

OBSERVATIONS ON WASTING AS A SIGN

OF DISEASE IN INFANCY.

T H E S I S

Submitted for the

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by

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SECTION 1.

INTRODUCTION.

The problem of the wasted infant is essentially a social question, in that it involves - amongst other factors - the subjects of maternity services, infant and child-welfare clinics and the provision of a pure milk supply.

The birth of the vitamin doctrine was spread over many years, at the end of the last and the beginning of the present centuries, but the doctrine brought about a rapid advance in our knowledge of the dietary requirements of the human organism, and the abandonment of many beliefs previously held.

It is now generally accepted that the "true-foods", or "proximate principles", are insufficient to satisfy the needs of the animal for growth and maintenance of health; and that there exists a number of other dietary components, the "vitamines" of Funk, or better, the "accessory food factors" which are essential to life and health, which the body cannot synthesise and which are neither protein, fat, carbohydrate nor salts. These components continue to receive considerable attention and their importance to the question of the proper feeding of infants is well realised.

The subject of infantile wasting has occupied the medical and lay mind for a long time, and although the condition is not so often seen now as formerly, it is still sufficiently common to form a source of great trouble and anxiety.

While the condition is often due to prematurity, and to organic disease (such as pyloric stenosis, and syphilis), improper feeding starts the large majority of cases.

In the present thesis, an attempt will be made to describe clearly the present day views on the relationship between wasting and gastro-intestinal upset in infancy, improper feeding and vitamin lack.

A series of personal cases of infantile disease will be described and an endeavour made generally to add, in a small degree, to our knowledge of the subject.

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SECTION 2.

In this section there will be given a brief historical outline of the writings of the principal workers in the fields of infantile wasting, the general deficiency disorders, the vitamins and the avitaminoses.

In the Goulstonian Lectures of 1924, (1) Parsons stated that Pemell in 1653, was the first English writer to refer to the condition of infantile wasting, that in 1746 John Astruc gave a very good description of the same condition, and that in his book in 1784, Michael Underwood, like many others, confused tuberculous peritonitis with this condition.

Dr. Charles West in his published lectures in 1848 clearly indicates the condition as a nutritional disorder.

In 1868 Eustace Smith, in his book "The Wasting Diseases of Children", also describes the picture well. In the third edition (1878) the first chapter is entitled "Simple atrophy from insufficient nourishment". The chapter is subdivided under two heads, "insufficient supply of food", and "unsuitable food"; and the first paragraph cannot be called out of date - "Imperfect nutrition constitutes the commonest form of disease, and furnishes the most frequent cause of death, in infants. Many thousand children die yearly in London alone for the simple reason that they are fed systematically and persistently upon food which they cannot digest.

And as long as the children of the poor are allowed to leave their schools utterly uninformed as to the duties which in after life they will be called upon to fulfil, so long this dreadful mortality may be expected to continue."

Owing to the frequency with which diarrhoea and vomiting accompanied the condition, most attention was directed to the alimentary canal and to morbid anatomy as a basis for the disease, and the morbid anatomy theory reached a zenith in 1880, but failed to survive owing to the lack of post-mortem changes.

In 1885 Escherich of Vienna, investigating the intestinal bacteriology, proved that the type of bacteria was dependent upon the kind of food taken.

For the next twenty years the opinion of paediatricians halted between the view attributable to Eustace Smith and Charles West, namely that atrophy was due to starvation (although Smith also thought that the cause might be difficulty in digesting protein), and the view based upon morbid anatomy.

In the American Journal of Diseases of Children (1912), Czerny published some important conclusions of his research work in Germany. His main theories and beliefs will be referred to later, but, as Parsons says, the main importance of Czerny's work lies in the fact that he emphasized the necessity of considering the infant as a whole and not only its food or alimentary tract

and also in demonstrating the harmlessness of protein.

In 1912 also, Finkelstein, another notable research worker in Germany, published in his book, a clinical classification of nutritional disorders.

Finkelstein's views, which, like those of Czerny, were based upon experiments that were afterwards disproved, will also be referred to later.

Owing to the fact that in June of that same year (1912), Casimir Funk, in his paper "The Etiology of the Deficiency Diseases," employed the term "vitamine" for the first time, a short review will be made here of the steps which had led up to his work. (2)

In 1881 Lunin first gave clear evidence for the existence of these factors "essential to life," and ten years later Socin came to the same point of view, but neither of these workers at the school of Bunge at Basel, attempted to complete the evidence.

Their observations were repeated and extended fourteen years later by the late Professor Pekelharing, who in 1905 gave a clear statement of the vitamin doctrine. "My intention is only to point out that there is a still unknown substance in milk, which, even in very small quantities, is of paramount importance to nutrition. If this substance is absent, the organism loses the power properly to assimilate the well-known principal parts of food, the appetite is lost, and with apparent abundance, the animals die of want. Undoubtedly the substance occurs not only in milk,

but in all sorts of foodstuffs both of vegetable and animal origin."

In 1897 Christiaan Eykman concluded from his researches of the previous seven years, that beri-beri resulted from the continuous consumption of decorticated rice; but he viewed the facts from the orthodox pathological standpoint of the time, namely, that the outer layers contained an "antidote."

In 1901 Grijn first put forward the true deficiency theory.

Eykman's observations were fully established in 1907 by Braddon and in 1909 by Fraser and Stanton.

In the first decade of the present century, "calorie supply", "protein-minima", and such factors still dominated the general conception of nutritional adequacy; but the next three years led to a change in outlook.

As a result of experiments in 1909, 1911 and 1912, carried out on mice, with diets subjected to prolonged extraction with alcohol and ether, Stepp remarks, "It is not impossible that unknown substances indispensable for life, go into solution with the lipoids, and that the latter thereby become what may be termed carriers for these substances."

In 1912 Hopkins published some results of his classical experiments of the previous six years in this country, carried out with food-mixtures composed of very completely purified proximate principles. As early as 1906 Hopkins had written: "But further, no animal can live upon a mixture of pure protein, fat and carbohydrate,

and even when the necessary inorganic material is carefully supplied, the animal cannot flourish. The field is almost unexplored but it is certain that there are many minor factors in all diets, of which the body takes account. In diseases such as rickets, and particularly in scurvy, we have had for long years knowledge of a dietetic factor, but though we know how to benefit these conditions empirically, the real errors in the diet are to this day quite obscure. They are, however, certainly of the kind which comprises these minimal qualitative factors that I am considering. Scurvy and rickets are conditions so severe that they force themselves upon our attention, but many other nutritive errors affect the health of individuals to a degree most important to themselves, and some of them depend upon unsuspected dietetic factors."

This brings us again to the work and writings of Funk, to whom we owe the term "vitamine," (which, without the "e", is now the class name) who helped greatly to advance our knowledge of the subject, and who did much to secure recognition of its importance. In 1911, when previous publications had awakened much fresh interest in the etiology and experimental cure of beri-beri, Funk made an almost pioneer effort to isolate the active curative substance from the rice polishings.

In his paper of June 1912, Funk reviewed the literature concerning beri-beri, scurvy and pellagra, and gave his opinion

(in advance of current thought) that the third, not less than the first two is to be numbered with deficiency diseases.

Funk believed that vitamins were amines. While not the first to express the view that vitamins are necessary for growth and general health, he is among the first to impress this view on scientific opinion.

Before outlining the steps in the investigation of the vitamins during the past twenty years, infantile marasmus is touched upon again, as regards recent work in Britain and America. In America much work has been done on the metabolism of atrophic infants. Marriott's writings in particular (1920-21) will be discussed later.

In Section 4 of this thesis some studies by Fife and Veeder in 1911 upon metabolism will be discussed, as also Parson's investigations in 1924.

In 1913, Osborne and Mendel (of Newhaven, Connecticut) wrote: "... it would seem as if a substance exerting a marked influence upon growth was present in butter." This was the outcome of their classical work, from 1911, on the relative nutritive value of various pure proteins; work which was erroneous however, owing to the use of lactose which was unpurified of milk vitamins absorbed into it.

In June 1913, (the same month as the above workers) McCallum and others (Wisconsin and Baltimore), on their studies from 1907

upon the nutrition of farm stock, recognised a factor essential to nutrition, associated with certain (but not all) fats.

In 1914, Osborne and Mendal first showed that cod liver oil contained what may now be called the "fat soluble complex." The therapeutic value of the oil had been known for a long time.

In 1915 McCallum and Davis made it clear that at least two accessory diet factors were essential for normal growth:-

- (1) fat soluble A
- (2) water soluble B.

From that year three vitamins were known, A, B and C.

In his work from 1918 - 1921 E. Mellanby recognised Rickets as a deficiency disease, and the anti-rachitic vitamin as the cornerstone in the etiology. He found that it was contained in some fats and that cod liver oil was a rich source.

In 1922 McCallum, with Simmonds and others, proved that there were two components in the "fat soluble complex."

That ultra-violet radiation is curative of Rickets was first shown by Huldshinsky in 1919-20; and in 1921 Hess showed that sunlight had the same power.

In 1924 Steenbock and Black found that ultra-violet radiation made potent against rickets fat-containing foods, previously inert against the disease; while in 1926 Peacock showed that the exposure of cod liver oil to light results in the loss of vitamin A. activity.

From his work from 1922-25 upon the relation of vitamin D. to

the cereal foods, E. Mellanby concluded that the latter contained an unfavourable agent (for which he suggested the name "toxamin") which was neutralised by a sufficiency of the vitamin.

In the B.M.J. of 12.11.32, E. Mellanby discusses the "Clinical applications of recent work on Bone Disease", while in the B.M.J. for 19.3.32, M. Mellanby and Harris reach important conclusions covering cereals, dental caries and vitamin D.

The anti beri-beri factor of the vitamin B. complex was discovered by Eykman in 1897.

Funk in 1912-13, first suggested that pellagra was due to vitamin deficiency, and advanced the theory that a factor was removed in the milling.

On work carried out from 1914-20, Goldberger (of the U.S.A. Bureau of Public Health) showed that dietary measures can prevent pellagra, and Wilson confirmed this in Egypt at the same time.

In 1920, Voegtlin, Neile and Hunter found an alcoholic extract of ox liver to be as good, therapeutically, as milk, eggs and meat.

In 1924, Goldberger and Tanner confirmed the value of milk and meat, and found that gelatin, butter and cod liver oil did not prevent pellagra.

In 1926, Goldberger and others discovered vitamin B₂, the pellagra-preventing factor.

B₃ was added to the list by Williams and Waterman in 1927-28,

and in 1929 Reader added B₄.

In 1930, Chick and Capping postulated the presence of the heat and alkali stable "factor Y." Chick in the Lancet of 12.8.33 reviews the "Current theories of the etiology of pellagra."

In 1651, Glisson gave a clear description of the signs of infantile scurvy; he recognised their nature and showed that they were not rachitic in origin. His work was entirely overlooked for over two hundred years.

In 1871, Ingerslev and in 1878, W.B. Cheadle pointed out the real cause, but general recognition and acceptance of the condition did not occur until 1883, when Sir Thomas Barlow's thorough investigations were published. Holst and Frohlich (1907 and 1912), and Chick and their colleagues are among the leading workers who have investigated this avitaminosis experimentally.

From 1919 onwards McCarrison has carried out important investigations into different aspects of deficiency disease.

During the past few years there has been great interest aroused in the nutritional anaemia of infancy by the work of H.M. Mackay who first drew attention to the condition in 1929.

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SECTION 3.

ETIOLOGY.

Divisions of childhood.

Introduction.

Mother's health and good obstetrics.

Early care.

Congenital conditions.

Unsuitable feeding - Faults in the food - proximate principles.

Faults in feeding technique.

Faults in the infant "Idiopathic atrophy", prematurity, certain organic conditions.

The Dyspepsias

Hutchison

Still

Thomson

Other causes of vomiting

Feer

Czerny

Finkelstein

Gastro-enteritis

Etiology, pathology, symptomatology, complications, principles of treatment.

"Pink Disease".

SECTION 3.

ETIOLOGY.

Professor McNeil (Lectures to Edinburgh students, 1931) divides childhood into three stages:-

Infancy - birth up to $2\frac{1}{2}$ years. "Early infancy" up to 1 year, and "later infancy" thereafter.

Early childhood - $2\frac{1}{2}$ to 5 or 6 years. At this period the rate of growth slows down, and there are no teething or school worries.

School age. Here "restrictions" make their appearance, and second dentition commences. It is a time of "stress" and certain diseases are prone to occur, e.g. rheumatism.

Parsons makes it his working rule that an infant is "wasted", if the weight is less than 80% of that "expected." To him the wasted infant is even more of a social problem than the rheumatic or tuberculous child.

In this section a short outline of the causes of wasting in early infancy will be given - that being the period at which the vast majority of cases occur. The principal causes will be selected for special discussion.

The pathogenesis of certain wasting and deficiency diseases will be treated of in Section 4, the different clinical pictures will be given in Section 5, and treatment will be dealt with in Section 6.

The importance of careful attention to the mother during

pregnancy and labour, and to the infant during the early days of its life, cannot be exaggerated in its effect upon growth and development. A great deal of good will be done, and certain disease processes prevented by regulating the woman's diet in pregnancy, and further, by impressing the mother strongly with the necessity and benefits of nursing her child herself. (See Section 6)

"To what extent marasmus is dependent upon abnormal nutrition is not known, but there is reason to believe that defective maternal feeding plays an important part in its etiology." (M.R.C. report 1932. Chapter XI, page 276.)

The importance of good midwifery to the infant is obvious; the rectification of malpresentations, the avoidance of injury to skull and abdomen, and the avoidance of a prolonged second stage of labour and the improper use of instruments.

Much mortality and morbidity will be prevented by especially careful attention to the infant in the first few days of life - mainly as regards preventing "chilling", and umbilical infection; and also by the satisfactory preparation of the mother's breasts and nipples during the last few weeks of pregnancy.

A considerable number of cases of malnutrition are due to congenital and developmental accidents, such as hare-lip and atresias of the alimentary tract. Mental deficiency is another very important cause, and others are congenital heart disease and

congenital cystic disease of the kidneys.

Derek R., aged 5 months. Weight $10\frac{3}{4}$ lbs. No vomiting, stools normal. Slight generalised cyanosis - no finger clubbing. X-ray showed liver on left side of abdomen, and apex of the heart turned to right.

Of the many causes of wasting arising later on, unsuitable feeding is universally recognised as the commonest, and this may be due to wrong food or to a faulty manner of feeding. Marasmus is rare among the breast-fed; marantic infants represent the failures of artificial feeding.

Faults in the food.

Qualitative faults are commoner than quantitative and "too strong" is commoner than "too weak." Excess of fat, either absolute or relative to the child's tolerance, is the commonest fault; it gives rise to a definite clinical picture, which occurred frequently with the use of the high cream dried milks. It is seldom wise to exceed 3.5% fat in a cow's milk mixture.

G.F. Still considers excess of sugar (giving rise to loose slimy motions) to be of quite common occurrence, and gives 5 - 8% as a good percentage for sugar, but Hutchison says that sugar is the least likely of the proximate principles to cause upset. (3) (4)

Holt remarks that the effects of high protein intake are little to be feared - contrary to former belief.

Starvation is a common cause of wasting. In hospital practice it is often due to excessively dilute "condensed milk." Inanition is commoner in the bottle-fed than in the breast-fed, but Thomson makes it a "golden rule" that insufficiency of milk is to be suspected if a breast-fed infant fails to gain ground.

Sheila B., aged 4 months. Weight $8\frac{1}{2}$ lbs. Past 3 months fed on different proprietary foods, finally milk to water - 1 part to 2, $\frac{3}{4}$ iii feeds. Had been vomiting slightly but steadily since birth. Diet built up to milk to water - 3 parts to 1, $\frac{3}{4}$ iv $\frac{3}{4}$ hourly, and infant gained 2 lbs. in 1 month.

Feer considers inanition to be comparatively frequent in the breast-fed, being due usually to over-feeding. (5)

To Holt (Chap. xviii), "too little" is the commonest mistake in infant feeding, and by impairing the tolerance for food, it gives rise to a vicious circle (6)

Starvation may also arise from pure inability to suck, whether mechanical or due to general weakness.

Faults in manner of feeding.

The intervals between feeds may be irregular or, regular but wrong, and here "too often" is far commoner than "tooseldom."

Too large a bulk of fluid causes some cases of wasting, which may be very difficult to treat. Other very faulty customs are to change the food too often and too suddenly.

Those cases of wasting which are not due to faulty feeding are

due to some abnormal condition in the infant itself.

There is one well recognised group, that of "primary" or "idiopathic" atrophy, the cause of which is unknown. These cases are all very young infants; and their progress is steadily downwards, there being apparently a true failure of assimilation.

Holt (Chap. xviii, p. 195) considers that a considerable number of premature infants fall into this group, but that the conception of "constitutional weakness" as a cause is not a satisfactory one.

The premature infant is very often wasted owing to the fact that, beside the general bodily and digestive weakness, it is metabolically extravagant.

Of the large group of organic conditions in infancy that will cause wasting, the other signs being inconspicuous, one very important condition which is by no means uncommon, "congenital pyloric stenosis", will be discussed later. (See Section 5)

One or two congenital conditions have already been mentioned. Congenital syphilis is considered by French writers to be a cause, but Findlay considers it very seldom responsible.

Congenital syphilis is an uncommon condition and one that is very apt to be overlooked. Four syphilitic infants have been seen in the last three months:-

- (A) Dorothy D. Admitted, aged 1 year with Broncho-pneumonia for four days. Weight 11 lbs. Spleen easily palpable, appetite good, stools normal. Transferred six weeks later

with nasal diphtheria.

(B) Arthur S. Admitted, aged 11 months and weight $12\frac{3}{4}$ lbs.

History of lost weight of 4 lbs with cough, pallor and breathlessness during past month. Spleen palpable.

Child was hoarse and right lower lobe was solid. (No empyema) Appetite and stools satisfactory.

Discharged to Outpatients after six weeks.

(C) Tom S. Attended Outpatients, aged 9 months, weight $13\frac{1}{2}$ lbs.

Gross frontal bossing of skull, very wide fontanelle, hoarse cry and running nose, palpable spleen.

(D) Geoffrey K. Admitted, aged 6 months, weight 10 lbs.

Losing weight past month. No diarrhoea or vomiting.

Wasting was present, then, in all of these.

Latent broncho-pneumonia and an empyema may very easily be missed as causes, and another easily overlooked cause is chronic constipation. This last condition is explained in some, but not all, cases by a too dilute milk, which leads to both wasting and constipation, but continual restlessness and insomnia also play a part.

Tuberculosis is uncommon in the first six months of life.

Chronic infection of the ear and of the urinary tract are important and easily overlooked causes of wasting.

Improper feeding has already been discussed. Persistent

ill-balance of the proximate principles of the diet, leads on to "dyspepsia." This condition forms a very large group of infantile upsets and causes many cases of infantile wasting, so that its own causation, pathology and treatment will be discussed in this section.

Hutchison states that few marasmic infants are not also dyspeptic. He says that fat excess is most likely, casein less and sugar least likely to cause upset, but that there is usually an impaired power of digestion of all the three proximate principles.

He says that the onset may be sudden or gradual and that the picture may be complicated by a secondary bowel infection.

Still states that a very large group of wasted infants result from gastro-intestinal upset, and especially from diarrhoea.

Thomson classifies "nutritional upset" very simply as :-

- (A) Acute (intoxication) group - toxic and febrile.
- (B) Chronic (marasmus group.

"In both there may be vomiting and undigested loose stools." (7)

He says that almost any disease process in infancy may lead to nutritional upset. In some cases the symptoms are due to the proximate principles of the food taken; more often they are due to contamination of the food either by:-

- (a) decomposition products, or
- (b) pathogenic organisms,

but most frequently of all the symptoms are due to disease elsewhere in the body - i.e. "parenteral infection." It is thus of first importance to examine the ears and the urine before accepting a "food disorder" as being the causal condition. He points out that the question is made very complex by the fact that more than one factor may be present at the same time, that one type of lesion leads to another, and that all cases cannot be brought into any one system.

To review the case history from birth is essential.

Vomiting is a symptom of a variety of infantile diseases. It must be separated first from the harmless regurgitation of some slight excess of the feed. It is very important to remember that hunger may be a cause of vomiting. Vomiting is also common in certain acute infections, especially in "influenza" and in pyelitis. In pyelitis there may even be visible "gastric peristalsis".

