T H E S I S

presented to

THE UNIVERSITY OF EDINBURGH

for the Degree of

D O C T O R OF M E D I C I N E

by

ALFRED IRVING SHEPHEARD-WALWYN.

(M.B., Ch.B.Edin.)

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

The subject of this discussion was suggested to me by two or three very interesting cases I met with when I was House Physician to Dr. Gibson in The Edinburgh Royal Infirmary.

On looking up the literature of the subject, I was struck with the paucity of our knowledge regarding this disease as well as other diseases affecting the blood and blood-forming organs.

That our scant knowledge as to the causation of these affections and the state of chaos which exists regarding their classification is very largely caused by the meagreness of dependable observations is irrefutable. Equally certain is it that our conceptions of these morbid conditions can be much aided by the truthful statement of the conditions found in connection with them.

For this reason, although I have found the subject in a tangle which I am unable to unravel, I have thought it would be useful to state the facts I have met with in the necessarily limited number of cases which I have been enabled to observe, in the hope that I may have been able to add a link to the chain of

facts which we still need for the comprehension of these rare but fatal diseases.

Owing to the fact that satisfactory examination of the blood is a comparatively recent undertaking, and that, in many instances, the reports of earlier writers are meagre, it follows that the history of splenic anæmia must be inseparably connected with that of other blood diseases to which it is closely allied.

Hippocrates[1] wrote on the association of splenic humour with dysentery, hæmorrhage, scrobutus and miasmatic diseases. Galen[2] described splenic hypertrophy in protracted autumnal fever and other cachetic states.

Malpighi,[3] Morgagni[4] and others observed splenic and lymphatic enlargement associated with pallor, hæmorrhages and emaciation which terminated fatally.

Nivet[5] also reports cases of splenic enlargement under the heading of rhachitis and scrofula, in which extensive glandular enlargement and cachexia developed during the course of the disease.

The older writers, therefore, clearly show us that they were familiar with enlargement of the spleen in wasting diseases and that they had also observed the condition in scrofula, rickets, syphilis, continued fevers and liver disease.

There are also old records of cases in which, without apparent cause, the spleen enlarged, hæmorrhages and cachexia supervened, and death followed.

The first attempt at differentiation of types of this disease was made by Hodgkin[6] in 1832. He reported a number of cases which showed an increase in the size of the lymph glands and spleen followed by emaciation, ascites, pallor, œdema and death. The blood, however, was not examined in any of the cases and in many instances the report is meagre. Undoubtedly, however, these cases included carcinoma, tuberculosis, sepsis, and probably, also cardiac disease.

In 1845, Bennet[7] published the report of a case of splenic hypertrophy in which the blood of the patient contained a great number of leucocytes resembling pus cells, and a month later Virchow[8] reported a similar case and correctly attributed the increase in number of the leucocytes to an actual augmentation of the leucocytes. He believed that the increase in leucocytes was due to splenic hypertrophy. Subsequently he evolved the doctrine of the disease, leukæmia, which he described as an affection characterised by cachexia, enlargement of the spleen and lymphatic glands and an increase in the number of leucocytes.

Other histological changes which he described.

were cellular hyperplasia of the lymphatic glands and spleen and infiltration of lymph cells in the tissues of the liver, lungs, kidneys and intestinal tract.

In 1868, the work of Neumann[9] and Bizzozero on the hæmopoietic function of the medulla of bone, gave rise to a new field of clinical observation, and soon, a sufficient number of cases of leukæmia was recognised in which profound changes in the medullary substance of the bone were present, to warrant a third subdivision of the disease viz:- "myelogenic leukæmia."

Shortly after Virchow's description of leukæmia, Bonfils[10], in 1856 published the first observation on this disease called after Hodgkin and he insisted on the absence of leukæmia. His article was quickly backed up by Trousseau[11], Woillez[12], Collin[13], Wunderlich[14], Greissinger[15], Muller[16], Wilkes[17] and others who observed cases which presented extraordinary swelling of the lymphatic glands and spleen, and many of the clinical features of leukæmia, but who also noticed that the number of leucocytes was not increased.

