PERNICIOUS ANAEMIA AND ITS RELATION TO THE LIVER.

Thesis submitted for the

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by

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Introduction.

The subject of Pernicious Anaemia is now receiving renewed attention owing to the great therapeutic advance made in its treatment, as a result of the Minot and Murphy diet - a well balanced diet rich in liver.

The scope of the present work is to review the subject of Pernicious Anaemia with special reference to its treatment by liver and to discuss the relationship of Pernicious Anaemia with the liver.

The cases hereafter described were, with two exceptions, under treatment in hospital in the wards of the Royal Infirmary or Glasgow and were diagnosed and treated as patients suffering from Pernicious Anaemia. The remaining two cases were discovered by me while making observations on the significance of paraesthesia of the hands and feet as possible early cases of Sub-acute Combined Sclerosis. Following a paper read by Hurst, (Hurst, British Medical Journal, p. 676, 1927) I thought that some nervous diseases were overlooked in their earliest phases by disregarding sensory disturbances. I concluded that persistent paraesthesia of hands and feet required further investigation.

I collected 200 cases where this disturbance of sensation was complained of either in the hands or feet. The majority of these cases had disturbed sensation of but a temporary nature, but those remaining were specially investigated by further examining the nervous system, giving a test meal, and examining

the blood. In this series of cases there were two, which in my opinion were early subacute combined sclerosis.

The liver has been an object of interest for centuries, even in the time of the ancients. Galen had decided views on the function of the liver. He regarded it as the organ of "sanguification". Galen saw the liver interposed between the heart and the gastro-intestinal tract, and intimately connected with each. Because of its position he inferred that the function of the liver was to transform chyle into blood. Galen's theory remained unchallenged until comparatively modern times, when Bartholin published his work on the lymphatics in which he declared that the liver was the bile producer. Harvey did not relinquish Galen's theory though he was aware of the existence of lacteals. He too considered the liver as the chief organ of sanguification.

During the Galenical period the liver was regarded as the seat of the soul. Clifford Allbutt writes that certain Chinese today believe the liver to be the centre of the circulatory system, and that the right radial pulse is an indication of the action of the liver, while the heart forms the left radial pulse.

Modern investigation on liver has confirmed Galen's theory. Modern physiology has shown that the larger proportion of aliment, after being acted upon by the gastro-intestinal tract, is picked up by the portal veins and carried to the

liver, where it is altered and made suitable for passing into the general circulation, i.e. it becomes sanguified. To recount some important sanguification processes we have (a) absorption and storing of certain fats from the blood, (b) controlling iron metabolism, (c) maintenance of blood sugar level, (d) converting ammonia into urea, (e) certain materials formed in the gastro-intestinal tract become detoxicated in the liver, (f) destruction of certain bacteria absorbed from the gastro-intestinal tract, and (g) the ingestion of liver causing a remission in pernicious anaemia.

The beneficial effect following the ingestion of liver has been appreciated for centuries. Crow's liver is treasured in China because of the improvement that results after debilitating conditions. Amongst savage races the fresh liver forms a staple part of their diet, due to the belief that it is a blood forming organ. This can be understood by the amount of blood this organ contains and its richness on ingestion.

The Aetiology of Pernicious Anaemia.

The aetiology of pernicious anaemia is very controversal and since the work of Minot and Murphy, who found the excellence of liver as a therapeutic agent, new interest in the aetiology of pernicious anaemia has been aroused.

1. Age, Sex, and Geographical Distribution of Pernicious Anaemia.

It has been found that the greatest incidence is between 40 and 60 years. Occasionally cases occur under twenty years of age, but cases reported under this age are rare and have to be carefully examined before being accepted as genuine. In infants the bone marrow tends to revert to the primitive type when stimulated and has great powers of regeneration. The stimulus may be of any kind and causes extra medullary islets in the bone marrow, while in the peripheral circulation embryonic cells are found. Certain cases of aplastic anaemia, leukaemia, and infantile purpura in infants would be difficult to be distinguished from the blood picture of pernicious anaemia.

Faber (1928) reported the occurrence of a very severe anaemia in two patients age 12½ months and 3 months respectively, who showed a striking clinical and haematological improvement as a result of giving liver extract. It is of interest that one of these cases had achlorhydria. This suggests a deficiency of a specific factor necessary for normal blood formation in Faber's cases and the therapeutic value of liver as a medium for the formation of mature red cells.

Cases of pernicious anaemia have occurred over 70 years of age though it must be remembered that the anaemia of old age resembles pernicious anaemia superficially. Senile anaemia is of the aplastic type and is due to lowered physiological activity.

Sex Incidence.

Both sexes are liable to the disease, but in my experience found that females are more liable. Possibly the puerperal type of pernicious anaemia may account for the difference in sex incidence. Authorities vary as to which actually preponderates.

Cornell (1927)collected the figures from widely separated countries and found that of a total of 1,726 cases, 819 occurred in males and 907 in females, while Calet (1916) in a series of 1,157 cases, found that 723 males were affected and 434 females. Gulland and Davidson in examining the sex incidence in 300 consecutive cases of pernicious anaemia found 159 in females and 141 in males.

Geographical Distribution.

Northern America and Northern Europe are its main locations and inhabitants of tropical and sub-tropical countries are seldom affected.

Cornell has produced figures which tend to show that in certain states of North America, there is a relatively high death rate of cases with pernicious anaemia. The death rates in Nova Scotia and Alberta are 4.8 and 4.3 per 100,000 of the

population respectively while in Ontario during the years 1922-1924 the death rate was nearly 15 per 100,000. Cornell does not advance a reason for the differences in incidence, but it is admitted to be exact.

c. Conditions which may have Megaloblastic Anaemia.

It is generally admitted that pernicious anaemia constitutes a pathological and chemical entity but not an etiological one. A megaloblastic anaemia may be found in malaria, syphilis, severe sepsis, cancer, sprue, pregnancy and bothriocephalus latus infection. Sprue is the only one of these conditions where a megalocytic anaemia is present relatively more, while in the others they are rare.

In a typical case of pernicious anaemia the haematological data are characteristic. These may be conveniently divided into three sections:-

A. Evidences of abnormal Blood Destruction - the oligo-cythaemia, the small microcytes, the phagocytosis of corpuscles by the clasmatocytes, the deposits of iron pigment, the abnormal features of the bile pigment metabolism, and fragmented erythrocytes.

B. Evidences of Abnormal Blood Formation.- the macrocytes, and larger microcytes of the circulation, also nucleated red blood cells and megaloblasts.

C. Evidences of Blood Regeneration.- the presence of immature red blood cells, such as reticulocytes, nucleated forms, an increased red blood cell count and higher haemoglobin percentage.

Evidence of a disturbed bile-pigment metabolism is shown by the hyperbilirubinaemia, the increased output of urobilinogen and urobilin by the liver, and the increased urobilin from the kidneys.

Van den Bergh has shown that the plasma bilirubin in pernicious anaemia behaves differently from the bilirubin associated with hepatic obstruction or disease as tested by the diazo-reaction. The lemon-yellow colour so often present is due to staining of the tissues by this bilirubin. As a rule severe anaemia is accompanied by hyperbilirubinaemia, but it is possible that a severe anaemia may be present without a marked hyperbilirubinaemia.

The other features of pernicious anaemia are achlorhydria, central nervous system degeneration and the phases of remission and relapse.

3. The Constitutional Factor in Pernicious Anaemia.

The constitutional factor in the production of diseased conditions is now admitted to be of aetiological importance. Hurst declares that patients suffering from gastric or duodenal ulcer have an ulcer diathesis.

Sprue, bothriocephalus latus infection, the anaemia of pregnancy, prolonged sepsis, syphilis, cancer and malaria may lead to severe anaemias which resemble pernicious anaemia. With the exception of sprue it is very exceptional that a megaloblastic anaemia is formed, it is usually normoblastic in type.

It is difficult to account, except by the inherent factor being in the host, that one person should develop a megaloblastic anaemia and another a normoblastic type, even though the type and severity of the underlying process may be the same. The tendency or diathesis may vary in degree and it may require only a small stimulus where the diathesis is marked to produce a megaloblastic anaemia.

Familial Incidence of Pernicious Anaemia.

Palmer Howard is said to be the first to note the familial incidence of pernicious anaemia. Klein in 1891 saw the disease in three brothers and sisters. Bramwell later described a family in which seven individuals in two generations had suffered from pernicious anaemia. Many other workers have since noticed its familial incidence. In examining the history of patients with pernicious anaemia it is a relatively frequent occurrence in my experience of relatives having died of "anaemia". Sub-acute combined degeneration of the cord has been proved to have hereditary influences.

Familial Incidence of Achlorhydria.

It is universally known that achlorhydria is a constant finding in pernicious anaemia, and it has been demonstrated that relatives of patients may have no free hydrochloric acid in the gastric juice, although there may be no anaemia.

Laelek examined 49 relatives of 20 cases of pernicious anaemia and found that 26 had complete or nearly complete achlorhydria.

Wemberg, as quoted by Piney, examined the blood of persons with familial achlorhydria and found Colour Index over unity, slight megalocytosis, and scanty blood platelets. They had however no anaemia.

Hurst, 1923, has confirmed the presence of achlorhydria in blood relatives and calls it the "achlorhydric gastric diathesis".

B. Latus Anaemia.

With the exception of Sprue, the B. Latus has a higher proportion of cases with megaloblastic anaemia than any other condition. It is recognised that only a small proportion of patients bearing this parasite develop the anaemia. Apparently there is no relationship between the development of the anaemia and the type of helminth.

Schaumann (1920) found evidence to support this view. He found that there were patients who had suffered from the parasite many years previously subsequently suffered from pernicious anaemia. Careful examination revealed that the parasite had been expelled. He also found that parasite-free relatives of patients suffering from tape-worm anaemia had a tendency to develop pernicious anaemia. These relatives had a higher incidence to develop pernicious anaemia though they migrated to countries where the B. Latus is not found.

Norway and Sweden have a high incidence of pernicious anaemia, in my opinion due to a constitutional predisposition to the disease and the frequent presence of B. Latus as the exciting cause.

It is alleged that there is a type of patient who developed pernicious anaemia. Addison (1855) noted that the disease occurred "chiefly in persons of a somewhat large and bulky frame". Most of the patients I have seen are of this build, but it may also occur in small, lean people. Maitland-Jones as well as other observers have noted the frequency of gray or white hair. Sheard (1924) noted in his cases that the change in colour of the hair occurred fifteen years earlier than the normal. He further noted, as others have, the frequency of very fine, soft hair.

Draper (1924) has taken very careful anthropological measurements in 45 cases of pernicious anaemia. Briefly summarised, as the result of these cases, he concludes that there is a particular type of individual who will develop the disease and that is a person whose measurements tend to approach the acromegalies.

There is then, from the above-mentioned facts, a considerable mass of evidence to support the contention of the existence of a constitutional predisposition to the disease, and that it is an essential factor in its production.

Achlorhydria.

In the literature there is a certain looseness in the terminology regarding achlorhydria and achylia gastrica. In both conditions there is an absence of free hydrochloric acid in the fasting gastric juice or during the process of digestion. In achlorhydria small amounts of hydrochloric acid and pepsin may be secreted, but the acid is immediately neutralised by

alkaline mucous secreted from the gastric glands. Combined acid may however be present. While in achylia gastrica there is a complete absence of any secretion of either acid or pepsin and therefore an absence of combined acid.

The absence of free hydrochloric acid in the stomach is of great diagnostic importance in pernicious anaemia. For about forty years it has been known of the constant association of achlorhydria with pernicious anaemia. Faber and Bloch, Levine and Ladd, Hurst, Faber and Gram have confirmed this result in their cases. This finding has been constant in my series of cases. Flint and Fenwick, both many years ago, drew attention to the frequency of an atrophic condition of the gastric mucous membrane as a post-mortem finding. There is not general agreement with this conclusion as some believe that the degeneration seen is due to post-mortem change.

So far as critically reported, achlorhydria precedes all other symptoms of pernicious anaemia. Riley reported two cases in which achlorhydria was present twenty and twenty-five years respectively before the onset of the disease. Hurst, Faber, Wilkinson, interalia, have reported cases in which achlorhydria preceded pernicious anaemia for varying periods. Hurst has moreover, shown that achlorhydria with or without the full picture of pernicious anaemia may exist in several members of the same family. The familial incidence of the disease is well recognised, and in view of these facts it is difficult to avoid the conclusion that, in the words of Hurst, "achlorhydria is an essential predisposing cause of the disease".

The condition of achlorhydria in pernicious anaemia is as permanent and usually more permanent than the disease. It does not alter with remissions, whether natural or as a result of treatment, and though the blood condition as a result of treatment may be normal for a long period, achlorhydria will still be found.

Achlorhydria is frequently present in diseases with no anaemia or if present may be associated with a secondary anaemia. Prolonged toxaemias or debilitating conditions reduce the fundamental activity of the stomach. Advanced carcinoma of the stomach is the only condition which approaches pernicious anaemia in the frequency of achlorhydria.

Achlorhydria may follow infective or toxic processes and is known as the acquired type. Chronic alcoholic gastritis, cirrhosis of the liver, pyorrhoea, etc., may cause achlorhydria, and so do gastrectomies.

Hurst reports of five cases in which pernicious anaemia followed removal of the stomach. As pointed out by Piney, since this operation is usually done for carcinoma, any subsequent pernicious anaemia would have to be carefully examined to rule out a secondary deposit of carcinoma in the bone marrow. There is not however, general agreement on the advent of pernicious anaemia following gastrectomy, as there is ample published evidence to show that gastrectomy patients are no more likely to pernicious anaemia than normal people.

If no pathological cause in the stomach or elsewhere can be found and especially if the achlorhydria has been known to be present since infancy, it is reasonable to assume that absence of free hydrochloric acid is an inborn error and would be classed as the constitutional type of achlorhydria. Modern works attribute this type of achlorhydria to be associated with pernicious anaemia in most cases. In my opinion this finding greatly supports the view that the constitutional factor is of great importance in pernicious anaemia.

The following are several of the alleged causes of this achlorhydria.

1. The Anaemia. This conception arose during the original discussion of the subject, but it can be dismissed because it is known that the achlorhydria out-dates the anaemia and persists even during a remission.

2. The Toxic or Infective Processes which also cause the other symptoms of the Disease. According to this theory the achlorhydria is the functional result of a toxic gastritis following prolonged irritation of toxins. In favour of this theory is that 20 - 30% of cases have a prodromal debility for many years previous to the disease. Against this view is that about 7% of patients have always been healthy and that there have been cases where gastric atrophy has not been found.

3. Constitutional Factors of Unknown Nature. This is the most common view. The theory admits achlorhydria to be of

constitutional origin not necessarily associated with gastritis. Hurst and Passey have shown that on post-mortem examination the gastric mucosa may be perfectly normal although achlorhydria was present. Hurst has further pointed out that a non-functioning gastric mucosa is more likely to have secondary injury than a functioning one, allowing the liability of mechanical irritation. The gastric secretion is an excellent antiseptic defence and its absence allows infection from bacteria-laden food and saliva from the unhealthy mouth. The theory regards gastric sepsis seems to be from secondary injury and invasion, and regards the achlorhydria of pernicious anaemia to be constitutional or even inherited.

The Significance of Achlorhydria.

1. Free hydrochloric acid is of great antiseptic value and is the natural protective barrier to infection from poisons and pathogenic organisms. Its absence causes an altered biochemical reaction of the contents in the small bowel, and allows an enormous growth of micro-organisms. As a result, there is infection from above and below, from above due to the notoriously septic mouth and below from the ascent of micro-organisms. The stomach and upper part of the small intestine contain in pernicious anaemia a bacterial flora similar as in the colon. Because the small intestine is known as the site of maximum absorption and also that the irritability of organisms is much greater than in the large bowel and that the factors necessary for toxin formation exist, it has been argued that

there must be auto-intoxication in these circumstances. The question of alimentary toxaemia will be gone into subsequently, but the strongest evidence against auto-intoxication as an etiological factor is the work of Knott, who demonstrated that after a remission brought about by the use of liver there was no appreciable difference in the fauna and flora of the lower bowel.

2. Absence of free hydrochloric acid does not affect digestion, Apparently healthy people may have achlorhydria and be perfectly well. Many cases of pernicious anaemia have at some time gastro-intestinal disturbances, but there is a proportion who have no disturbance. The pancreas takes up a bigger role in digestion when there is no peptic activity.

3. The work of Castle has increased the importance of achlorhydria. His work tends to show that the achlorhydria is associated with some constitutional secretory deficiency of an enzyme whose action is necessary for the elaboration from protein of the specific factor needed for normal blood formation. The importance of Castle's work and its exact significance will be discussed further with reference to the nature of the anti-anaemic principle.

Hypotheses regarding the Aetiology of Pernicious Anaemia.

For the past forty years two hypotheses have been held regarding the aetiology of pernicious anaemia. The haemopoietic system is the one principally affected in pernicious anaemia, but it is to be remembered that the frequent involvement of the gastro-intestinal and nervous systems and the phases of remission

and relapse, that any theory propounded must include these changes.

1. Bone Marrow Theory.

Pepper and Cohnheim, and later Ehrlich, satisfied themselves that the bone marrow was the primary pathological site of the disease which had reverted to an embryonic type, thus producing abnormal cells. They did not believe haemolysis as of great importance since the ceels of the reticulo-endothelial system, acting as phagocytes, caused this effect on the abnormal circulating cells. They did not satisfactorily explain why there occurred a megaloblastic degeneration of the bone marrow. Some believed it to be a developmental error while others explained the bone marrow changes to be the result of a toxin. This toxin was unknown and hypothetical and not proved.

Cohnheim demonstrated the fact which lies at the proper understanding of the disease, that the more active the bone marrow in respect of its blood-making function, the worse is the anaemia. An active bone marrow in other anaemias is associated with improvement in the anaemia. Marked activity of the bone marrow in pernicious anaemia is accompanied with relapse and increased anaemia. The bone marrow during the last and fatal relapse is seen at the height of its blood forming activity. This behaviour of the bone marrow is highly distinctive of pernicious anaemia. There are two possible explanations to account for the anaemia with an active bone marrow:-

(a) The red cells formed in the bone marrow are destroyed on liberation to the blood stream, or

(b) These cells are never liberated.

The anaemia according to the evidence is apparently maintained in both these ways. A powerful haemolytic element has been long liberated in pernicious anaemia and there has been a tendency to regard haemolysis as the sole cause. It is now held that the haemolysis is largely responsible for the anaemia.

c. Hunter's Theory.

Hunter's views represent the English School and they held that the primary site of the disease to be in the gastro-intestinal tract. A haemolytic toxin was thought to be absorbed from this tract and caused great blood destruction in the portal circulation. The bone-marrow changes were thought to be of a secondary compensatory nature. Hunter did not define the nature and origin of the haemolytic agent. He demonstrated by gravimetric analysis that the liver in pernicious anaemia contains more iron than the liver in other anaemias.

The Continental School, as represented by Cohnheim and Ehrlich paid little attention to siderosis and thought it due to iron medication. In the same way as Ehrlich held up the megaloblast as a specific finding, so did Hunter hold up hepatic siderosis. Hunter concluded from his results that the deposit of iron bearing pigment in the liver, was the result of abnormal blood destruction in the portal circulation.

It is of interest that McMaster, Rous and Larimore (1922) concluded from their experimental work that liver siderosis does not indicate any specific bodily site for blood destruction.

Hunter believed that a toxin produced from within the lumen of the gastro-intestinal tract, was being absorbed into the portal blood and there caused an intense destruction of blood corpuscles, the freed pigment from which was deposited in the liver. Hunter's hypothesis is important from the point of view that it was the first to explain the anaemia by extensive blood destruction. Hunter's theory is not accepted because;-

(a) There is no evidence of intravascular haemolysis in pernicious anaemia.

(b) No specific haemolytic agent has been found.

(c) The recent work of McMaster, Rous and Larimore, (1922) indicates that there is an increased iron content in the liver, kidneys and spleen in other blood conditions, and that the site of haemolysis may be elsewhere than the liver, also that the haemolysis may be the result of intravascular or intra-cellular blood destruction.

(d) It is known that haemolytic extracts can be obtained from the dead body of the B. Latus. Supporters of the theory of portal haemolysis have noted the association of this heleminth with pernicious anaemia and concluded that there must be a haemolysin in pernicious anaemia. Though a haemoly-

tic substance may be extracted from the parasite, there is no proof that it is absorbed. Further, it is known that only a small percentage of people who harbour the parasite develop a megaloblastic anaemia.

(e) Richter, Warthen and Isaac (1928) individually treated with liver extract several cases of pernicious anaemia resulting from B. Latus, with very satisfactory results. The anthelmintics were not given till the anaemia was in a marked state of remission. Liver or its extract not having any antihaemolytic or antiparasitic action is further proof that the anaemia could not be from any haemolysin from the parasite.

(f) When haemolytic agents such as haemolytic sera, B. Welchii toxin, etc. are injected into animals, an anaemia resembling pernicious anaemia is formed. The other points found in pernicious anaemia are not found such as degeneration of the central nervous system, leucopenia, and the phases of remission and relapse. A macrocytic, haemolytic anaemia is really formed as a result of these experiments.

(g) All agree to the presence of marked phagocytosis of red blood cells in pernicious anaemia by the cells in the reticulo-endothelial system and the disturbed state of the bile-pigment metabolism.

Peabody and Brown made a comparative study of the vertebral bone marrow in pernicious anaemia and in other diseases as well as in normal people killed as a result of accident, with

special reference to the phagocytosis of the red blood corpuscles by the reticulo-endothelial cells. They found that in pernicious anaemia the bone-marrow was highly phagocytic as to suggest this process of blood destruction to be a factor in the production of hyperbilirubinaemia. In the disease known as familial acholuric jaundice, where there is marked bone marrow activity, reticulocytes, possibly up to 25% of the total red cells, may be present in the peripheral circulation for long periods without increasing the total blood count. These reticulocytes are slightly immature red cells and normally constitute 1% of the circulating cells. If the red cell count remains stationary and the reticulocytes have this high percentage, it is obvious that the proportion of red cells represented by the reticulocytes must be daily destroyed. Nevertheless, the degree of siderosis in familial acholuric jaundice is very small in comparison to pernicious anaemia. The reason is that as soon as the iron is stored in the liver it is withdrawn for use in the hyperblastic bone marrow.

