

S P L E N I C A N A E M I A .

B Y

R O B E R T H E N R Y W A T S O N .

M.A. (Edin.) 1884. M.B. & C.M. (Edin.) 1893.

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ON SPLENIC ANAEMIA.

This disease, of which I wish to offer a more exhaustive account than is to be found in our language up to the present time, is both rare and obscure. Until recent years there were as many names for, as examples of, the disease on record.

Splenic Anaemia, the name first used by Griesinger, adopted by Banti, and now the common name.

Splenic Pseudo-leucaemia, of Lodi and Cantani;

Primary Splenomegaly, of Débove;

Idiopathic Splenic Tumour, of Mittler and Franzolini;

Simple Hypertrophy of the Spleen, of Henoeh and Wilks;

Splenic Cachexia;

Splenic Lymphadenoma;

Under one or other of these names a morbid condition has come to be recognised of which the earliest observations are cases briefly noted by Wells, by Squire and by Wilks, thus summarized by the last-named in "Wilks and Moxon"; "We have met with similar cases of simple hypertrophy of the spleen without leucaemia both in the living and in dead subjects.

They are generally, but not always, associated with anaemia, as, indeed, are all long-standing diseases of the spleen. These cases are the only ones that can be properly considered as pure examples of hypertrophy of the spleen. The cause of the enlargement is unknown, and the accompanying clinical phenomena need further investigation."

As an isolated case was observed here and there and passed almost unnoticed until Banti's monograph "Dell' Anemia Splenica" appeared in Florence in 1882. It comprised a record of three original cases with the first critical summary of previous observations. Banti gave form to the vague conceptions of the condition in a descriptive definition that may be thus abridged from the verbose sentence of the original: "Splenic Anaemia is a progressive, idiopathic anaemia, severe and indeed fatal, with idiopathic hypertrophy of the spleen and liver, without leucaemia, and generally accompanied by oedema, haemorrhage and irregular fever."

In 1891 Bruhl contributed to the "Archives Générales de Médecine" an elaborate discussion of the subject, based on 14 collected cases.

In June 1896, at a meeting of the Royal Medical and Chirurgical Society of London, a discussion initiated by Dr. Samuel West, brought to light a considerable number of unrecorded cases.

In August of the same year Dr. Frederick Taylor devoted to this disease a large part of his address on Anaemia, delivered before the British Medical Association.

These are the chief land-marks in the progress of our acquaintance with Splenic Anaemia.

No conspectus of the literature of the subject having been recently attempted, I have undertaken the task of revising Bruhl's critique, which was founded on 13 previous cases and 1 original case, with whatever extended knowledge may be gathered from 29 previous and 2 unrecorded cases.

I shall first submit a detailed report of a case occurring in my private practice and next a case for which I am indebted to the great kindness of my respected clinical teacher - Dr. J. O. Affleck. I shall then attempt a complete analysis of all the points of interest in the symptomatology and pathology of the recorded cases of the disease. A discussion

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of the diagnosis and treatment follows, and a full Bibliography of cases and allied medical literature will be found at the end of the Thesis.

Case I. SPLENIC ANAEMIA.
(Reported by R. H. Watson, M.B.)

Case of M... P..., Female, 18 yrs.

History and Present Condition.

M.P. is a girl of 18, the child of working-class parents. Her father is steady and healthy. Her mother has been for years addicted to the excessive use of alcohol and there is a tubercular taint in the maternal side of the family. The housing and general surroundings of the family have been good for their class. There is no trace of syphilis in the family nor of malaria in the district.

She is the 5th of a family of 8, one of whom died in childhood of tubercular meningitis. She was a healthy child, and had no illness till the age of 7, when she was run over by a horse and cart, and much injured about the face and legs. There was at that time no sign or symptom of injury to the abdomen, but bleeding was profuse from the other injuries. Her recovery was complete and she has never had any loss of blood since. Though always a small girl for her age and never of robust appearance, she kept a fresh complexion and rosy cheeks and seemed always "well

enough". At 14 she left school and was engaged in housework for a year during which she often complained of slight digestive derangements. She then tried dressmaking, but in six months gave it up as she began to look pale and felt worse for the confinement. About that time she was laid up with "Inflammation of the Bowels" for a few days. There was at the same time a swelling in the left hypochondrium (the seat of pain) which, she positively asserts, completely disappeared. On recovery, she obtained employment in a large bakery, where she remained without interruption until 3 days ago. During the last 4 months she had begun to fall off. Her colour became paler, she began to suffer from palpitation and breathlessness on exertion, and after a walk felt a sense of constriction about the waist that compelled her to have her dress "let out" more and more. This had, it seems, been treated as an ordinary Chlorosis and a temporary improvement was obtained from the use of Iron. Three days ago, however, she had to give in and take to bed, owing to weakness, giddiness and palpitation.

26. 3. 97.

I was called to see M.P. and found her in bed, complaining of headache, giddiness, palpitation, breathlessness, and of faintness whenever she raised her head from the pillow.

She is a small girl for her age, 4 ft. 9 inches in height, weighing about 7 stones, fairly muscular, with a fair amount of cutaneous fat, but poorly developed. Her chest measurement over the breasts is only $26\frac{1}{2}$ inches while the waist measures 27. The glandular masses of the mammae are not larger than walnuts, and she has never menstruated.

Her hair is hazel brown and very fine, the eyes of the same colour, while the skin is pallid with a tinge of the lemon-yellow of Pernicious Anaemia, a tint that is more marked on the ocular conjunctivae. All the mucosae exhibit the same pallor and the soft palate is of a deeper yellow than is seen elsewhere. The cheeks readily and frequently become deeply flushed. She is perspiring freely on the head and the hands are quite sodden, but perspiration is not noticeable on the general surface.

Her temperature is 104° F.

Circulatory System.

The cause of the palpitation complained of by the patient is readily seen and felt in an irregular heaving of the soft parts over the cardiac region. It is felt widely diffused over the front of the chest, the apex is moved a little outward, and the left edge of the heart is $\frac{1}{2}$ inch outside of the nipple line. On auscultation, a loud blowing systolic murmur is heard (and heard even on extra-auscultation) at all the areas, and indeed all over the cardiac region. It is least loud over the Pulmonary and Mitral Areas, so rough at the Aortic as to suggest more than a functional cause, very marked at the Tricuspid and conducted practically in all possible directions. There is no diastolic impurity of any account. The systolic murmur is easily recognised in the great vessels of the neck, and over the ophthalmic sinus. A systolic pulsation is plainly visible in the right External Jugular Vein, and on emptying it, it rapidly fills from below. There is therefore present an acute dilation of the heart, with insufficiency of the Tricuspid Valve. The nature of the murmurs at the other orifices remains uncertain.

The Radial Pulse is rapid, 160 to the minute, fairly regular, full, of low tension and sometimes almost dicrotic. All the beats of the heart are represented in the pulse.

Digestive System.

The lips are very pale, the teeth irregular and mostly carious, the gums pale, and the pharynx of a deep yellow colour. The tongue is large, pale, fissured on the upper surface and edges, and slightly furred. There is no enlargement of the papillae about its root, nor of the tonsils. Her appetite has been good all along and her bowels fairly regular.

There is a distinct fullness in the left hypochondrium, the only part of the abdomen where tenderness can be found. It is easy to define in this region a tumour reaching almost to the middle line, extending downward one inch below the umbilical level, and passing outward and upward in the left lumbar region to merge in the area of normal splenic dulness.

Gentle percussion gives a dull note all over this area. On palpation the anterior edge is not sharp, feeling at least $\frac{1}{2}$ inch in thickness, no notch can be recognised, but the tumour can be seen and felt to move with resp-

iration, and on placing the fingers of the right hand beneath the Erector Spinae and those of the left hand in front of the abdomen, the whole tumour can be easily recognised as an enlarged spleen.

The largest circumference of the abdomen over the tumour is $27\frac{1}{2}$ inches.

Glandular System.

There is not any enlargement of the liver, nor of any part of the lymphatic system open to examination; the glands of the abdomen and thorax, the superficial glands of the axilla and groin, and the lymphatic follicles of the pharynx.

Nervous System.

Except for the headache and giddiness, the palpitation and some general nervous excitement, the system is sound.

Respiratory System.

This shows no abnormality beyond the hyperpnoea.

Urinary System.

The urine at present is a febrile urine, diminished in quantity, yellow-brown in colour, of Specific Gravity 1025, highly acid and with no abnormal constituents.

Genital System.