(Holt, Chap xv.)

Rumination is another cause both of vomiting and of wasting, and this condition starts usually from the second to sixth month.

It must be remembered that vomiting due to "indigestion" may not come on for several hours after the feed has been ingested.

Habit is a potent factor in the continuance of vomiting once it has been started. Professor Feer describes two forms of "habitual infantile vomiting":-

(1) Spastic - of necessity, very similar to the vomiting of pyloric stenosis, and

(2) Atonic

Feer, also finds a satisfactory classification of the nutritional disturbances of infancy, militated against by the variety of causes and the intermingling and transition of the clinical pictures. He stresses, again, the consideration of the infant patient as a whole and the taking of a very accurate feeding history. Even so, diagnosis and treatment are very difficult.

Classified from the etiology, by Czerny and Keller, the nutritional disturbances fall into:-

Alimentary - the food given, being improper either qualitatively or quantitatively.

Infections - from mild cases (dyspepsia) to severe (intoxication).

Constitutional - including cases of pyloric stenosis and the "pre-dispositions."

Feer quotes Finkelstein as trying to classify the disturbance according to the degree of disturbance of function and injury to "tolerance" (in tolerance to changes in diet) that are present.

He himself combines both classifications, and lets the stools be guide to therapeutics, second to observing the

infant as a whole.

To Fear, diarrhoea and vomiting in an infant that is "up to weight," constitutes "simple dyspepsia;" a more severe case is toxic dyspepsia" or "alimentary intoxication;" diarrhoea in an undernourished infant is "decomposition;" while "milk feeding injury" is the condition in which the stools are of the formed, "fat soap" variety, and the weight of the infant is stationary.

In the breastfed, serious nutritional upset is uncommon and suggests "enteral" or "parenteral" infection, although it may be due to fat excess. But, (as stated before) inanition is comparatively frequent in the breastfed, being due, usually, to overfeeding.

Parsons sums up Czerny's theories in:- "atrophy is due to nutritional upset, and/or infection, superimposed on a constitutional anomaly, the two upsets being -

- (a) too much fat, and
- (b) too much carbohydrate

and the essential pathological factor being a demineralisation of the body."

Of Finkelstein, he says:- to him, "the sugar and salts of the diet were to blame."

The third section of Thomson's chapter IX (on the "Nutritional disorders of Infancy") is devoted to "gastroenteritis" etc. (The first two sections being devoted to the "Classification of Nutritional Disease," "Marasmus," and the fourth, and last, section, to "Ileocolitis.")

Mild forms of gastroenteritis, corresponding to Finkelstein's "Dyspepsia," are due to overfeeding, especially with carbohydrate, while severe forms ("intoxication") are due to infection, either from the ear, kidney or lung. Leucocytosis is present in these cases and acidosis may complicate.

Medical Annual 1933.

p.151. "The relation between otitis media in infancy, and gastrointestinal disturbance such as "summer diarrhoea" has long been a subject of controversy."

p.323. "Asherson is against the possibility of acute otitis being a cause of gastroenteritis. L. Findlay is also not in favour of such a hypothesis, and points out the marked differences between the two diseases in connection with their social and seasonal incidences."

Unfresh food may cause mild or severe cases, but the nature of the contamination causing "epidemic diarrhoea" has never been

discovered. Despite the worked reduction of mortality recently, the condition is still one of great importance. In the large majority of cases of diarrhoea, no specific organism can be held responsible. Less than 5% of severe cases occur in breast-fed, a fact which tends to discountenance an organismal etiology. Cases are quite commonly seen in winter and spring. The susceptibility of infants to diarrhoea has been attributed to their liability to "chill" and to the fact that the sterilising power of their stomach is small owing to their scanty hydrochloric acid.

Other factors which almost certainly play a very important part are anaemia (which is of remarkably common occurrence in infancy), and a deficiency of Vitamin A. These factors will be referred to in Section 4.

The important predisposing factors are:-

- (a) hot weather,
- (b) infections, and
- (c) artificial feeding.

It has been noticed that the acme of the death-rate coincides with the acme of the temperature.

Formerly, to explain these facts, the entire stress was laid upon the bacteria of milk, but in recent years attention has been focussing upon failure of the digestive secretions, (and Holt regards this as an important factor,) namely, a marked reduction

of gastric acidity and in the enzymes of the duodenal secretions

This may act in two different ways:-

either the undigested food in the intestine may favour the growth of certain bacteria,

or the altered reaction may effect the bacterial flora.

Two views are supported by evidence. The untoward effects are due to:-

- (1) fermentative bacteria acting upon carbohydrate; or
- (2) proteolytic bacteria.

Now, recent observations have thrown doubt upon the harmful nature of the fermentation products of carbohydrates.

Further, animal inoculation does not show any toxic action of the intestinal contents of these infants.

PATHOLOGY. There are usually no lesions in the intestines, but the kidneys may show tubular damage. The chemical pathology is more striking. Although the digestion of protein is little, that of fat and carbohydrate is markedly, affected. Much of the ingested fat is found in the stool, and moreover, the bulk of it is unsplit. The absorption of carbohydrate is usually affected and there is evidence that its intermediate metabolism is faulty.

The bloodsugar curve is not uncommonly of the diabetic type and there may be glycosuria. The loss of minerals in the

stools is quite as important as loss of water. The stools are alkaline, and if the loss of base is uncompensated, i.e. if kidney function is seriously impaired, acidosis may result. The minerals of the plasma and of the interstitial-tissue fluid, are chiefly potassium and phosphorus.

Although loss of interstitial-tissue fluids produces conspicuous changes, especially in the skin, the serious consequences of dehydration are due to cellular changes and the decrease in plasma volume which occur in severe cases.

Diminished plasma volume leads to increased viscosity of the blood, and an increase in the plasma proteins, together with the condition named by Rous "outlying acidosis."

There is accumulation of lactic acid, and impairment of renal function is common.

Pyrexia is one of the most striking manifestations of dehydration.

The symptoms, which are of all grades of severity, fall into two groups:-

- (1) The actual diarrhoea and vomiting, and
- (2) nervous symptoms, such as coma, and twitchings;

There may be marked languor.

The cause of the nervous symptoms is much debated.

Anhydraemia and its sequelae are probably the cause of the majority and yet a few serious cases are seen, especially where the infection is parenteral, in which for a time there is no diarrhoea, and in which the impression is roused that the diarrhoea is actually protective.

The observation that the diarrhoea does not start until after the elevation of temperature, is frequently a pointer to the infection being parenteral. Mellanby thought that the factor might be a toxic amine.

At any rate, it is generally accepted that acidosis is not responsible for the nervous symptoms.

Of the complications, secondary infections are very frequent; sclerema is uncommon, and almost invariably fatal, there being extreme depression and a state of hardening of the skin and subcutaneous tissues. Cachectic purpura is a grave complication; rectal prolapse may be persistent and troublesome.

Wasting may result from prolonged periods of difficulty of digestion and chronic diarrhoea.

In treatment the first step is to find the cause, whether food, or heat or parenteral infection (otitis media, mastoiditis, or pyelitis). The neurological symptoms are often very puzzling.

The principle indications in active treatment are first to treat any parenteral infection present, and then to remove the toxic foodstuffs from the body, to institute a period of starvation, and to assist the circulation.

Progress should be judged purely by the general condition.

The infant should be isolated, and starved of food for a "trial period" of six hours. Only in rare cases is starvation necessary for more than 24 hours. Gastric lavage will be of benefit if the vomiting persists to any degree; and the introduction of fluid by the mouth should always be attempted. Half strength normal saline is the best fluid; if glucose is given, most of it is excreted in the urine. Normal saline should always be given, also, hypodermically and intra-peritoneally, the latter route being the most satisfactory in all but the mildest cases. By this route 300 - 500 ccs. may be given within half an hour, but the peritoneal sac should never be distended by the fluid.

Holt considers that the main point in treating the complicating acidosis, is the prompt restoration of renal secretion and that this is best done by intravenous hypertonic glucose, 50 - 60 ccs. of a 10% solution are given in 10 - 15 minutes and always accompanied by hypodermic or intra-peritoneal

saline.

After the first day, breast milk is the first choice and protein milk the second. Mounting up from 3ss 4 hourly, and gradually replacing with 3ss milk, a sustenance diet should be reached in five days, if the infant is undernourished. Another successful regime is to give dilute lactic acid skimmed milk, 3ss 2 hourly for the second day, and by the fourth day 3ii 3 hourly. By the tenth day, diluted half cream dried milk may be given. Holt believes in some sour milk preparation to be given for some weeks into convalescence.

It is very important in this type of illness to prevent the onset of vitamin lack, and a dose of concentrated fat soluble vitamin preparation (such as "adexolin") should be given daily from the third day. If there is no evidence of anaemia, doses of ferri et ammon cit should be started by the tenth day.

In the early acute stage of the illness drugs are being used much less now than previously. One dose of castor oil or a small repeated dose of calomel is generally held to be beneficial. (12).

SECTION 4.

A. Pathogeneses of Infantile Atrophy.

Pathology and Bacteriology.

Metabolic processes

Czerny	Reactions of normal stools.
Finkelstein	The Mineral salts.
Holt	"Protein".
Thomson	"Fat and minerals".
Holt	"Fat".
Holt	(Appearance of normal stools)
Holt	Milchnahrschaden.
Fife & Veeder	"Fat".
Parsons	Series of cases, experiments on fat, conclusions.
Milchnahrschaden	Parsons, Feer, Hutchison, Fife & Veeder.
Fife & Veeder	Experiments.
T.R.Parsons	Nitrogen metabolism.
Holt	Pathology of marasmus.
Thomson	Fat dyspepsia and parenteral infection.
Marrriott	Pathology.
Holt	Carbohydrate tolerance and Malnahrschaden.
Spalding	Atrophy.
Eleanor Jones	Atrophy.
<u>Deficiencies.</u>	
McCarrison	Vitamins and the intestinal tract, and Relation of diets to thyroid.
Boyd	Thyroid gland.
McCarrison	Intestinal bacteria and the thyroid gland.

Complications. Pathology of "idiopathic oedema."
" " " "nutritional anaemia."

Prognosis.

Conclusions.

B. Pathogenesis of the Avitaminoses.

A. Introduction, chemistry, effects of deficiency, location.

D. Location, ergosterol, chemistry, action (Harris).

Rickets Blood chemistry, some clinical features.

Mellanby	Bone disease.
Langdon Brown	D deficiency and excess, and action of parathormone.
Holt	Parathyroid, lack and excess.
Boyd	Parathyroid.
Thomson	Tetany and its Etiology.
M.R.C. report	Tetany.

Treatment of Rickets. Vitamins and dental disease. Importance of D.

B. Complex Location, composition, deficiency.

Beri-beri Etiology, features in infancy.

Pellagra Features in adults, etiology.

Pellagra and Beri-beri.

Discussion on "Toxamins in foodstuffs."

C. Chemistry, action, location.

Scurvy Pathology, some clinical features.

C. Pathogenesis of the "intoxications".

Health.

Ketosis.

Acidosis. Acid - base balance.

Two causes of acidosis Excessive acid formation, inefficient acid excretion.

Conditions in which excess of acid is formed.

Thomson Periodic acidosis - clinical features, pathogenesis, treatment.

Reginald Miller Acidosis.

Conditions in which acid is inefficiently excreted.

CO₂ content in plasma.

2

"Compensation" and "decompensation".

Alkalosis. Two main causes, dangers of.

SECTION 4.

PATHOGENESIS OF INFANTILE ATROPHY.

Post-mortem, there are no characteristic lesions, even in the most severe examples.

Despite the work of Escherich, many years ago, and more recently of Brown and others at Toronto, it has so far proved impossible to correlate the different clinical pictures, with differences in the intestinal bacterial flora.

Normally in the newborn, the meconium is sterile. The chief organisms of the bottle-fed infant's stools are faecal streptococci and B. coli, while in the breast-fed, Gram-positive bacilli are in the majority.

In the breast-fed, the flora is saccharolytic, while in the bottle-fed, it is proteolytic and putrefactive. A lactose diet tends to change the latter flora to the former.

.....oOo.....

Up to Czerny's time, protein was the only food constituent which was thought could be harmful. This worker was the first to consider the "make up" of the infant, and he suggested that

at least certain types of nutritional disease, were due to the infant's "abnormal reactions" to the proximate principles, even if present in normal amounts.

Czerny exonerated protein from blame, and said that rather were the fat and carbohydrate at fault. He held that atrophy was due to nutritional upset, and, or, infective process on top of a constitutional anomaly; the two important food disturbances being:-

- (1) Milchnahrschaden - due to excess of fats in the milk and typified by the passage of pale, constipated, crumbly "soap stools", and
- (2) Mehlnahrschaden - due to too much carbohydrate - the stools being frequent, acid and green.

Here the wasting is occasionally marked by oedema.

In (1), he attributed the atrophy essentially to a demineralisation of the body, owing to an abstraction of alkalis from the tissues to neutralise the excess of fatty acid formed in the intestine owing to the low fat assimilative power.

This theory was based on experiments upon urinary ammonia by Keller in 1897 and Steinitz in 1903, which were later shown to be erroneous; but Czerny's writings made a great advance in two ways:-

- (A) by emphasizing the importance of considering the infant as a whole, and
- (B) by demonstrating the harmlessness of protein.

The reaction of the normal stool is generally more or less acid. Excess of fat increases this acidity, while protein excess leads to alkalinity. Carbohydrate excess produces very acid stools, but the watery motions of "summer diarrhoea" are distinctly alkaline.

Finkelstein in 1912, gave his clinical classification of nutritional disorders. He followed Jacques Loeb, and said, although admitting that there was considerable truth in Czerny's opinions, that it was the sugar fermentation, and the salts of the milk that predisposed to atrophy. Meyer's "whey exchange" experiments supported him but were later disproved. Finkelstein devised his special "protein milk" to combat this fermentation - having a high protein and a low sugar content.

He divided cases into:-

A. "Bilanz-storing" - or "disturbance of balance," because adequate calories did not lead to a gain in weight.

This corresponds to Czerny's "milchnahrschaden."

B. Dyspepsia

If mild, this condition was exemplified by a moderately diminished carbohydrate tolerance.

If severe, cases fell into two groups:-

(1) "alimentary decomposition" which occurred if the food contained plentiful fat, but little carbohydrate; and

(2) "alimentary intoxication" - the food containing much sugar and little fat.

He considered this last condition to be due, not to bacterial infection, but to the passage of whey salts through the unhealthy mucous membrane. Like protein and carbohydrate, the mineral salts are absolutely necessary for life.

Their absorption is favoured by acidity of the intestinal contents, and opposed by their alkalinity. As will be seen later, excess of fatty acid fixes the lime and so interferes with its absorption.

Of protein, Holt remarks,- symptoms of inadequate protein intake are not well-defined; such diets are often deficient in other respects, i.e. vitamins or minerals; and nutritional oedema may develop.

The effects of high protein intake are little to be feared, contrary to former belief. Undigested protein seldom appears in the stools, even in disease.

Thomson says of Fat Metabolism(p. 132) :- the interdependence of calcium, fat, and phosphorus absorption and utilisation is one of the most important fundamental features of infant metabolism. Normally, more than 95% of the fat in the diet is digested, and is present in the intestinal contents as free

fatty acid, or combined with calcium or other salts in the form of insoluble soaps. The amount of available salts (especially calcium) influences the relative proportion of fatty acid and soap. Calcium in excess leads to increased soap formation. This interferes with the absorption of fat and of calcium, and so to deficient retention of phosphorus, because phosphorus is only utilised in equal amount to calcium.

Of the fat in the diet, over 90% is absorbed from the intestine, and in health, the greater the amount given, the higher the absorption, while in disease, the reverse is the case: (e.g. coeliac disease.) Fat, or its derivatives, rarely form less than 30% of the total faecal output. It is important to remember that the fat content of the faeces does not necessarily bear any relationship to the proportion of the intake that is absorbed.

Holt (p. 105.) remarks that, under normal conditions, fat absorption is nearly complete. With breast milk, most infants retain 90-98%; and with cow's milk, 85-95%, the difference being largely due to the higher mineral content of cow's milk and not to differences in the character of the fat.....

Again, (p. 125.) a reduction of fat intake increases

the percentage of fat absorption, but a marked increase in intake diminishes it. (This remark opposes that of Thomson's quoted above.) The percentage of the fat intake, absorbed, however, is fairly constant, more so than the actual fat absorption.

Holt warns against overemphasizing the valuable information that the stools can give, regarding digestion.

The stools of the healthy nursing infant are acid, and seldom entirely homogeneous; of the handfed, firmer, paler and more alkaline. A diet in which there is excess of protein over carbohydrate, leads to the formation of alkaline, constipated stools.

(p. 106.) Prolonged feeding with raw cow's milk alone, without the addition of carbohydrate, may lead to the symptom complex known in Germany as Milchnährschaden, in which nutrition suffers. This has been attributed to lack of carbohydrate in the food, but possibly it is due in part to an inability properly to digest the other food constituents present in relatively higher amounts. Insoluble calcium soaps form a considerable part of the stools, and the latter are dry and crumbly.

With the addition of carbohydrate and a corresponding reduction of protein and fat in the diet, the condition is successfully treated and there is a rapid change in the stools.

Some experiments by Fife and Veeder in 1911, will be discussed later, but some of their remarks may be given here:-

On a fat free diet, a very small amount of fat is found in the stool:-

In the healthy infant, the normal absorption of ingested fat lies between 90 and 95%. The fat absorption is lowered in both acute and chronic nutritional disturbance, 10-50% (or more) of the ingested fat, being found in the faeces. In our own cases, the loss was 15-33%.

With "The wasting Diseases of Early Infancy" as his subject, Parsons delivered the Goulstonian Lectures of 1924. His classification was as follows:-

- (1) Simple atrophy.
- (2) Simple atrophy with dyspepsia i.e. with diarrhoea and vomiting, or with intolerance to fat, carbohydrate, or protein.
- (3) Simple atrophy with deprivation -
 - (a) deprivation of one of the proximate principles,
 - (b) deprivation of the vitamins.
- (4) Atrophy from other diseases. (Pyloric stenosis, pyelitis, syphs. T.B.s, etc.)

Each division has already been briefly dealt with, except for "fat intolerance," "carbohydrate intolerance" and "deprivation of vitamins.

Parsons describes the results of some original and strict

experiments on the fat digestion and absorption of wasted infants. Although he limited his investigations as far as possible to infants under the age of three months, Parson's series consisted of 100 infants under six months old, admitted to his care from 1920 to 1924. Of these, 68 were either first, second, or third in the family. In 19, there was a history of diarrhoea, but it occurred in 27 after admission; 72 had a history of vomiting, and this was "frequent" in 52; 40 had vomiting while in hospital. 46 had a history of constipation.

He attributes to Holt the following figures (which do not correspond to those figures of Holt, previously mentioned.)

- (1) In a breast fed infant, 99.2% of the fat in the milk ingested, is absorbed;
- (2) in an infant fed on cow's milk, 97.4% is absorbed; and gives a figure of his own (97.7%) for an atrophic infant fed on mixed cow's milk and skimmed cow's milk. He states the general rule:- "the percentage of fat in the faeces varies directly with the percentage of fat in the food."

Parsons found in his cases "as in Holt's series," that fatsplitting was good throughout (except in cases of diarrhoea in which a large amount of unsplit fat was passed,) and concluded

that there was no evidence of deficiency in pancreatic lipase either in atrophy or in pyloric stenosis. Further, from his own figures and those of Holt, he says:- "It is quite obvious that fat absorption (in the absence of diarrhoea) is normal in infantile atrophy and pyloric stenosis."

His further conclusions were:-

- (1) atrophic children show very good absorption figures for cow's milk modifications up to 3.3% of fat;
- (2) the absorption figures are also good for modifications of dried cow's milk up to 2.1% of fat; (indicating that high fat content dried milks are uneconomical from the fat standpoint, and may lead to "intolerance to fat," thus explaining the clinical experience that "halfcream dried milks" give better results than "whole cream.")

Parsons figures also showed that atrophic children on cow's milk can split larger amounts, and can absorb larger amounts of fat, than those indicated by Holt and Falles as necessary for healthy nursing children - viz 20 gms. of fat daily, increasing to 40 gms. at 6-7 months.

