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TWO CASES OF SPLENECTOMY FOR SPLENIC ANEMIA

A CLINICAL LECTURE, JAN. 21, 1920, TO THIRD-YEAR STUDENTS, TELLING
AN OLD STORY

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BOSTON

AND

A REPORT ON THE PATHOLOGIC CHANGES IN SPLENIC ANEMIA

(Written in 1900, but not Published)

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BALTIMORE

Gentlemen:—We went over together last week some patients with biliary disorders showing degrees of jaundice. One of them — Mary Jones, as you will recall — had a history of frequently recurring attacks of cholelithiasis over a period of nine years, but had never before been jaundiced. As her jaundice was rapidly fading, we arrived together at the conclusion that the common duct would be found free.

You saw the patient operated on subsequently by the resident, Dr. Cutler, and will remember that at an early stage of the procedure digital palpation led him to believe that there must be a stone in the common duct. After removing the gall-bladder, which was full of stones, he found that the impression of a deeper stone had been given to the finger by a pancreatic nodule which partly enveloped the lower portion of the duct.

It is well for you to bear in mind that this is not an uncommon observation, though less common now, I am sure, than in former days before it was pointed out — first by Mayo Robson, I believe — that chronic pancreatitis was a common accompaniment of cholelithiasis and often produced a degree of induration frequently mistaken on palpation, particularly through the inadequate openings then made, for malignant disease or for a large common duct stone.

Now, Mr. B——, will you tell me what you notice about this patient, named Alvin Landers, whom we may uncover for your inspection?

Third-Year Student.—"He appears to be jaundiced, but in his inguinal region there is a newly healed wound which suggests an operation."

Yes, he has a yellowish tint to his skin apparent also in his conjunctivae, quite unlike the color, as you will recall, of the gallstone cases you saw a week ago. But do you think this incision could have any relation to the skin discoloration, and, if not, what does it suggest to you?

Student.—"It looks like a recent hernia incision."

It is, I believe, and we will now hear the essential facts of his clinical story from Mr. A—.

Fourth-Year Student (clinical clerk).—"The patient is 35 years of age, a restaurant keeper, who entered the hospital January 1. He tells of having a small 'lump' in the right groin for five years, which gradually increased in size, and he has worn a truss for three years. The evening before admission, while straining at stool, the 'lump' suddenly enlarged and could not be reduced. Vomiting set in during the night; a physician was called, but he was unable to reduce the hernia and so sent him to the hospital the next morning. A diagnosis of strangulated indirect inguinal hernia was made. The hernia was immediately operated on under local anesthesia, and though the bowel was much discolored, the vessels were not thrombosed, and sufficiently good circulation returned into it to justify its replacement.

"On admission it was noticed that he was jaundiced, and it was learned that this condition had been present for fifteen years, ever since an attack of pain in the right upper quadrant, accompanied by nausea and vomiting which confined him to bed for six months. He states that during that illness he had dark-colored urine and clay-colored stools, and that he subsequently passed over 200 gallstones, but refused a proposed operation because of his mother's objections, for she is said to be even more yellow than he, and has had jaundice herself for many years and has done well without operation."

Now, Mr. B—, before we go into this story any further, what impression have you perhaps gained regarding this patient?

Third-Year Student.—"I think he must have some other trouble than the rupture for which he came to the hospital."

Yes, undoubtedly he has, although, as you have doubtless been told before this, it is the safest plan to attribute the symptoms which a patient presents to one underlying cause—a symptom complex—rather than to look for multiple causes. But here the conditions are somewhat different—an exception which proves the rule—for we have an acute complication on the part of an old rupture in a patient with some underlying trouble, and what do you think it may be?

Third-Year Student.—"It is very peculiar that he should have had such persistent jaundice if due to gallstones, and also that his mother has gallstones and jaundice."

It is peculiar, and, what is more, as Mr. A—— could tell us, we have since learned that he also has a brother who has chronic jaundice. Then, too, you have noted that his jaundice has a curious lemon-yellow tint, and, what is more, he has no evidence of bile in his urine, nor are his stools pale in color. Is it not the usual thing in cases of icterus to find bile in all the body fluids?

Student.—"I think so."

Yes, in all the body fluids except the cerebrospinal fluid, for, as I have told you, the choroid plexus, unless diseased or injured, is a filter so effective as to prevent the passage from the blood of all but a very few chemical substances. But here, with exception possibly of the blood, the fluids are not stained, not even the urine, and it is therefore what is called an acholuric jaundice. Now I may be trespassing on a subject you have not as yet covered and would like to ask the class whether they have any idea what may be wrong with this man in view of his history, and will ask those to raise their hands who know what we are likely to find on palpation of the abdomen. (Many of the class responded.) Some of you, at least, appear to have met with this condition in your medical lectures, and so, Mr. B——, will you let us know what you feel in this patient's belly?

Third-Year Student.—"He has a large mass on the left side which descends with respiration and I think must be his spleen. It reaches the level of the navel."

Yes, and what would you like to know next?

Third-Year Student.—"The findings in his blood."

Clinical Clerk.—"The blood shows 2,800,000 reds, 11,000 whites, and 60 per cent. hemoglobin. The differential is not remarkable—67 per cent. polymorphonuclears, 25 per cent. lymphocytes, and 20 per cent. eosinophils. The red cells do not show any departure from normal, but the fragility test made by Dr. Kebajian shows beginning hemolysis at 0.75 per cent., as against 0.46 per cent. for the control."

What, then, might be your diagnosis in this case, Mr. B——?

Third-Year Student.—"Hemolytic jaundice, probably of the congenital type."

And would you advise any treatment for the condition?

Third-Year Student.—"We have been told by Dr. M—— that splenectomy is of great benefit in these cases."

Yes, I think that is the prevailing idea, particularly regarding this family variety of splenomegaly. It is the type to which attention was first directed, I believe, by the students of Minkowski, of Chauffard

and of Vaquez, and it has been variously called congenital (or familial) hemolytic jaundice (or icterus), as you will.