(h) The increased stercobilin content of the faeces in cases of pernicious anaemia is generally held to be definite evidence of the importance of haemolysis in pernicious anaemia. The conclusions of Whipple (1922) are different from this evidence. Their theory is that in pernicious anaemia there is a deficient or abnormal blood production and not increased blood destruction. Whipple's conception of pernicious anaemia is that there is a scarcity of stroma building material or a disease of the stroma-forming cells of the marrow which limits

the output of red cell framework. There is also, according to Whipple, an excess of pigment material as proven by the high colour index. He adds that when a high colour index is met some deficiency in stroma construction should be suspected. Whipple's observations strengthen the view now commonly held that in pernicious anaemia there is abnormal and deficient blood formation and that haemolysis is of secondary importance.

In conclusion the hypothesis that pernicious anaemia is a result of portal haemolysis cannot be accepted from the above evidence, and that megaloblastic degeneration of the bone marrow is the chief cause and precedes the haemolysis.

Haemolytic Theory of Pernicious Anaemia.

Until recently the conception was held that pernicious anaemia was caused by a blood-destroying agent absorbed from the gastro-intestinal tract. The chief reason for hypothesizing a toxin was that in Bothriocephalus Anaemia the cause was supposed to be the autolytic products of the worm being absorbed by the intestine. The fact that no true haemolytic products have been found absorbable from the intestine does not prove logical reasoning. The "Haemolytic Theory" was conceived and the toxin, however produced, acted on the erythrocytes which were then removed from the circulation by the reticulo-endothelial system. No definite proof of a toxin exists and there is no haemolysis of a patient's serum in vitro. It was however supposed that the toxin was immediately absorbed to the erythrocytes which were then removed by the reticulo-endothelial cells.

Any toxin to be considered must produce:-

(a) Megaloblastic marrow reaction.

(b) Typical blood picture.

(c) Degeneration of the nervous system without increased neuroglial tissue.

(d) Phenomena of remissions and relapse.

Should a toxin be hypothesized, then because of the constant clinical and pathological picture in pernicious anaemia, there should be a uniform toxin - Subacute degeneration of the cord temporary without anaemia suggests plurality of toxins. The difference between "haemolytic" and "neurotoxic" cases might then be accounted for by difference in the strength of the toxin. To cause remissions the toxin would have to possess immunological properties or produced by a fluctuant mechanism. No such toxin has been shown to be specifically active within the body.

(a) Gastro-Intestinal Toxaemia.

Hunter's work on pernicious anaemia did not prove that alimentary toxaemia was the cause, yet he strongly supported this cause. He noticed the symptoms associated with the alimentary canal and having demonstrated that there was a higher percentage of iron pigment in the liver than in other anaemias he assumed that haemolysis took place in the portal system. Intestinal "auto-intoxication" being accepted by many as the cause of many diseased conditions including pernicious anaemia also because of the gastro-intestinal symptoms.

Alvarez did a great amount of work in support of intestinal intoxication. The fact that there are many poisons within the lumen of the bowel and little knowledge as to their individual absorbability by the mucosa is a great objection to this theory. The toxin suspected would have to be demonstrated to get in the circulation in a harmful condition or that there was increased absorption by the mucosa in pernicious anaemia.

Koessler as the result of his experiments, claims that there is in pernicious anaemia an increased absorption, but it has not been confirmed.

Iwao reported that tyramine, formed from tyrosine by B. Coli, when injected into the guinea pig causes a "pernicious" type of anaemia. The B. Coli is normally present in the bowel, it appeared that this work would support the theory of intestinal intoxication. Koessler and Harris failed to confirm this result.

Abnormal states of the gastro-intestinal tract have been suspected, especially chronic intestinal stenosis.. Seyderhelm produced a "macrocytic " anaemia in dogs by stenosing the small intestine near the ileo-caecal valve. He noticed the encroachment of colonic flora on the ileum in these dogs and in pernicious anaemia. The muscoa of the tract has also been under suspicion.

Cornell while experimenting with B. Welchii on dogs by attempting to implant the organism in the bowel, caused a temporary anaemia with typical anisocytosis and also diarrhoea.

No toxins have been proved to cause the typical changes as in pernicious anaemia.

(b) The Intestinal Flora.

Nearly every organism that inhabits the lumen of the intestine canal has been suspected of causing the disease. The B. Welchii, B. Coli and the Streptococci have each in turn been credited as the specific agent. No organism has been found specific.

(i) The B. Welchii Theory.

This anaerobic organism was first identified by Welchii to produce gas in the tissues during post-mortem examination. Hertz in 1906 suggested a possible connection between this organism and pernicious anaemia. He showed that the numbers of B. Welchii in the faeces of patients with pernicious anaemia were greatly increased as compared with the normal and other diseased conditions.

Kahn and Torrey, Moench, Nye and others confirmed this result. The strains of B. Welchii were not any different then in healthy people qualitatively and along with B. Coli and Streptococci are greatly increased in numbers. The demonstrated that B. Welchii is found at higher levels in the small intestine normally bacteria free, and that experimental evidence proves it to be haemolytic and to form an exotoxin. To prove that an organism is the causal agent in a disease, it must be present in every case and have some specific action or in every

case be present in excessive numbers or in abnormal situations. The fact that in a small percentage of cases the B. Welchii occurs numerically as in normal people is against this organism being the causal agent. Experimental evidence on animals by parenteral and enteral methods produce a marked anaemia which is secondary in type, but sometimes resembles pernicious anaemia, and the other features of pernicious anaemia, viz. the characteristic degeneration of the central nervous system, the achlorhydria, the phenomena of remission and relapse are absent. Achlorhydria is a constant feature in pernicious anaemia and it is postulated by Nye and others that the alkaline condition of the proximal ileum causes this part of the intestine to be colonic in organisms. The absence of acid allows pathogenic organisms from the mouth, nose, throat, and small intestine to multiply in the stomach. As the increase in organisms is secondary to the achlorhydria it cannot be claimed to be an etiological factor. The toxin has never been shown capable of absorption from the intestine and neither the toxin nor the serum be found agglutinative nor found it capable of complement fixation. The Welchii Antitoxin has been repeatedly administered to patients without visible benefit.

Knott has demonstrated that after a remission has been successfully brought about by the use of liver, there is no appreciable alteration in the flora and fauna of the lower bowel. This, in my opinion, is the strongest evidence that the bacteria and flora of the bowel have no causal relationship of pernicious anaemia.

There has been done a great deal of work in America investigating the Welchii bacillus, and the chief result found was that in rabbits, monkeys and pigeons, a profound anaemia resembling the pernicious type. It has not been proved that this anaemia bears any relationship to man. In France this theory still exerts a little influence in treatment. This is due to the work of Weinberg, who recently demonstrated that liver extract has a neutralizing effect upon Welchii toxin in vitro and also that liver extract given per rectum is efficient in producing a remission in pernicious anaemia. Because of these facts they claim that pernicious anaemia is due to the toxins from B. Welchii. In my opinion, Weinberg's work shows that liver extract neutralizes Welchii toxin and that liver can be successfully administered by the bowel.

(ii) The Streptococcus Theory.

William Hunter as the result of his work on the analysis of iron in the liver concluded that the siderosis was the result of blood destruction in the portal circulation. He attributed the haemolytic agent to a streptococcus which he discovered in the glossitic lesions in pernicious anaemia. Hunter claimed to have isolated this organism in a virulent state in pure culture. He attributed this organism as the cause of septic conditions seen to accompany or precede the anaemia. He did not, as some believe, claim that this was the cause of the anaemia. Haemolytic streptococci have been found in the gall bladder in cases of cholecystitis associated with pernicious anaemia. The search for a haemolytic agent has been

continuous since Hunter's treatise appeared. In 1927 Knott declared that specific strains of haemolytic organisms were of great aetiological importance. He found as did Hunter, large numbers of living streptococcus longus in the stomach contents of patients, and also increased in the saliva. Moench, Kahn and Torrey and others have shown however that haemolytic streptococci are rarely found in the faeces. Hurst is the leading exponent of the streptococcus theory as the cause of the disease. He first demonstrated that achlorhydria was constant in subacute combined degeneration as in pernicious anaemia. Hurst made cultures of the duodenal contents in his cases and found the strept. longus constantly. He viewed this organism, decomposed the unaltered protein which formed haemolytic and neurotoxic bodies which when absorbed caused the disease. Because this organism has not been found capable of forming these bodies nor capable of being absorbed by the intestine, this theory cannot hold. Experimentally the Strept. longus has been found capable of producing a pernicious type of anaemia, but this is neither constant nor form the other symptoms of pernicious anaemia.

(iii) The B. Coli Theory.

Adami in 1900 suggested that there was in pernicious anaemia a subinfection by haemolytic colon bacilli from the intestine. It was supposed that these strains of B. Coli invaded the bowel wall, and liberated haemolytic and neurotoxic endotoxins. Moench, Kahn and Torrey noted high counts of Bi Coli in the stools of pernicious anaemia patients, and so

did Seyderhelm, Faber and Grassmann. Lowenberg found that a culture of the duodenal contents showed B. Coli present in 85% cases and only 35% in uncomplicated achlorhydria. Nyfeldt experimentally produced in rabbits an anaemia and histological lesions resembling pernicious anaemia in seven out of sixteen cases, while the remaining nine developed a simple anaemia as a result of B. Coli injections. For reasons explained with B. Welchii and Streptococci the Coliform organism can be dismissed as an aetiological agent.

(b) Recent Views as to the Nature of the Disease.

Cohnheim's and Hunter's theories of pernicious anaemia held up to about four year's ago, when as a result of the successful treatment of the anaemia by liver or its extract, it took a subsidiary place. Influenced chiefly by the results of experiments on dogs by Whipple and R. Robbins, (1920), who found that certain glandular organs such as liver and kidneys had a remarkable regenerative effect on red blood corpuscles and haemoglobin, Minot and Murphy in 1923 decided to apply this knowledge on patients with anaemia. It should be pointed out that the animals experimented upon were suffering from a severe haemorrhagic anaemia. Minot and Murphy gave a well balanced diet rich in liver to patients with pernicious anaemia, They found that within a week an improvement of the blood picture and which continued, if the treatment was persisted in, so that the patient was able to leave hospital in good health in a matter of weeks. Similar results were

obtained on feeding with kidneys and certain other structures. Peabody (1927) as a result of tibial punctures in living patients found during the period of relapse the bone marrow to be crowded with megaloblasts, while during the period of remission following liver therapy, there was a return to normal of the histological appearance. The remission was ushered in by the appearance of a large number of immature red blood corpuscles known as reticulocytes. Peabody's observations on the alterations in the marrow correlates the appearance of the blood during remission and relapse. As a result of this work, the mammalian liver contains an unknown substance necessary for normal formation and maturation of blood and that its absence or diminution leads to the abnormal formation of cells found in pernicious anaemia.

Certain resemblances between pernicious anaemia with sprue, pellagra, and beri-beri suggest that pernicious anaemia may be a deficiency disease. Minot and Murphy found in their series of cases that many of their patients had been taking abnormal diets, with notable deficiency, in many cases, of red meats and an excess of fats. This latter fact did not appear in the history of my series of cases nor in the literature in this country.

McCollum suggested that the beneficial effects of liver therapy in pernicious anaemia depended on Vitamin E. which liver is known to contain. Cohn and West independently produced by a method of chemical fractioning a liver extract, which is believed to be a polypeptide on a nitrogenous base,

and certainly does not contain vitamin E.

There is the view that pernicious anaemia is due to a failure of manufacture of an internal secretion in the liver and thus resembles myxoedema or diabetes mellitus. In this case the specific factor would be known as a blood hormone. There are points of resemblance between the action of the effective liver principle in pernicious anaemia and that of insulin in diabetes mellitus.

The fact that the effective principle is found in the kidney as well as in the liver could not easily be explained. It is known that the liver has many functions and contains the principle effective in causing new formation of red cells and that the kidney an entirely unrelated organ should contain this antianaemic principle seems inexplicable.

Recent work throws some light on this problem and on the nature of this principle. It is now assumed by many that achlorhydria is at the root of pernicious anaemia. The constancy of achlorhydria in pernicious anaemia might have been regarded as either in the nature of cause or effect, but for the fact that records exist of many cases where the achlorhydria was present for years before the anaemia began. Also there have been cases of gastrectomy as a result of which the hydrochloric secreting portion was removed. An anaemia of the pernicious type followed. From this one may conclude that the achlorhydria is an aetiological agent in pernicious anaemia.

Formerly many held the view that achlorhydria allowed the development of abnormal fauna and flora in the bowel which caused an alimentary toxaemia. This hypothetical toxaemia was held to cause the abnormal anaemia. It was not until lately that another aspect was considered, that achlorhydria caused a disturbance of protein metabolism and that this abnormal protein metabolism was responsible for the blood condition. Working on this basis, W.B. Castle experimented on beef muscle which was subjected to normal gastric digestion. It was found that digested beef muscle developed an antianaemic principle which was not previously present. The fact that liver and the products of beef subjected to gastric digestion are identical in the nature of their actions permits one to postulate there being identical. Its presence in the kidneys is probably due to retention of the principle in small quantities.

Castle's work has not been entirely verified but present evidence appears favourable in this direction. The hypothesis is that hydrochloric acid in the stomach produces in the course of protein digestion some substance which is then stored in the liver and regulates the proper formation of blood. Its absence causes the absence of this substance which does not permit the red blood cells to mature. These immature red cells reach the peripheral circulation unchanged and then destroyed by the reticulo-endothelial system. This hypothesis plausibly explains the features of pernicious anaemia character of the bone marrow, the haemolysis and the anaemia.

(c) Effect of Liver Therapy in Pernicious Anaemia.

Minot and Murphy in 1926 reported on a series of cases of pernicious anaemia treated by a "special diet" which was a well balanced diet rich in liver. This diet was 120-240 gm. of cooked calf or beef liver; 120 gm. of red meat; about 300 gm. of vegetables; 250-500 gm. of fruit; 40 gm. of fat; an egg, 240 gm. of milk, dry bread, potatoes and cereals, in all a diet of 2,000 - 3,000 calories daily. They gave as the chief reason for the choice of diet the experimental work of Whipple and Robscheit-Robbins on the influence of blood regeneration. These workers found ample evidence of the importance of a full protein diet in the regeneration of blood in the secondary anaemia produced by haemorrhage. They also clearly demonstrated that the addition of iron materially assists blood regeneration. Minot and Murphy further stated that in their patients with pernicious anaemia they obtained the history of habitually eating excess of fat. They reported the results of this diet in 45 cases. Four out of this series died because they were so ill as not able to take liver. There were several who were unable to take the full diet at the beginning so that liver alone was given. All the patients improved under treatment remarkably. They observed a marked increase in the number of reticulated red cells after one week's treatment and noted that the percentage of reticulocytes come to normal by the end of the second week. Following this initial period the red cell count and haemoglobin percentage gradually improved and from four to six months treatment there had in most cases a normal blood picture.

The rate of improvement was greatest in those who had a low blood count. There were three patients in the series who relapsed because they had not taken their diet satisfactorily, who, on returning to the proper diet improved. To remain well the patients had to keep up their diet.

Minot and Murphy pointed out that in pernicious anaemia there occurs a natural remission accompanied by an increase of reticulocytes in the blood, and that an artificial remission can be produced regularly in a case within one week of treatment. They also showed that the remissions following liver therapy was greater and more sustaining than the natural one.

The next advance in treatment was by Cohn and others who prepared a liver fraction and produced excellent results on patients.

In 1927 Minot and Murphy reported on further cases, bringing the total number of cases treated by them up to 105. Three of the cases had died but none were from failure of treatment. A very full comprehensive paper was given by them in which was noted the improvement in the anaemia, and those symptoms associated with the gastro-intestinal tract and some nervous symptoms.

Since these cases have been reported by Meulengracht, Davidson, McCrie and Gulland;, East, Brewer, Wells and Fraser. The majority of their cases confirm the results of Minot and Murphy and those cases that failed can be explained by intercurrent disease, aplastic condition of the bone-marrow and inadequate dosage.

The Medical Research Council published a report on 34 cases treated with liver extract and all but two were found to result satisfactorily. The astonishing results as a result of liver therapy are so constant that a failure has to be examined carefully for other conditions simulating pernicious anaemia. There have been cases reported as pernicious anaemia which failed with liver therapy that later were found to be malignant condition of the stomach. Also cases of aplastic anaemia may simulate the pernicious type. The remission as shown by reticulocytes in the blood is so definite and constant that liver therapy is specific in pernicious anaemia and any case which does not respond is a doubtful one. In no other condition is the reticulocyte response to liver so high as in pernicious anaemia.

Prophylaxis of Pernicious Anaemia.

It has been established that there is a familial incidence and constitutional tendency in

pernicious anaemia. Observers have noted that children of parents with pernicious anaemia have a relative tendency to achlorhydria which is known to precede this anaemia. Those children who have normally functioning stomachs are not likely to develop pernicious anaemia. Achlorhydria being a known aetiological agent in pernicious anaemia has been administered by some with a view of prophylaxis. Continued administration of hydrochloric acid by mouth has not lessened the arrival of the anaemia nor even does it influence the acidity of the stomach as shown by test meal. An interesting point is that even when liver therapy is given to a case and the blood condition becomes normal, free hydrochloric acid does not return in the stomach. Nor does the administration of free hydrochloric acid with liver make any difference to gastric acidity. All cases of achlorhydria, where no organic disease has been found, should be kept under observation and if megaloblasts appear in the blood, to administer liver treatment. Nervous signs such as persistent paraesthesia may indicate early sub-acute combined sclerosis. This condition often precedes pernicious anaemia and the two diseases, or properly symptoms of the same disease, are commonly associated. Both achlorhydria and early megalo-blastic change have to be carefully watched and

liver treatment given early. I was fortunate to have in my cases two patients with persistent paraesthesia. They were kept under observation and the appearance of megaloblasts prompted administration of liver extract which caused an improvement of the paraesthesia and a return of normal blood picture.

In cases of pernicious anaemia it is advisable that all septic foci whether in the teeth, upper respiratory passages or elsewhere should be removed. There is on record patients who did not respond so well on liver treatment improved when their septic foci were removed. I saw one patient with pernicious anaemia, who, on removal of septic teeth, made a remarkable improvement with liver, who prior to this therapy did not make much headway.

Effect of Liver Therapy on Sub-acute Combined Sclerosis.

Pernicious anaemia is a disease in which the nervous system may become affected. Woltman (1919) reported that in his series of 150 cases roughly 80% cases had nervous symptoms, the majority of which had mild paraesthesias. Henneberg and Meulengracht individually corroborated this finding. Sub-acute combined sclerosis has received greater attention since the introduction of liver therapy.

There have been many reports that liver therapy leads to marked improvement in symptoms, but generally speaking, the results of investigators have been conflicting.

It has been established that sub-acute combined sclerosis may precede haematopoietic changes. Collier, reviewing the literature, states that no case under observation for pernicious anaemia, has been known to develop signs and symptoms of subacute combined sclerosis. This observation, however, is not consistent with the results of other workers in this country and also in America, where cases of subacute combined degeneration have been known to occur during excellent remissions following liver therapy.

Minot and Murphy, Cornell, etc. have reported that following liver therapy there is a distinct improvement in the blood picture, with little or no change in the nervous symptoms.

Cohn (1928) found there was increased neurological symptoms after the Minot and Murphy diet though there resulted an improved blood condition. Sturgis, Isaacs and Smith found that the improvement in the signs and symptoms of sub-acute combined sclerosis did not run parallel with the blood condition.

Ungley and Suzman reported a series of cases showing anaemia and marked nervous lesions in which liver treatment was successful in bringing about great improvement.

Wilkinson and Brockbank are of the opinion that once the deep reflexes have become affected, there is very little improvement in the nervous symptoms though the blood picture may be kept normal.

Brewer however states that where advanced nervous conditions are found, very little improvement can be looked for until the red blood cell count is about four millions per cmm.

An understanding of the underlying pathological process accounts for the divergence of reports by observers.

The pathological process passes through a series of changes at first scarcely perceptible and causes a complete degeneration of neurons and axis-cylinders, which is later replaced by sclerotic changes. Nerve cells and nerve fibres once destroyed cannot be replaced and cannot be regenerated with any form of treatment. If the deep reflexes are lost because of neuron destruction it must be permanent. There are cases in which the reflexes have returned but this is due to temporary disorganisation in the conducting mechanism of the nerve fibres.

The Babinski response may be obtained in

uraemia or epilepsy in the active phase and returns to normal response when the condition subsides. A toxic process could cause temporary changes which simulate organic disease.

In the majority of cases when first seen only mild paraesthesias are found which tend to improve with therapy only to return with inadequate treatment.

In cases where the nervous lesions are more advanced the response of the resultant treatment to liver therapy varies, depending as to whether there has been gross destruction of the nerve cells or temporary disorganisation. The majority of advanced cases have had permanent damage to the cells.

The majority of cases with subacute combined degeneration the neurological changes occur earlier than the blood condition. The hypothesis that the anaemia is the primary cause of the nervous system changes can be dismissed for the above reason and also because the majority of patients with pernicious anaemia seldom develop neurological conditions. It is possible to assume that the anaemia may devitalise the nerve cells and thus make conditions worse.

The constitutional factor, in my opinion, is a predisposing cause of the involvement of the

nervous system in pernicious anaemia, because of its presence in only 5% of cases, occurring frequently before the anaemia and also because it may be absent though the blood count is very low.

The intimate mechanism of the action of liver in this condition is unknown since the pathogenesis of pernicious anaemia is not known definitely.

While it is admitted that in liver there is a specific factor necessary for normal blood formation and that there is a deficiency of this factor in pernicious anaemia that accounts for the megaloblastic condition in the bone marrow, it is difficult to assume that the liver has a substance that keeps the nervous system normal. One would expect that should be a condition of the central nervous system in cases of advanced pernicious anaemia. Further it is known that cases of subacute combined degeneration may occur during a state of sustained remission of the anaemia following liver therapy.

