Observations ON CHRONIC SPLENOMEGALY IN CHILDHOOD: DIAGNOSIS AND TREATMENT.*

BY
ROBERT HUTCHISON, M.D., F.R.C.P.,

Physician to the London Hospital, and to the Hospital for
Sick Children, Great Ormond Street.

BEFORE proceeding to the differential diagnosis of the various splenomegalies of childhood, it is advisable to make sure that the abdominal tumour in question really is an enlarged spleen. Usually this is easy enough, but sometimes one is in doubt, especially as to the possibility that the tumour may be an enlarged left kidney or suprarenal. Sometimes the ordinary diagnostic criteria—that a large spleen does not extend back into the loin, that it has a sharp edge with a notch, that it crosses the middle line below the umbilicus, that the fingers cannot be passed between the tumour and the ribs, that the descending colon does not lie in front of it—all fail, and in that case it is important to remember that dullness extending above the level of the ninth rib in the mid-axillary line is in favour of the tumour being splenic. An x-ray examination, with pyelography if necessary, may help in the differentiation. I would only repeat that the difficulty of telling a splenic from a renal tumour is sometimes a real one, and that the methods of distinguishing them are worth discussion.

Having settled that the tumour is an enlarged spleen, it is necessary, before proceeding farther, to have some sort of classification of the different varieties of splenomegaly met with in childhood. The only satisfactory classification would be an etiological one, but of that our present knowledge does not allow, and I therefore propose, for purposes of discussion, to consider the subject under certain broad groups.

1. Tumours (Cysts, New Growths, Abscesses, etc.).

These are very rare, and for practical purposes undiagnosable. If diagnosed, the proper treatment, of course, would be surgical.

2. Chronic Infections.

Of these we have to consider tuberculosis, syphilis, lymphadenoma, and chronic sepsis.

In chronic tuberculosis splenomegaly is not likely to be the "presenting" sign, although in the acuter forms of tuberculosis in young infants enlargement of the spleen is very common. Cases are described, however, though I do not remember to have seen one myself, in which massive caseating tuberculosis leads to considerable splenomegaly. The spleen in such cases may be tender, and polycythaemia and some degree of cyanosis are said sometimes to be present. There will often, of course, be less conspicuous tuberculous lesions elsewhere. The proper treatment is splenectomy.

The relation of congenital syphilis to splenomegaly in childhood is very important, but I would suggest, for purposes of discussion, that its frequency as a factor in causing the condition tends to be exaggerated. After all, inherited syphilis is a comparatively rare disease, and so we may say that, although syphilis certainly very often leads to splenomegaly, yet not many cases of splenomegaly are due to syphilis. It is in infancy that a syphilitic enlargement of the spleen is most likely to be met with, but there is reason to believe that in later childhood—say, between the ages of 5 and 7—splenomegaly may be the only sign of a syphilitic taint, and it appears again about the age of puberty in association with syphilitic cirrhosis of the liver. In the pre-Wassermann days the tendency was to ascribe every splenomegaly of doubtful origin to syphilis, but since the introduction of that test I have been impressed by the frequency with which it is found to be negative in these circumstances. I am aware that in some undoubtedly syphilitic cases—in syphilitic cirrhosis, for instance—the

Wassermann reaction may be negative, and we might well discuss what degree of confidence we can place in it as a criterion of the presence or absence of a syphilitic taint. I would only point out that it is, after all, the only positive test we have in a case in which unmistakable objective signs of the disease are wanting, and if we are not to be able to trust it the whole question of the relation of syphilis to splenomegalies of obscure origin in childhood goes back into the melting-pot. It is all the more important that we should have some trustworthy test for the presence of syphilis, inasmuch as it has been suggested by Dr. Parkes Weber and others that an inherited taint may form a basis on which enlargement of the spleen—though not primarily due to syphilis—may develop more easily, or in a more exaggerated degree, than it does in a child whose heredity is not thus burdened. Although this view seems to me rather speculative, it would be of interest to have opinions upon it.

Where syphilis is believed to be the cause of a splenomegaly, vigorous antisyphilitic treatment must, of course, be adopted. In some cases, however, the changes in the spleen may have proceeded so far that they are unaffected by any form of drug treatment, and in that case splenectomy may be justifiable.

