross peristalsis. Six days later came the onset of profuse watery diarrhoea. I attended this woman throughout and no one who did so could fail to believe that

the whole illness was indeed one continuous illness.

A similar late onset of diarrhoea occurred in Case 22. Here it began on the 6th day of the illness.

The severity of the diarrhoea varied markedly. Usually it was of slight to moderate degree and the patient sometimes said that he 'could scarcely call it diarrhoea.' The stools were nearly always watery, the point being that they often occurred only 3 or 4 times daily.

Even when the patient had profuse watery diarrhoea his condition seldom if ever gave rise to anxiety (on the part of the doctor) e.g. on account of dehydration.

.....

Mrs. Beer (case 15 preceding group) suffered from profuse diarrhoea on the 3rd day of her acute illness. She was in a very weak state on the second day of her illness, verging on collapse, but she then had no diarrhoea.

.....

I concluded that in many cases the comparatively late onset of diarrhoea was very much against it being due to any infection (by food or otherwise) having been contracted less than a week and probably more, before.

NAUSEA.

This symptom was again difficult to assess numerically and if anything the number I quote (16 out of 50) is probably a definite underestimate.

In any case Nausea was a very prominent and important feature of the epidemic. The similarity of the complaint in so

many cases left no doubt that there definitely was an epidemic in the area.

Naturally, nausea became most obvious and noteworthy in the cases where vomiting at no time occurred.

To me the most convincing histories were as follows.
Thomas Collings, Case 9, lay awake all night trying to vomit. But he did not vomit.
Alex. Hewitt, case 23, all through the night he tried to vomit, but "nothing would come."
Cases 28 and 45 illustrate the type of case where the patient felt certain that he was going to vomit for say 24 hours but as it were just failed to vomit.

Intense nausea sometimes continued after vomiting had occurred. In several instances the patient had "wanted to be sick" for quite a long time before vomiting occurred (e.g. cases 15, 21) but as elsewhere stated nausea did not by any means precede vomiting, always.

Louisa Harrison (Case 2 preceding group) was intensely nauseated for a whole day prior to being sick. A noteworthy feature in these cases was that when vomiting did occur it was urgent as well as violent.

Nausea was the dominant symptom in the illness of Margaret Burdess (Case 3) who, however, did not, at any time, vomit.

.....

LOWER THORACIC AND ABDOMINAL PAIN.

This presented several interesting features and I think a study of the various pains encountered would be very instructive.

The absence of pain was remarkable in several cases, and in 2 of the cases reported the patient made a special point of stressing the surprise which this lack of pain occasioned (cases 32 and 38). In both illnesses the violence and frequency of the vomiting was probably more marked than in any others recorded in this series and there was not the slightest pain.

It was the exception for pain to be the leading symptom. In only 2 or 3 instances was I convinced that the pain could be classed as really severe.

The majority of the patients had epigastric pain, but in about a third of the cases in this series of cases pain in the region of the liver was complained of: this proportion was, I believe, maintained or exceeded in the epidemic in general. Examples illustrative of right sided pain are seen in cases 11, 19, and 31.

The last case is well worth our attention.

A 18 years old boy had vomited repeatedly, felt dizzy and very muddled, and his head ached. He had diarrhoea.
He complained of pain in the right chest. The location was such that it could just be covered by my hand placed horizon-

tally across his chest with its centre over the nipple. The pain was worse if he breathed deeply.

There was no evidence of pleurisy or indeed any pulmonary ailment. The boy told me that he had been so "swimmy" that he had swayed as he walked.

In Case 11, Thos. Knox, the pain also appeared to be related to the liver, and in case 19 the patient complained of very severe stabbing pains over the region of the liver anteriorly and in the asalia.

Occasionally, as for example in case 17, the patient complained of pain in the right subcostal region only. This was exceptional, more common being a central pain extending towards the right.

Sometimes the patient, considering the epidemic in general for a moment, complained of pain in the region of the liver, present only when he coughed. Case 49 provides an example.

There is no doubt that a marked tendency for the pain to include pain in the right side, was observed.

The patient sometimes complained of a feeling other than pain in the epigastrium. I include case 20 in the series as he expressed what I believe several patients wish to convey verbally but could not. He had pain in the epigastrium -- "it was more a 'fainting' sensation as if due to hunger and he thought he was going to have diarrhoea." He felt weak and "useless" and as if he "would die if he had given way to this sensation."

in the preceding group. GROUP 5 – page 548 et seq.

I have said that really severe pain is unusual; exceptional. I am equally convinced however that it does occur on occasion. In cases 9 and 13 in this group the pain was of acute onset and very severe: in each of these cases the pain was upper abdominal. In case 9 vomiting of alarming severity followed immediately but the other patient did not vomit then or later.

Mrs. Beer, who, it will be noted, showed a normal differential leucocyte count, was tender from the midline to the midclavicular line in the right subcostal region, and for some 2 or 3 inches below it. Pain was similarly situated.

A particularly suggestive distribution of pain, and this I several times encountered in the epidemic in general, was that described in Case 21: pain over the region of the liver in front and also just medial to the right shoulder joint just above the clavicle.

NERVOUS SYSTEM SYMPTOMS. A FEEING OF MENTAL DULNESS.

I have noted this symptom as occurring in 15 cases. The patients made special mention of ~~their~~ THIS symptom and it was really very distinctive. I had had no previous experience of my patients claiming to be mentally dull and it left me with no doubt that I was dealing with something new to me, when I had such a large number do so.

I can do no better than to quote several of the complaints made to me, and I think it would be better if I at times quote rather than paraphrase even if the language may appear rather undignified.

Case 1. She said that she had a heavy dull frontal headache. It is not a severe pain, in fact, "the pain is nothing," it is the "horrible, hazy, fuzzy feeling" of which she complains. It renders her slow to think.

The words underlined were really very typical of the complaint as made by most of the patients.

Case 5. She had "to exert all her will power to concentrate and prevent her mind from wandering -- or feeling stupid."

Case 7. She feels very "light headed" (This is not meant to signify "giddy") and says she feels "quite daft and sees the queerest things" when she closes her eyes.

I would say that this is less valuable evidence than in the two preceding cases.

Case 18. He felt "queer, cloudy and fogged mentally."

Case 25. Felt stupid, looked stupid, and knew he looked stupid.

Case 32. Headache was accompanied by the feeling that he is "not right in his mind." He feels stupid almost to the point of feeling he is going insane.

Case 41. A school teacher. His leading complaint was that he could not think clearly. He was "not himself" mentally. He said he was not alert, could not concentrate, and was "incapable of clear thinking."

I think these examples should serve to illustrate the type of complaint made, but other patients made complaints of a still different but associated nature. The complaint in these

cases was that the brain did not seem to be controlling the body properly, as the patients expressed themselves.

One young man, who manipulates a machine, found that he was in danger as he was "ages in removing his hand" after operating the machine. There was plenty of time to avoid the danger but "he felt as if his brain had very little command over his hand."

An intelligent woman "felt that the brain had lost the power to command the body" as she lay in bed, unable, for a short time only, to move her limbs or move her head from the pillow. Anyone reading Case History 42, the one in question, might well question the significance of this remark or even the significance of the symptoms described, if this was an isolated case.

When we find that her husband was ill one month before and consider his symptoms, Case 41, I think we are justified in asking if there can be any relation between the two illnesses.

Several times the patients were at pains to have me understand the sensation they had as illustrated below, quoting J. R. Hunter (Case 28).

This man was returning from his working place below ground in the mine to the cage, on his way home.

He walked out behind his workmate. He felt "powerless" and found that he was lagging behind. He said to his mate: "Are you hurrying, or am I slow?". It was not just a matter

of physical inability to keep up with his mate, he felt "as if he did not want to hurry, or perhaps, rather, that he could not produce the mental effort necessary to make his limbs keep up with his mate." He said it was "a queer sensation --- a powerless body and an almost powerless mind."

This was to me an extraordinary detailed description for a coal miner to give. I think that it describes the sensation which many summed up by saying that they felt muddled or "queer."

.....

Another symptom not uncommonly complained of in the epidemic was one of which I have seldom had experience in practice. The patient had a "feeling all over the body, not aches and pains, but as if the body was apart from her." Or again, at times "he felt as if he was not there." Others felt as if their limbs "were not there."

Quite frequently patients would tell me that they had to keep feeling their arms as they "seemed not to be there."

These complaints were made by people who did not know one another, who had obviously never heard of such a symptom, and who varied from the most stolid and unemotional to the frankly neurotic. Cases 12, 20, and 33 give examples of this symptom. It was a striking symptom in the case of Dorothy James (p.394). This 13 years old girl told me that she "often had a feeling that she had no legs on."

THROAT SYMPTOMS.

Throughout the epidemic the type of throat symptoms complained of presented distinctive features. The most striking symptom was the occurrence of a choking sensation in the throat. This is best illustrated in the series of cases described, in the illness of Edward Bate. This was no 'mere' globus hystericus. The 9 years old boy came home from school screaming that he was going to choke. If the reader refers to the record (case 27) he will note that the subsequent illness was marked by marked pyrexia of several days duration, marked vertigo, vomiting etc. Cases 16 and 38 give less striking illustrations of this choking sensation.

As 50 (or even 75) cases represent only a fraction of the illnesses encountered, I cannot include all instances in which this symptom occurred, but I would state that while I considered it to be due to, and in fact typical of, the epidemic illness, this symptom tended to occur in people who might be considered of a 'nervous' temperament.

Less dramatic but much more frequently encountered was the complaint of discomfort at the thyrohyoid level. I noticed that the patient seldom mentioned it without at the same time passing his fingers from side to side of the throat to demonstrate the level. Such a little occurrence as this may seem trifling to relate, but it was ~~only~~ VERY noticeable in a consulting room when it was carried out in the same way in many cases. More

often the discomfort was described as an ache (as in case 17) less frequently it was said to be associated with difficulty in swallowing (e.g. case 37). I had several patients who had marked dysphagia. I regret to note that I have not included an illustrative case. In two which I remember distinctly it was the patient's greatest worry. One complained that while he had a good appetite it took him a "ridiculous" time to eat his meals. Every time he swallowed the act had to be slow and deliberate, and it was performed with great difficulty The swallowing improved but I regret to say that the appetite failed and he had a typical attack of the illness.

Interference with voice production was noted in several cases (Cases 12 and 38). Both patients were nervous women.

VISUAL DISTURBANCES.

I must first of all emphasize that I was so intrigued by the visual symptoms that I have included practically all cases where this was a feature. It would have been more correct as regards the proportional representation of symptoms if I had included only one or two such cases. I have referred to it, and in some symptomatic detail, in no fewer than eleven cases and I feel that it would be best for the reader to refer to the histories in cases 2, 4, 5, 6, 7, 19, 25, 26, 30 and 47. (Also Cases 15, 16, and 20 in Series 5.).

It is interesting, I hope, to note the different ways in which the patients presented themselves with this symptom.

It will be noted that some patients complained of the visual disturbance after they had been ill for some time: for example, A. Richardson, Case 25, wished to be referred to the Eye Infirmary on the 17th day of his illness.

Mrs. Smith followed the reverse procedure as it were: she consulted me for gastro intestinal symptoms, presenting me with a report on her eyesight from the Eye Infirmary(C.47).

I think that the chief cause of the visual symptoms must have been a disturbance of accommodation. I was unable to detect any abnormality on opnthalmoscopic examination. The media and the fundus appeared normal.

It will be noted that after a time the patient could see an object clearly but there was this delay in accommodation whenever he looked at a fresh object. The inability to thread a needle was a nice demonstration of the upset.

It will be appreciated that in some instances when the patient used the term "black out" it was difficult to exclude the possibility of there having been a threatened fainting attack. In some instances, however, it was definitely a temporary partial blindness not so associated and it is worthy of note that not once did any of the patients faint throughout the whole epidemic. (LATER— once only.)

I might here mention that not only the Eye infirmary but the optician saw several of these patients. Several had consulted the dentist, the reason being that many suffered from a very offensive breath. (Example Case 4).

STABBING PAINS.

I noted the occurrence of stabbing or lancinating pains, and in 5 of the 50 in this series such pains were described. Two patients described sharp stabbing pains like needles being thrust in from the loin to the nape of the neck. Another had similar pains in the area between the temple and the neck and in one case they were localised to the left forearm. Rather different appeared to be the pain described by Ed. Bridges -- a pain striking proximally from the heel. I was the more interested in his illness as his son became jaundiced some 5 weeks after Bridges had consulted me.

The cases referred to in this paragraph are numbered 5, 21, 29, 39, 49.

WEAKNESS AND INCO-ORDINATION IN LIMBS.

A frequent complaint was of weakness or "powerlessness" in the limbs, usually accompanied by aching. It was not however the usual everyday complaint of vague aches and pains so commonly encountered in general practice.

Distinctive features were:- in the upper extremity the weakness was referred to the upper third of the area neighbouring on the shoulder joint. The patient noticed the weakness when she dressed her hair: or a coal miner noticed it when he tried to do anything about or above shoulder level.

In the lower extremity aching and weakness was most

frequently present on the anterolateral aspect of the thigh in its proximal third.

Occasionally a feeling of stiffness or clumsiness was described. One patient (case 1) said that her hands did not seem to manipulate things as she wanted them to: they felt clumsy, stiff, and "had not the usual feel about them."

The youth, Hewitt, Case 23, said his right hand felt very stiff and did not move easily, whilst the nervous Mrs Wilson had an exactly similar story. This time it was the left hand. (Case 12).

A surely unusual complaint was that made by patients who told me that they had to lift their legs out of bed in the morning with their hands. After a little movement the legs were said to act normally. I have been unable to include a good example of this symptom in the selection of cases I have here included but Case 25 illustrates a mild degree of the complaint and Case 49 shows a similar type of symptom, this time the shoulder and arm being affected.

PARAESTHESIA. ANAESTHESIA.

I was surprised to find on analysis that only one patient in the 50 mentioned had "pins and needles sensation" in the hand: ulnar distribution.

In the previous group Cases 12 and 13 (and another case referred to in Case history No 12) had this symptom.

It was on the whole a not very common symptom -- possibly it is such a distinctive symptom that one may be apt to

exaggerate its frequency --- I should estimate its incidence at not exceeding 4 per cent.

In several cases I discovered areas of complete analgesia and at times anaesthesia. Most frequently the patient could feel the prick of a pin, but he did not feel pain, he just felt it as a touch. In other cases anaesthesia was complete.

Case 24 illustrates such a finding.

BRADYCARDIA. PYREXIA.

The most interesting cases were those in which there was a decided pyrexia. The pulse temperature relation was very strikingly disturbed.

Considering Case 46 we find the pulse rate to be only 90 with a temperature of 103 ^{o} F.

Less striking is the pulse of 84 per minute with temperature 101 ^{o} F (case 32). When the temperature settled to 99 ^{o} F the pulse was 56 per minute.

A 9 years old boy showed a pulse rate of 116 with a temperature of 102 ^{o} F for 48 hours but next day a temperature of 101.5 ^{o}F was associated with the very low rate of 88 per minute. I could not help but compare this sudden alteration in the temperature-pulse relation with the finding in the case of Robinson, Cold Hesledon Group - 2nd illness.

Nor could I help but reflect that a markedly slow pulse in relation to a decided rise in temperature is encountered in relatively few diseases and that "jaundice" or infective hepatitis which was prevalent at this time was one of them.

Apart from cases in which such a definite rise of temperature occurred, however, bradycardia was not a striking feature.

The pulse was found very slow in one case in which a mild degree of pyrexia was noted, Temperature 99 ^{o} F. Pulse 54 per minute, but in another two instances it was increased in rate.

A boy of 14 years had the slow pulse rate of 54 per minute but apart from the cases mentioned the pulse was as often raised as slow.

In a few instances the pulse rate seemed to fluctuate abnormally: this no doubt being due to nervous exhaustion so commonly seen in the ambulant patients.

Mary A. Lawson Age 54 years.
11 Woods Terrace, Murton.

cf Lawson, Fife Street. Page 505 a.

Visited Sat 9Dec 1944.

She has not been well for about a month. She has felt tired and listless and very disinclined to do her usual work. Her appetite has been progressively poorer and after she has eaten even a little she has felt swollen and distended and can eat no more. She has taken a violent dislike to tea, to which she is very addicted normally. At times she is so sickly that she would welcome vomiting but she does not vomit. Her head at first felt tight, then swimmy -- now 9/12/44 she is at once giddy if she moves her head. Occipital pain is severe, and she has a heavy dull frontal headache; it is not a severe pain, in fact the pain "is nothing," it is the horrible hazy, fuzzy feeling of which she complains. It renders her 'slow to think'. She feels chilly at times and has heavy, cold sweats. Her hands and feet feel 'queer' --- she can only state that it feels as if they will not move freely or manipulate things as she wants them to. They feel clumsy, stiff, and "have not the usual feel about them."

She is lying in bed obviously quite incapable of doing anything --- as she says: "Useless."

Temperature normal.

Pulse 72.

Case 2.

Geo. Knox. Age 53 years.

6 North Doxford Terrace, Murton.

Consultation Wednesday 29. 11. 44.

He has felt out of sorts for 2 weeks: "vaguely not himself." He has been listless and disinterested in everything. On Monday he stayed off work as he felt chilly and had a head cold, and on Tuesday, when he worked, his eyes watered and felt irritable. He had occipital and supraorbital headache.

His arms ached and felt powerless -- this feeling and weakness being most marked in the arms next to the shoulders.

He makes no other complaint.

Pulse and temperature are normal. He looks "dead tired" and he feels it. Sleep is very restless and disturbed.

Consultation Sat 2.12.44. Low backache. Head cold.

Ravenous appetite.

Consultation Wed 6.12.44.

Complains of supraorbital headaches.

He says "Doctor, as I look at you writing that note I can see it quite clearly but if I turned to look at Dr. John writing I would have to steady my gaze for about ten seconds before I could see it clearly. I cannot see clearly until I steady my gaze. Is it all this 'carry on' or do I need glasses?"

Case 3.

Ruth Stephenson Age 58 years.

14 Dalton Ter. Murton.

Fri. 27/10/44. She felt weak and dizzy, listless and tired: she felt "half dead" going about. Now and again she felt shivery. Her back ached, her legs felt weak and weary and she had an occipital headache.

On 25/10/44 she had a very large loose motion early in the morning as if she had taken a dose of Epsom salts. This was unusual as she is of most regular habit.

These symptoms were so vague and so varying that at times she wondered if it was imagination. She did notice that her hands were tremulous as compared with her normal steadiness. She rested in bed on Sunday, 29th, and Monday, 30th October. On Wednesday, 1/11/44 at night and to-day, Thursday, 2/11/44 she was sick and had repeated attacks of diarrhoea.

For the past 4 days she has had pains in her left shoulder: also pains in the upper half of her forearms. The pains are very definite lancinating linear pains, "Like long needles thrusting into her."

She has a generalised tired aching as if she was very fatigued. She had "to exert all her will power to concentrate and prevent her mind wandering --- or feeling stupid. "

She feels as if she had not out of bed after a long severe illness.

Sat 4.11.44. Improved.

Case 4.

Angus Seed Age 23 years.

49 Dene Terrace, Murton.

Consultation 26 Dec 1944.

He was off work on Friday 22/12/44 on account of vomiting and interscapular aching. The aching is said to have been aggravated when he stood. He improved, but to-day Tuesday, 26/12/44 the vomiting has returned, he has an unpleasant taste in his mouth and he is aware of his unpleasant breath.

His vision is disturbed as follows:- On resuming the erect posture from a stooping position his vision is indistinct, also if he turns his head suddenly it is some time before he can "focus distinctly."

Like so many of these patients he asks me if his teeth are causing the trouble (they are perfect as are his gums): or if he requires glasses.

Pulse 76 Temperature no elevation.

NOTE. The unpleasant taste and breath sent many patients to the dentist, often unnecessarily.

Robert Parkinson Age 32 years.
11 West Avenue, Murton.

Consulted my partner Sun 7/11/44. Complained of pain and was tender in the right iliac fossa. Was told to report 10/1/45. Consultation Thurs. 10 Jan 1945. He was asked "Tell me when you first felt at all ill -- what you felt the matter: what has happened since then?" And he gave this history:

14 days ago he had pain in the epigastrium extending bilaterally to the anterior auxillary line. He felt sickly and giddy. He continued at his work, as he hates to be idle, but it was all he could do to carry on. At times he had a "black out" -- everything became blurred and then he could see nothing for a few seconds. However, the attacks soon passed off. When he went home he sat in the chair until bedtime.

When he is well he walks 2 or 3 miles each day to get some fresh air as his working conditions are unhealthy, and between times he is never still, busying himself with odd jobs. But now he is listless and just can't be bothered with anything. His sleep is fairly sound, but in the morning he feels as if he has had no sleep.

Seven days ago the epigastric pain eased off considerably but he began to have a pain simulating closely a right ureteric pain. It travelled from above downwards to the groin.

To-day he is slightly tender over this line at the lurch of the appendix. He is very constipated, which to him is unusual.

Hugh Robinson Age 28 years.

2 No. James Street, Murton.

Mon 8 Jan 1945. Consultation.

All last week he had a 'head cold' — his nose watered freely and he sneezed frequently. He had a throaty cough which aggravated a constant dull frontal headache.

On Monday, 8 January he had hiccough, belched much flatus and then vomited strenuously and urgently.

He had found for a few days that when he stood in a refuge hole in the pit he felt intensely dizzy as the set of tubs passed by.

He also found that when he read, the print went blurred and indistinct and his forehead ached and he felt dizzy.

Christina Wills Age 47 years.
20 Calvert Terrace, Murton.

Insurance Agent.

Fri 3 Nov 1944. Visit.

She gave the history (later) that for 2 or 3 weeks she has been crying as she could not do her housework as she likes to owing to weakness and an overpowering tired or lazy feeling.

On 31 Oct 1944 she took ill at the local picture house. The film notice "EXIT" on her left seemed to be leaving the wall and coming to hit her and she felt very giddy and as if she would faint. She managed to arrive at her home but then she was violently sick. She has vomited violently and repeatedly ever since.

To-day, 3 Nov. 1944, she is prostrated. She feels very "light headed" and says she feels quite "daft and sees the queerest things" when she closes her eyes. She complained of epigastric pain and of being intensely giddy if she raised her head. Temperature 99°F. Pulse 54 per minute.

Sun 5 Nov 1944.

Her eyes feel to be "out of focus as if she had a squint." They feel hot and burning. She feels very giddy if she looks left when her visual disturbance is most marked. Everything then seems to be rushing towards her and she has to close her eyes "in case these things hit her" (she knows this is an illusion).

Case 7 (continued). Mrs Wills.

Vomiting has ceased but she becomes intensely nauseated, has severe headache and is giddy if she raises her head.

I note that she has ~~worse~~ COARSE gyrating nystagmus for a second or two on opening her eyes.

Klein's Intradermal Histamine Test gave an interesting result. The wheal was a dirty yellow cream colour. Quite definite, in fact marked, but not yellow.

Sunday 12 Nov 1944.

Still sickly at once if she raises her head or looks left. She is very tender in the right subcostal region, especially, I think, in the region of the gall-bladder. She feels very listless. Insomnia.

By Sat 25 Nov 1944

She cannot "look at tea or coffee." She can eat date and bread sandwiches she finds.