A further view is that a hypothetical toxin causes the changes in the central nervous system. It is not necessary to postulate two toxins (a haemotoxin and neurotoxin) for a single toxin may affect the nervous or blood system or both should there be a predisposing constitutional weakness. The differences in reaction would depend to a great extent on the degree of constitutional weakness and

the blood system would be more affected in the majority of cases for this reason.

The liver diet can claim to arrest the progressive processes in subacute combined degeneration in the majority of cases. There can be no improvement in cases of advanced lesions of central nervous system though the anaemia usually does. The exact pathogenesis of the cord lesions remains unsettled.

3. A Review of the Status of the Liver.

(a) Nature of Substance acting beneficially in pernicious anaemia.

It has not as yet been possible to ascertain the nature of the active liver substance either by experimental or biological methods, so that any discussion on its nature must be speculative.

This especially refers to the discussion on the nature of the active principle as to whether it is a vitamin or an unknown hormone. This is the view expressed by Seyderhelm and Opitz (1928) with which one agrees.

Originally as much as 400-500 gms. of fresh liver together with a well balanced diet was given daily to patients with pernicious anaemia till a normal blood-count was reached. Many patients could not agree, because of the taste of liver, to carry out the treatment. An effective extract of liver containing the active principle was produced mainly on the work of Cohn working in Minot's laboratories. Cohn was able to concentrate one half pound of liver into .6 gm. of the affected principle. It has not been possible as yet to know what is the character of the effective principle. It is known to be soluble in water and insoluble in ether and alcohol. It is neither a protein, fat nor carbohydrate and there is no iron nor phosphorus in it.

Cohn declares it to be a nitrogenous base or polypeptide. His work was confined only to the liver and because the kidney has a similar, though not so powerful effect as liver, that organ must also have the effective principle. Up till recently it was difficult to understand why the kidney, an organ unrelated with the production of any blood constituent, should contain an antianaemic factor. The liver is intimately related throughout foetal and adult life with the blood.

At the present time great attention is paid to achlorhydria which is now accepted as an aetiological factor in pernicious anaemia. It is now agreed that achlorhydria is constantly present and precedes the blood condition in pernicious anaemia, also there have been cases where the anaemia has followed partial gastrectomy. As Piney has pointed out gastrectomy is often performed for carcinoma of the stomach which is associated with achlorhydria and if a secondary deposit was present in the bone marrow, it could produce a blood picture resembling pernicious anaemia, though the actual condition present would be an aplastic anaemia.

I submit these facts strongly point to achlorhydria being an aetiological agent in pernicious anaemia. Even the use of powerful gastric stimulants fail in producing a secretion.

Following the work of Castle there has resulted the theory that achlorhydria interferes with protein metabolism and that the abnormal products formed are responsible for the anaemia. Previously achlorhydria was held to permit the growth of abnormal flor and fauna in the alimentary canal which caused an alimentary toxaemia. This hypothetical toxin was alleged to cause pernicious anaemia. Castle fed patients suffering from Addison's anaemia with beef that had been predigested in a normal stomach, or with normal gastric juice in vitro, and obtained reticulocyte responses and increased red blood cell counts similar to those produced with liver. When beef which was given alone, or predigested with hydrochloric acid and commercial pepsin, or incubated with 150 gms. of mucous membrane of hog's stomach, there was no improvement. Wilkinson (1930) however, in his series of cases found that the mucous membrane of the hog's stomach was active in pernicious anaemia. In addition he found that the muscular layer of the hog's stomach, and desiccated preparations of the mucous membrane and muscular layer were successful in the treatment of the anaemia, proving as potent as liver. Sturgis, Isaacs and Sharp (1929) successfully treated three cases of pernicious anaemia with desiccated whole stomach. We have in our wards been equally successful with desiccated whole

stomach in two cases when ventriculin was administered.

We are at present aware that the action of liver, kidney, the products of gastric digestion of beef muscle and the hog's stomach wall are the same, and though there is no direct evidence, one may assume that the antianaemic principle in each is similar. Apparently this substance is formed in the stomach as a result of the digestion of protein and then stored in the liver, the latter being recognised as an organ which stores and regulates the products of digestion. The antianaemic principle present in the hog's stomach wall does not necessarily indicate that it is poured out from the stomach wall during the digestion of protein. The explanation would be that the action of the liver, kidney and stomach wall in pernicious anaemia was analogous to the pancreas in diabetes mellitus. It is acknowledged that insulin is found in various organs of the body in minute quantities, though the pancreas is the chief organ.

The probable process of events is as follows. In pernicious anaemia the substance formed as a result of protein digestion for the proper formation to maturity of red cells is absent. The achlorhydria causing abnormal protein metabolism and the effective principle formed normally during protein digestion is absent. The immature cells produced

in the bone marrow pass into the peripheral circulation unchanged and are then destroyed by the chasmatocytes of the reticulo-endothelial system, and this would account for the evidence of haemolysis. The role taken by the liver would be to store and regulate this effective substance and this reason would account for the large amount of the principle found in this organ.

Discussion on the Action of the Liver in pernicious anaemia.

There are at least three views on the action of the liver in pernicious anaemia:-

(a) That the liver produces a hormone which permits and promotes the maturation of the red cells.

(b) That the liver acts by producing a vitamine.

(c) That the liver acts by detoxicating the contents of the alimentary canal.

The effective principle known to be present in the liver being as yet not isolated and an unknown factor, causes a discussion on its nature to be hypothetical and allows only evidence pointing to its likelihood.

Minot and Murphy when they introduced their liver diet reported that the resemblance of certain symptoms and signs of pernicious anaemia with pellagra, beri-beri, sprue and diseases known to be

associated with a faulty diet, partly influenced them in choosing this therapy. It is very common for the latter diseases to have symptoms and signs relating to the central nervous, alimentary and haemopoietic systems which could be found in pernicious anaemia.

The liver is known to contain Vitamin E, and it was suggested by McCollum that the excellent results obtained from liver therapy was due to this vitamin. Cohn's work by preparing a liver fraction definitely disproves the presence of this or any other known vitamin. Whereas Vitamin E. is insoluble in water, the liver substance influencing pernicious anaemia proved to be soluble in water, precipitable in alcohol and insoluble in ether.

The true deficiency diseases such as scurvy, beri-beri-, are due to lack of accessory food factors, and the administration of liver in pernicious anaemia is as reliable as orange juice in scurvy. When a vitamin is withdrawn from the diet in normal people a true vitamin deficiency disease is always produced. Very few people take liver constantly and sufficiently as required by patients with pernicious anaemia to maintain a normal blood count. The evidence is more in favour of their being a deficiency or failure of the liver to manufacture an internal secretion. One could compare the

result of liver therapy in pernicious anaemia with thyroid in myxoedema or the action of iodine in exophthalmic goitre and could be classed as a hormone. It is known that hormones are higher specific substances secreted by specific cells in individual organs, while in pernicious anaemia the effective substance is found in various organs, e.g. liver, kidney, stomach wall. This is an argument against the hormonic view, but everyone agrees that insulin is manufactured in various organs in the body apart from the pancreas.

The work of Castle in 1928 is greatly in favour of the theory that there is a hormone deficiency in pernicious anaemia. He found that when beefsteak which had previously been acted upon by normal gastric juice had a similar action in pernicious anaemia as liver therapy. He was unable to produce the same result by means of beef artificially digested in vitro with hydrochloric acid along with with the other constituents of gastric juice. Beef previously digested in the stomach of patients with achlorhydria also failed to give the characteristic effects. This work tends to show that the stomach of the patient with pernicious anaemia lacks the effective blood regeneration principle found in normal people. There must be in normal gastric

juice an enzyme or hormone at present unidentified which is the specific factor in pernicious anaemia. The stomach produces the principle and is apparently stored in the liver where it is found in large proportion. According to the demands of the red cells this effective factor is used and causes the cells to become mature. The megaloblastic anaemias of pregnancy and sprue show frequently normal gastric digestion and for this reason it would be necessary to decide on a different site and cause of the anti-anaemic factor.

There is the view that the liver acts by detoxicating the contents of the alimentary canal. There has been a great amount of work with the supposed role of toxins in the disease which were believed to act as haemolysins. Herter and other workers classed pernicious anaemia to be due to alimentary toxaemia. There was one set of workers who believed that the toxins resulted from abnormal fermentation in the bowel and could be put right by diet. Other workers held that the organisms of the bowel were responsible for the formation of toxins. Faber, Kiralyfi, Grassmann et alia believed the B. Coli as the cause, Hurst the haemolytic streptococci, Kahn and Torrey and Moench the B. Welchii, while Davidson all the bowel organisms.

The toxins produced are hypothetical and have not been produced within the bowel, and it has not been proved that toxins can be absorbed through the mucous membrane of the bowel. These workers have only demonstrated that in pernicious anaemia the organisms of the bowel are found at a higher level than in normal people, and that in many cases there are increased numbers of organisms. These findings are very likely due to the achlorhydria which is constantly present and precedes the blood condition. The organisms would then be secondary and the result of effect and take no place in the aetiology of the disease.

Knott has demonstrated that following a remission after liver therapy there was no appreciable change in the bowel contents. This is strong evidence against believing that the bowel flora and fauna have an aetiological bearing in pernicious anaemia.

The Effect of the Liver on the White Cells.

A very characteristic finding in pernicious anaemia is the relatively diminished polymorphonuclear leucocyte count. A typical percentage count is polymorphs. 40, and lymphocytes 60, there being a relative lymphocytosis and the total white cell count is usually less than 5,000 per cmm. The lymphocytes are very little affected in pernicious anaemia as the disease does not disturb the lymphatic tissues.

The eosinophils are diminished. The polymorphonuclear leucocytes are known to undergo greater segmentation in pernicious anaemia. Cooke and Naegeli have done much observation in this direction and the common finding is to notice a "shift to the right", i.e. an increased number of cells with nuclei showing 3, 4, 5 or more lobes. In very severe cases primitive white cells are found in the peripheral circulation. Such cells as myeloblasts and myelocytes and metermyelocytes are found. Following successful liver therapy there is a disappearance of polymorphs with highly segmented nuclei, and there occurs a neutrophil leucocytosis and increase of eosinophils. A case I observed had a leucocyte count which rose from 4,000 to 9,000 following liver therapy.

Fleming (1929) reviewed the effects of liver treatment on the polynuclear leucocyte count of Cooke. The polynuclear count of Cooke is a modification of the Arneth count. The neutrophil leucocytes are classified in divisions, e.g. those with one lobe to the nucleus, two lobes to the nucleus, etc., till five lobes to the nucleus. In the polynuclear count described by Cooke and Ponder, the percentage of leucocytes with one lobe to the nucleus are multiplied by one, those with two lobes to the nucleus multiplied by two, etc., and similarly up to five.

All these numbers added together and divided by one hundred give the weighted mean number of lobes in each nucleus. In normal health the weighted mean number per leucocyte is about 2.75. Arneth (1920) observed there was a shift to the right, i.e. increased segmentation of nucleus, of the neutrophil nucleus, which accompanies the neutropenia which is characteristic of pernicious anaemia.

In pernicious anaemia there may be found cells with seven or eight lobes. A shift to the left has been noted in infective conditions. Arneth noted also a shift to the right in sprue and lymphatic leukaemia. According to Fleming, Carbonara (1929) reports there is a shift to the right associated with liver disease, an important observation if confirmed in view of the liver therapy in pernicious anaemia. Following successful liver therapy the total white cell count becomes normal and so does the polynuclear count of Cooke.

Secondary Actions of Liver given as Therapy.

(a) Liver Treatment in Secondary Anaemia.

Whipple and Robscheit-Robbins (1920) performed a series of experiments in which dogs kept in a condition of severe anaemia for long periods by bleeding. These dogs were fed on diets to discover which possessed the highest value as regenerator of blood cells and haemoglobin.

They demonstrated that the best effect was from the administration of liver or kidney. As a result of this work chiefly, Minot and Murphy decided to apply this therapy on anaemic patients. They expected that the benefit following the therapy on the secondary haemorrhagic anaemia in dogs would benefit patients with secondary anaemia. The reasoning was faulty as secondary anaemia in man has other factors. Fortunately patients with pernicious anaemia were included in the trial with results now known.

The secondary anaemias in man differ from the pernicious type in not being a clinical entity. They are divided roughly into two classes, (1) after a haemorrhage, (2) action of a toxin. When following upon acute haemorrhage it is impossible to distinguish between the effects of therapy and the natural recovery process. If associated with chronic haemorrhage the response to therapy is obscured by the possible continuance of the bleeding. In cases due to toxins an effort first of all must be made to remove them; when this has been accomplished it is impossible to differentiate the results of this treatment from that directed towards improving the anaemia. From these facts our knowledge of the effect of liver therapy in secondary anaemia in man cannot be precise.

The red cell count and haemoglobin content of the blood gives very little valuable information about the response to liver treatment, but the reticulocyte response is of help. Minot and Murphy, Stetson, Janet Vaughan and Dyke carried on observations on the effects of liver on secondary anaemia due to various causes. In some there was a reticulocyte response especially from those following a haemorrhage. The most marked response was in those secondary to haemorrhage, but was much below that produced in pernicious anaemia.

There was a case admitted into hospital during May 1929, a man aged 35, who had a haematemesis and malaena complicating a duodenal ulcer. The haemoglobin was 30% and the red cells 2,500,000 per cubic mm. At the end of a week the reticulocyte response was 5% of red cells. This did not keep up owing to slight recurrence of the haematemesis. A couple of weeks later he was given iron in addition and when examined two months later the red cell count was 4,000,000 and the haemoglobin 70%.

Powers and Murphy have arrived at the same conclusion that secondary anaemia following haemorrhage benefits from liver therapy, and found that the addition of iron enhances the effect of liver.

(b) Liver Treatment in Other Conditions.

Liver treatment has been attempted in other

conditions which are chiefly associated with a degree of anaemia. The response to treatment has been varied but in some there has been considerable success.

(1) Sprue. This disease characterised by typical diarrhoea and a severe anaemia is confined to the tropics and sub-tropics. The aetiology of the condition is still unknown. The anaemia in sprue may be so profound as to resemble the pernicious type and because of this some hold the view that there is a very close relationship between the anaemia of sprue and that in pernicious anaemia. Liver soup has been administered for many years as a therapy with not consistent success. There have not been many records on the results of liver in sprue, but in many cases where liver or its extract has been given an apparent cure has resulted. The diarrhoea ceases and the anaemia disappears. According to Bloomfield and Wyckoff a complete cure with liver is the rule and differs from pernicious anaemia where liver has to be continued.

(2) Anaemia of Pregnancy. Occasionally a profound anaemia is associated with pregnancy and little is known of its aetiology. This anaemia also may resemble the pernicious type of anaemia. The colour index is not so high as in pernicious anaemia and there may be leucocytosis present and free hydrochloric acid in the gastric juice.

There have not been many cases recorded on the treatment of this anaemia by liver, but in uncomplicated cases a typical response is expected. A typical temporary reticulocyte response occurs and is followed by an increase of red cells and the percentage of haemoglobin. The white cells at first increase but later become normal.

(3) Haemophilia. This is a hereditary disease, appearing only in males, but is transmitted by the females, and is characterised by marked prolongation of the coagulation time of the blood. Clinically it is distinguished by recurrent haemorrhages into the tissues and serous cavities and by prolonged bleeding from relatively slight wounds.

The liver has been recognised to be concerned with the mechanism governing the clotting of the blood. Pickering has recently applied liver therapy to the treatment of haemophilia. In three cases of haemophilia he was able to bring about a diminution of the clotting time of the blood as was afterwards proved in vitro. Pickering at first used a diet containing ½ lb. liver daily, which was later replaced by the commercial extract. This work seems promising and is of great interest as it appears that the effective principle in liver benefits the plasma besides the red cells. Nasse's view of

haemophilia was the persistence of a foetal type of constitution of the plasma, a view now supported by Pickering. The condition in pernicious anaemia is analogous as the view taken is that there is a failure in maturation of the red cells.

(4) The Leukaemias. This therapy has not been fully tested with the leukaemias. Both myeloid and lymphatic leukaemias vary much in their response to treatment, though in some cases considerable benefit was obtained. As to whether it could be attributed to the liver or to any other therapy given in addition cannot be gauged.

(5) Bothriocephalus Latus Anaemia. The B. Latus is not found in this country but is common in America and Northern Europe. The degree of anaemia may be of the pernicious type and in certain cases indistinguishable from that in pernicious anaemia. There may be achlorhydria, and hyperbilirubinaemia. The administration of liver in this anaemia and its response is similar to that in pernicious anaemia, and it is known to be similar even when the patient harbours the parasite. The great similarity between B. Latus anaemia and pernicious anaemia has been used as a basis for the belief in the toxic theory of pernicious anaemia.

(6) Aplastic Anaemia. Hayes Smith has claimed success with liver in a case of aplastic anaemia.

This result has not been corroborated and the pathology of the condition is not in favour of successful results.

(7) Acute Febrile Anaemia. Brill (1926) described this rare condition which is characterised by pyrexia and collapse and rapidly progressive anaemia, which proves fatal if not checked in about six weeks. Benhamore reported a case treated by liver and liver extract which was converted from a very severe anaemia to a normal blood count.

(8) Liver Treatment in the Dermatoses.

The response of liver therapy in dermatological conditions has not been tested. I saw a lady, aged 45 years, who had typical acne rosacea. Achlorhydria is invariably present in this condition and was so in this case. The evidences of anaemia caused a blood examination to be made, which resulted to be pernicious anaemia. Liver therapy did not affect the blood condition so easily nor did the skin condition clear up. The addition of hydrochloric acid medicinally to liver improved, caused a rise in the blood count and there disappeared the acne rosacea. Liver therapy has cleared up dermatoses associated with pernicious anaemia, e.g. Scaliness, pigmentation and skin lesions.

(c) Testing Preparations containing the Effective Principle.

The only way of testing preparations for its

activity in pernicious anaemia and other anaemias has been their use in known cases of pernicious anaemia. These cases are scarce now because of the universal application of treatment. Sabin conducted experiments upon the effect of the active principle on cultures of the blood islets of chick embryos in vitro. This work has not been concluded but it has been found that the blood islets from chick embryos incubated in Locke's solution there was no second division of the embryonic blood cells while second division took place in the presence of active extract. Should this work be corroborated and consistent in result, it will be of great assistance in measuring the activity of the effective principle.

(d) General Survey.

Observation on cases of pernicious anaemia by observers has shown that those with a marked icterus respond more readily and effectively to liver therapy than those who do not. Minot and Lee classified these types as (1) Haemolytic, (2) Myelotoxic. The haemolytic type shows great evidence of blood destruction and is characterised by frequent periods of remission and relapse. The myelotoxic type have only a little jaundice or icterus and have a chronic course. In the cases I observed this classification and the response to therapy held good. Apparently in pernicious anaemia the response to liver therapy points to the whole of the bone marrow cells being

disordered. Liver therapy has been shown to cause both the red and white cells to return to normal. The degree of affect varies, for in the haemolytic type the red cells are chiefly affected while in the myelotoxic type the white cells bear the brunt. The return of the normal from a low platelet count in a remission further supports the view that the whole of the haematopietic system is at fault.

Cases of gastritis with vomiting cause oral therapy if liver in pernicious anaemia useless. Various workers including Reznikoff gave liver per rectum with a typical reticulocyte response. American workers have claimed successful intravenous therapy of liver. This variation in administration permits greater success in the stage of relapse with its complications.

Prognosis.

The cases recorded show the beneficial results of liver in pernicious anaemia, also that good results follow the administration of ventriculin. A normal red cell count was not obtained but that is not always essential for good health.

Early in 1928 there was admitted a male patient whose red cell count was, 800,000 per cmm. and felt very tired. When the blood count reached 1½ millions he was able to play a round of golf. For domestic reasons he had to leave hospital.

Cases 11 and 12, which were early cases of subacute combined degeneration of the cord, their chief symptom, that of paraesthesia disappeared. It is perfectly obvious that cases which have gross destruction of the cord restoration of function is impossible, but that if liver therapy is introduced in the early stages of degeneration, not only is the degeneration arrested but the function is restored. The literature in this connection supports this view.

The ultimate prognosis in cases of pernicious anaemia is now very favourable but liver therapy given during a period of relapse does not produce a permanent cure. Liver therapy, the quantity varying in each case, must be kept up indefinitely to keep the patient well.

Minot and Murphy and others have recorded cases where relapse followed the absence of liver from the diet with a restoration when liver was included.

The vast majority of patients after being restored to health by liver continue achlorhydric. As, in my opinion, achlorhydria plays a very important role as the cause of pernicious anaemia, it is quite probable that the restoration of free hydrochloric acid to the gastric juice would indicate complete recovery. This question has not been settled. Seyderhelm and Opitz (1928) report the reappearance of free hydrochloric acid in the stomach in a case of pernicious anaemia treated with liver. It has not yet been established as to whether definite cure was obtained. Against this view is that by Gulland and Davidson who know of a limited number of cases of pernicious anaemia where gastric digestion was normal and free hydrochloric acid was found in the gastric juice.

The prognosis of pernicious anaemia can be held to be very good, though permanent cure cannot be promised. Providing liver therapy is maintained the patient's health is restored. Refractory cases to the therapy have been reported but in these full investigation has to be proceeded with for the possibility of complications and diagnosis and the potency of the liver fraction.

Soon after the discovery raw liver and cooked liver was given to patients, and some could not persevere with the treatment because of nausea. A possibility of renal damage in kidney cases made it unfavourable in these cases. The successful isolation of the liver fraction by Cohn allowed the administration of a liver extract which is less bulky, does no renal damage, and when mixed up with ordinary diet is quite palatable. It is known that liver extract can be potent when given per rectum and an American observer reports it can be given intravenously.

The price of liver prevents poor people from obtaining liver regularly and sufficiently. This is an economic problem and should be dealt with by the public authorities.

Conclusions.

1. The effective antianaemic principle is present in liver and restores a patient with pernicious anaemia to health. This principle is also present in the kidney, spleen, and wall of the stomach. The potency of the latter has been tested in cases with good results. A smaller quantity of liver fraction can be given than that from the kidney, stomach wall, or spleen, possibly because the principle is stored in the liver.