I do not know what others have told you, but I do not believe that it is at all clear whether the underlying fault in these conditions lies with the blood or with the spleen, or possibly elsewhere. The fact that symptomatic improvement has followed splenectomy speaks in favor of a splenic origin; others ascribe the disorder to a primary change in the blood, to the low osmotic resistance of the erythrocytes, or possibly to an imperfect blood formation or to some form of hemolysis of normal corpuscles due to an unknown chemical influence. This is a little vague, perhaps, but then, vagueness still characterizes our knowledge of blood-forming organs. Certainly, if the disease is hereditary it probably obeys Mendelian laws, and therefore should be much more common in affected families than the presence of icterus and splenomegaly would indicate, so that we may assume there are many milder cases unrecognized having neither jaundice nor large spleens. In short, the disease may possibly exist in the absence of the two outstanding symptoms which gave it its name. Nor is this unique.

Then, too, authorities are still equally indefinite in regard to the cause of the jaundice in the absence of cirrhosis or obstruction of the bile passages. Some ascribe it to the clogging of the biliary capillaries by an excess of viscid and highly pigmented bile, a consequence of blood destruction. On this I cannot pass.

This whole subject is one in which I am at this moment more interested from the standpoint of your fellow student than from that of a teacher, and as I have refreshed my mind regarding it before coming to this exercise, I will show you, for your benefit, the volumes I consulted. Here is a book you will find very useful, particularly because of its brevity of description and valuable bibliography. It is Barker's *Clinical Diagnosis of Internal Diseases*; and in this second volume there are a few pages devoted to the diseases of the spleen, where you can get your essential facts, up to 1916, very quickly and very briefly. You are given also, some of the more important references—in the author's estimation at least—so that you may run our prevailing ideas down to their source of origin. Such a treatise as this can serve you as a short cut to the *Index Catalogue* and *Index Medicus*, where, at your stage, you are likely to be swamped by the immense number of titles on a given subject.

But possibly this volume should have come first—the last edition of Osler's *Principles and Practice*; and, as I have told you before, it is perhaps the best jumping-off place for most subjects, whether surgical or medical, that you may wish to look up. You will find here under "Jaundice" a note about the hemolytic varieties, and the fact

that it was Chauffard who first pointed out the increased fragility of the red corpuscles — a note also on a hereditary form of icterus in infants, first described by Glaister, as well as this acholuric form before us which Minkowski reported. However, Osler does not feel that the disease is necessarily familial, though some writers have attempted to subdivide the cases into acquired and inherited types.

And there is another thing I may call to your attention which I had forgotten — namely, that in the icterus of the new-born, in contradistinction to other forms, the central nervous axis may be bile-stained, though I do not know whether this is also true of the cerebrospinal fluid in these cases, contrary to what I have told you.

Let us now turn to the section on the spleen, in the diseases of which Dr. Osler became interested, and to which he made important clinical contributions. Here you will find in the section on "Primary Splenomegaly with Anemia" a description of splenic anemia or Banti's disease, which he defines as "a primary disease of the spleen of unknown origin characterized by progressive enlargement, attacks of anemia, a tendency to hemorrhage, and in some cases a secondary cirrhosis of the liver with jaundice and ascites," and please observe that he says further, "The spleen itself is the seat of the disease, as is shown by the fact that complete recovery follows its removal."

You will note that the jaundice shown by Alvin Landers here has been an early and not a late symptom of his malady, and that there are no evidences of hepatic cirrhosis, nor have there been hemorrhages. Otherwise this brief description might cover the case of our patient well enough.

Osler, as you see, laid great emphasis on the tendency to hemorrhage, particularly hematemesis, as a special feature of Banti's disease, with recurring attacks often over many years, and he points out that the diagnosis of ulcer of the stomach may consequently be made. As I shall return to this again, I may read that "the bleeding may be of great severity. On several occasions one of my patients was brought into the hospital completely exsanguiné; in two the hemorrhage proved directly fatal; in a third the hemorrhage proved fatal ten days after a successful removal of the spleen . . . One patient had splenomegaly with repeated hemorrhages, and has now (1912) had more than twelve years of good health after splenectomy."

Again, under "Hemorrhage from the Stomach," Osler gives as causes passive congestion and splenomegaly, for he says (page 507) that "gastrorrhagia is by no means an uncommon symptom in enlarged spleen, and is explained by the intimate relations which exist between the vasa brevia and the splenic circulation." I quote this because the source of hemorrhage in these cases is another matter to which we will return.

Now let us go a little farther and turn to one of the systems of medicine which you will find in the school library if you do not happen to have succumbed yourself to a sales agent. Having already spoken of Osler's relation to the subject, you may turn to Modern Medicine or to Allbutt and Rolleston's System, in which there is also an exceedingly good chapter on diseases of the spleen, where you will find a still more elaborate presentation of the topic.

And lastly, to pursue the subject still farther without going to original sources, we may turn to some work of monographic form, and the most recent that I know of in English is this volume by Pearce, Krumbhaar and Frazier, on the spleen and anemia, which Dr. Cutler has loaned to me, so that here again, and proportionately in still greater detail, you will find this general topic gone into.

Thus in looking up a subject one proceeds, from a brief synopsis, to a textbook, to such short monographs as occur in standard system of medicine, to separately printed and larger monographs, and as a last court of appeal to the general literature of our journals through the agency of our great indices, and the results of so doing once on a time, fill this filing box as I shall tell you later; for twenty years ago, I would have had less need of consulting recent literature before coming to an exercise on this subject.

At that time this case would probably have been called primary splenomegaly or splenic anemia, or possibly splenic anemia with icterus, in view of this additional symptom; but of late years various types of splenomegaly with varying forms of anemia have come to be separated off, for one reason or another, from the cases which, in 1900, would probably have been grouped together — and may come to be again.

One might give a historical résumé of this process of separation somewhat as follows:

At first when we knew far less even than now of splenic function, enlargements of the organ were of course well recognized. They, for the most part, were secondary manifestations of some known disease process. Thus, we may dismiss, in our present consideration, the acute splenomegalies of various febrile states, the large spleen of chronic malaria and kala-azar, of syphilis, tuberculosis and echinococcus, the enlargement due to venous stasis of cardiac or hepatic origin.