Thereafter recovery was steady.

Jane Brown Age 31 years.

16 North Crescent, Cold Hesledon.

Sat. 4 Nov 1944. Visit.

On Thurs, 2 Nov 1944, she felt chilly, had an occipital headache which extended down on to her shoulders. Suddenly she began to suffer from diarrhoea and she wished she could vomit. She had a horrible taste in the mouth.

Pulse 108 Temperature 99.5

She is very tender over the liver in the epigastrium.

Mon 6 Nov 1944.

Epigastric and umbilical pain. 5 loose motions to-day.

Frontal headache and anorexia.

Pulse 94. Temperature 98.

Wed 8 Nov 1944.

Diarrhoea continues but less severe.

NOTE. For a day or two before this she had been out of sorts and had sent notes to me describing her symptoms, asking for tonics. She is said to have sat and looked at her housework -- cried because she could not do it. She had 'no' appetite and felt irritable and bad tempered.

Thomas Collings 25 years.

93 Toft Crescent, Murton.

(J. Bate, 13 Woods Ter. is his uncle q.v.)

Consultation Friday 5 Jan, 1945.

Yesterday, forenoon, he had a headache --- left supraorbital. But it lasted only 2 hours. At 10.30 p.m. he suddenly felt as if his head was going round and soon he felt intensely sickly. He lay awake all night trying to vomit. He had absolutely no pain then in either his head or his abdomen.

(It should be noted that he worked from 1 am to 9 am Thursday).

To-day he has had attacks of giddiness which make him think he is going to collapse, but the attack suddenly ceases only to return.

Case 10.

Freda B. Edwards Age 14 11/12 years.
4 Station Cottages, Murton.
SHOP ASSISTANT.

Wed 29 Nov 1944.

For the past 2 or 3 weeks she has felt tired and listless. When she came home from work she sat down apparently exhausted and frequently burst out crying for no apparent reason. (She says it was because she felt so weak and helpless).

Her mother became weary of her saying "Oh, I am tired", "I don't feel well", "I do feel poorly" etc. For the past ten days she has had a head cold with watery rhinorrhoea and she had frequent bouts of sneezing. She began to have a heavy feeling in the epigastrium and her appetite failed. She had fleeting attacks of giddiness.

On Sat 25 Nov 1944 she vomited half an hour after a light tea. The vomiting was urgent and repeated.

To-day she looks intensely sickly and sleepy. She feels "lifeless" and can hardly support herself in a chair.

She has a dull frontal headache and her head feels "muddled." I considered that her facies, posture, demeanour etc. were typical of this epidemic. She did not look severely nauseated.

Temperature 99.2° F. Pulse 68 per minute.

Thomas Knox Age 18 years.

6 Williams Road, Murton.

Consultation Sat 13 Jan 1945.

He felt out of sorts on Wednesday 10 Jan when he developed a head cold and a troublesome cough. Yesterday, 12 January, he stayed at home from work as he felt intensely dizzy, and at times he was afraid to stand up. When he stood he felt giddy and his head ached --at other times he had very little headache. He felt chilly. The appetite is extremely poor. Pain is complained of over the lower part of the right side of the chest in the posterior axillary line and an aching below the left breast "below his heart."

He finds difficulty in getting a good breath, as if he was constricted and now and then he feels compelled to sigh.

Tues 16 JAN 1945.

Yesterday he had pain in his back -- dorsal region. They were sharp like knife stabs and nearly made him shout -- later they steadied to a steady ache.

At midnight he began to have acute pain below the right nipple and generally over his liver anteriorly.

He is not tender in the epigastrium or in the right subcostal region.

Pulse 80. Temperature Normal.

Emma Jobling WILSON. Age 46 years.
13 South Crescent, Cold Hesledon.
(She is a nervous woman).

On Wed 8 Nov 1944 she felt poorly. She had a queer sensation all over her body: not aches and pains but more as if her body was apart from her. That night she was up on account of dyspn- (dyspnoea) oea and also on Thursday night and Friday night. She suffers from attacks of asthma (infrequent) but this did not seem quite the same.

On Sat 11 Nov 1944 she felt that her 'stomach' was all working -- she could see (and others, too, could see) the peristalsis and she was frightened by the movements and loud borborygmi and she panicked and wanted to rush out of doors-- and had to be restrained. She had a headache.

Sun 12 Nov 44. Pulse 100. Temperature 98.

At night she vomited. From 4 am to 9 am her breathing was difficult.

Mon 13 Nov 1944. She slept last night, and to-day she is better. She has had no appetite since the onset of her illness, and she is obstinately constipated. Her throat is not sore, but her voice fails at times. She feels as if there was something in her throat. Her left hand feels numb and at times cramped -- she has pins and needles in her fingers. This paraesthesia is of ulnar distribution. She complains of a horrible taste in the mouth -- oily or greasy.

Tuesday. She lost her voice - aphonia.

Case 12 (Continued)
E. J. WILSON.

Thurs 16 Nov 1944.

Urgent profuse watery diarrhoea.

Pulse 100

Temperature 98

She cannot stand owing to dizziness and weakness.

She feels extremely tired, as if she had been drugged.

Diarrhoea continued for a further 3 days.

Thereafter she made a gradual recovery.

This was a fairly severe illness and the patient lost weight, markedly.

Thomas Blades Age 51 years.
16 Luke Crescent, Murton.

Fri 5 Jan 1945. Consultation.

On Monday, 1 Jan 1945 he had a 'cold in the head and chest'. He had pain at the root of the nose and in the temples. Also his calves ached. He has eaten next to nothing 'this year.' He has a marked distaste for food. He says "I felt exhausted walking here to-night (880 yards), I had no wind to carry me. I have been short of breath for about 10 days. I find it as I come out bye. I cannot keep up with my mates, and I have to sit down and rest and let them go ahead."

His headache is now frontal and more severe. At 2 am he got ready to go to the pit but he was "lathered in a cold sweat" and behind his knees ached terribly.

I asked him if he had ever had influenza. Was it like this? He said no — it was different altogether.

1. He had found it coming on for 10 days.
2. He had never been short of breath before.
3. He had never before had such drenching cold sweats.
4. The headache and "Fuzzy dull" sensation were new to him.
5. The aching behind his knees had never occurred before. He stressed this point.
6. He had never had such a dislike for food.

Robert Inman Age 0 years.

18 Barwick Street, Murtoh.

Blacksmith. cf W. Deans.

Visited Tues 19 Dec 1944.

For the past 2 weeks or more he has suffered from a persistent head cold and aches and pains. He especially mentions that his arms felt weak around the shoulders and that he had no power to work at above the shoulder level.

He has also felt that he could not get enough sleep and was fatigued and listless - he just could not be bothered with anything.

He is a very versatile man and particularly interested in some domestic alterations which he is executing at present, but he has been unable to bring himself to complete this half finished work.

On Saturday 16 Dec he was suddenly and violently sick as he returned from work. He had not the slightest warning. He gradually improved until

Sat 23 Dec 1944 Diarrhoea occurred: scarcely any pain.

Sun 24 Dec 1944 No B. O.

Mon, Tues. 3 or 4 loose stools each day. They occurred especially after each meal and were said to be exactly like the motion resulting from taking Epsom Salts.

The associated pain was very slight.

Joseph Greenfield Age 43 years.

C. W. S. Undertaker.

Consulted me Monday 30 Oct 1944.

History.

Sat 28/10/44. P.m. After feeling sickly and wanting to be sick he vomited all through the night.

Sun 29/10/44. Diarrhoea occurred which has continued ever since.

Very urgent diarrhoea described as 'water and wind.'

Profuse sweating. Very weak. Complete loss of appetite.

Monday 30/10/44. Feels slightly sickly. Still mild diarrhoea.

Appetite returned -- a little.

Tongue very clean -- wet raw beef.

Pulse 66.

Thomas A. Hall Age 33 years.

20 Harrogate Ter. Murton.

(His mate is J. Hannaby). Later. Please ignore this reference.

Fri 29 Dec 1944. Consultation.

Yesterday he had a sore throat at the thyroid level and a choking sensation, which kept coming and going. His throat was not worse on swallowing. He had a dull supraorbital headache. He vomited twice and retched severely. He had no epigastric pain. He was chilly throughout last night when he rested badly. He did not sweat.

Pulse 60

Temperature Normal.

Mary Harris Age 8 years.

41 Talbot Street, Murton.

Attends Murton Council School. Teacher Mr. Porter.

Visited Tuesday 21/11/44.

She had a headache last night -- left temporal. She ate very little breakfast to-day and had no lunch or tea. She complained of pain under the right lower ribs and she is tender there. Has felt very sickly and made several attempts to vomit.

Her throat aches (she points to the thyrohyoid level) but she makes no complaint of dysphagia. She is listless and will neither talk nor do anything else.

Pulse 82

Temperature Normal.

She looks exhausted to a degree.

She remained in this state for about a week before beginning to improve.

Case 18.

Isaac Lowerson Age 40 years.

4 Dalton Terrace, Murton.

Thurs. 4 Jan 1945. Consultation.

Yesterday he arose as usual at 7.30 am. He felt queer -- he felt "cloudy and fogged" , mentally and physically he felt like one getting out of bed after a week's illness with influenza, i.e. weak and powerless. He continued thus until 4 pm. when he was seized with urgent vomiting, there being absolutely no warning. He began to have diarhoea, the frequent watery stools gradually decreasing in amount until he had a frequent urge to defaecate with little resulting stool.

To-day he has loss of appetite but there is no nausea.

Pulse 80

Temperature 98.4 °F.

David Jones Age 29 years.

22 Windsor Ter. Murton.

Fri 15/12/44.

He has had a head cold for 2 weeks: profuse watery rhinorrhoea with bouts of sneezing. Mild degree of conjunctivitis with epiphora. He feels tired, listless, and weak: he says he has never felt anything like he now does.

He appears absolutely exhausted. the appearance is arresting

Fri 22/12/44.

The head cold isbetter but he still has supraorbital aching. it is not severe but it 'nags' on. He has pain in the epigastrium, not severe, but at times he has exacerbations of more severe pain : this is most marked after food.

At times he has stabbing pain over the region of the liver anteriorly and in the axilla. These pains are severe.

Thursday, 28/12/44.

He thought he was getting better until to-day, when he has had a feeling as if there was crumb in his throat --- the feeling is of 24 hours duration.

He is worried about his eyes.

When he reads he feels dizzy, the print goes "askew and muddled", and then everything goes black. It is not like an impending faint but as if he was going to go blind.

Associated with this disorder of vision is a dull heavy frontal ache -- not a pain.

J. Hall 29 years.
77 Silver Street, Murton.

Coal Miner.

Consultation 26 Dec, 1944.

On the night of Thursday 21 December, 1944, he had pain in the epigastrium: it was more a "fainting" sensation as if due to hunger, and he thought he was going to have diarrhoea. He felt weak and useless and as if he "would die if he had given way to this sensation."

He had a copious watery stools. He has eaten practically nothing since then. Temperature 99°F. Pulse 88 per minute. At times he felt "as if he was not there." -- as if he was Dissociated from his body, as it were.

For the next few days he continued to have 3 or 4 loose stools daily and his appetite was very poor. The tongue was moist and very clean. He felt very exhausted, just as if he was convalescing after a severe illness. He looked extremely tired and sleepy.

Eliz. Hagan 55 years.
18 Princess Str. Murton.

Tues 2 Jan 1945. Consultation.

She had been feeling well when suddenly, on the night of Friday, she felt intensely sickly -- she wished she could vomit and eventually she did vomit. Since then, i.e. for 90 hours, she has vomited frequently, and promptly rejected all drinks or food taken in this period. She is very giddy. This she does not need to state, as it is obvious, and it is difficult to understand how she attended the surgery to-night. The giddiness is not constant but attacks occur several times every hour and are severe. She is extremely listless and cannot do a stroke of work.

When she gets up from a chair she feels that her head will hit the ceiling: and after this sensation or the attacks of giddiness she has profuse cold sweats.

She complained of unilateral frontal headache with attacks of sharp shooting pains going down into the neck from the temple - forehead, left sided. The pains "dart like needles."

The left side of the face becomes very red and she has a burning sensation there. Her friends remark on the redness of the face and wonder whether she has been sitting beside the fire--- which she has not been doing.

Pulse 96.

No elevation of temperature.

Joan Dullard 18 years.
9 Calvert Terrace, Murton.

Colliery Canteen Worker.

Visited Tues 12 Dec 1944.

Lying in bed with just a heavy cold in the head. It again impressed me as peuliar especially in this case to find a woman of 18 years lying in bed afebrile and with a normal pulse considering herself ill enough to absent herself from her work and call in a busy doctor.

And yet she made no further complaint, and I avoided any leading questions.

This disproportion between the complaint made and the degree of incapacity assumed, as it were, seemed typical of this epidemic, or many of the cases in this epidemic.
On Sunday, 17 Dec 1944 she retired to bed intending to go to work next morning, but at 1 am she was awakened with epigastric pain and she vomited frequently and violently. Diarrhoea began a few minutes later and continued with lessening frequency until Thursday, 21 Dec, 1944. She had frontal headache.

For five days she had no appetite.

She started work on Tues 2 Jan, 1945 at 10 p.m. At 10.30 pm she had heavy dull epigastric pain and diarrhoea.
Fri 5 Jan, 1945. Consultation.

The tongue is very moist. Pulse 96. Temperature normal.

She feels sickly to-day but still retains a fair appetite. There is slight constant dull headache. She has a chilly feeling in the epigastrium, alternating with a feeling of heat.

Alexander Hewitt. 15 years.
3 East View, Murton.

Factory Worker.

Visit Sun 12/11/44. He felt off colour on Thursday when he was sleepy and had pains in the epigastrium and suffered from frontal headache.

On Friday he had to stop work as the sound of the machinery made his headache intolerable. He had had a slight heavy headache for the previous 2 weeks. The epigastric pain was constant and accompanied by a heavy feeling.

To-day, 12/11/44, he has no appetite. His bowel action is not disturbed. His knees ache and his right hand feels very stiff and does not move easily. He feels that he "cannot find a resting place." If he sits he is uneasy, if he lies down he is uncomfortable, and "he does not know where to put himself."

The tongue is moist and looks abnormally clean. He is a carefree youth who makes light of his illness, but he cannot disguise his lazy, listless, drowsy appearance and his eyes look dull. Pulse 72. Temperature 98.

He improved and resumed work on Monday, 20th, but at night he was again ill. He had epigastric pain at work, and later had 4 or 5 very watery stools with a little intestinal colic. All through the night he tried to vomit but 'nothing would come'

To-day, Tuesday, he has complete loss of appetite and feels "fuzzy about the head" and tremulous especially in the legs. Pulse 88. Temperature 98°F.

27/11/44. Epigastric pain, headache occasionally. Tired through the day. Lies down but just has to get up.

Sun 3 Dec 1944. " Chest cold. " Occasional low abdominal pain. Good appetite. He is extremely listless. "I feel awful." Gets headaches if he sits down to do "home-work." Can't be bothered. Flat and dull.

CF Sat 9/12/44.

One month for very slight upset ;

Robert Chapman 26 years.
17 Wetherburn Av. Murton.

Tues 2 Jan 1945. Consultation.

For the past 2 weeksshe has been eating about half of his usual amount of food. On Sat 30/12/44 he had a slight frontal headache at night, and next day he could not eat at all--- complete loss of appetite. Since then he has had a slice or two of toast only. On Sun 31/12/44 he vomited. He afterwards felt intensely sick and tried to excite vomiting by tickling his throat. This led to him almost choking as something "seemed to go all wrong in his throat." He has had moderate diarrhoea since Sunday.

He feels extremely listless and cannot bother to do anything This feeling is so overpowering that he has to fight against it to do the slightest thing.

He has an aching pain in the right thigh -- anterior aspect- as if the thigh was tired and rather numb. A large area in the middle of the thigh is only very slightly sensitive to pin - prick -- a gross difference is discernable in the pin prick sensation when compared with the left thigh.

Pulse 72. Temperature 98°F.

Mon 8/1/45. He feels giddy at times: especially if he leans his head back in an 'easy' chair and then brings it forward. Diarrhoea and nausea almost gone.

Andrew Richardson 19 years.
58 Barnes Road, Murton.

Wed 27/12/44. Consultation.

He has felt shivery, sickly, and off his food since Sunday, 24 Dec, and he has had pain in his neck and the occiput. During this time he has "felt queer, wanting to go to bed and not do anything." His eyelids have felt heavy -- he found it an effort to keep them open. In the morning his legs ache, and at all times he has aching behind the knees.

His appearance is indeed striking, he looks almost as if he is walking in his sleep. He is pale, sleepy, heavy lidded, expressionless and stupid.
(Like other patients he said he knew he looked stupid).
His pulse varies markedly, 60 one minute, later 75, later 60, later 96. He does not complain of dizziness but he sways as I hold his wrist.

He improved slowly but gradually.

Tues 9 Jan 1945. Consultation.

To-day he asks for a letter to refer him to the Eye Infirmary. He states that last night he read a little -- the print soon became blurred and then even the book seemed to be very indistinct. He had a severe dull frontal headache, felt weak and ill and had to go to bed. In bed he is restless and cannot sleep. He gets out of bed and sits in the chair beside the fire, feels chilly and returns to bed finding sleep impossible.

He has pain at the thyrohyoid level when he swallows and also when he coughs.

He sits down to his meals with a good appetite, but after he has say half of a slice of bread he feels uncomfortable and distended and can eat no more. Frequently he vomits soon after food. He has a taste of 'the infirmary' in his mouth -- I think he means Ether. (There is acetone in the urine.)
Pulse is 90 and regular. Temperature not raised.

His lower limbs go stiff behind the knees and he has to move them with his hands, flexing and extending at the knee joint to make them move freely.

On examination of the eyes.

The upper lids look heavy and slightly ptosed.

Eye movements are full and there is no squint and no nystagmus. The pupils react normally to light and accommodation.

The vision is $^{6}/_{6}$ in each eye.

The discs and fundi are normal to ophthalmoscopic examination.

Joyce Taylor Age 20 years.
Travellers Rest, Murton.

Bar Attendant.

My partner asked me to visit this woman as the story seemed typical in many respects.

Tues. 28 Nov. 1944. History. She had had a 'head cold' attended by profuse watery rhinorrhoea for over a week when on Fri 24 Nov she felt very sickly and thought she was going to vomit. She had epigastric discomfort, not pain. Her head felt light and she had a supraorbital headache. She wondered if the whole upset was due to her eyes as she had thought for a few days that she would have to get glasses. For a few days if she looked right or left her head felt 'awful' and her vision was all "mixed up and disturbed." In fact, she had taken to turning bodily to avoid turning her eyes. She wished she could vomit but she did not vomit until just after supper.

She vomited again on Sat 25/11/1944.

The bowels are acting rather freely. She has had to go to bed owing to nausea and giddiness, which are not now troublesome unless she sits up.

Usually she gets out a great deal to visit friends, but for the "past 10 days she has been Cinderella." She could not bother to do anything, go anywhere, move or talk unless she was compelled to. She has been taking patent medicines(tonics) for the past 2 weeks.

Recovery was uneventful.

Edward Bate 9 years.

6 Watt Street, Murton.

Attends Murton Council School. Teacher: Mr. Wilkinson.

Visited Sat 25/11/44.

At school on Friday 24/11/44 he felt very dizzy. He came home screaming that he was going to choke. He had a headache. He was very pale but later became very flushed.

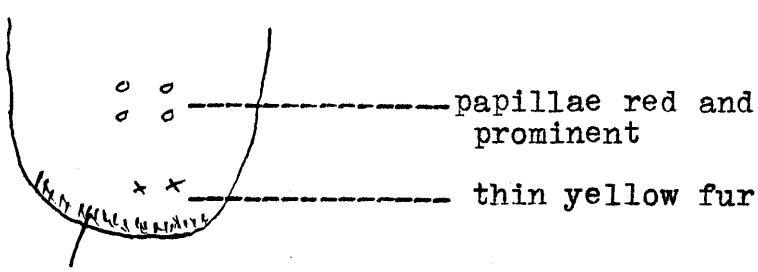
He vomited at 2 am on Saturday and sweated heavily. All night through he was delirious.

To-day, Sat 25/11/44, he complained of frontal headache. He dare not sit up on account of giddiness. "His head goes round."

He has a rough laryngeal cough -- the rough noise occurring when he coughs (expiratory) and complains of his throat hurting at level of Thyroid. His hand and forearm are seen to make involuntary jerking movements occasionally.

Pulse 120. Temperature 102° F.

Tongue.



(continued over.)

Sun 26/11/44. Vomited repeatedly. He is extremely giddy, and is terrified if I attempt to raise his head.

Temperature 102°F. Pulse 116 per minute. Respirations 28 per min.

In spite of the pyrexia he is very pale. His hands are very tremulous, and his hands and arms 'twitch' and jerk involuntarily.

The vertigo is not only subjective — he says that everything keeps on going round at times.

Mon 27/11/44. Temperature 101.5°F. Pulse 88 per minute.

This marked changeover in the pulse temperature relation is interesting. It occurred in the Robinsons (Cold Hesledon Group). Urine contains large amount of urobilinogen:nothing else abnormal.

The temperature settled gradually in 8 days. The tongue cleared and became rather raw (in appearance).

John Robert Hunter 28 years.
22 West Coronation Street, Murton.
~~of Nancy Abbott (Wembley)~~

Fri 5 Jan 1945. Visit.

He went to work at 2 am yesterday. At 9.30 am he finished work at the "coal face" and started his 1½ miles walk to the cage which would carry him to the 'surface.' He walked out behind his (work)'mate'. He felt powerless and found that he was lagging behind. He said to his mate "Are you hurrying, or am I slow?". It was not simply a matter of physical inability to keep up with his mate, he felt "as if he did not want to hurry, or perhaps rather that he could not produce the mental effort necessary to make his limbs keep up with his mate."

"It was a queer sensation --- a powerless body and an almost powerless mind."

When he arrived home he felt giddy and shivery --- his thighs ached above the knees anteriorly, and he had a continuous frontal headache, 'nagging on' all the time.

He felt sickly, and for 24 hours he has felt just on the verge of vomiting. Several times he has "all but vomited."

He has eaten nothing and has no desire to eat.

Pulse 78.

Albert Neal 29 years.

19 W. Coronation Street, Murton.

Wagonwayman.

Mon 15 Jan 1945. Visit.

He went to work at 4.30 am Sat 14 Jan, 1945, and returned home at midday. He had only half of his dinner as he began to have pain in the epigastrium. An hour later he vomited, and later diarrhoea commenced.

He felt giddy and cold, and he shivered.

From the loins to the nape of the neck he had an aching, with sharp shooting stabs of pain "like needles being thrust into him." This aching was associated with a sensation of stiffness so that he found it difficult to sit up in bed.

Proximal to his elbows he had had sharp darting pains. They seemed to strike inwards and 'proximal-wards'.

He is tender over the upper part of the rectus and he winces on firm palpation there.

Pulse 84

Temperature Normal.

(Appendic~~eitory~~ectomy Scar).

Moses Pine 14 years.
13 Woods Terrace, Murton.

Colliery Apprentice Joiner.

Wed 8/11/44.

He came home from work ill yesterday. He had a headache and his head felt fuzzy and intensely dizzy. As he walked home he felt as if he was swaying and everything seemed to be behaving in a very 'stupid' manner as he looked at it.