2. Achlorhydria must be stressed as a very important aetiological factor. Free hydrochloric acid in the stomach produces some substance in the course of protein digestion which regulates the proper formation of blood. With achlorhydria this substance is not formed and the haematopietic system becomes abnormal. The red blood cells do not mature and the other formed elements are affected but not to a great degree. The red cells formed in the marrow pass in their immature state into the blood stream where they are destroyed by the reticulo-endothelial system.

3. The antianaemic principle present in the liver, kidney, stomach wall, has not been isolated though an effective potent fraction has been formed. The nature of the effective principle has been ascribed to a hormone, vitamine, or detoxicating agent.

In my opinion the evidence is more in favour of the antianaemic principle being a hormone.

Against the vitaministic theory is the fact that average people partake of little liver and their blood formed elements keep in normal numbers. Also absence of liver in normal people does not form a deficiency disease. The numerous organisms found in the upper part of the bowel can be accounted for by the achlorhydria. The observations of Knott are against detoxicating agents. He showed that after a remission following liver therapy there is no appreciable difference in the flora of the lower bowel, this result, in my opinion, is against these organisms causing pernicious anaemia.

4. Liver therapy restores a patient with pernicious anaemia to normal health and relapse occurs when the specific factor is exhausted. This does not occur immediately as there is a certain quantity stored in the system and following the administration of the therapy the principle is again stored.

5. It is probable that once free hydrochloric acid is restored in the stomach, permanent cure will result. Liver therapy is too recent to decide if persistent therapy will restore this function.

6. Persistent paraesthesia of the hands and feet may be early cases of subacute combined degeneration. All cases with these symptoms should have a cytological examination and a fractional test meal performed. Liver therapy does arrest the degeneration and damage to the nervous system can be avoided if all cases with this paraesthesia are examined early.

7. All cases who have achlorhydria should be periodically examined as also near relatives of patients with pernicious anaemia. A slight megalocytosis should in these cases, especially with achlorhydria in the absence of any causal factor, be treated with liver therapy.

Case 1.

J.L. Male, age 69 years. Occupation: Railway Shunter.

Admitted. 2.7.28.

Dismissed. 13. 8. 28.

Result. Much improved.

Complaint. Increasing weakness of 18 months duration.

History. He was in good health and able to do hard work up till 18 months ago. At first felt appetite to be poor and had to stop work on January 18. 1928, because of a severe cough. The weakness became more pronounced and had to stay in bed for 2 months. He resumed work on March 22. 1928. The anorexia and weakness became progressively worse, and had to stop work on June 9. 1928. Two weeks before admission he had ringing noises in his ears and also headache which was worse at night and prevented sleep.

Past Illness. He developed erysipelas 20 years ago following a burn. At the age of 14 years his eye was removed following an accident.

Social Condition. Lives with his wife in one room and kitchen. The house is in a good state of repair. He smokes 1 oz. tobacco per week and is a teetotaler.

Present Condition. He lies comfortably in bed in any decubitus. The patient is of a heavy build and has a lemon yellow skin. His expression is listless and talks in a weak voice. The mucous membrane of the lips and conjunctivae were very pale. The pupils were of normal size and were equal and the sclerotics were pale. Pulse 96. Respirations 26. Temperature 97.

Family History. His parents died of old age. He has a wife, one daughter and two sons alive and well. Three of his children died during infancy from chest complications. A son aet 17 years died following a T.B. knee.

(a) Physical Examination of Digestive System. The lips were pale; eight decayed teeth were seen; the tongue was large, moist, and deeply fissured. The fauces and pharynx were pale and he complained of occasional dysphagia. His appetite was poor and had nausea when taking food - this symptom was present irrespective of the type of food. He was rather constipated.

Inspection of Abdomen. This appeared well nourished and of normal contour.

Palpation. There was marked rigidity in the epigastric region beginning about 3 inches above umbilicus and also slight tenderness in the left iliac fossa. The spleen was not palpable and the

liver was of normal size. Nothing abnormal could be felt in the abdomen.

Percussion. The spleen was slightly enlarged; the liver dullness was normal.

(b) Examination of the Respiratory System. He had a short dry cough and no expectoration. The respirations were 26 per minute, regular in rhythm, with poor expansion.

Inspection. Chest of normal shape.

Palpation. Nothing abnormal. Vocal fremitus normal.

Percussion. The lungs were resonant throughout and of normal pitch and resistance.

Auscultation. The breath sounds were vesicular, no adventitious sounds heard. There was normal vocal resonance.

(c) Examination of the Circulatory System. The pulse was 96 per minute, regular, normal tension but of small volume.

Heart. No abnormal pulsations seen. The apex beat seen and felt in 6th intercostal space 1 inch within the nipple line.

Percussion. The upper border of cardiac dullness was the 3rd interspace; left border 1 inch within the nipple line; the right border, the right sternal line.

Auscultation. The first sound at the apex was weak but the sounds were normal in the other areas.

(d) Examination of the Nervous System.

1. Motor functions. There was no spasm, tremor nor paralysis. The gait was normal and his strength feeble.

2. Sensory functions. These were normal.

3. Reflexes. The knee jerks were normal, the plantar reflex flexor, normal, abdominal reflexes, the biceps, triceps, supinator and pronator jerks were normal. The pupils were equal and reacted to light and accomodation.

4. Nothing abnormal on ophthalmoscopic examination and the special senses were normal.

(e) Genito-urinary System. Normal. Urine pale amber; acid; S.G. 1017; contains mucous and trace of acetone.

(f) Blood examination.

Red blood cells, 1,090,000

White blood cells 4,375

Haemoglobin 33%

Colour Index 1.51

A blood film showed anisocytosis and poikilocytosis. No nucleated reds.

Treatment.

3.7.28. ℞ Liq. acid hydrochlor dil. ℥i
Aquam ad ℥vi.
Sig. ℥ss with meals.

CASE 1

HAEMATOLOGICAL CHART.

Name

J. L

Age

69 years.

Disease

Pernicious Anaemia

Notes

DATE			2/7/28	9/7/28	16/7/28	23/7/28	30/7/28	6/8/28	13/8/28
RED BLOOD CORPUSCLES	HAEMOGLOBIN %	LEUCOCYTES	← LIVER →						
6,000,000	120	800,000							
		700,000							
5,500,000	110	600,000							
		500,000							
5,000,000	100	400,000							
		300,000							
4,500,000	90	200,000							
		175,000							
4,000,000	80	150,000							
		125,000							
3,500,000	70	100,000							
		90,000							
3,000,000	60	80,000							
		70,000							
2,500,000	50	60,000							
		50,000							
2,000,000	40	40,000							
		30,000							
1,500,000	30	28,000							
		26,000							
1,000,000	20	24,000							
		22,000							
500,000	10	20,000							
		19,000							
		18,000							
		17,000							
		16,000							
		15,000							
		14,000							
		13,000							
		12,000							
		11,000							
		10,000							
		9,000							
		8,000							
		7,000							
		6,000							
		5,000							
		4,000							
		3,000							
		2,000							

Reticulocytes % — 6% — 5% — 4% — 3% — 2% — 1%

Differential Count per cent.

POLYMORPHONUCLEAR NEUTROPHILS	52	48	50	58	60	70	66
" EOSINOPHILS	1	1	1·5	1	2	2	3
LYMPHOCYTES, SMALL	36	39	40	32	29	21	25
" LARGE MONONUCLEARS	8	9	7	6	8	5	6
MYELOCYTES, NEUTROPHILS	2	1·5	1·5	2	1		
" EOSINOPHILS	1	1·5	1	1			
NUCLEATED RED CELLS							

RED CORPUSCLES — BLACK HAEMOGLOBIN — RED LEUCOCYTES — ~~BLUE~~ Violet RETICULOCYTES ----

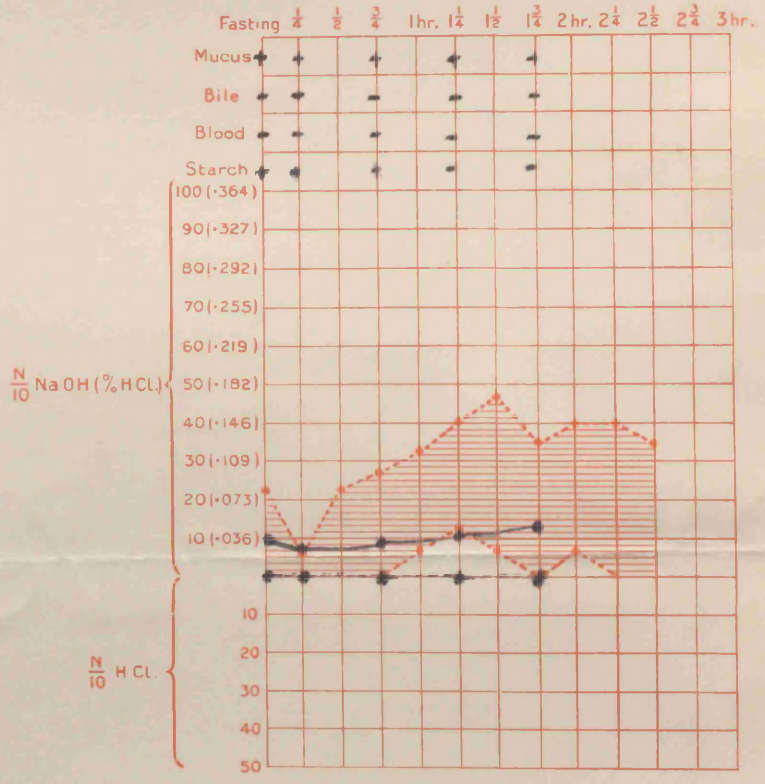
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

CASE I

GASTRO-INTESTINAL ANALYSIS.

Name of Patient J. L *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 2·7·28



Fasting Juice.

Volume. 7 cc.

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

——— · ——— represents total acidity.

Summary.

2. FÆCES.

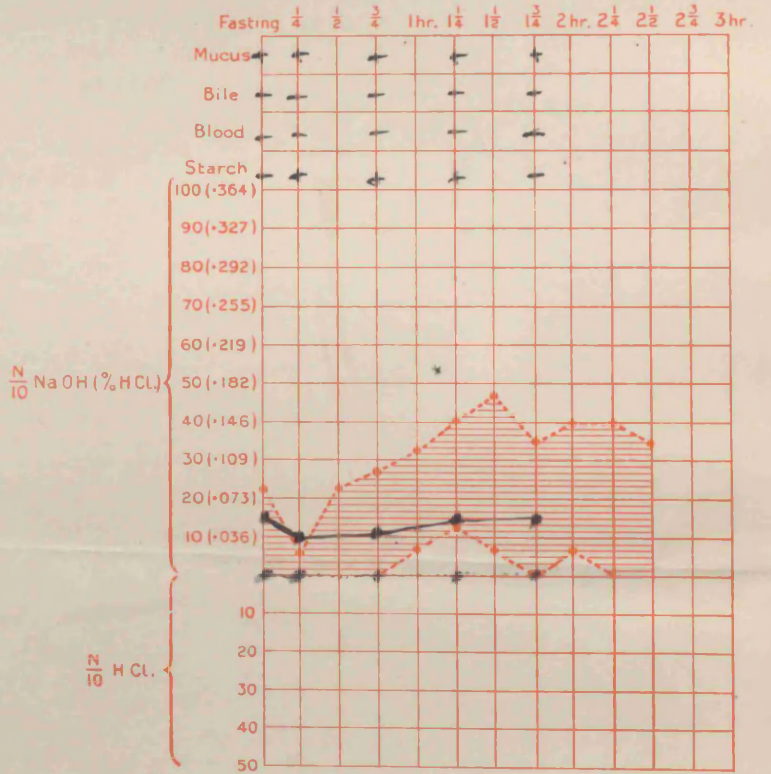
DOWN BROS., LTD. LONDON.

CASE I

GASTRO-INTESTINAL ANALYSIS.

Name of Patient J. L. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 10.8.28



Fasting Juice.

Volume. 4 cc.

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

———·———represents total acidity

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

6.7.28. ℞ Liq. arsenicalis hydrochlor. m. 36.
Aquæ ℥ vi.
Sig ℥ss t.i.d.

18.7.28. Liq. arsenic. hydrochlor. m. vii t.i.d.

6.8.28. Allowed up.

Diet. Milk.

3.7.28. Soup, pudding, tea and toast.

6 ozs. cooked liver.)
) Daily.
2 ozs. raw liver.)

Case 2.

A.D. Male. Age 36 years. Occupation. Farmer.

Admitted. 12.6.29.

Dismissed. 17.7.29.

Result. Much improved.

Complaint. General weakness during last 8 weeks.

Present Illness. About middle of March 1929 he noticed that he easily became drowsy and was not himself, also that his lips were pale and his skin a lemon yellow colour. He became sleepy when he sat down. On one occasion during April he fainted. His doctor gave him a tonic and advised teeth extraction - this made no improvement. He had later increasing difficulty in climbing stairs and for the past four weeks was confined to bed.

Past Health. As a child he had measles and whooping cough.

Family History. Father diet age 67 (unknown cause) and his mother age 66 of some 'blood' disease. A brother and sister died in infancy. He has 3 brothers and 3 sisters alive and well. He is unmarried.

Social Conditions. He lives in a farm which is airy and dry. His meals are regular and there is ample food. He drinks about six cups of strong tea daily, smokes 20 cigarettes daily and is teetotal.

Present State.

(a) External Surface. He lies comfortably in bed in any decubitus and appears well nourished. The skin is of a lemon yellow colour and has a languid expression. He had an arcus senilis, and very pale conjunctivae. His eyes were a little puffy and there was slight oedema of the ankles. There were no glandular enlargements.

Pulse 112. Temperature 97.6. Respirations 22.

(b) Nervous System. There were no motor disorders, no tremor, no paralysis, though because of his weakness he could not keep easily erect. There was no disturbance of sensation. The pupils of the eye were equal and of normal size and reacted to light and accomodation. The plantar reflex was flexor and there was no knee or ankle jerk. The arm jerks were difficult to elicit.

There were no vaso-motor nor trophic disorders. Vision was good and ophthalmoscopic examination revealed nothing abnormal.

(c) Circulatory System. He had occasional bouts of palpitation and dyspnoea on slight exertion.

Heart.

(1) Inspection. No abnormal pulsations, no bulgings nor depressions. The cardiac apex could not be seen.

(2) Palpation. The apex beat felt in 6th left interspace ½" from nipple line. No thrills felt.

(3) Percussion. Upper border 3rd rib; right border - right sternal margin, left border ½" within left nipple line.

(4) Auscultation. The heart sounds were normal except for a soft V.S. murmur at the apex. The arteries had a normal feeling, the pulse was regular, normal tension and volume.

(d) Respiratory System. This was normal.

(e) Alimentary System. The lips were pale and so were the gums, fauces and pharynx. His appetite was poor and was inclined to be constipated. Teeth carious.

The abdomen was of normal shape and palpation of the abdomen revealed it to be normal. The liver and spleen were normal.

HAEMATOLOGICAL CHART.

12.6.24

Name Case 2

A.D
Male

Age
36 yrs.

Disease
Pernicious Anaemia

Notes

DATE			17/6/24	19/6/24	26/6/24	3/7/24	10/7/24	17/7/24
REDBLOOD CORPUSCLES	HAEMO-GLOBIN %	LEUCO-CYTES	← LIVER →					
6,000,000	120	800,000						
		700,000						
5,500,000	110	600,000						
		500,000						
5,000,000	100	400,000						
		300,000						
4,500,000	90	200,000						
		175,000						
4,000,000	80	150,000						
		125,000						
3,500,000	70	100,000						
		90,000						
3,000,000	60	80,000						
		70,000						
2,500,000	50	60,000						
		50,000						
2,000,000	40	40,000						
		30,000						
1,500,000	30	28,000						
		26,000						
1,000,000	20	24,000						
		22,000						
500,000	10	20,000						
		19,000						
		18,000						
		17,000						
		16,000						
		15,000						
		14,000						
		13,000						
		12,000						
		11,000						
		10,000						
		9,000						
		8,000						
		7,000						
		6,000						
		5,000						
		4,000						
		3,000						
		2,000						

Reticulocytes 4%

Retic 3%

Retic 2%

Retic 1%

Differential Count per cent.						
POLYMORPHONUCLEAR NEUTROPHILS	56	56	50	58	62	65
" EOSINOPHILS	1	1	3	3	4	4
LYMPHOCYTES, SMALL	32	26	30	28	28	24
" LARGE MONONUCLEARS	10	8	10	3	4	5
MYELOCYTES, NEUTROPHILS	1	5	6	6	1	2
" EOSINOPHILS		4	4	2	1	
NUCLEATED RED CELLS						

RED CORPUSCLES – BLACK HAEMOGLOBIN – ~~RED~~ GREEN LEUCOCYTES – ~~BLUE~~ VIOLET RETICULOCYTES – – –

Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

CASE·2

GASTRO-INTESTINAL ANALYSIS.

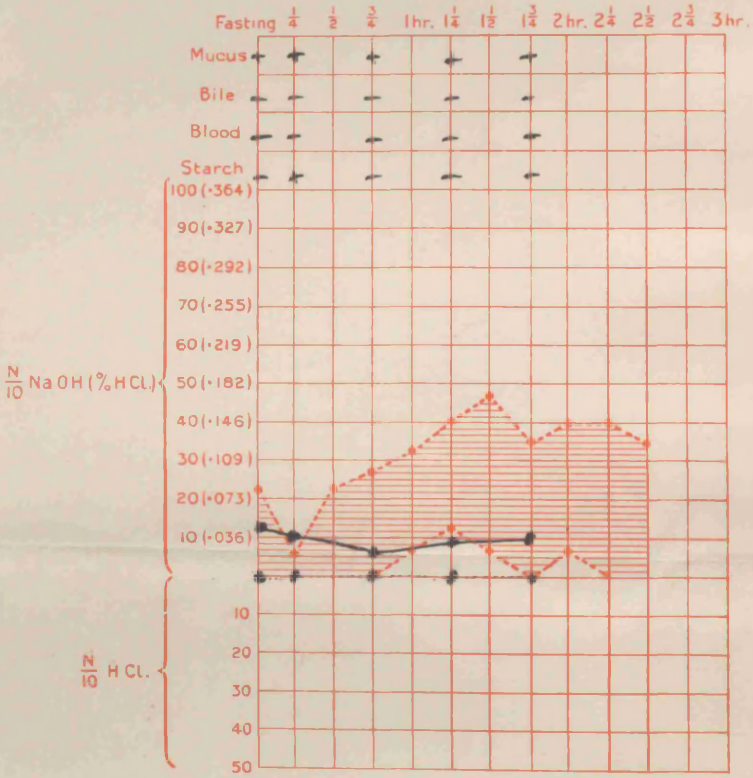
Name of Patient A·D *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 14·6·29

Fasting Juice.

Volume. 4·5 ccs.

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

————————represents total acidity

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

CASE 2

GASTRO-INTESTINAL ANALYSIS.

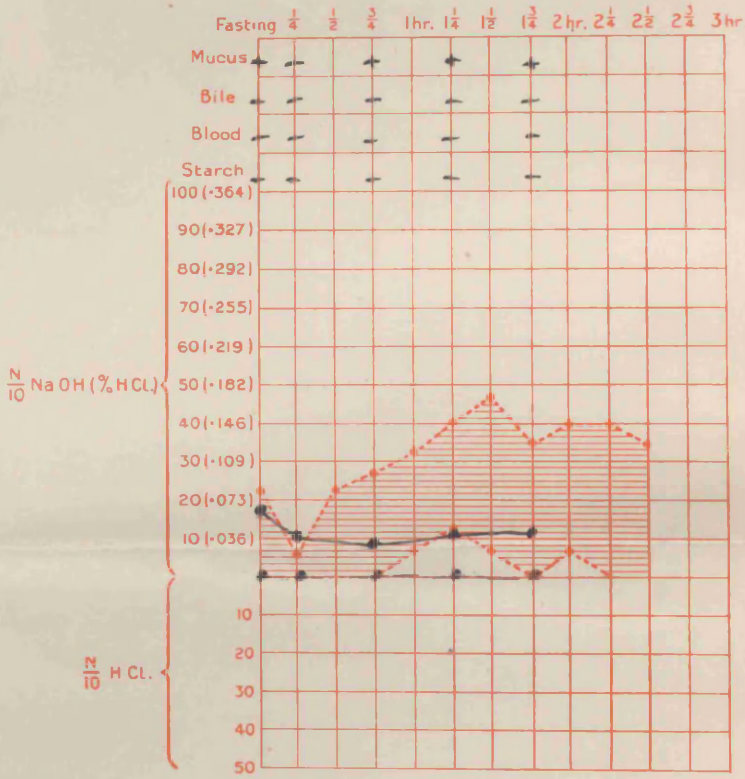
Name of Patient A. D *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 15. 7. 29

Fasting Juice.

Volume. 3 ccs.

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

———— - - - ————represents total acidity

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

(f) Genito-urinary System. This was normal.

Urine. Yellow colour. Acid. S.G. 1020, and had no abnormal constituents.

(g) Blood Examination. A film showed the red blood cells to contain megalocytes, megaloblasts. It also indicated poikilocytosis and polychromasia.

Red blood cells, 915,625.

White blood cells, 5,310.

Haemoglobin, 31.7.

Colour Index, 1.5.

Treatment. 19.6.29. Liq. arsenical m.3. tid. 22.6.29. Liq. arsenical. t.i.d. 28.6.29. Allowed up.

Diet. Soup, pudding, tea and bread.

14.6.29. Light diet and ½ lb. liver daily.

Case 3.

Mrs. A.S. Age 54. Occupation. Housewife.

Admitted. 15.10. 29.

Dismissed. 3.12.29.

Result. Greatly improved.

Complaint. Weakness of increasing severity for indefinite period, becoming more acute since the attack of pneumonia in August 1929.

History of Present Illness. The patient was operated upon for gall stones two years ago and has not been keeping well since.

She developed rheumatism in May 1929, which kept her in bed for two months. At the end of August she had pneumonia. Since then she has been feeling very weak and kept to bed. She was troubled with a cough and breathlessness, and felt heart thumping when trying to fall asleep. The colour of her skin was always pale but has been more so these past few weeks. Her appetite has been poor following the attack of pneumonia and since then has had occasional tingling sensations in the legs. She has had a sore mouth occasionally. She is not subject to headaches nor fainting attacks. Her bowels are constipated.