In order to distinguish these cases from leukæmia Trousseau suggested the name "Adenia", by which the French still recognise the disease. Wilkes called it anæmia lymphatica. Virchow described it as lymphosarcoma, Billroth[18] - as malignant lymphoma , and

[19] Cohnheim - as pseudoleukæmia.

The essential feature distinguishing the disease from leukæmia was an absence of increase in leucocytes. In many cases the lymph glands only were enlarged; in other cases there was enlargement of both the spleen and lymph glands.

More recently, a relatively small number of cases belonging to this class of disease has been reported in which the lymph glands were unaffected whilst the spleen was greatly enlarged.

This was really a splenic form of pseudo leukæmia. The first undoubted case of this kind described was by [4] Woillez in 1856, and the first case recognised as belonging to this type was described by [20] Gretzel from Greissenger's Clinic under the name of "Anæmia Splenica" this being the first time a case was reported under this heading. In reality, this case belongs more properly to the disease described by [21] Von Jaksch as "Anæmia Infantum" Pseudoleukemica. About the same time [13] Collin and [14] Wunderlich also called attention to this affection, whilst, a few years later, [16] Muller, [22] Landouzy and [23] Pye Smith wrote on the subject.

[24] In 1867, Strumpell reported several cases on which he had held autopsies and classed them under

the name 'Splenic Anæmia'. One of these cases has been largely quoted and Banti claims that it was undoubtedly a case of Progressive Pernicious Anæmia.[25]

Dr. H.C. Wood of Philadelphia in 1871 discussed a splenic variety of pseudoleukæmia.[26] It was Banti who, in 1882, first placed the affection on a working basis, reporting very fully 3 of his own cases, and collecting others which had been previously reported, and which he believes to belong to the same class. He kept the same term, Splenic Anæmia, which Greissinger had first applied to the disease.

In 1887[27] Pel and[28] Renvers, and in 1888,[29] Ebstein reported cases of pseudoleukæmia, but these nearly all belonged to the glandular variety.

Since this time, cases presenting the same clinical manifestations and pathological features have been described under various names.

In 1891[30] Bruhl, in an article entitled 'De La Splénomégalie Primitive' gave an admirable picture of the disease, and a report on 14 cases which he had collected from various literature.

In 1898,[31] Banti described a condition of splenomegaly with cirrhosis of the liver. This affection is still called after him, and, in all probability,

simply represents a terminal stage of true splenic anæmia.

In 1899,[32] Sippy and Wentworth gave a very full account of the work done on the subject up to that time.

Till the year 1900, not more than 25 cases of splenic anæmia were on record, and some of these even are doubtful. At this time, however,[33] Osler enlightened medicine regarding this affection with a report of 15 fresh cases observed by him, and two years later,[34] he added another 3 cases to his list, and gave a summary of 26 other cases.

Since this time, the distinct entity of the disease having been placed on a firmer base, and also owing to the fact that careful blood examination is ever increasing in frequency, many more isolated cases of this disease have been published.

Splenectomy, as a method of treatment in this disease was early advocated, and, up to the year 1890, had been performed four times with three recoveries. Since this time there have been numerous examples of its use, and in recent years, much work has been done on this subject by[35] Harris and Herzog.

Before going any further into the history, I think it wise to describe my own cases, so that I may later

be able to compare my findings and ideas with those of other observers.

CASE I.

Peter C., aged 36 years. By occupation he was a railway guard.

He was born in Grantown, has lived all his life in Scotland, and has never been abroad.

He was admitted to the Edinburgh Royal Infirmary under the charge of Dr. Gibson, on September 26th 1907 and he was, at that time, complaining of a tumour in the abdomen.

A letter from his doctor says:- "C. is a very nice fellow. He had a smash on the line and came to me later suffering from nephritis with a good deal of albumen, very anæmic and with aortic dilatation, also, if I remember rightly, headache and epistaxis. Liver was enlarged from backward pressure I thought, but, at that time I didn't detect any splenic enlargement."