He kept looking at things over his shoulder as each time he looked at anything a second glance made it appear to be in a different place or nearer or further away.

To-day he has complete loss of appetite. He feels sickly, and if he raiseshis head he feels sickly and dizzy.

Temperature 98°F. Pulse 54 (age 14 years).

Case 31.

George Jennings 12 years
11 Watt St. Murton.

Attending Murton Council School. Teacher, Mr. Gardiner.
Thurs 2/11/44. a.m. He vomited repeatedly, felt dizzy and very muddled, and his head ached. Sharp attack of diarrhoea.
Fri 3/11/44. He was "deadly white." Complained of pain in the right chest.

Visit Sat 4/11/44. He looks flushed -- the flush is dulled a little but he looks feverish. His temperature is normal. Pulse 72. The site of the right sided pain can be covered by the palm of the hand placed horizontally across the chest with the centre over the nipple. It was so sore that he cried with it. The pain is worse on deep breathing.

He has no cough and examination of the chest reveals NOTHING ABNORMAL. ~~Grab 7/1.~~ His skin is clammy. He states that he felt that his head was swimming and that he swayed as he walked.
Sun 5/11/44. Said to have been very flushed facially.
Mon 6/11/44. No return of appetite. Herpes on and around both lips -- extensive. Facies typically haggard but with red 'daub' on cheeks. Pulse 72. Pain in right side as before. Dizzy if he stands.
Fri 10/11/44. Herpes Labialis healed.

Robert W. Wood 45 years.

2 Stephenson St. Murton.

Visited Wed 29/11/44.

He felt chilly on Monday and shivered on Tuesday. Had a frontal headache, low backache, and his legs felt weak. The headache gave the impression of a commencing head cold which would not materialise. His tongue is coated andhe has absolutely no desire for food, but he is very thirsty. No bowel action during past 48 hours. (Very unusual) Feels weak.

Pulse 90 per minute. Temperature 99°F.

Thurs 30/11/44.

Diarrhoea and vomiting to-day. Both frequently repeated. Feels chilly. Severe occipital headache. Dull frontal headache which is not very severe but which is accompanied by the feeling that he is not "right in his mind." He feels stupid almost to the point of feeling that he is insane.
Pulse 96 per minute. Temperature 98°F. Dry tongue.
Sat 2 Dec 1944. Looks very tired, especially about his eyes. the conjunctival vessels are intensely injected. He has facial herpes round nose and top lip. He is sleepless and at times delirious. Complains bitterly of frontal headache, and of pains in front of the knees.

A short cough rather suggestive of Lobar P. is troublesome.

Pulse 84. Temperature 101°F.

I was unable to visit on Sunday.

(continued over

Mon 4/12/44.

Dry tongue. Vomited very frequently since 2.30 Sun 3 Dec.

The vomiting is effortless:- he has no epigastric pain.

Frontal headache continues.

Pulse 56 Temperature 99°F. Sleepless.

He says the vomiting is quite effortless --- it just seems to occur and is not even very upsetting. No epigastric pain or tenderness. No urobilinuria.

He gradually recovered when vomiting ceased Monday evening.

William Dean. 40 years.
Cragdale,

Visit Sun 12/11/44.

Three weeks ago he had pain across the epigastrium.

He feels that his present illness dates from then.

On Tues 5/11/44 he felt shivery in the evening and next day felt far from well. He particularly mentions that "his limbs felt as if they were not there."

Since Friday he has had a frontal headache and at night he had to "shove his supper down." He then felt very poorly--out of sorts and went to bed, but he did not sleep. He was up and down all night trying to be sick, and at length, Saturday 10 am, he did vomit. Then he began to have profuse watery diarrhoea. To-day, Sunday 12/11/44, he complains of discomfort above his "Adam's Apple."

He has a marked erythematus rash -- like a red blush -- all over his trunk, but nowhere else.

Mon 13/11/44. Diarrhoea easing. Temperature 100. Pulse 72. Appetite good. His right knee pains if he bends it and is tender to pressure especially at joint level. His tongue is coated but is clearing from the tip and sides.

Thurs 16/11/44. Pains in shoulders and knees. Otherwise well. Tender on pressure over inside of joint.

Sat 18/11/44. Came to surgery. Sent home on verge of collapse.

Tues 21/11/44. Exhausted and 'useless'. Complains of throat: when he swallows anything it seems to stick high up in his throat before it is swallowed.

Mon 4 Dec. 1944. Almost better but has epigastric pain off and on - not severe.

Mon 11 Dec 1944. Pain left side like renal colic.

Jos. Etherington 11 years.

21 Gray Av. Murton.

Attends Murton Council Schools. Teacher: Mr. Palmer.

Visit Wednesday, 29 Nov 1944.

He could not take drill at school on Thursday 23 Nov, 1944, as he felt weak behind the knees.

On Monday he suffered from dysphagia --- everything seemed too big to swallow, andhe had a heavy sensation in the epigastrium. "It felt like a stone."

On Tuesday at 4 pm he vomited several times and since then he has felt sickly. For 24 hours he was quite deaf in his left ear but it recovered completely.

He has an urticarial rash on both forearms — volar aspect.

Case 55.

Peter Laws 21 years. cf Stepfather,
J.W.Bate. Page 654.

13 Williams Road.

Consultation Wed 29 Dec 1944.

He states that he has not been well for 10 days --just rather tired and weary and taking little interest in his work or his hobbies.

He stayed at home on Monday 27/11/44 as he had a head cold.

He sneezed repeatedly and had a profuse watery rhinorrnoea.

On Tues 28/11/44 his cold seemed to have cleared up and he went to work, but he found that he was not equal to the exertion of his work -- and to-day he is again poorly.

Temperature is 98. Pulse 96.

He feels tired and rather weak, and he knows he could not manage his work. He looks extremely fatigued.

John Wm. Bate 50 years.

13 Williams Rd. Murton.

Coal Miner.

Wed, 13 Dec 1944 Consultation.

He states that on Thurs 7/12/44 he suffered from diarrhoea and vomiting. He improved but vomited on Tues and Wed, 11th and 12th December -- on each occasion only in the morning -- at 10.30 am. He, however, had no return of the diarrhoea. To-day he feels better but has occasional nausea and fleeting giddiness. He feels very weary and he cannot understand why he should be so weak. He presents the typical facies of the epidemic. There was little change until

Tues, 19 Dec 1944.

He felt sickly at night and had a "boiling sensation" in the epigastrium. He went to bed.

Suddenly he vomited all over the bed clothes. Through the night the vomiting was repeated, and he had profuse watery diarrhoea -- 6 or 7 motions.

Thursday 21 December. 1944.

He feels overpoweringly tired and sleepy.

At no time did I find the temperature to be elevated.

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Thomas Holmes 15 years
25 Hill Crescent, Murton.

Visit Thurs 12/10/44.

Retrospective. Wed 11 Oct 1944 Visit.

He complained of a sore throat at the thyrohyoid level and of difficulty and discomfort in swallowing. He had no rise of temperature, nor was there anything to see on examining the throat by the usual inspection. We wondered why he had sent for us (to put it mildly).
On Thursday 12th, he felt violently dizzy -- he could not stand -- and sickly, and this led on to violent vomiting which was frequently repeated. He had no pain.

The giddiness persisted for 3 or 4 days.

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Case 38.

Margaret Holmes 33 years.
25 Hill Crescent, Murton.

Visit Thursday 9/11/44. On Wednesday 8th she felt overpoweringly sleepy and tired. She felt that there was a lump in her throat. She had no desire to have tea -- no appetite, but she felt that in any case she would not be able to "get it down because of this lump."

She began to vomit and thought that she must die as the vomiting which she had with her appendicitis (for which she had an appendic~~eitary~~ectomy) did not compare with this attack. She had little or no pain apart from themuscular soreness due to the violence of the act of vomiting. She vomited practically nothing "just a little froth." Bowels acted in normal manner. My visit on Friday 10th. Temperature and pulse not disturbed. Her voice comes and goes. She is not hoarse.

Mrs. Mona Bowater 30 years.

13 No. Crescent, Cold Hesledon.

Visited Sat 11/11/44.

She felt off colour on Thursday shen she was cold, shivery, and had a terrible headache: he brow ached and she had a sensation of weight on the top of her head.

She had severe epigastric pain, and pains shot up her back -- like arrows darting or a knife stabbing.

She feels listless and weary and can't bebothered with anything. Her housework, normally to be admired, is neglected, and she can only sit, powerless to cope with it.

She nas absolutely no desire for food and she is dizzy -- she cannot stand or walk steadily without support.

Now, Sat, 11/11/44, her head feels light and she says that it feels 'stupid' ("daft"). She is incapable of thinking clearly , she says. Her brain seems "clouded or dazed."

Thurs 16/11/44.

Feels and looks as if she had been up all night.

She knows she looks tired. Her face feels tight and drawn.

Her head feels light and swimmy. Appetite improved.

Frank Penman Age 55 years

C/O Bell, 15 Dobson Ter. Murton.

Coal Miner.

Wed 15/11/44. Consultation.

On Mon 13/11/44 he felt cold across the shoulders and yesterday when he got out of bed he felt "queer" in his head--it was giddy and muddled. He went back to bed where he lay extremely tired and listless.

To-day he feels "useless" and has no desire for food. He has been inclined to have diarrhoea, he says, a few fairly copious watery stools but not very frequently repeated.

Temperature is normal. The tongue is lightly coated.

He vomited suddenly on Wednesday night: no warning and very distressing.

Sat 18/11/44. Tongue clearing, but still coated towards the back of the dorsum. His head is clearer and he does not feel so dull and stupid.

He continued weak and shaky for another 10 days.

His (only) leg aches and it feels cold and as if it was swelling: which it is not.

William Brown 53 years.

12 Porter Terrace, Murton.

Schoolteacher.

Tues 6 Dec 1944. Consultation.

He has felt ill since Thurs 1/12/44, suffering from a dull frontal headache. He is not concerned with the pain, which is not severe, but with a muddled fuzzy feeling --- his head seldom feeling 'clear.' Attacks of giddiness -- they are fleeting -- have occurred.

He has discomfort in the epigastrium and under his heart: it gives the impression of being due to flatulence. His appetite is fair but he finds that food aggravates his symptoms. The bowel action is not affected

He feels tired as if he was falling asleep all the time. Sat 9/12/44. He feels weak, and is still overpowered by tiredness. When he stands up his head seems to be floating. Mentally he is 'not himself.' He is not alert, cannot concnetrate, and is "incapable of clear thinking."

Jackson -- Bell

Edna Brown 49 years

Penman.

12 Porter Terrace, Murton. (15 Dobson Terrace).

Visited Mon 1 Jan 1945.

History:- For about a month she has felt out of sorts. Exactly 2 weeks ago, Mon 18 Dec 1944, she awoke at 5 a.m. feeling 'awful.' She had pain in the nape of the neck, associated with a stiff numb feeling. The sensation was rather like a faint, her head feeling as if it was floating away, as when one is in a lift which stops suddenly.

She could not move her limbs or raise her head from the pillow, and when she moved her head to either side she felt as if she'was going far away.' She felt that not only had her body lost the power to move but the brain had lost the power to command the body. Her husband gave her a very little whiskey and she vomited and retched violently thereafter.

In the morning she arose at 9 am and did a day's washing. But at 3 pm she had a sharp attack of vomiting with one watery stool and this attack was repeated at night. Since then until Sun 31/12/44 she carried on, at times feeling well and at other times having to rest owing to weakness.

Yesterday, Sun 31/12/44, she felt extremely listless and could not drive herself to do her house duties. To-day,1/1/45, she felt that she was going to be very ill. She was restless until 7 a.m. when she was attacked by violent diarrhoea and

vomiting, with epigastric and hypogastric pain. The vomiting has persisted, occurring at frequent intervals until now (11 p.m.) and the motions have been very frequent. The vomit is said to have looked exactly like the stool.

The tongue is thickly coated: the very edges are clean. The breath is unpleasant.

The pulse is 104. Temperature 97.6°F.

She has no headache, which she considers remarkable, as she suffers from severe headaches very often.

She is 49 11/12 years and her periods have occurred at 14 to 16 day intervals recently. Her last period terminated on Wednesday 27/12/44, and she has begun to menstruate again to-day.

Mary Ruby Askew 23 years.
21 NO. Crescent, Cold Hesledon.

Northern General Transport.

Mon 11/12/44 Consulted.

For two weeks she has had a tightness in her chest --- in her breathing, especially in the morning. She has had a cough, nothing much, but has a dull heavy frontal headache and the cough aggravates it.

She has pain in front of her knees.

She says "I don't feel well: terribly listless as if I could not be bothered. At times I get a fleeting giddiness."

She complained of a steady ache in the epigastrium and over the right lower ribs in front: and below this a pain keeps coming and going, which is sharp and rather stabbing.

Every now and again she feels slightly giddy: she thinks it is only if she looks upwards.

Sat. 16/12/44. Complained of pain in the thighs and shoulder girdles, and especially in the left upper arm, where it is accompanied by a feeling of powerlessness.

Emma Johnson 62 years. Mother of cf Askew.

21 No. Crescent, Cold Hesledon.

Visit Monday 15/1/45.

At teatime on Thurs 11/1/45, she suddenly felt a "turning over" sensation in her stomach -- it was an alarming sensation which she describes as a "commotion" -- she then had to rush to vomit. She had a right sided faceache and headache.

She had no pain in the epigastrium or anywhere in the abdomen. If she raises her head even a trifle she is intensely giddy -- she feels as if she is falling.

She is thirsty and has a bitter taste in her mouth.

Complete loss of appetite.

She says that she had a head cold and a cough before Thursday, 11/1/45.

Leslie Smith 20 years.

3 Turnbull Crescent, Murton.

Blacksmith. (cf Dean W.)

Consultation Mon 29 Jan 1945.

This man's first symptoms occurred on Mon 22 Jan, 1945, when he had pains in his thighs just above his patella. His legs felt weak just as if his knees were going to give way. He had a similar combination of symptoms in the right shoulder region -- aching and a feeling of powerlessness.

From Sat, 27/1/45, he has had marked loss of appetite and an alarming degree of giddiness --- he reeled about and had to "catch hold of things" to steady himself.

To-day, Monday, 29/1/45 he looks as if he was extremely exhausted physically, his features are drawn and his eyes appear sunken. His appearance is that of extreme lethargy and weariness. The features scarcely vary as he converses, and the general effect is to give him a tired and rather stupid look. He feels listless and very weak.

All to-day he has been on the verge of vomiting, and he has rushed to be sick on several occasions, but the 'vomitus' appears to reach his pharyngo-oesophageal level only.

He describes these attacks by saying "it is just as if you had put your finger in your throat to make yourself sick and the effect was not entirely successful."

George Dix Richardson 36 years.

13 No. James Street, Murton.

Coal Hewer.

Visit Sat 23 Dec 1944.

On Thurs, 21 Dec 1944, he suffered from frontal headache at work. At 3 am Friday he awoke with violent frontal headache which eased considerably by evening. He lay in bed on Friday feeling chilly but sweating profusely, lying in a pool of sweat in spite of several changesof pyjamas. His thighs ached, especially at the back.

To-day, again at 3 am, intense frontal headache recurred. Pulse 90 per min. - remarkably slow. Temperature 103°F. Resp. 22 p.m. He complained of marked frequency of micturition, only a few drops at a time -- no dysuria.
The urine was normal on examination. After my visit he had severe pains in the region of the hip joints, and later he vomited, which was followed by relief of the hip pains.
Sun 24 Dec 1944. Breathing easily and normally.Heavy sweating continues-- bouts of sweating followed by chilliness. Supra-orbital headache again at 5 a.m.and nocturnal frequency of micturition. Temperature 102.4°F. Pulse 84.

He makes no complaint, saying that he is really ill only from 3 a.m. to breakfast time.

Mon 25 Dec 1944. He says he is better. He looks better. Temperature 98. Pulse 66. His head now feels clear. He said that when he was at worst it felt like a tight band round it and someone was trying to pull his hair off.
Sat 6 Jan, 1945. Gradual convalescence. Aches behind knees and calves.

Joan Smith 55 years.
3 Turnbull Crescent, Murton.
(Sister of Jos. McNally, 51 Toft Cres. Daily contacts.)

Consultation Fri 15/12/44.

This woman handed me a report from the physician at Sunderland Eye Infirmary(my partner who had referred her was out on an urgent call) which report stated that the eyes were healthy and that her reading glasses were suitably correcting her refractory error.

She then gave the following history: For 3 weeks she had had pain in the occiput,neck and shoulders. She had never had such a headache before although she had suffered from pain on top of the head. It was a different headache, in position and character, altogether, and it was gradually increasing in severity. She had always had very good eyesight (she wears glasses for her work) but during this period it had become very markedly effected. She could not see to thread needles or do any close work, and if she looked quickly to either side everything appeared "misty and jumbled up,"-- indistinct.

She naturally attributed this new headache to the marked change in her vision and thought she required new glasses. These she acquired from a very ~~respectable~~ REPUTABLE source and it was when she still could not see clearly that she had asked my partner if he could refer her to the Eye Infirmary, with the result stated above.

To-night, 15 Dec 1944, she states that her visual trouble

Case 47 (Joan Smith) continued.

has almost cleared up, but that she is concerned about her indigestion. She has no desire for food and if she eats the food seems to lie like a stone in the epigastrium.

Further, she feels overpoweringly weary and lazy, and finds her work a great trouble. If she rests, leaning her head back in the chair, she feels so tired and listless that it is a great effort to sit forward from that position. (This peculiar occurrence was related to me by different patients).

She says that her eyelids seem to want to close as if they were too heavy to remain open.

This woman is normally healthy and uncomplaining. She has consulted me on only 3 occasions in the past 21 years.

Joseph McNally 40 years.
51 Toft Crescent, Murton.

(He is a very fit man, usually. Heavy work - filler.)
On Wed 8/11/44 he took ill at his work in the pit. He had vomiting and diarrhoea, the motions were soft and the colour of saffron, and occurred every 20 minutes for over 2 hours and then less often. The vomit was clear, in fact just like water, and it was also very severe and repeated.

The diarrhoea and vomiting cleared up in 72 hours and by Sat 11/11/44 he had begun to eat: having eaten nothing in the previous 48 hours. I visited him on Sat 11th (my partner had visited prior to this) and his coated tongue was clearing up from before backwards.

Thurs 30/11/44. Legs weak. Loss of weight readily noticed.

Tues 12/12/44 Consulted. He resumed work on Tuesday 5/12/44 and continued until Friday 8/12/44. But he has a heavy walk in bad conditions for 3½ miles to the cage (pit lift).

The exertion of this walk is too much for him and he has pain in the left hemithorax 6th and 9th ribs level and he is very dyspnoeic. He sweats profusely then too. He recovered fairly rapidly. He feels he has to sigh to get his breath: feeling tight and restricted. Appetite only poor yet. Pulse 108. Standing. Tongue coated. Can't sleep at nights. I note that his hand is very tremulous - complains that his legs were shaky. Again he tried to work on Mon 18 December.

TUES, 19 Dec 1944. Cannot continue at work. Looks weak and sickly, complains of marked dyspnoea and pain under left breast.

The pulse is 96 per minute.

Ed. Bridge 57 years.

Welfare Park House.

Consultation Sun 10/12/44.

He has had a head cold for the past 10 days: watery rhinorrhoea. He has had pains in the nape of his neck extending to his shoulders. He has a cough and it hurts him in the right subcostal region anteriorly over the liver and in the epigastrium. But he consulted me about pain in his left leg. The pain is described as not a cramp-like pain. It was severe for several hours yesterday, Sat 9/12/44. It originated in the Tendo Achilles neighbourhood and struck up to below the middle of the calf, when it stopped; the pain was frequently repeated and his leg felt useless. He says that the pain is very severe.

To-day there is no loss of power or sensory disturbance. Otherwise there is no abnormality on examination of the nervous system, and I believe Bridge has not had syphilis. This I naturally mention on account of the type of pain.

Wed 13/12/44. Pain in epigastrium and right subcostal region-very tender to palpation. Loss of appetite. Still has occasional attacks of pain -- "twitches of pains" in the left leg from the ankle to the calf. He feels very listless.

Sun 21/10/44. Complained of continued epigastric discomfort, the pain in the leg has now cleared up.

Bartholomew B. Soppitt. 20 years. cf W.Soppitt.
15 Beech Terrace, Murton.

Consultation Tues 28 Nov 1944.

On Sunday 26/11/44 morning on rising, his left arm from the elbow to the shoulder felt stiff and painful -- he could hardly lift it. With use and movement the stiffness wore off.

He enjoyed his dinner but vomited immediately after it. Since then he has had diarrhoea, which is apparently not severe. On Sunday night he had a dizzy headache, but in the morning felt better and went to work. At work he manipulates a machine -- he almost got caught in it. He had plenty of time to remove his hand as the machine action is slow and he is well used to the work. He saw that his hand was going to be caught, but somehow he was "ages" in removing his hand. He felt as if his brain had very little command over his hand.

To-day he looks sleepy and dazed and he is sweating. The temperature is normal. Flushed, sweating, "Face drawn." Pulse 70 with 6 extrasystoles.

He feels "bad altogether." The headache, dizziness, diarrhoea and painful stiffness of the left arm have all recurred worse than before.

He started work on 4 December, 1944, but worked only one day, complaining again on 5 December of being too weak to manage at work.

GROUP 7

The Elliotts,

25 Shinwell Terrace.

I am convinced that if we could fully understand and correlate the three illnesses which I will now proceed to describe, we would approach nearer to a solution of some of the problems of infective Hepatitis.

The sequence of events in this home was essentially as follows:

1. Dorothy B. Elliott, a 10 years old schoolgirl, had a particularly characteristic and well defined attack of the non-jaundiced type of illness.

2. Almost one month later, her brother, Joseph R. Elliott, was ill with infective Hepatitis accompanied by clinical jaundice.

3. In yet another month Dorothy B. Elliott began an illness strikingly similar to her first illness, albeit with distinguishing features very nicely portrayed, and now she became jaundiced.

.....

1. In examining the record of Dorothy's first illness, we find many points with which the Cold Hesledon and Bakery Epidemics have made us familiar.

On Tuesday, 14 November, 1944, we have the initial nausea, vertigo and in this instance diarrhoea. We have

the commonly encountered temporary rapid recovery and the return of symptoms in eight days, when I was called in. In addition, we have two very interesting symptoms (and these I encountered quite often in the epidemic). The first is the occurrence of pain just above the right clavicle, almost at its lateral extremity; the second is the complaint of pains in the groin, which are described as being "just like needles being thrust in." Again typical is the aggravation of headache, nausea and epigastric pain on assuming the erect posture.

Finally it is important, in relation to 3 above, to note that Dorothy had in this initial illness a well marked urticaria.

3. Let us no compare and contrast 3, her 2nd illness.

Again we have the biphasic illness:-

On 16 January, 1945, the onset with headache, vertigo, epigastric pain and anorexia --- then the interval (7 days) this time, not so strikingly symptom free --- and then the fully developed illness with the violent and frequent vomiting, the more severe epigastric pain, the headache and marked jaundice. Again we have the attacks of more severe epigastric pain coinciding with increase in the headache and vertigo. To complete the resemblance we have the return of the urticaria. The absence of the sharp lancinating pains in this illness is remarked.

