general and pulmonary condition in 1932 was normal; one child had had no symptoms, but there were signs of fibrosis at the base of one lung following collapse of the lower lobe, which was recognized in 1930 but for which no definite cause was ascertained on investigation; one had had no symptoms, but his general condition was poor, although there were no definite abnormal physical signs; one had bronchitis when the second test was done; one had rheumatic myocarditis at the time of the second test, but had had no pulmonary symptoms during the two years, and there were no abnormal signs in the lungs in 1932; one had enlarged and unhealthy tonsils in 1932, but was otherwise healthy; and one had slightly enlarged discrete cervical glands, which had remained unaltered since 1930. Three children under 5 years of age, who were positive in 1930, cannot be traced.

None of the children examined was ill, and with one exception their general condition was good. Although the numbers are small, it is interesting to note that of these twenty-four children under 5 years (two of whom were under 2) who had been infected with the tubercle bacillus none had had an acute dissemination of the disease, and none, except perhaps the child with cervical adenitis, had clinical tuberculosis.

CONCLUSIONS

The results of the repetition of the tuberculin test on 700 children whose ages varied from 1 to 15 years at the time of the first test show that allergy, once it is produced, persists in over 96 per cent. of cases throughout childhood.

A comparison of the different dilutions of old tuberculin which will produce a positive tuberculin reaction demonstrates the fact that there is a tendency for the degree of sensitivity to increase after an interval of one and a half to two years. Further, on separating the children into contact and non-contact groups, it is evident that a high degree of sensitivity in contact children is reached at an early age, whereas in a large percentage of non-contact children this degree of allergy is not reached at any age.

The absence of any development of clinical tuberculosis in 700 children during the period of one and a half to two years is interesting, more especially as this number includes two children of 1 to 2 years of age and seven under 3 years. That these children have remained apparently healthy throws doubt on the view which is held by some authors that a positive tuberculin reaction in a child under 2 years of age is evidence of active tuberculous disease.

SUMMARY

1. After an interval of one and a half to two years 700 children, 164 of whom were contact cases, were retested with tuberculin with the Mantoux method, and were examined for signs of tuberculosis.

2. Investigation has shown that in over 96 per cent. of cases positive reactors have remained positive after an interval of one and a half to two years. The change from negative to positive reaction, in at least thirty-one out of fifty-four cases, took place without any notable disturbance to the health of the child.

3. By using dilutions of 1 in 10,000, 1 in 1,000, and 1 in 100 O.T. it was shown that there is a tendency for the reactions to occur with higher dilutions of O.T. after one and a half to two years' interval.

4. Seven of the 700 children had pulmonary tuberculosis when first examined, but had improved in 1932. Of the remainder none has developed clinical tuberculosis. This number includes twenty-four who were under 5 years when first positive to the tuberculin test, and of these two were under 2 years of age.

We wish to express our thanks to the honorary medical staff of the hospital for permission to make use of their cases, and to the lady almoner, Miss Marx, for valuable help in tracing the children.

SEVERE ANAEMIA WITH ACHLORHYDRIA*

BY

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We come across three different clinical forms of severe anaemia associated with the absence of free hydrochloric acid from the gastric juice: (1) pernicious anaemia; (2) anaemia associated with carcinoma of the stomach; and (3) a form of anaemia of secondary type associated with neither of the above conditions.

