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University of Western Ontario

MEDICAL JOURNAL

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MEDICAL SCHOOL
VOLUME VIII. NUMBER 2

Epidemic Jaundice*

By J. L. BLAISDELL, B.Sc., M.D. (Tor.)
Senior Instructor in Pathology and Bacteriology, U. of W. O.

ALTHOUGH sporadic cases of so-called "Catarrhal Jaundice" are a commonplace of medical practice, jaundice occurring in epidemic form has seldom been reported in this country. During the last four months of 1938 an outbreak of this nature in the city of London, in which about 300 cases were observed, has aroused considerable interest. It was felt that owing to the unusual occurrence of such an epidemic in Ontario, a brief consideration of this subject might be of value.

While outbreaks of jaundice were mentioned in the writings of Hippocrates, the first actual description of an epidemic was made by Cleghorn in 1745. Many such outbreaks, chiefly among soldiers, were reported during the nineteenth century and within more recent years numerous observers have directed attention to the frequency of epidemics of jaundice in many countries of the world.

In 1886, Felix Weil described a type of jaundice which, in general, differed considerably from that commonly seen in sporadic and sometimes in epidemic form. Although, like the latter, the etiology was unknown, Weil's Disease usually could be distinguished by the severity of symptoms, tendency toward haemorrhage and frequency of renal involvement as well as by the long duration and high mortality rate of the disease. However, until the causative agent was discovered many years later, much confusion existed between Weil's Disease and other forms of jaundice. In 1915, the Japanese investigators Inado and Ito demonstrated a spirochaete, later termed "Leptospira Icterohaemorrhagiae," by Noguchi, as the etiological factor in Weil's Disease. The terms "Spirochaetal Jaundice," "Infectious Haemorrhagic Jaundice" and "Leptospirosis" have also been used to describe the condition. The latter term is to be preferred as recently it has been shown that the disease may occasionally occur without either jaundice or haemorrhage and that infection may sometimes fail to produce any characteristic clinical symptoms whatever. Investigations among sewer workers in London, England, have shown the presence of specific serum agglutinins in many individuals who gave no previous history

*Summary of a paper presented to the London Pathological Society in December, 1938, and as part of a Symposium on "Epidemic Jaundice" read before the London Academy of Medicine, January 5th. 1939.

of jaundice, so that sub-clinical forms of the infection are now recognized.

Although the differentiation of an outbreak of Epidemic Jaundice from Weil's Disease usually can be made from clinical and epidemiological findings alone, the diagnosis of any individual case may be difficult and must depend upon laboratory investigation. Weil's Disease is recognized either by the demonstration of the Leptospira in the blood or urine by guinea pig inoculation, or later in the disease by the presence of specific antibodies in the blood serum. These are shown by agglutination, adhesion or complement-fixation tests, by Pfeiffer's method, or by animal protection experiments.

The infection is transmitted to man from rats which harbor the Leptospira without developing the disease, the organisms being excreted in the urine. Thus Weil's Disease is largely restricted to those such as miners, sewer workers, butchers, etc., whose occupation exposes them to skin contact with moisture or moist soil contaminated by the urine of infected rats. Although Weil's Disease is not uncommon in European countries as well as in the East, only about 25 cases have been reported in the United States and only three have been observed in Canada. One of the latter cases, which terminated fatally, was carefully studied and reported by Edgar Bates in Toronto in 1926. Weil's Disease is seen either in the form of isolated, sporadic cases or in small outbreaks within certain occupational groups as we have mentioned. It is not transmitted from person to person and so does not occur in true epidemic form affecting the general population of a community. The possibility, however, of individual cases of Weil's Disease occurring during an epidemic of infectious jaundice, as recently reported in Detroit, must not be forgotten.

With this brief survey, we shall for a moment dismiss Weil's Disease from our discussion, bearing in mind, nevertheless, that the condition may occur in this Province, as Cameron and Irwin have shown that in Toronto a high percentage of rats harbour Leptospira Icterohaemorrhagiae capable of producing the typical disease in susceptible animals.

EPIDEMIC INFECTIVE JAUNDICE

Although jaundice of a mild type, occurring in epidemic form, has long been recognized, it is only recently that the widespread nature of these outbreaks has been appreciated. In 1912 Cockayne described a number of epidemics in America, Blumer in 1923 again drew attention to the problem and reported his studies of several hundred epidemics. In the years 1920-21-22, these outbreaks were particularly prevalent in the eastern United States, over 200 being reported in New York State alone. The disease has been described by a number of names, many of them inaccurate and misleading. This difficulty in terminology resulted from the confusion that existed not only between Weil's Disease and

other types of infectious jaundice but also among the various forms of non-spirochaetal jaundice themselves. The relationship of the common, sporadic form of the so-called "acute" or "simple" catarrhal jaundice to what was apparently the same disease occurring in epidemics also led to difficulty. The term "Epidemic Catarrhal Jaundice," which is usually applied, is undesirable as it implies a definite clinical entity and a characteristic pathological picture. That jaundice of unknown etiology, in sporadic or epidemic form, is of at least *two* clinically and pathologically distinct types, is now clearly recognized. One may thus classify infective types of jaundice (including Weil's Disease) as follows:

(1) EPIDEMIC INFECTIVE JAUNDICE (2 types)

(a) *Acute or Simple Catarrhal Jaundice*
(May also be sporadic. Commonly follows gastro-intestinal symptoms or respiratory infection. A type of "unobstructive," "resorptive" or "regurgitant" jaundice. Etiology unknown. Salmonelle group (?) Virus (?)

(b) *Infective Hepatic Jaundice (Mild Primary Hepatic Necrosis)*
(May also be sporadic. Not usually preceded by gastro-intestinal or other symptoms. No obstruction to biliary system. Probably a mild form of Acute Yellow Atrophy. Etiology unknown. Infection plus toxin (?)

(2) WEIL'S DISEASE OR LEPTOSPIROSIS
(Name should be noncommittal as both jaundice and haemorrhage may be absent. Probably many unrecognized cases. Etiology: Leptospira Icterohaemorrhagiae (rarely L. canicola).

It will be clear from the above classification that the term "Epidemic Infective Jaundice" is to be preferred in indicating all types of jaundice, apart from Weil's Disease, which may occur in epidemic form. This term does not limit one to a single clinical entity or pathological process, but rather includes the two separate and distinct forms of jaundice as we have shown.

Influenced by the original description of Stokes in 1839, Virchow stated that catarrhal jaundice resulted from inflammation of stomach and duodenum involving the common duct in a catarrhal swelling, with plugging of the lumen by mucus and desquamated epithelium, producing obstruction to the outflow of bile and dilatation of the biliary passages. Although Virchow described this condition in detail, he did not illustrate his discussion by any specific examples. As one of the mechanisms by which jaundice may be produced, Virchow's views have been confirmed by the post-mortem observation of a small number of actual cases, usually suffering accidental death. As the constant pathological picture to be found in *all* cases of so-called catarrhal

jaundice, however, this view was challenged by Heitler, later by Pal and finally by Eppinger who, in an epidemic of jaundice during the war, autopsied three cases dying of an unrelated condition and found, instead of gastro-duodenitis with biliary inflammation and obstruction, primary degenerative changes in the liver resembling a mild form of acute yellow atrophy. To this condition the term "infective" hepatic jaundice" or "mild primary hepatic necrosis" was later applied. However, the name "catarrhal jaundice," because of the familiarity of long usage, was not given up. It must be realized, however, that in the strict sense, the term should apply only to those cases in which an obstructive type of jaundice due to the pathological lesion described by Virchow exists, and not to include under it infective hepatic jaundice as recognized by Eppinger. The latter observer came to the conclusion that all types of so-called catarrhal jaundice were due to primary degenerative changes in liver and that no such process as Virchow described ever occurred. Strangely enough, some years later one of Eppinger's own patients, at the height of an attack of jaundice, committed suicide and he found to his disappointment the duodenitis, inflammation, swelling and occlusion of the common duct exactly as described by Virchow.

At the present time it is clearly recognized that epidemics of infectious jaundice may take the form of either Acute or Simple Catarrhal Jaundice, or Infective Hepatic Jaundice. Recently a great number of articles relating to this problem have appeared and many mild epidemics of jaundice have been described, particularly in England and in Sweden, as well as in the United States. Such epidemics, involving entire communities or occurring in institutions, affecting at times many hundreds of people, have been described by Pickles, Ramage, Bashford, Glover and Wilson, Sergeant, Bates, Montford, Fraser, Barber and many others. In Scandinavia they have been particularly studied by Wallgren.

Opinion differs as to the relative frequency of epidemics of Simple Catarrhal Jaundice and epidemics of Infective Hepatic Jaundice. It seems most probable, however, that the former is of more frequent occurrence. In some epidemics, both types may appear and in individual cases be quite indistinguishable as many clinical signs and symptoms are common to both. The conditions are, however, essentially dissimilar and when typical can often be distinguished. In nearly all of the epidemics recently reported, Leptospirosis as a possibility has been painstakingly excluded.

The two forms of Epidemic Infective Jaundice, namely Simple or Acute Catarrhal Jaundice and Infective Hepatic Jaundice, have been carefully described and differentiated by Hurst and Simpson of Guy's Hospital (1934) and by Barber (1937), the latter believing that epidemics are more frequently Infective Hepatic Jaundice than Simple

Catarrhal Jaundice. It must be borne in mind that both types may be found in the same epidemic. Molner, in Detroit, has informed me that since February 1938, 320 cases of jaundice, mostly among school children, have been reported in that city. Of these, 294 have been carefully studied, epidemiological histories being taken and blood agglutination tests for Leptospira carried out on all. In this large series, eight of the cases, or 2.7 per cent, proved to be Weil's Disease, among which three fatalities occurred. Thus it is possible that in epidemics any of the three types of jaundice, namely Simple Catarrhal Jaundice, Infective Hepatic Jaundice and occasionally Weil's Disease, may be represented.

Hurst and Simpson believe that in England most of the reported cases are examples of Simple Catarrhal Jaundice and are correctly diagnosed as such. The disease is chiefly one of children and young adults, tending to be extremely mild in character, sometimes without fever. Slight, transient icterus may be the only symptom of the disease. Epidemics occur chiefly in the fall and winter months and at times tend to recur annually. Close contact, overcrowding, etc., seem to be factors in the spread of the disease. Often several cases occur in one family, school or institution, and all observations point to transmission from person to person by direct contact, possibly through droplet infection. In Canada, only a very few epidemics have been reported, and in only one has the possibility of Spirochaetal infection been ruled out.

Although, generally speaking, Infective Hepatic Jaundice is mild, a few cases develop subacute yellow atrophy and die. It is the opinion of most observers that this type of liver damage is only a mild form of subacute yellow atrophy and the pathological changes to be found at autopsy are essentially the same, except in degree. A considerable number of fatal cases of this type, occurring in the course of epidemics, have been observed at autopsy, notably by Wallgren, Gaskell, and Klemperer. The duodenum and bile passages are completely normal, the essential lesion being a degeneration of liver cells often of periportal distribution. Often this is of rather mild character but is widespread and accompanied by areas of necrosis of varying extent. These milder changes are found in cases dying of some unrelated condition. Where death is due to the condition itself, the typical findings of subacute yellow atrophy are observed. It has been frequently pointed out, moreover, that the incidence of acute yellow atrophy rises sharply after some epidemics of infectious jaundice.