Now, do those facts suggest (A) that Dorothy had one illness passing through different stages ?

If so, it might be fair to assume from our preceding study that she was infected on, say, 25 October, 1944, giving an interval of some 3 months before jaundice appeared on 23 January, 1945.

Or alternatively (B) was this first attack an illness not related to infective Hepatitis ? --- (even if we admit that it may have predisposed to it.)

I would support the assumption A, and for the following reasons. There is in the first phase the very close clinical resemblance --- it could scarcely be closer --- between the two illnesses.

Next we have the pain so similar to 'shoulder tip' pain, suggesting an inflammatory lesion in the region of the liver or diaphragm.

Finally we have the story that Dorothy has been poorly "off and on" since her first illness. This story is not a vague generalisation but is accompanied by definite and very suggestive symptoms. The mother particularly stated that tea made Dorothy feel very sick --- here the possibility of the influence of suggestion would have to be allowed for: but then we are told that Dorothy could not keep up with other children as she was "short of breath." This last symptom could not have been due to suggestion as it was not known to either the patient or her mother to be a typical symptom.

The words "off and on" are important. Such fluctuation was repeatedly reported in the histories of the illnesses

(The writer realises that it will be impossible to incorporate more than a fraction of the observations and recordings made in the course of this epidemic, in the present work. He would therefore here state that dyspnoea was a very common feature of the prevalent 'non-jaundiced' illness. Frequently a miner, who had light work, would state that he could manage his work but as he had two or three miles to walk out-bye to the shaft he could not continue at work owing to a 'tightness in his chest', and dyspnoea. At first he began to tell his workmates to carry on without him and he proceeded slowly; but gradually he found that the dyspnoea was progressive and incapacitating.)

.....

2. Joseph R. Elliott, the brother, had an attack typical of infective Hepatitis with the occurrence of jaundice on 20 December, 1944, following a short prodromal illness. There appears to be no need to comment further upon his symptoms, which are presented in the accompanying case record, except to mention the absence of headache and the presence of conjunctivitis. The record makes obvious the relatively few symptoms. I would stress that like many of the jaundiced patients he looked heavy, dull and toxic but it was not quite the same appearance as that of his sister.

Her appearance, like that of son many of the patients who were not jaundiced at any time, suggested not so much a "toxaemia" --- it impressed one more as a complete mental and physical weariness and exhaustion.

.....

For the reasons stated I would interpret the happenings as being:

(a) Dorothy's original illness.

(b) infection passed to her brother who became jaundiced.

(c) Dorothy's illness ran a full course which terminated in her becoming jaundiced.

It would be helpful if the reader would here refer to the two illnesses in the cases of Iris Etherington, Brenda Robinson, and Brian Robinson at this stage.

Considered in conjunction with the two illnesses in the case of Dorothy B. Elliott they appeared to me to suggest that the virus of infective Hepatitis could have a longer 'life' in the body than we had been inclined to believe.

In the majority of the patients who became jaundiced the incubation period, where it could be estimated, was about a month, a little more or a little less. In such cases it was the general rule for the patient to make an apparently complete recovery. So far as I could judge the virus had then ceased to have any adverse affect on the patient.

The consideration of Dorothy Elliott's illness, especially when it is considered in conjunction with the three other illnesses mentioned above, made me think that, while this might be the general rule, exceptions could and did occur and their interpretation might be instructive.

Such exceptional cases might be accounted for by either:

A. Variation in the 'tropism' of the virus.

B. Variation in the mode of infection --- by inhalation or ingestion.

C. Variation in the 'soil' --- varying tissue susceptibilities in the patient, or variations in the defensive mechanism of the patient,

or any combination of A. B. and C.

Dorothy B. Elliott. 10 years.

25 Shinwell Terrace, Murton.

School : Murton Council. Teacher, Miss Redfern.

Visited Saturday, 25 Nov. 1944.

On Tuesday, 14/11/1944 she came home ill from school. She felt sickly but could not vomit, she suffered from diarrhoea and she was dizzy.

As she improved rapidly she returned to school.

On Wednesday, 22/11/44 she had epigastric pain and the diarrhoea recurred. She was chilly. At first pale, she later became flushed, especially her cheeks, which were as if daubed with dull red paint.

She cried with pains in the groin --- like needles thrusting in to her. She also complained of pain above the right clavicle medial to the shoulder joint.

To-day the tongue is clean. The mother says it was coated a few days ago.

Pulse 72. Temperature Normal.

Wednesday, 29 Nov., 1944. Diarrhoea again to-day. Epigastric pain. If she stands up she complains of headache, epigastric pain and nausea. Urticaria is present on the forearms, back of wrists and buttocks, and extends into the thighs.

2nd illness.

Tuesday, 16 January, 1945.

Pain in epigastrium. No appetite. Suboccipital headache. Dizzy. Tender right costal margin. At times epigastric pain headache, and dizziness "coincide".

Hiccough daily. Goes pale at times.Continued thus until Tuesday, 23 January, 1945. She vomited all last night; everything she took was promptly returned. She cried with epigastric pain and she had a frontal headache. Her breath is very offensive. She is markedly jaundiced. The urine is loaded with bile and urobilin (and phosphates). Urticaria left buttock since Sunday 21 January, 1945.

Pulse 64. Temperature normal. She is said to have been poorly "off and on" since 25/11/44; to have complained of dyspnoea --- couldn't keep up with other children, and tea made her feel very sick.

Joseph R. Elliott. 13 years.
25 Shinwell Terrace, Murton.
Murton Council School.
Teacher, Miss Flynn.

Visited Monday, 18/12/1944.

He was in bed. He had a heavy, dull, and sickly appearance and his expression altered very little during my visit.

He said that for a few days he had felt sickly and faint at times, and yesterday her had vomited several times. He complained of a sensation just like a heavy ball in the epigastrium.

He admitted to absolutely no headache.

The temperature was 98 and the pulse slow--66 per min.

The conjunctival vessels were injected, giving the eyes a markedly bloodshot appearance. But the appearance is not adequately described by calling it a conjunctivitis; there was a dirty discolouration of the conjunctivae which I have frequently observed in these cases (when jaundice did not later occur.)

By Wednesday the eyes were markedly jaundiced, and by Thursday the skin was noticeably yellow.

The urine contained Urobilin and Bile on Thursday, 21/12/1944, when the pulse was 60.

He complained then of nothing except loss of appetite.

GROUP 8

The patients affected in this group were members of three families named Newton, Forster, and Sugden, who lived in almost adjacent houses at Numbers 4, 5 and 7 Stephenson Street, Murton, respectively. It may be at once stated that cases of the infection occurred at the same time at Numbers 2, 3, and 6 Stephenson Street, Murton. I have selected the families mentioned for several reasons, viz:-

1. They were continually in intimate contact with each other; it would have been unusual not to find a Newton present, if one paid a visit to Forster's, and so on.
2. All the illnesses appeared to have a common original source.
3. After a fairly uniform period in each address, a case occurred accompanied by clinical jaundice.

The object of presenting this group, therefore, is to suggest that the three cases of infective Hepatitis with Jaundice all had their ultimate source in a case of illness not accompanied by jaundice--- and that this "non-jaundiced" illness had occurred several months before.

.....

On 22nd October, 1944, I was consulted by Mrs Mina Newton 4 Stephenson Street, Murton, whom I knew to be a particularly active and robust woman of 38 years. She told me that she

had been ill for one month. The illness began with vomiting, giddiness add headache. The headache was situated in the frontal and suboccipital regions. In 2 or 3 days she improved, only, however, to have a prompt relapse. She now wanted to be sick but she could not vomit. Most alarming, she thought that she was going blind at times; she consulted a colleague, who re-assured her, after examining her eyes. At this time she began to have "pins and needles" in her hands and feet, which "felt swollen." She had to rub them, especially in the mornings, to obtain relief. She said that her feet were swollen, but the swelling did not pit on pressure --- she had tried that !

Her chief complaint to me, 22 October, 1944, was of feeling exhausted, listless and "useless." She was pale and looked weary, exhausted and apathetic, strikingly contrasting with her usual alert and vivacious appearance.

On examination I found that she had a slow pulse, 52 per minute, and a normal temperature. Throughout this work I have avoided the use of the term "subicteric", and if I do employ it to describe Mrs. Newton's complaint, it is partly in order to describe the result of Klein's intradermal test in her case. The wheal was very obviously discoloured, in fact the response to the test was quite striking but the very critical might scarcely admit it to be a definite + ve. result --- the colour was a dirty "cream to yellow." Urobilinuria was marked.

A Differential White Cell Count showed:

Polymorph. Leuc.	63
Lymphocytes	36
Eosinophils.	1

From a consideration of her symptoms I concluded that she was suffering from the infection which later became so prevalent.

Especially suggestive were the visual disturbances, the pins and needles sensation, the Klein test and the bradycardia. Other symptoms, included in the case history, were pains above the elbows and knees and menstrual disturbance--again features which were frequently encountered.

.....

Bearing in mind, therefore, that Mrs Newton had been ill from about, say, 25 September, 1944, let us now tabulate the illnesses originating from her illness.

Name.	Age.	Date of illness	
Mina Newton	38	25 Sept. 1944 (approx)	
Anne Newton	14	29 Oct. 1944	4 Stephenson St.
Mary Newton	12	6 Nov. 1944	
William Newton	11	15 Nov. 1944	
Edna Newton	4	9 March.1945.	Jaundiced.
.....			
Elizabeth Forster	39	29 Oct. 1944	5 Stephenson St.
Moira Forster	10	6 Nov. 1944	
Chas. R. Forster	6	25 Nov. 1944	
Moira Forster	10	26 Feb. 1945.	Jaundiced.
.....			
Walter Sugden	35	30 Oct. 1944	7 Stephenson St.
Mrs. Sugden	35	18 Nov. 1944	
Frederick Sugden	21	13 Dec. 1944	
Mary Sugden	6	27 Jan. 1945.	Jaundiced.
Walter Sugden,Jr.	10	1 March.1945.	Jaundiced.
.....			

The case history of each of these illnesses is enclosed. They appear to leave no doubt that at least 12 of the 14 illnesses recorded, and very probably all, were representative of the epidemic ailment.

The question for immediate consideration is the relation

of the illnesses accompanied by jaundice, to the preceding illnesses not so accompanied.

The first possibility would be that they were not at all related. Mary Sugden, who became jaundiced on 27 January, 1945, may have introduced the infective hepatitis and infected her brother Walter, Moira Forster and Edna Newton-- (the table will facilitate easy reference.)

On that assumption it would however be fair comment to remark on the incubation period in the case of the last - named being at least on the **limit** of what is commonly accepted.

The case of Moira Forster might throw some light on the problem. She was ill on Monday, 6 November, 1944 --- the symptoms were headache, vomiting, giddiness, epigastric pain, listlessness, and indistinct vision --- she could not thread a needle. She looked sickly and pale and wan and she cried "if she was spoken to."

On February 26 she had almost exactly the same symptoms --- the visual disturbance was not present, but this time she was purged and she was jaundiced.

Not only were the symptoms which I have enumerated strikingly similar, but the child said it was "the same thing all over again", and the mother thought it was a repetition of the previous illness until jaundice became obvious.

I am convinced that Moira Forster's story is really that of one illness, or perhaps it would be better to say that the story pointed to the continued prolonged activity of one pathogenic agent, probably a virus. The case bears a striking resemblance to the story of Dorothy B. Elliott qv.

If we assume that Walter Sugden was probably infected from Mary Sugden we have still to consider the illnesses of Mary Sugden and Edna Newton, both of whom became jaundiced

I incline to the view that they both became infected from the non-jaundiced but sick members of their families rather than from an outside source. What justification is there for such a statement as this ?

There are 28 houses in Stephenson Street, and there are a further 28 houses in the street facing it, and at only a few yards distant.

THE DISTRIBUTION OF ILLNESSES WAS:-

Number in Street.	The Epidemic Illness	Jaundiced cases.
2 Stephenson Street	1	--
3 "	1	--
4 "	4	1
5 "	3	1
6 "	1	--
7 "	3	2
8-26 "	0	--
27 "	1	--
28 "	0	--
1--6 Watt Street	0	--
7 "	1	--
8-22 "	0	--
23 "	1	--
24-25-26 "	0	--
27 "	1	--
28 "	0	--
	17	4

To summarise: there were 17 cases of the epidemic illness in 56 neighbouring houses. No fewer than 10 of those cases occurred in 3 houses out of the 56. All 4 jaundiced patients resided in the same 3 houses.

I think that the above facts justify a bias in favour of the possibility of the illnesses attended by jaundice having their origin in the illnesses not so attended.

The interval between Moira Forster's two illnesses was 112 days.

It seemed significant that the ages of the children who became jaundiced were 4 years, 6 years, 10 years and 10 years

The circumstances allowed of the possibility of the incubation period where this "non-jaundic" illness led to a "jaundice illness" (if such a spread did occur) being a prolonged one.

As regards the mode of spread.

The distribution of the cases mainly in numbers 2 to 7 Stephenson Street (13 out of 17 cases) appears rather striking. It is not quite so striking when one has a "local knowledge" of the inhabitants. The householders in numbers 2 to 7, especially in numbers 4, 5, and 7, as I have already mentioned, are very friendly and are frequently to be found to be conversing in 'one another's homes.' I believe too that a fair amount of borrowing and lending of domestic materials takes place between them. The houses are all identical in every respect in the two

rows, and there was no apparent reason why numbers 2 to 7 should be 'picked out' from this point of view.

It still seemed definitely worthy of note that the children just across the street, in Watt Street, were not evidently infected except in one case. They must have played with the children in Stephenson Street at times, as the space between is used as a street 'playground.'

I could only conclude that in this group the actual visiting at each others houses determined the spread of the infection.

SYMPTOMATOLOGY.

The symptoms encountered in the four cases which exhibited jaundice were all present in the illnesses not attended by jaundice. The "non jaundiced illnessess" were in the main attended by more symptoms than the cases typical of infective Hepatitis --- as I have mentioned before they were more "poly symptomatic."

Interesting symptoms, apart from the anticipated headache, nausea, vomiting, epigastric pain and vertigo, were:

1. Visual Disturbances.
2. Complaint of pins and needles.
3. Dysphagia.
4. Rashes.

1. One patient was afraid she was going blind.

Another wondered whether the illness affected the eyesight as she "kept going blind."

Another found that everything went misty and indistinct if she altered her gaze. This I found to be a frequently repeated complaint in the course of the epidemic as a whole.

Very convincing was the complaint as made by two children. A boy could not do his sums or write, and a girl could not thread a needle --- owing to misty vision.

The visual disturbances were naturally alarming to many patients and they frequently had decided to obtain 'glasses' when further symptoms made them decide to seek medical advice.

2. Complaint of "Pins and Needles."

In one case this was complained of in the feet and hands: in another only the hands were affected. In each case it seemed to be very distressing.

3. Dysphagia.

In two cases the patient especially complained of difficulty in swallowing. The dysphagia was referred to the thyrohyoid level and appeared very puzzling to the patient.

4. In two cases a rash was a prominent feature of the illness. The brief history in the case of Wm. Newton is I think interesting. I think that <u>in the presence of an epidemic</u> he would be considered as a rather anomalous instance of the infection. The same remark applies in the case of C. R. Forster.

Only 3 Differential White Cell Counts were made in the group; all being from adults.

Polymorph Leuc.	63	45	54
Lymphocytes.	56	50	40
Monocytes.	-	2	-
Eosinophils.	1	3	6

I have the films.

Mrs. Mina Newton. Age 38 years.

4 Stephenson Street, Murton.

Sunday, 22 October, 1944. Visited.

History. About a month ago she took ill. She vomited, felt giddy and had a severe frontal and suboccipital headache. At times she "went blind." In two or three days she felt better and she dismissed the episode as being due to an acute gastric upset. No sooner did she feel almost better than she had a relapse. She now wanted to vomit but she could not vomit. The intervals of the "blindness" became worse, and she consulted a colleague who was then assisting us, and who reassured her. Since this consultation she has had frequent attacks of giddiness, complete anorexia, and she feels limp, listless and useless. Her sight continues to vary.

She complains bitterly of pins and needles in the hands and feet. This sensation is accompanied by a feeling that the hands are swollen. She obtains relief by vigorous rubbing, especially the first thing in the morning when the sensation is most troublesome. At times she wondered whether she might be pregnant as the nausea resembled nausea during pregnancy.

She has aching above the knees, around her wrists, and in her fingers.

On examination. The pulse is 52 per minute. The tongue is clean. She is not tender over the liver. Systolic apical

murmur. There is marked urobilinuria.

The Klein's Intradermal Test gives a + ve result, the wheal is of a dirty creamy yellow colour resembling the patient's complexion, which might be described as subicteric.

Differential White Cell Count.

Polymorph Leuc.	63
Lymphocytes.	36
Eos.	1

Tuesday, 31 October, 1944.

Gradual improvement with rest. Supraorbital headache persists. She describes both subjective and objective vertigo as having occurred previously -- "at times the bed was going round with me."

Tues, Wed., Thurs. 31 Oct., 1 Nov., 2 Nov., 1944.

She had completed her normal menstruation on 24/10/1944. She now had a slight return of the flow. She is normally of very regular menstrual habit.

Saturday. 4 November, 1944.

I was called to see her at 10.30 p.m.

She was seized with epigastric pain, she felt very sick and retched repeatedly, but only a little 'water' was vomited. In the end she dropped to the floor, "her legs gave way and she felt powerless."

After this attack recovery was uneventful.

The Apical systolic murmur "cleared up."

Anne Newton. Age 14 years.

4 Stephenson Street.

From Tuesday, 29 Oct., 1944 to 13 Nov., 1944, she was ill with an attack typical of many others described.

viz:- Giddiness, nausea, vomiting, frontal headache, and epigastric pain. Temperature 99.2°F. pulse 70 at onset, with gradual recovery.

On Monday, 27 Nov., 1944

She had another attack, differing from the above in some respects.

After a restless night between Sunday, 26th and the Monday she felt dizzy and sickly, and had epigastric pain. Her throat seemed to swell. She found that swallowing was difficult,--- she points to the level of the thyroid isthmus.

She could not manage to vomit.

The throat is very slightly inflamed -- swollen.

The cheeks look as if painted dull red and the rest of the face is extremely sallow -- not just pale.

Pulse 120

Temperature 101 ° F.

Wednesday, 29/11/44.

Pulse 84

Temperature 98 ° F.

Her voice keeps going "off and on."

Mary Newton. Age 12 years.

4 Stephenson Street.

Murton Council School.

Teacher: Miss Bramma.

Monday, 6 November, 1944.

She got out of bed this morning and she felt sick and thought that she was going to vomit. She says that she felt so sickly that she got up to try to be sick.

She then felt intensely dizzy and had a frontal headache.

The facies was characteristic.

She rapidly recovered normal health - in a few days.

William Newton. Age 11 years.

4 Stephenson St.

Murton Council School.

Teacher: Mr. W. Palmer.

Wed. 15/11/44 Visit.

Since Sunday, 12th, he has had a supraorbital headache. He has not been able to do his "sums and his writing" at school as his vision kept on going misty.

Now and again he feels very dizzy and as if he is going to vomit. He has complete loss of appetite.

Palpation of the epigastrium immediately leads to nausea. Temperature normal. Pulse 90.

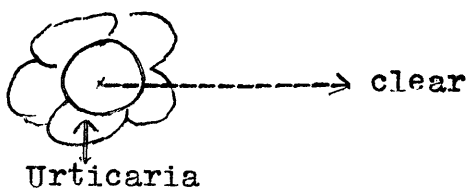
He looks listless and dazed.

He returned to school on Monday, 27/11/44.

I was recalled to visit him on Friday, 1 December, 1944.

He had a rash on both legs. The lesions were composed of a clear central circle surrounded by a sort of erythematous rosette:-

URTICARIAL



and were intensely itchy.

He returned to school on Tuesday, 12 Dec., 1944. That day he again felt sick.

Visited Wed.13 Dec.,1944. Complains of headache. Has felt dizzy all day. Fainted. He is very pale. The lips are dry and fissured. It is obvious that he is unstable on his feet as one feels his pulse. Pulse 80. Temperature normal.

Subsequent recovery was uneventful.

Newton, Edna. Age 4 years.

4 Stephenson Street, Murton.

This child became jaundiced on 9 March, 1945.

For a week she had been lazy and sleepy. Her appetite remained fairly good throughout the illness.

The urine was bile stained, the faeces were pale.

She complained of her eyes being irritable --- she had some conjunctivitis and blepharitis.

The liver was palpable and tender.

Severe supraorbital headache. Cold clammy skin.

Differential white cell count.

Polymorph Leuc.	65
Lymphocytes.	30
Monocytes.	2.
Eosin.	3.

3/4/45. Feels much better.

Elizabeth Forster. Age 39 years.

5 Stephenson Street.

Visited Tuesday, 31/10/1944.

History. "On Sunday, 29th, when I got up out of bed I felt dizzy and had to sit down. I felt that my head was floating. I then vomited. My forearms felt weak and useless."

This floating feeling and dizziness goes off and she feels fairly well, but it returns, and again she feels 'powerless.'

She is sitting with her legs up on two chairs, and is tired and weak and powerless, and just wants to sleep. She asks "Does it affect your eyes ? Now and then things go misty as if I were going blind, and I find myself blinking to take it away."

Pulse 72. Temperature Normal. Bowel action normal, regular.

Severe supraorbital headache. Cold clammy skin.

Differential white cell count.

Polymorph Leuc.	45
Lymphocytes.	50
Monocytes.	2.
Eosin.	3.

3/11/44. Feels much better.

Note she did not maintain this improvement.

Tues. 7/11/44. She vomited in a 'bus — she vomited only froth and felt very dizzy and sickly and fuzzy-headed all that day. She felt chilly. She sweated profusely and frequently. Recovery was protracted.

Moira Forster. Age 10 years.

5 Stephenson St.

Murton Council School.

Teacher: Miss Redfern.

Monday 6/11/44. Vomited in school. Very giddy. Frontal headache. Said to have been "white as death." Epigastric pain. She "cries if she is spoken to." She has an extremely heavy, tired (locally expressively termed a "hangy") look.

She is dull, apathetic and weak.

Pulse 96 Temperature normal.

Wednesday, 8/11/44.

She feels dizzy and she cannot thread a needle as she can't see clearly.

.....

2nd Attack.

26 February, 1945.

Epigastric pain. Headache. Vomiting.

Diarrhoea. Is giddy. Vision is slightly indistinct.

Jaundiced 26 February, 1945.

Charles Robinson Forster. Age 6 years.

5 Stephenson St.

Visited Sat. 25/11/44.

Giant urticaria left thigh.

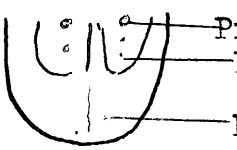
Erythematous rash all over the body -especially the trunk-- the mother thought it was Scarlet Fever yesterday, but to-day realised it was different.No punctate element.

He looks listless and exhausted and is sitting limply in a chair.

Monday 27/11/44.

Loss of appetite: feels sick and giddy. Epigastric pain. He has a very pale and sickly look. Tongue strikingly clean. Pulse 75 Temperature normal. No headache.

Tues. 28/11/44. Complains all the time of epigastric pain.