I

Pernicious anaemia shows all the characteristic signs and symptoms met with in severe anaemia due to any cause. But it may or may not show, in addition, certain other features affecting the alimentary tract, as sore tongue, nausea, vomiting, and diarrhoea, or the nervous system as postero-lateral sclerosis. But the final decision must rest on the blood examination, and this is characteristic and absolutely diagnostic. There is great diminution both of the red corpuscles and of the haemoglobin, but the special feature is that the red corpuscles are proportionately more reduced than the haemoglobin, so that each corpuscle on the average contains *more* haemoglobin than does a normal red corpuscle. This is expressed in the statement that the colour index is above 1. Accordingly on examining a film it is recognized that on the average the corpuscles are larger than normal. This may be confirmed by an elaborate process of measurement, though this is rarely necessary. The presence of these large corpuscles, macrocytes, is a characteristic feature of the anaemia, and is found in no other condition, except certain unusual and rarely met with conditions. There is also marked variation in size. In addition to the macrocytes, microcytes—corpuscles smaller than normal—are encountered, and their presence makes the macrocytic condition more strikingly evident than even the raised colour index would indicate. In addition to this macrocytosis and anisocytosis there is marked departure from the normal shape—poikilocytosis—and the corpuscles may be oval or pear-shaped or depart still more from the normal rounded form. It is not that an occasional corpuscle here or there departs from its natural form (that may happen in any kind of severe anaemia), but that the great majority do so, and one may have to look carefully for any of the normal round shape. This tendency for the corpuscles to be oval† instead of round is one that I have emphasized for a long time back, and is sometimes even more striking than the large average size. There are other departures from the normal—the presence of nucleated and abnormally staining red corpuscles, departures from the normal proportions of the various forms of leucocytes, and diminution of the blood platelets—but the features of the red corpuscles that I have already described are the most important, and are in themselves diagnostic.

A good many patients with pernicious anaemia appear to digest their food well and maintain their body weight. But on looking through my record of cases over the last twenty or thirty years I come across a fair number of patients with pernicious anaemia in whom anorexia or complete loss of any inclination for food was present. This is a symptom that one had commonly come to associate with absence of free hydrochloric acid from the gastric juice, and accordingly in these patients I was accustomed to use medicinal doses of hydrochloric or

* Post-graduate lecture, Manchester Royal Infirmary, November 29th, 1932.

† On showing a film of his patient's blood to one practitioner, who had a clear recollection of his biological days, he exclaimed, "Why! it's just like frog's blood."

nitro-hydrochloric acid in the treatment. But it was only a comparatively small proportion of the cases that showed these symptoms, and it was only in these occasional cases that one judged, on clinical grounds, achlorhydria to be present. Of recent years, however, since direct chemical investigation by fractional test meals has become more common, it has been demonstrated that *all* cases of pernicious anaemia, practically without exception, have complete achlorhydria, although only a minority of them show that anorexia which one commonly associated with achlorhydria. It proves, in point of fact, to be complete achylia gastrica—that is, there is absence of pepsin as well—and it seems remarkable that so many of these patients are able to digest and assimilate their food as well as they do.

II

The anaemia associated with carcinoma of the stomach closely resembles that of pernicious anaemia, and on ordinary clinical grounds there is great difficulty in discriminating between the two. They both commonly show symptoms of severe anaemia associated with gastric symptoms, pain after food, nausea, vomiting, and anorexia, of varying severity. If there is a history of sore tongue or of nervous symptoms the diagnosis of pernicious anaemia is indicated, but these symptoms are by no means always present.

It is becoming more and more fully recognized how frequently these two conditions have, in past years, been confused. I can recall most vividly a patient being picked out in the wards of a Poor Law hospital as a typical case of pernicious anaemia by one of our leading physicians to be utilized in an examination in clinical medicine. It was only when the blood was examined actually in the examination room that the true nature of the condition was demonstrated, and this was confirmed by necropsy a few months later. And the confusion, in either direction, may lead to most serious and regrettable results. I can recall not a few cases of carcinoma of the stomach that have been treated for long periods as being cases of pernicious anaemia, naturally without avail. In some of these I have seen the patient with the diagnosis already made for me (maybe on the word of a clinical research laboratory) in the hopeful expectation that I should be able to advise a line of treatment that would lead to amelioration and cure, and when I came to investigate it the case proved to be rather one of carcinoma of the stomach, and I was obliged to give the expectant friends an absolutely hopeless, instead of a hopeful, prognosis. And, moreover, valuable time had been lost during which perhaps surgical treatment might have been of some avail. On the other hand, cases that have really been pernicious anaemia have been regarded as carcinoma of the stomach and, in the feeling that nothing could be done for them in consequence, they have steadily got worse without the effective and successful treatment that was available having received a trial.