No physical examination was made, but from the rudimentary condition of the mammae, and the amenorrhoea it is evident that puberty has not arrived.

Progress of case under Observation.

27.3.97. Temperature, Pulse and Respiration are falling. No abdominal pain. In absence of the proper instruments for examination of the blood, I was only able to regard the case as one of extreme and dangerous anaemia, either pernicious or leucocythaemia. For treatment I could not attempt more than absolute rest and quiet, frequent light diet, a little alcoholic stimulation, and Arsenic, begun in doses of 5 drops of Fowler's Solution thrice daily.

28.3.97. Patient still improving, though the pain has returned in the left side.

29.3.97. She is sleeping much and taking food better.

30.3.97. Temperature rising again, and the patient is very weak and restless.

31.3.97. T. 102° . The palpitation is very bad and she is fainting at almost every movement.

3.4.97. She is improving very slowly, but

gastric pain immediately after each dose of arsenic compels me to reduce the amount.

4.4.97. The instruments of Thoma and Gowers having been obtained, the blood was found to show 1,600,000 red corpuscles or 32% and 28% of haemoglobin. The white corpuscles were only 6,000. This definitely excludes leucocythaemia and almost certainly excludes Pernicious Anaemia. The case was therefore regarded provisionally as one of true Splenic Anaemia of Banti.

5.4.97. I was called late at night to find the patient suffering from intense pain in the left hypochondrium and epigastrium, radiating into the left shoulder and left lumbar region. T.100, Pulse 125, small and jerky. She was ghastly pale, lying crouched up in bed and unable to move, sick, with moist skin and dilated pupils, in short in a state of shock suggesting renal or hepatic colic. There was extreme tenderness over the spleen and on auscultation friction sounds were distinctly heard. It was no doubt a "splenic crisis" due to perisplenitis. The condition was rapidly alleviated by morphine, given hypodermically and hot fomentations over the seat of inflammation.

6.4.97 The patient is again pretty comfortable but as she was very sensitive to the ill effects of even small doses of Arsenic, I resolved to give Bone Marrow a trial. She was ordered 6 oz. a day, to be taken in the fresh condition, and calf, rather than ox marrow, as often as the former could be procured. For two weeks she made slow but evident progress. She remained in bed, slept well, took a good supply of light food, mostly milk food and eggs, and the 6 oz. of marrow did not seem to overtask her digestion. She remained free from pain,

After the 10th she never felt giddy on rising, and only rarely after unusual excitement was conscious of palpitation. Her colour improved daily, and by the 13th she was requesting to be allowed to leave her bed.

21.4.97 There was on that day a distinct suggestion of jaundice in conjunctivae and skin, but no sign of bile in the urine.

24.4.97 During last night she had a severe attack of abdominal pain, probably another "splenic crisis" and this morning was found to be deeply jaundiced over the whole body. By evening the urine

showed presence of bile acids and pigments.

As I could not be sure as to the nature of this jaundice, whether so-called "haemolytic" or due to over-loading of the liver with fat from the marrow. I reduced the dose of marrow to 3 ounces daily and added 12 ounces of Bourboule Water (equal to 1/22 grain of Arsenious Acid) with abundance of milk and soda for food. In two days the jaundice was almost completely gone, and on the 4th her colour was more natural and healthy than at any time since she came under my care. A slight trace of the jaundice seemed to linger about the conjunctivae for some weeks. From this time she maintained a constant and steady improvement. The blood count kept varying between 55% and 70%, the spleen gradually became ^{both} smaller and softer, the circulation regained strength and regularity, and the general nutrition and strength of the patient improved. She was allowed to leave her bed ~~for~~ for a few hours, and soon was able to take advantage of the season and sit out of doors in direct sunshine.

On May 4th her weight was 6 stones, 12 lbs. On May 10th a careful examination of the heart showed that the condition had altered and improved consider-

ably. Even with a little exercise no palpitation had been felt for some time. The left border of the heart was distinctly within the nipple line. There was no sign of Tricuspid Regurgitation, and the systolic murmur heard at all the areas possibly, though not certainly, originated at the Pulmonary Orifice, where it was certainly much more pronounced. On May 19th she was found to be passing a large quantity of Uric Acid in a highly acid urine, a copious deposit appearing within 6 hours of micturition. The arsenic she was now taking was stopped (Bone marrow having been stopped on account of the onset of warm weather) and for 8 days nothing was given but Dilute Nitrohydrochloric Acid 10 m, t.in d. before meals with 10 grains of Salicylic Acid after meals. By this time the urine was again clear, mildly acid, and no uric acid could be seen in 24 hours.

The patient was sent to the country for more sunshine and rest in the open air than could be got at home. In a fortnight she returned much improved. Menstruation had appeared for the first time in the preceding week. Her blood did not seem to have suffered in any way and her weight had increased now

to $7\frac{1}{2}$ stones.

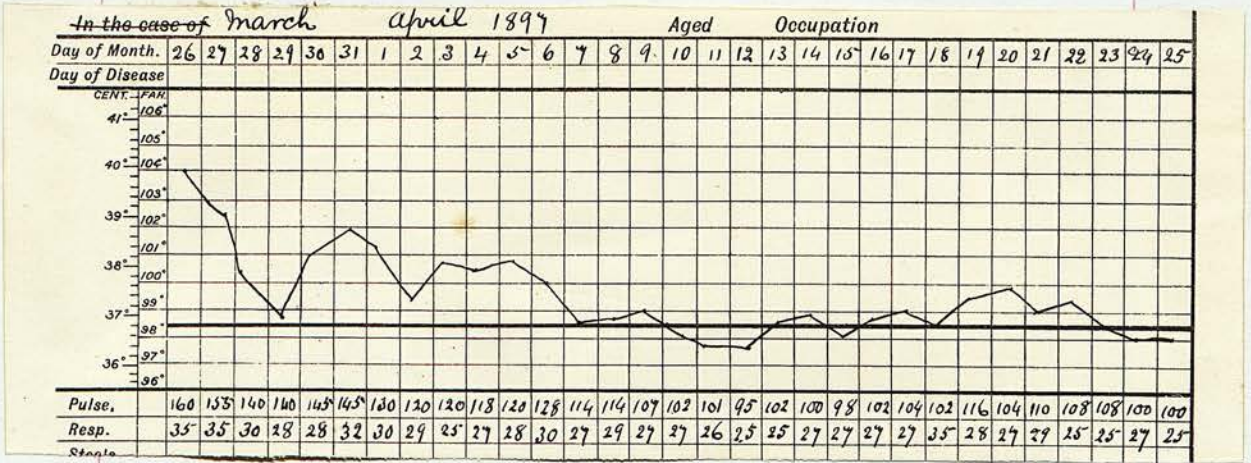
The death of a near relative on the 7th of June was almost disastrous to the patient. On the 11th I found her again very ill. Pulse 145, with much irregularity of the heart's action and sickly pallor of the skin. weak, sleepless, unable to take food, and complaining of headache. The spleen was again as large as at first, and the blood count showed a serious fall. Believing that the relapse was due entirely to mental causes, no change was made in the treatment beyond insisting on absolute rest for body and mind. The condition became rather worse for three days, then steadily improved, and in 2 weeks she was again up to her best.

For the following two months she continued to improve on the whole, although there were fluctuations in the condition of the blood and spleen, her general health remained good, she was able to be out for a few hours every day, and I was pressed to allow her to return to work.