Tongue 

Wed. 29/11/44. Pain in epigastrium continues.

No appetite and feels very sickly.

Saturday, 2 Dec., 1944.

Angioneurotic oedeme face and lips.

Hands and fingers very itchy.

Walter Sugden Age 35 years.

7 Stephenson Street.

History. Consulted me monday 30/10/1944.

For about 3 weeks he has felt weak, tired and listless. He has gone to work, and sat 'in the house' doing nothing, and not desiring to bother with anything.

For the past 4 days he has had pain in the small of the back and across the shoulders -- at the back, and the tired feeling has become almost overpowering.

His appetite has become progressively poorer in the past week, especially in the mornings: and the last 2 days he has felt very giddy, especially on rising. He has then also felt sickly but he has <u>not</u> vomited.

30/10/44. Typical dead tired facies. Pulse 72. Temp. normal.

Monday 30/10/44.

Differential White Cell Count.

Polymorph	54
Lymphocytes	40
Eosin.	6

Resumed work 6 November, 1944.

.....

Monday, 25 December, 1944.

Diarrhoea. Very little pain.

Not profuse nor very frequent.

Mrs. Sugden. Age 34 years.
7 Stephenson Street, Murton.

Saturday 18 November, 1944. Visited.

For a few days her fingers have "kept going into pins and needles." She had pain across the upper abdomen yesterday. She has been troubled with a heavy headache -- "it is not a pain really, it is just heavy." She does not feel sick, but whenever she sits down to eat she immediately "feels full and her appetite goes." She has a dull sickly facies, which combined with the marked conjunctival injection gives her an appearance suggestive of exhaustion and loss of sleep.

He tongue appears peeled like a scarlet fever tongue --- the papillae are prominent.

Mon. 27 Nov., 1944.

She complains of a continuous nausea, "exactly as if she was pregnant," and of pain and a feeling of weight and constriction right across the chest below the nipple level. For the past 3 days she has vomited 3 or 4 times daily. She has not only felt sick at the sight of food, she has actually vomited then -- this is especially marked with tea.

The nausea is accompanied by a sensation that her stomach is rolling and turning over.

She has frontal headache, and she is frequently very giddy and at no time is she quite stable.

Her vision is indistinct: this is very marked if she looks to either side.

Frederick Sugden. 21 years.
7 Stephenson St.

Wed. 13 Dec. 1944.

He has a watery nasal discharge and complains of a dull heavy frontal headache which makes his head feel "fuzzy."

He feels tired and listless and he looks sleepy and seedy. At times he is very giddy. Although he complains of sore throat and that he cannot swallow, there is nil ti find on examination. The difficulty in swallowing is said to occur at the thyrohyoid level and he has to help each bolus down with a drink. Pulse 72. Temperature normal.

.....

Mary Sugden. 6 years.
7 Stephenson St.

Murton Council School. Teacher, Miss Penk.

Visited Saturday, 27/1/45.

She no sooner got out of bed to-day than she started to vomit. Even sips of water have been promptly rejected.

She is definitely jaundiced. She complains of pain over the liver anteriorly, but of absolutely nothing else. She is tender on pressure over the right subcostal margin but I could not palpate the liver. Temperature is 99°F. Pulse 100.

Tues. 30/1/45.

She is more deeply jaundiced, but her condition is improved in so far as the vomiting has ceased and she is beginning to eat a little. The urine is acid. S.G. 1020. Bile is present in moderate amount. Urobilin is present. There is no albumin nor is there any other abnormality.

Walter Sugden. Age 10 years.
7 Stephenson St.

Murton Council School. Teacher, Mr. W. Brown.

Thursday, 1 March, 1945. Visited.

His sister was jaundiced on 27 Jan., 1945. Walter complained of epigastric pain and of feeling sick at that time, but he did not vomit.

A week ago he complained of abdominal pain and wanted to vomit, but he could not be sick. He was very listless. He began to vomit on Sat. 24/2/44 and continued to suffer from acute abdominal pain and vomiting until early to-day. Dr. McIntyre, who was attending, was relieved to find Walter jaundiced to-day, "fearing appendicitis."

To-day the liver is palpable.

Pulse 96 per minute. Temperature 98°F.

He says he feels "top heavy" -- very giddy, especially if he sits up. The urine contained urobilin and bile.

The faeces were clay coloured.

THREE FATAL ILNESSES.

During the period covered in the review of the illnesses in the Murton area, there were 3 fatal illnesses which presented features so/sufficiently uncommon as to merit our consideration.

The case of Ernest Scothern is the only one of the 3 illnesses which resembled an attack of infective hepatitis accompanied by jaundice. The illness was of 3 months' duration and I have made the history as brief as possible consistent with providing the reader with a general outline of its course and its main features. The main features will be seen to be the onset, with vertigo, nausea and vomiting. Severe headaches and mental confusion, with an irregular high temperature, in the presence of a rather troublesome cough raised suspicion of a lobar pneumonia: but this tentative diagnosis was not upheld by subsequent events. In 4 weeks time he appeared to be likely to die, only to stage a remarkable recovery.

Six weeks after he became ill, bile appeared in the urine and the liver was found to be very enlarged. This appearance of bile in the urine was followed by marked improvement in the patient's physical and mental condition. He began to eat, became lucid, and complained of feeling "doped" and sleepy. The bilirubinaria persisted for a week, urobilinuria persisted.

After being absent for 18 days, bile again appeared in the urine, he re-commenced to vomit and his appetite again failed. The liver was now diminished in size. Twitching movements of the hands and forearms preceded the occurrence of a position seen in tetany. He now became completely apathetic and incontinent and the Babinski response became 'extensor', bilaterally. The pulse became irregular in force and rhythm prior to his death.

During this time I was naturally keen to try the effect of methionine but unfortunately a supply was not available.

I think the history as later detailed is consistent with a diagnosis of infective hepatitis.

The next fatal illness was that of Arthur Cowley. I was completely misled by the history in this case as may be readily appreciated by a perusal of his case record: the more so as his brother and the son of his brother were at the same time absent from work and under my care: further it was indeed a rare event for any of the 3 men to be absent from work.

There were two facts which should be noted. Cowley looked very pale and, although he was of a very pale complexion normally, this did attract my attention in view of his moderate degree of pyrexia, 101°F. Further, the lymphocytes numbered only 12% of his total leucocyte count, and this I

considered to be quite atypical of infective hepatitis.

Nevertheless, the history which he gave me absolutely spontaneously, will be seen to closely mimic many others which I have recorded. In the presence of the prevailing epidemic, his gradual loss of appetite and especially the fact that he "had no fancy for a cigarette" which he particularly remarked, were obviously misleading.

Although Cowley's death was therefore probably not related to infective hepatitis, I think that it merits mention, and I therefore include a record of his illness, and the illnesses of his brother and nephew.

I am indebted to Dr. Cookson for his assistance with the post mortem materials which I submitted to him and for the microphotograph of the septal infarct which I include.

The last of the three fatal illnesses concerned Violet Cutmore, a woman of 55 years.

Her 15 years old son, John Cutmore, had been attended by my partner, some 3 weeks before Mrs. Cutmore sent for us to attend her. My partner had no reason to take especial notice of the son's illness; it appeared to be exactly similar to very numerous cases which we were then attending. The boy's facies, general appearance, posture, demeanour and complaints had led my partner to label his illness 'hepatitis,' ----

not that there was any proof that the lad had indeed a 'hepatitis', but because the obvious lethargy, the absence of temperature rise etc. were so unlike any previous epidemic which we had seen and, as I have previously stated, we believed that the illnesses were related to the 'jaundice' epidemic.

At times, Violet Cutmore had suffered from bronchitis, and for the first week of her absence from work she had no reason to suspect that her illness was anything but a recurrence of this bronchitis. But after a week, the symptoms altered, for she then had a severe headache and her head felt heavy and muddled ("fuzzy"). After a short interval of apparent recovery, she became giddy and thereafter we find a picture of a rapidly ascending myelitis, associated with encephalitis. The early symptoms of this rapidly fatal illness, from the time of our attendance that is, were rather misleading, and I feel that in view of the "nervous system symptoms" which I have elsewhere detailed as occurring in the epidemic illness in Murton, the history of Mrs. Cutmore's illness calls for our close interest and consideration.

Repeated vomiting was accompanied by right sided lower abdominal pain, which was also present in the lower dorsal and lumbar regions posteriorly, again only on the right side. At first the pain had not been continuous but it was severe. Particularly interesting and arresting was her description---

"as if she was being stabbed by a thick dart or needle." This was exactly the wording used by some patients as the reader will remember.

Later the pain became more continuous "a continuous burning ache with superadded bursts of finer and shorter dart-like pains."

On examination, I found a band of hyperaesthesia--hyperalgesia, corresponding to the 7th to 12th dorsal segments of the cord.

The reader can read of the subsequent complete paralysis and almost completely anaesthesia of the legs etc., which supervened in this short tragic illness. The ascending spinal lesion became associated with marked neck rigidity before the fatal termination.

Whether or not John Cutmore had infected his mother I thought it possible that the mother's illness was due to an infection with the prevalent virus illness. Some time previously I had attended a youth who worked at Young's Garage with Cutmore. This lad's illness was of the gastro intestinal type and obviously infectious as his mother <u>also</u> became ill some 4 weeks later with similar vertigo, nausea, vomiting, headache and upper abdominal pain (Details could be provided) In the immediately following section of this work I refer to the illness of Verna Edwards which was mild but rather resembles Mrs. Cutmore's illness, in some respects.

ERNEST SCOTHERN. Age 65 years.

11 New Pilgrim Street, Murton.

Retired Coal Miner.

This man had the light duty of "knocking up" people to go to work. He worked not more than 2 hours daily.
The illness lasted 3 months before its fatal termination.
I did not attend him in the early stages of the illness.
History. (I am indebted to Dr. J.H.McIntyre for his assistance)
Tues. 26/9/1944.

Sudden onset of vertigo and nausea which was followed by violent vomiting which continued for several hours, and thereafter recurred 4 or 5 times daily. He struggled on with his light duties for 5 days and is said to have appeared on the verge of collapse.

Sat. 30/9/44.

He was forced to go to bed as he could not "hold up" any longer. Next day, Sunday 1/10/44 he vomited frequently, but the vomiting ceased thereafter. He became mildly disorientated, then very confused and presently delirious. When lucid, he complained of a dreadful headache. He had a troublesome cough. Dr. McIntyre thought that Scothern possibly had a pneumonia, but he was not at all satisfied with this provisional diagnosis. There was no response to Sulphapyridine. After some fluctuation the

condition deteriorated --- delirium, at first noisy, became quieter -- and Scothern became progressively weaker. He took no solids and he was constipated. The temperature was extremely irregular, varying up to 103.5°F. There was a suspicion of dullness to percussion posteriorly --- right lower lobe. He continued thus until

Wed. 25 Oct. 1944.

I saw him. He was lying like a log "obviously" moribund. The relatives were opposed to unnecessary interference and investigation and I rather accepted their view.

.....

During this period I had discussed with Dr. McIntyre, who was in attendance, the possibility of the condition being a cholaemia due to hepatitis. The urine was examined daily but at no time did it contain bile. The output was low and the specific gravity always exceeded 1020. At no time was albumin present in the urine.

On Monday, 6 Nov. 1944

his urine was found to contain bile. It was very deeply bile stained. The specific gravity was 1024. There was no albumin. Urobilin was present. I now attended Scothern at Dr. McIntyre's request. On examination: The liver is palpable and tender 3 fingers' breadth below the right costal margin. The patient is fairly lucid, more so at intervals. Pulse is 72 per minute. Temperature is 98°F. He is

not jaundiced. He particularly states that his headache is much easier. Emaciation is now, naturally, extreme. He was obese before his illness.

Klein's intradermal Histamin Test is negative.

Differential White Cell Count.

Polymorphs.	61
Lymphocytes.	36
Eosinophils.	1
Monocytes.	2

Until Saturday 11 Nov 1944

He was obviously improving gradually. Throughout his illness he has taken glucose and concentrated orange juice as a drink very freely -- he was thirsty. Now he tries to chew bread and jam but he either can not or will not swallow a bolus, which he eventually 'spits out,' after rolling it about in his mouth.

His blood pressure which I had known to be $\frac{156}{84}$ before his illness, is to-day $\frac{125}{75}$ mm. Hg.

There is obvious twitching of the face and hands. He has restless nights --- I think this is more an objective than a subjective 'symptom'.

Until Tues 14 Nov 1944

Improvement continues. He complains that he feels "doped" and extremely sleepy. He is chewing more food but still not swallowing the bolus -- he says he

can swallow the "juice" only. There is now no bilirubinuria but urobilinuria persists.

Until Tues 21 Nov 1944

Steady well marked improvement. Begun to eat. Not so thirsty. He ate oranges, Heinz Beans, an egg or two, biscuits etc. Much brighter and feels that he will now recover. Tongue moist. The liver was no longer palpable. Thereafter, he improved markedly and promised to stage a truly wonderful recovery.

I again ceased attending him, and did not see him until Dr. McIntyre requested me to do so on

Monday 11 December 1944.

He is said to have been rapidly regaining strength until Sat, 2 Dec 1944, when he vomited in the early morning. Since then his condition has at first gradually and then rapidly deteriorated.

On examination.

There is again marked bilirubinuria. The liver dulness is diminished -- there is no tympanites and the finding is definite. Mentally the deterioration is striking. He is dull and apathetic and interrogation is very difficult. In contrast to the earlier stage of the illness he is not constipated. Loss of appetite is again marked but not complete. His hands, fingers and forearms twitch --(very like Walshaw's, Cold Hesledon Group). Pulse 96 per minute. Temperature 101°F. Dribbling incontinence is noted.

Tuesday 12 Dec 1944

Pulse 72 per minute. Temperature 102°F. Respirations 28 to 30 per minute. Short cough. There are again a few medium fine chales and a doubtful dull note on percussion, over the right lower lobe posteriorly.

He gradually drifted into a condition as described under "Wed 25 Oct 1944", except that he was not comatose. The hands which were extremely tremulous as well as exhibiting involuntary jerky movements assumed a position characteristic of Tetany. The Babinski response became extensor. He became completely apathetic and incontinent. The pulse became very irregular both in rhythm and force.

He died on 22nd December, 1944.

.....

I was not granted a supply of methionine owing to "service" priority demands.

Otherwise treatment was dictated by the patient's condition re appetite etc.

He took glucose with concentrated orange juice as a beverage freely throughout the major part of this time.

ARTHUR COWLEY. Age 48 years.

41 Toft Crescent, Murton.

Coal Miner.

Mon 6 Nov. 1944. Visited.

History. It is practically verbatim.

For 7 or 8 days he has felt out of sorts and remained indoors on his return from work. He was not able to go out at nights. He felt he must be taking a chill as he had "cold shiverings" frequently. Sat 4/11/44 at 4 p.m. he went to bed. (the hour is explained by his 'shift' at work).

He was seized with epigastric pain which persisted until 6/11/44. He felt suddenly violently sick and on rising to go to vomit he was intensely dizzy -- in fact he could not stand. His head was, and has remained, heavy and dull. He had one sharp fleeting pain like a stab on the top of the head.

He is very pale and he certainly looks afebrile, but his temperature is 101°F and the pulse is regular in rhythm and force at 120 per minute. He has no desire for food and no fancy for a cigarette.

Unfortunately no total white cell count was made.

Differential White Cell Count.

Polymorph. 86

Lymphocytes. 12

Monocytes. 2

Wed 8 Nov 1944

He is said to have had a very bad night the night of Mon-Tues 6th-7th Nov 1944. He was restless and he shivered and sweated. He still complains of epigastric pain and is tender in that region but not markedly so. He stresses his illness through Monday night. However he states that he feels much better now, and his temperature and pulse have dropped. Temperature 98.4°F. Pulse 84 per minute.

Fri. 10 Nov. 1944

He professes to feeling very much better, just feeling a little shaky and weak. He is sitting up fully dressed and practically dismisses me with "Oh, I am quite all right now, Doctor."

(I afterwards learned that he had been out on Thursday evening).

This man persisted in returning to work on Sunday 12 Nov., 1944, when he worked 14 hours. On Monday he worked 8 hours. Soon after returning from work on Monday 13/11/44 he ate a hearty, bulky meal. He then went to the outside lavatory.

There he was found lying dead, in his vomit, some few minutes later.

Post Mortem Examination

The heart, the spleen and the kidney were removed. The stomach, duodenum and gall bladder were removed "all in one." The organs were submitted to examination by Dr. Cookson, Pathologist, Sunderland Royal Infirmary.

proceeding p. 414.

Ref { Arthur Cowley
aged 48. 41 Toft Crescent – Morton

Dear Dr MacRae

Here is the micro-photo
showing the heart lesion in your P.M. case as alive
as you will see there is evidence of healed infarct
The lesion was from the septum.

Yours sincerely.
Stacpoole Sowry.

The cardiac musculature appeared, generally, healthy, particularly so. Three small fibrotic areas were clearly visible. The anterior mitral cusp was thus slightly affected. The valve was competent.

A fibrotic lesion on the septum was submitted to microscopic examination.

Dr. Cookson considered that the history and the post mortem findings signified a cardiac death. The liver which appeared healthy was not submitted to microscopic (section) examinaton.

The stomach, duodenum, kidneys and spleen appeared "healthy."

A microphotograph of the infarct present on the septum is provided.

John Cowley Age 19 years.

3 Williams Road, Murton.

Sat 4/11/44.

States that on Monday 30/10/44 he had a pain in the right subcostal (anteriorly) area and above. The pain extended across the 10 D.V. level at the back if he bent. He also had pain in his shoulders but only if he used his arms. He had no headache: his appetite is good: no giddiness.

He is very tender on gentle deep palpation in right subcostal region and he is very thirsty. The tongue is moist with a definite thin Rhubarb- Soda coloured fur.

The pulse is 60. Temperature Normal.

John Cowley

3 Williams Road, Murton.

Mon 6/11/1944.

Complains of headache right supraorbital, especially. He feels tired and when he stands the thick (upper part) of the thighs feel painful --- when he sits down his arms and shoulders feel useless. He is not dizzy and his appetite is as normal. He does not complain of abdominal pain.

The tongue is clean. He is tender subcostally--right.

Pulse 60. Temperature 98.2°F.

~~Blood Test---6/11/44.~~

Wed. 8/11/44. He states that his shoulders feel as if they were not there. He has to move them to feel that they are there.

He has pain in the epigastrium and right subcostal region which is aggravated if he coughs a little.

The nares are skinned and the nose is obstructed by crusts.

There are 3 or 4 erythematous blotches on the face the size of a sixpence. He complains of headache - supraorbital to occipital and down to angle of the jaw. Pulse 72.

He has low back ache if he lifts anything.

John Cutmore. 15 Years.

21 Edison Street, Murton.

Employed at Young's Garage, Sunderland.

Fri. 5 Jan, 1945.

At night he had a frontal headache and his legs ached. He felt weak and remained in bed until Sunday, expecting to be fit to resume work on Monday 8 Jan, 1945. He had a troublesome cough which hurt his throat. On Monday he was unfit to go to work as he felt very tired, lazy and listless, in fact this feeling appeared to be out of all proportion to the antecedent illness. I did not attend him but my partner said that "Cutmore was just another of those illnesses," the facies, appearance, and obvious apathy and lethargy following a trifling illness had seemed to him to be typical of the outbreak.

Violet Cutmore. 55 years.

21 Edison Street, Murton.

'Bus (N.G.T.) conductress.

Visited

Friday 26 Jan 1945.

This woman was seen in consultation with my partner, in the evening.

From Monday 15/1/45 until Monday 22/1/45 she had a flare up of her (chronic) bronchitis. On the latter date she felt intensely sick after breakfast and wished to vomit but she did not vomit. She had a severe frontal headache and her head felt heavy and "fuzzy": she felt that she wanted to keep her eyes closed to ease the head symptoms. After shivering near the fire she went to bed where she recovered by Tuesday morning and then she got up and about and felt quite better all day.

On Wed 24/1/45 she had pain in her abdomen centred at about the umbilicus and extending right around her trunk. She felt intensely giddy at intervals and she had to keep sitting down. There was no nausea. The condition on Thursday was unaltered.

To-day she tried to get out of bed, but she found that her legs would not support her: they just crumpled up under her weight. Later she commenced to vomit and has done so repeatedly since. All drinks are promptly rejected and she

is sick even if she does not drink. The vomit has been yellow brown and bile stained. She has sent for us three times to-day complaining of severe pain in the right side of the abdomen, especially the lower abdomen, and in the lower dorsal lumbar regions posteriorly. The pain is said to be intolerable. On Wednesday and Thursday, she states, the pain was severe in this region, but it was not continuous: it was as if she was being stabbed by a thick dart or needle. To-day there is a constant burning ache with superadded bursts of finer and shorter dart-like pains.

The bowels have been confined since Tuesday.

The output of urine is said to be reduced, markedly.

The pulse is 68 per minute. Temperature is normal.

Sat. 27/1/1945. Sent at 2 a.m. as pain was so severe. She looked pale, pinched and exhausted.

On examination there is an area of hyperaesthesia on the right corresponding to the 7th to 12th Dorsal segments of the cord. On stroking lightly across the abdomen the hyperalgesia was very noticeable at the midline anteriorly and it could be similarly demonstrated posteriorly and at the upper and lower limits of the zone. The ankle jerk was absent on the right side and the big toe was upgoing in Babinski's test. The knee jerks were present. Urobilinogenuria was marked.

Sunday. 28 Jan 1945 The face is flushed. Temperature is 99.2 and the pulse 84 per minute. She told me that she feels numb

up to the neck. When the nurse administered an anema Mrs. Cutmore did not feel the operation. Also she has aching in the right axilla and a feeling that her right arm is going to be affected. There is no stabbing pain. She is thirsty. The bowels are still confined. The urine, which was kept for me, contains a heavy deposit of urates but no other abnormal constituent bile, urobilin, sugar, albumin or acetine, is present. She has passed no urine for 8 hours but the bladder is not distended.

She is completely anaesthetic in both interior extremities- no notice is taken of deep pin pricks and musclejoint, touch, temperature and vibration sensations are lost.

The knee jerks and ankle jerks are absent bilaterally but the big toes are "downgoing" --- the response is not marked especially on the left. (A change from yesterday.)

The loss of sensation extends a little higher on the right where it reaches the 4th Dorsal Spinal Segmentary distribution, on the left sensation is absent until 6th Dorsal Segment Zone is reached.

The vibration sense extended rather lower on both sides, a fact influenced possibly by two factors.

First the vibrations would probably be conducted upwards by the chest wall and again the limits of anaesthesia on the trunk are not sharply demarcated in one respect. There is a belt of some 1 to 2 inches wide where heavy pricks are

detected but not light pricks.

At night the level of anaesthesia had risen -- I examined quickly, almost casually, to avoid alarming the patient. The level on the right was the 3rd Dorsal Spinal Segment area. The area in the upper arm and axilla corresponded to the same segment. The pulse is 84 and the temperature has risen to 100.2°F. She complains of an ache over the occiput.

The reflexes are unaltered in both arms -- she is inclined to think that the feeling (pain touch heat vibration) is more acute on the left side.

Monday, 29 Jan 1945.

Respiratory embarrassment is apparent, shallow rapid breathing. She has an almost incessant weak ineffectual cough --- she feels that "the phlegm is lodging in her throat."