The etiology of epidemic infective jaundice is at the present time unknown. In certain cases it would appear that possibly organisms of the Paratyphoid group might play a part as instances have been described where various organisms could be demonstrated or where the formation of specific immune substances had occurred. It would appear, however, that infective jaundice is not a disease of specific bacterial etiology but may be induced by a variety of infections, perhaps in some

COMPARISON OF WEIL'S DISEASE AND EPIDEMIC INFECTIVE JAUNDICE

WEIL'S DISEASE	EPIDEMIC JAUNDICE
INCIDENCE—Very uncommon in America; only about 25 cases reported.	Very common; many hundreds of epidemics have been reported in the United States.
SEASONAL INCIDENCE — No seasonal incidence in indoor workers.	Mostly in fall and winter months.
AGE AND SEX INCIDENCE—Practically all cases in adult males, except in sporadic cases.	Chiefly a disease of children. (70 per cent in 50 epidemics studied by Blumer.)
OCCUPATION—Occurs in those exposed to water, soil, etc., contaminated by urine of infected rats. Commonest in miners, butchers, fish cleaners, field workers, sewer workers, etc.	No relationship to occupation except where crowding and close contact are factors.
TRANSMISSION—Usually through skin contact with material containing leptospira from rats. Not transmitted from person to person or through gastro-intestinal tract. Can be transmitted to some animals, as guinea pigs.	Probably from person to person through direct contact or droplet infection. Possibly at times through gastro-intestinal tract or by fomites (?). Cannot be reproduced in animals.
EPIDEMIOLOGY—No true epidemics affecting general population. Either sporadic or in small outbreaks within certain occupational groups.	Occurs in true epidemics, affecting general population of community, institution, school, barracks, etc.
SIGNS AND SYMPTOMS—	
Often very severe or fatal. In outbreak, always have some severe cases.	Usually very mild. No epidemic with many severe cases.
Haemorrhages common and often widespread.	Haemorrhages absent or mild epistaxis.
Kidneys usually involved. May have elevated N. P. N.	No renal involvement or slight albuminuria only.
Nervous manifestations common—convulsions, delirium, etc., occasionally meningitis.	Usually headache only.
Jaundice increases to about tenth day.	Jaundice at height in two to four days.
Jaundice lasts about three weeks.	Jaundice often transient; often disappears in a few days.
Convalescence often prolonged and may have "after-fever."	Convalescence usually rapid, with no "after-fever."
MORTALITY (Untreated)—	
Varies up to 50 per cent. In reported cases in United States, 41 per cent.	Practically nil.

cases associated with the action of unknown toxic substances. In certain epidemics the jaundice is preceded by upper respiratory symptoms which have suggested to some the possibility of a virus infection.

Occasionally, a case of jaundice may present such severe symptoms that it may easily suggest Weil's Disease, and, as we have seen, the latter may be so mild as to be confused with the former. While differentiation upon a clinical basis may be quite impossible in any *individual* case, the general character of the outbreak or epidemic is, however, usually apparent. No epidemics of Simple Catarrhal Jaundice have ever been recorded in which the *majority* of cases resembled Weil's Disease and, conversely, no outbreaks of Weil's Disease have ever been reported in which there were no serious cases. In general, therefore, from the character of the outbreak and the degree of severity in the *majority* of cases, a clinical differentiation of Epidemic Infective Jaundice can be accurately made. The characteristic features of the two conditions may be compared in the following manner: See Page 48.

SUMMARY

(1) Epidemics of Jaundice, while rarely reported in Canada, have been frequently described in many parts of the world.

(2) Infective Jaundice, excluding Leptospirosis, occurring sporadically or in epidemics may take the form of either Acute Catarrhal Jaundice or Infective Hepatic Jaundice.

(3) The cases recently reported in this district constitute an epidemic of what would appear to be Acute Catarrhal Jaundice. All cases have been of relatively mild character, the majority in children, and no fatalities have occurred.

(4) No evidence of Weil's Disease has been found, although only a small number of cases have been investigated bacteriologically.

(5) Although only three cases of Weil's Disease have been reported in Canada, the possibility of its occurrence in this district must be borne in mind, particularly as a number of cases have been recently reported in a neighboring city (Detroit).

(6) The etiology of Epidemic Infective Jaundice at present is unknown.

STATISTICS

Don't have anything to do with averages. Recently the Ministry of Health issued a Blue Book mentioning a mysterious malady which affected people of "an average age of forty-five." Doctors declared that they knew nothing of such a disease — and then it was discovered that the only persons who had ever had it were a baby aged twelve months and a man of ninety.—*Sir Thomas Inskip*, JOURNAL OF THE CANADIAN DENTAL ASSOCIATION.

The Modern Concept of Gastic Cancer

By HERBERT J. LIPSON '38

WHEN one considers the fact that 38,000 persons in the United States die annually from cancer of the stomach and that in 90% of cases the lesion could be satisfactorily removed if treated early, the need of more concentrated attention to early symptomatology of this disease is keenly felt. Moreover, when it is realized that carcinoma of the stomach is a disease of persons of the civilized world where a "high cancer mortality is an indication of general prosperity," the necessity for early diagnosis becomes apparent.

This disease is responsible for 42.8% of deaths from all types of cancer. It affects men three times more frequently than women, the average age incidence being 53 years. The average duration of symptoms is 11 months.

Etiology. The cause of cancer remains one of the obscure problems in medicine. According to most authorities heredity unquestionably plays a role. Whether it is due to a genetic change in one or more of the somatic cells, or due to an embryonal rest or whether it is simply because of the inheritance of certain anatomic or physiological peculiarities, no one ventures to say. There is evidence to disprove the theories that it is due to a germ or virus, or that it is due to diet, or an increase or decrease of any vitamin. It has also been shown that there is no real basis for the belief that syphilis favors or tuberculosis antagonizes the development of cancer. There is of course much experimental evidence that repeated traumatic or chronic irritations of various kinds, such as chemical, physical, bacterial, may produce cancer.

The occurrence of malignant degeneration in gastric ulcer has long been a debated question and the frequency of its occurrence has been shown to be somewhere between 5% and 10%.

Pathology. Ewing has pointed out that gastric cancer may begin in several different ways. It may commence:

(a) "As a localized overgrowth affecting previously normal cells which show atypical overnutrition and overgrowth.

(b) "As a focal hyperplastic gastritis at multiple points.

(c) "As a breaking up of the tubular gland with infiltration over the mucosa of malignant epithelial cells while the superficial epithelium and ducts remain intact.

(d) "In congenital or acquired structural abnormalities."

Whatever the beginning, all carcinomata of the stomach may be classified pathologically as follows:

(a) Polypoid or Medullary ca.

(b) Ulcerating ca.

(c) Diffuse carcinomatosis or linitis plastica.

The Polypoid type forms a large bulky tumor mass which projects

Editor's Note: This article was written as part of the work under the new block system of clinical clerking.

into the lumen of the stomach. Ulceration may or may not occur. This form is usually an adenocarcinoma. It is less malignant than the other types.

The Ulcerating carcinoma is the commonest form seen. It is a sessile growth occurring mainly on the lesser curvature of the stomach near the pylorus. Frequently it forms an annular constriction "sitting on the lesser curvature like a saddle." The growth contains an ulcer of varying size up to three or four inches in diameter. This tumor is for the most part scirrhous in character.

Diffuse carcinomatosis is quite rare. No real tumor can be seen but the stomach wall is greatly thickened. For this reason it has been likened to a "leather bottle." The process may be localized in the pyloric region or be diffuse throughout the whole stomach.

So called Colloid cancer is not a special type but rather a degenerative change which the tumor has undergone. Any of the previously described cancers may be transformed into a soft jelly-like transparent growth to which we ascribe the term Colloid.

As to the site of the growth, 90% occur in the pyloric third. Of these 75% originate in the lesser curvature fairly close to the pylorus. About 4% occur on the posterior wall; only 3% occur at the cardiac end.

The extension of gastric cancer is either local, to the lymph nodes, or distant organs. Local spread occurs in the submucous coat but the

THE MODERN CONCEPT OF GASTRIC CANCER

entire thickness of the stomach wall may be penetrated whence the tumor cells may be spread over the abdomen. It is in this fashion that Krukenberg's tumor of the ovary arises. Spread to the lymph nodes involves first the regional nodes but there may be distant extension along the thoracic duct, and the supraclavicular and cervical glands may be involved, especially on the left side. Extension to distant organs occurs via the blood stream whence the liver is involved first. Metastases may also be found in lungs, central nervous system, kidneys and bones.

Symptomatology. The various perceptible changes are "governed largely by the site and extent of the lesion and especially by the degree of motor impairment it has caused." A growth at the pylorus will produce different symptoms from one at the cardia particularly if obstruction has occurred at either orifice. A lesion confined to the pars media, whether on the lesser curvature, anterior or posterior wall, may be silent until well advanced. A small ulcerating lesion may mimic the clinical syndrome characteristic of a benign ulcer. It may respond favorably to treatment at the outset but later prove to be a malignancy.

"Symptoms making up the generally accepted criteria for the diagnosis of cancer, i.e., abdominal pain, nausea, vomiting, emaciation and cachexia, are late manifestations due to ulceration, secondary infec-

tion and obstruction, and when they occur the patient has lost his chance for cure by surgery or any other treatment."

Lord Moynihan emphasizes that "there are no symptoms pathognomonic of cancer of stomach; the symptoms are suggestive, not conclusive. The safest procedure is to consider the case a cancer until proven otherwise."

Vague indigestion such as a sensation of an empty stomach one or two hours after eating or a hunger-like distress coming on in a previously normal individual of 40 or over should bring the possibility of gastric cancer to mind. Where there is the slightest suggestion of associated weight loss a complete gastro-intestinal study should be undertaken. Finney and Carson regard loss of appetite and stomach consciousness the most important early symptom. Barney Brooks maintains the earliest feature is consciousness of something unusual in digestion. In an analysis of 291 cases over a period of nine years (1928-1936) at the Lahey Clinic frequency of incidence of symptoms was as follows:

	1928 - 1934 195 cases	1935 - 1936 96 cases
Indigestion	70%	92%
Anexoria	40	70
Pain	30	70
Vomiting	28	20
Weight Loss	25	83
Constipation	7	15
Dysphagia	4	5
Hemorrhage	4	4
Mass	1.5	2
Anemia	—	10
Tarry Stool	—	10

Thus while the full blown picture of gastric carcinoma is easily diagnosed, it becomes exceedingly important to recognize early symptoms as follows:

(a) Indigestion: Recently developed vague symptoms of epigastric distress; stomach consciousness.
(b) Anorexia: Gradually increasing loss of appetite.
(c) General Malaise: Condition of lowered vitality, of obscure origin, associated with fatigability and a slight loss of weight.
(d) Pain: Indefinite and associated with a known history of chronic gastric ulcer.

Such information as a history of gastric ulcer with changes in or a recent intensification of symptoms may prove of much value. Unexplained anemias or a family history of carcinoma should lead one to investigate more thoroughly.

Diagnosis. To reveal an underlying malignancy we have at present many methods at our disposal. Together with the symptomatology as

described above there is little reason for overlooking this disease. When, from the symptoms presented, one suspects a tumor in the stomach the following methods should be utilized in confirming the suspicion:

(1) Gastric Analysis. While this is not very important in the early stages, it may help pick up the odd case.

(2) Occult Blood in Stools: This is of value in early diagnosis if found but its absence does not disprove the presence of cancer.

(3) Blood Study. Anemia, while it is not seen early in most cases, may be found.

(4) Gastroscopic Examination. This method is particularly valuable in determining early lesions of the fundus. For lesions of the pylorus its value is not great.