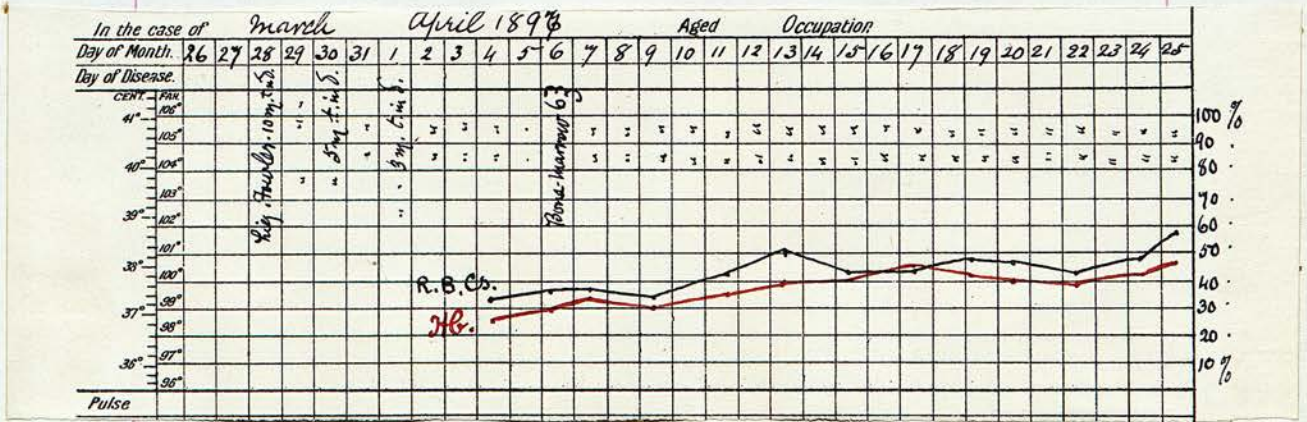
At the end of July her weight was $7\frac{1}{2}$ stones. The only remaining morbid signs of which she was conscious were a tendency to swelling at the ankles in

the evening, and a considerable falling of the hair. This symptom was no doubt due to the Arsenic which she was now taking in large doses, but as it soon became less marked and as a slight neuritis of both hands, attributed to the same cause, had already passed off without reduction of the dose, I continued to push the drug. At the end of October, 7½ months after coming under my observation, she was going about all day, doing light indoor duties. The spleen remained much as it had been for the last three months, and, as there were no urgent symptoms, at the pressing request of herself and her people, I stopped treatment by drugs and released her from restrictions of any kind. Up to the present time (Jan. 1898) she remains in much the same condition.

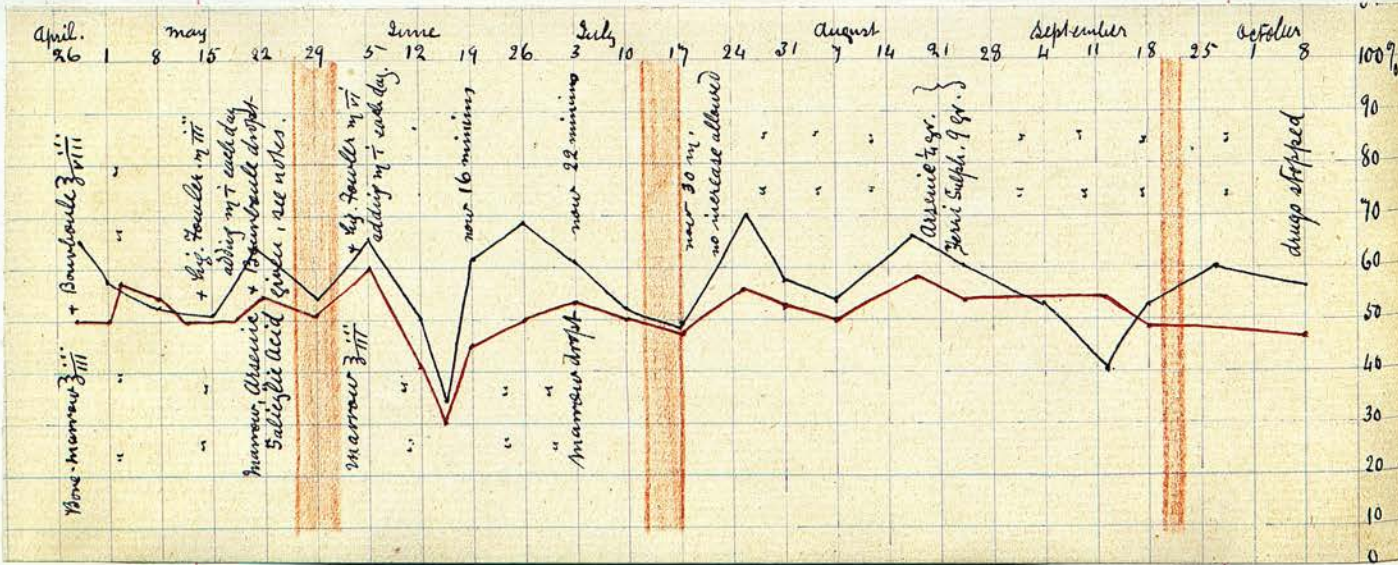
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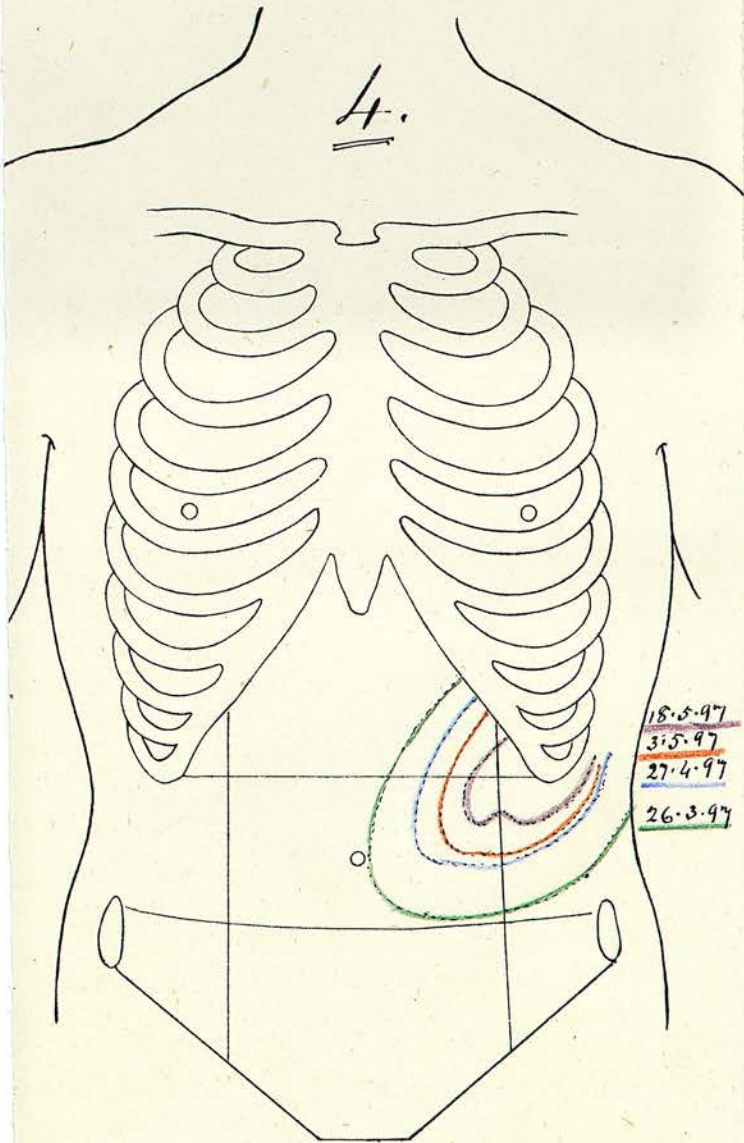
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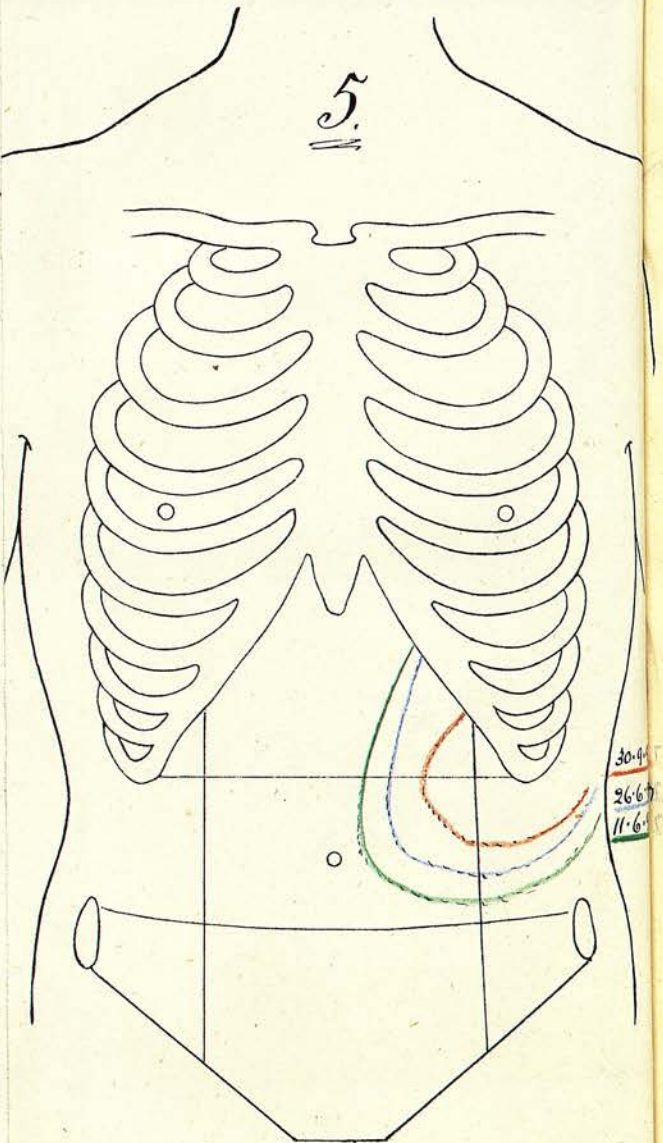
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18.5.97
31.5.97
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26.3.97

YOUNG J. PENTLAND
EDINBURGH.