History:-

His father died in old age. His mother is, at present, alive and well and has always been a very healthy woman.

He knows nothing of his grandparents.

He has 3 brothers and 2 sisters living, all of whom enjoy excellent health.

1 brother died as the result of an accident.

1 brother died with acute tubercular pulmonary

phthisis.

He is a married man and has 3 healthy children. No children have died, and his wife has had no miscarriages.

Patient has, for many years, been occupied as a railway guard on a goods train on the Highland Line. He is accustomed to a regular and substantial diet, has a comfortable home and is not, at his work, much exposed to vicissitudes of weather.

He says he has always been a very steady man, that he was never more than a moderate drinker, and that he is practically a non-smoker.

He had scarlet fever in childhood, and , apart from this, has never had any serious illness. He denies syphilis and other venereal trouble, and says he was never subject to rheumatism.

On Feb. 4th of this year (1907) he had a fall on the railway, which resulted in a cut face and a severe shaking, and he dates his illness from this time.

He felt weak and unfit for his work, becoming faint and breathless with slight exertion. He has done no work since the time of his accident.

At the beginning of March he lost his appetite and commenced to vomit his food regularly, about one hour after every meal. He had no pain or nausea in connection with his vomiting, and the vomited matter

was greenish, and never dark or suggestive of blood.

Soon after this, in the middle of last April, he felt unusual throbbing in his throat, which did not trouble him, but which has continued up to the present time.

The vomiting continued till the beginning of June, by which time he had lost considerably in strength and weight. It then gradually subsided, and he has only vomited occasionally during the past three months.

By the commencement of June, he became too weak to remain on his feet, and took to his bed. He called in his doctor who told him he was suffering from kidney disease. Not content with this, he called in another doctor, who told him that his kidneys were perfectly healthy, but that his heart was dilated.

Although he felt in no way improved, being extremely weak, he became so weary of his bed that, towards the end of July, he got up and walked about as much as he could. Shortly after this, his feet and ankles commenced to swell and he was forced to again take to his bed about the middle of August, since which time he has been unable to rise. He says that, during the last month, he has experienced a beating sensation in the chest and neck, and occasionally in the head, and that the mere act of sitting up in bed

had been sufficient to make him breathless.

Four days ago (Sept. 22nd) his doctor discovered 'a lump' in the abdomen, and recommended him to Dr. Gibson for admission.

He has had no pain, either in the chest or abdomen and says that he has had no epistaxis, malæna or bleeding from any other source.

On Admission:-

He is a well built healthy looking man. He has rather an alert, anxious expression, and his complexion is somewhat pale and sallow. He says he feels easy and comfortable and has no pain in any region. He lies with equal comfort in any position.

His height is 5 ft. 8½ inches, and his weight 10 st. 6¾ lbs.