(5) X-Ray. This is the most important method and should be utilized frequently. However, Horsely claims even a negative finding does not exclude early malignancy. In his opinion the patient should have the benefit of an abdominal exploration.

Differential Diagnosis. Before a definite diagnosis of gastric carcinoma can be made there are several diseases which must be ruled out, if possible. Eusterman and Balfour divide these into intrinsic and extrinsic conditions.

Of the intrinsic conditions the following must be considered:

(1) Peptic Ulcer. This condition is difficult to distinguish from gastric cancer but if resort is made to Sara Jordan's method a distinction can be made. The patient is put to bed on strict Sippy management for three weeks. If at the end of this time there is still blood in the stool and X-Ray does not show improvement, or if symptoms are not relieved, the case is one of gastric carcinoma.

(2) Benign Tumors. There is a marked absence of gastric disturbance. Anemia is very apparent and is of the secondary type. Pyloric obstruction is infrequent. X-Ray will prove their presence.

(3) Gastric Syphilis. Patient is younger; 85% of cases have achlorhydria. Other clinical evidence of syphilis will be present. Antiluetic treatment will usually clear up the symptoms rapidly.

Extrinsic conditions to be differentiated from gastric carcinoma are:

(1) Cancer of Pancreas. This usually results in pain. X-Ray will show the absence of an actual filling defect in the stomach. Carbohydrate metabolism will usually be disturbed, often hyperglycemia, but in cases of islet cell tumor hypoglycemia will occur.

(2) Cancer of Gall Bladder and Liver. Pain, anemia, slight jaundice and emaciation are early features. The liver is usually

enlarged. Cholecystography will usually show a malignant gall bladder.

(3) Gall Bladder Infection and Gallstones. Occult blood in the stool is absent. The use of the Graham-Cole test will point out the presence of gall bladder disease.

(4) Intestinal Neoplasms. Change in habits of defaecation and pain in the lower abdomen plus gastro-intestinal X-Ray studies will usually decide the diagnosis.

(5) Pernicious Anemia. In this condition the red cell count is lower than in gastric cancer. The color index is over 1. Nucleated red cells will be present. Loss of weight is not a feature here. Negative X-Ray findings will confirm the presence of this condition.

Treatment. Surgery offers the only hope for cure. Attempts at medical treatment in early stages are to be condemned. Lord Moynihan laments the fact that "the success of medical treatment in early cases of cancer is one of the causes of the high mortality from this disease." Every patient should have the benefit of exploration unless the disease can be proved incurable.

The determination of curability and hence the application of surgical measures depends on the following factors:

(1) Metastases in supraclavicular lymph nodes, peritoneum of rectal shelf, liver, umbilicus and thorax must be absent.

(2) Multiple tumors are inoperable.

(3) A small fixed tumor is difficult to remove.

(4) When pain is pronounced it indicates extra-gastric involvement and when referred posteriorly it is incurable.

(5) If patient has dysphagia it indicates encroachment on to the cardia. This is inoperable.

The methods of operative treatment can be divided into those which are palliative in aim and those which attempt a cure.

(a) Palliative Operations:
  (1) Gastro-jejunostomy.
  (2) Exclusion of growth.
  (3) Resection of growth.
  (4) Gastrostomy.
  (5) Jejunostomy.

(b) Radical Operations:
  (1) Partial gastrectomy.
  (2) Total gastrectomy.

Whatever the procedure elected it is most important that the patient should be properly prepared pre-operatively and that post-operative care be carefully given.

Prognosis. Balfour on a study of 4,793 cases concludes that "Cancer

of the stomach in its early stages is so situated that in 90% of cases the lesion can be satisfactorily removed."

When the growth and regional lymph nodes can be thoroughly extirpated 30% of cases will have a five year cure. The expectation of life in those cases which exploration reveals inoperable is five months. Where gastro-enterostomy is done life expectation is six months.

If the growth can be removed there are certain factors which determine the prognosis:

(1) Age of Patient. A higher percentage of five year survivals is found among older patients, 45 - 54 years, than younger patients, 35 - 44 years.

(2) Duration of Symptoms. The percentage of five year survivals is higher in those patients whose symptoms were of longer duration (12 months).

(3) Gastric Acidity. Among those patients whose secretory functions are normal the percentage of five year cures is greater.

(4) Size, Situation and Extension of Lesion. There is a greater expectation of life among patients who have a larger lesion. The nearer the lesion is to the pylorus the more difficult it is to cure. Removable lesions in the body of the stomach result in a greater rate of survival than those near or involving the pylorus.

More important in the prognosis of gastric malignancy is the degree of malignancy based on Broder's classification:

Grades 1 & 2—63% alive 5 years after operation.
55% alive 10 years after operation.

Grades 3 & 4—20% alive 5 years after operation.

Conclusion. The present outlook in carcinoma of the stomach is a poor one. For improvement the patient is not dependent upon the surgeon as upon the physician from whom he first seeks advice. It is to the physician that the lot of early diagnosis of gastric cancer falls.

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The Ovarian and Placental Sex Hormones

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SO far as is known, the ovary produces two hormones, and perhaps a third. One of these is the oestrogenic female sex hormone (folliculin, oestrin) which is secreted in the follicular fluid, also in the granulosa cells about the follicle. It is not exclusively an ovary-produced hormone as it is excreted abundantly by castrates, in whom it appears to be derived mainly from the adrenal cortex and the anterior pituitary. Moreover, oestrogenic substances occur in plants, minerals (even in anthracite coal) and in male animals and man.

The oestrogenic hormone is responsible, in the female, for the development of some secondary sex characteristics, e.g., the plumage of birds, the reddening of the sexual skin of monkeys, etc. In rodents, at oestrus, the uterine cornua secrete a fluid which distends them very markedly and uterine rhythmicity is increased. Moreover, pseudopregnancy cannot be produced at that time by irritating foreign bodies introduced to contact the endometrium. Oestrin seems to be responsible for the growth of the nipple and the lactiferous duct tree of the mammal. In mice of cancerous strains, there is very strong evidence that oestrin is carcinogenic to the breast (the site of spontaneous cancers in these strains). Oestrin seems to be largely responsible for animal behaviour and general spontaneous activity, not sexual activity alone. It even determines certain reflex times, and perhaps affects psychic states, as at the human menopause. In immature rodents, it induces puberty and perhaps it controls the same phenomenon in the human being. At least, it is not excreted normally until puberty in our species but is found regularly thereafter.

In some rodents, oestrin relaxes the pubic symphysis. In the guinea pig, and perhaps in the human, it acts with the relaxin of the corpus luteum to accomplish the same effect.

Injected into rats, mice, rabbits and guinea pigs, at least, it can produce abortion. Given to the human, it can produce only uterine haemorrhage in early pregnancy and huge doses are required to elicit even that.

Oestrin was thought to exist in the human in both free and combined forms, of which the former was obtainable from the latter by simple hydrolysis. However, some doubt of this has developed recently.

In the urine of the human female, it is excreted principally from the 10th to the 19th days of the cycle—in other words, during late maturation, ovulation and early formation of the corpus luteum. There is a second excretion from the 21st to the 24th days for reasons unknown. Before the menses, there is a rapid fall. Starting late in the second half of pregnancy, the amount excreted rises gradually and falls back to zero a few days after parturition. However, in the blood

stream, the concentration of oestrin is often highest at times when it is lowest in the urine, indicating how unreliable is the assay of urinary oestrin as an index of the status of the body's oestrin.

Oestrogenic substances in large doses depress the activity of the anterior pituitary in respect, at least, to its gonadotropic, mammatropic and thyreotropic functions. Indeed, there may be a sort of reciprocal relationship between the ovary and the anterior pituitary. After ovariectomy, the so-called castration cells develop in the pituitary. Oestrin administration causes them to disappear.

A word about the carcinogenic background of oestrin is appropriate. In 1915, Japanese investigators found that tar applied for long periods of time to the skin produced skin cancer locally. It was shown finally that a tricyclic phenanthrene nucleus was common to such carcinogenic agents. Some of the tumors so produced even metastasized. Such carcinogens are not selective of their substrate tissue and can produce either carcinoma or sarcoma. They can produce cancer without previous tissue stimulation. These substances differ only quantitatively from other substances such as arsenic, the aniline materials given off by certain parasites, etc., which in their own right occasionally appear to cause cancers; chemically, they resemble closely substances such as cholesterol, bile acids, ergosterol, vitamin D, testis hormone, and especially oestrin. However, other substances quite as closely related to these carcinogens are phenanthrene derivatives such as digitalis, strophanthin, codeine and morphine. It has been found very recently that even the penta-carbon ring is not an essential, as it is the position of the double bonds that really counts most in determining carcinogenic power.

Mice of cancer strains cease to develop cancer if the ovaries are removed. The later the operation, the higher is the cancer rate; the prevention of reproduction also reduces the cancer rate.

There are several oestrins now known, and the term which is coming into use to replace "oestrin" or "female sex hormone" is oestrogen. For example, this chemical "family" contains ketohydroxy oestrin or oestrone. Also there are trihydroxyoestrin or oestriol, an ester of oestriol called emmenin, dihydroestrin or oestradiol, hippulin, equilin, and the water-soluble unstable substance described independently by Engel of Vienna and myself. Many other substances act as weak oestrogens. Indeed, the list of such substances is growing very rapidly.

We do not know how much oestrin the body produces, how much is in our food, how, and in what form, certain organs utilize it (although the evidence now accumulating points to oestradiol or dihydroestrin as the physiological follicular hormone), how much of it is destroyed and where; what percentage of it is eliminated and what the proportions between blood and urinary oestrins mean. All assays differ, depending on the method used. To illustrate this, Schwenke pointed out that, if the a-folliculin were excreted as the hydrate, its potency would drop

from 8,000,000 or 10,000,000 mouse units to 70,000 mouse units per gram.

A word about the relation of female to male sex hormones is indicated. The male hormone seems to be always in female urine, although it is not found in the faeces. The urine of both the mare and the stallion, and the testis of the stallion are the richest commercial sources of oestrin. The two hormones differ only by one molecule of water and an atom of carbon. The female hormone is always to be found in male urine. In both sexes, according to Zondek, the male hormone is produced first. Then, in the female, this is dehydrated. More and more evidence goes to show that either gonad may produce either male or female hormones. Accordingly, we find instances of intersexuality in which female characters dominate but the only gonads are testes. A case has been reported where menopausal symptoms ensued upon removal of the testes. Korenchevsky, also a group of Austrian workers, have advanced the idea recently that the male and female hormones act as synergists.

In the frog, the gamete coming from the cortex becomes an oocyte and that from the medulla a spermatocyte. If the germ cells are so facultative, the hormones might be also! We can, indeed, look forward to a time in the near future when intersexual humans may be treated by rational means, rather than by seclusion and detention.

Oestrin in dogs has reproduced experimentally the hypertrophy of the lower part of the ureteral sheath, and even of the ureteral wall and mucosa, seen in pregnancy. The ureteral dilatation above the pelvic brim probably is not due to oestrin but rather to progesterone.

The corpus luteum secretes both oestrin and progesterone, the latter predominating. Abramson has recently indicated that it may also produce relaxin in the human. The function of progesterone is to stimulate the endometrium in order to make it receptive to the ovum by the time the latter reaches the uterus and in some way it prepares the way for the decidua basalis and the placenta. If the corpus luteum is removed early in pregnancy, there is a failure of implantation but if this has already occurred, the pregnancy is terminated prematurely in most mammals and to a limited extent in man. Recently, it has been shown by Eberhardt and others, that progesterone is contained in, and probably secreted by, the placenta of the human female, so that the latter can replace the corpus luteum, relatively, early in pregnancy. Hence abortion need not necessarily ensue upon removal of the human corpus luteum.