A second step, and a most important one, was the recognition by Virchow and others of a splenic enlargement associated with a leukemia.

A third chapter would properly record the recognition of cases not due to the ordinary causes given above nor associated with an increase of white cells in the blood and therefore called "pseudoleukemias" by Cohnheim.

Then as a *fourth step* came Banti's first monograph in 1883, describing splenic anemia which was withdrawn from the nonleukemic splenomegalies, and at about the same time in France came Bruhl's papers on splénomégalie primitive. Both Banti and Bruhl, doubtless provisionally, included numerous allied disorders, and Banti, in the belief that the spleen was the seat of the disease, advocated its removal.

As a *fifth step*, Gaucher separated off from splenic anemia of the Banti type a form with a peculiar histologic picture, characterized by masses of endothelial cells in the spleen and by hypertrophy of the liver. At about the same time —

A *sixth step* — a side step possibly — was taken by von Jaksch, who gave the name pseudoleukemia infantum to a form of splenic anemia which had been recognized in infants even before his time.

And then, finally, this disease, hemolytic jaundice, was separated off, and some are attempting to split this up into acquired (Hyem-Widal) and familial (Minkowski-Chauffard) types. This is the sort of thing that usually happens, and we are probably not through yet with these clinical distinctions, though probably many of them have much in common, and if Banti disclaims this progeny for splenic anemia, they at least were hatched in the same pseudoleukemic nest.

Now I wish to approach from a different angle these conditions of splenomegaly with anemia, in the surgical aspects of which I was once greatly interested.

STUDIES FROM OLD CASE-BOOKS

I shall take advantage of the occasion to speak to you of the value of case records and why it is we put the names of these patients on the board, and keep referring to them, because as I told you early in your year I wanted you to remember each of these clinical cases that you see, as patients, rather than merely as examples of some given symptom, such for example as jaundice in this man who has just gone out.

I have brought in here, to show you, a volume entitled "Studies of Old Case-Books," by Sir James Paget, whose life I hope all of you will some day read. The book contains accounts of some odd cases and conditions, with chapter headings such as "Diabetic Gangrene," "Ununited Fractures in Children," "Use of Will for Health," and so on, but what I want to quote are some paragraphs from his preface. He says:

Few things of the kind seem to be more useless than old case-books. To the writer himself they may have some value and even great personal interest: he may profitably study himself in them as well as some of the facts which he has recorded.

Then he goes on to say:

Thus as one looks through volume after volume, they seem to prove nothing but a waste of time, till one reflects that the present use of old case-books is no just estimate of their value in past years. For, to say nothing of the materials they may have supplied for work already done in lectures or in books and papers published at various times, they were among the very best means of self-education. The habit of recording facts is nearly essential to the habit of accurately observing and remembering them. That which we intend to record we are bound and may be induced to observe carefully, and the very act of carefully recording is nearly equivalent to a renewed observation. Thinking of this and of their personal interest to myself, I ought, perhaps, to have been content with the good service that my case-books have rendered to me and with the hope that they have been, in some measure, indirectly useful to others.

Now your attention has been called to this old volume of Paget's, because I wish to show you the accumulations which I have here of two old case reports concerning which I have much the same feeling that he has expressed in the quotation I have read to you. I show them to you also because I want you to learn to accumulate facts and material for yourselves through what you may learn in your various clinics and in your use of the journals in the library which I have so often urged you to get in the habit of going over. If you do nothing more than to jot down references to these articles, to which I have called your attention, and to put them with the notes which you must have already taken down about splenic diseases, together with one or two case reports of patients that may have been shown to you, like Alvin Landers this morning; and if you will keep this little collection of your own up to date by occasional additions from what you run across in your reading, you will build up a textbook of your own—one very much better than anything you can buy bound in covers, which must necessarily quickly become antiquated. By this means, when the time comes to need them, you will be able to recall your facts infinitely better than in any other way.

This old filing box which, until this morning, had certainly not been opened since 1910, is labeled "Spleen," and it represents some ancient accumulations regarding this topic which is under consideration, and I will tell you the story.

There came to the Johns Hopkins Hospital, March 9, 1898, a man, aged 33, C. D. B. by name, a farmer from Fincastle, Va., complaining of dyspepsia, and hemorrhages from the stomach and bowels. These he had had for nine years, the loss of blood at times having been sudden and very profuse, the attacks coming possibly once every twelve months. I remember him as a little fellow with a curious brownish coloration of the skin and a big spleen which was taken to

be an ague-cake doubtless in view of his place of domicile. He had a marked anemia, with hemoglobin of 25 per cent., about 3,000,000 reds, and a leukopenia of 2,800 cells. His gastric examination (this was before the days of bismuth roentgen-ray studies you will observe) showed a slightly dilated stomach with visible peristalsis, and a test meal showed a considerable hyperacidity. He was discharged, and returned to the hospital again on October 26, with his blood picture somewhat improved. A presumptive diagnosis had been made of bleeding peptic ulcer and he was transferred to the surgical service for operation.

Being the resident surgeon at the time, the case fell to my lot, but it was just at this period, as I remember it, that the first edition of Allbutt's System was published. I had invested in a set of the volumes and by chance had read Samuel West's article in Vol. V, p. 539, on splenic anemia. The condition seemed to fit the case of this man so exactly that I remember going over to Dr. Osler's house with some needless trepidation, the evening of the patient's transfer, to ask him if he did not think it was possibly a case of splenic anemia, and if I found no sign of pyloric ulcer would he mind letting me take out the man's spleen, because there had been one or two promising cases referred to by West. As was characteristic of him under such circumstances, he said, "Go ahead, young man, and do what you think best."

So the next day I made a primary exploration on the right side, found nothing, and then proceeded through a new incision to take out his spleen. It was very adherent, and I had a good deal of difficulty from bleeding during the separation of the adhesions under the diaphragm, but, nevertheless, in spite of his anemia, he recovered.¹

There is a tradition, as you know, in most clinics, that when rare conditions turn up they often come in pairs, and while this Mr. C. D. B. was still in hospital, another patient, Mr. W. H., 30 years of age, was admitted to Dr. Osler's wards² with a very similar history: a large spleen extending to the umbilicus and several attacks of profuse hematemesis occurring over an eleven-year period. The blood picture was very much the same, there was the same muddy brownish tint to the skin, and he complained similarly of some upper abdominal soreness.