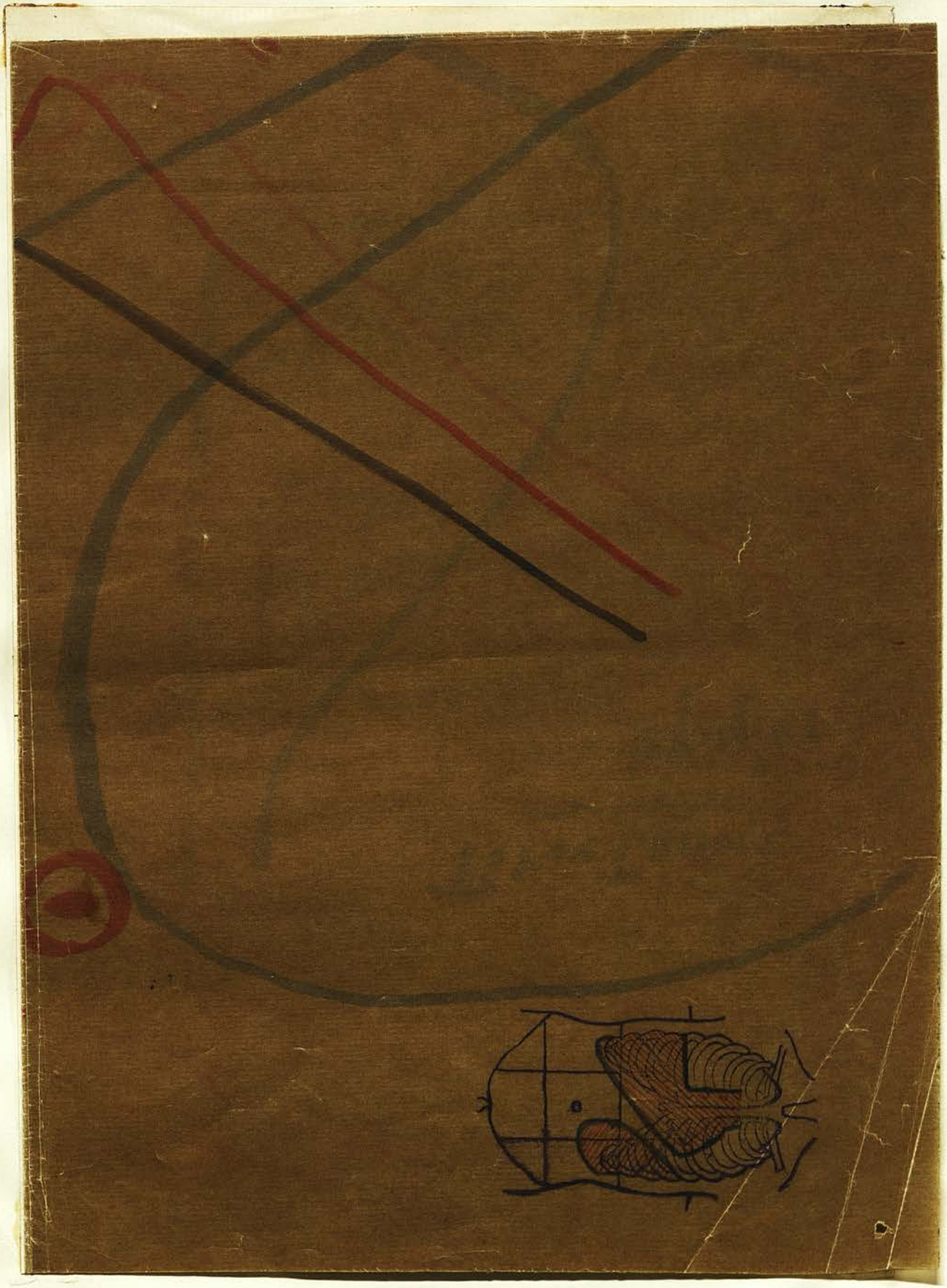
Circulatory System:-

He says he never has any præcordial pain, but that he often experiences a beating sensation in the chest, neck and head.

He does not complain either of faintness or dizziness, but says that he becomes short of breath on the slightest exertion.

The præcordia are well formed, and show neither bulging nor retraction.

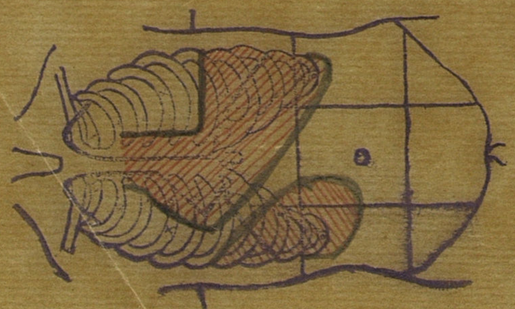
Diffuse, heaving pulsation in observed in 4th and 5th left interspaces, and there is very obvious arterial pulsation in episgastrium , episternal notch



Tracing from Case I, denoting the size of the heart, liver and Spleen.

Peter Crowe

27.9.'07



and carotid arteries, whilst the temporal arteries are seen to pulsate forcibly. Beyond this, the patient showed a well-marked capillary pulse, as evidenced by pressure on the nails and Tache Cerebrale.