Although it is useful only during pregnancy, the corpus luteum occurs in each menstrual cycle in apparent anticipation of pregnancy and produces the typical premenstrual endometrium. During sexual life in the human female, it is therefore functional for about half the time.

The principal hormone of the corpus luteum, as has been said, is progesterone or corporin. It was synthesized two years ago in Germany

and the United States. It cannot be given orally but must be administered subcutaneously in oil. It will produce typical pregnancy changes in the uteri of castrated rabbits. Kaufman has been able to produce menses, by means of progesterone in castrated women who had been primed just previously with huge doses of oestrin. It is standardized on rabbits. It renders the normal uterine muscle quiescent, inhibits the reaction of that muscle to pituitrin and is able to inhibit the effect of oestrin on such muscle by doses about $\frac{1}{11}$ to $\frac{1}{20}$ as large as the doses of oestrin.

Relaxin was found by Hisaw in the corpora lutea of the guinea pig, in which animals it causes relaxation of the symphysis pubis, without which parturition would not be possible. In the human, pubic separation appears to depend upon a similar hormonal mechanism, oestrin acting to prime the joint for the action of the relaxin.

Progesterone is very expensive on account of its elaborate process of preparation, even by the newer synthetic methods. Fully 80 human corpora lutea are required to yield one rabbit unit of progesterone. When prepared by extraction methods, therefore, sows' corpora lutea are utilized.

It has been definitely shown to be as effective as vitamin E in preventing abortion in women who threaten to abort or are habitual aborters. It has been used in menorrhagia, dysmenorrhoea and lately for after-pains, although in most cases no deficiency of progesterone can be demonstrated in the blood of any such patients.

The common biological test for the presence of an oestrogen is the Allen-Doisey test. Mature young mice weighing 20 to 25 grams (about three months old) are used. They are castrated by the dorsal approach and isolated for at least two weeks. Then the supposed oestrogenic material is injected subcutaneously in six divided doses over a period of 48 hours, and the test is read in 72 hours. A positive oestrus smear can be obtained in the vagina, and the uterine cornua are enormously engorged and distended.

Menstruation is primarily an ovary-controlled phenomenon. Its processes are studied best by means of endometrial transplants inserted in the anterior chamber of the eye. Some six to twelve hours before the onset of bleeding one can see vasoconstriction. This lasts about a day, after which subepithelial haematomata develop and small papillae appear. The papillae rupture and bleed either irregularly or in sequence. Only tiny bits of desquamated epithelium are cast off on the first day and re-epithelization begins at once from the depths of the mucosal glands.

In primates, menstruation occurs if there is ovariectomy, or damage to large follicles, or excision of corpora lutea, or if there is section of the nervous connections to the ovaries either peripherally or in the cord. After the cord section regular menstrual cycles are resumed.

The essential phenomenon preparatory to menstruation is oestrin

stimulation of growth in the accessory genitalia, i.e., vagina, uterus, tubes and mammae. Endometrial proliferation is extremely rapid. Withdrawal of the hormone eventuates in haemorrhage after from two to nine days. In normal monkeys and occasionally in young women "menstruation" occurs without ovulation, so it would seem that progesterone is scarcely an essential for the appearance of menses. Adding progesterone to oestrin-treated animals delays the onset of the menses, but only for a few days. Menstruation occurs within three to four days of its withdrawal. The typical premenstrual endometrium is built up by extensive proliferation of new vessels and tissue cells.

After many attempts had been made, Hisaw and his co-workers were able, in both mice and monkeys, to produce ovulation of a whole litter of eggs by means of effecting a proper balance between the follicle-stimulating and the luteinizing fractions of anterior pituitary extracts. It is conceivable that sterility may be due, occasionally at least, to a corresponding defect of such stimulation.

Ovulation in monkeys and humans has been found to occur nearly always on the 12th to the 19th day of the cycle. This is the basis of the sterility theory of Ogino and Knaus.

Huebscher, by proper doses of oestrin, actually made a woman 80 years of age menstruate, and checked the findings by curettage.

The Placenta

The importance of the placenta as an endocrine gland has been recognized latest of all. It is only within the last two years, indeed, that it has been shown to be the source of progesterone in the human, thus explaining an ancient puzzle—that not all women in early pregnancy aborted when the corpus luteum was removed at laparotomy. Whether or not it is the source of oestrogenic substance or merely a reservoir for it is still a subject of debate but the evidence is gradually preponderating in favour of the former view.

It is now generally held that quite early in its functional life the placenta secretes and conserves large supplies of gonadotropic, oestrogenic and lutein hormones. It is the Maginot line of pregnancy; hence the far-reaching effects of functional disturbances of the placenta and the importance of therapy designed to conserve its function.

Moreover, early in pregnancy the placenta produces and retains relatively huge quantities of acetylcholine. The uterus is one of the few viscera analyzed to date containing none. As acetylcholine and choline are very effective in increasing the tone and rhythmicity of all smooth muscle and are especially active on the pregnant uterus near term, this would appear to have some significance. Add to this the fact that the placenta near term contains relatively much smaller quantities of choline and aectylcholine by weight than in early pregnancy, but that near term the blood begins to display it, and we catch a glimpse of a possible accessory or primary factor in the aetiology of the onset of labour.

The Life and Work of Richard Bright*

By EDWIN L. BROWN '40

WHEN one attempts to write about a man long since dead, it is necessary to refer to the historical documents of his period. Because we cannot make this man's personal acquaintance, we must do the next best thing and read what his contemporaries and friends had to say of him. Moreover, we must read any writings which he may have published, in order to arrive at an estimate of his achievements, his abilities, and his character. Fortunately, for our edification, such information about Richard Bright is readily procurable, for not only is the work written about him very extensive but he himself published numerous articles and books.

Richard Bright was born at Bristol on September 28, 1789, the third son of Richard Bright of the banking firm of Ames, Bright, and Cove. He was sent to school at Bristol, and in 1808 he began to study medicine at Edinburgh. Little has been written about his boyhood days, so apparently this period of his life was uneventful.

In 1810, however, a very interesting thing occurred when Bright accompanied Sir George Mackenzie on his trip to Iceland and contributed notes on botany and zoology to the latter's "Travels in Iceland." No doubt this period in Bright's life did much to develop his powers of observation and to materially broaden his outlook. It would indeed be interesting to learn what prompted Bright to abruptly interrupt his medical studies in favour of this travelling. No mention is made of this in the book but Mackenzie speaks of Bright's pleasing manners, his cheerful and ready exertion, and his undeviating good humour. Another side of Bright's life is brought out in the book and this is his artistic ability. The book is beautifully illustrated and many of the drawings are by Bright.

When he returned from Iceland, he started his clinical work at Guy's Hospital, London, where he lived in the house of a resident officer for two years, the beginning of the forty years or so he was to be connected with this institution. In 1812 he returned to Edinburgh, and on September 13, 1813, he graduated M.D. and read a paper "On Gangrene" to the Royal Medical Society. From Edinburgh Bright went to Cambridge with the idea of obtaining a degree there, but he only stayed two terms, finding that his studies were hampered by strict college discipline.

In 1814, he went on an extensive tour through Hungary, Austria, Germany and Belgium, taking advantage of his opportunities to learn French and German, and upon his return to publish a large book entitled "Travels from Vienna through Lower Hungary." This is really a very remarkable book, being written as it was by a medical man, and it

*This article won the Rowntree Prize in Medical History for 1938.

serves to exemplify Bright's wonderful powers of observation and description, his learnedness and his artistic ability. It is a great compliment to Bright's ability that, at the time, this book was considered a valuable contribution to the statistics and social condition of Hungary.

In December 1816 he was admitted a licentiate of The Royal College of Physicians, and shortly after this time he served as assistant physician to the London Fever Hospital, where he suffered from an almost fatal attack of fever.

Now we enter upon the most interesting part of this man's life, his professional career, which he fully embarked upon in 1820, when he started up his private practice in Bloomsbury Square, London. In the same year he became assistant physician at Guy's Hospital, and it was in connection with this institution, where he remained until 1843, that he was to do his famous work. He at once became noted for his untiring energy and for his extreme devotion to the pathological investigation of all his cases. It has been said of Bright that he was one of the first to appreciate that the progress of medical science was to depend largely upon the study of the pathological changes in disease. From this time on, Bright's progress was rapid. In 1821 he was elected F.R.S. and in 1824 he was appointed full physician at Guy's, where he began to lecture on medicine. Some years later he became associated with Addison, in this lectureship, and for many years the two renowned men worked together to raise the fame of the hospital.

In 1827 Bright published his "Reports of Medical Cases Selected with a View of Illustrating the Symptoms and Cure of Diseases by a Reference to Morbid Anatomy," which at once made his name famous. We may pause to note that the very title of his book expressed the extreme importance which Bright attached to the study of pathology. These Reports contain accounts of cerebral and liver disease which, in themselves, would have established his reputation as a morbid anatomist, but above all they contained a full account of dropsy and its relationship to the morbid condition of the kidney, with which Bright's name will forever be associated. It is a tremendous compliment to Bright's observational powers, when one considers that before his time renal disease was practically unknown. The strange thing is that dropsy had been recognized for such a long time and yet its relationship to the kidney had been undiscovered. Although Blackhall had pointed out, in 1813, that in many cases of dropsy he had found the urine to be albuminous, yet he failed entirely to implicate the kidney in the disease, In fact it is doubtful if, at this time, the kidneys were even removed at autopsy. Shortly after this, Dr. Wells investigated the subject very thoroughly but he too missed the role played by the kidney.

Such was the state of affairs when Bright stepped into the picture and before he left the scene was to be markedly changed. The most famous part of his "Medical Reports" is the first 126 pages of Volume 1,

and this section is entitled "Cases Illustrative of Some of the Appearances Observable on the Examination of Diseases Terminating in Dropsical Effusion." He first makes the statement that one great cause of dropsy is venous obstruction, but immediately goes on to say, "There are other appearances to which I think too little attention has hitherto been paid. They are those evidences of organic disease which occasionally present themselves in the structure of the kidney, and which, whether they are to be considered as the cause of the dropsical effusion or as the consequence of some other disease, cannot be unimportant." Bright then states that in many of these kidney conditions, associated with dropsy, he found an albuminous urine more or less coagulable on the application of heat and "I have never yet examined the body of a patient dying with dropsy attended with coagulable urine in whom some obvious derangement was not discovered in the kidneys;" and, "In all cases in which I have observed the albuminous urine, it has appeared to me that the kidney has itself acted a more important part, and has been more deranged both functionally and organically than has generally been imagined. . . It is now nearly twelve years since I first observed the altered structure of the kidney in a patient who had died dropsical; and I have still the slight drawing which I then made. It was not, however, till within the last two years that I had an opportunity of connecting these appearances with any particular symptoms, and since that time I have added several observations. I shall now detail a few cases, beginning with the two first, in which I had an opportunity of connecting the fact of the coagulation of the urine with the disorganized state of the kidneys." Then Bright presented the clinical notes on twenty-three cases and the post-mortem findings in each. The first case, a man named John King, was a classical example of what we now know as chronic Bright's Disease and Bright clearly and fully described the clinical aspect as well as the post-mortem findings. In spite of the fact that the sectio cadaveris presented acute pericarditis, enlarged heart, edema of the lungs and ascites, Bright inclined to the opinion that "the disease of the kidney was the first established," and that the other conditions were all secondary. About the kidneys themselves he said, "The kidneys were completely granulated throughout; externally the surface rough and uneven; internally all traces of natural organization nearly gone, except in the tubal parts. This is a well marked example of a granulated condition of the kidneys, connected with the secretion of coagulable urine."