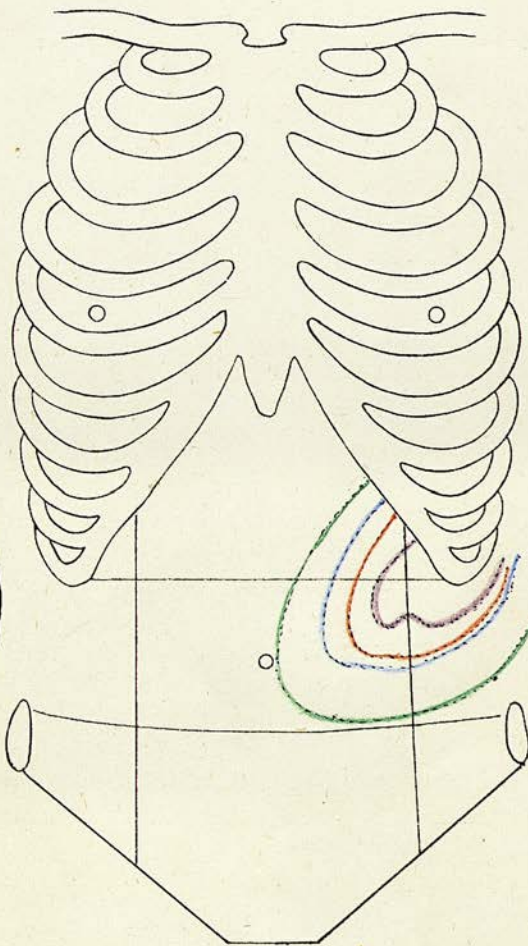
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YOUNG J. PENTLAND
EDINBURGH.

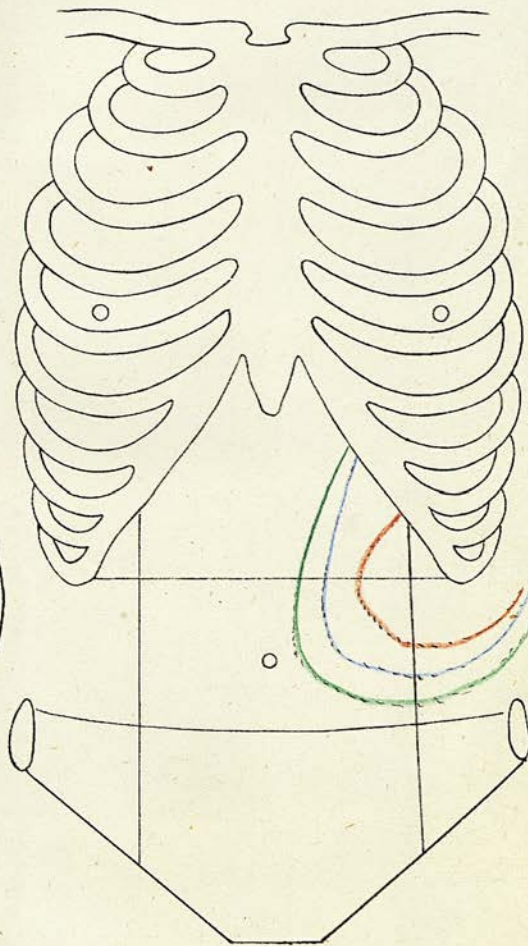
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18.5.97
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YOUNG J. PENTLAND.
EDINBURGH.

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30.4
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YOUNG J. PENTLAND.
EDINBURGH.

Explanation of Diagrams.

- Diagram 1. Shows the daily temperature, Pulse and Respiration for the first four weeks.
2. Gives the Blood-record, together with the drugs administered daily for the same period.
 3. Gives Blood-record and treatment and the menstrual history for the next six months.
 4. Shows the size of the spleen from March to the end of May.
 5. Shows same from relapse in June to the end of October.

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Case II. SPLENIC ANAEMIA.

From Dr. J. O. Affleck - Edin. Royal Infirmary)

Case of M -- H -- , Male, 29 yrs.

M- H-, age 29 years, a coalminer, presented himself complaining of a dragging pain low in the abdomen, epistaxis, weakness, deafness and cough.

Duration

About 14 weeks.

History.

Family history good. Personal history bad; he has been addicted to the use of alcohol, has worked very long hours in an unhealthy pit. He suffered from Enteritis and Axillary Lymphangitis 10 years ago. He has had gonorrhoea. Recently he suffered for some weeks from pain in the belly, "like inflammation". He has had severe epistaxis five times.

Admitted to the Wards of Dr. Affleck, Severe epistaxis recurred next day Temperature irregular, ranging from 99°F to 101°F. Gums not scorbutic. Spasmodic diarrhoea present. Blood showed Haemocytes 42%, Haemoglobin 35%, leucocytes 60,000, and a few nucleated red corpuscles. Spleen very large. Respiratory signs in the chest caused some suspicion

of early Phthisis. There was a presystolic mitral murmur present. The liver gradually enlarged. Purpura was observed on one occasion, and haematuria occurred several times. The anaemia improved somewhat under increasing doses of Arsenic and Salol. The leucocytes varied all the time from 30,000 to 100,000. Epistaxis recurred frequently. The temperature varied throughout from about 98° in the morning to about 102° in the evening, once rising to 104°.

He was discharged in four months, much improved. Two months later he returned in very poor condition, suffering mostly from cough and from Cystitis. The state of the blood was still much better than formerly, being - haemocytes 70%, haemoglobin 50% leucocytes 7,000. Temperature, as before. He suffered much from acute pain about the liver and spleen, gradually sank, and died three weeks after readmission.

Post-Mortem Examination (by Dr.R.Muir).

The lung affection was found to be Anthracosis, not Phthisis. The heart showed vegetations on both aortic and mitral valves.

The liver showed venous congestion and fatty

degeneration with many lymphoid nodules.

The spleen weighed 40 ounces, showed one old infarction, and was darker in colour than the leucocythaemic spleen. Malpighian bodies distinct. Organ firm in consistence but not hard. The whole change is a diffuse hyperplasia with much vascular engorgement.

Bone marrow red, but not very markedly so.

A peculiar form of cell was observed in this case by Dr. Muir, never seen by him in any other blood. It resembled a round epithelial cell and is to be reported on by him at an early date.

ANALYSIS OF 31 CASES OF SPLENIC ANAEMIA.Course and Prognosis.Course.

The two cases that have now been related give a fair idea of the ordinary course of Splenic Anaemia. Bruhl speaks of three stages:

1. Stage of Asthenia, or latent stage, marked by general loss of strength, and *occasional attacks of Perisplenitis.*
2. Stage of Anaemia and Splenomegaly (When cases come under observation).
3. Stage of Cachexia, going on to Marasmus, and Death.

This order is not quite invariable. Perisplenitis may occur at any stage, or may be absent throughout. Moreover, it is difficult from the records to maintain the distinction of the first and second stages, as it is generally impossible to say whether asthenia or anaemia was the first event. Bruhl's assertion of the priority of asthenia must depend on the accuracy of Collin's report alone.

Duration.

The duration of the disease before coming under observation can be ascertained in 18 cases, and in most of these it has been by far the larger part

of the whole course of the disease. Collin alone seems to have observed a case in the early stage of Asthenia - Bruhl's latent stage. The average duration of the others, previous to observation, is less than two years. The Issue is practically always fatal. Only one trustworthy record of complete recovery is to hand - Köster's, and it is too recent to be pronounced permanent. The total duration can be estimated in 17 cases, of which the most acute terminated in a little more than three months, the most chronic in six years, while the average duration of the 17 was $2\frac{1}{4}$ years. For reasons to be considered later we may remark that these extremes and that average correspond exactly (Gowers & Fagge) with those met with in Leucocythaemia and in Hodgkin's Disease.