1. The case was subsequently referred to in all of Osler's three papers: (1) "On Splenic Anemia," *Am. J. M. Sc.*, January, 1900, Case IV; (2) "Chronic Splenic Enlargement with Recurrent Gastro-Intestinal Hemorrhages," *Edinburgh M. J.*, May, 1899, p. 447, Case II; (3) "Anemia Splenica," *Tr. Assn. Am. Physicians*, 1902, Case IV.

2. Osler refers to him as Mr. A. B. in his first paper, Case V, second paper, Case III, and third paper (after operation) Case V.

This man also was operated on, and in addition to the large spleen there was found some ascites and a slightly cirrhotic liver. The same surgical difficulties were encountered from dense adhesions due to a perisplenitis, and I well remember his being kept in the operating room inverted on the table until the following day, as it seemed unsafe to move him.

He made an excellent operative recovery and his wound healed; but on the tenth day he had a sudden profuse vomiting of dark blood, fully 2 liters or more in amount, and died almost before the attendants could reach his bedside. At autopsy it was found that the bleeding had come from an esophageal varix, and I pass around this very beautiful water-color made by Mr. August Horne, one of the artists then in Dr. Kelly's clinic, which shows the lesion.

So far as I have been able to determine this morning in looking over these accounts of splenic anemia, Dr. Osler in particular laid stress on hematemesis, and his impression was doubtless colored by these early cases. So far as I am aware, also, this was the first and perhaps the only case in which the bleeding was shown to come from an esophageal varix, for I have read you the note in Osler's Practice in which he ascribes the hematemesis to capillary hemorrhages from the stomach. Esophageal varices of course are common enough and may occasionally be a source of fatal hemorrhage in extreme passive congestion either of cardiac or hepatic origin. In both of these patients, however, that I have referred to, the changes in the liver were insignificant, at least in gross appearances, for though in Banti's disease proper there is a terminal stage of cirrhosis with ascites, this was not apparent in Case I, and but very slightly in evidence in Case II. Disease of the portal vessels, irrespective of stasis, was a feature of the disease Banti called attention to, and it may have some bearing on this symptom of recurrent bleeding.

Now let us return to this box, not only that I may show you what these accumulations are, but that I may tell you the end-results of the story of our friend from Fincastle. I do so particularly because I want to warn you as well as my junior surgical colleagues here lest there be too great enthusiasm over splenectomies for these obscure diseases.

I am led the more to do so because Mr. B—— has told us that in this patient we have just seen, splenectomy is the proper procedure, but I am not at all sure but that the boy's mother is correct in believing that she has lived as long with her hemolytic jaundice as she would have done if her spleen had been removed. I find that in the hospital records here there have been seven cases of splenectomy for the following conditions: splenic anemia, 1; splenomegaly, 2; pernicious anemia, 2; fever, cause unknown, 1, and chronic splenitis, 1; not a

Water color sketch by August Horne of the esophageal varices with perforation, leading to fatal hemorrhage in the second case.

very large series, and I will show you two recent articles on the subject, one of them from the Mayo Clinic, where possibly the largest experience has been had with these particular operations.

Unless the spleen is very adherent and very large and unless the patient is unduly anemic and in poor health, its removal is not an operation of exceptional magnitude; and unquestionably when we are reaching out for some therapeutic measure in regard to a possible cure of an obscure disease the temptation is strong to remove an organ which evidently participates in the disease, if it is removable, even though it may not be the primary source of the disorder. We must not, however, be misled under the circumstances by mere operative recoveries into the belief that the patient has necessarily been benefited — benefited in the way that Alvin Landers has been by his hernia operation, which you will recognize as having been an urgent and possibly life-saving procedure.

I feel a little conscious-smitten when I find that the case of Mr. C. D. B. — has gotten into the literature as one of the early recoveries and possible cures of Banti's disease by removal of the spleen — particularly as *two cases*. For here is a much-quoted article by Gaston Torrance, on "Splenectomy in Banti's Disease," reprinted from the *Annals of Surgery* for January, 1908. Thirty-six cases were then collected, of which that of C. D. B. — was XII, and it states that "he made a good recovery and gained 30 lbs. in weight;" also that "he was reported living and well eight years later, with no return of the hemorrhages." Case XIII of the same series is evidently the same patient and accredited to my then chief, Dr. Halsted. There had been eight recoveries out of the eleven preceding cases, going back to one by Spencer Wells in 1865. These favorable reports — especially when a success is counted twice — unquestionably are what encourage subsequent operations. This is quite proper, and it is natural that we should continue with these measures, but we must not let ourselves be blinded by incomplete reports of these operative recoveries.

Now let us return again to our filing box and see what happened to the patient from Fincastle, Va. Here, in this old rubber band, is a package of cards labeled "Splenic Anemia," with some fifty or sixty references collected in 1900, and you may imagine what the collected literature of the subject must be today. You will find it in the Index Catalogue when you need it.

Here is a bundle of notes on the diseases of the spleen and their surgical treatment, and here are several starts at the writing of a paper on the subject, finally abandoned. One of them begins: "Nebular as they are, these are essentially borderline conditions of medicine and surgery, and consequently of interest to all," and further, that "some day order may come out of chaos and the disorders now classified as

'pseudoleukemia,' of which Banti's disease appears to be a type, may be found to represent a great diversity of conditions." Some of this might have been written today. And here is a postoperative chart by Dr. Follis who was then a fourth-year medical student like some of you here, and he industriously followed this man's blood for two months after the operation, with an almost daily differential count—and you know what this means—though I do not know that we observed anything especially noteworthy except a well-marked poikilocytosis after the operation. And here—a letter from Dr. Osler urging that these cases be written up from a surgical standpoint. And a bundle of reprints on the spleen and its diseases, among them Banti's two papers with a manuscript translation of one of them, made by some one, I've forgotten who. Then a package of some twenty letters from the patient from about as many addresses. For your information as well as entertainment I will quote from some of them, for they are in part amusing and in part tragic. This of March 15, 1900:

Dear Sir men of good business have advised me to write to the Hospital as it is well known there can be no advertisement put out that will represent the Hospital as well as the scares on my body. I can readily see and know and have knowed for some time that I can send many afflicted people there that never will come until they see what has bin don for me. I wrote to Dr. Henry M. Herd on this mail will you see him and pleas have a talk with him and youall can tell me what is the very bes salery they can pay me as I can see some time ago the people I can induce to come it will be a big thing pleas let me hear from you and all about the matter very Respectfully.