Fat indigestion, concluded Parsons, occurs in atrophy under two conditions:-

- (1) when diarrhoea develops; (here, "peristaltic hurry" makes fat splitting poor;) and
- (2) with the use of high fat content dried milks; (here, the

fat splitting is good, but the stools are large, with a considerable content of soap and free fatty acid).

Parsons emphasised the rarity of "Milchnährschaden," (it only occurred in one case of his series;) and says, "..... the presence of fat and soap curds in the stools is not certain evidence of fat indigestion; in my experience the "soap stool" is not an abnormal one, unless it is very bulky, in which case there may be diminished fat absorption.

Professor Feer remarks that "Milchnährschaden" is due to an unsatisfied high carbohydrate requirement, and that malt sugar may be necessary in obstinate cases.

Hutchison, although granting that the study of the stools does give some guide to the nature of the feeding error, is unable to reconcile the classifications of Finkelstein and of Czerny and Keller with the bedside conditions. Discussing their own experiments (to be soon referred to,) Fife and Veeder remark "..... in none of the periods was the so-called 'soap-stool' of Czerny's 'milk injury', or Finkelstein's 'balance disturbance' present."

Holt (p. 125) describes two kinds of curds that may be observed in the stools of milk fed infants;

(1) When the stools are loose, there are liable to be found small yellowish - white curds, consisting almost entirely of neutral fat. This is an indication that fat is

being incompletely digested; and

(2) large, smooth, firm, yellowish brown curds, white on cross section; they are sometimes seen in the stools of those fed on raw milk, are composed of coagulated casein in an envelope of soap, and are of no pathological significance.

In 1911, Fife and Veeder undertook some studies of the metabolism of two atrophic infants, in order to determine:-

- (A) the absorption of fat under the influence of different proportions of fat and carbohydrate; and
- (B) the influence of the varying quantities of the fat and carbohydrate on the nitrogen metabolism.

The two infants were:-

- (1) Albert: weight 10 lbs. 8ozs.; age 9/12;
father tuberculous, mother mentally deficient;
the infant's weight was stationary for the two months between admission and investigation; and
- (2) Edward - aged 10/12, weight 11 lbs: 10 ozs.,
family history negative.

The results of the study were similar in the two cases, and the following conditions were noted:-

- (a) fat absorption was less than in normal infants, although the two infants were able to absorb large quantities of fat.
- (b) The percentage absorption was better with a large amount of fat in the food, than with low amounts.

Although they say that fat and carbohydrate differ from protein in that they may be substituted for one another within certain limits, yet they found:-

(c) that the amount of carbohydrate in the diet did not influence the fat absorption.

(d) The amount of fat in the form of soaps in the faeces was neither proportional to the amount of calcium in the faeces, nor to the amount of carbohydrate in the food.

(e) Both the actual and percentage amounts of soaps were greater when the fat intake was low, and the investigators consider that this shows that the infants were not atrophic as a result of "fat injury."

Regarding that part of their study concerned with the nitrogen metabolism they say:"it is generally accepted that the amount of nitrogen in the faeces is not proportionate to, nor dependent on, the amount of nitrogen in the food;" and that therefore, the study of the nitrogen absorption is of little or no value; but that the "nitrogen retention" is important, that is, the balance between the output (in the urine and faeces) and the intake.

T. R. Parsons, however, says (p. 91.):- "We can decide

whether the tissues of a subject are wasting permanently, or whether they are being repaired, by comparing the food nitrogen with the nitrogen in the urine and faeces. The food nitrogen, less that in the faeces, indicates the nitrogen absorbed from the alimentary canal. A comparison of this last with the urinary nitrogen, indicates the "nitrogen retention."

Neither the growing organism nor a starving man, can ever be in "nitrogen equilibrium."

(P. 58). One of the most fundamental reactions in the whole of the chemistry of the body is that of "deamination," by which the "amino" groups of the amino-acids - those end products of protein digestion, and the starting point of protein utilisation and synthesis - are split off; and the noncombustible, and therefore useless, nitrogen that they contain eliminated in urea. The liver is the only site of urea formation.

(P.77). In general, it will not be possible to decide what proportion of the total urea excreted is of exogenous, and what of endogenous (i.e. tissue breakdown) origin. But certain constituents are present in the urine that are entirely endogenous in origin - of these creatinine is the chief. There is a remarkable constancy of production of

creatinine, it is not present in any ordinary articles of diet, and it is very easily estimated. Its total output in the 24 hours, is the same, whether exercise is indulged in or not.

Another short extraction from Holt:-

(p. 195) Infants dying of marasmus, show no characteristic lesions. Evidences of morbid physiology (during life) are far more striking than the anatomical changes - there may be marked suppression of the digestive secretions.

In uncomplicated cases there is very little evidence of impaired fat and carbohydrate digestion and absorption.

Evidences of starvation dominate the picture. Combustion of the body tissues is reflected in the marked negative balances of nitrogen and minerals. A vicious circle arises from the fact that the basal metabolic requirements become steadily higher owing to the growth in surface area and the loss of subcutaneous fat.

To return to Fife and Veeder's conclusions:-

(f) the nitrogen retention was greater than in normal infants of the same age and weight.

"This may be due to their beginning on a period of convalescence,

as both children started in to improve from the moment they were placed on the metabolic bed in the first period." (i.e. "period" of experiment.)

"Nitrogen retention was very good in all our periods."

(g) Increasing the amount of carbohydrate produced an increased nitrogen retention, but the nitrogen retention was not influenced by the amount of fat in the food.

Thomson's three causes of marasmus ("or Bilanzstörung,") are:-

- 1. inanition,
- 2. fat dyspepsia,
- 3. parenteral infection.

Certain children, he says, undoubtedly have a reduced tolerance to fat, with the passage of large crumbly motions, a condition corresponding to Czerny's "milchnährschaden," and Finkelstein's "bilanzstörung." The digestion and absorption of fat are, however, quite normal.

The form of the motions is due to excessive amounts of insoluble soaps, which need excessive amounts of calcium and magnesium, the absorption of which is therefore interfered with. In more severe cases, it is thought that salts are actually extracted from the body; but, in many cases, there is shown to be no diminution in salt retention.

Further, it has been disproved that excess of fat in the gut interferes with the absorption of sugar.

"Whatever the explanation, it is a definite clinical entity that occurred frequently with the use of "full cream" dried milks."

Thomson considers that parenteral infection may cause wasting by :-

- (1) affecting the appetite,
- (2) raising the metabolic rate,
- (3) the action of toxins.

Marriott considered that atrophy was due to a long continued partial starvation. He believed that there, was actual destruction of the body tissues, and he attached importance to the diminution in the rate of blood flow, which he thought was present, together with a diminution in the blood volume, and in the blood cells and protein.

Marriott postulated a period of repair to explain the well-known clinical fact that the weight may be stationary for long periods in atrophic infants, despite a fairly large fluid intake. He believed that the greater liability to atrophy of handfed infant over the breast fed, was due to the greater buffer value of cow's milk.

(Holt, p. 120.) "The "higher buffer value" of cow's milk is due to its greater protein and phosphate content, these factors combining with and neutralising, additions of acid. Despite many digestive disorders having been attributed to this higher buffer value, no good evidence of harm has been presented.

Holt, (p. 273, p. 107) describes two other clinical pictures, "often associated with one or other of the avitaminoses."

One, "nutritional oedema," will be discussed later. (see under "Complications.")

The other, "a less well-defined syndrome," is the "mehlnehrschaden" of Czerny and Keller (1928.) This is seen after the excessive administration of carbohydrate, in the form of cereals and proprietary foods. It is not to be regarded as a specific carbohydrate injury, but rather as a deficiency of other foodstuffs, - proteins, and vitamins. The clinical picture is similar to the "partial vitamin B. deficiency," of Hoobler. There is often a rapid increase in weight, without a proportionate increase in strength; the child is flabby and often rickety and the resistance to infection is low. Holt

considers that it is only partly true that excess of carbohydrate ferments in the intestine and leads to diarrhoea. The normal infant tolerates sugar in large amounts, but if infection is present, this tolerance breaks down, and fermentation of the unabsorbed sugar may occur. Fermentation may therefore, be the result of, and not the cause of, nutritional upset.

Spalding in 1909, attributed "failure of developement" largely to food intoxication caused by improper feeding, particularly to a too-early recourse to artificial feeding, and to a too-high percentage of fat in the feed. This latter factor could also account for some cases of failure with breastfeeding. (14).

He considered that excess of carbohydrate leads to fermentation, and also to "intoxication" from an upset of fat digestion; while excess of fat extracted valuable alkalis from the body.

Eleanor Jones, (1910) said:- "the etiology of infantile atrophy (or Parrot's "athrepsia") is a mooted question, but a scanty and incongruous kind of food is probably the main factor." (15).

To her, the sequence of events was:- gastrointestinal upset, leading to putrefaction and the formation of organic

poisons (especially acids,) which are absorbed and poison the organism.

She quotes Rubner and Heubner as concluding that the work of digestion is much more laborious in the artificially fed than in the breast fed, and that therefore more calories are necessary in the former.

"It is a common fact that the artificially fed needs more food, secretes more urine and is more restless than the breast fed."

"Good breastmilk is the strongest safeguard against the condition."

In the Medical Research Council's report on vitamins, 1932, we read in Ch. XI. ("Vitamins for Mother and Infant."):--

(p. 276.) "To what extent marasmus is dependent upon abnormal nutrition, is not known, but there is reason to believe that defective maternal feeding plays an important part in its etiology. Supplementary vitamin foods are very useful in marasmus and retarded progress, often leading to marked improvement. Some cases respond well to Ultraviolet Radiation, after failing to do so with cod liver oil.

"Scurvy and rickets are frequent in those reared upon proprietary infant foods."

Holt remarks (p.194.) that deficiency syndromes (of protein, minerals or vitamins) may be superadded to the picture of malnutrition.

Boyd considers that McCarrison's results obtained in experimentally-produced deficiency disease in animals, resemble the findings in marasmic infants; and further, that the conception of intestinal lesions - particularly in children, - the result of a faulty dietary, may assume considerable importance in the future. (10).

Before indicating some of McCarrison's numerous experimental results, it must be emphasized how greatly different animals vary in their susceptibility to different vitamin deficiencies - examples being, that:-

- (1) it has never been possible to produce Rickets in kittens; &
- (2) rats never show the characteristic effects of a scorbutic diet, while guinea-pigs are especially susceptible.

After describing the effects which McCarrison produced in monkeys and birds by means of diets deficient in vitamins B. and C. (namely, the well-marked thinning of the wall and dilatation of the stomach and intestines, resulting in invasion by bacteria; and

also, particularly, the degeneration of Averbach's myenteric plexus;)

Boyd, (p. 319.) sums up:-

"It appears, therefore, that the health of the gastrointestinal tract depends upon the presence of accessory food factors in the diet, and in particular upon B. and C. vitamins, B.-lack giving rise to a picture resembling some forms of colitis, while C.-lack produces congestion and haemorrhagic lesions."

McCarrison has published the results of a large amount of work on - "The Pathogenesis of Deficiency Disease." The tenth of his series of articles, describes - "the effects of some food deficiencies and excesses on the thyroid gland." (16).

These are his conclusions:-

- (1) Diets deficient in vitamins lead to a reduction in size and weight of the thyroid gland.
- (2) Diets deficient in vitamins render the thyroid gland susceptible to the noxious action of intestinal bacteria, or of their products, with resultant atrophic and necrotic changes.
- (3) A scorbutic diet of crushed oats and autoclaved milk may cause in guinea pigs considerable enlargement of the thyroid gland. The enlargement is, in the main, the result of congestion and haemorrhagic infiltration of its

tissues.

- (4) Diets containing adequate provisions of vitamins, but excessively rich in protein and fats, induce in the thyroid gland of pigeons in confinement, marked degrees of hyperplasia, the extent of the hyperplasia being largely dependent on the duration of the organ's exposure to the gastrigenous influences induced by the excessive protein and fat content of the food.

(Boyd, p. 493, remarks that, during life, the thyroid is continually being acted upon by various stimuli, - chemical, bacterial, psychic, all tending to induce hyperplasia. When the action of these ceases, involution sets in. Boyd wonders why the thyroid gland should be such an apparent exception to the rule that tissues acted upon by toxins, do less, rather than more, work than usual.

He states that whenever the iodine content of the thyroid falls below .1%, hyperplasia results, but that this hyperplasia is neither necessarily nor even commonly associated with hyperthyroid symptoms. He instances the quite frequent and marked compensatory hyperplasia in myxoedema and cretinism.

McCarrison also found that:-

- (5) The addition of onions to a dietary excessively rich in



proteins and fats, while containing at the same time an abundance of vitamins, markedly retards the development of thyroid hyperplasia, and the tendency to acinar "budding" in pigeons living in confinement.

The beneficial influence of the onions is held to be due, in part at least, to their action in restraining the growth of putrefactive types of bacteria in the gastrointestinal tract and in retarding the absorption of their products.

It is suggested that "succus alii" might prove of benefit in restraining the hyperplasia of Graves' disease.

- (6) The changes in the parathyroids induced by a diet deficient in vitamins and excessively rich in starch and fat, appear to be related in their origin, to intestinal anaerobes; the noxious action of which, is greatly favoured by the defective diet.

Other points mentioned by McCarrison are:-

(A) "excessive proteid diet alone, all other hygienic conditions being perfect, will not, as Forsyth has shown (Lancet 1907, July, 20th.) cause thyroid hypertrophy."

(B) "In the present experiments, overfeeding was the

main causal agent in the production of the goitres." unhygienic conditions of life were important.

McCarrison sums up as follows:- (17).

- (1) With the possible exception of the thymus and adrenal glands, no organ of the body is more sensitive to food conditions than the thyroid gland, and its sensitivity is greatest in early life.
- (2) Vitamin insufficiency has an important relation to goitre.

The more perfect the constitution of the diet, the more normal is the thyroid gland, both as to its size and as to its action.

The complications of Marasmus are quickly reviewed:-

- (1) Secondary local infections are very common, - in the form of thrush, furunculosis of the skin, otitis media, or bacillus coli pyelitis. Enteritis and bronchopneumonia are especially dangerous.
- (2) Nutritional anaemia, and the effects of lack of one or more vitamins, are common.
- (3) Subnormal temperature, purpura, and oedema, are grave and not uncommon complications.

(4) Rectal prolapse may be a very troublesome occurrence in rapid wasting.

The pathology of the complication "idiopathic oedema" is very uncertain.

Holt considers (ch. XXVII.) that "nutritional oedema" is most often seen in severe malnutrition when the diet has consisted largely of carbohydrate. The plasma protein is reduced. (Panton and Marrock, p. 90, remarks:-- (11).

"When the total protein falls below 5 mgms. per 100 ccs. of plasma, general oedema usually appears.")

The condition may be due to a deficiency of protein or of certain amino-acids in the diet. It may be identical with the "war oedema" and "famine oedema" of older patients - and also with the "wet" form of beri-beri.

The serous cavities are seldom involved.

Of the same subject, Thomson says:--

"One of the commonest and most interesting forms of oedema in young infants is that seen in defective excretion of salts from the body. Excess of salts (and also of sugar) in the young infant's diet, is apt to cause increased retention of fluid even in health, and still more during sickness."

Usually, there is no noticeable superficial oedema, but in the newborn and in the premature, it may go on to obvious dropsy.

In infantile atrophy, oedema is especially prone to occur. Also, it is not uncommon in babies of a few weeks' old, who are being overfed.

The condition requires thorough dietetic treatment and not the mere withholding of salt; although the less sugar and salt that there is, the more rapidly does recovery take place. In oedema occurring in the course of chronic diarrhoea, subcutaneous injection of adrenalin, minims 5. twice daily, seems often to accelerate its disappearance. (Hume, B. M.J., 1911. II.478)

The question of infantile anaemia, requires special mention.

It is essential to remember that the vitamins, which will shortly be discussed, are not the only nutritional factors that matter. Among the most striking of recent work is that of Mackay who has shown how surprisingly common iron deficiency is, in infants.

The infant with nutritional anaemia, although pale, is frequently well-grown and well-nourished.

Normally, iron stores are laid down in the liver and spleen during the last few weeks of foetal life, and these stores fall progressively from birth to the end of the lactation period. Premature infants are therefore particularly liable to anaemia, because they have not had time to make up their stores, and because neither breast nor cow's milk contains sufficient

iron for the needs of the growing babe; and cow's milk has less iron (and copper) than breast milk.

The addition of copper to the therapeutic iron, has been found to bring about a far quicker response in haemoglobin formation, than does iron alone. Copper has no such effect in the absence of iron and its action is thus a definitely catalytic one.

Copper is also stored in the liver.

This nutritional anaemia of infancy is very easily prevented. The premature child must have iron at an early date, while the full term infant should be given it from the seventh month onwards.

Prognosis. The outlook for the wasted infant is always a doubtful one, even while progress is satisfactory. Those cases are worse in which no apparent cause can be found.

Intercurrent diarrhoea and pulmonary infection (the latter may affect the temperature to a very minor extent) are especially to be feared.

When it does occur, recovery is surprisingly complete.

Fatality as a rule, is due to intercurrent infection, but sudden death from no apparent cause is not uncommon; and this collapse may be quiet and unexpected.

Conclusions Regarding Pathogenesis.

We are concerned with the infant who is wasted, but in whom no other signs of disease can be found to account for the wasting. The child was born at term, there is no pyloric obstruction, no gastroenteritis, syphilis, or infection of the ear or urinary tract.

The impression received by the author after a few months' work with infants, is that, in the majority of cases, (apart from the primary conditions named) there is evidence in the "feeding history," of a considerable period of time, over which the food intake has been insufficient. (see section 5.)

To Thomson, "inanition" is one of the three great causes of marasmus.

The clinical picture is one of starvation, while no characteristic lesions are found, postmortem.

It is almost universally accepted that in cases of wasting - uncomplicated by diarrhoea - the splitting and absorption of fat, and the digestion and absorption of carbohydrate, are unimpaired. It has, however, also been well recognised for a long time, that certain children have a reduced tolerance to fat, with the passage of large crumbly stools, a condition corresponding to the "milchnährschaden" of Czerny, and one which

Holt considers can arise from prolonged feeding with raw cow's milk alone. Here again, the digestion and absorption of fat are normal. This definite clinical entity occurred frequently with the use of fullcream dried milks, and was thought to be due to a diminished retention of salts in the body. This was disproved, and the real explanation is still doubtful.

Excess of carbohydrate will apparently only lead to nutritional upset, if the presence of some infection has lead to a reduction of tolerance to this proximate principle; and it is probable that the "mehlnährschaden" of Czerny is due, rather to lack of protein and vitamins than to carbohydrate "injury."

Defective feeding of the mother is an important factor in the causation of wasting in the child, and supplementary vitamin feeds are very useful to marantics, as deficiency syndromes are liable to be superimposed on the picture of wasting.

The results have been given above of a tithe of McCarrison's work; some, suggesting that the effects of vitamins deficiency may be found especially in the gastrointestinal tract; others, indicating the presence of a relationship between certain excesses and deficiencies of

diet, the size of the thyroid gland, and the activity of certain intestinal organisms.

It was in 1926, that Harrington showed that thyroxin (the active principle of the thyroid gland) is derived, not from tryptophane, as Kendall had thought, but from tyrosine, another of those amino-acids which are essential for animal life.

Thyroxine is an iodine derivative arising from two molecules of tyrosine.

It must also be remembered that adrenaline is also closely related in chemical constitution to tyrosine.

McCarrison is strongly of opinion that infected water is the main factor in the etiology of endemic goitre, while Marine maintains that lack of iodine is all important.

The mechanism of the beneficial action of iodine in hyperthyroidism is unknown. McCarrison considers that it acts as a strong intestinal antiseptic, but he showed that excess of fat leads to thyroid hyperplasia, even though abundance of iodine be given. If the action is a chemical one upon the thyroid, it is difficult to explain its cessation after two or three weeks.

It is possible that one action of the thyroid is to keep the intestinal bacteria below a certain level of activity, by

means of a particular concentration of iodine in the blood.

It will be seen that the question of the pathogenesis of wasting is closely connected to that of the necessity to the young animal, of a diet well-balanced and adequate in all respects.

(B) Pathogenesis of the Avitaminoses.