Lymphadenoma as a cause of enlargement of the spleen, without there being evidence of the disease in the glands, must be very rare. For my own part, I have never met with an instance of it, though cases have been described by others,¹ and I do not see how it can be diagnosed with certainty. If diagnosed, the appropriate treatment would be the application of x rays to the tumour.

Chronic sepsis has been put forward as a cause of splenomegaly, as of most other things. Dr. Gordon Ward,² for instance, regards it as of considerable importance, though I think on rather insufficient grounds. That splenomegaly may be the presenting sign in cases of very chronic infective endocarditis (*endocarditis lenta*) is certain, but I doubt if cases of this very chronic type are ever met with in childhood; and of "intestinal sepsis" as a cause of enlarged spleen we know nothing.

3. Tropical Splenomegalies.

Chronic protozoal infections, as in malaria and kala-azar, may cause great enlargement of the spleen in children, but as the diagnosis and treatment of these diseases is the same as in adults we need not discuss them.

4. Splenomegaly in Metabolic Diseases.

We have here chiefly to discuss the part played by rickets. This has been almost as much disputed as the role of syphilis in producing splenomegaly, and, I believe, fully as much exaggerated. That severe rickets tends to be accompanied by some degree of enlargement of the spleen is undeniable, though in some cases the organ is not so much enlarged as pushed down by deformity of the ribs; but I would suggest, for purposes of discussion, that rickets alone is not an important factor in the production of splenomegaly, especially nowadays. The same may be said, with even greater truth, of waxy disease, which we need rarely think of when the nature of an enlarged spleen is under discussion.

5. Gaucher's Disease.

Gaucher's disease should, I suppose, now be included under the metabolic disorders associated with splenomegaly. It is rare, though probably not so rare as is believed, and is to be diagnosed by its familial, though not hereditary, incidence, and, above all, by the demonstration of the characteristic endothelioid cells in the product of a splenic puncture.³ Opinions as to the value of splenectomy in the Gaucher cases are divergent. The operation cannot certainly be regarded as a cure, seeing that the disease is one which is not confined to the spleen, but affects the whole reticulo-endothelial system throughout the body. If the splenic tumour is causing local discomfort, however, its removal would appear to be justified.

6. Splenomegaly in Diseases of the Blood.

We have here to consider the leukaemias, splenic anaemia of infancy (anaemia pseudo-leukaemica infantum of von Jaksch), acholuric jaundice, purpura, and erythraemia.

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The *leukaemias* we may dismiss in a word. In childhood they are almost always acute, and therefore not a cause of chronic splenomegaly. I have only once seen a case of chronic myeloid leukaemia in a child—a boy of 12—and for practical purposes leukaemia as the cause of a chronically enlarged spleen in childhood need not be considered. If suspected, a blood count would at once establish the diagnosis.

The *splenic anaemia of infancy* is in an altogether different category. It used to be relatively common, and when I was giving the Goulstonian Lectures twenty-five years ago I had no difficulty in collecting notes of a large number of cases, all of which had been under my own observation. In recent years, however, it has become rare, and I have not seen a typical case now for a long time. I do not propose to discuss the nature of this disease, and whether it is merely the result of a haemopoietic reaction to various debilitating influences in childhood, or whether it is—as I at least hold—a disease *sui generis*. For our present purpose it is sufficient to point out that it should not be diagnosed after the age of 3, although it is true that the enlarged spleen may persist beyond that age, when the anaemia has passed off, before gradually disappearing. In that case, however, there should be a clear history of the disease in the earlier years. The blood picture in the acute phase is characteristic.

In considering the treatment of this form it is to be remembered that the disease tends to spontaneous recovery in the great majority of cases, given suitable hygienic measures. I do not myself consider that splenectomy is ever called for in it, as the operation must be highly dangerous in the severe forms and is unnecessary in the milder. Some successful cases have, however, been reported by Ashby and Southam,⁴ but I think it probable that these would have recovered without operation. Whether x-ray treatment is of any use I am not sure. In the few cases in which I have tried it the results have been disappointing, but others⁵ have been more fortunate. At least, it cannot do any harm.

I need not say much about the splenomegaly of *acholuric jaundice*; it is now well recognized as a not uncommon occurrence, and the diagnosis can be established with certainty from the characteristic increased fragility of the red cells. There is also no doubt that splenectomy is the only effective form of treatment.