So far as I know, Dr. Hurd did not take advantage of this, for two years later, Aug. 12, 1902, we find our patient peddling a patent medicine and attributing his recovery to it.

Dear Friend your letter was received last eavening well I am at home now I got sick. I am trying to introduce A.I.M. will send you one of my circulars *Please* read it and when you cannot stop blood just call on me for I never fail they like me the company as an agent though I worked to hard. Doctor say I Kneed rest and I have liver trouble Kneed some Kind of a mild liver Meadicine all the time A.I.M. is to Strong for me to take very much of it. if I was not one of those Push go ahead Kind of fellows I wouldnt be able to do anything at all now you seem to always have so much busines on hand you will never take time to write only a word or too sit up one hour later some night and write a long letter you could do this if you would well when I was operated on I weighed 157 I now weighe near about 140 they say anything that has its spleen removed natural grows thin guess I will dwindle to nothing finaly now write me soon and send me your Picture, &c.

A year later finds him married and on a farm—complaining of

Rheumatism I guess I am subject to it all through my body some of it maybe due to me handling the Pruning Shers my mussles seam to be harder than when I come here hard work has made them hard I guess. When I get up of

morning I spit up some saliva very bloody looking or almost blood itself. I taken some of the Mineral about a yer ago and lots of hard blood Passed from me at Stools for 3 or 4 times just like I used to pass when I had those hemorages etc.

Here I must have lost track of him, for there are some returned letters, and there is a gap of six years till 1909, when this from a new address:

Dear Doctor one week ago today I was taken with a severe hemorage threw up as much as a pint of blood lost over three quarts of blood all together most of it passed through my bowels this time when I use to have those hemorages eleven years ago before I come to the hospital I would vomate as much as a gallon to a gallon and a half the Dr. come to see me the second day the first day he said I must have blood ulcer or cancer of the stomach and that he wanted to go home and read up my case, etc.

A wise doctor, particularly as he said the next day:

I dont think you have blood ulcer or cancer since I have read up on Dr. Oslers work and he did not give me any medicine at all only told me to take a dose or too of oil and I don so. I can begin to eat a little something again everybody tells me I work to hard, etc.

A good soul, as you will see, but just how much he has benefited by his splenectomy there may be some justifiable doubt.³ The matter might be argued both ways; and it might be said that otherwise he would certainly by this time have been in the stage of cirrhosis and ascites. Who can tell?

But the last and most important document in this box is a description by W. G. MacCallum, of the pathologic changes in the spleens of these two patients, which well deserves publication even after these twenty years, if for no other reason than to show how little additional knowledge we have at the present day.

Now Gentlemen, I do not mean to imply by what I have told you at this exercise that these are the only books of reference, for there are of course many others equally valuable, in our own and foreign tongues. The main thing is for you to get accustomed to certain sources of information, so that you can pick up a subject in its essential details and know how to follow it to its full elaboration.

Nor do I mean to imply from what I have told you of the keeping of case records or subject records that this is the only way, for each of you must work out a method more or less applicable to his own characteristics of work. The essential thing is to remember that medicine

3. Since this clinic I have again heard from this man (Feb. 13, 1920, twenty-one years since his operation) and he reports another hemorrhage in July of 1918 when he vomited about a quart of blood which he attributes to pitching hay, and he still works too hard and would like a position here because he once worked at an asylum in Osawotomie, Kan., and has "the name of being a fine salesman but he doesn't say it boastingly."

is a rapidly changing subject, that no one can keep pace with all branches of it, that if you are going to succeed you will have to be a student of medicine the rest of your days, that this is the time, if any, to establish good habits of work and to learn how to assemble facts relating to disease as they come to your knowledge, so that they may hereafter be useful to you.

You must remember, too, that just as the physician may be deluded by blind faith in regard to the efficacy of drugs, so may the surgeon be misled by his operations — the capacity for self-deception is strongly developed in all of us. It is well to keep a reasonably skeptical attitude regarding cures, for then you are never vexed when you find you have been in the wrong. You can learn to practice medicine successfully with a very few drugs well used, and will become the better surgeons for conservatism in the use of the scalpel.

To return for a moment to our patient with hemolytic jaundice, whose spleen it is proposed to remove. I see no reason why it should not be done, but at the same time feel some sympathy for his mother's point of view. The risks are not great and, so far as we know, it at least should do no harm, but in the present stage of our ignorance of these disorders, not knowing indeed whether the spleen is the primary seat of the disease, we at least should feel obligated to take every advantage of such an operation to advance our knowledge, by following the case through for a reasonable time before letting it get into medical literature as a presumptive cure. This is a temptation to which the guild of surgeons is particularly prone.

THE PATHOLOGICAL CHANGES IN SPLENIC ANEMIA

BY W. G. MAC CALLUM

Of the pathologic examinations carried out in cases of so-called splenic anemia, the most satisfactory are those of Banti, Harris and Herzog, Sippy, Bovaird and Gaucher. Others are very brief indeed and generally limited to the macroscopic inspection of the organs. The cases described by these authors are, however, not homogeneous in their character — those of Bovaird and Gaucher being apparently quite different from those described by Banti, and later by Sippy and Harris and Herzog. With the types described by Bovaird, we have in the other cases nothing exactly comparable. The enormous widening of the venous channels in the pulp with the proliferation of the endothelial cells is not found by Banti in his case. Banti found merely a diffuse new growth of interstitial connective tissue throughout the pulp marking out the venous channels, and a change which he considers primary in the malpighian bodies leading to their sclerosis. These changes, even when taken together with the other details which Banti brings forward, do not seem sufficiently characteristic from the

anatomic point of view to justify the classification of the condition as a separate disease. Such a classification must rest until an etiologic factor is determined largely on the clinical course of the disease. Nevertheless, the objective anatomic description of the cases before us may furnish a clue in time to the etiologic factor.