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Etiological Considerations.

Previous Condition.

The details of the previous condition are given in 18 cases. Of these 3 suffered from haemorrhage, severe or recurrent (too long before to consider it as a symptom), 2 from Influenza, 2 had a tubercular heredity, and 3 are said to have enjoyed previously uninterrupted good health. One patient thought a

blow over the spleen was the cause of her illness, and the others are credited to various debilitating causes.

Age Incidence.

We find the age of the patient stated in 26 cases. In the 8 female cases the age varies from 3 to 72, but in the males, all, with one exception, (a boy of nine) were in early adult life, from 20 to 45, with a total average of 31.

Sex Incidence.

The cases I am able to accept provisionally as Splenic Anaemias amount in all to 31, of which 23 are in the male sex, 8 in the female, a proportion (roughly) of 3 to 1. Bruhl's statement is therefore still accurate. "The disease may occur at all ages, but is most common in adult males."

Symptomatology.

Early Symptoms.

The early symptoms of Splenic Anaemia are very indefinite, owing to the fact that cases are practically never seen until the disease is far advanced.

In the case of the patient whom Collin believes he saw in the first stage of the disease, nothing was

discovered by him beyond a slight jaundice and the patient's complaint of occasional pain about the left side. Four months after this the man returned to Collin with Splenic Anaemia already in an advanced stage. In all the other cases we have to rely on the patient's own observation of his early condition.

The majority of cases seem to indicate an invasion of the disease only by a gradually increasing general debility, anorexia, and pallor (13 cases). Frequently (8 cases) the earliest complaint is of spontaneous haemorrhage, epistaxis being much the most frequent form. Much less common are abdominal pains (4) splenic pains (3), breathlessness (4), diarrhoea, vomiting and other digestive troubles (3), palpitation (2), recurrent feverish attacks, oedema, and recurrent jaundice (1 each.)

Considering, however, that all of these are the common complications of the disease as seen under treatment, i.e. in more advanced stages, and that we have only the patient's authority for the stage at which they appeared, it is evident that although they are the earliest known symptoms, we cannot conclude that they represent the earliest stages of the disease.

Splenic Crisis

A typical "splenic crisis" has been sufficiently described in the report of the case of M.P. It is an attack marked by acute paroxysmal pain and tenderness about the left hypochondrium, generally accompanied by sickness, vomiting, diarrhoea and pyrexia, often by jaundice and sometimes by left basal pleurisy. But for the constant site of pain it would commonly be mistaken for hepatic colic. It is recorded as present in 9 of the cases. It may occur only once, or may recur many times in each case. It cannot be said to be more frequent at one stage than at another. It is probably (Bruhl and Taylor) due to perisplenitis, though this was seen post mortem in only 3 cases. In 2 more infarctions were present, perhaps both producing and concealing the local perisplenitis. It is not clear, however, that this is the whole explanation. In leucocythaemia both infarctions and perisplenitis are as commonly met with, but no attacks comparable with the "Splenic Crisis" are found.

Condition of Spleen during life.

In every case the splenomegaly is very advanced when first observed; "énorme" is Bruhl's constant

description. Curiously enough it does not seem ever to have increased much after the first measurements. A diminution of size coincident with general improvement of the patient, is rare, but has been observed by Strumpell, Köster and myself, while, on the other hand, a diminishing spleen has frequently been noted while the patient was going from bad to worse, and especially in the last days of life. (Compare this with the diminution of the large glands of Hodgkin's Disease, observed before death - Fagge.). It may here be noted in passing that from the recent researches of Campbell Clark, it seems possible that some of the symptoms of the disease, namely, the tendency to pyrexia, the rapidity (often out of proportion to the temperature) and low tension of the pulse, the soft, moist condition and ready flushing of the skin, may be partly dependent on a true increase of function accompanying the anatomical hypertrophy of the spleen.

Enlarged Liver.

Some enlargement of the liver is a very frequent accompaniment of the splenomegaly, rarely with tenderness. An enlargement from "slight" to "great" is recorded in 12 cases, while in three only is there

a report of a liver of normal size.

Jaundice.

This has been seen in six cases, most often occurring along with a splenic crisis. The authors mention the colour of the skin; the supplementary evidence of faeces and urine does not appear in any, an important omission in a disease in which the skin commonly suggests a slight jaundice. The jaundice of splenic anaemia is evidently not merely an accumulation in the superficial vessels of waste colouring matter from the blood, since careful examination of the blood of M.P. at the time of her severe attack showed no sign whatever of a rapid blood change. It is probably of two different origins. When it occurs at a "splenic crisis" it may be due to "shock" acting through a nervous constriction of the ~~bowel~~ bile passages. When it occurs apart from such a crisis it is probably due to a gradual constriction of the same ducts by lymphomatous growth. In the latter case it is likely to be less sudden but to last longer.

Haemorrhage. (Spontaneous).

This, another of the classical symptoms, is present in less than half the cases, 13 in all.

Epistaxis is much the most common form, occurring in 11 cases, haematuria^{emebis} in 3, while there is one observation for each of the following:- Melaena, haematuria, purpura, retinal haemorrhage, and bleeding from the gums.

Cardiac Murmurs.

Are probably as constant as in other grave anaemias. In only one case is their absence noted. From the frequency of post-mortem evidence of endocarditis, it is probable that in many cases at least the murmurs are organic, rather than functional.

Oedema.

Dropsical effusions are by no means as frequent as Bruhl seems to indicate; ascites appearing in 4 cases, general oedema in 3, oedema confined to the legs in 3, while in West's case a sudden and severe oedema laryngis compelled immediate recourse to tracheotomy.

Movements of the Bowels.

Bruhl's statement that "constipation is the rule, diarrhoea the exception" is probably a clerical error. There is no record of constipation. In only 7 cases is the state of the bowels mentioned, and in all of

these diarrhoea was present.

A priori we should have expected the pressure of the enormous spleen to cause obstruction rather than irritation of the bowels. I suspect that careful examination of the intestine in the diarrhoeal cases would have shown some affection of the lymphoid patches. This has not been noted, however, except by ^{Murray-Leslie} ~~Leslie Murray~~ and Williamson.

Urine.

The accounts of the urine are extremely scanty. In no case does it seem to have been like the chlorotic urine, large in quantity, of low Specific Gravity and very deficient in colouring matter. It is generally scanty, very acid, with urea varying from 10 to 45 grammes in the day. Albuminuria was observed in 4 cases, haematuria in 1.

The urine in my own case was examined once a week, or more often when indicated. It was throughout about normal in quantity, of Specific Gravity 1020 to 1030, always acid, sometimes abnormally acid, rather dark in colour, on account of excess of normal pigments, and never shewed the presence of albumin, blood or sugar. The condition of the urine during the

jaundice in April and during the "Uric Acid Crisis" in May has already been mentioned. The daily ~~see~~ excretion of Urea varied very little, and within normal limits, during the whole course of observation.

Fever.

In all cases the temperature is high, either continuously or rising at intervals. It is apt to rise high (as far as 104^oF) on the occurrence of a Splenic Crisis. West found his case at 103^oF, and it remained "high" all the time. The cases of Affleck and of Williamson showed a temperature that may be described as "hectic", ranging throughout from 99^o in the morning to 102^o in the evening.

Various Symptoms.

Headache, buzzing in the ears and sweating are occasional symptoms. Emaciation, though rare, does occur.

Fatal Complications.

Two cases died in indirect consequence of the treatment adopted, Banti's 3rd case from haemorrhage after Splenectomy, and Lodi's from septicaemia after transfusion. One died of Pneumonia, one of the perforating of a Gastric Ulcer, and one of the per-

forating of an Intestinal Ulcer. All the rest seem to have died from general asthenia.

The Blood.

In the recorded cases of Splenic Anaemia, the observations on the blood are the most disappointing. They may be tabulated as follows:-

Red Corpuscles.

1. Normal. - much variation in size (Williamson).
2. Nucleated. - present in small numbers (Affleck)
3. Blood-plates. - no observations.
4. Microcytes. - common (Banti, Bruhl, Köster).
5. Macrocytes - always absent (Bruhl, Köster).
6. Poikilocytes. - present (Banti, Taylor, Köster, Williamson).
absent (Bruhl).

White Corpuscles.