Bright continued his investigations into renal disease and his next allusions were delivered in 1833 in his Goulstonian lectures and in an article in the "Guy's Hospital Reports" of the same year. In these publications Bright described the varieties of kidneys found in the post-mortem room and alluded to various symptoms and laboratory findings. If there ever was any doubt as to the originality of Bright's unique discovery it can readily be dispelled by the two following quotations.

Firstly, "I enlarge a little upon this topic—the indication of disease derived from an albuminous condition of the urine—for I am fully convinced that it is a fact that much important disease arises in connection with those derangements of the kidneys which lead to admixture of albumin with the urine, a connection which had not until very lately been in the least suspected—which now that it has been pointed out, fails not to show itself with the course of every month amongst the casualties of almost every hospital in the British Dominions." And secondly, "My conviction is complete as to the existence of some decided connection between the three facts—anasarca, coagulable urine and diseased function going on to diseased structure of the kidney." That the importance of Bright's discovery was fully appreciated at the time is seen in a review of the work in Lancet, which says, "Dr. Bright thinks that too little attention has been paid to disease of the kidney. To this point we call the attention of our readers, and hope that those physicians who are morbid anatomists will never open the body of a person who has died of dropsy without a careful examination of the internal structure of the kidney."

Bright was not content with the tremendous advances he had already made in connection with renal disease but continued his efforts with renewed vigour and in 1836 published his final and most extensive communication upon the subject. This article appears in the Guy's Hospital Reports of that year and it is, beyond doubt, one of the medical classics. The first part of the discussion deals with the etiology, history and symptoms of renal diseases, ten case accounts with comments and finally the treatment. The second part contains a tabular view of the pathology of one hundred cases. In everything Bright's descriptions were extremely complete and accurate and with the exception of one or two facts derived by means of instruments he did not possess (he only had a candle and a spoon with which to test for albumin in the urine) nothing has since been added to his accounts. Thus he described scarlatina and exposure to cold as causative agents and among the signs and symptoms were hematuria, oedema, pain in the loins, uraemia, pericarditis and peritonitis, convulsions, indistinct vision and blindness, and a hard pulse. But what is more important, Bright fully appreciated the fact that all these symptoms were directly due to the disease in the kidneys, as he said, "But one question may be asked in this place: Do we always find such lesion of the kidney as to bear us out in the belief that the peculiar condition of the urine, to which I have already referred, shows that the disease, call it what we may, is connected necessarily and essentially with the derangement of that organ? After ten years attentive—though, perhaps, I must not say completely impartial observation—I am ready to answer this question in the affirmative."

With respect to the treatment of the condition, Bright discussed many factors, stressing especially the maintenance of the function of the skin and the necessity for warm clothing, but at the beginning of

his paper he was forced to say, "It is, indeed, an humiliating confession that, although much attention has been directed to this disease for nearly ten years, yet little or nothing has been done towards devising a method of permanent relief, when the disease has been confirmed." And yet, at the present time, we find nothing much can be done as we find the following statement in one of the latest medical texts (Cecil, 1937): "A hundred years later we must amplify this apology of Bright with the equally humiliating confession that we, today, cannot cure the disease."

Although Bright published nothing more, upon what is now known as Bright's Disease, he pursued his investigations along with some of his pupils and colleagues. During this period two entire wards, devoted only to renal cases, were put under his supervision and the results of their investigations were published by Drs. Barlow and Rees in 1842. This report entirely corroborated Bright's earlier findings in all details. Moreover, Bright and his followers discovered that in these renal cases there was a marked retention of urea in the blood and they postulated the theory that this uraemia was the cause of many of the symptoms such as the cerebral disturbances and the inflammation of the serous surfaces.

Thus, we arrive at the conclusion of the discussion upon this very remarkable series of papers. When we consider that Bright's investigations, into what was at that time a new disease, were so complete and correct in all details, that in the hundred years since, only one or two facts have been added, we must admit that the papers are almost unique in medical literature.

Here, after a consideration of the work which has made his name famous, let us pause to consider the character of mind which was brought to bear, with such fruitful results, upon one of the most difficult problems in the entire range of medicine. We have seen, from his early publications, that he was a man of clear and vigorous intellect which was well nourished by experience and education. Moreover, his activities were many and varied for he was a traveller, a linguist, an artist and a writer. But above all, Bright was endowed with two great characteristics which, undoubtedly, chiefly account for his success. He was an indefatigable worker and his powers of observation were phenomenal. Although, strange as it may seem, most men find it easier to theorize than to see actual fact, Bright was one of those rare individuals who possessed the ability to observe the most minute detail. Added to this he possessed a still rarer ability in being able to correlate his observations. But, to do justice to his memory, we cannot stop here, for upon referring to the many comments written about him, we find that Richard Bright was possessed of many more virtues and worthy characteristics. Among these there is one other for which he was eminently distinguished and that was his truthfulness. This honesty in scientific investigation is no ordinary virtue and for it Bright was rewarded in the fact that he had to retract or correct so little of his

many observations and conclusions. He is described, by those who had the privilege of knowing him, as being a man of remarkably even temper, very considerate towards the failings of others, but very severe in the discipline of his own mind. Is it any wonder that this man, possessed with such an independence of thought and untiring energy, was able to contribute perhaps more than any other man to the medical knowledge of his day?

So much time has been spent in the discussion of Bright's work upon renal disease that the reader might well get the idea that this is all he did. Nothing is farther from the truth. Although Bright will, forever, be remembered in connection with the disease that bears his name, there is scarcely a disease of the body to which he did not pay considerable attention and moreover, many of his findings would have been enough, in themselves, to bring fame to an already illustrious name. In the second volume of his "Medical Cases," Bright devotes most of the space to a consideration of nervous diseases. In fact, Bright probably felt more interest in diseases of the brain than in any other and an examination of his writings serves well to exemplify the indefatigable industry he used in tracing them to their source. He wrote a very excellent survey of cerebral haemorrhages with forty cases as examples. He also discussed meningitis, hydrocephalus, cerebral abscess and other brain conditions, but his most original discovery, in this field, was in connection with certain epileptic seizures which we now know as Jacksonian epilepsy. Bright was the first to differentiate this condition from generalized epilepsy by insisting that the seizures were due to a localized affection because of "the degree of consciousness which was observed to be retained during the fits." He was able to localize the side of the brain the lesion was on and corroborated his statements in the post-mortem room. This localization of the lesion and also his excellent work upon aphasia, where he states "that the symptoms which arise in cerebral and spinal diseases are actually the results . . . of the lesions which the different parts of the nervous system have suffered," shows that Bright was one of the first to postulate the theory of cerebral localization, so well substantiated since his time.

He also investigated, very thoroughly, the subject of rheumatism and its various complications, especially its relationship to chorea and pericarditis. Sir Samuel Wilkes, who wrote the "Biographical History of Guy's Hospital," believes that Bright was the first one to describe a mitral murmur in connection with chorea.

The last contribution that Bright made to the literature of his profession was a series of monographs upon abdominal tumours, which appeared in Guy's Hospital Reports and later were reprinted as a separate book called "Clinical Memoirs on Abdominal Tumours and Intumescence," edited by Dr. G. Hilaro Barlow. Bright's death did not permit him to finish these memoirs. In the Editor's Preface, Barlow

wrote a great tribute to Dr. Bright which, though it has been often quoted, can well bear being repeated here. "There has been no English physician, perhaps none of any country, since the time of Harvey, who has effected not only so great an advance in the knowledge of particular diseases but also so great a revolution in our habits of thought, and methods of investigating morbid phenomena and tracing the etiology of disease, as has the late Dr. Richard Bright." Barlow points out that although Bright's papers upon abdominal tumours do not suggest any new doctrines, they are especially valuable as examples of care and accuracy in observing and recording observations. This statement applies to all of Bright's work and his papers should be read by everyone who appreciates the descriptions of a master.

In this book, Bright gave the first description of hydatid cysts, anticipating by quite some time similar observations made in Germany. Of the other subjects discussed the most original statements are made in connection with diseases of the pancreas and duodenum. It might be well to mention at this time that Bright described many other abdominal conditions, which are not included in the scope of this book. Thus he was the first to describe (but not name) acute yellow atrophy of the liver in connection with an admirable paper he wrote entitled "Observations on Jaundice" (Guy's Hospital Reports, Vol. 1, 1836). He was also the first man to describe a case of Addison's Disease, but he did not connect the symptoms with the suprarenals, although in his report he says "the only marked disease was in the renal capsules; both of which were enlarged, lobulated and the seat of morbid deposits apparently of a scrofulous character . . ." Thus in the disease that bears his colleague's name he did everything but say that the symptoms and the lesions were connected. The specimens obtained in this autopsy are still in Guy's museum as the earliest examples illustrating the pathology of this disease.

Although in his earlier years Bright's practice was not very extensive, his publications on renal disease and other subjects gradually attracted general attention and won for him a first class practice. In 1832 he was elected, with great acclaim, by Sir H. Halford, a Fellow of the College of Physicians. He married, first, a daughter of Dr. William Babington, and secondly, a daughter of Mr. Benjamin Follett. He had three sons and two daughters and of the sons one was Dr. Bright of Cannes and the other was the famous historian, the Reverend James Bright, master of University College, Oxford. Bright was an excellent father and husband, enjoying nothing better than being in the company of his family and looking after their welfare.

He retired from his position at Guy's in 1843, and took up residence at Saville Row, where he died, at the age of sixty-nine years, on December 16, 1858. A post-mortem was done on his body and it was discovered that he had suffered from diseased aortic valves and an enlarged heart. His kidneys were in perfect health, so he did not, as has often

been claimed, die of the disease which he had made his own (which is supposed to be a characteristic of medical men).

Richard Bright is one of the most famous physicians of modern times. Through his great discoveries and writings he won for himself an enviable position in the medical profession, both at home and abroad, in his own time and for evermore. This position, as we have seen, was not easily obtained but was the result of many years of unswerving energy of purpose and unceasing labour. It is true that he was endowed with many of Nature's best gifts but we must remember that he was constantly exercising these powers in order to derive the most benefit from them. This position, once obtained, he held by his pleasing manners, his honourable conduct, his extensive knowledge of all diseases, and the extreme pains he took to investigate every last detail of all his cases.

There is no better way to close this biography than to quote the eulogium which appeared in the Lancet (Vol. 1, 1859, p. 183), which not only expressed the opinion of Bright held by his colleagues but also that which will be held for all time to come: "The sudden and unexpected demise of Dr. Bright has created a deep impression of grief and regret, such as only a sense of irretrievable loss could occasion. In him all feel that the medical profession of England has lost one of the most original, observant and philosophic minds that have ever contributed to the glory and the usefulness of the body. A man of peculiar independence of thought, of high morale, and untiring energy, he has contributed more than, perhaps, any other to form the medical opinion of his day. With the acute application of truth which with him was almost an instinct, he was foremost to perceive that the progress of medical science must now greatly depend upon the successful study of pathological changes; and by the singular devotion to pathological investigation which characterized his career, he was at once enabled to accomplish investigations which have immortalized his name, while he gave a beneficial impulse to the whole science."

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Bright, R—Abdominal Tumours and Intumescence; 1860.

At Newport, R.I., there stands a monument to Michele Felice Corne, who first dared to eat a tomato, despite the age-old superstition that tomatoes were poisonous. Thus he gave the world one of its most prized vegetables.—THE PATHFINDER.