Previous Illnesses. Her health has been good up till ten years when she had an attack of acute gastritis. Two years later she was kept under observation in the hospital for gall stones, but was not operated upon. Two years ago she was operated in a Nursing Home for gall stones. In May 1929 she was in bed with rheumatism and at the end of August 1929 had an attack of pneumonia.

Family History. Her mother died from an unknown cause and her father died from bronchitis. A brother died following asthma and she has one sister alive. Of 12 children there are 8 living, one died 4/12 year, another following an injury, and two after pneumonia.

Social History. She lives in a 2 room and kitchen house which is damp.

Present Condition. The patient lies comfortable in bed in any decubitus. Her complexion is pale and her skin is of a lemon yellow colour. She appears well built and nourished and the skin is dry and smooth. There are no palpable glands but she has a large scar in the epigastric region where she was operated on. There is some oedema of the ankles. W.R. negative.

(a) Nervous System. There are no motor disorders but her strength is feeble, and there are no sensory disturbances. The pupils are of equal and normal size and react to light and accomodation. The plantar reflex is flexor, there is a knee-jerk and arm reflexes, and the superficial reflexes of the body were present. There are no trophic or vasomotor disorders and eye examination proved normal.

(b) Cardio-vascular System. The pulse rate was 84 per minute, regular in force and rhythm, small pulse and moderately easy to compress. No cardiac impulse seen or felt in chest.

Percussion. Upper border of cardiac dullness was the 3rd left interspace. Right border - was the left sternal margin; the left border - 10 cm. from the middle line. The cardiac apex was in the 6th interspace ½" from the mid-clavicular line.

Auscultation. The heart sounds were regular and not very strong in character. The first sound at the apex was abrupt, and there are no adventitious sounds.

(c) Respiratory Sounds. The chest was symmetrical in shape and the breathing was 20 per minute and regular. There was slightly increased vocal fremitus of the left base. On percussion there was an impaired note in the back of the chest and there was dullness of the left base. The respiratory murmur is harsh and there is tubular breathing over the left base. Rhonchi heard all over the chest and vocal resonance was increased over the left base.

(d) Alimentary System. The lips were very pale and the tongue pale, smooth and slightly fissured. There was a large amount of adipose tissue in the abdominal wall, but there was no pain, tenderness nor rigidity. The liver, spleen and kidneys were not palpable and on percussion the spleen and liver were of normal size. There was an area showing increased resistance and dullness to percussion just below the left costal margin.

Urine. Alkaline, dark amber colour, S.G. 1016, deposit of phosphates and a trace of albumin.

(e) Blood Examination. 15.10.29. Blood film shows red blood corpuscles, nucleated reds, punctate basopenlia, polymorphs.

Red Blood Cells 600,000

White Blood Cells, 6,000

Haemoglobin, 20%

Colour Index, 1.7.

Treatment.

16.10.29. Liq. arsenicalis m.iii. t.i.d.

(Stopped 22.10.29.)

16.10.29. Neo Kharsivan, .6 gms. Liver extract.

22.10.29. ℞ Liq. acid hydrochlordil ʒiv.

Liq. arsenic hydrochlr. m. 36.

Aqua. ʒ vi.

Sig. ʒʃo. t.i.d. ℞

Neokharsivan, .6gm.

28.10. 29. Antiphlogestine over the chest.

28.10. 29. Neo Kharsivan, .6 gms.

4.11.29. Neo Kharsivan, .6 gms.

13.11.29. ℞

Liq. Arsenicalis ʒi

Acid hydrochlordil ʒ vi.

Aqua ad ʒ vi.

Sig. ʒʃo. t.i.d. (Stopped 21.11.29)

21.11.29. ℞ Acid hydrochlor dil ʒ vi.

Aqua ad ʒ vi.

Sig. ʒʃo. with meals.

R. Neo Kharsivan .6 gms.

30. 11. 29. Neo Kharsivan .6 gms.

Diet. Milk, tea, soup.

27.10.29. Puddings, poached egg, tea, bread, fish.

3.11.29. ¼ liver daily.

CASE 3

HAEMATOLOGICAL CHART.

Name

Mrs A.S.

Age

54 yrs.

Disease

Pernicious Anaemia

Notes

DATE	13/10/24	22/10/24	29/10/24	5/11/24	12/11/24	19/11/24	26/11/24	3/12/24
POLYMORPHONUCLEAR NEUTROPHILS	50	52	51	54	56	62	60	66
" EOSINOPHILS	½	1	2	2	2	3	4	3
LYMPHOCYTES, SMALL	30	28	30	28	26	30	29	24
" LARGE MONONUCLEARS	10	12	8	7	10	3	6	5
MYELOCYTES, NEUTROPHILS	6½	5	6	5	6	1	2	2
" EOSINOPHILS	3	2	3	4	2	1	1	
NUCLEATED RED CELLS								

Differential Count per cent.

REDBLOOD CORPUSCLES	HAEMOGLOBIN %	LEUCOCYTES
6,000,000	120	800,000
		700,000
5,500,000	110	600,000
		500,000
5,000,000	100	400,000
		300,000
4,500,000	90	200,000
		175,000
4,000,000	80	150,000
		125,000
3,500,000	70	100,000
		90,000
3,000,000	60	80,000
		70,000
2,500,000	50	60,000
		50,000
2,000,000	40	40,000
		30,000
1,500,000	30	28,000
		26,000
1,000,000	20	24,000
		22,000
500,000	10	20,000
		19,000
		18,000
		17,000
		16,000
		15,000
		14,000
		13,000
		12,000
		11,000
		10,000
		9,000
		8,000
		7,000
		6,000
		5,000
		4,000
		3,000
		2,000

Liver Extract

Liver Extract + ½ lb liver daily

Reticulocytes %

6% 5% 4% 3% 2% 1%

RED CORPUSCLES — BLACK HAEMOGLOBIN — ~~RED~~ Green LEUCOCYTES — ~~BLUE~~ Violet Reticulocytes .....

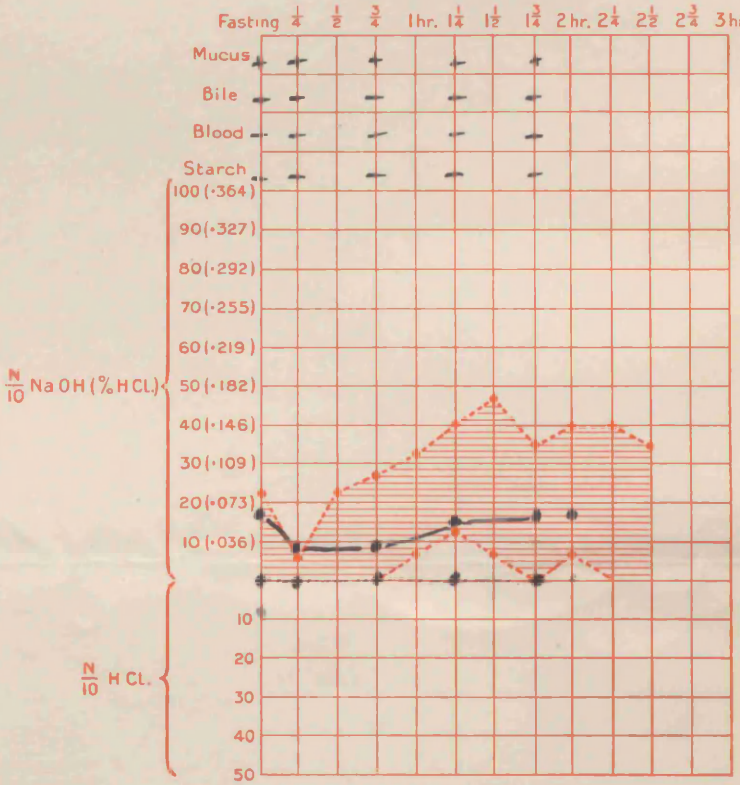
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull

CASE 3

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs. A.S. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 20.10.29



Fasting Juice.

Volume. 7 cc.

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

———— represents total acidity.

Summary.

2. FÆCES.

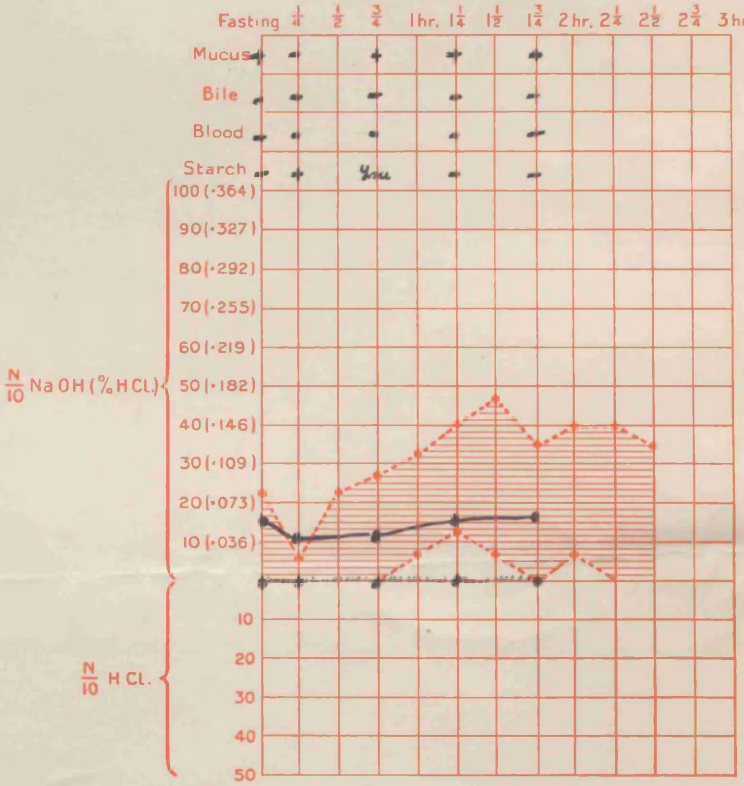
DOWN BROS., LTD., LONDON.

ASE.3

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs A. S *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 2·12·29



Fasting Juice.

Volume. 5 cms

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2–2½ hours).

———————— represents free HCl.

———·—·—·— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 4.

M.M., Female, age 39 years. Occupation. Housewife.

Admitted. 4.11.28.

Dismissed. 7.1.29.

Result. Much improved.

Complaint. Breathlessness and pain across the chest on exertion.

History of Present Illness. Patient has been weak and anaemic for the past 5 years and was treated with tonics without benefit. For the past 12 months she has noticed her feet and ankles swell on standing. She cannot walk on the level beyond 200 yards without having a rest. Occasionally she has fainting attacks when stooping. These symptoms have become progressively worse during the past 2 months. Liver had not been taken.

Previous Health. She had measles and bronchitis as a child. At the age of 8 years enlarged glands in the neck which had been present for some time broke down.

Social Conditions. She lives in a 3 room and kitchen house with a husband and five children.

Family History. Her father died of pneumonia. Her mother, three brothers and one sister are alive and well.

Present Condition. Pulse 84. Respirations 24. Temperature 98.

The patient lies comfortably in bed any any decubitus. Her complexion is pale and the skin has a yellowish tint, which is dry to the touch. The pupils are rather large and equal in size. There is an old irregular scar in the neck. The mucous membrane are very pale. She is of average build and appears well nourished. No glands are enlarged.

(a) Cardio-vascular System. The pulse rate is 84 per minute, regular, easily compressed, low volume. The arteries are scarcely palpable. The Heart. The praecordial area does not show any abnormal pulsations. The apex beat can be seen and felt in the 6th left interspace, 11 cms. from the mid sternal line. Upper border of the heart is the 3rd interspace. Left border of the heart is 12 cms. from the mid sternal line. Right border of the heart is left sternal line.

(b) Respiratory System. Both sides of the chest are not quite symmetrical. There is slight bulging in the 3rd and 4th interspaces. The borders of the lung were normal. On percussion there was normal lung resonance, and on auscultation the R.M. was vesicular.

(c) Digestive System. The lips are pale and there are ten carious teeth. The tongue is flabby, moist and slightly fissured, and the fauces and pharynx are pale. Her appetite is

very poor and she has occasional attacks of diarrhoea. The spleen, liver and kidneys were not palpable, though the spleen on percussion was a little enlarged. Nothing abnormal could be felt in the abdomen.

(d) Nervous System. There were no motor, sensory or trophic disorders. The pupils reacted to light and accomodation, the plantar reflex was flexor, the knee reflex was difficult to elicit. There was no abdominal reflexes; the arm reflexes were present. There was no disturbance of vision or of the special senses.

(e) Genito-Urinary System. This was normal. Menstruation was irregular and scanty. The urine was yellow, S.G. 1018, acid, and contained a trace of acetone.

(f) Examination of the Blood. This proved negative with a Wasserman Test. Blood film showed megalocytes, megaloblasts, monocytes, anisocytosis and a few polymorphs.

Red Blood Cells, 1,220,000

White Blood Cells. 4,500.

Haemoglobin, 25%

Colour Index. 1.1

Treatment.

7.11.28. Liq. Arsenicalis m.iii t.i.d.

11.11.28. Liq. Arsenicalis m. v. t.i.d.

18.12.28. Liq. Arsenicalis m.vi. t.i.d.

21. 12. 29. Allowed up.

31.12.28. ℞ Liq. acid hydrochlor. dil 3ss.

Aqua 3 vi

Sig. 3ss with food.

Diet.

Soup, pudding and toast.

Liver stopped 9.11.28.

10.11.28. Liver extract.

5.12.28. Full diet.

CASE 4

HAEMATOLOGICAL CHART.

Name

M·M

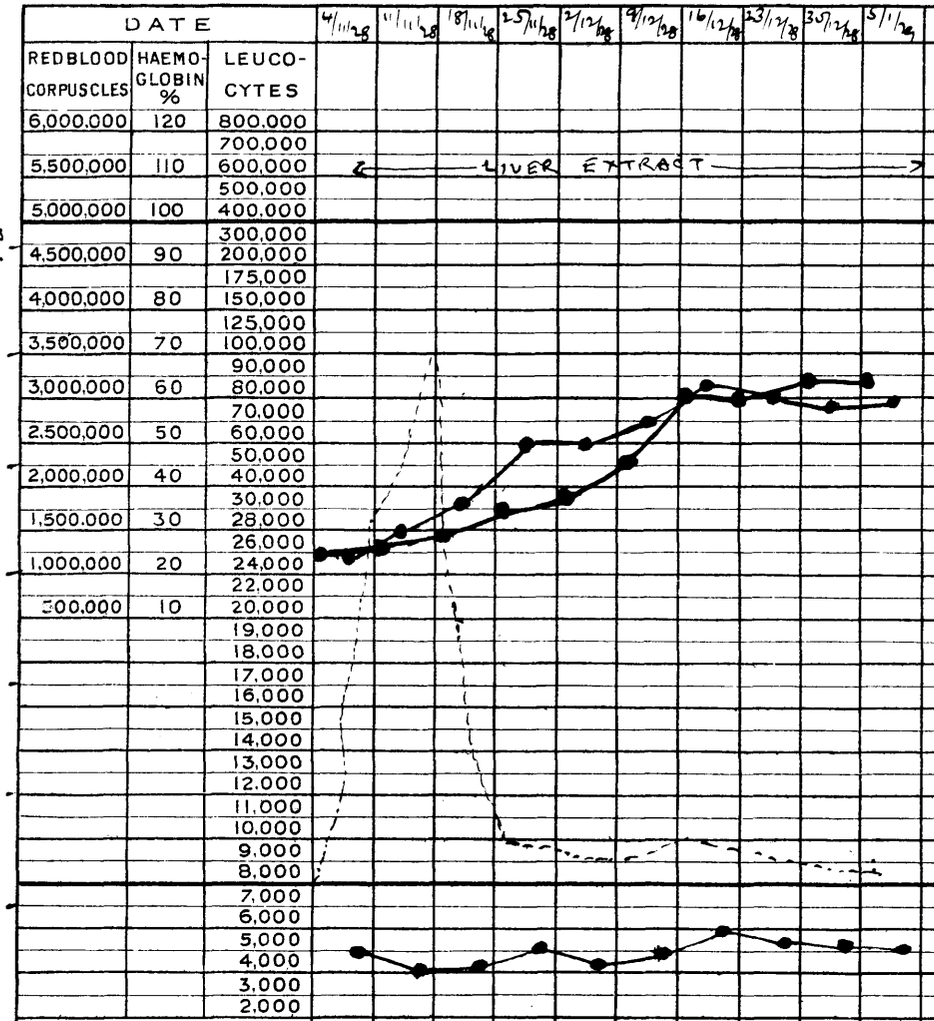
Age

39 yrs

Disease

Pernicious Anaemia

Notes



Differential Count per cent.

POLYMORPHONUCLEAR NEUTROPHILS	50	49	50	54	52	58	55	60	60	62
" EOSINOPHILS	1	1	2	3	2	5	1	4	3	5
LYMPHOCYTES, SMALL	32	32	29	28	29	22	30	26	25	22
" LARGE MONONUCLEARS	10	6	8	5	10	7	9	6	8	10
MYELOCYTES, NEUTROPHILS	4	8	6	8	4	5	4	3	2	1
" EOSINOPHILS	3	4	5	2	3	2	2	1	2	
NUCLEATED RED CELLS										

RED CORPUSCLES — BLACK HAEMOGLOBIN — RED LEUCOCYTES — ~~BLUE~~ Violet Reticulocytes - - - - -

Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

CASE 4

GASTRO-INTESTINAL ANALYSIS.

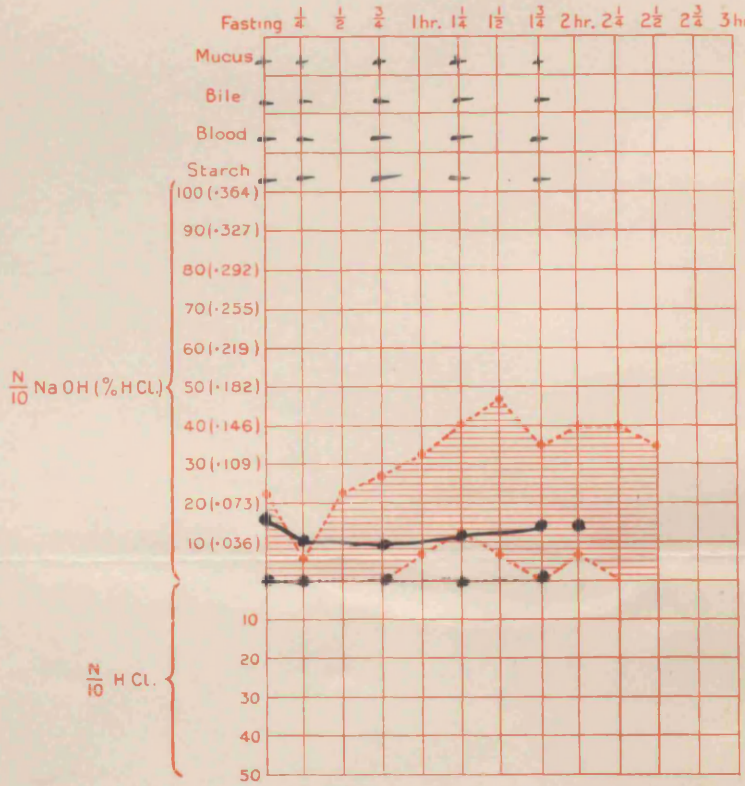
Name of Patient Mrs. M. M. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 7.11.28

Fasting Juice.

Volume. 3cc.

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

..... represents free HCl.

——·——·—— represents total acidity.

Summary.

2. FÆCES.

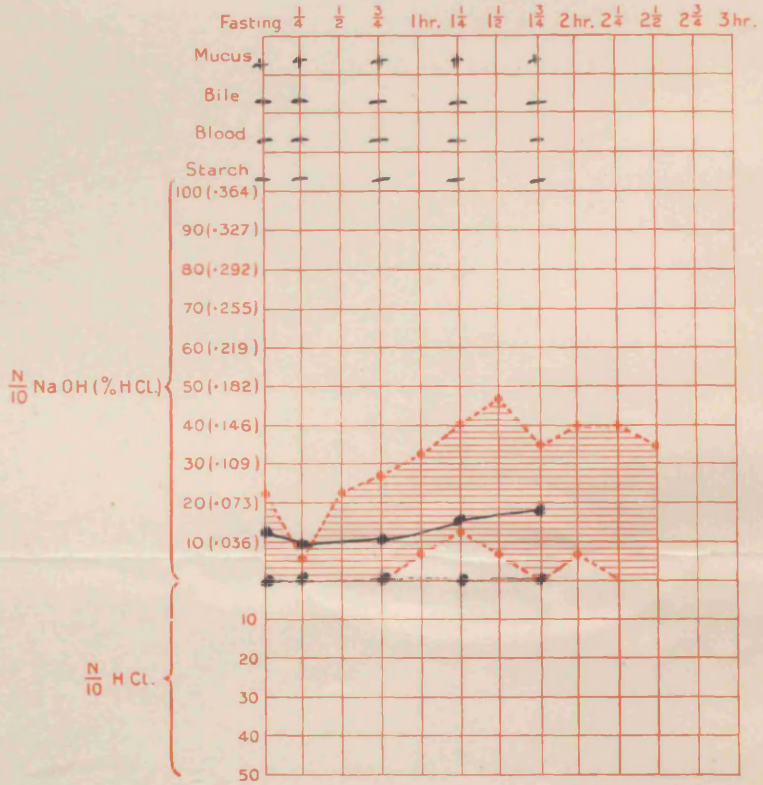
DOWN BROS., LTD., LONDON.

CASE 4

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs. M. M. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 29.12.28



Fasting Juice.

Volume. 4 ccs.

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

..... represents free HCl.

——— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 5.

Mrs. A.Sc. Age 54 years. Occupation. Housewife.

Admitted. 29.12.29.

Dismissed. 21.2.30.

Result. Good.

Complaint. Troublesome cough of two week's duration.