Mononuclear, small; - excess of these much the most marked change (Williamson).

" large; - absent (Williamson).

Polynuclear, eosinophilic; - Köster finds a few, Williamson none.

The Haemoglobin at first observation in each case, is found to range from 17% to 68% (average 41%)

The Haemocytes at the same times range from 20% to 79% (Average 62%)

The proportion of the red corpuscles present is always superior to that of the Haemoglobin by about 20%, i.e., the anaemia is of the Chlorotic type.

The number of Leucocytes present is in many cases about normal, but in several an occasional leucocytosis appears, sometimes, as once in Affleck's case, reaching ~~to~~ a high degree. This is believed by Bruhl to be entirely attributable to intercurrent complications such as fever, or inflammations. From the cases encountered since Bruhl's publication it is therefore impossible to do more than repeat his conclusion that "there is no change in the blood that is ^{granular} ~~pathogenic~~ of Splenic Anaemia".

My own observations are little, if at all, more satisfactory. In the odd hours of a general practice and with the limited resources of a country surgery, not much can be done, but I have examined the blood more than 100 times in 6 months, by means of Thomas' Haemocytometer and Gowers' Haemoglobinometer, and have prepared slides of the blood either unstained, or fixed and stained by Gulland's method, and by Ehrlich's Haematoxylin-Eosin Method.

The examination by differential stains for the

various granules described by Ehrlich gave no result whatever and may be omitted. The rest I shall summarize as briefly as possible.

Coagulability. The time required for coagulation was distinctly increased.

Specific Gravity. Tested on many occasions, was always about 1045.

Blood Value. The progress of the blood as to the proportion of red corpuscles and haemoglobin can be traced on the charts on Page 18. It is obvious that the so-called "chlorotic type" is much less marked in this than in most cases.

Rouleaux. Were at first very slow to form, but in this respect, the blood gradually improved.

Microscopic Examination.

I. Red Corpuscles.

- (1) Normal Corpuscles. For number see Chart. They varied much in size all through. The megalocytes were estimated at first at 7% of the total number of haemocytes. The proportion steadily diminished as the patient improved, and in two months was no more than 1½%. This observation is of interest as the converse of Gilbert's that a steady increase of this form (up to as much as 30% in some extreme cases) is always prognostic of a fatal issue.
- (2) Nucleated Red Corpuscles. Absent throughout.
- (3) Blood Plates. Normal in number, with a distinct increase in the later months (due to menstruation? see Gilbert et Lion; or due to the use of Arsenic?)

(4) Poikilocytes.

Never observed except when probably due to methods of preparation.

II. Leucocytes.

The total number varied from 3,000 to 7,000 per cm.

<u>Varieties.</u>	<u>Percentage.</u>	<u>Normal.</u> (Gundobin)
Small mononuclear.	19	24-30
Large Mononuclear.	6½	3-6
Polynuclear neutrophiles.	72	60-75
Eosinophiles.	2½	1-2

These percentages represent the average of a long series of enumerations, among which there was so little variation that it is unnecessary to give them in full. The only point on which I would remark is that the small mononuclear leucocytes, increase of which was found by Williamson to be the most marked change, are, on the contrary, rather diminished in number.

PATHOLOGICAL ANATOMY .

Out of 31 cases of Splenic Anaemia I find records of post-mortem examination in 17. The principal facts observed are the following.

Spleen.

The spleen, an organ weighing in the healthy subject some 5 or 6 oz., is always enormously enlarged, the recorded weights ranging from 40 to 208 oz. It is almost always firm in consistence and dark in colour. Much the most frequent change is a general overgrowth of the trabecular framework, accompanied in the early stage by distension and engorgement of the sinuses, and becoming in the later a cirrhosis (the lymphoid tissue becoming fibroid) with constriction and all but obliteration of the sinuses and even of the Malpighian Bodies. In 2 cases there was practically nothing but general vascular engorgement to be seen by the naked eye. In one case Splenic Abscess was found. Perisplenitis is not uncommon (3) and infarctions have been recognised 4 times.

The contents of the sinuses vary, most likely with the stage of the cirrhosis, and the leucocytes may

be very few (3 cases). Free iron has been found in the spleen by Williamson, but was searched for unsuccessfully by West. The remarkable cells containing a large number of red corpuscles, described by Williamson, were carefully searched for by Dr. Muir in Affleck's case, but without success.

Lymphatic Glands.

In only one case, but that is crucial, was any involvement of the glandular system found post-mortem, *viz.* in Woillez' case, where the two mesenteric glands were shown to be in exactly the same "Hyperplastic" condition as the spleen.

Liver.

It is reported enlarged in 11 cases, weighing as much as 93 oz. in West's case. The nature of the change is seldom mentioned, but it seems most often to have been lymphomatous or cirrhotic according to its stage, similar, in fact, to the condition common to Leucocythaemia and Hodgkin's Disease. Affleck's case showed venous congestion with fatty degeneration and a few lymphomatous nodules. Free iron has not been found in the liver.

Pancreas.

This gland has not been reported on except by Stanley, who, in both of his two cases, found it "cirrhotic" like the spleen.

Bone Marrow.

It is frequently (5 cases) found redder than normal, with a smaller proportion of fat. Williamson found no free iron, but many large corpuscle-containing cells, similar to those he saw in the spleen in the same case.

Supra-Renal Bodies.

They have been twice found fatty and atrophic.

Heart.

Endocarditis with vegetations on the valves has been observed in three cases.

DIAGNOSIS.

In the consideration of Splenic Anaemia, accurate diagnosis is at once of supreme importance and of the greatest difficulty. So important is it, in the case of a disease both obscure and rare, to admit none but absolutely unquestionable cases, that I have been compelled to exclude about a dozen reported by various observers. From the fact that eminent physicians have on more than one occasion found a confident diagnosis negatived by post-mortem evidence, we must conclude that the symptoms and course of Splenic Anaemia may be simulated by quite different conditions. I am again indebted to Dr. Affleck for one such case, perhaps more instructive than a successful diagnosis. Very briefly it is as follows:-

Waxy Disease.

W.W., aet. 27, a tailor to trade. Complained of progressive weakness and indigestion for 6 months, with abdominal pain, diarrhoea and cough for 4 weeks.

Family History fair.

Personal history fair, no alcoholism, workshop badly ventilated. Suffered from epistaxis at intervals for one year, and latterly almost every

second day.

Admitted to Edinburgh Royal Infirmary. Skin is pallid, yellowish.

Blood - Haemocytes 84% Haemoglobin 52% Leucocytes 40,000.

Temperature varies from 97° to 101°F.

Palpitation, mitral systolic murmur.

Liver large, and spleen very large.

Patient was treated with arsenic 30m. daily; but made more improvement on Bone Marrow tabloids, 2 grs., thrice daily.

An attack of jaundice occurred, but no bile was found in the urine. The splenic tumour became much smaller, patient improved considerably and left the hospital.

The case was considered to be Splenic Anaemia. The patient returned a few months later, much worse, and soon died.

Post mortem the spleen was a large waxy spleen; and the whole case one of general waxy disease of unascertained origin.

Syphilis.

It is hardly necessary to insist on the import-

ance of excluding Syphilis, since the case of Coup-land and Gould showed that Splenic Anaemia can be simulated in its entirety by that disease.

Sarcoma.

Can nearly in every case be recognised by its previous occurrence in other organs. Primary splenic sarcoma is even more rare than Splenic Anaemia.

(Weichselbaum).

Ulcerative Endocarditis.

"A swollen and tender spleen with pyrexia and a cardiac bruit is a certain sign of ulcerative endocarditis" (Fagge). The previous history and the subsequent course would probably soon differentiate the two conditions, yet it would be extremely difficult to exclude Splenic Anaemia on the spot if one were called to such a case of Ulcerative Endocarditis as that reported by Dr. Lauder Brunton in Edin. Med. Journ. May 1897.

Hypertrophic Cirrhosis of the Liver.

This would not often give trouble except in the case of children, when the spleen is often of very large size - the "Splénomegalic hepatic cirrhosis" of Gilbert ^{and} ~~et~~ Fournier.

Anaemia Infantum.

(Pseudo-leucaemia^c of Von Jaksch.) This rare disease, and the splenic anaemias in children so frequent in Italy and in America (see Somma, Koplik and Warner) need not be discussed, partly because they occur at an age when Splenic Anaemia of Banti is almost unknown, and partly because they would lead us into the interesting, but certainly foreign land of malaria.