Gonococcal Arthritis

By H. J. D. JAY, B.A.
Meds '38

CASE REPORT

Patient, M. W., female, age 17. Admitted to Victoria Hospital October 11th, 1938, complaining of:

(1) Severe pain generalized on dorsum and palm of left hand.

(2) Generalized swelling of left hand.

History of Present Illness. Patient noticed severe pain which came on suddenly on dorsum of left hand, beginning at the wrist joint and later severe tenderness was noticed in area of hypothenar eminence. This pain rapidly became generalized and was accompanied by marked swelling of left hand. Patient also gave a vague history of trauma to dorsum of left hand. (This may play an important part in subsequent discussion.)

Past History.

(1) Growing pains at 6 or 7 years of age.

(2) Scarlet Fever at 8 years of age. (This introduces the factor of possible Rheumatic Fever.) All other past illnesses are irrelevant.

Functional Inquiry. When patient questioned about menstruation, said her periods were irregular, twenty-eight to thirty-four days.

Physical Examination. Patient was well nourished young female, lying in bed with left hand elevated on a pillow. She seemed to be suffering excruciating pain, yet looked remarkably well. No signs of toxemia.

Important Findings. Breasts: Nipples were flat, with prominent, pimply Montgomery tubercles.

Extremities—Left Hand:

(1) There was a diffuse swelling of left hand over dorsum and obliteration of the normal palmar contour.

(2) Pain at base of fingers 3, 4 and 5, dorsally, more marked on extension. There was also marked tenderness on pressure in hypothenar area and in mid-posterior portion of wrist.

(3) Movement:
   (a) Wrist joint could be flexed and extended a slight degree without undue pain.
   (b) Fingers were held in a position of flexion but could be extended and flexed without undue pain.

(4) There was no sign of epitrochlear or axillary lymph gland in-

PROGRESS NOTES

On admission, patient's temperature was 102.5°. Due to oblitera-

Editor's Note: This article was written as part of the work in the new block system of clinical clerking.

tion of palmar contour, a diagnosis of mid palmar space infection was made and drainage of dorsum and mid palmar space was instituted. Temperature dropped after drainage to 100° but cultures of serum from incisions were negative. X-ray of hand on October 12th and 20th showed no evidence of fracture or osteomyelitis. Patient's hand was treated with hot fomentations and radiant heat although no positive findings of infection could be obtained.

On re-examining the patient and questioning her, we found she was two months pregnant, so a question of G. C. Arthritis arose. On October 31st smears from urethra, vagina and cervix were taken but no gonnococci observed. Another X-ray was taken on October 29th and definite rarefaction and osteoporosis of the trapezium, trapezoid, os magnum and the bases of the proximal ends of adjoining metacarpals of the index and middle fingers suggested infective osteoarthritis. A G.C. complement fixation test was done on November 8th and reported strongly positive.

Patient was treated with short wave to left hand daily and given Prontylin, grs. 10 q 6 h for three days. (An important finding—with the use of Prontylin the red blood cell count dropped from normal to 3,000,000 cells.) Patient progressed favourably under the treatment, swelling in hand subsided, and was discharged to return to physiotherapy three times a week.

DISCUSSION OF G. C. ARTHRITIS

History and Etiology. The earliest discussions of G. C. Arthritis in England were those of John Hunter and Astley Cooper. After the discovery of the Gonococcus by Neisser in 1879, the organism was found in the joint fluid and later in the blood and lymph stream of patients suffering from acute Arthritis. This definitely established the etiology of the condition. In a series of thirteen thousand cases of Gonorrhea studied by Lees, Arthritis occurred as a complication in 2.9 per cent. The incidence in men was 3.3 per cent and in women 1.8 per cent. Joint complications in Gonorrhea were four to five times as common in men as in women. The joints affected: the knee, making up over 50 per cent of the cases; with ankle, wrist and olecranon in order of frequency.

Pathology. As Keefer and others have pointed out, the pathological picture of G. C. Arthritis depends on the tissue response to a direct invasion of the joint by the Gonococcus. The synovial membrane shows the characteristic inflammatory reaction with a more or less leukocytic infiltration. This commonly progresses to the point of bone involvement with destruction, and fibrous adhesions are formed leading to a permanently stiff joint. Some investigators believe the destruction is not due to the Gonococcus but rather is a sensitization reaction to the products of metabolism of the organism since it has been impossible in many cases to isolate the Gonococcus from the exudate or surrounding tissues.

Clinical Course. Gonococcal Arthritis may occur at any stage of Gonorrhea but in men there is usually an infection of the posterior urethra and in females the common foci of infection are the cervix and Fallopian tubes. Eighty-five per cent of the cases give a history of a Polyarthritis with dull pains in the joints without swelling. This usually persists for a period of a week when some predisposing cause, such as,

(1) lack of treatment,
(2) too active exercise during the acute stage,
(3) trauma to a joint,

may cause a flare-up with monoarticular involvement. However, as Osler states, "variability and obstinacy are the two most distinguishing features of the disease," and thus we must be prepared to meet it in many clinical forms. The commonest types of these are:

(1) Arthralgia, in which there are pains about the joint but no clinical signs of disease in the joint.
(2) Polyarthritic type, a local inflammation with severe pain and extensive swelling, usually monoarticular.
(3) Chronic Hydrarthrosis. This usually involves the knee. There is extensive swelling but no pain or redness or signs of acute inflammation.
(4) Bursal and Synovial forms, attacking chiefly the periostium, the tendons and their sheaths, and usually accompanied with marked myositis and muscle atrophy.
(5) Spondylitis. This is a specific involvement of the lower spine.
(6) Exostoses, particularly of the os calcis.

DIAGNOSIS

As we have mentioned above, there are a great number of clinical forms but there are certain essentials that must be followed in making a diagnosis. The first essential, although it is not specific for G. C. Arthritis, is:

(1) A classification of diseases of the joints based on etiology. A simple classification is:
    (a) Joint diseases of known etiology;
        1. traumatic; i.e., fractures into joints, dislocations, etc.
        2. infectious; i.e., G. C., T. B., Streptococcus, etc.
        3. neuropathic; i.e., associated with tabes, syringo-myelia and leprosy.
        4. metabolic; i.e., associated with gout, etc.
        5. constitutional; i.e., associated with hemophilia.
        6. anaphylactic; i.e., arthritis associated with serum sickness.
    (b) Joint diseases of uncertain etiology;
        1. degenerative joint disease.
        2. rheumatoid arthritis.
        3. rheumatic fever.

(2) History taking:
Usually in this condition it is very difficult to obtain a good history and it is necessary to use careful judgment and tact in eliciting history of venereal infection. However, a history of contact, followed by a yellowish discharge three to twenty days after exposure and a later involvement of prostate or tubes a few weeks or months after the acute phase, is of great import. Often coincidental with the above or at some later date the history usually reveals transitory involvements of many joints.

(3) Physical examination:
(a) *Inspection.* General inspection usually reveals a patient who looks remarkably well. There are little signs of toxemia, loss of weight or prostration. The general condition is good. Local inspection usually reveals a swollen, brawny, hot, tender joint hyper extended, with extensive swelling and involvement of tissue above and below the joint, much more so than in the non-specific joint infections.
(b) *Palpation.* On palpation one is at once impressed with the exquisite pain any manipulation causes patient. The pain is comparable to that of acute osteomyelitis and usually sedatives are necessary to control the patient. As we see, the local symptoms are out of all proportion to the general symptoms.

(4) Laboratory aids:
(a) *Examination of discharge from genito-urinary tract by smears and cultures.* In acute cases, positive smears are obtained in 40 per cent of suspects and 60 per cent show positive cultures. Warren gets a higher percentage of positive cultures approximating 100 per cent by following a strict bacteriological technique. In women he takes cultures of the discharge from the cervix during the last two days before and two days following the menses. In males without discharge he carefully massages the prostate, then washes out the urethra with sterile saline and cultures this.
(b) *Complement Fixation Test.* The work of Hinton, Bauer and Warren has proven that the Complement Fixation Test is of great value in the diagnosis of G. C. Arthritis. 206 cases of arthritis in which no history of G. C. or physical manifestations of the disease were present gave 91.3 per cent negative tests. 36 persons who had no organic disease gave 100 per cent negative tests, whereas 68 patients having a proven or probable G. C. Arthritis gave 91.9 per cent positive tests. The test is not alto-

gether conclusive since the Gonococcus must be present for at least ten days to four weeks before the test becomes positive, and if the disease and complement remain localized the test may never become positive; but research has shown that a positive test will be correct in 90 per cent of the cases.

Complications

(1) Myositis and a variety of skin conditions occur, especially hyperkeratosis of the palms and soles.
(2) Sciatica, usually secondary to spondylitis.
(3) Iritis, which is especially prone to occur with successive attacks.

Prognosis depends on:

(1) The virulence of the offending G. C. strain.
(2) The persistence of the local infection.
(3) The resistance of the individual.
(4) The promptness with which the appropriate treatment is instituted. In early acute cases the outlook is good unless there is a purulent arthritis, in which case some disability will probably remain. If damage of the articular surfaces has occurred, there is never complete restoration of joint function.

TREATMENT

Essentials of treatment are:

(1) Treat the original focus of infection.
(2) Deal with the infected joint locally and relieve the pain and prevent adhesions.
(3) Administer treatment to influence blood-borne infection.

METHODS

Hyperpyrexia. It has been aptly demonstrated that Gonococci can be destroyed at a level and duration of temperature within the limits of human tissue tolerance and safety. Several agents, such as the malarial organism, G. C. vaccine, typhoid vaccines, intramuscular milk, peptone, horse serum, and a host of other proteins have been used to raise the systemic temperature. In recent years Diathermy has been used for the same effect. Three techniques have been developed:

(a) General systemic hyperpyrexia.
(b) Localized pelvic hyperpyrexia.
(c) A combination of the two above.

As Warren and colleagues of Rochester have shown, they could kill all strains of Gonococci at a temperature of 106.7° F. in 6 to 26 hours, and Boerner and Santos have shown that the Gonococci are destroyed in half the time when a temperature of 111.2° F. was used, hence the combined systemic and local elevation of temperature is used — the systemic elevation at 106° F. and the local pelvic foci raised to 111° F. The pelvic heating is produced by Diathermy — the active electrode

inserted in the vagina or rectum and the temperature of 111° F. maintained for 3½ hours. The systemic elevation may be obtained by the use of the above mentioned methods or a water bath, and maintained for 5 to 6 hours at about 105° F. or 106° F.

In a series of sixteen cases of Arthritis (previously treated locally by tapping, immobilization, traction, Diathermy and X-Ray, either alone or in combination), when treated with the combined systemic and local hyperpyrexia for an average of two treatments the patients were relieved of their symptoms. Follow-up periods ranging from six months to a year and a half failed to reveal any foci of G. C. infection.

Treatment with specific antitoxin. The recently introduced antitoxin produced by Parke, Davis & Co. has been reported a great success. In a series of 27 cases of acute Gonococcal Arthritis, eight cleared up in 4 weeks, six in 6 weeks, one in 7 weeks, two in 8 weeks, two in 10 weeks, two in 12 weeks, one in 24 weeks and one in 40 weeks. The joint appeared normal and generally had full mobility in a week with a permanent result. In the chronic G. C. Arthritis, the patients were usually able to walk and to use their arms and hands without disability, and to leave the hospital within 18 to 21 days instead of the usual five or six weeks. In the series of eleven chronic arthritic cases, one relapsed, but after a second series of injections no relapse occurred over a period of a month's observation. This work was carried out by T. Anwyl-Davies of St. Thomas Hospital, and was carefully controlled. There was no severe reaction with the antitoxin; there was no severe pyrexia, and he concluded that the antitoxin was specific.