Present History. Patient aware of suffering from pernicious anaemia for the past nine months. She was treated for this illness but did not keep up the liver treatment regularly. She feels very exhausted and has become progressively weak. After a chill two weeks previously she has been troubled with a cough.

Previous Health. She had only measles as a child.

Social Conditions. Her house contains 2 rooms and a kitchen, which is dry.

Family History. Father died of old age. Mother following a cerebral haemorrhage. She has two sisters and one brother alive and well. Her husband and three children are keeping well.

Present Condition. She lies in bed in the dorsal deculitus and is rather restless because of the cough. Her face is pale and appears languid. The mucous membranes are pale and the pupils are of normal size and equal. She is well built and

looks well nourished. The skin is of a lemon yellow tint which has almost a velvety feel. There are no glandular enlargements. Temperature 98.2

(a) Nervous System. The motor, sensory and vaso-motor systems are normal except for the muscles being flabby. The eye reflexes are normal, The plantar reflex is flexor. K.J. is present; the arm jerks are present and so are the superficial reflexes of the abdomen. The vision sense is normal and so are the other special senses. The cranial nerves are normal.

(b) Cardio-vascular System. The pulse rate is 84 per minute, regular, normal tension and volume. The praecordial area reveals no abnormal pulsations, and the cardiac impulse can be seen and felt in the 6th left interspace 10 cms. from the left sternal line.

Upper border of cardiac dullness is 4th rib.

Left " " " " " ½" within mid-clavicular line.

Right border of cardiac dullness is left sternal line.

Auscultation. The heart sounds are not absolutely regular, but they are regular and of good quality. There is a soft V.S. Murmur at the apex.

(c) Respiratory System. The chest wall is symmetrical and expands well with respiration. The percussion note is resonant throughout and the R.M. is vesicular. Occasional rales are heard and there is prolonged expirations. She has a loose cough and a clear frothy spit.

(d) Digestive System. The mucous membranes of the lips are very pale; the tongue is pale and moist; she has anorexia and the bowels are regular. The spleen and liver are normal in size. Nothing abnormal could be felt in the abdomen. Ten septic teeth in upper jaw.

(e) Genito-Urinary System. This was normal, the urine was acid, pale amber; S.G. 1012, and there is a deposit of pink urates.

Examination of the Blood. The W.R. was negative. A blood film revealed megalocytes, and megaloblasts, polychromasia, normocytes, polymorphs and eosinophils.

Red Blood Cells, 3,140,000

White Blood Cells, 6,200.

Haemoglobin, 76%

C.I. 1.2.

Treatment.

30. 12. 29. ℞
Ammon. Carb. ʒi
Tinct. ~~Tallae~~ ʒii
Chlorodyne ʒiii
Aquam ad ʒvi.

Sig. ʒi t.i.d.

20. 1. 30. Emulsion ʒi t.i.d.

25.1.30. Allowed up.

Diet. Soup, pudding, tea and bread.

31.12. 29. Liver.

14.1. 30. Poached eggs.

19.1.30. Light diet.

CASE 5 29.12.29

HAEMATOLOGICAL CHART.

Name

MRS. A.S

Age

54 yrs

Disease

Pernicious Anaemia

Notes

Condition improved after extracting teeth

DATE	22/12/29	5/1/30	12/1/30	19/1/30	26/1/30	2/2/30	9/2/30	16/2/30
REDBLOOD CORPUSCLES / HAEMOGLOBIN % / LEUCOCYTES	LIVER							
Differential Count per cent.								
POLYMORPHONUCLEAR NEUTROPHILS	55	52	56	64	67	58	64	68
" EOSINOPHILS	2	2	3	4	5	3	3	4
LYMPHOCYTES, SMALL	24	28	26	24	22	29	23	20
" LARGE MONONUCLEARS	8	7	8	4	4	6	5	4
MYELOCYTES, NEUTROPHILS	7	6	5	3	1	4	4	2
" EOSINOPHILS	4	5	2	1	1		1	2
NUCLEATED RED CELLS								

Teeth extracted

Reticulocytes %

RED CORPUSCLES — BLACK HAEMOGLOBIN — RED LEUCOCYTES — ~~BLUE~~ GREEN VIOLET RETICULOCYTES

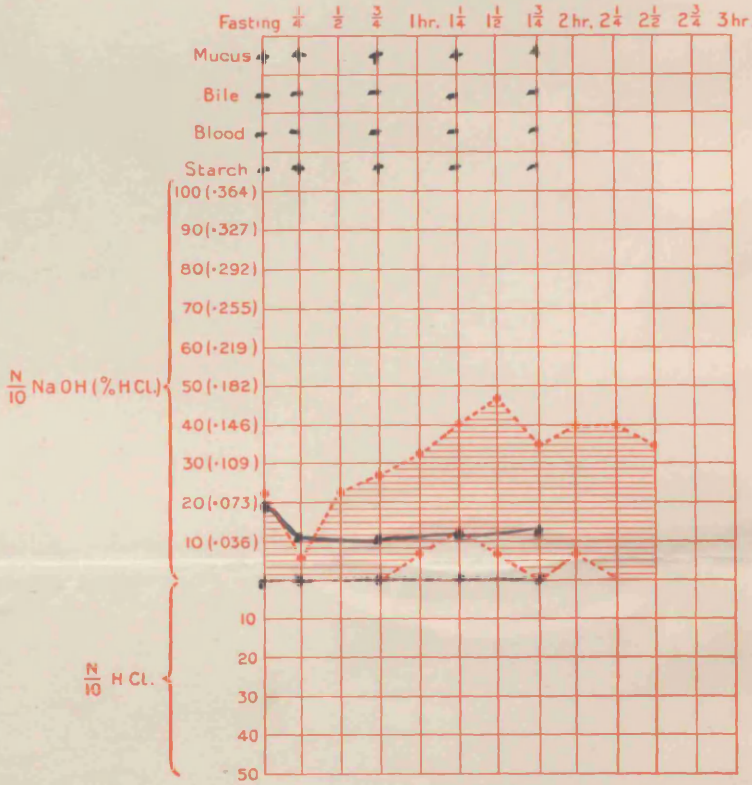
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., H.

CASE 5

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mr A.S *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 30.12.29



Fasting Juice.

Volume. 8 cm.

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

———— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON

CASE 5

GASTRO-INTESTINAL ANALYSIS.

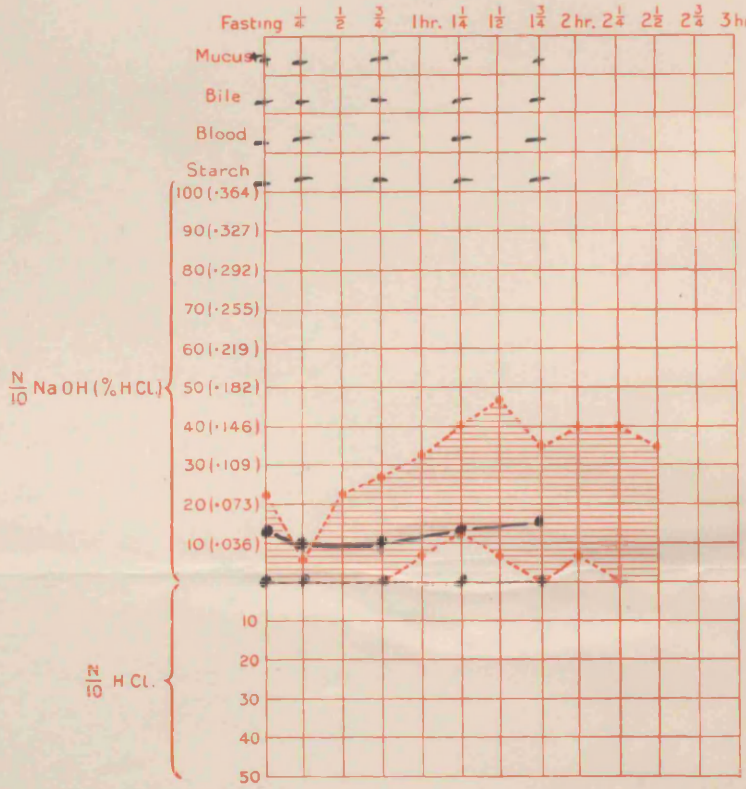
Name of Patient Mrs. A. S. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 18.2.30

Fasting Juice.

Volume 6 ccs.

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

..... represents free HCl.

——— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 6.

Miss S.G. Age 64 years. Occupation. Domestic servant. Spinster.

Admitted. 24.3.30.

Dismissed. 20.5.30.

Result. Good.

Complaint. Is of weakness becoming more pronounced during the past few weeks.

History of Present Illness. She has always remained in good health but noticed about 3 months ago that she became more easily fatigued and could not perform her work. Attacks of giddiness and faintness became more frequent in the past two months and had to keep in bed. Her doctor gave her tonics which did not have much effect. She has always been rather pale but it became more pronounced lately. Liver previously not taken.

History of Previous Illnesses. She had measles, chicken pox and whooping cough as a child. During the past 10 years she noticed that she got frequent colds which made her cough; those colds were more frequent in the winter time but they were not so severe as to confine her to bed.

Family History. Both her parents died from old age. She remembers that an uncle (her father's brother) died from anaemia; she has two sisters who are

alive and well.

Social Condition. She lives at the home of her mistress. Her room and time for recreation is good. Pulse 94. Temperature 98.2. Respirations 20.

Present State. She lies comfortably in bed and looks very pale, her features are broad and she is of average size; the skin is lemon yellow and is dry to the touch; the mucous membranes are very pale; the pupils of the eye are of normal size and are equal; the sclerotics are very pale. She appears well nourished and the hair of her head is brittle; the eyebrows are rather scanty; no glands could be felt.

(a) Nervous System. The muscles are flabby but there is no wasting or paralysis. Tactile and thermal sense could not be fully appreciated in the right foot and leg.

Reflexes. Plantar reflex was flexor, the knee jerks were difficult to elicit, the abdominal reflex were present. The arm reflexes were present, and the eyes reacted to light and accomodation. Ophthalmoscopic examination revealed nother abnormal. The special senses and the cranial nerves were normal.

(b) Cardio-vascular System. The pulse

rate was 94 per minute, regular, normal tension, small volume, but not equal in force. The praecordial area was free of any abnormal pulsations or thrills. The cardiac apex was in the 6th interspace, 12 cms. from the mid-sternal line, and extended 1". Boundaries of the Heart. Upper border 3rd interspace: left border, mid-clavicular line; right border, right border of the sternum. Auscultation. The first sound at the apex was weak and there was more than the normal interval between the 1st and 2nd sounds. The sounds in the other cardiac areas were feeble in character. There were no adventitious sounds.

(c) Respiratory System. The boundaries of the lungs were normal; the character of the respirations were normal; the R.M. was vesicular though an occasional rale could be heard at the left base.

(d) Digestive System. The lips were very pale; she was edentulous; the fauces and pharynx were normal; the tongue was try and slightly fissured. The abdomen was pendulous because of excessive fat round the umbilical and hypogastric regions. The spleen was palpable and the liver of normal size. Nothing abnormal could be found in the abdomen.

(e) Genito-Urinary System. This was normal, The urine was highly coloured, acid, and there was a deposit of urates. S.G. 1020.

(f) Blood Examination. The W.R. was negative. A blood film showed megalocytes, megaloblasts, anisocytosis, poikilocytosis, normocytes and polymorphs.

Red Blood Cells, 2,415,000

White Blood Cells, 6,800

Haemoglobin, 57%

C.I. 1.2

Treatment.

24.3.30. ℞ Potass. Iodide. ℥iii

Ammon. Carb. gr. 36.

Tinc.digitalis. m.36.

Aquam ad ℥ vi.

Sig. ℥ss. t.i.d.

26.3.30. Tab. Atropin. gr. 7½ i nocte.

Diet. Tea, pudding, toast, fish, liver.

CASE 6

HAEMATOLOGICAL CHART.

Name 24.3.30

Mrs S.G

Age

64 yrs.

Disease

Pernicious Anaemia

Notes

DATE	24/3/30	31/3/30	7/4/30	14/4/30	21/4/30	28/4/30	5/5/30	12/5/30	19/5/30
RED BLOOD CORPUSCLES / HAEMOGLOBIN % / LEUCOCYTES			LIVER						
6,000,000 / 120 / 800,000									
700,000									
5,500,000 / 110 / 600,000									
500,000									
5,000,000 / 100 / 400,000									
Reticulocytes % 300,000									
4,500,000 / 90 / 200,000									
175,000									
4,000,000 / 80 / 150,000									
125,000									
3,500,000 / 70 / 100,000									
90,000									
3,000,000 / 60 / 80,000									
70,000									
2,500,000 / 50 / 60,000									
50,000									
2,000,000 / 40 / 40,000									
30,000									
1,500,000 / 30 / 28,000									
26,000									
1,000,000 / 20 / 24,000									
22,000									
500,000 / 10 / 20,000									
19,000									
18,000									
17,000									
16,000									
15,000									
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12,000									
11,000									
10,000									
9,000									
8,000									
7,000									
6,000									
5,000									
4,000									
3,000									
2,000									

Differential Count per cent.

POLYMORPHONUCLEAR NEUTROPHILS	60	68	54	57	52	58	63	62	64
" EOSINOPHILS	1	1	1	2	1	2	3	3	5
LYMPHOCYTES, SMALL	25	30	25	26	27	27	26	25	22
" LARGE MONONUCLEARS	6	8	9	7	6	7	4	5	6
MYELOCYTES, NEUTROPHILS	6	8	9	6	10	8	3	3	2
" EOSINOPHILS	2	5	2	2	4	3	1	2	1
NUCLEATED RED CELLS									

RED CORPUSCLES – BLACK HAEMOGLOBIN – ~~RED~~ Green LEUCOCYTES – ~~BLUE~~ Violet Reticulocytes

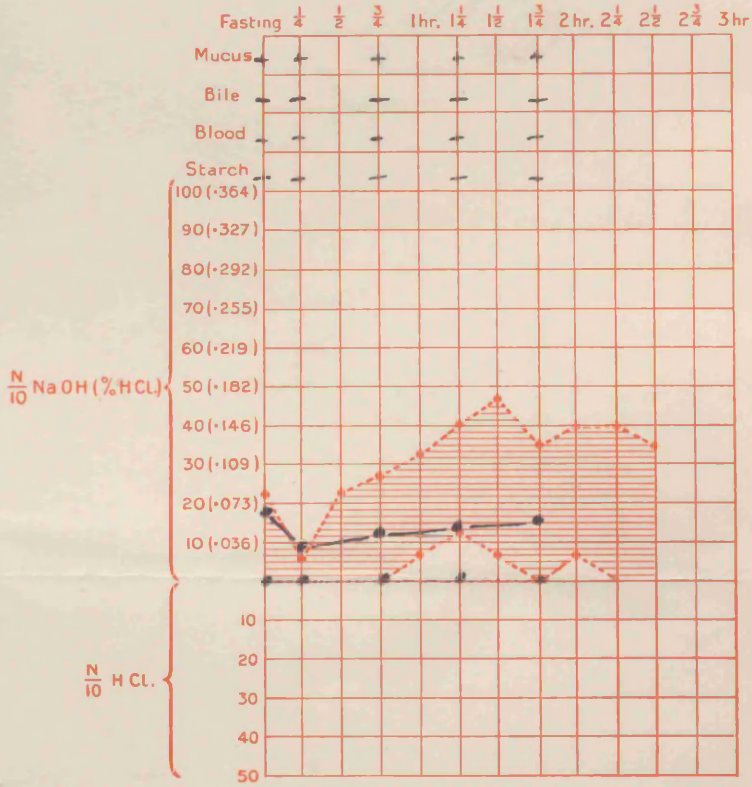
Designed by Edward Turton, M.D., B.Sc., M.R.C.P. Hull.

CASE 6

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mr. S.G *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 17.5.30



Fasting Juice.

Volume.

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

– – – – – represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

CASE 6

GASTRO-INTESTINAL ANALYSIS.

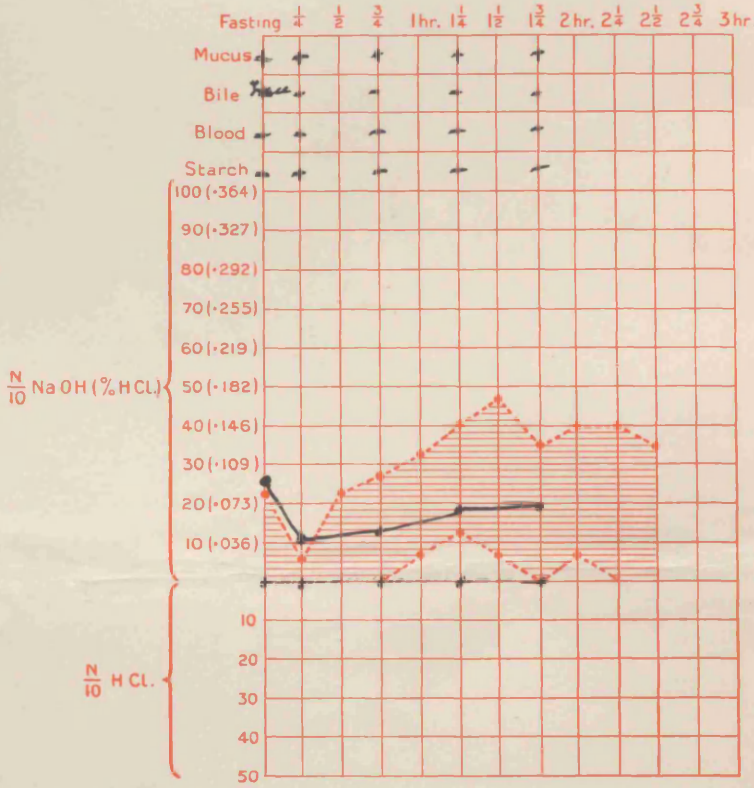
Name of Patient Mrs. S.G *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 25·3·30

Fasting Juice.

Volume. 4 cc.

Cells.



One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

– – – – – represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 7.

Mrs . E.P. Age 43 years. Occupation. Book-keeper.

Admitted. 24.3.30.

Dismissed. 17.5.30.

Result. Much improved.

Complaint. Of weakness which has become progressively worse during the last three years.

History of Present Illness. For the past five years she has not been in good health. It commenced with listlessness and not being able to concentrate. She usually felt drowsy in the afternoon. Since about three years she noticed that she easily became fatigued. This became gradually worse and for the past four months had to keep in bed. She was subject to frontal headaches and had no appetite for food. If food was taken she frequently vomited it. This vomiting after food became more frequent and was almost after every meal. She noticed her skin becoming more sallow lately and that she has lost much weight. The bowels are regular.

Previous Illness. Except for "rheumatic" pains in the hands and feet which she had a year ago for six months, her health has been good.

Family History. She stays with her parents who are alive and well and so are her two brothers and sister. Social Condition. Along with her parents she lives in a 2 room and kitchen which is clean and airy. Present Condition. Pulse 96. Respirations 20. Temperature. 98.6.

She lies comfortably in bed in any decubitus. Her complexion is sallow - almost jaundiced. The conjunctivae are of a bluish tint and the sclerotics are pale. Psoriasis is present in the arms and legs. The mucous membranes are very pale. The skin is yellowish-white and is dry. She is of spare build and is thin. There are no enlarged superficial glands.

(a) Cardio-vascular System. The pulse rate is 96 per minute, regular in rate and rhythm and is of good volume and tension. The apex beat is palpable in the 5th interspace in the nipple line. Heart Boundaries. The upper boundary is in the 3rd interspace; right border, left side of the sternum; left border is in the nipple line. On auscultation the heart sounds are normal and a soft V.S. murmur is heard all over the praecordium.

(b) Respiratory System. The chest is symmetrical and is resonant on percussion. The breath sounds are vesicular.

(c) Digestive System. The tongue is clean and moist; she has false teeth. The spleen is just palpable; the liver extends half-way to the umbilicus in the middle line and 1" below the costal margin in the mid-clavicular line - it is also slightly tender on palpation. Nothing except scyballous matter in the left iliac fossa could be felt in the abdomen.

(e) Nervous System. The muscles are flabby and there are no sensory nor trophic disturbances. The plantor reflex was flexor. K.J.s. were present; the arm reflexes and abdominal reflexes were present. The pupils reacted to light and accomodation. There was no disturbance in vision and the special senses were normal.

(f) Blood Examination. The W.R. was negative. A blood film showed megalocytosis and poikilocytosis.

Red Blood Cells, 930,000

White Blood Cells, 3,200

Haemoglobin, 36%

Colour Index, 2.

(g) Genito-Urinary System. This was normal. The urine was pale amber, neutral and the S.G. 1022.

Treatment.

26.3.30. Liq. arsenicalis m iv. t.i.d.

28.3.30. Ventriculin ½ vial four times daily.

5.4.30. ℞

Acid hydrochlor dil ℥i.

Aqua. ℥vi.

Sig. ℥ss with meals.

2.5.30. Allowed up.

Diet. ½ lb. liver daily.

Stopped 28.3.30.

Light diet.

CASE 7

HAEMATOLOGICAL CHART.

24.3.30

Name

14 yrs. E.P.