The conditions which demand fuller examination are the primary anaemias, Chlorosis and Pernicious Anaemia, and, finally, Leucocythaemia and Hodgkin's Disease.

Chlorosis.

Uncomplicated typical chlorosis can scarcely be mistaken for Splenic Anaemia. In chlorosis, splenomegaly and spontaneous haemorrhage are unknown and the disease is "never directly fatal" (Fagge). Oedema is never of great extent, constipation is common and the disease is all but confined to young females. Splenic Anaemia is certainly not a severe or fatal type of Chlorosis. The blood changes are altogether different. The leucocytes in chlorosis show a marked excess of

large mononuclear forms, (Wentworth, Cabot, etc.) which is certainly not the case in Splenic Anaemia. The reduction of the specific gravity of the blood in Chlorosis, perhaps its most marked feature, (down to 1032 Lloyd Jones), is greater than in Splenic Anaemia.

Above all, the age incidence and sex incidence of the two diseases show that there is no relation between them.

Chlorosis with Gastric Ulcer.

It may at the same time be worth remark that a physician called for the first time to see a young woman suffering from Splenic Anaemia during a splenic crisis, as I have been, would be very apt to diagnose Chlorosis with perforated Gastric Ulcer. That diagnosis can be avoided by attention to the history, the precise seat of pain and of tenderness, the presence or absence of fever, and careful physical examination of the splenic tumour to distinguish it from peritoneal effusion.

Pernicious Anaemia

This disease at first sight seems to compare closely with Splenic Anaemia, in that it ~~has~~^{is} a severe and indeed fatal anaemia, occurring most commonly in the adult, marked by rapid progressive asthenia and

irregular fever and frequently by spontaneous haemorrhage and local oedema. It differs from Splenic Anaemia in its more rapid course, and in showing no greater incidence in the male sex. The most frequent spontaneous haemorrhage in Pernicious Anaemia, viz., retinal haemorrhage, is the least frequent in splenic anaemia, and though the spleen may (rarely) be found enlarged in pernicious anaemia, it is never comparable with the enormous spleen which is the rule in Splenic Anaemia.

The Pathological Anatomy of the two diseases differs entirely, the fatty degeneration of the heart, diaphragm and other viscera, and the deposit of free iron in the liver which are prominent in pernicious anaemia, being hardly noticed in splenic.

The condition of the blood is so different that I place it in tabular form:

<u>Pernicious.</u>	<u>Splenic.</u>
Haemocytes, very low.	Not so low.
Poikilocytosis marked.	rare.
Microcytes. common.	variable.
Megalocytes.	{always lower than corpuscles.
Haemoglobin high in proportion to corpuscles.	
Neucleated Haemocytes - common.	absent.
Leucocytes.	
Mononuclear cells increased.	Not increased.
Eosinophilic " " "	" "

These conditions establish a clear diagnosis between the two diseases, the stress of the morbid process lying in the one on the formed elements of the blood, and in the other, on the spleen.

Leucocythaemia.

The typical splenic form of this disease is not hard to distinguish from Splenic Anaemia. Although resembling the latter in being an anaemia with enormous spleen, most common in adults from 20 to 50, and more than twice as frequent in the male as in the female, and showing, moreover, complications such as Epistaxis, that make the clinical pictures very similar, leucocythaemia is, vulgarly, at once distinguished by the presence of Leucocytes in great excess. But when we examine the cases more closely, we find it impossible to state the essential difference so simply. The blood in leucocythaemia, while always anaemic, need not even be constantly "leucocytotic", for an excess of leucocytes that is no more than slight or occasional is recognised by most authorities (Fagge in loco). Again, soon after Bennet's and Virchow's discovery of the splenic type, there very rapidly followed the recognition of the forms known as Lymphatic and Myelog-

enous and the very rare form known as "Leucémie Intestinale" of Béhier. Before long, again, it was ascertained that a pure form is very rare indeed, so that the "spleno-myelogenous" form is now commonly regarded as the "type" of the disease. The marked difference in the kinds of leucocytes present show whether glands, spleen or bones are most affected in any single case, but this rather tends to indicate that the primary lesion is not in the blood, but is localised or disseminated or all but generalised, as the case may be, in the lymphoid tissues of the body.

Hodgkin's Disease.

In the case of Hodgkin's Disease also, the typical case is quite distinct from the typical Splenic Anaemia. Here the enlargement of the lymphatic glands, most frequently superficial, is the first event, followed by anaemia, and, often after a long interval, by enlargement of the spleen. It seems to occur mostly at an earlier age than Splenic Anaemia. Not only is the typical clinical picture different, but the typical pathological lesion, the "hard bake spleen" of Hodgkin's Disease is, so far, unknown in Splenic Anaemia. The mere order of invasion, how-

ever, can hardly be depended upon for a pathological distinction of two diseases, and there are many points of similarity in the clinical position. There is the same incidence on the male sex, the same tendency to more or less oedema. Occasional haemorrhages occur in both and in both epistaxis is the most common form. In both leucocytosis, while generally absent, may be present, and may even reach a high degree. In both the temperature is variable, but is most often irregular with occasional exacerbations. Even so inexplicable a phenomenon as the diminution of the spleen in the last days of life in Splenic Anaemia is paralleled in Hodgkin's Disease by a diminution of the enlarged glands (Fagge). So close may the resemblance be that ~~many~~ cases have been recorded in which eminent observers, alive to the accepted distinctions of the two diseases, have, even after post-mortem examination, been in doubt, or at least leave the reader in doubt, as to the final diagnosis. For examples:

1. Pye-Smith (1870) a case supposed to be Hodgkin, where the spleen alone was affected.
2. Pye-Smith (1874) where spleen and liver, both enormous, seemed to be affected with Hodgkin's Disease, but no glandular affection could be traced.

3. Wilks, a case diagnosed as similar to No.1, but post-mortem some deep glands in the abdomen were found affected.
4. ~~Leslie Murray~~ ^{Murray-Leslie} - a case believed by him to be Splenic Anaemia, where the liver and the lymphatic ^{oid} patches of the intestine were found in the same condition as the spleen.
5. Gretsel's case of Hodgkin's Disease, where the spleen was enlarged for "several" years before the glands became involved.
6. Concato's case of Splenic Anaemia, where post-mortem some mesenteric glands were found affected. (Reference mislaid).
7. Woillez' case, exactly similar.
8. Taylor's case of Splenic Anaemia, where two glands, one in the neck and one in the axilla, were found in a state of hyperplasia.

It would thus appear that, if the definition of Bruhl, "the absence of lymphomata is absolute and pathogenic", is to be rigidly adhered to, ^{gnomonic} the diagnosis of Splenic Anaemia cannot be made during life, since it is always possible that extension to the glands may become evident during life or after death. But it seems to me impracticable to maintain an absolute separation of two diseases on so slender a basis. Besides, even the post mortem evidence is not decisive, for the "hard bake spleen" is not the only condition found in indisputable cases of Hodgkin's disease,

(Goodhart and Ziegler). "The pathological anatomy", says Fagge, "is unessential . . . The spleen may present only an indefinite mottling, or its tissue may be uniformly red or homogeneous," a condition that would, but for the granular enlargement, have been accepted as the typical spleen of splenic anaemia. We may, in my opinion, infer that while the extreme variations of the two conditions are certainly considerable, we are not entitled to call these extreme cases the types of two distinct pathological entities, and that the correspondence in sex and age incidence, course, symptoms and ultimate pathology (a lymphoid hyperplasia) outweighs these variations in rational import. The opinion that Splenic Anaemia is merely a splenic variety of Hodgkin's Disease, was the opinion of Banti, and has been adopted by Wunderlich and apparently by Ziegler in his latest edition (1897, p.113).

For my own part, I believe we may attempt a more comprehensive generalization. It is true, of course, that progress in medical, as in all other, science is mainly a process of differentiation or specialisation, yet it is sometimes evident that the

microscopic habit has carried us too far, and that a halt must be called in the march of analysis to synthesise as much as may be of what has been analysed. We have valuable examples of this in the syntheses by Leyden, Gowers, and others, of the old Bulbar Paralysis, My-atrophic Lateral Sclerosis and Progressive Muscular Atrophy into one group, or the generalisation of many of the forms of bullous skin diseases that is known by the name of Duhring.

In relation to the present subject, Jaccoud has suggested a "diathèse lymphogène," and without subscribing to the French mania for diatheses, I believe we may, with advantage, consider Leucocythaemia, Hodgkin's Disease, and Splenic Anaemia from this point of view.