Sulphanilamide. During the past year, numerous favourable reports on the treatment of G. C. Arthritis with Prontylin were published. The usual dosage is 10 - 15 gr. q. 6 h. for three days, with rest period of one week, and repeat if necessary. I was not able to find large series of cases treated with this drug.

General Surgical Measures. In the main, these consist of rest to the joint during the acute exacerbation, with early movement both active and passive as soon as the acute stage has subsided.

The very severe cases must be treated as a synovitis of pyogenic origin, either by tapping or open drainage and washing out the joint cavity.

I wish to thank A. J. Grace, M.D., F.R.C.S., through whose kindness I am permitted to publish the case report, and R. A. Johnston, M.D., F.R.C.S., for his able advice and constructive criticism in the preparation of this article.

California canned peaches are eaten instead of "hot dogs" by many patrons of English amusement parks and carnivals. Small cans of the fruit are sold complete with can opener and spoon.—FOOD FIELD REPORTER.

Abstracts

THE USE OF MALE SEX HORMONES

By E. W. RICHES

Practitioner, CXL; 60: 1938

The hormones to be considered are (i) Gonadotropic hormone or prolan which is probably secreted by the anterior pituitary. It stimulates the testis to produce its own internal secretion, the true male sex hormone. (ii) Gonadal hormone or male sex hormone. It is available as testosterone acetate or propionate.

Their clinical uses are:

(a) Gonadotropic hormone: (1) Undescended testes: The recommended dosage is 500 rat units twice weekly, continued 6 - 12 weeks if necessary. If no results after three months a period of rest for three months is advisable. Failure of descent may be due to abnormally short cord or abnormal fixity but even in such cases hormonal therapy makes subsequent orchidopexy easier. (2) Azoospermia: Gonadotropic hormone indicated when condition not due to mechanical blockage as in gonococcal infections. (3) Impotence: Hormonal therapy helpful when impotence not due to organic causes.

(b) Gonadal Hormone: (1) Hypogonadism: Where there is retarded development of secondary sex characteristics associated with atropic testicles, gonadal hormone is indicated. (2) Eunuchoidism: Sexual function without ejaculation can be maintained by a weekly dose of 40 mgm. (3) Acne of puberty: Sometimes it will respond to testosterone. (4) Enlarged prostate: Hormonal treatment of this condition is still in the experimental stage but thus far it has shown great promise.

—B. C. BROWN '40.

DRUG THERAPY IN CORONARY DISEASE

By HARRY GOLD, *M.D.*

J.A.M.A., 112:1, 1939.

There are at present no drugs which will influence the course of any organic lesion in the cardiac muscle or in the coronary arteries. Drug therapy in coronary disease is therefore directed to the relief of pain apprehension anxiety, and restlessness, congestive heart failure, paroxysmal dyspnea, shock, and disorders of heart rhythm.

Nitrites. Used to abolish the pain of effort angina. They do this by decreasing the ischemia (which is the cause of the pain) rather than by dulling perception of the pain. There is no danger (with therapeutic doses) of causing harm from over-use, of setting up a tolerance to them, or of habituation.

Xanthines. Theobromine and theophylline, which have been highly praised as pain relievers in angina pectoris, are now thought to be of little value for that purpose. Aminophylline, which has been used to reduce the size of scars produced by coronary thrombosis, has been proven to be of no value.

Morphine is indicated in coronary thrombosis with severe pain, anxiety and paroxysmal dsypnea, in which case it relieves pain, gives rise to a sense of well-being and abolishes any disposition to move about. Ordinarily these patients are tolerant to morphine because the pain acts as an antidote to poisoning. If, however, the pain subsides more or less spontaneously after large doses of morphia are given, symptoms of morphine poisoning occur: constipation with abdominal distention, urinary retention, vomiting and increased susceptibility to ventricular ectopic rhythms. The best general plan of administration is to give ¼ grain doses of morphine sulphate subcutaneously at intervals of not less than one-half hour, until pain is relieved or diminished. Not more than 1 gr. in 12 hours should be given.

Barbiturates are sedatives, and are used to reduce nervous excitability and so reduce the number and severity of attacks of effort angina; to control the fear, anxiety and restlessness which accompany acute coronary thrombosis; to

reduce the susceptibility of the heart to ectopic rhythms.

Digitalis is indicated in coronary thrombosis only in two conditions: cardiac failure and disordered rhythm (fibrillation, flutter and paroxysmal tachycardia) with or without failure.

Quinidine is indicated in coronary disease only when there is a disordered rhythm whose return to normal must be hastened (most cases subside spontaneously if left long enough). If signs of congestive heart failure are present, digitalis is preferred. The use of quinidine routinely as a prophylactic measure against ventricular tachycardia is without sufficient merit to warrant it.

Diuretics are used in patients with congestive heart failure and attacks of paroxysmal dyspnea. Such patients should also receive digitalis.

Papaverine exerts a mild depressent action in animal experiments but is of little or no value in control of cardiac pain.

Iodides have been used in coronary sclerosis but are of no value except where syphilis is the underlying cause.

Tissue extracts have been widely exploited as "heart hormones" (due to the vasodilator substances which they contain) in the control of angina but are of very doubtful value.

Emergency measures for acute coronary thrombosis: (a) *epinephrine* is of some value during an Adams-Stokes attack, and in acute pulmonary edema if the systemic pressure is low. (b) *Posterior pituitary extract* should not be used to raise the systemic pressure because it constricts the coronary arteries. (c) *Caffeine, metrazol, coramine* and intravenous *dextrose* are of no apparent use.

—THOMSON ROOS '40.

A RENAL FUNCTION TEST FOR OFFICE PRACTICE

By P. C. ESCHWEILER, M.D.

Med. Times; 66:571, 1938.

Available for use in any office practice, this practical application of the valuable renal dilution and concentration tests should appeal to every practitioner.

A 2 cup (pint) size aluminum measuring cup, containing 8 standard screw cap dispensing bottles 4½ inches long and 1 inch in diameter (which are the specimen bottles and allow the use of a regular urinometer bulb) is given to the patient, along with a card of directions for the test. It may be run on a Sunday or day off duty, and has this to recommend it:

(1) Equipment easily obtainable; (2) simple diet easily measured by the patient; (3) neat method for patient to measure, collect and return urine specimens; (4) elimination of transfer of specimens from collection bottles to urinometer for measurement of specific gravity; (5) use of a meal containing 100 grams of carbohydrate as a glucose tolerance test to determine presence of an asymptomatic glycosuria.

The specimen direction sheet accompanying this article contains specific instructions to the patient for procedure and diet on the day of the test.

—K. SYMINGTON '40.

HYPERTENSION A CENTURY AFTER BRIGHT

By R. W. SCOTT

J.A.M.A., 111:2460, 1938.

Richard Bright first described the co-existence of arteriosclerosis, cardiac hypertrophy and chronic renal disease one hundred and two years ago. He attributed this condition, now called essential hypertension, to increased peripheral resistance due to renal disease. Gull and Sutton in 1872 ascribed the condition to widespread vascular disease, and regarded the renal lesions as purely secondary. Allbutt in 1915 said hypertension was due to generalized vasoconstriction unrelated to renal disease. Even in 1934 Fishberg stated that "sometimes hypertension is produced by renal disease but more often it is not."

Goldblatt and his associates, beginning in 1932, produced experimental hypertension lasting weeks by constricting the renal artery of a dog by a special clamp designed to permit any degree of occlusion. The blood pressure returned promptly to its former level by removal of the ischemic kidney or release of the clamp. A benign essential hypertension was thus produced. Further narrowing of both renal arteries resulted in uremia and death, or the counterpart of malignant hypertension. Clamping the aorta below the level of the renal arteries had no effect on blood pressure. Scott claims from that evidence that the renal

vascular disease produces likewise a varying degree of ischemia; a humoral substance is liberated from the kidney, constricting the peripheral arterioles, and thus elevating the blood pressure.

The author believes that Goldblatt's work is applicable to human beings, and declares enthusiastically that Bright is vindicated.

—JULIAN PRIVER '40.

RADIOACTIVE IRON AND ITS METABOLISM IN ANEMIA

By P. F. HAHN, W. F. BALE, E. O. LAWRENCE *and* G. H. WHIPPLE

J.A.M.A.; 111:2285, 1938.

During the past eight months, radioactive iron has been used as a tool in the studies of iron metabolism in dogs. This radioactive iron is prepared from Fe 58 isotope by deuteron bombardment. Its beta ray activity with a half life of forty-seven days makes this isotope useful as a labelled iron that may be followed in metabolism experiments, even after mixture with the ordinary iron of the body.

Five dogs were maintained on a diet low in iron and kept anaemic by frequent bleeding. This has been shown to affect the depletion of iron stores. They were then fed iron containing the radioactive isotope on one or several occasions and the absorption of iron was followed by analysis of the circulating blood fractions.

In another series of experiments, radioactive iron was fed to three normal dogs with iron stores well filled, as the result of previous feeding of soluble iron salts and intravenous injections of neutral colloidal iron.

It is immediately apparent, even in this short series, that the non-anemic animal absorbs but little of the iron fed. The rapid appearance of radioactive iron in the red blood cells is of great interest. Further experimentation is necessary to indicate the relationship of this iron to the hemoglobin of the various types of red blood cells (nucleated, immature and mature).

The evidence appears convincing that, in dogs under the conditions of these experiments, absorption of iron is dependent on the need of the body for iron.

—B. J. SCHUMM '40.

EXPERIMENTAL GASTRIC ULCER (Pitressin Episodes)

By A. J. NEDZEL

Archives of Pathology; 26:988, 1938.

The author presents a detailed study of ulcer formation due to the pressor episodes evoked by the injection of pitressin. Experiments were carried out by intravenous injection of pitressin into normal healthy dogs. Observations showed that 37 per cent of the animals developed lesions in the stomach and duodenum varying from small erosions to large ulcers and these were located in places common to the same lesions in man. Pitressin evokes a spasm of small blood vessels and muscular tissues and creates anoxia of parenchymatous cells which if prolonged will cause necrosis. These experiments point to a conditioning of the blood vessels as the immediate cause of ulcer formation and indicate that the "spasm theory" is the most logical to explain the periodicity in the appearance as well as the frequent multiplicity of acute peptic ulcers and their tendency to wide and irregular distribution. Depending on constitutional, seasonal, endocrine, emotional, traumatic and meteorological variatious vascular incoordination may be sufficient to lead to prolonged anoxia with the resulting development of peptic ulcers. It therefore appears that peptic ulcers should be regarded as a local expression of a vascular disfunction.

—B. PALMER '41.

"TUBERCULOSIS OF THE UTERUS: REPORT OF CASE"

C. F. TESSMER, M.D., *Fellow in Pathology*

Proceedings of the Staff Meetings of the Mayo Clinic; 13:46, 1938.

A white married woman, aged 68 years, complained chiefly of purulent vaginal drainage of one week's duration, which contained no blood. A similar occurrence had taken place five or six years previously. The only related symptom was a mild, chronic, slightly productive cough, present since youth.

A diagnosis of pyometra was made, and the possibility of a malignant lesion considered. Dilatation and curettage were performed and examination of the tissue showed a purulent endometritis and tuberculosis. Hysterectomy and bi-

lateral salpingo-oophorectomy was performed by Dr. J. M. Waugh.