In *purpura*—even in the chronic forms—splenomegaly is not likely to be the presenting sign, and I only mention it here because in that variety of the disease in which the platelets are greatly diminished removal of the spleen is now generally agreed to be very beneficial.

I doubt whether true erythraemia (Osler-Vaquez disease) is ever a cause of chronic splenomegaly in childhood, but it is interesting to note that polycythaemia is sometimes a feature in cases of syphilitic splenomegaly.⁶

7. Splenomegaly Associated with Cirrhosis of the Liver.

We now come to that interesting group of cases in which an enlarged spleen is associated with cirrhosis of the liver. Three forms of cirrhosis with splenomegaly—excluding for the moment Banti's disease—may be distinguished.

(a) *Idiopathic Non-alcoholic Progressive Cirrhosis* (Parkes Weber).⁷—This is a cirrhosis of unknown cause, which resembles the ordinary portal cirrhosis of adults, runs a fairly rapid course, and often terminates in haematemesis. The spleen is always enlarged to some degree, but in certain of the cases is so conspicuous and early a feature as to be the "presenting" sign, and these have been spoken of as cases of "splenomegalic cirrhosis," or cirrhosis with "splenic predominance." Their diagnosis from Banti's disease is not easy, and will be considered later, and whether or not they are suitable cases for splenectomy demands discussion. Some writers—Thursfield⁸ for example—maintain that the operation in these cases is almost invariably fatal, but I am not at all sure that this is true. In the following case, for instance, if, as I believe, it must be included in this group, splenectomy appeared to effect a cure.

The patient was a boy aged 12, who was admitted for bleeding from the gums with a history of always having bruised easily. His spleen was enlarged down to the umbilicus, and the liver

was easily palpable. The red cells numbered $4\frac{1}{2}$ million, with 70 per cent. of haemoglobin, and the white cells 1,600. The Wassermann reaction was negative, both in the patient and in his mother. Four months later he was readmitted with ascites. The spleen was removed, and at the operation the liver was found to be cirrhotic. Twelve years later he was in excellent health.

The question of splenectomy in these cases is, I repeat, one for discussion.

(b) *Syphilitic Cirrhosis with Splenomegaly*.—These cases are met with in later childhood about the time when interstitial keratitis and the other signs of "late syphilis" manifest themselves, and I have already said that there is reason to believe that they do not always give a positive Wassermann reaction, and that, if antisyphilitic treatment fails, removal of the spleen may be justified.

(c) *Splenomegaly with Biliary Cirrhosis*.—These are the cases described by Gilbert and Fournier,⁹ and are believed to be the form which Hanot's cirrhosis takes in the child. They are said to be characterized by the presence of a much enlarged spleen, recurring jaundice, finger-clubbing, and impairment of growth, but without ascites. Now I am very sceptical as to the existence of Hanot's cirrhosis at all, and still more sceptical as to the occurrence of such cases in the child. I once thought I had such a case—I have described it elsewhere¹⁰—but it proved *post mortem* to be a case of partial obliteration of the bile ducts, presumably of congenital origin. I shall, however, be interested to hear the opinions of others on the subject.

8. Splenomegaly the Result of Splenic Thrombosis.

That thrombosis of the splenic vein could cause enlargement of the spleen was denied by Osler,¹¹ yet there seems to be no doubt that it does happen. I have myself seen two cases in the adult in which this was proved at the necropsy to be the cause, and a case of it has been published by Parkes Weber.¹² Wallgren,¹³ in an important paper, has drawn attention to it as a cause of splenomegaly in children, and believes that it is commoner than is supposed, but that it has hitherto been confused with Banti's disease. He describes the leading features of the syndrome as splenomegaly, anaemia with leucopenia, and slight ascites. Sooner or later haematemesis sets in, and after a bleeding the volume of the spleen *shrinks*—this, he believes, does not happen after haematemesis in Banti's disease or in cirrhosis—and at the same time a temporary leucocytosis appears. The liver in all of his cases coming to necropsy was found to be normal.