Sir Walter Fletcher has said:- "Many diseases of environment are under our potential control already. Diseases like scurvy, beri-beri, rickets and pellagra, are due to deficiencies of particular vitamins in the food. No doubt, other abnormalities of body, including forms of mental weakness, will be found to be due to similar deficiencies either in childhood or during embryonic life, and we know already, though not yet in enough detail, that deficiencies in diet diminish the resistance of the body to infective disease." (18)

Vitamins are mostly exogenous hormones, and we are dependent for them, in the main, upon vegetable life, as the animal body has very little power of manufacturing them.

Vitamin A. has a provisional formula, the skeleton of which is the same as that of a synthetic perfume called "Ionine."

Carotene, although not identical with A., is converted

into it, when fed to an animal and stored in its liver.

A matter of great practical importance is the fact that A. is easily destroyed by oxidation.

Severe vit A. deficiency rarely, if ever, occurs alone, but there is a considerable and growing amount of evidence that deficiency of a slight grade is not uncommon among the infants of the poorest sections of the population the this country.

The primary effect of a deficiency of vit A. is to cause a characteristic abnormality of certain cell structures, especially of mucous membrane cells and nerve cells.

Briefly, deficiency of A. leads to:-

- (1) Poor growth.
- (2) Xerophthalmia - this is one of the most specific ill effects.
- (3) Hemeralopia or "night blindness" - often unrecognised, although one of the earliest manifestations. The condition can readily be detected (by means of the Birch-Hirschfield photometer) - and cured.

Hemeralopia is apparently accounted for by the special sensitivity to vit. lack on the part of sensory fibres, demonstrated by Mellanby, as compared with the motor fibres.

- (4) Susceptibility to infection. (Green and Mellanby, 1930.)

Vit A. however, is only anti-infective in a limited way; there is

no change in the general immunity.

Dr. Helen Mackay, from her own observations, regards a susceptibility to skin affections as "probably the first sign of vit A. deficiency in infants." (19)

There is no satisfactory evidence that A. lack is responsible for any of the usual respiratory or intestinal infections of children in this country.

(5) Very important effect of increased susceptibility of the central nervous system to toxic influences.

Mellanby showed that in the absence of A., animals developed lesions similar to those found in "subacute combined degeneration" of the cord; lesions which were aggravated by the administration of wheat germ, or of ergot, but completely overcome by adequate A., showing that the rigid dictum is no longer tenable, that a cord tract, once degenerated, can never recover.

Langdon-Brown puts the question: whether the absence of hydrochloric acid and of Castles' "Intrinsic factor" prevents the body utilising vitA. just as it prevents the proper maturation of the red blood corpuscle. (20).

Vit A. is also responsible for the perfect structure of the marginal epithelium of the gums, and

(6) Pyorrhoea. Results when there is lack of it. (This

will be referred to again.)

Shortage of A. seems most likely to occur in young children, and the infant receives very little in utero and from its mother's milk, necessitating ample extra provision, especially at the time of weaning.

Holt, (ch. XXII) points out that the infant patients of A. deficiency, fall into two classes:-

- (1) those with poor fat assimilation, owing to chronic nutritional upset; and
- (2) those fed on a poor fat diet.

Vitamin A. is abundant in cod liver oil, and especially so in halibut liver oil; in these, it is accompanied by vitamin D.

In codlivers, accumulation of the vitamins occurs as the fish age, thus giving oils of high value. It is unknown whether the same applies to the high values in halibut liver oils. It has been found that live steam liberates the oil from cod livers much more readily than from halibut livers.

(Peacock in 1926, showed that the exposure of codliver oil to the light, results in the loss of its vit A. activity.) A. is also abundant in the livers of the ordinary food animals (ox, sheep and pig,) from which D. is absent; and A. also differs from D. in being moderately abundant in green

vegetables, carrot, etc. as Carotene, which is the "provitamin" to A. and of equal biological value to it.

It may be said that no common foodstuff contains the fat soluble companion D. in abundance; (making supplementary dosage of this factor essential in children.)

Egg yolk is the only known foodstuff containing anti-rachitic power to any extent.

Milk, which contains all the known vitamins, only has a nominal and inadequate degree of anti-rachitic power.

It was partly this rarity of D. in natural foods that lead Hess and his fellows to call it the "anti-rachitic factor" and not a "vitamin."

Prior to Mellanby's demonstration (in 1918-19) of the anti-rachitic vitamin as the cornerstone, many hypothesis were held regarding the etiology of rickets.

These roughly were:-

- (1) dietetic,
- (2) environmental, and
- (3) infective.

In 1919, Holdschinsky showed that ultraviolet radiation cured rickets in humans; five years later, Hess showed that these rays

made inert foods patent against human and rat rickets, and the next year, Hess suggested that the radiated ergosterol was produced just under the skin.

The discovery that radiated ergosterol has a profound influence upon ossification, is of far reaching significance.

Ergosterol has a formula of $C_{28}H_{44}O$. It is apparently a derivative of di-benz-anthracene. "Calciferol," the synthetic antirachitic factor is isomeric with the ergosterol from which it is obtained. The nature of the intramolecular re-arrangement produced by the ultraviolet rays, is unknown.

In the Gaulstonian lectures for 1934, Dodds gives an account of "The Hormones and their Chemical Relations." (21)

He refers to the extensive investigations of Kennaway and his colleagues, which showed that those hydrocarbons which are capable of producing "tar cancer," belong to the group of condensed carbon ring compounds derived from di-benz-anthracene; and describes his own experiments with two of these compounds, showing that each of them possessed a dual activity; namely, the power of carcinogenesis, and the power of oestrogenesis.

Pointing out that vit D. is also included in this condensed carbon ring group of compounds, he claims to have shown that this molecule also, may possess two entirely separate

physiological effects, namely, anti-rachitic and oestrogenic activity.

He sums up:- "Whether the phenomena associated with rickets, malignant disease and sex activity are all related, or whether all the locks are capable of being opened by skeleton keys, remains yet to be proved."

The relation of vit D. to calcium and phosphorus metabolism, is the only instance in the present knowledge of vitamins, where it is possible to state the function of a vitamin in terms of chemistry.

The mode of action of vit D. is summed up by Harris as follows:- (22)

"Vitamin D. causes an increased "net absorption" of calcium or phosphate (the two are mutually interdependent) from the intestine - that is, more calcium and phosphate are absorbed from the gut, or less are excreted back from the body into the gut." (Sir Walter Fletcher remarks:-" There still remains for study, the attractive physico-chemical problem of how it is exactly that this calciferol molecule exerts its special influence upon the living cells of the intestinal wall, and exactly why, without it, they cannot do their work of effecting the passage of calcium salts into the

blood, but not back again.')

"Thus the level of the phosphate and/or calcium in the blood rises and, as a secondary mechanical result of this, extra calcium phosphate is precipitated out into the bone. That is, the amount of calcification in the bone depends entirely upon the amount of calcium and phosphorus in the blood: there is no fundamental error in the bone in rickets, but the fault is with the blood, and rickets is in this sense "a disease of the blood." If the blood phosphate and calcium can be kept at the right level, sufficient bone salt is put down and so rickets does not develop, or if it is already present, healing is brought about. This reasoning explains why in vitamin D. deficiency (rickets) one has an excessive loss of phosphate or calcium in the stools, a low blood phosphate, and, in some circumstances, low blood calcium - hence and inadequate deposition of calcium salts in the bone. (As Holt says:- (ch.XXV. p.242.) In active rickets, there is a diminished retention of calcium and phosphorus.

The rachitic child is a prey to minor variations in the mineral balance of his diet.

Ergosterol increases the holding power of the blood, for

calcium and phosphorus.) Whereas, in contrast, with too large doses of vitamin D, we get the reverse picture - increased absorption, hypercalcaemia and/or hypophosphataemia, and a resulting excessive degree of calcification."

The results of other clinicians and workers vary but slightly from this concise summary:-

Thomson - on Rickets.

The blood calcium is always within normal limits in uncomplicated cases; but it is lowered if tetany complicates.

The lowering of the normal 4-5 mgms. per cent. of inorganic phosphorus content is recognised as one of the most constant and delicate tests for active rachitic mischief. (But we see in M.R.C. report, p.49:- "Some say that a low blood phosphorus is not an infallible test for rickets.")

The bony changes are of two kinds:-

- (1) There is a general softening, and
- (2) At the point of ossification, there is an "exaggerated preparation with diminished accomplishment."

Thomson describes how in 1838, Guerin, with a calcium poor diet, produced a condition of osteoporosis, but not rickets, and in 1922, McCallum and his co-workers, feeding rats with a phosphorus poor diet, produced histologically

true rickets. These latter also found that, so long as the phosphorus and calcium in the diet were properly balanced and adequate in amount, rickets would not develop despite complete absence of vit D. Thomson does not consider rickets a true avitaminosis, since two independent factors can lead to it:-

- (1) deficiency of phosphorus, and
- (2) deficiency of D;

but he wonders how the rat rickets can be related to child rickets, as phosphorus deficiency can be definitely excluded in the latter, (human milk containing much less phosphorus than does cow's milk.)

He remarks upon the undoubted varying susceptibility of different infants, to rickets; and that the degree of maturity of the newborn is a factor of the first importance, the premature infant almost invariably developing the disease to some extent.

The fundamental observation that, without growth, rickets cannot result, explains the fact that it is seldom present in marantic infants, but is apt to supervene in cretinous children treated with thyroid gland preparations.

Clinically, rickets is most prevalent in late Winter and early Spring, less common during the Autumn.

The rickety child may or may not be thin; often, he is

unusually fat. Thomson considers that anaemia and pyrexia occur only with complications; also that definite enlargement of the spleen is invariably due to some complication such as tuberculosis, syphilis, anaemia, or chronic pyogenic infection.

Holt considers that anaemia is a frequent accompaniment of rickets, and that in rickets the resistance to infections, especially respiratory, is feeble.

Thomson considers that rickets is distinctly rare in Coeliac disease, but that a degree of osteoporosis is the rule in this disease, and may be very marked. He points out that in Coeliac disease:-

- (1) growth is arrested - explaining the absence of rickets, and
- (2) fat, protein, carbohydrate, calcium and phosphorus, are all poorly absorbed.

The condition Renal Rickets in which Ford (1931) showed that there was a parallel diminished retention of calcium and phosphorus (just as in infantile rickets,) responds neither to vit D, irradiated ergosterol, or ultraviolet radiation.

These are Mellanby's views on bone disease:- (23)

In the normal animal, the structure of bone is the out-

come of a struggle between two influences:-

- (a) tending to perfect formation and calcification, and
- (b) tending to produce comparatively soft bone.

Perfect calcification is assisted by:-

- (1) adequate calcium and phosphorus, and
- (2) adequate vitamin D - either from food or synthesized by the skin, from sunlight or U.V.R.

Perfect calcification is prevented by:-

- (1) foods which produce growth, without supplying adequate calcium, and
- (2) foods which produce growth and also interfere with the retention of calcium in the body.

Perfect bone formation is stimulated by:-

milk,
cheese,
butter,
egg yolk,
meat fat,
fish fat,

all of which contain vitamin D, and the first, second and fourth, much calcium and phosphorus.

Lean meat, white fish, and most vegetable fats, stimulate growth without supplying enough calcium, while cereals (bread, oatmeal, maize and rice) hinder calcification.

(In 1922, 1925, Mellanby suggested the name "toxamin" for the unfavourable agent in cereals, neutralised by

sufficiency of vit. D. M. Mellanby, and Pattison, concluded that "cereals hinder the prevention of dental caries by vit. D." (24). This latter subject will be referred to again.)

Vegetables and fruits are indifferent in their action, save for the calcium contained in some of them, especially in green vegetables. These last, also sometimes contain - if recently in the sun - small amounts of D.

The vitamin C. content of fruit and vegetables, defends the bones from scorbutic influences. Unlike the bones, the tooth, once formed, remains practically unchanged.

Even in adults, when growth has ceased, bone is constantly being absorbed and reformed; thus, a long period of diet poor in calcium, may lead to osteomalacia.

Mellanby proceeds to discuss the subject of: treatment of rickets, standardisation of vit. D. and hypervitaminosis D.

Prevention of Rickets apart from the very important attention to surroundings, lies in giving extra milk, and extra vit. D. because many samples (about 10%) of cow and human milk do not contain enough D. for the perfect formation of bone in early life.

As a preventive, 3i - 3iii of cod-liver oil daily, is ample. ("The smaller dose from birth.") Cod-liver oil is also rich

in A. and iodine, which are often deficient in ordinary diet.

Cereals should be forbidden for the first 9/12 of life, and only allowed in very small amounts for the first two years. The great drawback is the high cost of milk.

The rachitic child should also be given 2 gms. of bone ash daily. (Calcium phosphate.)

Standardisation of Vit. D. has been procured by the definition of an international unit of its activity; cod liver oil containing from 100 to 250 units per ccm. according as to whether it is "ordinary" or "good." D. has now been isolated as calciferol and intensely active preparations are now procurable; for ordinary purposes 3000 units per ccm. is strong enough.

Hypervitaminosis D. is little to be feared if the infant is also given milk in plenty.

There is a real danger of calcification of the renal vessels and tubules if concentrated preparations are given to marantic infants not getting milk in plenty. 20 ccms. of cod liver oil daily (2000 - 3000 units of D.) is enough to cure rickets under ordinary diet conditions.

Langdon Brown points out that the salient point in Vit. D.

deficiency, is a decrease in the net absorption of calcium, (i.e. the gross absorption, less that amount re-excreted into the bowel,) and that in clinical rickets the blood phosphorus and calcium may both be low. (25)

Excess of vit. D. produces;-

- (1) increased net absorption,
- (2) tendency to a high blood calcium and phosphorus,
- (3) excessive formation of densely calcified new bone, and
- (4) deposit of calcium in the soft tissues - especially the kidneys and aorta (which two structures are notably rich in phosphatase, the enzyme concerned with the deposit of calcium.)

With the maximum toxic excess of D., a reabsorption of bone occurs, if there is no increased provision of calcium in the diet.

He describes how hypervitaminosis D. (which is impossible with natural foods) recalls the condition of hyperparathyroidism, but that the several important differences between them may lead to a clearer conception of calcium metabolism.

Parathormone, the very active extract discovered by Collip in 1925, merely raises the blood calcium by withdrawing calcium from the bones. There is increased excretion of calcium through the kidneys but not sufficient to prevent

the blood calcium being abnormally high. The blood phosphorus is lowered, owing to increased excretion in the urine. Langdon Brown remarks that, just as haemoglobin carries oxygen from the air to the deepest tissues, so vit. D. carries sunlight to the darkest parts of the body.

Holt, (ch.LXIX.) notes that:-

- (1) hypo secretion of the parathyroids, leads to tetany with diminished blood calcium, and markedly increased inorganic phosphate. "The Calcium phosphorus product is always higher than in rachitic tetany." There is diminished excretion of calcium and phosphorus in the urine.
- (2) Parathyroid hyperplasia is commonly found in rickets, and may be a compensatory phenomenon which prevents most children with rickets, developing tetany.

(Boyd, ch.XI. - remarking that all the vertebrates have parathyroid glands, except fish, says we have no known histological criteria on which we may gauge the activity of the glands. Parathyroidectomy leads to a great drop in blood calcium excretion in the urine, while the "blood phosphorus is in uninverse proportion to the calcium.")

- (3) Parathyroid hormone given to a normal individual leads

to a rise in serum calcium, a drop in the serum phosphate and an increased excretion of calcium and phosphorus in the urine.

(Parathyroid tumour, says Boyd, leads to hypersecretion, with:-

- (1) blood calcium high but much excreted in the urine.
- (2) low blood phosphorus.)

Thomson finds it difficult to express the true relationship between rickets and tetany. Tetany is a frequent accompaniment of rickets; it is occasionally associated with severe gastro-enteritis, or any marked alkalatic state of the blood (e.g. in pyloric stenosis; or the hyperpnoea of post-encephalitis.)

Only a small proportion of children with rickets develop tetany, and the latter condition almost seems to "prefer" the very mildest of cases, some of the most severe cases of rickets never suffering from it.

Another instance of difference between the two conditions is that florid rickets is seldom met with in the poorly nourished, while tetany - especially latent, is by no means uncommon in malnutrition.

One of the most delicate tests for spasmophilia (active tetany) is a lowering of the blood calcium to 5 to 7.5 mgms. %. Inorganic phosphorous is usually, but not invariably, raised.

(Holt, chap. XXVI, considers that the phosphorous is low,

normal or occasionally high.)

Thomson discusses the three views held regarding the etiology of tetany:-

(1) Calcium depletion - the one serious objection is that the fall of blood calcium is not proportionate to the severity of the condition. Further, in 1923, the virtue of calcium chloride was found to depend, not on the calcium, but on the power to induce acidosis.

(2) Alkalosis - in 1918, Howland and Marriott found tetany to occur after the treatment with sodii bicarb, of acidosis complicating gastroenteritis; while in 1920, Collip and Backhus observed it to occur after forced breathing. Freudenberg and Gyorgy firmly believe that an alkalatic state of the blood and tissue juices (to which state there is a tendency in rickets and tetany) acts by interfering with the ionisation and physiological activity of calcium.

(3) Guanidine poisoning due to parathyroid dysfunction.

In 1912, W. F. Koch found methyl guanidine in the urine

of parathyroidectomised dogs; and in 1916, Paton and Findlay found it in the urine of children with idiopathic tetany.

This theory received strong support in 1931, when Morris Watson and Morris found that guanidine poisoning leads to a fall in blood calcium, and a definite, though slight, alkalosis.

Thomson considers that the tendency to alkalosis in rickets, favours the action of the toxic element guanidine.

On p.64, of M.R.C. Report, we read:- The lowering of the blood calcium in tetany is connected with deficiency of vit. D. and adequate cod liver oil prevents tetany as it does rickets.

Irradiated ergosterol is more rapid and may raise the serum calcium to normal in 10-14 days. Large doses of calcium - or ammonium - chloride, will rapidly alleviate the acute symptoms; the salting administered combining with the plasma bicarbonate and so liberating hydrogen ions.

Med. Annual 1933, p.329.:-

There is evidence that focal sepsis may be an important factor in increasing the severity of tetany, and in preventing its successful treatment.

Specific Treatment of Rickets.

A. Prophylactic - ultraviolet radiation is quite unnecessary.

Harris urges the commencement of prophylaxis at the age of six weeks, starting with a daily dose of 250-500 international units of vit. D., and rising to 1,500. This last, (which is contained in " $4\frac{3}{4}$ teaspoons" of "good cod liver Oil,") is the standard prophylactic dose for children of 1-2 years and upwards, the dose to be continued for "some years" after two.

B. In Curative treatment, Thomson considers that, if anything, ultraviolet radiation cures, in the shortest time.

Miss Harriette Cluik considers that these rays are only of use when it is desired to raise the calcium content of the blood. The general opinion is that ultraviolet radiation is unsatisfactory, in that it takes time, is expensive, and does not supply the valuable vit. A.

Langdon Brown recommends 1 mgm. of irradiated ergosterol as an adequate daily dose for the average case of rickets, and recalls the occurrence of renal calculi after the continued administration of 4 mgms. daily.

To Harris, "irradiated ergosterol seems undoubtedly the method of choice." For a severe case of rickets in infants of 1-2, the daily dose of D. should be 5,000 international units. (This corresponds to .5 mgm. of ordinary

solid irradiated ergosterol, or 15 teaspoonfuls of good cod liver oil. Harris further notes that, 1 gm. of calciferol = 4 gms. of ordinary irradiated ergosterol = 4,000,000 gms. of cod liver oil.)

Harris recommends 3,000 units daily as sufficient for milder cases of rickets, but remarks, "Mellanby has more recently found that in practice, 3,000 units is generally a sufficient dose."

For the human, says Harris, the toxic is indeed quite close to the optimum curative dose.

In the "Lancet" (21. 10. 33. p.911.) Spence reports "Clinical tests of the antirachitic activity of calciferol," while a leader in the same number (p.927) says:- "Calciferol irrefutably cures human rickets in doses of 3, 6 and 9,000 international units of vit. D. daily. Even 3,000 must be more than the nominal curative dose." (26) (27).

Only a small group of wavelengths is capable of forming calciferol from ergosterol, the valuable portion of the spectrum being that between 260 and 315 μ μ .

.....

The Relation of Vitamins to Dental Disease.