The specimen weighed 80 gms. and contained multiple fibromyomas in the uterus. The endometrium was thin, and on microscopic examination revealed a tuberculous lesion. Similar lesions were scattered throughout the body and fundus, but none were found in the cervix or Fallopian tubes.

This case is unusual because of the patient's age of 68 years and the involvement of both endometrium and myometrium without involvement of the tubes. The latter indicates that the infection was probably hematogenous in origin, whereas most cases of tuberculosis of the uterus are caused by descending infection from above.

According to many authors, the frequency of involvement of the uterus in tuberculosis of the genitalia is second only to that of the Fallopian tubes, and accompanies it in about 50 per cent of cases. Tuberculosis of the uterus hardly ever invades the myometrium.

—J. W. BABB '41.

LUMPS IN THE BREAST

By RUSSEL HOWARD, F.R.C.S., C.B.E.

The Clinical Journal; LXVII:45, 1938.

The author takes the stand that, to be effective, diagnosis of a lump in the breast must be made at the earliest possible time, before any of the typical signs develop. Therefore he suggests that "the sign of a cancer of the breast is a lump in the breast—simply that and nothing more." No accurate diagnosis is possible at the time when operative procedure gives the best results. He advocates the excision of the lump, with the patient's permission to do a radical removal of the breast if it is thought advisable.

At operation, three situations arise: (1) the lump is innocent, so the breast is sutured at once to restore shape; (2) the lump is undoubtedly malignant; (3) the diagnosis is still doubtful. In either case, a radical removal is then done.

The author believes that chronic interstitial mastitis cannot be diagnosed from cancer, in the early stages, and often does become malignant. If it consists of a single lump, it should be removed and examined. If there are multiple small lumps, removal should be advised but not urged. Removal is never regretted.

—WILLIAM PACE '41.

A DOUBLE SYRINGE FOR THE ADMINISTRATION OF PROTAMINE ZINC AND UNMODIFIED INSULIN

By E. M. WATSON

Can. Med. Assn. J.; 40:1, 1939.

Experience has shown that, due to the slow mobilization of protamine zinc insulin in the blood stream, many patients require some unmodified insulin in addition to control their disease, especially in the acute form. Marked elevation of the blood sugar has been noted soon after the ingestion of carbohydrate when protamine zinc insulin was given alone. This postprandial hyperglycaemia and accompanying glycosuria has been most successfully combated by the administration of a combination of protamine zinc and unmodified insulin. To obtain the most satisfying results from this procedure it has been found necessary to inject these two insulins separately, as apparently most of the unmodified insulin is converted into protamine insulin.

In order to avoid a multiplicity of injections, a unique double-barrelled syringe has been designed by the author and used with gratifying results. The instrument consists of two 2 c.c. syringes supported on a frame and connected with a needle by means of a Y-shaped adapter fitted with a three-way metal stopcock.

A quantity of each type of insulin is drawn into its respective syringe; the adapter is then fitted with a rather long needle and inserted deep into the subcutaneous tissues. The unmodified insulin is first deposited, the needle is then withdrawn slightly and inserted in a different direction to deposit the protamine zinc insulin.

Excellent results have been obtained by the use of this method as shown by all-day blood sugar curves. Another advantage claimed is that several patients may be treated in a short time by merely changing the needles between injections.

—J. D. MCINNES '40.

Editorial

THE FIRST STEP

EARLY last spring a group of medical students from four Canadian Medical Schools met in Room 110 at Hart House, University of Toronto. These men were brought together through a common desire to organize Canadian medical students and internes for the purpose of advancing the interests of both the individual and the group, to strengthen our relations with the Medical Profession in this country and to discuss, and solve if possible, the common problems of men studying medicine in Canada. Because of the immediate necessity for such an organization and because of a real desire on the part of these men to do something about it, a working plan was drawn up. The babe had been born, the mucus had been cleared from its throat and it was crying lustily.

On February 4th, 1939, after a year of intensive body building, the brain child will take its first step. At this time the first conference of the Canadian Association of Medical Students and Internes will be held in Toronto. Plans have been developed weeks in advance and a large programme is to be considered. Among the timely topics to be discussed are co-operative book stores, government help in lowering the high rates of active tuberculosis in medical students, and a central bureau of information for men seeking interne appointments.

A capable body of men, led by a capable leader in the person of Paul McGeoy of Toronto, can carry only part of the burden if such an undertaking is to be a success. We are hoping for the full co-operation of every Canadian medical student of other schools as well as Western in order that the child's steps may not falter.

Book Reviews

THE FUNDAMENTALS OF INTERNAL MEDICINE

WALLACE M. YATES, M.D.

(1021 pp., Illustrated, Indexed. D. Appleton, Century Co., New York, 1938)

This text is one which should prove to be of value to the student who is commencing the study of clinical medicine, particularly internal medicine. The book is written primarily for this purpose. In no way is it intended for reference work, but appears to be excellent material for reviewing purposes. Throughout the book the author has attempted to present an unbiased view of the topic under discussion, both as to the nature of the condition and to treatment. Only the more universally accepted and proven methods of treatment are outlined. A bibliography appears at the end of each section.

For these reasons, Yates' *Textbook of Internal Medicine* should prove to be a popular one.

—W. E. CRYSLER, M.D., '38.

THE HORSE AND BUGGY DOCTOR

By ARTHUR E. HERTZLER, M.D.

(First Edition 322 pp., Illustrated, $3.00. Harper & Brothers, New York)

This is the autobiography of a country doctor who has actively participated in the tremendous changes wrought in medicine in the past fifty years. He is now Professor of Surgery in a large American university and a prominent figure in his field. To be more exact, since the author is still in the height of his life work, it is not in the true sense an autobiography but a history of his own times. In his own words, he is only "in the last half of the seventh inning."

The book deals intimately with the author's early life, his education and practice. Throughout it is amply studded with numerous anecdotes and humorous incidents which add greatly to its attractiveness. Of particular interest is the account of medical education used fifty years ago. The usual practice was to read medicine with an established practitioner called a preceptor. This was followed by two years in a medical school. The course consisted of two series of lectures of five months each. All the lectures were given to the whole student body at the same time so that each student heard the same lectures twice, once each year.

Perhaps the most remarkable thing in the whole book is the tracing of the advances in medical science which were made in this time. Of his early medical practice he says: "The country doctor's activities had less to do with the saving of life than with relieving a patient's pain and mental suffering." From this he progressed through further education to the later stages of his practice, where, by means of "kitchen surgery," he was able to save many lives.

The book includes a very interesting chapter dealing with two years of study that Dr. Hertzler spent in Germany, where he met and studied under such eminent men as Virchow, Waldeyer, Klebs and Zeit. Following this the author gives a very detailed description of "kitchen surgery" as compared with modern hospital surgery. The results obtained, considering the circumstances, were very excellent, although there is a surprising lack of accounts of those cases which failed to get well.

The author devotes much space to a consideration of his own private hospital which he built at considerable expense, trouble and disappointment.

The last two chapters deal with the psychology of treating patients, and medicine as it is today. The former, indeed, is a masterpiece, such that could only be written by a wise and experienced practitioner. From it the young student of medicine can derive much that will serve him in good stead, while the learned will know only too well how true to life it is.

Let it be said in résumé that the book's greatest value lies in the fact that it is a good and acurate record of the old country practitioner, which, as the author points out in the preface, it was intended to be. Nevertheless, it contains much comment about modern medical education and the relation of doctor and public health administration, which, although the reader may have difficulty in reconciling completely with his own ideas, certainly provides much food for thought.

—E. L. BROWN, '40.

HOW TO CONQUER CONSTIPATION

By J. F. MONTAQUE, M.D.,

Medical Director, New York Intestinal Sanatarium

(244 pp., Indexed, $1.50. J. B. Lippincott Co., Philadelphia, 1938)

Dedicated to "The Law of Diminishing Returns," written in a popular vein, and a sequel to "TROUBLES WE DON'T TALK ABOUT" by the same author, this book should have a favourable reception by both a thinking laiety who "suffer in silence, linger in doubt and carry on in despair," and a profession overwhelmed by an army of insistent drug house salesmen, each with the "perfect" product.

Dr. Montaque brings us the kernel hulled from the chaff of remedies

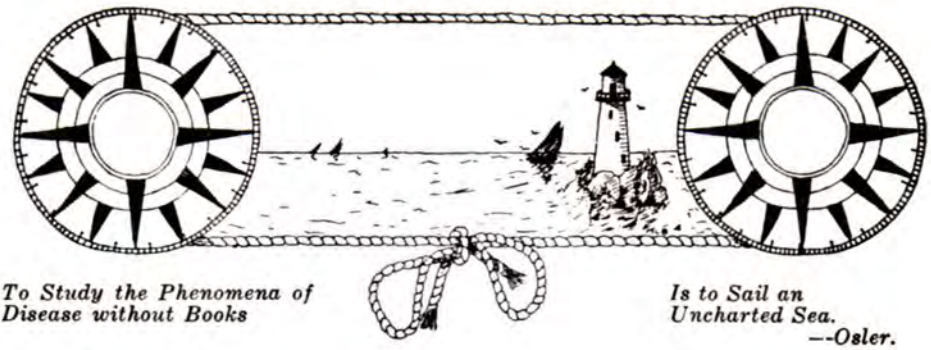
cluttering up the family medicine chest. Many useful hints on diagnosis, complications and effective treatment of this commonest of gastro-intestinal complaints are given. For the bewildered average person, to whom this book will primarily appeal, he presents a logical, physiological explanation of his many abdominal complaints, and the mechanism of action of the remedies popularly used. All this comes from a wide experience as a leading specialist in gastro-enterology in New York City—an experience which fully qualifies him to speak authoritatively and give instructions of incontestable value.

The book is divided into two main parts. Part One, "The Patient Asks . . ." is subdivided into fifty short chapters devoted to frank discussion of questions the patient asks the practitioner. For example: "How About Laxatives?" "But, Doctor, Is There Such a Thing As Auto-Intoxication?" "What Do Doctors Recommend?" "How Can I Establish the Habit?" "Good Old Castor Oil!" "Does Cigarette Smoking Help Constipation?"

Part Two, entitled "The Doctor Suggests . . ." constitutes a down-to-the-earth discussion of methods of control of constiptaion in infancy, childhood, adolescence, adulthood and old age.

Throughout, the author tells the truth without fear or favor, in an appealing, concise, yet complete manner. The book may well take a place in the crusade of preventive medicine.

—K. D. SYMINGTON, B.A., '40.



To Study the Phenomena of Disease without Books

Is to Sail an Uncharted Sea.
—Osler.

RECENT ACCESSIONS TO THE MEDICAL SCHOOL LIBRARY

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BALD HEADS

To a doctor a bald head is worth five thousand dollars a year. Many a practitioner without a practice worth the name would part with a fairly round sum for a good, cheerful, amiable bald head.

And what is said of the medical profession is applicable all around, with certain modifications. A bald head stands for wisdom in many a business concern, and draws customers. It favors the assumption of mature philosophy, and makes an impression on people who judge by appearances.

The father of a family gains much from his denuded scalp. It is that more than anything else which gives him the character of a jolly, hearty, generous man which he enjoys. Capped with a profusion of hair he would immediately sink in estimation. His very act of mopping the perspiration from the top of his head raises friendly feelings.

As to ladies, one does not venture an opinion, never having seen a bald-headed woman nor heard of one. Of men, however, it must be repeated, the world would be the loser by the extermination of all those whose character is bodily proclaimed by the graceful bumps and gentle depressions of a bare skull.—HEALTH DIGEST.