Pinprick is now felt at the same level on either side, at the 3rd rib anteriorly. There is a dim appreciation of really heavy hammering on the Tendo Achilles and a little proximal to it. There is no response to Babinski's test -- knee jerks, ankle jerks and abdominal contractions are lost.

She complains of occipital, suboccipital and neck pain. There is marked neck rigidity. She swallows only 3T sips of water "as she cannot raise her head to swallow." She was able to push herself up on to the pillows if she slid down in the

bed until 6 a.m. to-day -- now she cannot, "as she cannot bend her neck to help in the movement."

The right arm is not used -- she says it feels weak. She can use it however and its power is quite good.

The reflexes in the upper extremity are present and rather brisk.

The pupils are almost pinpoint -- any reaction to light or accommodation can not be (therefore) discerned.

Some 30 oz. of urine were obtained by cutheter.

The urine is acid: there is no deposit.

S. G. 1022.

Albumin. A trace.

Sugar. Nil

Acetone. Present in large amount.

No Pus-blood or bile.

No urobilinogen.

Some rather Uncommon Illnesses which occurred During the Period under veview.

SOME RATHER UNCOMMON ILLNESSES WHICH OCCURRED DURING THE PERIOD UNDER REVIEW.

In the last three months of 1944, when the epidemic in Murton reached its peak, there were several rather unusual illnesses which I consider may be of significance in relation to that epidemic.

I have no proof indeed that they were related to the epidemic in general, but yet I think it would be well to refer to a few of such illnesses to allow the reader to consider whether they are at all significant.

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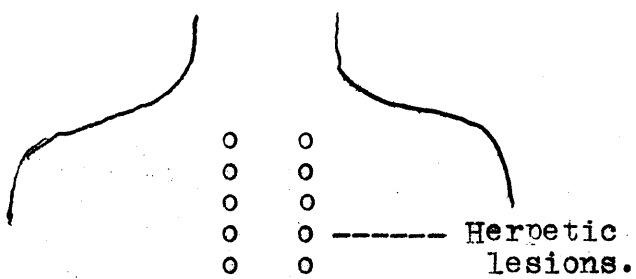
(1). In my experience bilateral herpes zester has been an uncommon illness and this is the view of van Rooyen and Rhodes[1]. I include the history of such an illness: it occurred in a young woman, Verna Edwards, who consulted me on the 21st October, 1944. The prodromal symptoms were interesting. For 14 days, or so, she had been so tired and listless that she had almost fallen asleep at work. On return from her work she rested until she had to go to work next day. Normally she is an extremely robust and active girl and enjoys very 'robust' health. Later she developed an upper respiratory catarrh, described as a head cold with a cough which pained her chest --this during the 2nd week of the prodromal stage. After this she had to come home ill, from work. She vomited

and she developed pain in the neck and across the shoulders. When I saw her her on 21st October 1944, she looked pale and exhausted and the facies were otherwise "expressionless." She also presented a most striking symmetrical herpetic eruption which was accurately localized next to the vertebral column centering on the 1st Dorsal vertibra, and not extending laterally. The Differential Leucovyte count was

Polymorphs. Leuco.	71 %
Lymphocytes	27 %
Eosinophils.	2 %

This mild illness, especially as regards the prodromata, was not unlike that of Violet Cutmore's fatal illness, just referred to. I was unable to find any possible source of this infection.



(2). As I have previously stated that several cases of atypical pneumonia occurred at this time, reference to such a case appears to be indicated. In the absence of radiological confirmation, examination of the sputum etc., my account can only be regarded as suggestive on the clinical evidence.

I would first refer to the illness of Robert Turnbull, a man aged 62 years, the history of whose illness I provide later. It is easy to be wise after the event, and it may be considered that the initial cold shivering should have made me think of pneumonia. But there was nothing during the first five days of Turnbull's illness to suggest such a diagnosis. He breathed easily without hurry or discomfort. He coughed a little, but that was usual for him. The striking feature of his illness was that he slept, and slept. His temperature ranged from 100 to 102°F, his pulse was relatively very slow, not exceeding 100, and at times only 76 per minute. He had to be awakened to take drinks and food. He was <u>easily</u> awakened and after the first two days he enjoyed his meals. But whenever he finished his meal he would fall asleep. In fact he reminded me strikingly of Walshaw (Cold Hesledon group ? atypical pneumonia with encephalomyelitis.) although he was obviously not so ill. Like Walshaw he would converse intelligently and apparently brightly but once the conversation was interrupted Turnbull immediately fell asleep, even when I remained in the room. He made no complaint on the

6th day of his illness, in fact he said "I feel comfortable lying here." He had no headache. It was only after he had been ill a week that his respiratory rate rose, apparently almost abruptly to 40 per minute. The breathing varied markedly in rhythm and depth, and for the first time his appearance, apart from his symptoms, was worrying. He still continued to sleep but in another 48 hours he began to improve, and thereafter he made an uneventful recovery.

When he had recovered he had no recollection of 3 days of his illness.

(3). While Turnbull's illness did eventually give a definite indication of at least including a pneumonic condition, the illness of Jean Bartram, a 12 years old girl, gave more vague and subtle indications of possible pulmonary involvement. It presents features which I regard as being particularly interesting and, to me, uncommon, and moreover it can be regarded as typical of several illnesses which occurred in our practice in October to December, 1944. A reference to her 'case record' will show that her illness began with a mild pyrexia, general malaise, headache, backache and pain at the thyrohyoid level when she swallowed. In 4 or 5 days she had improved and got up out of bed a little. My partner, who was in attendance, was therefore surprised to find that she was again ill on the 8th day of her illness. He noted that she felt that her breathing was

restricted on the right side, where she had pain round the lower ribs. As her condition deteriorated as witnessed by her appearance, her increasing weakness, progressive anorexia and continued pyrexia, he asked me to see her. The 'biphasic' nature of her illness reminded me of the Cold Hesledon patients, among others. The sense of tightness or restriction of breathing, with pain in the right chest low down was a symptom with which I was now familiar as was the occurrence of headache and giddiness when she sat up. She appeared weak and utterly exhausted and yet I felt that the prognosis was probably good. Her fingers 'twitched' and she was sleepless at night when she sweated very heavily.

The pulse was at first slow in relation to the temperature rise. Giddiness and repeated vomiting were the next features of her illness. Mensuration showed the right half of the chest to be 1" to 1½" larger than the left at the level of the 10th Dorsal Spine. An uncommon feature present in this case was that the glands along the posterior border of the stermomastoid were slightly swollen and tender.

Urobilinuria was marked. There was no dulness to percussion over the right side of the chest posteriorly, there was an occasional rhâle and I thought that the right side moved slightly less freely than the left. The impression formed after examination of the chest was, that while there was little to be found, the slight physical signs present

were all right sided and that if there was any type of pneumonia present it was probably in the right lower lobe.

But the striking symptom of the disease was the marked prostration and of this the girl complained. She looked utterly limp and exhausted and her remark to me on this matter was:- "Oh, Doctor, I do feel awful. I am so weak."

This was the type of complaint to which I have previously referred and with which I was becoming familiar. Although she continued to vomit I observed on the 15th day that the tongue was beginning to desquamate, and this I interpreted as a good 'prognostic', as indeed it proved: recovery soon followed

This illness presented, then, some features typical of the prevalent epidemic and it seemed at least possible that an atypical pneumonia may also have been present.

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(4). Finally, I would very briefly comment on the illness of Lilly Skeen. I did not see this child until she was convalescent. My partner, who attended during the illness, thought that the history was interesting and unusual. I record the history later. The interesting feature of the girl's illness was not the pneumonia, which, I am told, was typical of a lobar pneumonia; the illness responded to treatment with sulphapyridine and when I examined her the physical signs were those of a resolving lobar pneumonia. But very unusual was the story of the prodromal phase of the illness.

For 6 days prior to the doctor being called upon, the girl had been absent from school. She had not been "bad enough to send for the doctor." In fact her symptoms had been as it were 'negative'. The story was a familiar one, in its initial phases. She sat limply in the chair all day, we were told, not talking, not moving unless forced to, completely listless and apthetic. The mother said that the child seemed dull and rather stupid "as if she needed a good shaking to brighten her up!" She admitted to a heavy dull frontal headache and at times she felt "chilly." It was only when the improvement which was anticipated from day to day failed to materialize that my partner was consulted.

My interpretation of this illness was that it was an instance of an initial virus infection being complicated by a bacterial pneumonia.

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It can be confidently stated that the majority of the illnesses featuring pneumonia in Murton during the winter of 1944 were in many respects quite unlike the pneumonia as prevalent there in the preceding 21 years. I encountered illnesses like that of Jean Bartram where I suspected the diagnosis to be "primary atypical pneumonia." (cf Cold Hesledon Group).

The illness of Walshaw (Cold Hesledon Group q.v.) and of Turnbull and Skeen, just described, are offered in support of my assertion that pneumonia in Murton during the period

reviewed was frequently, with regard to the prodromata, clinical course and physical findings of a "NOT TYPICAL" type.

.....

I was interested to observe that Turnbull carries the bread trays into the Co-operative Society Grocery Department: the bread being delivered from the local bakery where the epidemic already described occurred: and to further notice that the only other employee so engaged, at times, had a very severe attack of the epidemic illness not however accompanied by pneumonia.

Reference.

1. van Rooyen. C. E. and Rhodes A.J.
Virus Diseases in Man London 1940. p 137.

VERNA EDWARDS. Age 18 years.

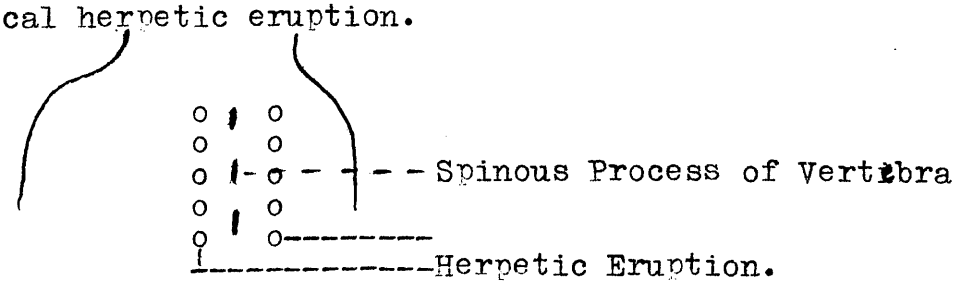
58 Calvert Terrace, Murton.

Sat. 21 Oct 1944. Consultation.

She states that for the past 2 weeks she has felt tired, listless, and "run down" -- almost falling asleep at her work. When her day's work was over she lay down on the couch and could do nothing more. Last Saturday, 14 October, 1944, she developed an upper respiratory catarrh -- described as a "head cold" and sore chest with painful cough. She rested until Monday, when she returned to work, somewhat better but not well: she meantime having pain over the left lower ribs on 16th October. She continued at work on 16th, 17th and 18th October, but on Thursday, the 19th, she came home ill.

She vomited, and she had severe pain across the shoulders (posteriorly) up into her neck, especially suboccipitally. She went to bed completely exhausted, until to-day.

To-day she consulted me re bilateral herpes: a most striking symmetrical herpetic eruption.



Apart from the dull, pale, expressionless facies there was nil else of note. The tongue was clean.

Differential White Cell Count.

Polymorph	71
Lymphocyte	27
Eosin.	2

ROBERT TURNBULL. Age 61 years.

52 Williams Road, Murton.

Co-operative Society Grocer.

History.

Obtained on my visit to him on Tuesday 3 Oct, 1944. For the past 2 weeks he had felt tired. On Sunday 1 Oct,1944, he felt chilly in the evening. On Monday, 3 Oct, he felt well and worked until 12.30 p.m., his lunch hour. Just then he felt suddenly very weak and chilly and he shivered. He struggled home, sat in a chair and fell asleep. He took no lunch as he felt sickly. However he returned to work, where he had great difficulty in keeping awake -- "he was almost overpowered with sleepiness."

At 5.30 p.m. he returned home and went to bed, and presently he vomited repeatedly. He retched violently but vomited only a little mucus. He sweated freely.

Tues 3 Oct 1944, Wednesday and Thursday.

He slept practically all day, each day.

As described in the text, he dropped off to sleep whenever his attention was not strenuously 'held'. I could find nothing else on examination and he did not seem to be very ill, although the lethargy was rather disturbing. The highest temperature noted (on my visits only, of course) was 100.8°F. The pulse was relatively slow, 76 to 86 per minute. Vomiting and nausea rapidly cleared up and the appetite returned.

Friday, 6 Oct 1944 2 p.m.

"Sleep, sleep, sleep all day" his wife states.

I was now worried about his condition but he looked not at all ill. He said that he was feeling much better. He was eating well and had eaten a generous breakfast at 8 a.m. I asked him how he felt or if he had any complaints. He replied: "I feel comfortable lying here. I have no pain at all." At no time had he headache.
However the temperature was 100.6°F. The pulse very slow at 76 per minute.
6 p.m. Temperature 102°F. Pulse 100. He states that he is "Fine. I have a good appetite and would like some beer!" The bowels have acted thrice to-day but the colour is normal and the motions formed though rather soft.

Up to this date his breathing had been regular and unhurried.

Sat 7 Oct 1944.

The condition is obviously altered. This I noticed as I entered the bedroom. The respirations are hurried -- 40 per minute. They vary markedly in depth and the rhythm is very irregular. Whilst the temperature is now 101°F. the pulse rate has risen to 124 per minute. These are all striking changes. He had a restless night: he still slept soundly but he "moaned and groaned and was restless." He appeared to be very ill. The appetite remained good and he had to be awakened for his meals.

There was evidence of a left basal pneumonia --- dulness to percussion was sufficiently marked to be described as definite.

Throughout the illness he had a cough. (He has a chronic cough always, when not ill).

The sputum is mucoid with an occasional fleck of blood. In 48 hoursthe temperature was normal in rate and rhythm. Coincident with this improvement, his drowsiness became less marked.

He made an interrupted recovery.

The illness may be compared with Walshaw (Cold Hesledon Group.)

JEAN BARTRAM. 12 years.

1 Ash Terrace, Murton, Durham.

Attending Seaham Secondary School.

First seen by colleague Tues 21/11/44

First seen by me Thurs 30/11/44.

History.

Monday 20 Nov 1944.

She was ill when she returned from school complaining of backache (12th Dorsal Vertibral level), frontal headache, of feeling 'not well' and of a sore throat. The throat was sore only when she swallowed, the level of soreness being Thyrohyoid. She was seen by a colleague on Tuesday. She had a slight rise of temperature and she remained in bed until Friday 24/11/44, it being considered that she had an "influenzal chill."

She was sitting up out of bed on Friday evening, Saturday, Sunday and Monday morning, when she felt that she was taking ill again.

Mon 27 Nov 1944

I am told that her temperature was 101°F. and the pulse 96 per minute. On Monday night she had a pain in the right chest low down, to the front and side and she felt that her breathing was restricted. Her appetite which had been poor to fair became definitely very poor, and she became obstinately constipated.

She continued in this way until I saw here on

Thurs 30 Nov 1944.

She looks very pale, weak and exhausted. If she sits up she has a frontal headache and feels giddy. Her chest feels tight and her breathing is said to feel 'restricted.' Pulse 96 per minute. Temperature 101°F.

Friday 1 Dec 1944

Liver palpable and tender. The edge is down more than a finger's breadth. She feels drowsy but she cannot sleep at night. The facies is dull apathetic and wan. The fingers and the hands "twitch." Pulse 112 per minute. Temperature 101.5°F.

Saturday 2 Dec 1944.

Vomited several times. She complains of discomfort in the epigastrium and she feels as "if blown up with wind." Still sleepless at night. Small tender glands behind sterno-mastoid. Mouth dry. Feels very giddy. Urobilinuria is very marked. Pulse 112 per minute. Temperature 99.8°F. She looks ill. "Oh, Doctor," she says, "I feel awful. I am so weak."

I found that the right side of the chest measured 1" to 1½" more than the left: an occasional rhale over the right lowerlower lobe posteriorly and ? slight dulness to percussion. On Sunday and Monday, 3rd and 4th December, she vomited twice each day, retching severely. The tongue is thickly coated

but the papillae are showing red. The skin shows a pale lemon tint. I considered that the desquamation of the tongue was a 'good sign' and believing this illness to be a variant of the prevailing epidemic illness I gave a good prognosis, as in those cases improvement followed desquamation.

She did improve. Next day, after a good night's sleep, she looked better. The temperature was normal and the pulse 76 per minute.

The improvement was probably by crisis.

At no time was there any respiratory hurry or distress.

I regarded the illness as comparable with others in the Cold Hesledon Group (q.v.) and that there may have been an atypical pneumonia.

LILY SKEEN. Age 12 years.

5 Barwick Street, Murton.

Attending Murton Council School. Teacher, Miss Bramma.

The history is partly retrospective.

Written on Saturday 25/11/44 when I visited her.

She has been off school ill from Monday 13/11/44 and she had no medical attention until Monday 20/11/44.

During this first week she did not seem ill enough to warrant calling in her busy doctor.

She complained of heavy frontal headache and she felt chilly at times. Her appetite was poor to the extreme. She sat in the chair each day, listless, apathetic and looking as the people here express it "hangy and washed out."

She was pale and had dark shadows around her sunken eyes. All this time she had a slight cough.

As the improvement anticipated from day to day did not materialise the doctor was called in and on Tuesday he diagnosed left lobar pneumonia, treating ir with M. B. 693. To-day Saturday 25/11/44 there is evidence of a resolving pneumonia with redux 'creps' and dull percussion note.

Temperature, pulse and respirations are normal.

I think this has been a case where pneumonia has complicated an initial virus infection.

The Interpretation of the Simultaneous Occurrence of the Two Epidemic Illnesses.

THE INTERPRETATION OF THE SIMULTANEOUS OCCURRENCE OF THE TWO EPIDEMIC ILLNESSES.

An epidemic of an illness accompanied by jaundice and undoubtedly typical of infective hepatitis as it has been described by others, has been discussed.

I have attempted to provide the reader with an impression of another series of illnesses which occurred in the area throughout the same period. I fear that I may have included among the records, accounts of illnesses which it may be thought allow of an interpretation differing from the one which I now suggest.

But I venture to hope and think that taking a broad view of the illnesses as they occurred and comparing the groups at Cold Hesledon and Dalton le Dale, at the local bakery, and in Murton in general, it can only be concluded that there was an epidemic illness in the area in 1944-1945.

Further I believe that an impartial critic would agree with me in remarking on the definite resemblance between the symptoms of the infective hepatitis epidemic, and the other concomitant epidemic.

In fact, on referring to the tables of symptoms on pages x 251,314,460, the similarity might without any exaggeration be 555,556,591 termed striking if not remarkable.

What could be the explanation of the occurrence of those

x Modified Tables reproduced in page 765 et seq.

two so similar epidemics in the area ?

Either it was a coincidence, or else they were related.

The more I saw of the illnesses, the less could I credit that the two epidemics were unrelated. It was not simply a matter of the most frequently encountered symptoms being common to both epidemic illnesses. When one considered the minutiae of the symptomatology the resemblances were as impressive, and in fact, to me, they were particularly convincing.

Such resemblances I can demonstrate, and in fact I trust that they have not escaped the notice of the reader. But there were resemblances which it is beyond the power of my inexperienced and untalented pen to adequately illustrate. When something entirely new presents itself to a general practitioner of over 20 years' experience, and when that something new keeps on presenting itself, it is certain to arouse his interest and curiosity. I would make only one modest claim as a result of my stated length of service in practice, and that is this:- I had seen a variety of epidemic illnesses, I had listened to the complaints of my patients with, I trusted, the average degree of intefest and attention during those epidemics, and I felt that I was able to assess whether a complaint or a symptom complex was an unusual one: an unusual one at least in this area.

Certainly it can be stated that the illnesses in the Murton

area in 1944-1945 presented features with which I had previously been unfamiliar.

I wondered whether others had described epidemics in which the symptomatology resembled that encountered in this outbreak. One rather similar outbreak had been described by Bradley[1] under the title "Epidemic Nausea and Vomiting." Bradley stated that the condition had previously been described as having occurred in Denmark where it was widespread in 1935: in a boarding school in Thanet in 1936: and in Hayling Island in 1939.

This "Epidemic Nausea and Vomiting" did, on the closest inspection, bear a striking resemblance to the Murton epidemic. What were the chief symptoms?

They were:— Vomiting.
Nausea.
Vertigo.
Aches.
Diarrhoea

Bradley illustrated the relative frequency of some symptoms in one group as follows:

Population at risk	55
Vomiting without diarrhoea	11
Vomiting with Diarrhoea	7
Diarrhoea only	1
Nausea	7
Total cases	26

To examine in a little closer detail. Bradley discussing the symptoms seriatim stated:-

Vomiting. This was said to be the most characteristic

sign. It was said to tend in young people to be projectile and of great urgency. For instance sleeping children awoke at night and vomited before they could get out of bed. "On the other hand projectile vomiting was by no means invariable and a large proportion of the cases, particularly adults, did not vomit, or vomited only after a prolonged period of nausea."

Well, so far as this symptom went, I believe I could write the above as truthfully, to describe the Murton epidemic.

Nausea.

This occurred with the vomiting, or more characteristically "preceded it for a period of hours or even days, and in several cases persisted unaccompanied by emesis."

The records of the Murton Epidemic give numerous parallels. We have seen where one patient would want to be sick and try to make himself sick to no effect: then suddenly he would vomit violently. Another patient would be intensely nauseated and even rush to vomit and yet his illness would not feature vomiting as a symptom at any part of its course.

Vertigo.

Quoting Bradley's paragraph:-

"Nausea often included a sense of instability and dizziness. A desire to fall over or faint was present in some cases and patients disliked sitting up for this reason, but in few instances only did dizziness amount to true vertigo."

The underlining of the words above is the writer's.

Nothing more typical of the Murton epidemic could have been penned. For the rest of the quotation it was as applicable to the Murton illnesses as any such brief comment could be.

Aches, and Pains.

Again the resemblance is extremely marked.

The almost invariable presence of "some degree" of frontal headache; the occurrence, presumably less frequently, of occipital headache; the fluctuation of the headaches, not persistent but tending to come and go ---this description by Bradley would be equally applicable to the Murton epidemic.

"Pain from colic was conspicuously absent," in Bradley's series. I would prefer to say that it was very conspicuously uncommon in the Murton outbreak.

Diarrhoea.

Bradley stresses that diarrhoea was not severe. In the present series of cases, Bradley's description of watery stools, with hurried rather than very frequent action of the bowels, would apply to the great majority of cases.

So far, it may be agreed that the two outbreaks --- the one reported by Bradley and the other occurring in Murton-- show a similarity which might well indicate that they were in fact almost identical.

The further consideration will, I think, serve to further suggest that the illnesses were one and the same.

Under the heading "Physical Signs" Bradley goes on:--
"Central Nervous System."

"When a group of these cases were seen together the impression that the central nervous system was primarily involved was a strong one, particularly when signs of gastritis or enteritis were absent. There was no evidence of dehydration, severe intoxication or collapse. Routine examination of the central nervous system failed to detect any recognized signs apart from a suspicion of mydriasis with sluggish ocular reflexes. Widely dilated pupils were observed in some children on the first and second days of the disorder. Although the school children remained limp and tired for a few days, they returned to classwork when nausea and vomiting had ceased, and their teachers did not notice any lack of co-ordination, precision or concentration following the attack."