And yet a suitable blood examination will conclusively discriminate between the two conditions and remove any possibility of confusion. The two are, from the point of view of the type of anaemia, diametrically opposed. In carcinoma the haemoglobin is reduced to a greater degree than the number of red corpuscles. The colour index therefore is below unity, often only 0.5 or 0.6. The red corpuscles accordingly are on the average smaller than normal; they appear thin and washed out. The majority of the corpuscles are of even size and of the normal round shape; there may be some variation in size and shape, but it is insignificant compared with the degree of variation met with in pernicious anaemia. The leucocytes are commonly somewhat increased (as compared with a leucopenia), and there is often a high percentage—12 to 15 per cent.—of large mononuclears, and the blood platelets are

increased instead of being greatly diminished or absent as in pernicious anaemia.

The characters of the red corpuscles stamp the condition as typically a microcytic anaemia, as also is the anaemia of chlorosis and of all forms of secondary anaemia, and indeed of all forms of anaemia, with insignificant exceptions, other than pernicious anaemia. The slides that I show you now of the blood in pernicious anaemia, in the anaemia of carcinoma of the stomach, and in other forms of secondary anaemia will clearly demonstrate this.*

It appears to be cases of carcinoma at the *cardiac end* of the stomach that produce the most profound degrees of anaemia, and further, as the pylorus is not obstructed, the gastric symptoms, pain and vomiting, are often comparatively inconspicuous, and any tumour is concealed under the edge of the ribs and may not be palpable until the very late stages.

As the result of accumulated experience of these two types of anaemia one came to assume with considerable confidence that cases of severe anaemia with gastric symptoms in which the blood examination did not reveal the features of pernicious anaemia, especially in elderly persons, were to be regarded as carcinoma of the stomach. And in the main the further course of the illness, the resistance to treatment, and the steady progress to a fatal termination, with or without necropsy, confirmed the correctness of the diagnosis. With the advance of x-ray examination of the stomach the detection clinically of early carcinoma was rendered easier, and occasionally (unfortunately only too seldom) surgical intervention was possible, with greater or less success.

III

But as time went on and numbers of cases accumulated, occasional exceptions to this generalization began to be noticeable. Patients with severe anaemia were seen with the blood showing the features of a secondary type and not of pernicious anaemia, who had gastric symptoms and complete achlorhydria, but who showed no evidence of carcinoma of the stomach on x-ray examination, and who, instead of getting steadily worse and dying, made a more or less complete recovery under medicinal treatment. And it is especially of recent years, when a routine investigation of the gastric activity in all cases of severe anaemia has become more common, that the frequency of the condition has become to be generally recognized. But the recognition is, in point of fact, by no means of recent date. As far back as 1909 and 1913 a number of cases were very completely described by Knud Faber, and since then many writers, particularly in Scandinavian literature, have described cases, and these have been well summarized in a recent paper by E. Meulengrath. The condition has attracted less attention in this country, and in spite of its long recognition has hardly obtained entry to our textbooks. The name which has been most commonly applied to the disease has been "simple achylic anaemia," but the term "simple achlorhydric anaemia" has been suggested as more accurate, since though the absence of hydrochloric acid is well established it is not quite so definitely proved that pepsin is always absent from the gastric juice.† Witts, in a recent paper, has described cases that have come under his care under the heading of "chronic microcytic anaemia." The term is an

* The lecture was illustrated by a series of lantern slides of the blood in various forms of anaemia.

† The meaning of the word "achylia" presents some uncertainty. If it is translated as "absence of chyle" it can have no true relation to any process of gastric digestion, since the chyle is the product of digestion in the small intestine. If it is translated more literally as "absence of juice" then achylia gastrica would signify absence of the gastric juice. Einhorn appears to have used it as connoting absence of the ferments of the gastric juice, which is certainly not what it means literally. If we use it to denote absence of the specific digestive power of the gastric juice it would cover an absence of ferments or acid, or both.

unfortunate one, since, as I have said, with rare exceptions all cases of anaemia, other than pernicious anaemia, are microcytic, and to appear to limit the term to one specific form seems to me inaccurate and unscientific. I see no adequate reason to depart from the established and sufficiently accurate name "simple achylic anaemia."