He is of opinion that the thrombosis of the splenic vein is the result of trauma or of an "infection," and that it leads to engorgement of the spleen and dilatation of the veins at the lower end of the oesophagus, rupture of one of which causes the haematemesis, with temporary subsidence of the splenic tumour. Wallgren believes that the prognosis in these cases is bad unless splenectomy is performed.

I believe that the following case may be regarded as one of splenic thrombosis.

The patient was a boy aged 5. Two years before admission he vomited a teacupful of blood, and this was repeated one year later, and again one week before his admission to hospital. He had had no other illness except whooping-cough when he was 4. He was a pallid, weakly, but not ill-nourished child, with a "biscuit tinge" of skin. The spleen was palpable and the liver extended one inch below the costal margin. There were a few small palpable glands in the axillae. A blood count showed red cells 1,160,000, white cells 5,620, haemoglobin below 30 per cent. A few normoblasts were present. The differential count was normal. The Wassermann reaction was negative. Ten days after admission he vomited an ounce of bright red blood, and at the same time his temperature rose to 103° F. The white cells were at this time 12,000. There is no note as to the effect of the haemorrhage on the size of the spleen. He was transfused, but with only temporary benefit, and died two weeks after his admission.

At necropsy the spleen was four times the normal size, firm and tough. There was *ante-mortem* thrombosis of the splenic vein, and also recent clotting in some of the mesenteric veins. The liver was large, pale, not cirrhotic. There were a few small varices at the lower end of the oesophagus.

9. Splenic Anaemia of Adult Type and Banti's Disease.

It will be generally agreed, I think, that "splenic anaemia" and "Banti's disease" are to some extent diagnostic "rag-bags" into which are thrown all the cases of enlarged spleen that cannot be placed in any other category. None the less it will be admitted that cases to

which these terms are applicable have a real existence in the adult, and the question for us to-day is whether they are also met with in childhood. Now, seeing that the splenic anaemia of adults is of its essence a very prolonged disease, the final stage of which, when cirrhosis of the liver has supervened (so-called Banti's disease) is only reached after some years, it follows that Banti's disease at least is not likely to be met with whilst the patient is still a child. In spite of this I think the diagnosis "Banti's disease" is sometimes justified in childhood, as in the following case.

A boy of 12 was known to have had an enlarged spleen for five years. The liver was not enlarged. The blood count showed 2,750,000 red cells, 45.1 per cent. of haemoglobin, and 3,400 white cells. Wassermann test negative. Haematemesis supervened, after which the spleen was decidedly smaller for some days. There was no leucocytosis during or after the haemorrhage. Splenectomy was performed, and at the operation the liver "seemed to be the seat of early cirrhosis." His subsequent history is unknown.

The difficulty, of course, is to distinguish such cases from those of idiopathic cirrhosis "with splenic predominance," already referred to. It can only be done if the history shows that the spleen was enlarged for some years (as in the above case) before signs of cirrhosis supervened, for the cases of idiopathic cirrhosis seem to run their whole course in a comparatively short space of time. There is little doubt, too, that cases of splenomegaly due to splenic thrombosis must often have been included under the term "splenic anaemia or Banti's disease," and so, probably, have some syphilitic cases and some of acholuric jaundice.

It is sometimes asserted that the presence of leucopenia puts a case in the category of splenic anaemia rather than of idiopathic cirrhosis, but to this I cannot agree. In the case of idiopathic cirrhosis with splenic predominance which was described earlier in this paper, for instance, leucopenia was present, and my own view is that leucopenia tends to be a feature of most chronic splenomegalies, no matter of what origin, and that little diagnostic value can be assigned to it.

The treatment for splenic anaemia of the adult type, we should all agree, is splenectomy, but whether the operation is worth doing after cirrhosis has supervened—that is, in Banti's disease—is a matter for consideration.

In conclusion, I would suggest as the most important points for us to discuss: (1) the part played by syphilis and rickets in the production of chronic splenomegaly; (2) the nature of idiopathic cirrhosis with "splenic predominance" and its differentiation from Banti's disease; (3) the existence or otherwise of biliary cirrhosis with splenomegaly; (4) the frequency of splenic thrombosis as a cause of enlarged spleen and its diagnosis from other forms of splenomegaly; (5) the occurrence of cases of splenic anaemia of the adult type and its sequel, Banti's disease, in childhood.