I have quoted this paragraph in full, because it got down, as it were, to Bradley's impression of the epidemic. I have previously tried to convey to the reader the impression made on me when a series of those cases were seen. On pages 252-254 319, 524 I discuss the matter at some length, and I would advise and request the reader to again peruse those pages and compare them with the exerpt from Bradley's article. Bradley, the expert investigator, formed his impressions in an inspection and review lasting a few days. The writer, an amateur novice,

hoped that the fact that he had spent a year in forming his impressions, might excuse his temerity in comparing such impressions as he had formed, with those of such an eminent epidemiologist.

Bradley's description, it was described as a preliminary report, is obviously curtailed to dimensions feasible in an article in the British Medical Journal. I think the words: "when a group of those cases were seen together" are significant.

I have stressed that the facies, posture and general appearance, as well as the demeanour and the address of the patient, created an unmistakable and indeed distinctive impression. I have compared that impression with that occurring in Encephalitis lethargica in 1924. I felt that we are entitled to think that in some similar way some closely comparable impression was formed by Bradley. The reference to the ocular reflexes etc. is particularly interesting. It may be considered that the histories of visual disturbances which are given in this work indeed do much to establish the identity of the two outbreaks, and may even possibly help to illustrate that the general practitioner can do much to substantiate and augment the findings of the expert.

Temperature and Pulse.

It is interesting to note that while Bradley did not find bradycardia in his cases, he states that Gray did so. The occasional occurrence of bradycardia

in the present (Murton) series has been noted and especially I have remarked on it as being conspicuous when there was a moderate to sharp rise of temperature.

Alimentary System.

Bradley's cases showed a moist tongue. I have remarked on how frequently the tongue was moist, and this even when the patient complained of the mouth being dry. The changes in the tongue, the light fur and the prominent papillae etc., are strikingly similar to those seen in Murton. In the more seriously ill patients at Murton the changes seen above were preceded by an initial phase during which the tongue was uniformly coated and not so moist. Here again the similarities far outweigh the differences especially as we note that some of the cases at Murton were ill for a more prolonged period, and some of the cases were rather severe. In all ambulant cases and in all mildly to moderately ill patients in Murton, a moist tongue was typical of the outbreak.

.....

There was apparently one definite difference between the Epidemic Nausea and Vomiting of Rischel and Henningson (Denmark), Miller and Raven (Thanet), Gray (Hayling Island) and Bradley and the illness at Murton. That was that the former illness had an incubation period of 2 to 7 days, whereas I considered that the Murton illness had an incubation period of about a month (18 to 35 days). Bradley said "the

incubation period was probably within the range of from 2 to 7 days, but could not be determined accurately."

I feel that if we consider carefully all the data of the outbreak as Bradley recorded it, we can equally well support the view that the incubation period may have been in the neighbourhood of 3 to 5 weeks.

For instance, when discussing "family outbreaks" he writes: "By asking a few individual patients whether their friends or acquaintances had suffered from a similar condition, a number of family outbreaks were brought to light. Chronologically the earliest involvement detected preceded the present events by 5 weeks." (Bradley's account recorded observations made on Oct 30 to Nov. 3, 1943.)

We are not told to which patient this particular family was related, or which patient was friendly with them.

But the next reference to a family outbreak does tell us that M, a schoolgirl evacuee, was ill on 8 Oct, 1942, and that on the 10 October, J., another evacuee, was ill. Now, the two girls, M and J were membersof the 6th Form, which remained well until 3 weeks afterwards. Of the remaining 18 girls in the form, nine became ill -- On Oct 28 (one case), Oct 30 (two cases) Oct 31 (one case), Nov 2 (one case), Nov 3 (two cases), Nov 4 (one case) Nov 11 (one case) respectively.

By assuming that M might have been a possible source of infection from say 6th October, and that J may have consti-

tuted a source of infection until say 12 October, we would see that an incubation period ofnot less than 22 days need be assumed and similarly that in no case need it have exceeded 50 days, if we regard M and J as the source of all the infection in the 6th Form.

A reference to the original article in the British Medical Journal makes one or two facts clear.

The disease among the boarders was encountered mainly as an explosive outbreak, and there was a remarkably heavy attack rate, in the region of 50 per cent.

Bradley says "The timing of the outbreak on the sixth form girls was entirely different. All these girls lived in billets or with their families." As we have seen "M" and "J" (see above) were ill on 8th and 10th October, and 5 out of 18 of the girls in the form were ill between Oct 28th and Nov 11th as already detailed.

Bradley says that on November 5 at least 27 children out of 181 had been attacked and fresh cases were occurring.

Incidentally the report bore a very close resemblance to the report made by Cookson when he compared and contrasted the incidence and timing of attacks of Epidemic Hepatitis as they occurred in (a) elementary schools and (b) residential nurseries in Gloucestershire in 1943. It would indeed be difficult to find 2 reports dealing with 2 presumably different diseases which were so strikingly alike.

I considered that here we had yet anotner very suggestive similarity between infective Hepatitis and this Epidemic Nausea and Vomiting which I considered to be so remarkably like the epidemic in Murton.

I would sum up the comparison between the Murton epidemic and that described by Bradley by saying that they appeared to be very much alike: and that they strongly resembled infective Hepatitis in symptomatology and probably in their incubation periods and modes of spread.

.....

A final word in Epidemic Nausea and Vomiting, again a quotation from the article cited.

"Although the disease is of minor significance clinically & economically it may give rise to considerable administrative uncertainty. Those who are unfamiliar with the clinical and epidemiological picture may be led to suspect food poisoning or dysentery and be stampeded into ineffectual and wasteful action. It is important that at the present time "Epidemic Nausea" should be considered in the differential diagnosis of all outbreaks of gastro enteritis....."

This not only made me think of Dr. Wilkin's gastro enteritis epidemic following upon his epidemic of jaundice (see page 279) or of the cases which had presented as apparently gastro enteritis in Murton. When I visited a medical colleague, I would look over the counterfoils in his National Health Insurance Certificate of Incapacity books,

and there I saw entered - "gastritis", "enteritis", "gastro enteritis", "gastric influenze" etc. very frequently.

My friends agreed that it was unusual, at least for us in County Durham, to have such an outbreak occurring in the winter months and also still continuing in March (I write this page on 13/3/1945.)

"Gastric Influenza." That was a diagnosis which frankly I had never had the courage to make. It may so be that I have simply not numbered an outbreak of gastric influenza among my experiences since I qualified. I can only state that what I have read about it, what I have othefwise heard about it, and my experience in general practice, left me unconvinced that there was a definite clinical entity "Gastric influenza"; granted that my experience and my reading might both be considered inadequate to justify the forming of such an opinion. But in practice one does form such opinions and while it is possibly taking a safer line to say that every case or group of cases should be approached with an open mind, decisions have to be made, and a little well-considered bias is sometimes inevitable and indeed possibly not to be condemned.

I decided to compare the Murton epidemic with some of the descriptions given of epidemics of gastric influenza. Horder and Gow's contribution to Price's Textbook of the Practice of Medicine (London 1942) read:--

"The gastro intestinal type.

More strictly, perhaps, the gastric and the intestinal types. These types are less common in pandemics and epidemics than in small endemics and in sporadic cases. The gastric cases are quite common, and some of the milder endemics seem to breed true to a remarkable degree in this respect, leading to a very constant clinical picture of an illness with acute, even abrupt, onset, vomiting, marked anorexia, epigastric and umbilical tenderness, and general prostration. Considerable difficulty often arises in diagnosis; even when there are several casesof a similar kind prevalent. Jaundice of a catarrhal kind is not very uncommon as a complication."

This paragraph interested me greatly. The very brief description, or summary of the symptoms, bore a very close resemblance to those of the illnesses at Murton.

Even the abrupt onset, the only apparent difference in the symptomatology, had been frequently observed at Murton, (although it had been preceded by prodromal symptoms.) FREQUENTLY ✓

As will be readily understood, I was very interested in the mention of catarrhal jaundice as a not very uncommon complication.

A further reason why I did not regard many of the "gastro intestinal" cases in the Murton outbreak as being of an influenzal type was that in my reading of very recent articles

on influenza, the absence of any reference to gastric influenza was conspicuous.

Van Rooyen and Rhodes[2], who deal with the disease, or diseases, at some length, do not mention gastric influenza in their "Virus Diseases of Man." (1940).

Nor does Stewart-Harris describe gastric influenza in the abridgement of his Goulstonian lectures which he delivered to the Royal College of Physicians in January, 1945. Although he discusses in some detail the diagnosis of influenza and even the question of the differential diagnosis of the types of influenza -- e.g. influenza A., influenza B., and influenza Y- he makes no reference to cases of the type described above by Horder and Gow.

I was convinced that the epidemic in Murton was not an epidemic of gastric influenza; I suspected that the "gastritis" "gastro enteritis" and "gastric influenza" of my colleagues was the same illness as I had encountered in Murton.

In fact I wondered if there was no such disease as gastric influenza, what the gastro intestinal type of influenza, as above described by Horder and Gow, really was.

The reader may think it an impertinence on my part, but I was convinced that the correct way for me to reason out this matter was not to say that the Murton cases resembled the "gastric influenza" of Horder and Gow -- but on the contrary to say that the casesof Horder and Gow resembled the cases at Murton.

Indeed the resemblance to the cases at Murton was rendered the more striking by the fact that cases of "jaundice" were present in the communities at the same time.

Of topical interest is a question by a correspondent in the British Medical Journal of 21st April, 1945. It is as follows:-

"I have been attending many cases of abdominal influenza with severe and continuous pain in the upper abdomen, slight vomiting but no bowel action. The pain persists for 10 days, gradually lessening. Sometimes there was a less severe repetition. The temperature is about 100 - 102°F....."

The answer given reads: (the reader must judge of its "standing").

"We may take leave to doubt whether such a condition as "abdominal influenza" actually exists. Certainly there seems to be no evidence that influenza virus or antibodies have been demonstrated in cases so classified. Most illnesses of this kind are salmonella infections, acquired from water, food, or carriers..... A less common cause of symptoms of this type is a sub-icteric attack of infective Hepatitis."

Here we not only had the opinion that there was, probably, no such thing as abdominal influenza, but the statement that some of the cases really represented sub-icteric attacks of infective hepatitis.

To recapitulate in trying to find a description of an

outbreak similar to the outbreak which occurred in Murton in 1944 and 1945 I had considered Epidemic Nausea and Vomiting and Gastric Influenza.

I had concluded that Epidemic Nausea and Vomiting not only bore a remarkable similarity to the Murton outbreak but that (like the latter) it had many points of resemblance symptomatologically and epidemiologically to infective Hepatitis.

I believed that gastric influenza was a misnomer and I further believed that there were indications that some of the cases or series of cases may have closely resembled the outbreak at Murton.

The so called Gastric Influenza of Horder and Gow referred to catarrhal jaundice as a not very uncommon complication. My colleagues' cases of so called gastric influenza were occurring in communities where infective hepatitis was present or had recently occurred.

Finally the Murton epidemic began after and continued throughout the occurrence of infective Hepatitis in Murton.

In trying to correlate the facts which I had observed, I began to think that a likely explanation might be:-

Infective Hepatitis, sub-icteric casesof infective hepatitis, the Murton epidemic (excluding jaundice patients for the present)Bradley's outbreak of Epidemic Nausea and Vomiting Dr. Wilkin's uncommon outbreak of gastro-enteritis, my neighbouring colleagues' cases of gastric influenza, and many

of the series of cases of gastric influenza described by others; they might all be essentially variations in the one basic disease: or they might all be diseases due to one agent, probably a virus.

Having considered the matter so far from a broad viewpoint, including in the consideration the work of others, let us return to the rather narrower but closer comparisons which we can base on the two local epidemics.

In a recent report of "an outbreak of jaundice with signs in the nervous system" Byrne and Taylor[3] remark on the scant reference in the literature to lesions of the nervous system in casesof infective hepatitis.

I consider that a careful study of their very brief article will go a long way towards convincing the reader that I may well be justified in believing that the two epidemics in Murton were related. The authors point out that

1. In 170 cases studied by Cameron (1943) the only neurological sign noted was a temporary paresis of accommodation in two cases.

2. Newman (1942) refers to severe headache and to the occasional occurrence of paraesthesia in the limbs.

3. Brain (1943) refers to one case in which unilateral convulsions and a hemiplegia togetner with mild polyneuritic signs, preceded theonset of jaundice.

4. Tescher (1944) describes a case where a generalized polyneuritis was followed one week later by jaundice (during an epidemic of infective hepatitis). They then refer to their 'own cases', numbering five. "The cases which are the subject of this note show the association of lesions of the nervous system with jaundice in several individuals being in close proximity." The 4 men -one was an officer - went sick within 48 hours of each other, the symptoms including:- severe headache, dizziness, pyrexia, pains behind the eyes, a "pins and needles" or tingling sensation in the arms and legs, loss of muscular power especially in the lower limbs.

Some degree of dimness of vision was noticed by each of the patients. Later we are told that there was definite sensory loss in the thigh, on the anterior surface in one case and, in another, along the posterior surface.

The cerebro spinal fluid was abnormal in 3 of the cases. In two, a clot developed 15 minutes after the fluid had been withdrawn. The protein content was increased in 5 cases. Cell counts were 23, 14 and 11 lymphocytes per c.mm.

Three of the five patients made a complete recovery within two months. In the remaining two "a mild residual spastic paresis of the lower limbs, with in one case sensory loss peripherally, was still present several months later."

The authors considered that the cases represented "a condition characterised by the association of jaundice with meningitis, peripheral neuritis, and less constantly, myelitis."

I must remark on the fact that "the total and differential white counts were normal."

.....

Which of the symptoms enumerated had been seen in Murton? I have mentioned as occurring among the jaundiced cases (page 459) in my series.

"Pins and needles sensation" -- Tingling -in the hands.

Visual Disturbances.

Disturbance of Hearing.

Disturbance of Voice.

Disturbance of Micturition.

Now it seemed very significant that in the epidemic of which jaundice was not a feature the neurological manifestation were similar to those which I have enumerated as occurring in the jaundiced patients and also resembled the symptoms collected by Byrne and Taylor in the article referred to.

Let us briefly consider the neurological symptoms as they have been mentioned in each section of this work.

Cold Hesledon Group. (pages 165,-276).

"Visual disturbance - an inability to see clearly especially after looking in an altered direction was noted in 2 cases.... the appearance of drooping of the eyelids was also very marked."

(Pins and needles) Paresthesia in the hands associated with little darting "needle-like" pains in the fingers and hands

were described in one case.

I also included a reference to a sensation as if the throat was swollen at the thyrohyoid level, and that some patients said that it required an effort to swallow.

Several of the patients felt drowsy all day and kept falling asleep, but at night they could not sleep.

Bakery Group (pages 314 to 326).

Among the neurological symptoms mentioned were:-- Pains in the limbs, ptosis, complaint of marked mental dulness, insomnia, paraesthesiae, visual disturbance, transient deafness nocturnal enuresis. Lethargy was marked. The facies suggested that the illness must have affected the central nervous system.

Non Jaundiced cases at Murton.

In the 25 cases considered in pages 548 to 589in addition to the listlessness and lethargy which were noted in all groups -- I include references to aches and pains, "pins and needles", visual disturbances, "shooting" or stabbing pains.

In the 50 cases considered in pages 590-669 the further references to neurological symptoms include mention and discussion of visual disturbances, in no fewer than 11(selected) cases: a sensation of choking or dysphagia in 6;stabbing pains in 5 instances. Weakness of the limbs and inco-ordination were noted. A peculiar complaint was that the patient sometimes felt as if a limb "was not there," as described in the text. Further, I have dealt at some length, with a "feeling of mental dulness." Areas of analgesia and anaesthesia were

discovered in a few cases -- occurring in the lower limbs.

From this brief catalogue of the nervous symptoms encountered in the patients who were jaundiced and in those who were not jaundiced, it may appear that the resemblance between nervous manifestations in both epidemics is not only interesting but arresting. To complete the resemblance I should add that disturbances of voice, of hearing and of micturition also occurred in the non jaundiced cases as well as in jaundice patients: and they are described in the text.

The symptoms also bear close comparison with those as described by Byrne and Taylor as occurring in the outbreaks described by others, and the small series of cases which they illustrate. The reader can readily appreciate this if he remembers or refers to the extract from their article. The fatal illnesses of T. Walshaw (page 216) and V. Cutmore(p719) are also worthy of the reader's consideration in this connection.

From such considerations as those which I have detailed in this section of the work, and from other circumstances which I have attempted to relate, the reader may have observed in the course of this work generally, I came to believe that the two epidemics occurring in Murton in 1944/1945 were closely related.

I believed that several of the illnesses definitely represented instances of sub-icteric infective hepatitis.

For example there seemed no reasonable doubt that William and Henry Lavery (page 536) were infected by their jaundiced sister and suffered from sub-icteric infective hepatitis. The symptoms in the illnessesof those two children could not be distinguished from those found in the illnesses of many others who likewise did not become jaundiced, but in the case of whom we could not trace contact with a jaundiced patient.

It would be correct to state that I thought therefore that we had had in the area an epidemic of infective hepatitis accompanied by jaundice, and an epidemic of sub-icteric infective hepatitis --- but I think that this would be over-simplifying the position. It is frequently stated that an epidemic as encountered in an area like Murton, with a polulation of 10,000) frequently really comprises several minor epidemics -- for instance, I have remarked elsewhere (page 379) that the jaundiced patients were not all infected in Murton.

Similarly, I have no doubt, several of the patients who did not become jaundiced may have acquired their infection outside of the area. It would be anticipated therefore that, assuming the epidemics were due to a virus, there might be different strains of the causative virus present in Murton at the same time.

The virus of infective hepatitis possesses hepatotropic and neurotropic properties. I assumed that these properties might be present in varying proportion in various strains of the virus.

In this way we could understand the absence of jaundice in, for instance, the Bakery illnesses: the virus presumably being more markedly neurotropic and not so hepatotropic as in the early cases at Cold Hesledon. But even in the Bakery Group of cases, where no case of jaundice occurred, I believed that the symptoms were not to be fully explained by the action of a purely neurotropic virus.

In this connection it should be noted, as a reference to the case histories on pages 334 to 374 will show, that the onset of symptoms frequently occurred at a time when the blood sugar level would be relatively low, e.g. 5 am. to 8 am. (This was, indeed, a finding which I observed in a fairly large number of cases: not only in the Bakery outbreak). A consideration of the symptoms will reveal a marked resemblance in many cases to those of a mild hypoglycaemia --- the general feeling of weakness and listlessness, the mild mental vagueness and confusion, the dimness or mistiness of vision, the occurrence of "black outs", heavy sweatings and the moist tongue were all points of similarity which occurred to me. I wondered whether there might be a fleeting hypoglycaemia, but I was unable to have the blood sugar estimated

at the onset of the illnesses. Such a hypoglycaemia might have been due to a temporary derangement of the liver function of glycogenesis, and, if it did indeed occur as I suspected, it would point to the action of an hepatotropic virus.

The presence of two or more strains of the virus and variations in the response of different individuals to infection would account for the differences in the clinical picture of the resulting illnesses.

Considering the illnesses in which jaundice did not occur— in many cases the resemblance to the "jaundiced illness" was extremely close, in others the 'nervous' element in the symptomatology was more prominent, and many illnesses showed symptoms intermediate between those two groups.

Thus while many of the illnesses could be stated confidently to typify sub-icteric hepatitis and would be assumed to be due to the virus of infective hepatitis, a group of cases such as those at the bakery seemed to point to the presence of a virus possessing properties which were less actively hepato-tropic and relatively more neurotropic.

In the following pages I have reproduced for the convenience of the reader simplified tables of the Symptomatology in each group of cases which has previously been described.

While this will allow of a rough and ready comparison at a glance, reference to the original tables will ultimately be more satisfactory.

I also reproduce for comparison modified tables of the Symptomatology as described on pages 121 et seq in Homologous Serum Jaundice.

In order to keep this work within reasonable bounds I do not propose to proceed to a detailed comparison of the symptoms in Homologous Serum Jaundice and in the illnesses at Murton which included Jaundice as a symptom, and those in which Jaundice was not a feature.

Such comparison the reader can easily make for himself from the data which I have already provided.

I would particularly ask him to compare the less frequently encountered symptoms.

COLD HESLEDON GROUP. GROUP 1.

See Page 251.

Symptomatology.

Headache
Vomiting
Nausea
Anorexia
Vertigo
Abdominal Pain
Diarrhoea
Lethargy
Pains in Limbs
Paræsthesia
Bronchitis
Atypical pneumonia
Conjunctivitis
Epistaxis
Feeling of Chill
Dysphagia
Rhinorrhoea
Visual Disturbances
Biphasic illness
Typical Facies
Temperature
Urobilinuria
Jaundice
Relative Lymphocytosis

BAKERY GROUP. GROUP 3 (See page 514).

Symptomatology. 22 Cases considered.

1. A relative lymphocytosis occurred in all 15 patients whose differential white cell count was estimated.

	Cases
2. Headache	16
3. Nausea	16
4. Giddiness	15
5. Abdominal Pain (a) Majority were tender	13
6. Vomiting	12
7. Lethargy	12
8. Marked Anorexia	11
9. Diarrhoea	9
10. Pains in the limbs	9
11. Marked Feeling of Weakness	8
12. Heavy Sweating	7
13. Rhinorrhoea (mainly in relapses or recurrences)	6
14. Conjunctivitis	5
15. "Ptosis"	5
16. Bronchitis	5
17. Distinct from 15. Tightness round the chest: a sense of restriction or constriction	5
18. Marked Mental dulness, complaint of	5
19. The facies of the disease	Very frequently typical.

Additional. Insomnia. Paraesthesia, Cramps, 'Bad taste,' Visual disturbance, Transient deafness, Nocturnal enuresis, Menstrual disturbance, Feeling of 'chill,' Urobilinuria, Itch.

The onset frequently occurred at certain times of day.

Relapse occurred in 5 cases.

Recurrence occurred in 3 cases.

"JAUNDICED ILLNESSES IN MURTON" GROUP 4.

See Page 460.

Number in Group 44

Excluding Cases A and B... 42

Jaundice..... 41

Bile in urine but no jaundice...1

Jaundice but no bile in urine...1

Vomiting	30
Abdominal Pain	29
Anorexia	27
Marked Lethargy	27
Headache	18
Vertigo	14
Skin eruptions	8
Liver palpable	7
Upper Respiratory catarrh	7
Itchiness of skin	7
Conjunctivitis	6
Diarrhoea	4
Marked constipation	3
Association with Parotitis	2
Hiccough	2
Herpes Simplex	1

A relative lymphocytosis was present in all, 8 cases, in which the examination was conducted.

Also noted. Pains in the limbs

Pins and needles sensation.

Visual Disturbances.

Disturbance of Hearing.

Disturbance of Voice.

Disturbance of Micturition.

Noteworthy was the condition of the tongue.

"NON JAUNDICED" ILLNESSES IN MURTON. GROUP 5.

See page 556.

These are the cases in which a differential leucocyte count was made.