The two types of dental defect commonly found in man are:-

- (a) dental caries, and
- (b) periodontal disease (including pyorrhoea alveolaris.)

Vit. D. deals with the structure of the tooth and of the alveolar bone, while A. deals with the structure of the marginal epithelium of the gums.

In guineapigs, vit. C. also plays a part.

It appears safe to conclude that adequate D. is of greater importance in determining the perfect development of the teeth, than an abundant or carefully balanced supply of calcium and phosphorus. There is considerable evidence to show that dietetic factors and especially vit. D. determine to a large extent the resistance of children's teeth to dental caries.

For practical purposes, the ideal to aim at is, by correct feeding during prenatal life, infancy and childhood, to encourage the production of normal or perfect teeth in the adult. This, with a continuance of a sound dietetic régime throughout life, should result in a very greatly diminished

incidence of dental caries in the community.

It is of fundamental importance to give A. and D. during the early developmental period, if the periodontal tissues are to resist disease, a large supply of them, given later - even from the fifth month onwards - does not entirely compensate for deficiency in early period of life; although A. in large doses may prevent the spread of the pathological condition.

(The work of Zilva and Wells, has clearly shown that in guineapigs, the dental tissues are peculiarly susceptible to deficiency of C. It remains to be tested whether this applies to man or not.)

(Dogs and rats are relatively insusceptible to C. lack.)

Vit. D. is the principal factor that determines the occurrence of:-

rickets,
defective teeth, and
infantile tetany.

.....

Vitamin B. Complex.

The knowledge of this is imperfect owing to the conflicting statements by different workers, regarding solubility and stability.

The richest sources of the complex are the bran and germ (embryo) of dry cereals, such as wheat and rice. Yeast contains all the members of the complex abundantly, as also does its extract. (Marmite.)

B₁. This is the more heat labile antineuritis (i.e. anti beri-beri) factor, discovered by Eijkman in 1897. It is necessary for life and growth; and is the only fraction of which there is any definite knowledge, being probably a nitrogenous base, containing sulphur.

B₂ is the more heat stable "Pellagra-Preventing" factor of Goldberger and others (1926.) It is necessary for the prevention of dermatitis in rats.

(B₃ is the heat labile factor in yeast and whole wheat, which Williams and Waterman found, in 1927-28, to be necessary for the full normal nutrition of the pigeon.

B₄ is Reader's heat and alkali labile factor (1929,) present in yeast, and necessary for the rat.

Factor Y. of Chick and Capping (1930) - heat and alkali

stable, and present in yeast and many other foods, but lacking from egg white.)

In general, B₂ accompanies B₁ in ordinary foodstuffs. Hen's egg white, appears to be unique in containing the former, but being devoid of the latter; whilst the yolk contains B₁ alone.

Ultraviolet radiation destroys B₂ and to a less extent, B₁. Yeast is the richest known source of B₁, and is unaffected in this respect by autolysis and extraction.

Parsons remarks that maize alone, contains B₁ without B₂, but it is more generally accepted that the fact that maize does not greatly differ from other cereals in its B₂ content, makes it so difficult to explain the epidemiology of pellagra in terms of B₂ deficiency.

In vit. B. deficiency, carbohydrate metabolism cannot proceed normally, and lactic acid accumulates; this leads to slowing of the heart, and, from its acid on the central nervous system, convulsive symptoms.

It was Funk, (1914,) who first showed that polyneuritis in pigeons (as typified by "head retraction,") was more rapidly produced by B. Deficiency, the greater the amount of carbohydrate ingested by the birds.

There is also some relation between vit. B. and protein metabolism.

McCarrison found that B₁-lack lead to enlargement of the suprarenals in pigeons.

The disease "Beri-beri" - including the infantile variety - is almost universal in certain parts of the globe, but there is little evidence of serious lack in Great Britain and the U.S.A., although some recent American experiments have resulted in very suggestive growth and weight charts.

The disease, which has a high mortality, is generally accepted to be of dietetic origin. The presence of two forms of the disease - namely, the dry or wasting form, and the wet or oedematous form - suggests that it may eventually prove to be a syndrome and not a clinical entity.

In 1928, McCarrison considered that the disease was, in part at least, a toxæmia.

In countries where beri-beri is prevalent, diets are invariably ill-balanced, and it is probably unwise to regard the problem in the tropics as being solely a question of polished or unpolished rice.

Infantile beri-beri occurs among breastfed babies in

the Philippines and in the Island of Nauru in the Pacific, whose mothers have the disease. Andrews showed that it was attributable to B.-lack in the maternal milk.

In adults, there is a latent period of apparently not less than 90 days. In infants the disease is typified by restlessness, loss of appetite, and later, cardiac failure. Fever is absent and prompt treatment may save.

In 1928, Hoobler suggested that infantile malnutrition might be due to a partial deficiency of the anti-neuritic factor; and his especial symptom complex was one of loss of appetite and weight, fretfulness, and stiffness of the limbs and neck.

Holt considers the relationship as not yet established. It is generally considered worth while, however, to bear B₁ deficiency in mind as a possible cause of poor development in infancy.

At present there is no convincing clinical evidence to show that the B. complex determines the normal functioning of the human bowel, and so it is unnecessary to assume that B. deficiency causes the constipation so common among western peoples.

Pellagra. - A disease, seen at almost all ages,

though comparatively rare in very young infants, - occurs preeminently in the warm months.

The incidence is very high in the U.S.A. (120,000 cases in 1927, with a mortality of about 40%,) but Harris does not consider it a disease of children; and in 1919, did not find a single case in a nursing child.

Recent workers in Denmark, have shown that Pellagra is commoner in that country than was once thought, and especially so in insane institutions. (Lancet, 24.6.33. p.1356.)

It is well recognised that children of pellagrous parents are often born in a very poor nutritive condition, not diagnosable as pellagra, but probably referable to it.

The symptoms are characteristic and easily recognised, the rash, very symmetrical and non-irritant, the diarrhoea, as a rule, (vomiting being rare,) and the nervous symptoms.

Pellagra is almost exclusively a maize eater's disease; its appearance being rare among consumers of other materials.

Theories of the etiology of pellagra and of beri-beri have run a similar historical course, - from diet to microbes and back to diet again.

Beri-beri, is related to B₁ deficiency, but the exact

relationship between pellagra and an error in diet, still remains to be shown conclusively.

Theories of Etiology.

(1) Amino-acid deficiency theory. The importance of such a deficiency in the causation of pellagra, is difficult to assess.

(2) Theory of absence of a "pellagra preventive" factor in milled maize. It was Funk, who, in 1912-13, first suggested that pellagra was due to a vitamin deficiency, and advanced a theory that a factor was removed in the milling process.

Despite the work of Voegtlin (et al) in 1920 - (who found the therapeutic value of an alcoholic extract of ox liver to be as great as that of milk, eggs and meat;) and despite the discovery of the factor known as B₂; it is not yet justifiable to assume that pellagra and B₂ deficiency are synonymous, because of certain facts, such as, millet and rice are low in B₂ content, and yet are rarely associated with pellagra.

Pellagra and Beri-beri.

Diets composed almost exclusively of milled rice and refined wheat flour, are commonly found among populations liable to beri-beri, but this disease is rarely recorded

among maize-eaters. There is possibly enough B₁ in the latter's diet to let them subsist long enough on this diet to develop pellagra, supposing the latter disease to be due to B₂ deficiency and to occur after a longer depletion period than beri-beri.

Further, it is possible that the eater of milled rice alone, dies of ber-beri before he can get pellagra.

(3) The "maize toxin" theory of pellagra, is still held officially in Italy. This suggests the presence in maize of a positive "pellagra-producing" factor, perhaps operative only in the absence of a "pellagra-preventing" factor.

Thus the pellagra-preventive factor may neutralise a toxin rather than make up a deficiency, just as vit. D. neutralises the anti-calcifying effect of certain cereals, although it also makes up a deficiency.

Many points therefore, remain obscure.

Harriette Chick makes the following speculative suggestion:- "Pellagra is caused by a toxic substance derived from a maize diet, which can be corrected by sufficient good protein, or perhaps by sufficient vit. B₂ (which is found to accompany good protein.) (28).

Chick again gives the analogy of Mellanby's cereal

to draw an analogy between this disease and those infections
that arise as a result of a diet lacking in vit. A.

These are difficulties that arise from the unfortunate
acceptance of a direct causal relationship between the vitamins

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"toxamin" and vit. D; and also suggests a relationship be-
tween the increasing prevalence of pellagra in the U.S.A.
among severe alcohol addicts; and the fact that the liquor
may be distilled from maize products insufficient food being
taken to neutralise the poison.

The Danish workers mentioned previously, found that
even when the dietary was sufficiently mixed, and apparently
contained adequate B₂, severe pellagra might develop if
chronic disease of the gastrointestinal tract impaired the
absorption of food. The mental patient who refuses to eat
seems to be particularly liable to contract pellagra on the
slops with which he is forcibly fed. (29).

It is of great importance that the conception of the
presence of "toxomins" in the normal basic foodstuffs,
should be thoroughly tested or abandoned. If true, it
would be of fundamental importance.

The theory does not explain the seasonal appearance,
subsidence and recurrence of pellagra.

The possibility that infection plays a part in the
etiology has not been proved untenable. It may be possible

to draw an analogy between this disease and those infections that arise as a result of a diet lacking in vit. A.

These are difficulties that arise from the unfortunate acceptance of a direct causal relationship between the vitamins and certain diseases. (It is appropriate to recall here that Rickets will not develop in the absence of Vit. D. if the proportion of calcium and phosphorus in the diet is near optimal; but D. corrects the absorption and assimilation of calcium and phosphorus when these are supplied in unsuitable proportions.)

Vitamin C. has been definitely isolated, and is identical with an acid - "ascorbic acid" - of the formula $C_6H_8O_6$. This is present in lemons and cabbage, and also in the suprarenal cortex. Red pepper is its most abundant source.

This acid is probably an oxidation product of a hexose sugar. It possesses a labile hydrogen atom whereby it can exist in an oxidised and in a reduced form and so possibly play a part in the catalysis of tissue oxidations. (9)

It effectively protects guinea pigs against scurvy, and has recently been shown to cure the disease in humans. (30)

Harris maintains that, in vit. C. deficiency, the primary failure is in the function of certain highly active cells - odontoblasts, ameloblasts, etc. - and that other changes observed, are secondary to this effect.

C. is very easily decomposed - being destroyed by:-

- (1) keeping,
- (2) exposure to air,
- (3) double heating.

Posteurising destroys it, especially if copper be present.

Lemon juice, tinned whole tomatoes, green vegetables, and raw swede juice, are all rich in this factor. Milk is a variable, but by no means rich, source. Scurvy may occur in the breastfed, but appears to be rare.

Vit. C. is found in nature associated primarily with living plant tissues, in which active metabolic processes are still proceeding. This is in marked contrast to the anti beri-beri factor of which dry seeds form one of the principal sources.

In Scurvy - there is rarefaction of the long bones, and atrophy of the other tissues, although McCarrison maintains that the adrenals are enlarged. The capillary endothelium is swollen and degenerated and Hess and Fish showed in 1914,

that it was this morbid change that was responsible for the haemorrhages. Besides a secondary anaemia, there is no marked change in the blood picture (although in guineapigs, there are degenerative changes in the bone marrow.)

Clinically, almost all cases fall between the sixth and fourteenth month. There is an undoubted individual susceptibility. Unlike ordinary malnutrition, growth in length as well as in weight is seriously interfered with in longstanding cases. Emaciation is not marked, but asthenia is extreme.

Petechiae and subcutaneous haemorrhages are rare, and bleeding from the mucosae uncommon. The essential lesion is a subperiosteal blood extravasation; haematuria is the only common external haemorrhage, making urinary microscopy of great diagnostic significance. There may be well marked "pitting on pressure." The temperature is very erratic, and liability to infections is marked.

Harris maintains that lack of C. leads to faulty formation of the dental enamel, and is probably a contributory cause of dental caries.

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C. Pathogenesis of the "Intoxications." (Acidosis and Alkalosis.)

Thomson and Holt are agreed that during health, the blood and tissue juices of the body are slightly but definitely alkaline.

Panton and Marrack however, say that the reaction of the body fluids, lies near that of water, which is a very weak acid, having a hydrogen ion content of $\frac{1}{5,500,000}$ at 37°C.

(The hydrogen ion content, or C_H , is the number of gms. of H. ion per litre.)

Acetone in the urine, indicates acetonæmia which is the same as ketosis, but it no more gives a clue to the underlying pathological process, than does the temperature in a febrile condition.

Acidosis is a condition of diminution of plasma bicarbonate due either to accumulation of acids (other than carbon dioxide,) or to a diminution of base in the plasma.

It is customary to express the plasma bicarbonate as the number of ccs. of C^O_2 present combined as bicarbonate in 100 ccs. of plasma.

Thomson remarks that, a true acid state of the blood never occurs; the ultimate factor in determining the reaction

of the blood is the ratio between the free CO_2 (normally 1/20th of the whole,) and that combined with the base; or thus:-

$$C_H = \frac{\text{H}_2\text{C}^{\text{O}}_3 \text{ concentration}}{\text{bicarbonate concentration}} \times \text{constant.}$$

Normal	55-70ccs.	CO_2 in 100 ccs. of plasma.
slight acidosis	45-55 "	" " " " " "
moderate "	30-45 "	" " " " " "
severe "	30 "	" " " " " "
moderate alkalosis	70-90 "	" " " " " "
severe "	90-120"	" " " " " "

(Panton & Marrack. p.94.)

As regards acetone bodies; normally, in 100 ccs. of blood plasma, there may be from .000-.006 gms. of β hydroxybutyric acid. With starvation, this may rise to .04 gms., and in diabetic ketosis, up to .15 gms.

Acetonaemia (or ketosis) may induce acidoses, but in the vast majority of cases, it does not do so.

Thomson points out that to diagnose acidosis, there must be evidence of a change in the acid base balance, either from estimation of the CO_2 content, or from the symptom of hyperpnoea. (A reduction of the proportion of carbonic acid is an index of acidosis, and an increase in its

proportion, an index of alkalosis; and yet it is important to remember that a lowered CO_2 content, does not always signify acidosis, since it may be the primary change (for example, from overventilation of the lungs.)

The clinical history must therefore decide whether a particular CO_2 content spells acidosis or alkalosis.)

The retention of acetone bodies is of greater clinical importance than the amount excreted, and the retention varies considerably with the efficiency of the kidneys. Thus a ketogenic diet may lead to marked acidosis, and yet no symptoms may arise, the acidosis being "compensated" for by the functional activity of the excretory organs.

The body is protected against changes in the reaction of the plasma by:-

- (1) the "buffer action" of the blood, and
- (2) by the excretory action of the lungs, kidneys, and intestines.

Acidosis may follow from two main causes:-

- (a) Excessive formation or ingestion of acid; and
 - (B) Inefficient excretion of acid.
- † (c) A third cause is described, resulting in acidosis in infants with acute gastroenteritis. Here, the cause is the

loss of base in the alkaline stools, together with the starvation owing to the vomiting.)

(a) Excessive formation of acid may occur normally after severe exertion.

The chief pathological condition under this heading is ketosis, especially diabetic ketosis, but it must be strongly emphasized again that acidosis does not invariably occur in ketosis, and still less are all forms of acidosis due to ketosis.

Anaesthetic acidosis - is a milder condition. (Thomson, however, considers "postanaesthetic acidosis" to be a rare condition. It can occur even after ether administration. It is usually fatal, and fatty degeneration, and even necrosis of liver and kidneys is found post mortem.)

A therapeutic acidosis, by giving ammonium or calcium chloride, is induced in treating infantile tetany.

Salicylate poisoning is very apt to arise, with symptoms of acidosis, if salicylates are given unaccompanied by sodium bicarbonate. The cause is not yet definitely understood, but ketosis is not the chief factor.

The severity of the condition is unrelated to the amount of salicylate ions present.

Morris and Graham (Arch. Dis. Child, 1931,) showed the

importance of the part played by the excretory function of the kidneys.

The clinical entity, "periodic acidosis," or "cyclical vomiting," is an important one.

The pathogenesis is still obscure, but there is apparently a spontaneous acidosis which arises at intervals of the greatest regularity in any individual case - commonly every one, two or three months.

Thomson considers the first title preferable, because vomiting may be absent, and the clinical picture one of pharyngitis, bronchitis or colitis.

If present, the vomiting starts suddenly, for no apparent reason: the condition may become worse with great rapidity. Fever may or may not be present: the bowels are constipated as a rule. There is collapse in severe cases. Examination is negative save for the presence of acetonuria and perhaps some abdominal tenderness. The vomiting may suddenly cease when death appears imminent.

The onset of the condition is usually in the second or third year: the patient is essentially of the non-hospital class, and is commonly "highly strung" and nervous.

There is a tendency to spontaneous recovery after

puberty, but the condition may continue, or may relapse later as "migraine."

Pathogenesis. As stated, this is still obscure. Thomson definitely puts aside "autointoxication" from the bowel, and "food idiosyncrosy." He considers that "overstrain" is not a contributing factor, and points out that an attack seldom occurs during a period of observation. A "ketogenic diet" when given to one of these patients, will neither induce an attack nor exacerbate one, when given deliverately at the outset.

During an attack, the blood sugar may be unduly low, but as a rule is not so. The Laevulose test, however, shows the hepatic functions to be impaired.

Thomson considers the condition to be in great part "nervous;" and wonders whether the nervous phenomenon affects the hepatic nerves, causing an inhibition of deamination; and again, whether the impairment of liver function interferes with oxidation, and predisposes to hypoglycaemia.

He considers dieting of little avail in prophylaxis; and that sod. bicarb. in half drachm. doses, thrice daily for 12-18 months, is the best preventive. In active treatment, he gives small frequent doses of sod. bicarb; but

recommends 10% glucose intravenously as the quickest method.

Professor Feer notes (p. 314) that at autopsy on one of his two fatal cases, the findings were entirely negative.

Reginald Miller (31) believes that definite organic conditions are responsible for a much larger proportion of cases of "so called acidoses in children" than is generally accepted. He instances specially, the not uncommon "chronic appendix", and the rarer conditions of atonic stomach and duodenal ileus.

Setting aside these cases, he further believes that three factors are at work.

(1) The attack is started by an intense poisoning of the liver; witness the pale stools; and the post mortem finding of fatty degeneration of the liver.

(2) The presence of intestinal toxæmia is incontestable; the stools are foul and contain mucus.

(3) There is a lowering of the "glycogen reserve" but "in the very numerous instances where intestinal toxæmia is at all profound, glucose therapy is a complete failure," and the intestine needs prolonged treatment, before a cure results.

"It seems we must no longer invoke a ketosis as the cause of the symptoms."

(b) Inefficient excretion of acid:

This occurs when the kidneys are severely damaged, and is the commonest form of acidosis. There is retention of phosphoric and sulphuric acids; but defective formation of ammonia also plays a part.

There is a moderated degree of acidosis in the uraemic state.

It is to be remembered that changes in the plasma bicarbonate are accompanied by proportional changes in the CO_2 tension of the alveolar air, provided that:-

- (1) the hydrogen ion content of the blood plasma is constant, and
- (2) there is no interference with the gas exchange between the blood and the air in the lungs.

The carbonic acid concentration of the plasma is raised by:-

- (1) severe exercise,
- (2) disease of the heart and lungs, and
- (3) breathing excess of CO_2 ;

and it is reduced by:-

hyperpnoea.

The normal hydrogen ion concentration of the plasma lies from, pH. 7.3-7.5.

Down to pH. 6.9, and up to pH 7.8, are pathological.

Changes in the respiratory exchange compensate to some extent for changes in the plasma bicarbonate, so that the hydrogen ion concentration is kept fairly constant, - for example, if the bicarbonate is reduced, hyperpnoea occurs and so reduces the carbonic acid concentration. Thus, we have a "compensated" and an "incompensated" form, of both acidosis and alkalosis.

"Compensation" is much more successful in the acidosis of diabetic ketosis, than in the acidosis of nephritis, - owing to the great hyperpnoea in the former.

(The symptoms of diabetic coma are due, not to the reduction of plasma bicarbonate - the "acidosis" - but to the actual acetone bodies.)

In heart and lung disease, hyperpnoea usually occurs to prevent the accumulation of CO_2 , and even to reduce it to below normal. In hysteria, and especially in hyperpiesis, the hyperpnoea reduces the H. ion concentration.