From *the first case*, we have for anatomic study only the spleen with a macroscopic observation as to the condition of the liver at the time of operation.

Note of Dr. Flexner on the spleen, Nov. 10, 1898:

Spleen measures 18 by 11.5 by 2.5-4.5 cm. and weighs 730 gm. Its anterior edge is rounded—notch partially obliterated. Inferior anterior half of capsule thickened, white and opaque. In the central portion there are lines of calcareous deposit. The capsule is thickened generally but not uniformly, elevated plaques being scattered over the surface. Old adhesions exist over the inferior and posterior border as far back as the hilum which bound the spleen to the diaphragm. Gastrosplenic omentum is adherent to the anterior edge. Cut surface exhibits a remarkable uniformity—its general color is deep salmon or reddish brown only variegated by very prominent trabeculae. The malpighian bodies cannot be made out at all.

A few noncalcareous thrombi, oval in shape, are found in branches of the splenic veins—one was concentrically striated. The consistence of the spleen is very much increased.

Splenic Artery: There is some thickening of the wall which is practically always present in adults, and a moderate degree of tortuosity. Intima generally is smooth. There are, however, thickened opaque plaques situated at the points of branching at the hilum of the spleen.

Splenic vein is apparently normal. What remains of a lymph gland on the hilum of the spleen is easily made out and perhaps enlarged.

Microscopically, one finds the trabeculae definitely increased in thickness throughout the section; the capsule, however, is not markedly thickened. The malpighian bodies are less numerous than in a normal spleen; many of them are quite normal in appearance, while others are abnormal only in their very small size. These immature nodules surrounding small arteries occur in the pulp at quite a distance from the coarse trabeculae. In a few of the larger and more normal looking bodies, there is the pale central area in which the cells lying on the reticulum have a large vesicular nucleus, contrasting with the more deeply staining nucleus of the smaller lymphoid cells. In many instances, as will be observed again in the next case, the central portion of the nodule is occupied by a dense mass of the small lymphoid cells, the peripheral cells being slightly larger and less closely arranged. No progressive sclerotic process such as Banti described is seen in these malpighian bodies, nor has it been possible to find any fibrous nodules which might have resulted from such sclerosis. The fine reticulum normally supporting the lymphoid cells is perhaps a little coarser than normal. None of the hyaline masses enclosing cells and

fragments of nuclei, such as Banti described, are found here, although it may be mentioned in passing that it is by no means unusual to find such masses in the greatest variety of conditions, and they can therefore hardly be considered in any way characteristic of this disease.

In the red splenic pulp the changes are definite enough to attract immediate attention; but before detailing them it may be well to review briefly the main points in the histology of this tissue as brought out in the recent papers of Weidenreich, Mall, Thoma and others. The question as to whether or not there is an open or closed blood circulation we may leave aside, as it scarcely concerns us here. More important for the comprehension of these changes is the excellent description of Weidenreich of the minute structure of the venules and arterioles, and the intervening tissue which goes to make up the red pulp. The walls of the arterioles present no especial peculiarities if we except the curious sheath which covers the vessels just before their termination in the capillaries. The wider venules into which these capillaries empty, however, have a very remarkable structure. They are of almost uniform width and lie closely plaited together so as to constitute the greater bulk of the tissue. Their walls consist of a basketwork or network of circular and communicating fibrils very much like the markings on a tracheid vessel in the wood of a plant stem, inside of which there is an extremely delicate basement membrane on which the elongated lining endothelial cells are longitudinally arranged. There has been some discussion as to the nature of the circular fibrils. They stain weakly with Weigert's elastic stain, also with the phosphomolybdic hematoxylin of Mallory, and resist for a time pancreatic digestion so that they may be isolated by digesting a section on a slide.

The endothelial cells have a long, narrow cell body; the nucleus, which has one or two indentations, lies in an expansion of the protoplasm in the middle, and is somewhat elevated above the basement membrane so that in cross section of the venule it projects into the lumen. Between these venules there is a supporting reticulum, the fibrils of which anastomose with those forming the network about the venules. Definite connective cells and fibers are present also in small numbers, and there are in the meshes of the network abundant free cells including red blood corpuscles, polymorphonuclear leukocytes and other wandering cells of the type of the lymphoid and plasma cells. In certain conditions, such as acute infection with the pyogenic cocci, we may have an acute splenic tumor, the chief characteristic of which is the great increase in these free cells which form the true pulp cells of the spleen, in contrast with that type of acute splenic tumor which occurs with typhoid fever and in which the hyperemia and endothelial proliferation dominate the picture.

In the case before us, we have, as was mentioned before this digression, changes which are obvious at the first glance. The splenic pulp is markedly poor in cells and the venous channels, ordinarily very thin walled, and to be outlined only with some difficulty on account of their being masked by the great number of cells, are here stouter and extraordinarily distinct. All of the features described above are extremely evident. The intervening tissue, however, has been converted into a fibrillated mass containing only a very few cells of the types usually seen there. Rounded mononuclear cells closely resembling plasma cells are most abundant; polymorphonuclear leukocytes are sometimes seen, and mononuclear and polymorphonuclear eosinophils are quite numerous. There is, as one can determine by suitable stains, a great increase in the connective tissue between the venules. Wavy strands of white fibrous tissue course along here although, as mentioned by various writers, there is no evidence of cell proliferation to give rise to all that new tissue. They lean to the view that the cells of connective tissue nature already present produce more interstitial substance and thus cause the sclerosis of the tissue.