As regards treatment, debate must chiefly centre round the question of splenectomy. As to this, I would agree with Dr. Leonard Parsons¹⁴ that the cases suitable for this operation are those which show a negative Wassermann reaction, no enlargement of lymphatic glands, and no characteristic leucocytic picture, but in which there is some degree of anaemia, associated with (1) leucopenia, or (2) increased fragility of the red cells, or (3) haematemesis. There may be difference of opinion, however, as to the advisability of removing the spleen in Gaucher's disease and in cases with cirrhosis of the liver, whether of the idiopathic or Banti variety, even although these fall within the limits of the above criteria.

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A full bibliography will be found in a paper by Sir Humphry Rolleston entitled "Diagnosis and Treatment of Splenic Enlargement in Children" (*British Medical Journal*, 1925, ii, 1099), which was the opening paper of a discussion on this subject in the Section for the Study of Disease in Children of the Royal Society of Medicine on November 27th, 1925.

AUTOTOXAEMIA AS A FACTOR IN THE CAUSATION OF PSYCHOSES.*

BY

PROFESSOR W. WEYGANDT, M.D.,
Hamburg.

In psychiatry, as in other spheres of medical science, the history of medicine unveils precursors of many a modern theory. The modern fever therapeutics of psychoses recall memories as far back as Hippocrates and Galenus.

In the course of the past century a great change has taken place in the doctrine of the cause of psychoses. Formerly the psychic cause was represented as the only, or at least the most important, one. As late as 1827 Heinroth disputed the fact that fever might be a cause of mental derangement; he emphasized that even in the case of alcoholism the moral origin of all mental disorders could be recognized, and that even in the case of injuries to the head the spiritual life must not be forgotten as a cause.

With the advances of normal and pathological anatomy of the central nervous system, however, the doctrine became more and more firmly settled that mental derangements are cerebral diseases, and that a morbid influence of the brain represents the cause of mental disorders. But the external causes were frequently overestimated. Forty years ago the cause of paralysis was regarded as lying in sexual excesses, overexertion, congestion, injuries to the skull, overheating of the skull, long-enduring shocks, alcoholism, becoming prematurely aged, the climacterics, interruptions or derangements in menstruation, together with certain psychical influences, such as excitement or grief.

Very gradually the doctrine of syphilis being the cause of paralysis opened up new paths of research, and its correctness was finally proved in 1911 by Noguchi tracing the *Spirochaete pallida* in the brain.

As early as 1889 Kraepelin taught in connexion with paralysis that numerous symptoms must be regarded as a direct consequence of the degeneration of certain trophic nerve tracts. In 1896 he described dementia praecox and general paralysis as metabolic diseases.

The later doctrine was accepted, but for all that derangement of the digestive processes is of material importance among the symptoms of paralysis; in this connexion syphilis of the organs must also be mentioned, as well as an increased tendency of the bones to fracture. As to the pathogeny, it is assumed by numerous authors that not only are the symptoms caused directly by the spirochaete, but that a number of these may also be caused by toxic agents produced by the spirochaetes. I regard the lipomatosis that frequently occurs in advanced stages of paralysis as a secondary metabolic derangement, the region of the hypophysis being disturbed by hydrocephalus internus, and abnormal adiposity being thus induced.

The doctrine that dementia praecox is a metabolic disease or autointoxication was based on corporeal symptoms and relations—for example, on changes in the reflexes, mechanical excitability of the facial nerve, mechanical excitability of the muscles, dermatography, a peculiar change in the skin, and possibly, too, on disorders in the thyroid glands, and the relations as regards puberty, menstruation, pregnancy, etc. Kraepelin also called attention to an hereditary disposition in 70 per cent. of the cases, and also to inherent symptoms of degeneration.

The realization by a large number of alienists that an endogenous cause of the disease must be assumed, above all, the study of nerve disorders based upon disease in the blood glands or the glands of internal secretion, has induced an intensive investigation of these factors for decades past. This biological observation and investigation of mental derangements is the more important because cerebral anatomy has not fulfilled the great hopes that were entertained in regard to it. Psychology, too, has not led to very satisfying results, either as regards experimental study or psycho-analysis.

* A paper read in opening a discussion in the Section of Mental Diseases and Neurology of the Annual Meeting of the British Medical Association, Cardiff, 1926.