The distressing hyperpnoea, however, seen in hyperpiesis is not due to acidosis.

The fact that the reduction of the H.ion concentration of the blood, alone, often leads to ketosis, illustrates the fallacy of calling ketosis, acidosis.

Alkalosis - is the condition of increased plasma bicarbonate, due to loss of acid or increase of base.

Alkalosis may result from:-

- (a) the ingestion of alkalis, (as in the treatment of gastric ulcer, of ketosis, or of nephritis;) and
- (b) the loss of acids; this occurs especially in acute high intestinal obstruction; also in other conditions accompanied by profuse vomiting, e.g. pyloric stenosis.

Overventilation of the lungs, by an excessive loss of CO_2 , may lead to alkalosis.

In alkalosis, whatever the cause, there is an increased mechanical and electrical excitability of the nervous system.

Alkalosis is a much more dangerous condition than acidosis, because of:-

- (1) the activity of the respiratory centre is depressed, and
- (2) the greater stability of the haemoglobin and oxygen compound. This increased stability results from the diminution of H. ion content of the plasma, and it checks the transfer of the oxygen from the blood of the tissues.

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SECTION 5.

Clinical Features.

In this section, three clinical pictures will be briefly examined:-

- (1) marasmus,
- (2) pyloric stenosis,
- (3) "Pink Disease."

Marasmus.

In the early stages, there is a failure to gain weight, and the appetite may be lost. (It is not uncommon, however, for the weight to be stationary for one or two weeks in the healthy infant of less than six months old.) As a rule there is no vomiting, and the stools are normal but they may be pale and crumbly, or the small loose and dark "hunger stools." As the condition proceeds, there is a definite loss of weight, and a liability to infection arises. The temperature is unsteady but tends to be subnormal; the respirations are irregular and of Cheyne Stokes type; the motions may be normal, but are frequently bulky, pale and soapy, or small and dark green, containing mucus.

It is not widely enough known that starvation not infrequently leads to vomiting and even to diarrhoea - although the motions are small and not to be mistaken for

the stool of enteritis. The advanced case has the look of the "toothless old man." The appetite is more often lost than preserved. Vomiting and diarrhoea are easily provoked.

Whether the wasting is due to starvation, excess of fat in the diet, or to a chronic infection, the clinical picture is the same. Nor is there any radical difference in the toxic symptoms and evidences of gastrointestinal indigestion (vomiting and diarrhoea) with anhydraemia, whether the exciting toxin is produced locally by decomposing food or pathogenic organisms, or whether the bowel is damaged by toxins produced at a distance.

Parenteral infections, however, are seldom accompanied by the degree of dehydration so typical of acute gastro-enteritis.

It must be repeated that one type of lesion leads to another, and in most cases, more than one factor is at play either simultaneously or alternately.

During the five months from 1.2.34. - 1.6.34, 146 children below the age of 1 year were admitted to the Sheffield Children's Hospital.

Of these, 55 were surgical cases; the 91 medical cases were composed of:-

pylorospasm	-	2
congenital pyloric stenosis	-	11
convulsions	-	8
chest conditions	-	11
"dyspepsia" (D.V. constipation, marasmus, prematurity.)	-	41
extras	-	18
		91

41 cases of dyspepsia.

9 cases died: - mortality 22%

(1) S.N. (m) $7\frac{1}{2}$ lbs. at 12 weeks. History of constipation and loss of weight; evidence of underfeeding;

4 days after admission. P.M. nil. characteristic.

A.T. (m) twelfth child. 10 lbs. at birth; D & V.

since breast feeding stopped at 1 week. $6\frac{1}{4}$ lbs. at 3 weeks; died 7 days later with fever, and slow

irregular respirations: P.M. nil. characteristic.

D.H. (f) $6\frac{1}{4}$ lbs. at 2 months. Wasting since breast stopped at 5 weeks. Generalised soft oedema gradually

developed from below upwards; died after 6 days.

(Periods of marked hypothermia.) M.P. - hydrothorax

and peritoneal fluid++ : kidneys satisfactory.

- (4) N.B.(m.) PINK DISEASE. $13\frac{1}{2}$ lbs. at 9 months.
one month's history of trunk rash, wasting anorexia,
constipation, redness of hands and feet. No cough or
vomiting. Flabby muscles. Collapsed 12 days after
admission after several loose yellow stools.
P.M. nil. characteristic.
- (5) D.E.(m.) $5\frac{1}{4}$ lbs. at $2\frac{1}{2}$ weeks. Died after 27 days of
stationary weight; for last 2 days, had dyspnoea with
evidence of "collapse of upper aperture of larynx."
- (6) C.W.(m.) 7 weeks old. D.& V. 4 days. Died same day.
- (7) C.H.(m.) 10 months. D.& V. 4 days. Died same day.
(Admitted 14 days after C.W.)
- (8) D.S.(f.) 6 months. D.& V. 7days. Died same day.
(admitted same day as C.H.)
- (9) M.A.(f.) 11 lbs. at 5 months. Eczema for past 2 months.
died after 15 days of anorexia and loss of weight.

(All these infants were "wasted." i.e. were less than 80%
of their expected weight.)

8 cases were of a mild nature.

	<u>Days in Hospital.</u>
(1) <u>H.T.</u> (m.) 13 lbs. at 4/12. 1/52 of diarrhoea.	7.
(2) <u>B.S.</u> (f.) 16 lbs. at 5/12. vomiting occasionally.	6.
(3) <u>E.R.</u> (f.) 18 lbs. at 9/12. Diarrhoea.	9.

Days in Hospital.

- (4) K.S.(m.) 13 lbs. at 7/12.
Constipation. 8.
- (5) H.R.(m.) 12 $\frac{1}{2}$ lbs. at 2/12.
D.&V. 1 week. 8.
- (6) J.B.(f.) 14 lbs. at 5/12.
D.&V. 1 week. 4.
- (7) H.B.(m.) 18 lbs. at 9/12.
Constipation. 6.

(None of these infants was wasted.)

NAME.	AGE MONTHS.	SEX.	WT. LBS.	HISTORY.	DAYS IN HOSP.	TREATMENT.	PROGRESS.
W.C.	1/12.	m.	6 $\frac{1}{4}$.	"wasting" since breast stopped at 2/52.	18.	Full milk by 3rd. month.	10 lbs at 6/12.
J.A.	7/12.	f.	11 $\frac{1}{4}$.	10th child, breast-fed. Pink Disease 3/12 history.	83.	m/w : 2/1. Vitamins.	17 lbs at 10/12.
E.H.	4/12.	m.	8 $\frac{1}{2}$.	ii Nestles t.i.d. from 2/52 wasting.	40.	Protein milk - skimmed - full milk.	12 lbs. at 6/12.
D.S.	6 $\frac{1}{2}$ mths	m.	12 $\frac{1}{2}$.	C. & G. from 1/52 old.D. & V. - 1/52.	66.	Calomel, sherry whey, protein milk, intra-peritoneal saline.	16 lbs at 10/12.
J.McC.	10/12.	m.	13.	Breast-fed 3/52 D. & V. 2/52.	29.	Calomel, sherry whey, protein milk.	19 lbs at 13/12.
G.H.	4/12.	m.	6 $\frac{1}{2}$.	Costive and vomiting from age 2/52.	22.	Raised in 4 weeks to m/w : 2/1.	13 lbs. at 8/12.
A.W.	7/12.	m.	11 $\frac{1}{2}$.	Costive and vomiting since birth.	18.	$\frac{1}{2}$ cream Cow & gate.	Untraced.
N.L.	3/12.	f.	11 $\frac{1}{2}$.	D. & V.	30.	Calomel, breast and protein milk. m/w : 2/1 in 3 weeks.	16 lbs at 8/12.

NAME.	AGE MONTHS.	SEX.	WT. LBS.	HISTORY.	DAYS IN HOSP.	TREATMENT.	PROGRESS.
A.C.	3/52.	f.	6 $\frac{1}{4}$.	3 days D. & V	52.	Calomel, sherry whey m/w : 2/1 in 6 weeks.	9 lbs at 4/12.
M.P.	4 $\frac{1}{2}$ mths.	f.	7.	Wasting since pertussis.	12.	m/w : 2/1 3 v. 3-hourly.	11 lbs. at 6/12.
A.B.	1/12.	m.	6 1/3	Bengers from 1/52 old, wasting & vomiting	25.	$\frac{1}{2}$ cream C. & Gate - m/w = parts.	10 lbs. at 4/12.
V.C.	3/52.	f.	7 $\frac{1}{4}$.	D. & V. 1 day.	20.	Calomel, protein milk, m/w = parts in 1 week	10 lbs. at 3/12.
R.C.	2 $\frac{1}{2}$ mths.	m.	5 $\frac{1}{4}$.	1/52 vomiting.	11.	Calomel, protein milk m/w = parts in 1 week	9 lbs. at 4/12.
T.B.	3 $\frac{1}{2}$ mths.	f.	6 $\frac{1}{2}$.	Wasting since pertussis 2/12 ago.	50.	Protein milk, $\frac{1}{2}$ cream C. & G., intraperitoneal saline.	9 lbs. at 6/12.
M.B.	2/12.	f.	10.	Diarrhoea 1 week.	25.	m/w : 2/1 in 2 weeks.	14 lbs. at 5/12.
T.H.	9/12.	f.	7 $\frac{1}{4}$.	2 $\frac{1}{2}$ lbs. at birth, rusks & Nestles, wasting & costive, no vomiting	5.	(Nasal Diphtheria).	Untraced.

NAME.	AGE MONTHS.	SEX.	WT. LBS.	HISTORY.	DAYS IN HOSP.	TREATMENT.	PROGRESS.
M.P.	1/3 mth f.	f.	4.	4½ lbs at birth, 6/52 premature. No vomiting.	52.	At 2/12 reached ½ cream C. & G. 3 iii - 3 iv.	9¼ lbs. at 4/12.
J.W.	2/12.	m.	9.	Fed on Nestles, chronic vomiting, stools normal.	47.	½ cream C. & G. m/w : 2/1.	13 lbs. at 6/12.
J.W.	5/12.	f.	5½.	Wasting 1/12, costive & vomiting 2 weeks.	61.	m/w : 2/1.	8 lbs. at 8/12.

On Parson's "80%" standard, all the above 19 infants were wasted except:-

- N.L.
- V.C.
- M.B.
- J.W. (m)

D.S.)
A.C.) are on the border line.
A.B.)

Pyloric Stenosis.

This condition, the diagnosis of which rests upon:-

- (1) marked visible gastric peristalsis,
- (2) palpable thickening of the pylorus,

is perhaps commoner than is generally realised. When seen, the patient is aged less than four months. Symptoms are very rarely "congenital", and rarely start after eight weeks of age. The variation in the history is seen in the accompanying table. Sometimes an obstinate refusal to suck is found early in the case.

Although the association of vomiting with constipation is suggestive, there are exceptions in both directions. Also, feeble gastric peristalsis may be seen in chronic vomiting and in constipation. Still considers that only in very rare instances is the pylorus not palpable. (palpable in 309 out of 312 cases). In a recent analysis of 145 cases operated on at the Royal Edinburgh Hospital for Sick Children during the 12 year period, 1922-33 inclusive, Wallace and Wevill report that a palpable tumour in the pyloric region was noted in only 24% before operation. (43)

Still considers too that recurrence after Rammstedt's operation is very rare; if it occurs it is within 7 to 10 days of the operation and is to be diagnosed from the recurrence of forcible vomiting, and not by visible peristalsis or a palpable pylorus, both of which may be present without recurrence of the obstruction.

NAME.	SEX.	ADMISSION.		LENGTH OF HISTORY.	OPERATION RAMMSTEDTS.	DISCHARGE		PROGRESS.
		DATE.	AGE.			WT.	DATE.	
Healey.	m.	2.2.34.	2/12.	6.14 $\frac{1}{2}$	G.A. 5.2.34.	22.2.34.	7.1.3 $\frac{1}{2}$	17 lbs. at 7/12.
Helliwell.	f.	3.3.34.	6/52.	10.2 $\frac{3}{4}$	G.A. 13.3.34.	4.4.34.	10.12 $\frac{3}{4}$	14 lbs. at 6/12.
Mawhood.	m.	12.3.34	1/12.	6.3 $\frac{3}{4}$	Bowels satisf. wasting and vomiting 17 days. 2nd child	G.A. 14.3.34. Collapsed 18 hrs. after op- eration and died.		
Berry.	m.	4.4.34.	5/52.	4 $\frac{1}{2}$ lbs.	2nd child, costive & vomiting since birth.	Died in 4 days, pneumonia.		
Atkin.	m.	5.4.34.	9/52.	9 $\frac{1}{2}$ lbs.	Bowels regular vomiting since birth, worse for past 1/52; vomited for several days after opera- tion.	G.A. 9.4.34. 14 lbs. at 5/12.		

NAME.	SEX.	ADMISSION.		LENGTH OF HISTORY.	OPERATION	DISCHARGE		PROGRESS.
		DATE.	AGE.			WT.	DATE.	
Watkinson	m.	17.4.34	1/12.	Bowels satisf. vomiting 2/52, only child.	L.A. 23.4.34.	12.5.34.	5.13}	10½ lbs. at 3/12.
Staples.	m.	28.4.34	6/52.	Costive & vomiting 2/52 only child.	L.A. 2.5.34.	18.5.34.	9.6}	13 lbs. at 4/12.
Langrish.	m.	10.5.34	11/52	Costive & vomiting since birth.	G.A. Same day.	Died 5 days later; diarrhoea no fever.		
King.	f.	28.5.34	11/52	Costive since birth, vomiting 5 weeks; projectile & losing weight 1/52.	L.A. 31.5.34.			12½ lbs. at 4/12.
Smart, C. (twin)	m.	30.5.34	2/12.	Bowels satisf., vomiting 5/52.	L.A. 31.5.34.	18.6.34.		9 lbs. at 3/12.

NAME.	SEX.	ADMISSION		LENGTH OF HISTORY.	OPERATION	DISCHARGE		PROGRESS
		DATE.	AGE.			WT.	DATE.	
B. Smart. (twin)	m.	30.5.34	2/12.	6.1 $\frac{1}{2}$	L.A. 31.5.34.	18.6.34.		9 $\frac{1}{2}$ lbs. at 5/12.
Swallow.	m.	18.6.34	6/52.	5 $\frac{1}{2}$ lbs.	L.A. 21.6.34.			Gained 1 lb. in 10 days.

Twelve cases operated upon in 4 $\frac{1}{2}$ months; 3 died.

In the following cases, gastric peristalsis was visible for a few days.

- Wood, m. Admitted on 3.2.34. 5/12 old. 8.53. "Gonorrhoeal ophthalmia". From 14.2.34 - 19.2.34. forcible vomiting, stools loose and slightly green, moderate gastric peristalsis seen.
Discharged 13.4.34. 9lbs.
? Pylorospasm.
- Hibbert m. Admitted 6.12.33. 5/12. 6.113. "Wasting". 1/12 premature. Vomiting and constipation after admission. 23.12.33. Large gastric residue 9 hours after Bc. meal. 24.1.34. Gastric peristalsis seen for first and only time. 2.2.34. "Feeds well"; bowels satisfactory; weight stationary for past 6/52.
9.3.34. Discharged - 9.103.
Probably inanition.
- Shaw, m. Admitted 10.2.34. 10/52. 9.33. Costive, forcible vomiting past 1/52. Well-worked visible peristalsis. 20.2.34. "No vomiting past 4 days; stools normal". 26.2.34. Discharged 9.13.
Pylorospasm.

PINK DISEASE is another condition in which the most striking feature may be a loss of weight and appetite. The majority of patients are from 9 months to 2 years old, but may be from 3 months to 4 years. Characteristics are restlessness, irritability and wretchedness. Photophobia is important. The bowels are more often costive than loose, and there is no spontaneous vomiting.

Profuse sweating and an irritable meat rash on the trunk are soon followed by a bluish red rash on the hands and feet where there is also some swelling but no true oedema and no increase in heat. These areas are very irritable.

Hypotoma of the muscles is marked and early. There is tachycardia and a moderate leucocytosis, but the polymorphs are in normal proportion.

The following are some of the points from a recent review of 100 cases at Birmingham:- (Lancet. 21.4.34. p. 857)

1. The disease may begin at any time throughout the year, with a predominance in the early spring months.
2. Sexes are equal, and the state of physical welfare frequently first class, the disease not uncommonly starting during breast feeding.
3. A sudden onset is unusual. As a rule it is preceded by some infection of the upper respiratory tract.
4. Fever is absent in 90% of cases.
5. The course is protracted - a moderate case lasts about 100 days - and as a rule the younger the child, the shorter the duration.
6. The essentials of treatment are:-
 - (a) the avoidance of superadded infection,
 - and (b) the provision of good nursing and an adequate food supply.
7. Etiology. A microbial agent of low infectivity is considered to be the most likely cause. The addition of vitamins, or other special food factors, such as liver, to the diet, was not found beneficial.

Moreover, severe anorexia has often to be contended with - if

necessary by the stomach tube.

8. Prognosis - 14 out of 100 died in hospital, mostly of broncho-pneumonia, in none was any mental or physical defect found.

(Notes on 2 cases are seen in the list of personal cases of wasting noted. One died.)

Inability to nurse.

Defects in breast-feeding

Insufficiency,
poorly milk.

Not-nursing.

Artificial feeding

Principles,
cow's milk,
whole milk feeding.

Imagined,
Milk,
Infants,
Milk,
System.

Feeding the average
infant.

Kilbuck,
Fitchman,
Milk,
Milk.

Feeding the weakly
infant.

Glaxo,
sterilized,
Crisol,
condensed,
milk.

Responsibility to
cow's milk.

Scott's milk,
protein milk,
Anso's milk.

Preparatory foods.

Further principles.

SECTION VI.

TREATMENT.

Breast-feeding.

Diet in pregnancy.

Breast milk Vitamins in,
characters of.

Inability to nurse.

Defects in breast-feeding Insufficiency,
irregularity,
faulty milk.

Wet-nursing.

Artificial feeding ... Principles,
cow's milk,
whole milk feeding.

Longnead,
Still,
Hutchison,
Holt,
Thomson.

feeding the average
infant.

Edinburgh,
Hutchison,
Holt,
Still.

feeding the weakly
infant.

Citrated,
peptonised,
dried,
condensed,
whey.

Hypersensitivity to
cow's milk.

Goat's milk,
Protein milk,
Asses' milk.

Proprietary foods.

Further principles.

Treatment of Marasmus.

General,
dietetic.

Hutchison,
Holt,
Spalding,
Thomson,
Parsons.

RECAPITULATION

TREATMENT

The advantages of The premature both to mother and infant,
infant.

The Preparation of Cow's
Milk.

Vitamins and Milk.

Vitamins in infancy.

Vitamins and human diets.

The importance of an abundant supply of Vitamin D, and of calcium, for the satisfactory structure of the skeleton and health of the embryo, has been touched upon.

It would be hard to overstate the beneficial results both direct and indirect, which accrue from the careful feeding of the pregnant woman. Not only Vitamin D is essential for the expectant and as well as for the nursing mother, but so much to protect the young, as to improve the calcium assimilation of the mother herself and help her to replace the large amount of minerals lost to the child or in her milk.

Fat soluble vitamins give a certain degree of protection against puerperal sepsis; besides deficiency of iron, Vitamins A, and B, are probably implicated in the etiology of the toxemia of pregnancy and of the puerperium.

SECTION VI.

TREATMENT

The advantages of breast-feeding, both to mother and infant, are obvious, and will be discussed no further than to point out that these advantages are not by any means fully enjoyed, either from ignorance, or from the lack of opportunity owing to poor social circumstances, many women being unable to nurse, owing to their engaging in work away from home.

The importance of an abundant supply of Vitamin D, and of calcium, for the satisfactory structure of the skeleton and teeth of the embryo, has been touched upon.

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The pregnant woman, therefore, must have a diet rich in vitamins, especially the fat soluble vitamins. If she is poor, she should receive daily, one drachm of cod-liver oil and a gramme of bone ash, and this applies equally to the period of lactation.

Breast milk may be grossly deficient in one or other of the vitamins; lack of A. is possibly the cause of slight degrees of xerophthalma; rickets is common among the breast-fed, and there is good evidence that these may also suffer from the lack of B. vitamins.