Age

43 years

Disease

Pernicious Anaemia

Notes

Liver given 24.3.30
Vill 28.3.30

Ventriculin given daily from 28.3.30

DATE	24/3/30	31/3/30	7/4/30	14/4/30	21/4/30	28/4/30	5/5/30	12/5/30
RED BLOOD CORPUSCLES / HAEMOGLOBIN % / LEUCOCYTES	LIVER			VENTRICULIN				
6,000,000 / 120 / 800,000								
700,000								
5,500,000 / 110 / 600,000								
500,000								
5,000,000 / 100 / 400,000								
Reticulocytes 7% — 300,000								
4,500,000 / 90 / 200,000								
175,000								
4,000,000 / 80 / 150,000								
125,000								
3,500,000 / 70 / 100,000								
6% — 90,000								
3,000,000 / 60 / 80,000								
70,000								
2,500,000 / 50 / 60,000								
50,000								
5% — 2,000,000 / 40 / 40,000								
30,000								
1,500,000 / 30 / 28,000								
26,000								
1,000,000 / 20 / 24,000								
4% — 22,000								
500,000 / 10 / 20,000								
19,000								
18,000								
17,000								
3% — 16,000								
15,000								
14,000								
13,000								
12,000								
2% — 11,000								
10,000								
9,000								
8,000								
1% — 7,000								
6,000								
5,000								
4,000								
3,000								
2,000								
Differential Count per cent. — POLYMORPHONUCLEAR NEUTROPHILS	52	58	60	63	60	65	62	66
" EOSINOPHILS	1	1	3	2	4	3	3	5
LYMPHOCYTES, SMALL	30	29	25	28	22	21	22	24
" LARGE MONONUCLEARS	7	6	4	4	4	6	5	3
MYELOCYTES, NEUTROPHILS	8	6	6	2	7	4	6	2
" EOSINOPHILS	2	1	2	1	3	1	2	
NUCLEATED RED CELLS								

RED CORPUSCLES — BLACK HAEMOGLOBIN — ~~RED~~ Blue LEUCOCYTES — ~~BLUE~~ Green Reticulocytes ----

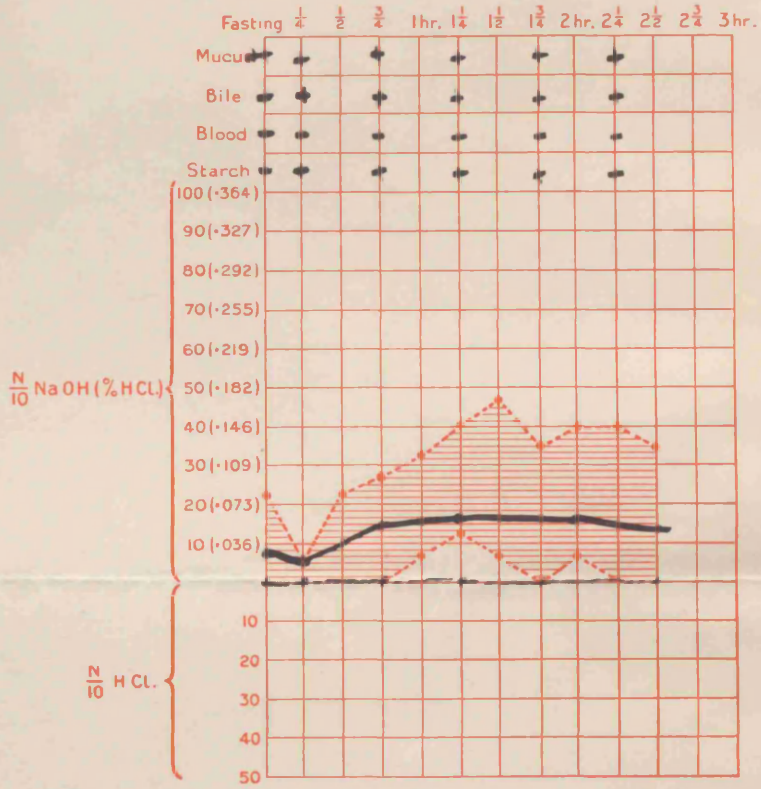
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

CASE 7

GASTRO-INTESTINAL ANALYSIS.

Name of Patient ~~[illegible]~~ Mrs E.P. *Ward* 4 *Bed*

1. FRACTIONAL TEST-MEAL. Date. 4.6.30



Fasting Juice.

Volume. 5cc.

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

— — — — — represents total acidity.

Summary.

Residual Juice 12cc

2. FÆCES.

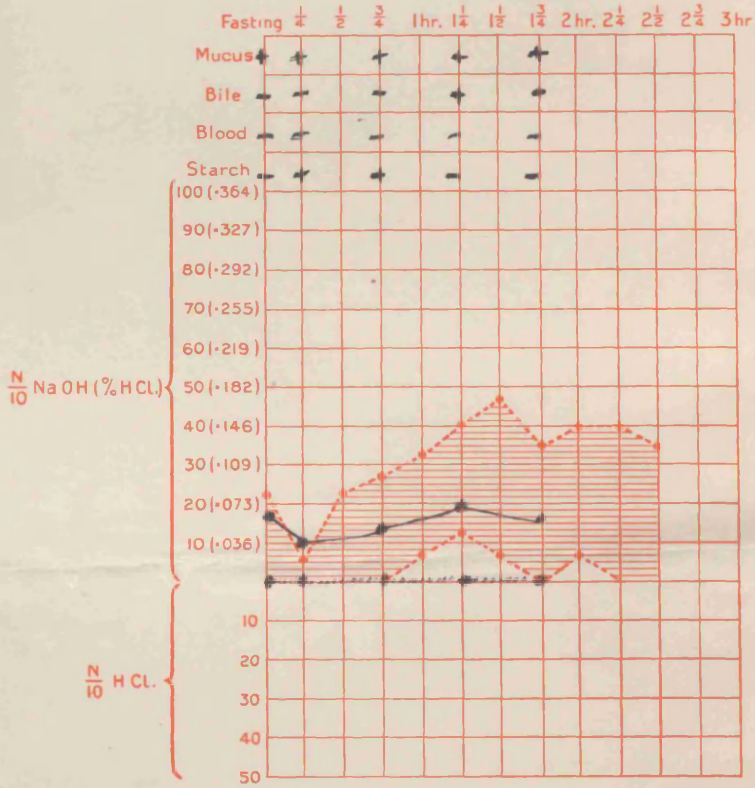
DOWN BROS., LTD., LONDON.

CASE 7

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs E. P *Ward* 1 *Bed*

1. FRACTIONAL TEST-MEAL. Date. 10.5.30



The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

— — — — — represents total acidity.

Fasting Juice.

Volume. 2 ccs

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 8.

Mrs. I.M. Age 45 years. Occupation. Housewife.

Admitted. 5.10.29.

Dismissed. 3.12.29.

Result. Good.

Complaint. Of "bloodlessness" for over two years and loss of appetite for one year.

History of Present Illness. Menorrhagia commenced two years ago, her periods having increased from 3 days to 1 week. This occurred occasionally at the beginning but for the past year excessive menstrual periods occurred regularly. She noticed her complexion becoming paler and there was also loss of appetite and vomiting after solid food. The anorexia became more marked and she vomited occasionally after food. During the past year she has lost weight. The anorexia and vomiting was worse during a period. Her skin has been dry for at least 2 years and has been constipated for many years. She has had no disturbance of locomotion or sensation. For the past week she has had a short dry cough.

History of Previous Illnesses. She has always enjoyed good health.

Family History. Her father is alive and well; her mother died following child-birth; there is

one sister alive and well and one died from an unknown cause; a brother died aet. 17 years of intestinal trouble. She has a husband and six healthy children. One boy died of septicaemia following an accident. She had no miscarriages.

Social Conditions. She lives in a house with 3 rooms and a kitchen. It is roomy and comfortable. Her meals are regular.

Present Condition. Temperature 98.4. Pulse 120. Respiration 24. The patient lies comfortably in bed in any decubitus and makes no complaint while resting in bed. She appears well nourished, the mucous membranes are pale and the skin is of a lemon yellow colour. The skin is dry and fissured and the hair is thin and dry.

(a) Circulatory System. The pulse is regular in rate, but the volume varies from moderate to small; the tension is consistently low and the arteries are not sclerosed.

The Heart. The apex beat is neither visible nor palpable but on auscultation is found in the 5th interspace 4" from the middle line.

Boundaries. Right border of heart is ¾" to the right of the mid-sternal line; upper border - 3rd rib; left border mid-clavicular line. The heart sounds are of fiar quality and there is a definite

blowing V.S. murmur which can be heard over the praecordium and the axilla, but best over the apex. There are no other adventitious sounds.

(b) Respiratory System. The chest is symmetrical in shape and there is a fair excursion during respiration. The lungs are resonant in percussion and the R.M. is vesicular. There are no adventitious sounds.

(c) Nervous System. There are no motor, trophic nor sensory disturbance. The knee and ankle jerks are exaggerated, and ankle and patellar clonus is easily obtained, this especially in the right leg. The plantar reflex is flexor; no abdominal reflexes; and the biceps, triceps and supinator jerks are active. The pupils of the eye are of equal size and react to light and accomodation. There is no external ocular palsy but there is a tendency to a coarse lateral nystagmus which is most marked when looking to the right. The special senses are normal.

(d) Digestive Tract. The tongue is fissured and beefy. The upper teeth are artificial and there are four unhealthy stumps in the lower jaw. The upper part of the abdomen is slightly rigid and there is some hepatic tenderness which extends from

from the 4th instespace to ½" below the right costal margin. The spleen is 1" below the costal margin. The kidney is not palpable.

(e) Genito-Urinary System. Nothing abnormal found. The urine is alkaline. S.G. 1022. deposit of phosphates and mucous; no abnormal constituents.

(f) Blood Examination. The Wassermann Reaction is negative.

Red Blood Cells, 740,000

White Blood Cells, 3,600.

Haemoglobin, 22%

C.I. 1.3.

A blood film showed megalocytosis, megaloblasts, polychromasia, and normocytes.

Treatment.

7.10.29. Liq. arsenical m. iii. t.i.d.

11.10.29. Test meal.

13.10.29. ℞ Pepsin

Acid hydrochlor. dil.

Aquam 3 vi.

Sig. 3ß with meals.

25.10.29. Test meal.

26.10.29. ℞ Pepsin 3 ṯp

Acid hydrochlor dil 3 i

Aqua ad 3 vi.

Sig. 3ss. with food.

21.11.29. Allowed up.

Diet. Milk.

7.10.29. ½ lb. liver daily. (Stopped 10.10.29)

10.10.29. Liver Extract.

2.11.29. ¼ lb. liver daily.

CASE 8

HAEMATOLOGICAL CHART.

Name 5.10.25

MRS. I. M.

Age

45 yrs

Disease

Pernicious anaemia

Notes

DATE	5/10/25	13/10/25	19/10/25	26/10/25	2/11/25	9/11/25	16/11/25	23/11/25	30/11/25
POLYMORPHONUCLEAR NEUTROPHILS	52	58	59	55	61	60	64	62	68
" EOSINOPHILS	1	2		2	1	2	3	2	3
LYMPHOCYTES, SMALL	27	26	30	27	23	26	24	25	22
" LARGE MONONUCLEARS	9	6	4	8	5	4	4	5	4
MYELOCYTES, NEUTROPHILS	8	7	5	7	8	6	4	5	3
" EOSINOPHILS	3	1	2	1	2	2	1	1	
NUCLEATED RED CELLS									

Differential Count per cent.

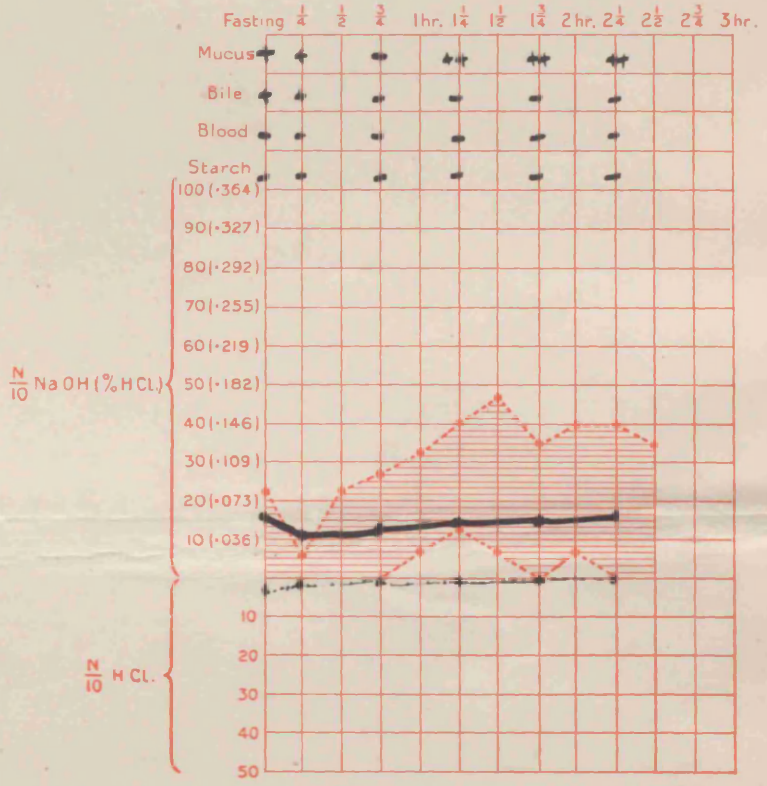
RED CORPUSCLES — BLACK HAEMOGLOBIN — ~~RED~~ Green LEUCOCYTES — ~~BLUE~~ Violet Reticulocytes - - - - -

CASE 8

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs. M. *Ward* V *Bed*

1. FRACTIONAL TEST-MEAL. Date. 11. 10. 29



Fasting Juice.

Volume. 12 c.c.

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

————represents total acidity.

Summary. No residual juice

2. FÆCES.

DOWN BROS. LTD., LONDON.

CASE 8

GASTRO-INTESTINAL ANALYSIS.

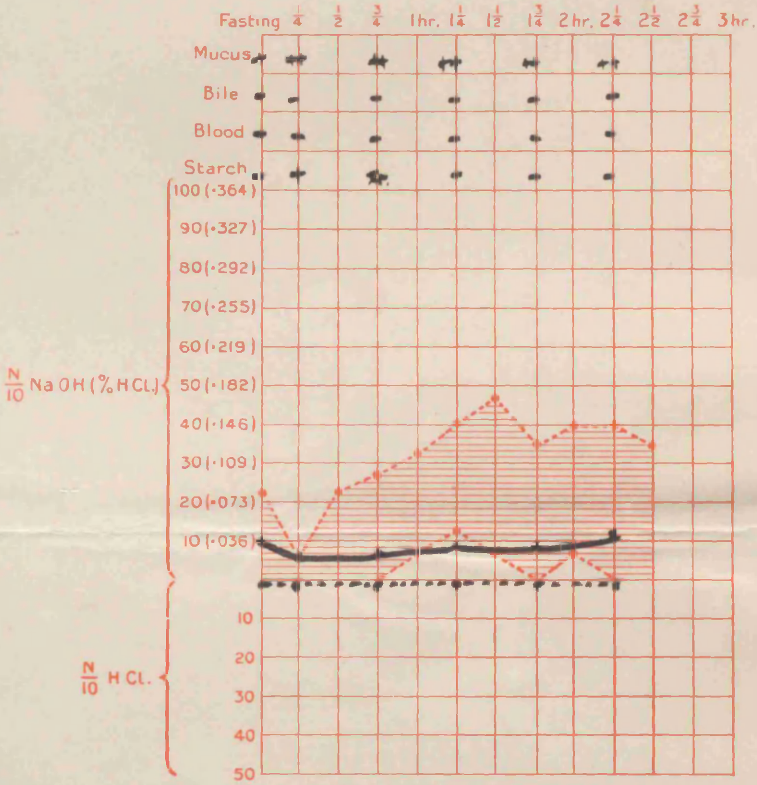
Name of Patient Mrs. M. *Ward* V *Bed*

I. FRACTIONAL TEST-MEAL. Date. 25·10·29

Fasting Juice.

Volume 20 ccs

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

..................represents free HCl.

——— ———represents total acidity

Summary. Residual Juice 5 ccs

There is excess of mucus in all specimens

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 9.

Mrs. S.S., age 41. Occupation. Housewife.

Admitted. 4.3.29.

Dismissed. 23.4.29.

Result. Much improved.

Complaint. Weakness and swelling of legs for the past 2 years.

History of Present Illness. Five years ago she noticed that she was becoming weaker. This became worse and now she becomes fatigued on the slightest exertion. She is subject to fainting attacks especially after stooping. Three years ago her feet began to swell and for the past 6 weeks her ankles are also swollen. When walking she has a sensation as if walking on carpet. Liver not previously taken.

Previous Illnesses. She had scarlatina aet. 10 yrs. and a severe uterine haemorrhage 11 years ago.

Family History. Her mother died of dropsy aged 63 years, and her father of senility. She is an only child and has four children who are healthy.

Social Condition. She lives with her husband and children in a single room and kitchen; the house is damp. She takes her meals regularly.

Present Condition. Pulse 94, Temperature 97. Respirations 22. She lies comfortably in bed in any decubitus. Her skin is very pale, almost jaundiced in colour and dry. She appears well built. The mucous membranes and sclerotics are very pale. The pupils are of normal size and equal.

(a) Cardio vascular System. The pulse rate is 94 per minute, regular, normal volume, and tension. The cardiac apex could be seen and felt in the 5th interspace 10 cms. from the mid-sternal line.

Borders of the Heart. The upper border is in the 3rd interspace, the right border in the left sternal line. The left border ¼" within the mid-clavicular line.

On auscultation the heart sounds are normal in character, but there is a soft V.S. murmur best heard at the apex.

(b) Respiratory System. The chest is symmetrical and there is only a small excursion with respiration. The lung note on percussion is resonant and on auscultation the R.M. is vesicular. There are no adventitious sounds.

(c) Nervous System. The muscles are well formed though flabby. There is paraesthesia for

for touch and temperature, senses on the soles of the foot. The eyes react normally to light and accomodation, the arm jerks are present, so are the abdominal reflexes, the K.J. is difficult to obtain; the plantar response is flexor and Romberg's sign is found. Ophthalmoscopic examination is normal and the special senses are normal.

(d) Digestive System. The lips are very pale, the teeth in the upper jaw, (9) are carious; the tonsils are unhealthy. The spleen and liver are of normal size, the kidney are not palpable and nothing abnormal could be found in the abdomen.

(e) Genito-Urinary System. This was normal. The urine was pale yellow, neutral, S.G. 1022., no abnormal constituents.

(f) Blood Examination. The Wassermann Reaction was negative. A blood film revealed anisocytosis, poikilocytosis, megalocytes and normocytes.

Red Blood Cell count, 1,200,000

White Blood Cell count, 4,700.

Haemoglobin, 20%

C.I. 1.2.

Treatment.

7.3.29. Liq. arsenicalis m.iii t.i.d.

6.4.29. ℞ Acid hydrochlor dil ℥vi.

Aqua. ℥ vi.

Sig. ℥ss with food.

12.4.29. Massage.

19.4.29. ℞ Acid Hydrochlor dil ℥i.

Aqua ℥ vi.

Sig. ℥ss. with food.

Diet. Milk.

6.3.29. Soup, pudding, tea and bread.

7.3.29. ½ lb. liver daily.

14.3.29. ¼ lb. liver and liver extract daily.

CASE 9

HAEMATOLOGICAL CHART.

Name Mrs. S.S

Age 41

Disease Pernicious Anaemia

Notes

DATE	4/3/26	11/3/26	18/3/26	25/3/26	1/4/26	8/4/26	15/4/26	22/4/26
POLYMORPHONUCLEAR NEUTROPHILS	58	60	62	60	61	64	62	66
" EOSINOPHILS	1	1	2	2	2	3	3	4
LYMPHOCYTES, SMALL	26	24	20	20	22	21	20	23
" LARGE MONONUCLEARS	5	5	6	5	6	7	6	5
MYELOCYTES, NEUTROPHILS	7	8	8	10	8	4	7	2
" EOSINOPHILS	3	2	2	3	1	1	1	
NUCLEATED RED CELLS								

Differential Count per cent.

RED CORPUSCLES — BLACK HAEMOGLOBIN — RED LEUCOCYTES — ~~BLUE~~ Violet Reticulocytes ---

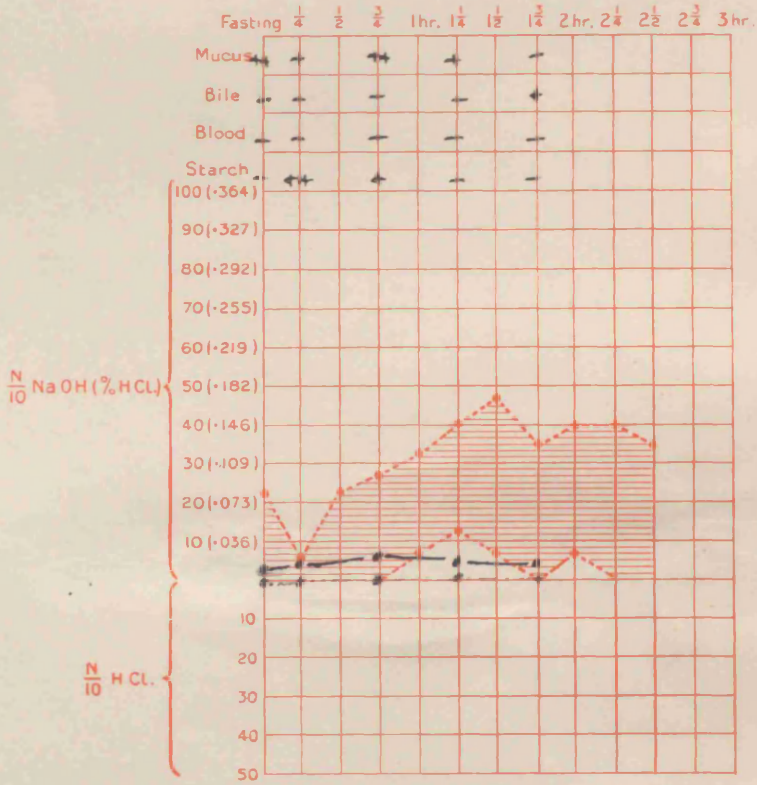
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

CASE 9

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs S S . *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 5 . 3 . 29



Fasting Juice.

Volume. 11 ccs.