The condition is met with much more commonly in women than in men, usually between the ages of 30 and 50, and in some it is associated with varying degrees of menorrhagia. So far no features of the blood have been described which would distinguish it from any variety of severe secondary anaemia. The treatment is generally straightforward and satisfactory. Full doses of iron, with or without hydrochloric acid and pepsin, usually produce rapid amelioration. Ferri et ammon. cit. in doses of 20 to 30 grains three times a day has been the form I have employed. This is in my experience the blandest and most easily taken form of iron, but it has long been recognized that it must be given in full doses, and that doses of less than 20 grains are much less effective in bringing about an improvement. I have tried the addition

of small doses of copper and manganese without any apparent benefit, but small doses of arsenic and of digitalis do appear to increase the effectiveness of the iron.

I should like to add that preparations of liver and of stomach have no special effect in these cases. In pernicious anaemia there is a definite and rapid response on the part of the bone marrow to treatment with these preparations as shown by the appearance of a high proportion of reticulocytes in the blood, but these cases of simple achylic anaemia show no such reticulocyte response to treatment with liver or stomach. I resent the action of some of our manufacturing chemists in pushing on the market special and expensive combinations of liver and stomach with iron for the treatment of such cases, which are no more effective than the simple and inexpensive pharmacopoeial preparations.

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CONGENITAL ABSENCE OF THE VAGINA

BY

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Operative measures for the formation of an artificial vagina are undertaken either to rectify a congenital abnormality or to reconstruct a vagina in cases where the natural canal has been destroyed as a result of parturition or consequent upon inflammation.

The purpose of this paper is to record a case of congenital absence of the vagina which I have had the opportunity of treating. These cases are so few in number that the recording of every example is important as an aid to surgeons confronted with a similar problem.

The patient was a woman 32 years of age, of normal appearance. Until her marriage four years previously she was unaware of any abnormality beyond the fact that she had never menstruated. She had regular monthly menses, but no menstrual flow. After marriage the impossibility of coitus became apparent, and resulted in domestic unhappiness. This finally caused her to consult her family practitioner, who discovered the abnormality. He invited me to see the patient with a view to rectifying the condition if possible.

On examination one found that the secondary sexual characteristics were normal, as were also the external genitals. When the labia were separated a small depression, suggesting in appearance and position an imperforate hymen, was seen. There was no evidence of haematocolpos. On rectal examination no cervix uteri could be felt, and no further information regarding the uterine

adnexa was obtained. The probability of the absence of the vaginal canal, and the proposed method of forming a vagina, with the operative risks and ultimate possibilities, were explained to the patient, who readily gave consent to the suggested procedure.

Three methods of forming an artificial vagina have been described and performed with varying degrees of success. (1) Turning in pedicled flaps of skin. This method carries the minimum risk, but the subsequent contraction of the new canal makes it the least satisfactory. (2) The method described by Schubert of adapting a portion of the rectum. (3) The method described by Baldwin in 1904, and successfully performed by him in 1907, of utilizing a loop of small intestine. From a survey of the literature

this appeared to me to give the most satisfactory permanent results, and was therefore employed in this case.

The operation was carried out as follows. The patient was first placed in the lithotomy position and a transverse incision made between the labia minora. The cellular tissue between the rectum and bladder opened up easily, but there was no trace of a vaginal canal. This separation was carried out to the highest possible point. A pair of long artery forceps was then intro-

duced into this space, and fixed securely in position by packing gauze round it. The position of the patient was then changed to the Trendelenburg, and the abdomen was opened by a median subumbilical incision.

The first striking feature found intraperitoneally was that the left kidney was lying on the brim of the true pelvis. This abnormality is mentioned by Pemberton as being present in several of the cases recorded; he suggests, therefore, a preliminary cystoscopy with ureter catheterization and x-ray examination to ascertain the location of the ureters. On examining the pelvic viscera the ovaries were

FIG. 1.—Shows the method of drawing down the isolated loop of ileum. The end of this loop is shown open, and the other closed by suture. In the actual operation both ends were closed before the loop was drawn down; the continuity of the bowel had also been restored before this stage was reached.

FIG. 2.—Shows the operation completed.