There is now no doubt that the best policy is to give a vitamin supplement both to the mother and to the child, because of the fact that supplements given to the mother may never reach the child.

Human colostrom is alkaline in reaction and has a higher percentage of protein and salts than ordinary human milk.

Human milk is amphoteric while cow's milk is distinctly acid.

Human milk varies slightly in composition from time to time, but it changes little as lactation proceeds. No galactagogue is so satisfactory as the suction of the infant. It is to be remembered that the lactalbumen contains the amino-acid tryptophane essential for growth.

Certain conditions definitely contraindicate maternal nursing; e.g. pulmonary tuberculosis, nephritis and exophthalmic goitre. Regarding the presence of breast sepsis opinions vary.

Apart from these conditions, a considerable percentage of British women (the number is apparently smaller on the continent) are genuinely unable to nurse their children. Apart from these little understood cases, there are many that are due to want of perseverance.

Ability to suckle may vary with the pregnancies, so that previous failure does not necessarily mean further failure.

With the breast-fed, the weight chart should be the guide to whether the milk is suitable. Fretfulness and vomiting should not be taken too much into account.

If the breast-fed infant is "dyspeptic" and loses weight, analysis of the milk may be carried out, but this analysis is only of help in a small minority of cases. A sample from the middle third of the breast contents, or a mixed sample from the whole breast must be obtained.

The specific gravity reading is no guide unless the percentage of fat or protein present is known.

A series of "test feeds" will determine whether the infant is drawing sufficient food from the breast. If the supply is deficient the mother should be encouraged, and a more liberal diet and longer periods of rest prescribed, if possible. If this fails, hand feeds should be substituted two or three times daily for

the breast feeds. If this is insufficient the child should be weaned from the breast.

Insufficiency, then, is the commonest defect in breast-feeding. A scanty milk may lead to the signs of "colic" and, occasionally to the passage of loose green stools. The milk, again, may be too profuse, leading to the excess being "posseted".

A fault in the milk itself is the last thing to be thought of. The question of the intervals between feeds and the regularity of the feeding should be carefully gone into. If these are satisfactory, the milk sufficient and the child not thriving, it should be carefully examined for an infection of the ear or urinary tract or for the presence of pyloric stenosis; vomiting may be due to any of these conditions and even in the last the stools, though small, may be loose and green.

During acute maternal illness, it is better to wean temporarily; also, the child should be gradually weaned, should pregnancy supervene.

Breast milk itself does disagree by no means infrequently, and analysis does not always reveal the cause.

In some cases, an abnormally high protein content leads to the passage of stools that are green, but not unduly loose; excess of fats, and of protein more rarely, causes loose green stools, but the same picture is given by too large feeds.

The baby itself is frequently at fault, some infants being remarkably intolerant of fat, and others of carbohydrate, even in that percentage present in the mother's milk.

Exercise will reduce the protein and fat content of the mother's milk, while shortening the interval between feeds will increase the protein content.

There are several methods of overcoming the difficulty of excessively rich breast milk:-

1. The infant may be put for 4 - 5 minutes to each of the breasts.
2. It may be given $3 \frac{3}{4}$ of plain water before each feed, or
3. gr. ii of citrate of soda may be given in a little water before feeds.

The difficulties of wet-nursing are great, and yet the benefit is often very striking. The nurse's health is all important, but the size of the breasts is no guide. She should be treated with kindness and consideration. In most cases the nurse's own child should be fed entirely by hand.

The subject of artificial feeding is probably the most important in the whole field of therapeutics. And yet it would not hold this place if the laity could be made to under-

stand the saving of health, labour and expense brought about by breast-feeding.

One of the most important precepts in this subject is that of "individualisation". It is essential that each infant should be fed according to its own digestive capabilities and its own changing clinical condition.

No one method is universally applicable; certain rules should be observed and simplicity aimed at above all.

The different ways of modifying cow's milk to suit the infantile digestion have always given rise to considerable difference of opinion, and an effort will be made here to reconcile certain varying opinions.

The relatively large protein content of cow's milk has always been the stumbling block to clinicians; it is very important to remember however that, bulk for bulk, cow's milk protein only has half the essential tryptophane content of human milk; any dilution of cow's milk will reduce the percentage itself still further, and also reduce the amount of the necessary salts, e.g. iron. (Human milk with gr. $1/40$ of ferric oxide per $1\frac{3}{4}$ pints, has three times the iron content of cow's milk, and yet both frequently contain insufficient for the infant's needs.)

Thomson considers that for the great majority of infants no modification of the milk is necessary save boiling or pasteurising, and that it is generally, though not universally, admitted that even the newborn can digest and assimilate undiluted cow's milk. He points out that it has still to be proven that an excessive protein content, at least within limits, has harmful effects. The fundamental fact that the different proteins are not quantitatively replaceable must be remembered.

Professor Budin at his Paris centre in 1892 was the first to advocate this whole milk feeding of infants; and Vallue upheld the method in 1894. In 1895 Sir Alwroth Wright first suggested the administration of gr. i - ii of citrate of soda per ounce of whole milk, while in 1904 at Great Ormond Street, first combined citration with dilution.

Marriott recommended the acidifying of whole milk with dilute lactic acid, but Thomson found no better results from this, and considered that it might cause vomiting.

At a meeting in 1910, Langmead pleaded for the use of undiluted citrated milk in wasted children, and described a consecutive series of 80 cases so treated. (32).

As disadvantages of dilution he pointed out that:-

1. The increased bulk of fluid might lead to atony of the stomach,
2. there is the necessity of adding cream and sugar -(the

former might contain harmful preservatives), and

3. the toughness of the milk curd is left unaffected.

The advantages of the whole milk method were:-

1. It is a simple method.

2. the feed is as digestible as "condensed" and "desiccated" milks, and

3. citrated whole milk "agrees" better than does diluted.

Remarking that milk in any form is unsuitable in epidemic diarrhoea, Langmead mentioned the few disadvantages and limitations of the method:-

1. The chief disadvantage is the excess of protein, but this is passed by the bowel;

2. oedema may result from too large dosage with citrate,

3. the occurrence of "acid dyspepsia" (as shown by distress after food), may require the addition of sodium bicarbonate to the feed.

Langmead's method was to give gr.ii of sodium citrate to each 3i of milk ordered.

He remarks that his experience with the method in infants under the age of 2 weeks is very small; and that citration can usually be omitted by the age of 6 months, unless the babe is weakly.

All of his series of 80 cases gained in weight over many weeks. At the first attendance, the ages were from 3 weeks to 4 months; 4 were under 5 lbs. in weight and 10 others were 6 lbs. or less.

One died of epidemic diarrhoea; two apparently developed rickets.

In the discussion later, Poynton said: "If a child went wrong on full milk, it did so badly, and might require weeks to get right again". Therefore, in dealing with small babies, he started with citrated and diluted milk, increasing the strength of the milk and the proportion of the soda.

Regarding whole milk feeding, Still remarks that some infants not only tolerate it, but do so even when unable to digest diluted or even peptonised. Half a teaspoon of sugar should be added to each 3 iii of boiled milk; in some cases, the addition of nitrate of soda is necessary. Still found that from $\frac{2}{3}$ - $\frac{3}{4}$ the usual quantity of food was sufficient. The two main causes of the method failing are:-

1. Too large feeds.
2. Too rich milk - e.g. milk from Jersey cows.

The method is successful in:-

1. Many healthy infants;
2. Infants wasting as a result of too small a gastric capacity, and

3. several cases of wasting which do not fall into a definite group.

Hutchison remarks that citrated whole milk feeding often seems to succeed in strong and healthy babies, and Holt, that, some robust infants will thrive on pure cow's milk, but it is unsuitable for the majority.

Having given these opinions regarding whole milk feeding, we shall look next at the general opinion regarding the feeding of the average infant which is deprived of the breast milk from its early days.

As stated before, Thomson considered that some modification of cow's milk was only necessary in the great minority of cases, but that these cases fell mostly among the newborn and in the presence of disease. He considered also that the estimation of the amount of feed for each infant appeared to be the greatest stumbling block in the whole of infant feeding. Sufficiency is the all important point; each infant should be fed according to its age, unless very emaciated.

He quotes "healthy average" figures of Rubner and Heubner:-

For the first	3/12	of life	the infant	needs	45	cals	per lb	body	weight.
" "	2nd.	" "	" "	" "	40	" "	" "	" "	" "
" "	3rd.	" "	" "	" "	35	" "	" "	" "	" "
" "	4th.	" "	" "	" "	30	" "	" "	" "	" "

(It is recalled that all whole milks yield about 20 calories per 3i., skimmed milk 15, and separated milk 10.

Sugar yields 120 cal. per 3i., and wheat and oat-flour 100.)

The following table demonstrates the present Edinburgh teaching.

These points are to be noticed:-

- (a) At 3 weeks the infant is getting equal parts of milk and water, also sugar.
- (b) At the age of 3 months the infant is getting undiluted milk and sugar, and
- (c) the sugar can be increased up to $3\frac{1}{2}$ daily, especially if the baby is active.
- (d) Fruit juice is given from the end of the 6th week, and between feeds.
- (e) Cod-liver oil (3ss t.i.d.) starts at 2 months.

RATIONS FOR 24 HOURS.

AGE.	OUNCES.			NO. OF FEEDS.	S. PER FEED.	CALORIES.
	MILK.	WATER.	SUGAR.			
1 day	-	2-3	-	5-6	$\frac{1}{2}$	
2 days	1	5	$\frac{1}{4}$	6	1	
3 "	$1\frac{1}{2}$	6	$\frac{1}{4}$	6	$1\frac{1}{4}$	
4 "	2	7	$\frac{1}{2}$	6	$1\frac{1}{2}$	
5 "	$2\frac{1}{2}$	8	$\frac{3}{4}$	6	$1\frac{3}{4}$	
6 "	$3\frac{1}{2}$	$8\frac{1}{2}$	$\frac{3}{4}$	6	2	
7 "	4	8	$\frac{3}{4}$	6	2	160

To end of:-

2nd. week	7	8	1	6	$2\frac{1}{2}$	260
3rd. week	9	9	1	6	3	300
4th. "	10	8	1	6	3	320
6th. "	16	7	1	5	$4\frac{1}{2}$	440
2nd. month	20	5	1	5	5	520
$2\frac{1}{2}$ months	24	1	1	5	5	600
3 "	25	0	1	5	$5\frac{1}{2}$	620
4 "	$27\frac{1}{2}$	0	1	5	6	670
5 "	30	0	1	5	6	720

(i.e. 50 cal
per lb if $1\frac{1}{4}$ lbs)

Hutchison uses a mixture composed of equal parts of milk and water, to each 3 vi of which 2 teaspoons each of dextrimaltose cream are added:- or in Hospital practice, 1 teaspoon of cod-liver oil emulsion, in place of the cream.

He gives 3 i of this 3 hourly for each month of age, (but again stresses individualisation,) and considers that milk and water equal parts should be the rule up to 6 months, thereafter 2 parts of milk to one of water, and by 9 months pure milk.

It is agreed that wey is the ideal diluent for cow's milk but it is troublesome to prepare and expensive.

Barley water is best avoided as it is a 1 - 2% solution of starch in water; although it makes the curd slightly less tough. Water, then, is the preferable diluent.

As stated before, Holt considers that the majority of bottle-fed infants require modified cow's milk, but that previously efforts to render cow's milk more digestible not infrequently led to failure because the energy requirements were not met, or because some essential amino acid, vitamin or mineral constituent was inadequately supplied.

He describes his own routine after discussing some general feeding principles.

Holt boils the milk for safety (warning that the process

He considers that the most successful cow milk modifications have certain features in common - a reduction in protein and fat and an increase of carbohydrate. A diet with protein content in excess of the carbohydrate may eventually lead to malnutrition - the picture of Milchnahrschaden in which there is:-

- (1) an increased requirement of water;
 - (2) an increased energy requirement (because of the marked "specific dynamic action" of the protein),
- and there may be (3) a tax on the digestive capacity.

But, on a cow's milk diet, the digestion and absorption of protein is very complete, even in grave nutritional disorder.

As regards fat, most infants can take a high proportion of cow's milk fat; moreover, it is doubtful whether intolerance is more likely with the fat of cow's milk, than with that of human milk.

Holt's preference for the routine infant feed, is to give a food isocaloric with breast milk (i.e. 20 calories per 3i).

This is composed of:- whole milk 3vii.
water 3iii.
sugar 3ss.

protein	gives	15%	of	calories,
fat	"	35%	"	"
carbohydrate	"	50%	"	"

Holt boils the milk for safety (remarking that the process

also makes the milk more digestible). If raw or pasteurised milk is used, a mixture yielding only 12 - 15 calories per 3i should be used for the first few days.

Still strongly maintains that the large quantity of curd is the one great obstacle in the digestion of cow's milk.

(Roughly it may be said that cow's milk contains 4% each of protein, fat and carbohydrate, while human milk contains 2% protein, 4% fat and 6% of carbohydrate.

The 4% of protein in cow's milk is made up of 3.25% of casein and .75% of lactalbumen; while the 2% protein in human milk is only .6% casein and 1.4% lactalbumen.

The curd of milk is composed of casein with some fat globules entangled in it).

Still remarks that with the poor, we often have to be content with simple dilution and addition of sugar (cream being hard to get and of doubtful quality)

From experience Still favours the following concentrations:=-

	<u>Milk.</u>	<u>Water.</u>
At birth	1	4.
" 1 week	1	3
" 1 month	1	2
" 2 months	1	1½
" 3 "	1	1
" 6 "	2	1
" 9 "	3	1

Still considers that the breast-fed can be fed 3 hourly almost from birth; with the bottle-fed the interval should not be so long

as this, until after $2\frac{1}{2}$ months of age. He discusses methods of correcting the fat deficiency present in any dilution of cow's milk; "top milk" and "gravity cream" are unsatisfactory, while centrifugal or separated cream is much better. (This contains an average of 48% of fat.)

Artificial cream is cheap and free from the tubercle bacillus.

Any deficiency in sugar is easy to correct, and extreme exactitude is unnecessary.

Lactose is less laxative and less rapidly absorbed than the other sugars.

We have examined the mixture favoured by different workers in "hand-feeding" the average infant.

What of the more weakly infant.

Hutchison commences with a more digestible food -

- (a) if the infant is unable to digest his " $\frac{1}{2}$ " and " $\frac{1}{2}$ " mixture,
- (b) if the infant is "delicate", and
- (c) "indeed, in most under $\frac{3}{12}$ old".

In order of ascending digestibility, he names citrated, dried, condensed and peptonised milks; with the wet nurse as a last resort.

Still, to whom the commonest difficulty in infant feeding is "curd indigestion", induced in many cases by insufficient

dilution of milk during the first few weeks of life, describes methods of assisting curd digestion when moderate dilution is insufficient.

He remarks that insufficient dilution is a much commoner source of trouble than excessive dilution; and that some infants show from the very outset an extraordinary intolerance to cow curd.

(1) Sodium citrate, he considers, is best where there is only slight difficulty with digestion. A dose of gr.1 per $\frac{3}{4}$ i of milk forms the sodium paracasein which is much less tough than the calcium paracasein. Sodium citrate tends to constipation and large doses may cause oedema.

If there is no improvement with citrate of soda, Still strongly advocates partial peptonisation before recourse to the patent foods.

(The method of citration is being used less and less nowadays; it is agreed that at most it should not be used more than temporarily.)

(2) Peptonisation. By allowing 1 measureful of the "peptogenic powder" to act for half an hour upon 1 pint of the milk and water mixture (without any added sugar) the peptic digestion of the milk is performed before it enters the baby's stomach.

The possibility of scurvy used to be the main objection to this method. Apart from that it, also, is a method for temporary use only; the return to unpeptonised milk later should be very gradual.

(3) Hutchison has faith in a "half cream" dried milk, for the very young, delicate or dyspeptic infant, provided that fruit juice is given daily. "Dried milk" is cow's milk evaporated to a fine powder.

The "dried milks", such as Cow & Gate, and Glaxo, are so composed that 1 part in 8 parts of water makes a solution roughly equivalent to full cow's milk. The "curd" is a more flocculent one, but if the milk is made by the "roller process", the fat is apt to be imperfectly emulsified; the "spray process" does not have this disadvantage. The dried milks are essentially scorbutic, but contain few bacteria compared with fresh milk and the tubercle bacillus very rarely. (Because of this cleanness, Holt welcomes the present increase in the use of the dried milks).

The " $\frac{1}{2}$ cream" dried milks are deficient in fat soluble vitamins.

Moreover, many infants will not tolerate dried milk.

(4) As regards condensed milk, that is, cow's milk sterilised at 212° and evaporated in vacuo, Hutchison finds the "full cream sweetened" type very useful for young and delicate infants, provided cod-liver oil emulsion is administered at the same time; but he

never gives such a preparation after the 4th month and rarely after the 3rd.

Two average teaspoons to 3iii of water makes a preparation containing:-

Protein	1.1%
Fat	1.2%
Sugar	6.7%

Still grudgingly admits the unsweetened condensed milks to be less objectionable than other patent foods, and that the curd is more easily digested than in cow's milk. They should be used within 36 hours of opening the tin, as they lack the preservative effect of the cane sugar.

Thomson finds condensed milk of very temporary use, and that it may produce a deceptive gain in weight owing to retention of water in the tissues. He favours the unsweetened variety.

In the occasional and difficult case in which full peptonisation fails to assist the digestion of cow's milk curd; it is agreed that the infant should be fed on a

- (5) whey basis. Whey contains .8% protein (essentially lactalbumen).
.2% fat.
and about 4.5% sugar.

Hutchison favours enrichment of the whey with one of the pancreatised foods, such as Bengers or Savory and Moores', standing for a good while before boiling up, so that the starch may be thoroughly converted.

A dextrinised food, such as Mellin's, may also be added to whey.

Later the whey should be very gradually replaced by milk - one or two teaspoons in each bottle.

Still considers that the addition of one drachm of cream (48%) and $\frac{1}{2}$ teaspoon of lactose to each ʒiii of whey, makes a good food for many weeks if necessary.

(He describes his own cheaper method with tartaric acid, but has found it to fail at times).

He also favours "sherry whey" (or "white wine whey") as an emergency food, and considers that it is very good in emaciation, and exhaustion, especially if there is much vomiting. It serves best if small feeds are necessary; ʒiii hourly at 6 months of age would be an exceptionally large feed.

Whey feeding will fail in those few infants who are intolerant of cow's milk however it may be modified.

Holt considers that intolerance to cow's milk protein is, in nearly all cases, only to the lactalbumen and that boiling will lead to success. In hypersensitivity to casein, heating will not succeed, and a change to a milk of another species will be necessary.

Goat's milk is then useful. This is very similar to cow's milk; if the animals are clean the taste is indistinguishable.

Like the ass the goat is immune to tuberculosis, but the possibility of undulant fever being carried necessitates sterilisation of the milk.

Synthetic milk may also be useful here - i.e. with protein and fat derived from some other source than milk. Thus, Almata may be used for the first three months of life, diluted 1 to 8 with water only. Milk may be added to it after that age.

Holt remarks that food allergy is not necessarily of life-long duration, but he urges the institution of desensitisation, without waiting for the gradual disappearance of the condition.

If whey feeding fails Still considers that a condensed or dried food will succeed now and then, but that asses' milk is a better though expensive temporary measure. It is very weak in both protein and fat.

Thomson, as mentioned, maintains that some modification is only required in the great minority of infants, but cases are more numerous among the newborn and in the presence of disease.

(1) He considers protein milk (the "eiweiss milch" of Finkelstein and Meyer) to be the best borne modification in the newborn.

The fundamental principle is a reduction of the salt content to that of breast milk. The percentage of sugar and fats is also

low; the protein remains high. Thus the antifermentative effect is retained and the irritant effect lessened. The figures are:-

Protein	3%
Fat	2.5%
Sugar	1.5%
Salts	.5% (chiefly calcium salts).

It is very good also in

- (a) diarrhoea and enteritis;
- (b) atrepsis with low fat tolerance.

In the newborn, sugar may be added when the stools show good digestion; cow's milk should gradually replace the other.

Holt gives the figures as:-

Protein	3.75%	13 calories per 3i.
Fat	3.0 - 3.5%	
Carbohydrate	1.8%	

and remarks that it is useful in acute and chronic nutritional upset, especially if accompanied by diarrhoea.