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

————————represents total acidity

Summary. no free HCl. Stomach empty after 1¾ hrs

Trace of charcoal in first 2 specimens

2. FÆCES.

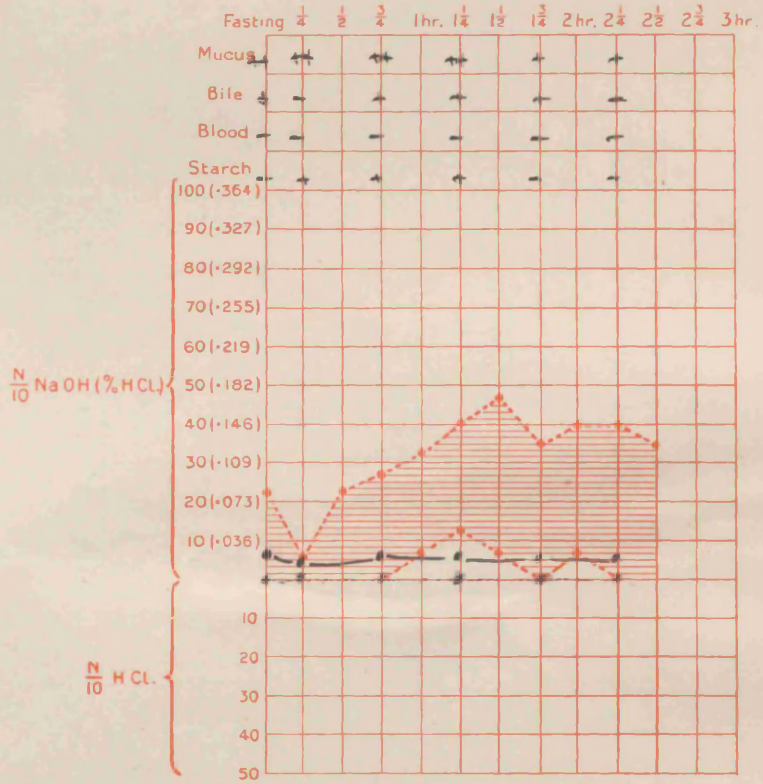
DOWN BROS., LTD., LONDON.

ASE 9

GASTRO-INTESTINAL ANALYSIS.

Name of Patient Mrs S.S. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 19.3.29



Fasting Juice.

Volume. 13 cc.

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

————————represents total acidity

Summary.

Trace of charcoal in fasting juice

2. FÆCES.

DOWN BROS., LTD., LONDON.

ASE 9

GASTRO-INTESTINAL ANALYSIS.

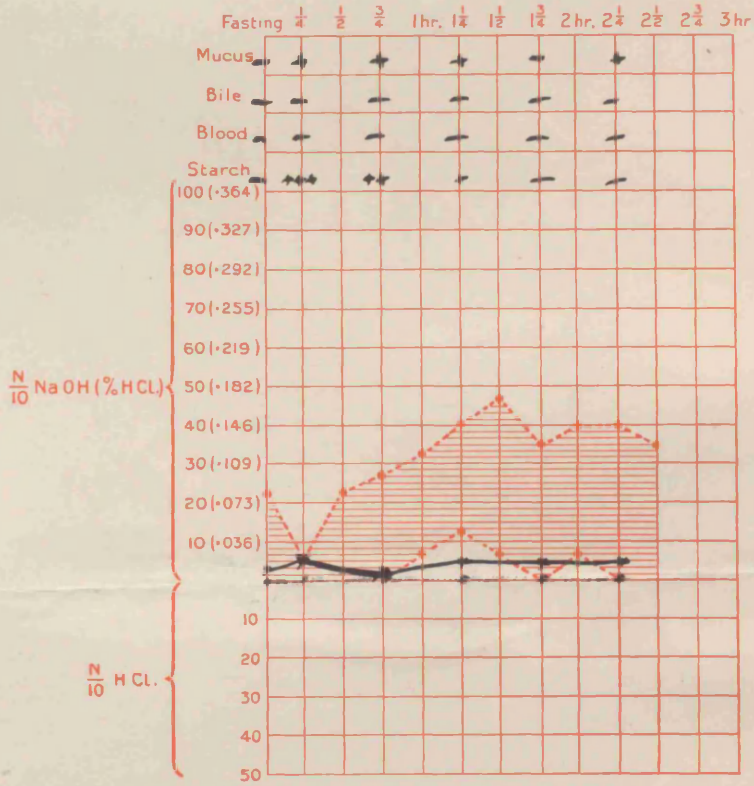
Name of Patient Mrs. S.S. ~~[illegible]~~ *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 12.4.24

Fasting Juice.

Volume. 9 cc.

Cells.



One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——— represents free HCl.

——— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 10.

J.M. Age 61. Occupation. Clerk.

Admitted. 3.9.29.

Dismissed. 14.11.29.

Result. Good.

Complaint. Of weakness and lack of energy of about 2 years duration.

History of Present Illness. The onset had been gradual and noticed that he became easily tired. This became more pronounced during the four months prior to admission. He noticed the colour of his skin becoming sallow about 18 months ago; he has always been constipated. He had not taken liver previously.

History of Previous Illness. He always enjoyed good health up till the present illness.

Family History. His parents died of senility; an aunt of gastric cancer. His wife and two sons are in good health.

Social Conditions. With his wife he lives in a 2 room and kitchen house which is comfortable.

Present Condition. Pulse 90. Temperature 98.2. Respirations 20. He lies comfortably in bed in any decubitus and is of spare build and a sallow complexion.

The sclera of the eyes appear jaundiced. He does not appear to have lost weight, his skin is dry and smooth, the mucous membranes are very pale, and his voice is hoarse.

(a) Cardio-vascular System. The pulse rate is 90 per minute, regular, normal tension and volume. The apex beat could be seen and felt in the 6th intercostal space, ½" within the mammary line. Boundaries of the Heart. Upper border, 3rd rib; right border - left sternal line; left border 10 cms. from the mid-sternal line. On auscultation the heart sounds are normal.

(b) Respiratory System. The chest is symmetrical, normal excursion with respiration. The lungs are resonant in percussion and the R.M. is vesicular.

(c) Nervous System. There is no disturbance of the motor, sensory or vaso-motor systems. The plantar reflex is flexor, the K.J., arm jerks and abdominal reflexes are brisk. The eyes react normally to light and accomodation. The special senses are normal.

(d) Digestive System. His lips are pale, has a set of false teeth; the spleen is barely palpable; the liver is normal, and nothing abnormal could be felt in the abdomen.

(e) Genito-Urinary System. This is quite normal. The urine is amber coloured, acid, S.G. 1018, no abnormal constituents.

(f) Blood Examination. The Wassermann Reaction is negative. A blood film showed anisocytosis, poikilocytosis, megaloblasts and polychromasia.

Red Blood Cell count, 1,820,000

White Blood Cell count, 6,800.

Haemoglobin. 50%

C.I. 1.36.

Treatment.

Ventriculin. Daily.

4.9.29. ℞ Acid Hydrochlor dil 3vi.

Aqua. 3vi.

Sig 3ii. with food.

Diet. Milk.

Puddings, tea, toast.

11.9.29. Light diet.

CASE 10

HAEMATOLOGICAL CHART.

Name 3.9.24

J. M.

male

Age

61

Disease

Pernicious Anaemia

Notes

Ventriculin given daily

DATE	3/9/24	10/9/24	17/9/24	24/9/24	1/10/24	8/10/24	15/10/24	22/10/24	29/10/24	6/11/24	10/11/24
POLYMORPHONUCLEAR NEUTROPHILS	59	62	60	64	62	59	64	62	65	67	70
" EOSINOPHILS	1	2	1	3	2	2	2	4	3	4	4
LYMPHOCYTES, SMALL	28	24	27	26	24	26	23	21	22	20	19
" LARGE MONONUCLEARS	4	3	2	2	3	4	3	5	2	3	2
MYELOCYTES, NEUTROPHILS	7	6	8	4	7	7	6	7	8	5	4
" EOSINOPHILS	1	3	2	1	2	2	2	1	2	1	1
NUCLEATED RED CELLS											

Differential Count per cent.

RED CORPUSCLES – BLACK HAEMOGLOBIN – RED (Green) LEUCOCYTES – BLUE (Violet) RETICULOCYTES

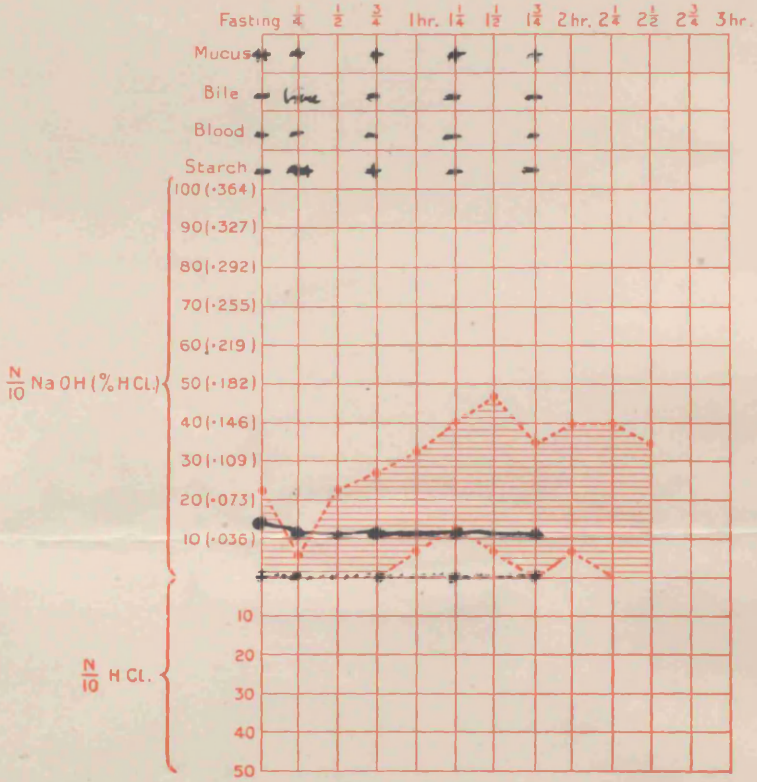
Designed by Edward Turton, M.D., B.Sc., M.R.C.P., Hull.

ASE 10

GASTRO-INTESTINAL ANALYSIS.

Name of Patient J. M *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 3·9·29



Fasting Juice.

Volume. 5 ccs

Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

————————represents total acidity.

Summary.

2. FÆCES.

DOWN BROS. LTD. LONDON.

CASE 10

GASTRO-INTESTINAL ANALYSIS.

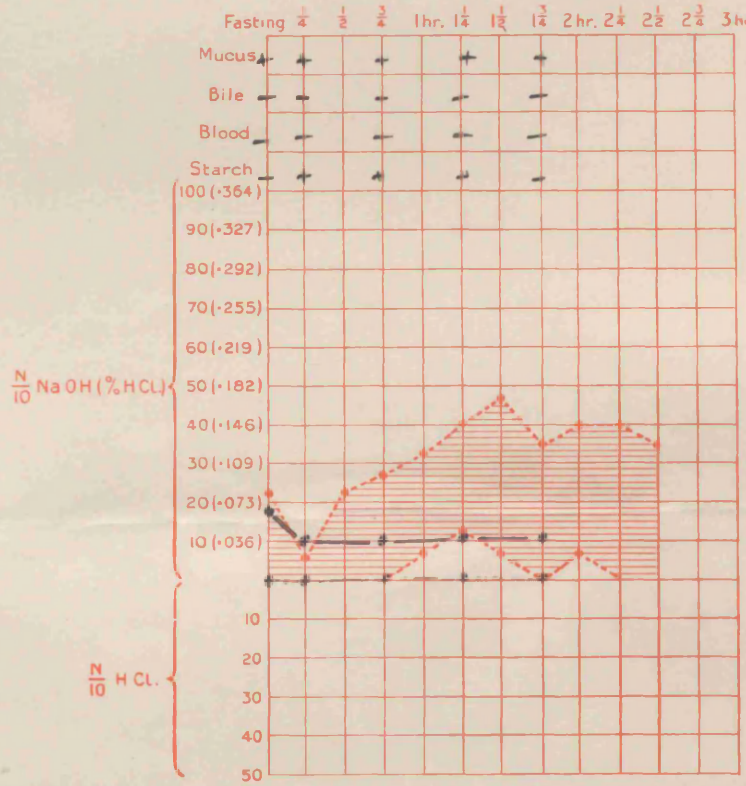
Name of Patient J. M. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 7. 11. 29

Fasting Juice.

Volume.

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

———— ————represents total acidity

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 11.

A.D. Male. Occupation. Carpenter. Age 39 years. Single.

Complaint. Of weakness and tingling of the legs and feet.

History of Present Condition. The patient noticed that about a year ago that he had a peculiar sensation in his feet when walking as if he were "walking on velvet". He felt uncomfortable when ascending or descending stairs but he did not stumble even in the dark. These symptoms commenced insidiously and later developed a tingling sensation in his legs and feet. These symptoms persisted and he consulted me about it.

History of Previous Illness. He has always enjoyed good health and has never been abroad.

Family History. His parents are alive and well and so are his two sisters and brother. An uncle (by marriage) had died of "anaemia". There was no history of familial nervous disorder.

Social Conditions. He lives with his parents in a 3 room apartment which is comfortable.

Present condition. 5.2.28. Pulse 80. Temperature 98.2. Respirations 20. He appears healthy, well nourished, good colouring of his skin, has a set of

false teeth and his hair is turning gray. No enlarged glands felt.

(a) Nervous System. There was no motor disorder nor tremor, and has no paralysis and has normal strength. The gait was steady and he puts his feet down deliberately but it was not abnormal. He is apt to sway when standing with his eyes closed. There is no wasting or hypertrophy of nay muscle. Nystagmus is absent and the eye muscles are normal.

Sensory disorders were only present in the feet. Thermal, tactile, and pain senses could not be fully appreciated especially on the soles of the feet. The plantar reflex was flexor, the knee-jerks and abdominal reflexes were exaggerated; the arm jerks were normal, and the eyes reacted to light and accomodation. The special senses were normal and so were the cranial nerves.

(b) The circulatory, respiratory and genito-urinary systems were normal. The digestive system was normal on physical examination, but a fractional test meal revealed complete achylia.

(c) Blood Examination. The Wassermann Test was negative. A blood film revealed a normal picture.

Red Blood Cell Count, 5,200,000

White Blood Cell Count, 6,000

Haemoglobin, 88%

Treatment. A mixture containing arsenic, and hydrochloric acid and pepsin was prescribed, along with massage of his feet.

Subsequent History. Monthly examinations were made with very little change in the paraesthesia of the feet.

Blood Examination. (6.7.28) The Wassermann test was negative. A blood picture showed slight anisocytosis and poikilocytosis.

Red Blood Cell Count, 5,120,000

White Blood Cell Count, 6,090.

Haemoglobin, 90%

Gastric Anchysis. Revealed a complete achylia.

Treatment. Recognising the case as an early pernicious anaemia with subacute combined degeneration of the cord. ½ lb. of cooked liver was ordered daily in addition.

7.9.28. The blood picture became normal. The gastric achylia persisted, and the paraesthesia had disappeared entirely.

10.12.28. The patient kept well and there was no sensory disturbance. He was now taking ¼ lb. liver daily.

17.5.29. He is now in a satisfactory condition. Blood examination is normal. ¼ lb. liver is taken daily.

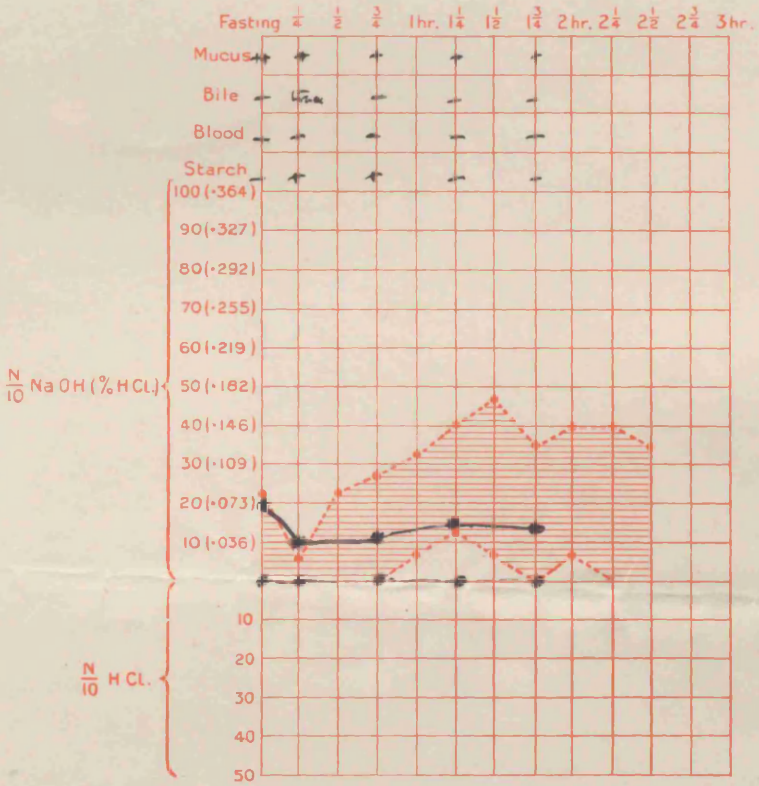
8.4.30. Paraesthesia still absent. Blood picture and count normal. Liver extract is taken daily. Achylia gastrica found on giving test meal.

ASE II

GASTRO-INTESTINAL ANALYSIS.

Name of Patient A-D. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 5.2.28



Fasting Juice.

Volume. 8

Cells.

One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

.....represents free HCl.

———·———represents total acidity

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Case 12.

J.McN. Male, age 48. Occupation. Labourer. Married.

Complaint. Of numbness of the right hand and both feet of three years duration.

History of Present Illness. This disturbance of sensation commenced insidiously about three years ago. At first it did not trouble him but for approximately 5 months it became worse and was associated with weakness of the right hand.

History of Previous Illnesses. As a child he had measles and chicken pox. Five years ago in January 1924 he had an attack of influenza which caused him to be off work for six weeks.

Family History. His father died of a "seizure", his mother of old age. Two brothers and two sisters are alive and well. One brother died from pneumonia. There is no family history of a blood or nervous disease.

Social Conditions. With his wife and three sons he lives in a 2 room and kitchen house which is dry and in a good state of repair. He obtains his meals regularly, drinks about four pints of beer a week, and smokes 2 ozs. of tobacco.

Present Condition. 25.9.29. Pulse 74. Respirations, 22. Temperature 98. He is well built and has a 'ruddy' complexion. His gait is steady and firm, though after walking for about 200 yards he feels tired. The mucous membranes are normal, the skin is white and of good consistence. No enlarged glands could be found.

(a) Nervous System. There is a degree of weakness of the right hand. There is no paralysis nor atrophy. No ocular palsy could be found and no nystagmus. The thermal and tactile senses are absent in the soles of the feet.

The eyes reacted to light and accomodation; the arm jerks, superficial abdominal reflexes, the knee-jerks and ankle jerks were present; the plantar response was flexor. Ophthalmoscopic examination was normal.

(b) The circulatory, respiratory, digestive, and urogenital organs were normal. The urine was highly coloured, S.G. 1022, acid, and contained urates. Gastric analysis after a test meal showed achylia.

(c) Blood Examination. The Wassermann Test was negative. A blood picture was found normal.

Red Blood Cell Count, 4,980,000

White Blood Cell Count, 6,400

Haemoglobin, 85%

Treatment. Pepsin, hydrochloric acid, and arsenic was given with an improvement which only lasted 2 months.

Subsequent History. Monthly examinations of the blood and gastric contents were made. On 27.2.30 a blood film definitely showed anisocytosis. A blood count was normal. Liver extract equivalent to ½ lb was given with a return of a normal blood picture and a disappearance of paraesthesia.

28.5.30. The patient feels quite well and takes liver extract daily. The blood examination was normal and achylia gastrica was still found.

CASE 12

GASTRO-INTESTINAL ANALYSIS.

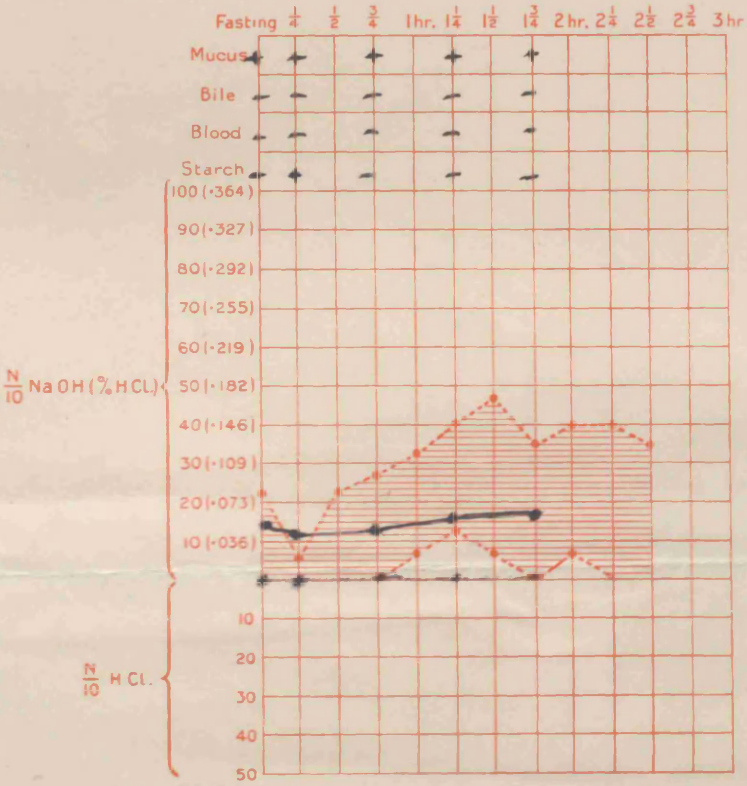
Name of Patient J. McN. *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 26.9.29

Fasting Juice.

Volume 3

Cells.



One Hour Fraction

Free HCl.

Active HCl

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

———— represents total acidity.

Summary.

2. FÆCES.

DOWN BROS., LTD., LONDON.

Comment.

In the series of twelve cases all improved with treatment. Cases 1,2,3,4,5,6,7, and 9 responded to liver or its extract. It has been found that the extract was as effective, easier to take, and as economical as whole liver. In cases 7 and 10, Ventriculin, a desiccated preparation of hog's stomach, produced good results. Cases 11 and 12 are taken from a series of cases where persistent paraesthesia of the hands or feet or both was investigated. These patients (11 and 12) as well as the rest of the series were examined cytologically and the stomach contents analysed. Both the cases were early pernicious anaemia and subacute combined degeneration and yielded to liver therapy.

It is very important that all cases of persistent paraesthesia of the hands and feet should be thoroughly examined and a cytological examination and a fractional test-meal performed. The possibility of early subacute combined degeneration must be remebered.

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