A careful perusal of the best clinical accounts in recent works on General Medicine, leaves the reader with the impression that for ultimate diagnosis he must await the decision of the pathological anatomist, while, on the other hand, Zeigler for the pathologists expressly states that in the case of both spleen and glands, the histological structure being "anatomically identical", reference must be made to the living blood

for diagnosis. The three diseases may be classed as a form of disease most common in early adult life, though not unknown at any age, affecting the male sex from twice to thrice as often as the female, producing progressive asthenia with anaemia and all the general symptoms of anaemia, with frequent spontaneous haemorrhages, with oedema more frequent and general than occurs in a simple anaemia, and with irregular, occasional or periodic fever. In all three varieties the prognosis is extremely and equally unfavourable, and in all the progress under treatment is marked by the same total failure of Iron alone, and the occasional or temporary success of Arsenic, Oxygen and Bone-marrow. In all the seat of the lesion is the lymphoid tissue in one or more structures or organs, in some cases (Hodgkin's disease) there being evident hyperplasia of that tissue in spleen, lymphatic glands, bone-marrow, liver, kidneys and lungs, in fact (if the patient lives long enough) wherever lymphoid tissue is normally found. In other cases (Splenic Anaemia) the hyperplasia is confined to the spleen, In all varieties, the conditions of the glands, bone-marrow, and liver correspond. Why in any case one



part should be attacked previous to, more than, or to the exclusion of another, we are not in a position to say, so long as we are quite ignorant of the ultimate cause of the hyperplasia. Finally, in all varieties the results on the blood are, though not the same, yet comparable. In all there is anaemia, tending, as do most secondary anaemias, to the Chlorotic type, and in all an excess of Leucocytes may or may not be present, their number being probably directly proportional to the extent of the affection of the lymphoid tissue, and inversely proportional to the stage of the pathological change, i.e. to the progress from a hyperplastic (productive) condition to a cirrhotic (obstructive or destructive) condition. The same supposition may be true of the number of each form of leucocyte, but this may be almost impossible to establish, since a productive change in some of the organs producing any form may coincide with an obstructive or even a destructive stage in other organs having the same function.

CONCLUSIONS AS TO ETIOLOGY & PATHOGENESIS.

From this investigation of all the available data as to Splenic Anaemia, and from comparison of the results with the recognised facts of Leucocythaemia and Hodgkin's Disease I conclude that from the standpoint of clinical convenience and of pathological anatomy, the three are no more than varied manifestations of the same morbid process. To go beyond this, or to affirm that the three are only varieties of one "disease" is impossible until more is ascertained about their ultimate etiology. As to the nature of the ultimate cause or (more probably) causes, when we consider how general the process often is from the beginning, it does not seem likely to be of the nature of a new growth. There is, of course, the bacteriological field to investigate. Given a disease with high fever, large spleen and frequent endocarditis, one is bound now-a-days to "chercher le microbe". Bruhl, however, failed in many attempts to find microbes in the blood in Splenic Anaemia; Williamson found none in the spleen or in the cardiac vegetations after death, and I have been as unsuccessful as both.

In Leucocythaemia, on the other hand, every observer has found a ^{germ}~~germ~~ of his own, Bonardi a staphylococcus, Touton a protozoon and Kelsch & Vaillard a bacillus (See Wurtz), while in Hodgkin's Disease the results are equally indecisive, except for the observations of Brentano and Tangl, Cordua and others as to the frequency of tubercular infection.

To draw this discussion to a close, it seems to me

1. That cases of so-called Splenic Anaemia want more careful observation and investigation than they have in most cases received.
2. That the histological examination of the blood is not likely to throw light on the nature though indicating the main situation or stage of the morbid process and its cause.
3. That no case can be accepted as certainly not Hodgkin's Disease nor Leucocythaemia (not to speak of Waxy Disease, Syphilis, etc.) until after post-mortem examination.
4. That for the present Splenic Anaemia cannot be accepted as a disease per se, but must be provisionally placed as the most local form of Lymphoid Hyperplasia.

TREATMENT OF SPLENIC ANAEMIA.

So long as the etiology is unknown it is impossible to claim any treatment as a rational cure for the disease, while the uniformly fatal issue up to the present time proves that empiric treatment has no permanent value.

All authorities agree that Iron alone is of no use whatever, seldom showing any improvement even temporarily.

From the use of Arsenic, alone or combined with Iron, from Bone-marrow and from Oxygen considerable benefit can always be obtained for a time. Köster claims complete recovery from advanced Splenic Anaemia in 3 months, from the administration of Arsenic and Quinine with 4 litres of Oxygen daily in a case previously going down under Arsenic and Quinine alone. Taylor, on the other hand, obtained only a temporary improvement from Arsenic and Iodides with as much as 30 litres of Oxygen daily.

While Arsenic is antiseptic, it also, like Iron and Bone-marrow, stimulates the growth of bone (the chief blood-forming tissue) and, according to Binz is a means of indirectly supplying oxygen to the tissues.

In severe cases a trial might be made of injection of arsenic or quinine into the spleen.

Transfusion of blood has been used with apparent temporary benefit, but, promising as were the early results, it has been, as far as I can gather, finally abandoned as a mode of treatment in primary anaemias.

Splenectomy has been tried in one of two cases with transitory benefit. Banti, Wells, Taylor & Gould have given their opinion in favour of this radical treatment of the splenomegaly. The danger of the operation is rapidly becoming less with improved technique, Spanton's mortality-tables showing already no more than 37% of deaths. In the improvement after splenectomy there is perhaps some slight confirmation of the theory of microbic origin, from the fact that the main constitutional result of the removal of this organ is an increase of the bactericidal action of the blood and consequently a greater power of recovery from infective processes (Blumreich & Jacoby). Besides we must allow that whatever the nature of the cause of the disease of the spleen, so long as no change can be traced outside of that organ,

removal of the spleen may mean removal of the origo mali.

In regard to the treatment of my patient M. P. there are two details worthy of mention.

(1) The use of Bourboule Water as an introduction to the administration of Arsenic. It was taken with ease and benefit when very small doses of Arsenic in other forms were rejected. It is to be remembered that apart from the Arsenic it contains, Bourboule Water is practically blood-serum.

(2) The very large amount of Bone-marrow taken without disturbance of digestion. As much as 6 oz. was taken daily for several weeks, twice as much as the largest dose I have read of. (Fraser & Barr). It is of course true that the marrow usually administered consists of nothing but fat (Stockman) but even fat is a stimulant to the blood-forming tissues (Nasse etc.)

The treatment of Splenic Anaemia therefore must be conducted on general principles.

1. We can conserve the patient's energies by complete rest, better in open air and sunshine when possible.
2. We can supply a light, nutritious, blood-forming mixed diet.

3. We can directly stimulate reformation of the blood by the use of the drugs already named.
4. And in the last resort (or better, perhaps, at an early stage) splenectomy may be tried with a fair prospect of considerable temporary improvement and a chance, remote it must be confessed, of permanent cure.

LIST OF CASES OF SPLENIC ANAEMIA.

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Affleck	In present communication.	1.
Banti.	a) Dell' Anemia Splenica - Florence, 1882.	3.
Beale.	Royal Med. & Chir. Soc. June, 1896.	1.
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Collin.	Bul. de la Soc. Méd. des Hôpitaux 1862.	1.
Coupland.	Royal Med. & Chir. Soc., June, 1896.	1.
Degle.	Wiener Med. Presse - 1891.	1.
Gossage.	Westmin. Hospital Reports - 1895.	1.
Koster.	Centralbl. für innere Medizin, Jan. 1896.	1.
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Lodi.	Trattato della Leucemia, 1880.	1.
Muller.	Anaemia Perniciosa - 1877.	1.
	Berlin. Klinische Wochensch., 1867.	2.
Potain.	La Semaine Médicale, 1887.	1.
Squire.	see Wilks & Moxon's Pathology, &c.	1.
Stanley.	Brit. Med. Journal. 23.11.95.	2.
Strumpell.	Archiv. der Heilkunde, T. 17.18.	1.

a) This work is very rare. Probably only one copy exists in Britain (and that is in private hands) but the substance of it is given in French by Bruhl.

		Cases
Taylor	Royal Med. & Chir. Soc. June 1896.	2.
	^{Guy'} Grey' s Hospital Reports 1896.	1.
Wells.	See Wilks & Moxon's Pathology.	1.
West	Royal Med. & Chir. Soc., June 1896.	1.
Wilks.	Lancet, July, 1861.	1.
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