The venules are not distended and do not reach the size ordinarily seen in cases of advanced chronic passive congestion, the condition which perhaps most of all resembles that seen here. They are not even filled with blood in the section, although of course that fact may be due to the draining of the spleen of its blood at the time of the operation. Many mononuclear cells are seen in these venules as well as in the large veins. They may be in large part desquamated endothelial cells, since they are by no means so abundant in the peripheral portions of the section, or in sections in which the fixation of the tissue has been very accurately carried out.

A neighboring lymph gland shows no especial pathologic alterations. There is no deposit of pigment of any sort — no phagocytic cells are to be seen, nor are there any other evidences in the spleen of an active hemolysis. One or two miliary tubercles with beginning necrosis of the center and giant cells are found in the pulp.

In the second case the spleen was removed successfully and the death of the patient occurred ten days later from an extensive hemorrhage from a dilated esophageal vein.

The macroscopic examination of the spleen was recorded in the following note:

Spleen removed by Dr. Cushing. Spleen is much enlarged. Dr. Cushing said that it is much smaller now that blood is expressed than before the operation. It weighs 1,000 gm. and measures 25.5 by 14.5 by 8.5 cm. It is somewhat irregularly lobulated.

The capsule is not much thickened in general, but presents lines of opacity forming a network.

Over the convex surface is an area 11 by 4 cm. where the capsule is much thickened and contains calcified plates. There are a few small nodules of such thickening scattered here and there over surface. The vessels at the hilum are not thrombosed. The arteries are markedly sclerosed. The veins appear normal and rather wide. The main splenic vein measures 2 cm. in circumference; i. e., about 7 mm. in diameter.

The spleen in general is soft and flabby and is not dense and firm as in the case of a spleen of chronic passive congestion. It has rather a pale color. On section the spleen has a similar pale red color. The malpighian bodies are seen with great difficulty. They are apparently diminished in size. The blood vessels are very prominent. The walls are thickened and opaque, gaping open on cut section. The trabeculae are also much increased in relation to the pulp. The pulp is somewhat translucent, and trabeculae can be seen as opaque lines running beneath the cut surface. The spleen though soft is extremely tough, reminding one of very soft rubber. A small portion can be crushed only with difficulty by the fingers. The pulp is thus not friable, and this character together with a slight translucency gives one the impression that there is an increase in the connective tissue throughout. It has nothing of the opaque velvety appearance of acute splenic tumor, and the cut surface is quite smooth and glistening.

Autopsy. MacCallum. Jan. 9, 1900. Autopsy No. 1469.

Anatomic Diagnosis: *Primitive splenomegaly. Operation for removal of spleen. Cirrhosis of liver. Interstitial pancreatitis. Hemorrhage from esophageal varix.*

The body is that of a well nourished man, 165 cm in length. There is a wound in the left hypochondrium 20 cm. in length which extends to the crest of the ileum. It is completely closed by sutures. The peritoneal cavity contains about 100 c.c. of blood-stained fluid.

The thoracic viscera are practically normal except for a slight arteriosclerotic thickening of the aortic valves.

The liver weighs 1,300 gm., and measures 24.5 by 14.5 by 9.5 cm. It is distinctly smaller than normal. The surface is roughened, but not definitely hobnailed. It is yellowish brown in color with a slight greenish tint, and both from the outside and on the cut surface has a translucent appearance. The consistence is firmer and more elastic than normal. The lobules are not very sharply outlined, but interlobular strands of grayish tissue can be made out here and there. The portal vein at its entrance into the liver is occluded by a thrombus.

The peritoneum about the site of the operation is not injected. There is no hemorrhage and no peritonitis, except that the omentum and stomach are delicately adherent to the diaphragm. The diaphragm is somewhat congested, and severed veins are everywhere plugged with dark thrombi. The splenic artery is tortuous in its course over the tail of the pancreas where it is ligated. The splenic vein is wide and accompanies the artery; it is also ligated. Both are occluded by thrombi of which that in the artery is firm and lamellated. The wall of the vein is perhaps slightly thickened. The thrombus in the lumen, which has a central softened portion, extends along the vein into the portal, where it rolls up and occludes the vein at the hilum of the liver. The inferior mesenteric, diaphragmatic and gastric veins and left renal veins are occluded by thrombi. That in the portal vein is, however, limited to the hilum of the liver.

The stomach and duodenum are distended with bloody fluid and clots, the stomach containing over a liter. The gastric mucosa is pale and normal looking. One or two thrombosed submucous veins are seen through the mucosa. In the esophagus at its lower end there are widely dilated submucous veins, most of which seem to be thrombosed. One just beneath the mucosa is apparently the source of the hemorrhage, for there is a small punched out ulcer opening directly into it, as shown in the illustration.

The pancreas was slightly injured at the tip of the tail and there are scattered areas of fat necrosis in the neighborhood.

The kidneys are large, but show no especial pathologic alterations. In the fat about the splenic flexure of the colon there is an accessory spleen about 2 cm. in diameter resembling, on section, the main spleen. The inguinal and femoral glands are enlarged, white and firm.

Bone marrow of the femur is pale purplish red in color and quite firm. The fat is quite masked by the cellular elements.

All the organs are very anemic and the heart's blood thin and watery.

Microscopically, the changes are most marked in the spleen and liver. The bone marrow proves to be exceedingly rich in cells of the types usually found in actively proliferating marrow. Erythroblasts are very numerous indeed. The lymph glands show no characteristic abnormality. Special attention at that time was not directed to the hemolymph glands, and none of them can be found in the preserved material.

The accessory spleen is completely necrotic, its vessels being thrombosed and entirely occluded. What remains of the architecture, however, is enough to show that it had undergone the same changes as the main spleen. The kidneys microscopically are practically normal, except for a very insignificant increase of connective tissue in certain areas. In the pancreas there is a well marked chronic interlobular and intralobular pancreatitis without very extensive degenerative changes in the parenchyma cells. The changes in the liver are very slight as compared with those in the spleen. There is a cirrhosis, that is, there is an increase in the connective tissue in the portal spaces, but this is not an extensive new formation of tissue, such as one sees in alcoholic cirrhosis. The bands of fibrous tissue are narrow and have not the appearance of having been recently formed—they are instead very dense and poor in cells—newly formed bile ducts are almost entirely wanting in them. The liver cells show a good deal of fatty degeneration, and there is great inequality in the size of their nuclei.