On palpation, the cardiac impulse is observed to be diffuse and forcible, and a thrill, systolic in time is made out over the base of the heart.

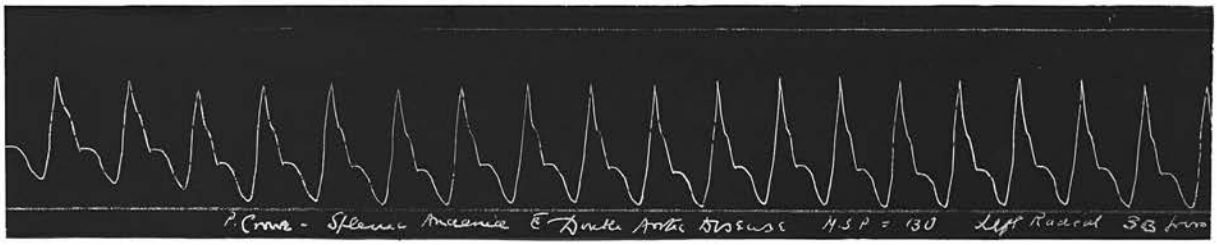
On percussion, the area of cardiac dulness is found to be slightly increased:-

At the level of the 3rd interspace, the left border of the heart lies 2¾ inches to the left of the midsternum; in the 4th and 5th interspaces, the left border lies 4 in. and 4½ inches to the left of midsternum, and the apex lies at the level of the upper border of 6th rib, 4¾ in. to the left of midsternum. The upper level of liver dulness lies at the lower border of the 5th rib in the right mammary line. The right border of the heart lies 1¼ in. to the right of midsternum in 3rd and 4th interspaces. (See Chart)

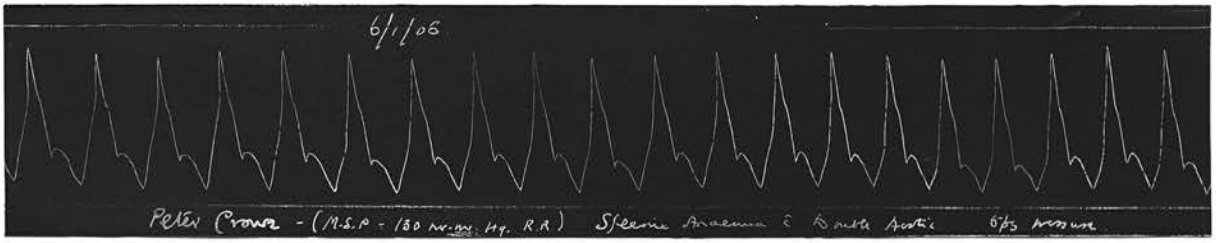
On Auscultation:-

In the mitral area, there is a soft, blowing systolic murmur, which has its maximum intensity at the apex, and which is propagated outwards into the axilla, and inwards to the left border of the sternum. The 2nd sound is reduplicated and accentuated.

with 2½ ounces pressure.



with 3 ounces pressure.



with 5 ounces pressure.

Sphygmographic Tracings from the left radial pulse of Case I.

In the Aortic Area there is a loud, rough systolic bruit, which has a slightly musical quality, and which is propagated into the subclavian vessels. The second sound is replaced by a murmur having a soft character, which is most plainly heard over midsternum at the level of 3rd interspace, and which can be fairly made out in the tricuspid area.

In the pulmonary and tricuspid areas, both sounds appear to be closed, though the aortic murmurs can be heard in these areas.

The Pulse in the radial vessels is perfectly regular, both in its frequency and force. It is - simultaneous, and of equal strength on the two sides.