(2) Of peptonised milk Thomson remarks that it was an old favourite in nutritional disease, but is now going out of fashion.

It is useful, however, in stenosis and spasm of the pylorus.

After touching upon condensed and dried milk (vide supra) Thomson remarks that asses' milk is of good temporary use in young infants and in the indigestion of coeliac disease. The fat and protein content is low, but there is plentiful lactalbumen and the milk may be given undiluted and raw. Cod-liver oil should be given at the same time.

Thomson considers that the proprietary foods are expensive and misleading. He classifies them into milk, malted and farinaceous foods.

It is generally agreed that the administration of starch should only be begun about the 8th or 9th month and then very gradually. (In the first 6 months of life there is only a very small amount of saliva and pancreatic juice).

Hutchison warns against their routine use and Still strongly advocates partial peptonisation before having recourse to them.

Still divides them into 2 groups:-

- (a) those intended as substitutes for fresh cow's milk (these are essentially the "dried milks"),
- and (b) those intended as additions to fresh cow's milk.

It is well recognised that of these foods:-

- (1) in nearly all of them, there is a serious deficiency in fat,
- (2) many have too little protein,
- (3) most have far too much carbohydrate, and
- (4) all are more or less scorbutic.

Even Still however admits that there are certain conditions under which the intelligent use of these foods is advisable; thus, a feed with a low curd and fat content may be necessary for a short time. (contrary to Holt, he considers that many infants can

not take as large a proportion of cow's milk fat as they can of breast milk).

He points out that a gain in weight is not, of course, proof of a good food; and that evil results, in the form of rickets or scurvy, may appear for weeks or months.

He believes also (in contrast to Fife and Veeders' conclusions) that excess of carbohydrates interferes with fat assimilation; and again that a low fat, high carbohydrate diet lowers resistance and induces intestinal catarrh.

He stresses the simple methods of adopting fresh milk.

Still touches upon some other general points in infant feeding. He denounces the practice of "leaving it to the nurse". He considers that too large a bulk of fluid is one of the commonest faults in infant feeding; if the child is unsatisfied and the stools well digested, the proportion of milk to water should be increased, not the bulk of the feed.

"Nursery milk" is to be avoided, an account of its especial richness and also the fact that it may be dirtier. The milk from a shorthorn herd is the best.

Regarding cream, this should never be added to a whole-milk feed; and 3% of fat should be the upper limit in an artificial feed. Cream contains preservatives and is as dangerous

as milk, as regards the tubercle bacillus.

There are other very important principles to be carried out in infant feeding.

Changes in the feed should be made as seldom as possible, and as gradually as possible; only one change should be made at a time, (except of course, when acute illness necessitates reduction).

Hot weather requires a reduction in the food and an increase in the water intake.

In infection there is no close relationship between the severity of the condition and the degree of nutritional upset.

We may mention here another beneficial modification of cow's milk, the method of thickening, which is useful in curing a baby of such bad habits as airsucking and ruminating.

The 2nd six months of life should see the transition to a mixed diet, in the form of vegetables, meat products, fruit and eggs, and cereals in small amounts.

When there is considerable solid food in the diet, caloric estimation is inaccurate and the appetite becomes a more satisfactory guide to sufficiency.

With this background of infant feeding, we shall examine the principles of treatment of the wasted infant.

The importance of prophylaxis is again stressed. Treatment embraces the whole subject of infantile feeding, in addition to the treatment of the non-dietetic causes of wasting.

Very careful nursing and mothering and infinite patience are foremost in the principles of treatment. Much can be done to prevent the occurrence of secondary infections. Warmth is of far greater importance than fresh air, and the room temperature must be kept at 65°.

Feeding must be done very cautiously and any change made reluctantly and gradually.

Still remarks that where the cause is a digestive disorder, a weak food is commonly the right food; and he starts treatment with veal broth, (with lactose 3 i to 3 iiii). This is followed by dilute asses' milk, if weak peptonised cow's milk cannot be assimilated.

He notes that half cream dried milk is of temporary use; and that Thursfield (Arch. Dis. Child. Feb. 1927, p. 49) recommended banana pulp mixture.

If breast milk is unobtainable, Hutchison starts with a sweetened condensed milk or half cream dried milk. Then, if the stools show fat indigestion, he feeds on a whey basis with

either Mellin's food or a modified starchy food. If the stools show casein indigestion, he gives a dried milk or a fully peptonised or citrated mixture. In those cases, "fortunately less common", where there is sugar indigestion, he finds protein milk often very useful.

(7% is quite a normal strength for the sugar in solution in the infant's bottle feed. Intolerance to this quite reasonable percentage is not uncommon; as is shown by watery diarrhoea and the explosive passage of faeces, due to the fermentation, and excoriation of the buttocks. There omission of the additional sugar in the feed will often cause the condition to clear up).

Holt favours an acidified evaporated or dried milk if breast milk is unobtainable. He stresses the need for sufficiency, advancing cautiously up to even 100 calories per lb. of body weight. He considers that generally the most successful high caloric feedings are those with a high carbohydrate content, but that this should not be given for longer than a few weeks.

The "calories per body weight" system originated in France, with Budin and Heubner. It is a quantitative rather than a qualitative guide and a variable one at that.

The system of "percentage feeding", originating in America, helped to place infant feeding on a scientific basis, but tended to lead to overfeeding.

The essential rule is to feed each infant according to its clinical power of digestion. A careful record is kept of the food given and its effect upon the child. It is enough if the percentages and the calories are calculated at intervals.

These are some of the points stressed by Spalding in 1909 in discussing "The feeding of immature and atrophic infants". (14)

He found that "gavage" or feeding by the stomach tube was usually necessary at the outset, and he started an immature infant (judged, not by age, but by weight of less than $4\frac{1}{2}$ lbs) with a 5% sugar solution, gradually replaced by whey. The atrophic infant he started with whey, gradually replaced with a 10% milk mixture, increasing to 30 and 40% of milk. He warned against "letting the fat calories run too high", and considered that the wasted do better when the ratio of fat percentage to protein percentage is not greater than two to one.

Regarding the acidified milk mentioned by Holt, this is the preparation strongly favoured by Marriott, who brought the milk to a pH of about 4, by adding to a pint of milk a drachm of the U.S.P. lactic acid (85%). Holt was not convinced that the average infant progressed better on acid milks, but he believed that it had an advantage in acute and chronic nutritional upset.

We have seen that Thomson finds marasmus to be due to:-

inanition,
fat dyspepsia
and parenteral infection.

For inanution, the diet should be gradually built up; for parenteral infection, protein milk or albumen milk is best, together with the treatment of the suppurative focus in ear or urinary tract.

It is agreed upon that marantic infants very commonly ill-tolerate fat.

Thomson found fat dyspepsia a definite clinical entity and treated it with diluted milk, or better with undiluted milk deprived of some of its fat, i.e. skim milk. (The skim milk usually on sale is unfit for infants). A half cream dried milk may be used but the fat can easily be reduced in ordinary milk by allowing it to stand and skimming the risen cream.

A skim milk contains from 1.5 - 1.75% fat.

Parsons concluded from his experiments that fat indigestion occurs in infantile atrophy under two conditions:-

(a) When diarrhoea develops, the peristaltic hurry may lead to poor splitting of the fat. This should be treated by giving a low fat diet, containing a less fermentable carbohydrate (such as dextrimaltose). If the infant is not very enfeebled, a short preliminary period of starvation is often useful.

(b) If a high fat content dried milk is given, large stools may be passed, containing excess of soap and free fatty acid.

Although here the fat splitting is good, treatment consists in giving a lower fat content dried milk, or the ordinary cow's milk mixture.

Three additional factors that are sometimes of use in cases of infantile wasting are mentioned here.

Thyroid extract has been suggested from time to time over the past many years, with varying results.

Insulin has sometimes been found to stimulate the appetite.

Preparations of Vitamin B, may be used, although there is not yet any convincing proof of their value.

At the present time, in the treatment of the premature infant, attention is concentrated upon the three very important heads of:-

- (1) warmth,
- (2) sufficiency of fluid and food, and
- (3) protection against infection. (33) (34).

(1) General opinion is against the use of an incubator, but in favour of the electric blanket.

The baby should not be bathed until it weighs 5 lbs. and then only if vigorous, and upon alternate days.

Most do best if their body temperature is kept at about 99°.

(2) The need for breast milk is always urgent and may be vital.

At first, diluted with an equal amount of normal glucose saline and given every two or two and a half hours, most cases will take it undiluted by the end of a fortnight. Failing breast milk a condensed sweetened milk is favoured; others prefer fully peptonised and diluted milk. A dried milk containing 1% fat and 1% casein is also satisfactory.

In America protein milk is popular; in this country the nearest approach to it would be an acidified dried milk, either half cream or humanised.

The caloric needs range from 60 - 100 per lb. of body weight, but a period of weeks often passes before the full requirements can be met.

(3) The nurse in charge of the infant should wear a mask to prevent the onset of a droplet infection. Some practice the injection of parental whole blood to increase the antibodies - a course of 10 injections of from 3 - 5 c.cs. on alternate days.

Nutritional anaemia and a degree of rickets will develop in nearly every case of prematurity unless especial precautions are taken to prevent their onset. Iron and ammonium citrate, and a concentrated fat-soluble vitamin preparation must be given from the beginning of the 2nd. or 3rd. milk.

Preparation of Cow's Milk.

The leaders in medicine are universally agreed that an increased consumption of milk (the "perfect food") would have undoubted advantages to the community; but also, that the existing milk supply is not safe. (38), (39), (40), (41), (42).

In the incidence of tuberculosis of bovine origin, Great Britain is behind other countries, notably the United States of America and Canada.

The tubercle bacillus is found in from 3% to 15% of samples of cow's milk, and it has been found even in certified milk. The development of tuberculosis free herds is a long process and at present all milk other than:-

(i) Certified, or

(ii) Grade A. (Tuberculin tested) -

Should be pasteurised or boiled.

This would obviate the risk of tuberculosis and other diseases.

"Low temperature" pasteurisation (i.e. holding the milk for thirty minutes at a temperature of 145°F. to 150°F. and cooling rapidly to 45°F.) causes no diminution in the nutritive value of the milk, that cannot easily be remedied by the simple addition of orange juice and cod liver oil. (Cod liver oil has 500 times the anti-rachitic potency of fresh milk.)

There is no evidence that the enzymes of milk (which are partially destroyed by pasteurisation) are of any importance in nutrition. From fresh milk they are destroyed in the gastro-intestinal tract.

It is to be remembered that pasteurised milk sours in the same way as a good quality fresh milk.

Where adequate pasteurisation is at present impracticable, the milk should be boiled before use. (The difficulty of the altered taste of boiled milk is however an insuperable one with some children)

The question of the vitamin content of milk is not yet settled. It is generally accepted that both human and cow's milk contains surprisingly little vitamin D. This matter was the subject of editorial comment in the Lancet of 2.12.33. (p. 1269), which included the following remarks:- "... Sherman, (Amer. Journal of Public Health, October 1933. p. 1031) contests the general opinion that cow's milk is on the whole, a poor source of vitamins ...

... The following are methods of increasing the vitamin content of milk - especially useful where smokiness diminishes the anti-rachitic value of sunlight:-

- (a) the addition of a vitamin D. concentrate of the milk;

- (b) irradiation of the milk, with suitable carbon arc arc lights.

(It is to be noted that different preparations of irradiated milks, still vary considerably in their activities.)

- (c) addition of irradiated yeast to the cow's diet.

- (d) irradiation of the cow itself, (a method at present under investigation.)

... The comment urges the clinician to make his own practical observations and remarks that "few will disagree with Dr. Chalmers Watson's main thesis (Scot. Journal of Agric. Oct. 1933. p. 394) that our present knowledge of the nutritive factors in cow's milk is very inadequate." (35)

(Dr. Chalmers Watson has long maintained that "much of the present teaching of the laboratory on vitamins is either entirely erroneous or at least unproven.") (36)

The following is a summary of the teaching accepted at present, regarding vitamin supplies in infancy:-

1. All infants should be breast fed up to the age of 8 or 9 months; even if breastfed, each should receive daily two teaspoonfuls of orange juice and $3i - ii$ of cod liver oil. (The larger dose from age of 5 months.)

2. Extra vitamins are even more essential to:-

- (a) those infants that are partially or entirely hand fed.

(b) those infants at the time of, or following weaning, because then, some of the foods given, e.g. cereals, make a special demand on the vitamin supply.

3. Probably, the risk of defective calcification of the teeth is greatest at the weaning period, when the cusps of the molar teeth are joining up.

4. The fact that the liver stores such large quantities of Vitamin A. (when the food is rich in it) is an indication of its importance in the animal economy.

5. Egg yolk contains plentiful Vitamins A. and D. and should be given to all artificially fed infants after the age of 3 months - half to one egg daily.

6. When partly or entirely artificially fed, cow's milk should form the bulk of the diet up to the age of 8-9 months, and the basis of the diet for one year afterwards. At no time in the first year after weaning should an infant receive less than one to two pints daily, and after this not less than one pint.

7. Little is known of the normal infants requirements, of the "B-complex," but small amounts of "marmite" should be given daily.

8. Vegetable purees should be given from the 6th month and, as early as possible, some iron-rich supplement (meat, gravy, spinach, egg, etc.)

Mackay in 1931 showed the especial benefit of iron and ammonium citrate due to the contained traces of manganese and copper.

Some recent and controlled experiments carried out on school children at Peterhead, with the administration of vitamins A. and D. supplements, had results which were disappointing when compared with the good results of a previous experiment with milk supplements. (37)

Vitamin deficiency in man is rarely, if ever, complete, and is generally associated with a partial shortage of other important substances.

The milk supplements had made good these associated deficiencies.

Partial deficiency of one or more of the "accessory substances" leads to much subnormal health and development, and even incidence of disease; and the results may be very serious when such partial deficiencies occur in very early life, and a sufficiency later may fail to make good, damage caused by a deficiency in youth.

Latent deficiency disease is a real thing and not an imaginary concept.

Hard work, pregnancy and lactation (as stated before) are conditions calling for extra supplies of vitamins, and it must be remembered that a mixed diet, formerly regarded as excellent, may in reality be defective.

In sickness and convalescence, when the dietary is necessarily restricted, therapeutic vitamin concentrates are the best safeguard.

Hess found that "Eiweiss - Milch", the well-known preparation given to dyspeptic infants, was an excellent diet for producing rickets. Fat dyspepsia is undoubtedly a reality, and then the fat intake should be greatly diminished, but it is essential that a vitamin concentrate should be given at the same time.

Regarding fruits also, the period of reduction should be made as short as possible. (Adequate vitamins are essential in diabetic diets.)

The problem of adequate Vitamin A. is not such a difficult one as with some of the other vitamins, and it can be cheaply solved wherever vegetables are grown. Vitamin A. is little damaged by ordinary cooking.

Skimmed and separated milk should never be used as a substitute for full milk in young children, but it forms a cheap

and valuable source of protein and salts for those of school age and should be largely used in poor families.

The position may be summed up:-

The vitamins present us with the means of attaining an ideal, namely the eradication of deficiency diseases.

Cereals form about 60% of the diet of the poor and milk, butter, eggs and vegetables are costly. Thus, even the cheapest sustenance diet is beyond the reach of many unemployed persons.

The fault lies largely with the mal-organisation of society, and the failure to apply or realise the knowledge already won by science.

C O N C L U S I O N S .

(1) "Wasting" is common amongst poor-class infants.

The careful management of pregnancy, labour, the early days of infancy, and of breast feeding, is a factor of vast importance in prophylaxis.

(2) The main cause - unsuitable feeding - is preventable by lay and medical education.

(3) It is essential to diagnose between a "functional" and an "organic dyspepsia", since wasting may result from a considerable number of organic conditions.

(4) Persistence in unsuitable feeding leads to "dyspepsia", which form a large group of infantile "upsets", and which is a frequent cause of wasting.

The causation, pathology and treatment of "dyspepsia" (including "summer diarrhoea") are discussed.

(5) Congenital pyloric stenosis is not a rare condition and should be constantly born in mind. The age and general condition of the infant, and the length and type of history, vary very considerably. Visible gastric peristalsis occurs to a slight extent, in certain other, less common conditions.

(6) "Pink disease" - the cause as yet unknown - may lead to a considerable degree of wasting, even in the breast fed. The diagnosis is usually easy.

(7) In childhood, there is a very important interdependence between the absorption and utilization of fat, calcium and phosphorus. Thomson considers the three main causes

of wasting to be:- inattention,
fat dyspepsia,
parental infection;

even in the second of these however, namely cases in which there is a reduced tolerance to fat as shown by the passage of large crumbly and pale motions (the "milchnährschaden" of Czerny, and Finkelstein's "bilanzstörung"), the digestion and absorption of fat are quite normal.

(8) Fat splitting and absorption is normal in infantile atrophy and in pyloric stenosis; but in atrophy, fat indigestion occurs under two conditions:-

- (a) if diarrhoea develops, and
- (b) with the use of the high fat content dried milks.

(9) Starvation is a frequent cause of wasting and the "mehlnährschaden" of Czerny and Keller is due rather to a deficiency of protein, vitamins and minerals, than to an excess of carbohydrate. Such deficiency syndromes may be superadded to the picture of malnutrition.

(10) The effects of a high protein intake are little to be feared.

- (11) The presence of infection is an important factor in reducing the carbohydrate tolerance.
- (12) It is suggested that the estimation of the urinary creatinine of wasted infants, would, by indicating the extent of tissue breakdown, at least be of assistance in prognosis.
- (13) In infantile atrophy, no characteristic lesions are found post-mortem, even in the most severe cases.
- (14) Animals vary greatly in their susceptibility to the various vitamin deficiencies, a fact which necessitates the very cautious interpretation of animal experiments in relation to human disease.
- (15) In some animals, the health of the gastro-intestinal tract depends upon the presence of accessory food factors in the diet.
- (16) The thyroid gland is very sensitive to food conditions, and especially so in early life.
- (17) The pathology of idiopathic oedema is uncertain, but the condition requires thorough dietetic treatment.
- (18) The important and common "nutritional anaemia" of infancy, is preventable.
- (19) A slight degree of vitamin A. deficiency is not uncommon in poor children. Milk is a poor source of A. and D, and supplementary dosage of these vitamins is necessary in

infancy, especially at the time of weaning.

(20) Egg yolk is the only known foodstuff containing anti-rachitic power, to any extent.

(21) Some workers are investigating the possibility of a relationship between the phenomena associated with rickets, malignant disease, and sex activity.

(22) Vitamin D. prevents tetany, as it prevents Rickets; it also promotes perfect tooth formation.

(23) Several important points regarding the etiology and pathogenesis of Pellagra, remain obscure. The conception of the presence of "toxamins" in the normal basic foodstuffs should be thoroughly tested or abandoned.

(24) Certain factors in acidosis and alkalosis are discussed. The pathogenesis of "cyclical vomiting" is still obscure. Ketosis is, in all probability, not the cause.

(25) Of 146 infants below 1 year of age admitted to the Sheffield Childrens' Hospital from 1.2.34. to 1.6.34, 91 were "medical" cases. Of these 91, 41 were "dyspeptic", and 11 had congenital pyloric stenosis (including twin brothers). These two groups are discussed in greater detail.

(26) The importance to the infant, of an adequate diet for the mother, and instruction and perseverance in breast-feeding, is obvious, but neglected. Only thus is the subject

of artificial feeding one of the most important in the whole field of therapeutics.

(27) The great benefits of special dietaries (including the administration of vitamin preparations) will be more extensively enjoyed when time and intensive teaching increases the faith in them.

(28) Factors in the failure of breast-feeding are discussed.

(29) Every hand fed baby should be raised, as quickly as is compatible with its digestion, to a diet of full (boiled or pasteurised) cow's milk, with an added one ounce of sugar daily. The majority consider that full milk should be reached by three months of age; others consider this too strong for those below nine months of age.

(30) The more digestible modifications required by special cases (especially in wasting and in prematurity) are discussed. The dried milks ("half-cream"), which cost a little more than fresh milk, are acceptedly the next choice.

(31) "Partial vitamin deficiency" is no vague theory and the employment of the vitamins (especially in infancy) abounds with practical applications, which are of vital value to the practitioner, but which are by no means fully realised. The fault of this lies partly in the mal-organisation of society.

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