The veins in the submucosa of the stomach, especially about the cardiac orifice, are distended with blood.

The sections of the spleen show no definite thickening of the capsule; the trabeculae, however, are much thickened. The alterations of the pulp and malpighian bodies resemble in general those seen in the first case. The malpighian bodies are not numerous. Indeed, as compared with the normal spleen, very few of them are to be found in a

section; but this may, of course, be due to the enormous increase in the bulk of the red splenic pulp which separates them widely. They are in general normal in appearance with the exception of a diffuse thickening of the reticulum. Often there is the frequently described central area with large pale nuclei in many of which mitotic figures are visible — fragments of nuclei and occasionally fine fragments of hyaline material are seen between these cells. None have undergone any extensive sclerosis, and it has not been possible to find one completely converted into a fibrous mass.

The red splenic pulp is greatly increased in amount — there must be a great new formation of vessels, because the increase in the interstitial tissue alone does not seem to be sufficient to account for the enormous enlargement of the spleen. The pulp too consists, as in the preceding case, almost exclusively of closely matted venules whose walls are rather more definite than normal, but which are not dilated to a diameter greater than normal. In the interstices there is a distinct increase in the connective tissue which runs in wavy lines between the venules. Mallory's connective tissue stain brings out a fairly dense network in which the venules lie. In digested and stained preparations, however, the reticulum which becomes isolated as a delicate basketwork does not appear to be very greatly thickened over the normal, and indeed the individual venules are not especially stouter than the normal. Nor in all parts is the distribution of the new connective tissue homogeneous — there are areas in which the venules lie immediately together, while just adjacent to them there are bundles of connective tissue fibers separating the blood channels. Apparently, therefore, the change in the bulk and consistence of the red splenic pulp is due to a great increase in the venules and their closer packing together on account of the lack of abundant pulp cells together with a definite formation of new connective tissue throughout.

As in the preceding case the cells in the interstices are very few in number. Those which are left are of the lymphoid and plasma cell type with some polymorphonuclear leukocytes and relatively abundant mononuclear and polymorphonuclear eosinophils, some of which are so large as to form very striking objects. Large giant cells also sometimes occur in these spaces; they are irregular in outline and contain several nuclei clumped together in the middle.

Here, as in the lymph glands, the tests for iron holding pigment were negative.

Finally, we have the spleen from the case reported by Dr. Osler⁴ as Case XVI. This spleen was also enormously enlarged, measuring 24 by 14 by 7 cm. The surface is somewhat roughened by shreds of

4. Osler, William: *Anemia Splenica* (second paper), *Tr. A. Am. Phys.*, 1902.

old adhesions, but the capsule was not particularly thickened. On section, it has the same semitranslucent grayish lilac or grayish red color as in the preceding case; the cut surface is quite smooth and sinks slightly into a concavity. The malpighian bodies are not at all prominent, but the trabeculae and vessels are quite conspicuous. The spleen has the elastic rubbery consistence described for the others. The blood vessels at the hilum are somewhat dilated, but show no other abnormalities.

Microscopically, the trabeculae are very inconspicuous and indefinitely outlined; they seem to merge into the surrounding tissue. There are a few small hemorrhages in the splenic substance beneath the capsule as well as elsewhere scattered in the pulp; probably these were due to the handling of the spleen during the operation.

The splenic pulp is pale and anemic, and there are strands of pale staining connective tissue running throughout it and separating quite widely the venules. The new growth of connective tissue is far more marked here than in the other cases, and with Mallory's stain gives a blue meshwork of coarse fibers with very narrow meshes. The venules, indeed, seem narrower than normal. The basketwork of the reticulum fibrils in the spleen about the venules seems to be denser than normal; it is very intimately associated with the connective tissue of new growth.

The connective tissue between the channels is exceedingly poor in cells; it stains pale pink and has a finely fibrillated appearance; with Mallory's stain it takes a deep blue and the fibrillation is more evident. Definite connective tissue cells are relatively few in number, and no evidence of mitosis has been made out. Free cells of the lymphoid and plasma cell type occur, however, sparingly distributed, and there are quite numerous mononuclear and polymorphonuclear eosinophils. The last are so abundant as to be quite a striking feature in the section, occurring also in the blood channels.

The malpighian bodies are few in number in a section, but are practically normal. The central cells are generally the smaller and more closely crowded together, while the peripheral are larger and more loosely arranged; large epithelioid cells occur scattered among them. There is no evidence of any primary sclerosis of this part of the tissue. They rarely show any centers of active cell proliferation, and areas of cell degeneration and hyaline necrosis are quite as rare.

In these three cases, therefore, we have practically identical conditions in the spleen. In all, the malpighian bodies show practically no pathologic changes of any significance. They are scattered by the changes in the pulp and often small, but no more characteristic changes occur. In the pulp, there is apparently a great increase in the number of the venules which are not dilated, but from the loss of cellular tissue

between them have come to compose the greater part of the tissue. The basketwork of fibrils surrounding these venules seems not to be much altered, but there is a definite new growth of connective tissue between the venules. The endophlebitis described by Banti has not been made out in these cases. There is no evidence of great hemolysis in the spleen or elsewhere in the body, if we except the regenerative activity of the bone marrow. In one of these cases the man is apparently well two years after the splenectomy; in one there is slight cirrhosis of the liver, while in the third we have no evidence as to the condition of the liver. Speculation as to the nature of the process will probably lead to no definite result. Certainly the condition is not such as is characteristic of the ordinary chronic passive congestion; there are no extravasations of blood with hematoidin formation, no such widening of the venules, and withal a far greater new growth of connective tissue than is ordinarily found in the spleen of chronic passive congestion. There can be no question of malarial infection as an etiologic factor, for there is nothing in the history to indicate this, and there is none of the characteristic malarial pigmentation. It does not seem unreasonable to suppose that some toxin perhaps with a mild hemolytic action may act primarily to produce an enlargement and induration of the spleen and later a cirrhosis of the liver.