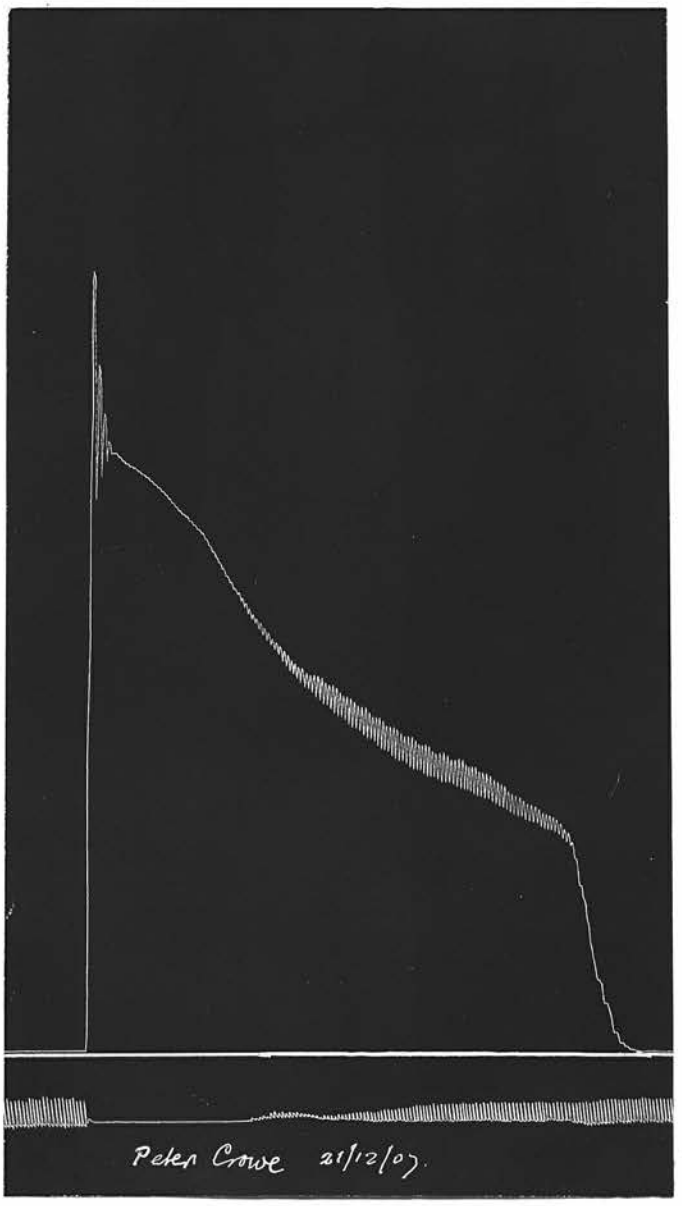
Its frequency is 86 per minute.

It has a moderately rapid rise and fall and its apex is poorly sustained.

The maximum systolic pressure, as read by the sphygmomanometers of Riva Rocci, Erlanger and Dr. G.A. Gibson is equal to 160 millimetres of Hg. and the diastolic pressure is equal to 85 mm. of Hg. (See Tracings). The vessel walls are soft and show no undue thickening. (See Tracings).

Hæmopoietic System:-

No enlargement of any of the lymphatic glands is manifest.



Sphygmomanometer Tracing from Case I.
Recorded by Dr. G. A. Gibson's Sphygmomanometer.

The liver is not enlarged. It extends from the lower border of the 5th rib, to ¾ inch below the costal margin, both in the left nipple line.

The spleen is very much enlarged. Anteriorly it reaches down to the level of the umbilicus, and to within ½ inch of the middle line. Posteriorly, dulness, apparently splenic, extends as far up as the 8th rib in the scapula line (See Tracing).

On palpation the anteriorly border can be distinctly felt, and also the presence of a slight notch on this border. The surface of splenic tumour feels perfectly smooth, and the tumour itself is firm and immovable. Manipulation of the tumour causes no discomfort.

Blood.

On admission, the blood was found to be much impoverished, the Red Blood Corpuscles being diminished almost exactly in proportion to the Hæmoglobin. The White Blood Corpuscles were also found to be much diminished in number.

A blood count showed:-

Erythrocytes -	2,250,000	) per cubic millimetre.
Leucocytes -	3,600	)
Hæmoglobin -	45%	

Name Case 1. Age ..... Clinical Clerks { .....