Number of illnesses.....25

Average Lymphocyte count..44%

Lethargy.....21

Headache.....17

Vomiting.....15

Lower Thoracic and Abdominal pain.....14

Vertigo.....13

Anorexia.....12

Aches and pains..... 5

"Pins and needles"..... 4

Diarrhoea..... 4

Visual Disturbance..... 3

"Joint" Pains..... 4

Also noted.

Relapse	Urticaria
Epistaxis	"Shooting" pains
Menstrual Disturbance.	Conjunctivitis.

JAUNDICED ILLNESSES IN MURTON. GROUP 6.

See Page 591.

NUMBER OF CASES DESCRIBED.....50.

Vomiting	30
Vertigo	25
Headache	25
Lethargy	24
Anorexia	21
Diarrhoea	18
Nausea	16
Upper Respiratory Catarrh	14
Abdominal pain	13
A feeling of mental dullness	15
Visual disturbances	11
Sensation of choking Dysphagia etc.	6
Stabbing Pains (darts, needles)	5
Marked prodromata	15

Also noted were Weakness and in-cordination in the limbs, Bradycardia, Relapses, Skin Rashes, Dyspnoea, Insomnia, Urobilinogenuria, "Tight feeling" in the chest, a peculiar sensation that the limbs were "not there."

HOMOLOGOUS SERUM JAUNDICE. See Page 124.

Presenting symptoms in order of frequency.

Loss of appetite
Nausea
Lassitude
Epigastric pain
Bad taste in mouth
Constipation
Vomiting and retching
Headache
Diarrhoea
Upper abdominal pain
Flatulence
Giddiness
Fever
Backache
Joint pains
Mental depression
Itchiness (pruritus).
Sore throat
Insomnia
Heartburn
Pain at back of the neck
Blackout
Palpitation
Muscle pains
Blood vision
Hiccough
Dysphagia

Liver enlarged
Bile in urine
Jaundice
Spleen enlarged
Light stools
Skin rashes

HOMOLOGOUS SERUM JAUNDICE. See Page 125.

Aggregate Symptoms in Order of Frequency.

Anorexia
Nausea
Epigastric pain
Bad taste in mouth
Vomiting or retching
Lassitude
Constipation
Headache
Upper abdominal pain
Diarrhoea
Flatulence
Giddiness
Backache
Joint pains
Insomnia
Fever
Itchiness (pruritus)
Heartburn
Mental depression
Sore throat
Pain in back
Hiccough
Muscle pains
Palpitation
Blurred vision
Dysphagia
Biliary colic
Pain at back of neck
Blackout
Dysuria. Urinary incontinence
Deafness. Profuse sweats.
Extreme restlessness.

REFERENCES.

1. Bradley W.H. B. M. J. 1943 Vol 1 p 309

2. van Rooyan C.E. and Rhodes A.J. Virus Dis. in man. p 540. London 1940.

3. Byrne E. A. J., and Taylor G. F. B. M. J. 1945. p 477.

BRIEF REVIEW, SUMMARY AND CONCLUSIONS.

Part I of this work calls for little descriptive comment at this stage. The contents of this section of the work are summarised in the table which precedes it.

After a brief reference to the finer anatomy of the liver lobule, I have discussed the more important features of the physiology of the liver. A discussion on 'jaundice' is followed by a review of the liver function tests.

The recent pathological findings in 'hepatitis' are then detailed. Next I include a section on diet and hepatitis.

Comparatively recent findings and views on post arsphenamine and homologous serum jaundice are discussed. After devoting a section to viruses and their role in the diseases of man, I conclude the first part of this work by indicating the present day views on the epidemiology of infective hepatitis.

.....

Part II constitutes the section of the thesis dealing with the original observations of the writer.

In it I have attempted to provide the reader with an account of an epidemic of infective hepatitis which occurred in Murton, County Durham, area, commencing in the spring of 1944 and continuing for over a year.

My original intention was to determine if possible

1. The incubation period.

2. The mode of spread.

3. The symptomatology.

Presently I shall summarise the findings and my views in each of those matters. 1, 2, and 3.

4. Whilst I had originally intended to limit my observations to the occurrence of cases of infective hepatitis, I subsequently devoted much of my time and studyto other cases of an illness which assumed epidemic proportions, and which I considered was related to the infective hepatitis epidemic. They were illnesses of a type which had not occurred, or certainly not occurred in anything approaching such large numbers, in the Murton area in the past 21 years. An attempt has been made to justify the suggestion that the numerous illnesses referred to were indeed related to infective hepatitis. The incubation period, the mode of spread, and the detailed symptomatology are discussed and compared with those obtaining in infective hepatitis. A large number of differential leucocyte counts are provided in this comparison.

5. I have compared the epidemic illnesses at Murton, including the 'bakery outbreak', which did not feature jaundice, with Bradley's account of "Epidemic Nausea and Vomiting" and with accounts of epidemics of so-called "Gastric Influenza": and I have sought to imply that the

Murton epidemic illnesses may be identical or very closely related to the former and to at least some of the latter.

6. The acceptance, or serious consideration of my theory of the relation of this epidemic illness, 4, to the epidemic of infective hepatitis might throw light on the epidemiology not only of infective hepatitis but of many other infectious illnesses. A tentative suggestion has been made as to how an epidemic may apparently 'disappear' from a community only to re-appear at some later date.

7. It is further suggested that a consideration of this review of the two epidemic illnesses which occurred in this area in 1944-1945 may offer the reader, so interested, food for thought and material for consideration with regard to the life history, or the fate, of viruses in the human body.

8. I consider that a careful study of several of the illnesses encountered and described may have a bearing on the aetiology of post arsenical and homologous serum jaundice. Such illnesses may indicate how the serum of patients who have 'never' suffered from an illness featuring jaundice, may have become icterogenic.

1. THE INCUBATION PERIOD IN INFECTIVE HEPATITIS.

This is usually stated to be from 3 to 5 weeks, and with this generalization I agree.

The shortest period I believed to be 18 days (Sheach to Oliver. "Infective Hepatitis in Murton") I could not deny the possibility that it may have been a little longer.

The longest period was 36 days. A period of 35 days was indicated in 2 or 3 instances in the Cold Hesledon epidemic. I was very greatly interested in those cases in which the patient had been infected outside Murton.

By far my most interesting and convincing evidence came from the far distant Elgin. I feel that the illnesses of the brothers SHEACH, one being ill in Elgin, the other being my patient in Murton, do illustrate satisfactorily and convincingly that the incubation period was 28 to 24 days from infection to the onset of symptoms; and 36 to 32 days to the onset of jaundice. The account of the circumstances of the brothers' illnesses is included in "Infective Hepatitis in Murton" and I refer the reader to this account hoping that it will convince him, as it impressed me. Throughout the work I have stated the incubation periods where evidence allowed of their being estimated.

Whilst my findings in general agreed with those generally accepted I thought it likely that the incubation period may be very occasionally probably, as long as 2, 3, or 4 months.

Two illnesses appeared definitely to point to this occasional occurrence. The reader is referred to the illnesses of Dorothy B. Elliott ("The Elliotts" page 670) and to the comparable illnesses of Moira Forster (Forster Sugden Newton Group, page 679).

My interpretation of the illnesses was that they probably pointed to incubation periods of about 3 months and 4 months respectively. Less convincing to me, although still suggestive, were the illnesses of Iris Etherington where the incubation period may have approximated to 3 months; I have referred to her illnesses in the Cold Hesledon epidemic under the heading "The Vague Illness prior to the Jaundiced Illness," "Uncommon illnesses," and "Argument and Interpretation."

2. THE MODE OF SPREAD.

This is dealt with at some length as a leading feature of this study, especially in the section of the thesis entitled "Infective Hepatitis in Murton."

I believed that the disease was not spread by any form of aerial infection but by 'contact.' By 'contact' I mean actual contact with an infected patient, or contact with something which such a patient has handled, or consumption of food which has similarly been contaminated. Faecal contamination via the fingers was considered to be a likely agent in the spread of the disease.

The sources of the epidemic were believed to be relatively fairly numerous: or, as has been elsewhere stated, the epidemic really constituted the aggregate of several component epidemics.

In this way, whilst the possibility of a spread in the schools was not denied it was definitely not the predominant method of spread. The facts pointed to the spread being dependant on very intimate association and the home was a much more important factor than the school. It seemed likely that the contamination of foodstuffs after purchase was in part responsible for the influence of the home and intimate social intercourse on the spread of the disease.

I believed that locality had nothing to do in itself with the spread of the disease. Mere proximity did not determine the spread; it simply acted by favouring more intimate association and contact, direct or indirect. Children who sat, as it were, 'ringed round' an infected child did not become jaundiced, nor did they develop illnesses which might indicate either mild or anomalous attacks.

My view was that the infection was not always contracted from a person who was jaundiced but that people suffering from atypical or mild attacks were probably an important source of infection. I believed that the manifestations of such attacks were more protean than had hitherto been suggested. At the end of 5 of this group, I reproduce a summary of my views on the spread of the infection from patient to patient.

3. The SYMPTOMATOLOGY.

This has been reviewed in respect of the Cold Hesledon patients and in the Murton patients, in the appropriate sections of the work. I have described and commented upon the commonly encountered symptoms such as jaundice, vomiting, abdominal pain, anorexia, lethargy, headache, constipation or diarrhoea, upper respiratory catarrh, itching of the skin, and vertigo, and in 8 cases I have recorded the findings of the differential leucocyte count. Whilst I trust that the records of such symptoms are sufficiently stressed and detailed, I have felt that many of them are symptoms common to many of the more vague and indefinite infections and illnesses frequently encountered in general practice.

I therefore took particular note of symptoms which because of their rather uncommon occurrence in practice may be accepted as being more distinctive. The reader will learn, from the narrative, of the striking visual disturbances which were not uncommonly remarked.

The media, the fundus of the eye and the optic disc showed no abnormalities and I ascribed the symptoms mainly to disturbance of accommodation.

Paraesthesia was occasionally noted: it was described as a "pins and needles" sensation.

Perhaps more striking were 'darting pains' -- they varied from very small fine darting pains to rather coarser pains of

the same type, and I thought that they assumed especial significance when we consider the recent accounts of neurological manifestations in infective hepatitis; to me they suggested that the illnesses of Walshaw (Cold Hesledon Group) and Cutmore (3 Fatal Illnesses) may have been caused by the same virus.

The complaint that an arm felt "as if it was not there" was made several times and the patients actually kept feeling the arm with the unaffected hand to dispel this illusion.

Disturbances of hearing, of voice, and of micturition are mentioned.

In the sections entitled "3 Fatal Illnesses" and "Some Uncommon Illnesses" I have invited the reader to study the case histories recorded and to consider in the light of the symptomatology of the epidemic as a whole, my suggestion that the majority of these illnesses were related to the epidemic illness.

4. The Epidemic Illness in which Jaundice was not a Symptom. Its relation to Infective Hepatitis.

Throughout the work generally and more especially in the sections "The Outbreak at the Bakery"

"Non Jaundiced Patients at Murton - The Differential Leucocyte Count"

"Non Jaundiced patients at Murton. A Typical Cross section of the Epidemic"

I have made frequent and, in some respects, detailed reference to the occurrence of a "new" illness in the area.

In all there will be over 100 histories of such illnesses. These 100 cases were selected from some 600 illnesses which I recorded in this way during the 12 months under review.

In order to attempt to illustrate the resemblances between this "new" illness and the cases of Infective Hepatitis, a resemblance which not only I myself but many of my more intelligent and observant patients and friends had noticed, I was keen to find some test which might be convincing.

The occurrence of subicteric tints of the conjunctiva and skin did not attract me as being a suitable test. Above all it was a test too readily influenced by 'suggestion' and I had to avoid looking at the illnesses with a 'jaundiced eye.' Although I employed Klein's Intradermal Histamine test I thought that the reading of the reaction was again

open to this same objection.

The differential leucocyte count appealed to me as a possibly convincing comparative test. I thought that the finding of a relative lymphocytosis in this "new" illness comparable to the findings in infective hepatitis would be impressive. I therefore made films in a considerable number of the illnesses, and I have reproduced the counts in probably upwards of 60 cases. The great majority of those blood films I have preserved as tangible evidence.

Here I must state that the actual counts were made for me by Dr. R. B. Thompson, then Senior Medical Registrar to Professor Nattrass at the Royal Victoria Infirmary, Newcastle. Not only was he an experienced haematologist, but I could not have dealt with such a large number of films in the really few spare moments, with which the rest of my observations, in addition to my practice duties, left me daily. (This the reader may credit and understand when he remembers that I have recorded only a fraction of the work which I did in this period.)

I am now aware that a relative lymphocytosis occurs in many infections and that I possibly attached too great significance to its occurrence in the early stages of this enquiry.

Nevertheless I think that the findings which I have recorded are of significance as <u>one</u> feature in the comparison

of the symptomatology of the two epidemics.

As a check on the significance of the leucocyte counts I have arranged to have the total and differential leucocyte counts in the Bakery Group re-estimated to compare with the findings during the epidemic.

It is however on a comparison of the symptoms --- the history of the illnesses and the patients' complaints mainly -- that I have based my views.

In the preceding paragraph, 3, I have drawn attention to several less common but possibly more distinctive symptoms. The occurrence of such symptoms in both the epidemic featuring jaundice and the epidemic in which jaundice did not occur is discussed.

Additional symptoms commented upon include dysphagia always presenting at the thyrohyoid level; conjunctivitis and photophobia; disturbed sleep rhythm. In some cases in which jaundice did not occur the temperature--pulse ratio varied in a peculiar manner. The pulse remained slow in the presence of pyrexia at first but later rose to assume the usual relation. I have enumerated the skin eruptions met with and described the changes in the tongue. A striking feature was that muscle soreness, stiffness, or aches were complained of in certain well defined positions -- e. g. above the patellae.

The onset of symptoms in the early morning made me wonder

whether this might be occasioned by the relatively low blood sugar level present then. Right shoulder tip pain occurred in an occasional case. A feeling of constriction, of restriction in breathing sometimes accompanied by dyspnoea on exertion is recorded. Especially have I stressed the facies of the disease and the feeling of extreme fatigue and languor which dominated the picture.

In several instances I have analysed individual symptoms to permit of more intimate and detailed comparison.
5. In such a way have I sought to demonstrate, or at least suggest, that the "new" illness was related to infective hepatitis. The 'Bakery outbreak' to which I allot special mention tells of such an outbreak in a compact group of workers.

The incubation period, the mode of spread, and the symptomatology including the leucocyte counts, were all I believed similar to those found in my study of infective hepatitis. In many ways I consider this 'Bakery outbreak' to be an important feature of this work. The cases are comparatively few and they allow of ready comparison with not only cases of infective hepatitis but, as I have illustrated, with epidemics of Epidemic Nausea and Vomiting and Gastric Influenza. Such a comparison is contained in "The Interpretation of the Simultaneous Occurrence of the Two Epidemic Illnesses," where all cases of the 'new' illness are considered in the discussion.

Further note on the "Spread of the infection."

I am now in a position to supplement paragraph 2 by including here a summary of my views in the case-to-case spread of the infection ---a similar summary is included on page 449.

(a) A person who was jaundiced could infect another person, who, in turn, in about a month would become jaundiced.

(b) A person who was jaundiced could infect another person who might develop an illness so closely resembling a fully developed picture of infective hepatitis that the only difference was that jaundice did not occur.

(c) A jaundiced person might infect another person who might develop an illness less closely simulating " a fully developed infective hepatitis" than did (b): frequently the difference between (b) and (c) lay in the relative prominence of "nervous" symptoms and the less prominent gastro-intestinal symptoms, both, in the latter group.

(d) A person who contracted an infection leading as in (b) to an illness simulating infective hepatitis but without jaundice, might continue to harbour that infection and, subsequently, two or three months later, become jaundiced: the virus at this late stage exerting its full hepatotoxic action.

(e) A person such as Dorothy Elliott (see "The Elliotts") group (d) above, could in the early stages of her initial

illness, infect others, and such others might become jaundiced.

(f) A person such as (b) and (c) above, who suffered from the 'epidemic' illness might convey the infection to others.

Such others would in most instances suffer from an illness of the type described under (b) or (c), but in the case of (b) certainly and in the case of (c) possibly, and I thought only occasionally, such others might become jaundiced.

6. I have entitled a small section of the work --- "The Epidemic. Genesis, Course and Exodus." I suggest that the epidemic does not simply exhaust itself after all or a particular percentage of the susceptibles have been infected but that the epidemic illness gradually becomes less distinctive, or specific. I suggest that the virus responsible for the disease probably remains in the community in an altered state between epidemics.

In this connection I would mention that I have recently had another case of infective hepatitis. I attended Alan Shaw for a typical attack of infective hepatitis with jaundice which began on 10 July, 1945.

His twin brother was ill on 5 June, 1945. I did not attend him, but the history was of an illness identical with Alan's except that jaundice did not occur or was not observed.

Neither child had been away from home and I believe that the infection was contracted in Murton. My theory is that the infection had not really 'disappeared' from the community in this interval.

7 and 8.

These suggestions are considered in several portions of the work but more especially in the section entitled

"Infective Hepatitis in Murton."

My impression based on a consideration of the 3 illnesses of the "Elliott" children, and of others detailed, and in the light of my study in general, is that infective hepatitis is spread by a virus in an unaltered state, probably via the excreta, mainly the faeces: whereas post arsphenamine and homologous serum jaundice are caused by the virus which has been altered in the human body.

It may well be that the diversity of the incubation periods may not therefore be determined so much by the route of introduction of the icterogenic agent, as by the fact that the agent introduced by various routes may not, in fact, be identical, in each case. To me it seems that a pathogenic agent which is present in the 'prima via' and in the faeces is certain to be considerably modified after it enters the human blood stream.

Careful clinical observation of several patients led me to believe that the virus of infective hepatitis frequently

existed for a long time in the body and that its distribution in the tissues might be more widespread than would be inferred by a literal interpretation of the term "hepatitis."

I have attempted to indicate how a consideration of the life history or fate of the virus in the body, as deduced from such illnesses may throw light on the problems of post arsephenamine and homologous serum jaundice.

Finally, whilst I have not provided the reader with a detailed comparison of the symptoms encountered in Homologous Serum Jaundice and in the illnesses at Murton, which did not feature jaundice, I have nevertheless provided sufficient data for the making of such a comparison. Indeed, in the section of the work devoted to Homologous Serum Jaundice on Pages 121 to 146 I have made several references to such a comparison.

A study of that section of the work will illustrate the similarities and this the work generally will supplement.

The Prevalence of an Epidemic Disease in Great Britain.

The Prevalence of an Epidemic Illness in Great Britain.

N.B.

When one has devoted every spare moment of a whole year to the investigation of an epidemic, as I have done, it is only to be anticipated that he should at one moment be strongly convinced of the definite identity of that epidemic, and that at other times he may wonder whether his study has tended to be an obsession: in this way one may question the value of the observations which he has made.

I have already referred to the prevalence of epidemic diarrhoea etc. as reported in the lay and medical Press. I have quoted Dr. Wilkins' letter and now I should like to refer to one other letter.

In November, 1944, I wrote to the employers of a patient whom I attended for an attack of the epidemic illness to inquire re illnesses among her fellow workers. The reply which I received was possibly none the less suggestive by reason of having been written by a lay person. I retained for inspection the original reply which was in accord with the information which I, at other times, (e.g. in the Bakery Outbreak) received on verbal inquiry.

"In order to assist your investigation, I have looked through the "sick notes" which we have filed, and on finding several cases of "Gastritis" recently I

have questioned three girls who are now back at work.

The following are the names of the girls, their doctors and the symptoms as they gave them to me. They do not sit close to each other.

L. Stubbs. (Dr. H.) "Sick note" 24 Oct. 1944 -Gastritis. Felt sick and dizzy at work - also stomach pains. Went home, and was treated by doctor for "anaemia." No diarrhoea.

Two weeks later was about to come to work when sickness, dizziness and stomach pains recurred. Vomited and had diarrhoea. Two days later rash broke out all over body - this cleared in about 2 days. Was away from work for further 2 weeks - a month in all.

A. Nash. (Dr. S.) "Sick note" 23 Oct 1944.-Gastritis.

Felt sick and dizzy and had stomach pains. Was in bed two days, but off work for two weeks under treatment. Rest of family all suffered in the same way and in a more severe form. Was told she was anaemic. Although back at work, fainted at "pictures" a few nights ago and frequently gets a dizzy feeling which soon passes off. No diarrhoea, no actual vomiting.

J. Winlow. (Dr. S.) "Sick note" 6 July, 1944-Gastritis.

Felt sick and dizzy, bad headache, pain in stomach.

Off work one week."

Finally I provide a cutting from the British Medical Journal of 11 August, 1945, which comprises an excerpt from an editorial article, dealing with the question of this epidemic illness.

The reference to Bradley's article is very interesting, in view of my earlier detailed discussion and analysis of 'his' epidemic.

Further comment is, I think, unnecessary.

The reader may be interested to note that I submitted this thesis to the bookbinders on 23rd August, 1945.

logically it is distinct from herpetic stomatitis; specific antibodies appeared in the blood of affected children.

It may be noted that an epidemic form of nausea, diarrhoea, and vomiting among adults, often diagnosed as "gastric flu," has in recent years been observed both here and in the U.S.A. Reimann and his colleagues[2] have given a detailed account of this type of infection, which they believe may be due to an air-borne enterotropic virus. Most commonly the first complaint is of epigastric discomfort and nausea (like sea-sickness), followed in a few hours by vomiting. Diarrhoea, if it occurs, is characterized by considerable abdominal discomfort. There is only slight fever or none at all, and the symptoms clear up in 1 to 2 days. Very few patients feel ill enough to go to bed or to call in a doctor. The syndrome is similar to that described in this *Journal* two years ago by Bradley,[3] except that diarrhoea was not prominent in the outbreaks he recorded. Hyperaemic tongue papillae and injected fauces, like the early stages of a streptococcal throat infection, were, however, commonly noted among his cases. Although there is apparently no special seasonal incidence for this infection, many of the recorded outbreaks occurred in late autumn. Attempts to isolate a specific bacterium or virus have failed, but Reimann and his colleagues reported some success in the transfer of infection to human volunteers who inhaled the sprayed filtered nasopharyngeal washings or stools of affected patients.

E P I L O G U E

EPILOGUE

When I first confessed my intention to embark upom a course of study to improve my knowledge of medicine, and with a view to the possibility of obtaining higher academic qualifications, to a learned and mature colleague, he counselled me in these words:-

"Don't forget the chicken ! " .

To be certain as to his meaning, I asked him to explain the phrase, and he explained that if confronted with a meal consisting of a chicken and all the accessory foods which, as we commonly say, "go with it", one should remember that the chicken is the main article of diet.

In the same way, the study of medicine has many byways which may detract the student from the main avenues.

Apparently my mentor thought I was tooprone to explore the byways.

He was learned; he was mature; perhaps he was right.

I feel that in the work which I have presented I have paid more attention to the accessory foods and relatively less to the chicken; I have left the arterial roads to explore the byways. How often do we find that the byways are so much more interesting than the main roads in any countryside! Certainly they lead us closer to the truths and secrets of nature.

If I have proved anything, or given any information that may lead others to the truth in the matters discussed, I may have justified my meanderings in the byways.

And I may respectfully suggest to my mentor that we add to his counsel the words, again colloquially expressed:

"Don't forget what goes with the chicken ! "

The End.