Blood. Date.	26·9·04.	30·9·04.	14·10·04.	1·11·04.	4·12·04.	24·12·04.	Start.	Treatment.	Stop.	Diet.
R.B.C.	2·250·000	2·300·000	3·410·000	4·000·000	3·300·000	1·850·000				
Hb.	46%	45%	60%	70%	62%	35%				
W.B.C.	3·600	3·200	2·700	3·100	5·000	3·800				
Film :—		Film :—	Film :—	Film :—	Film :—	Film :—				
Polymorphs	73%	56%	53%	64%	54%	53%				
Lymphocytes	23%	35%	43%	31%	38%	40%				
Large Monos	3%	5%	4%	3%	6%	4%				
Eosinophils	–	2%	–	2%	1%	2%				
Mast Cells	1%	2%	–		1%	1%				
Comments :—										
No nucleated red cells. No poikelocytosis or polychromatophilia.		As before.	As before.	As before.	As before.	As before.				

Date.	Urine.	Blood Pressure.	Sputum.	Gastric Contents.	Additional Facts.

Diet Sheet 1. – showing the differential blood counts at different dates.

Colour Index = 1.

Examination of a blood film showed:-

Polymorphonuclear Leutrophils	- 73%
Lymphocytes	- 23%
Large Mononuclears	- 3%
Mast Cells.	- 1%

There were no nucleated red blood corpuscles, nor was there any polychromatophilia, and the erythrocytes were well formed and fairly uniform in size (See Chart 4).

Alimentary System:-

He has excellent teeth, his gums are healthy and his tongue clean.

He says his appetite is excellent, and that he has no pain or discomfort in relation to food. He now vomits very occasionally, the vomit consisting simply of food taken - the vomited matter has never been coffee-coloured.

The bowels move regularly once daily, and the motions are healthy and have never contained blood.

The abdomen moves freely with respration and shows no undue rigidity.

Palpation and percussion reveal the splenic tumour above described.

The lower edge of the liver is palpable. It feels firm and has a smooth surface.

There is no fluid in the abdomen, and no enlarged glands are palpable.

The stomach is pushed over to the middle line, and lies more vertically than is normally the case.

The motions show no signs of intestinal parasites, and the ova of ankylostoma were carefully hunted for with negative result.

Nervous System:-

He is an exceptionally intelligent man, and , though somewhat anxious, shows no undue excitement. His superficial and deep reflexes are all healthy.

The Pupils are moderately dilated, equal and regular, and react briskly both to light and accommodation. Ophthalmoscopic examination shows healthy discs and fundi, and there are no retinal hæmorrhages.

Integumentary System:-

The skin has a faint yellowish colouration. The subcutaneous tissue is abundantly represented all over the body. There are no purpuric spots or skin hæmorrhages.

Urinary System:-

He has no discomfort of difficulty with micturition.

He is passing about 60 oz. of urine daily. He has never noticed any blood in his urine.

The urine shows:-

An acid reaction; a specific gravity of 1015.

It contains no blood, albumen, or other abnormal constituent.

He passes about 450 grains of urea daily.

As a result of this examination, at the time of the patient's admission, we were forced to the conclusion that this was a case of Splenic Anæmia, and that it was complicated by aortic disease of unknown origin.

Progress:-

During the first 10 days of his stay in the ward there was very little change in his condition. As the 4 hourly chart shows, the temperature was swinging between 98° and 101°, reaching its height about 11 p.m.

The only alteration in the blood during this period was, that the lymphocyte count increased to 35%, the total number of leucocytes remaining, as on admission, much below normal, and only reaching, on

Oct. 3rd. - 2,600.

On Oct.1st we prescribed mv. of Liq.Arsenicalis for him, three times daily, and on Oct. 7th, this was increased to mx ter in die. He had vomited 3 or 4 times during the past week, almost immediately after his food. The vomit was not particularly sour, and only consisted of returned food. By Oct. 9th he was feeling better, he had not vomited again, had gained 4 lbs in weight, the erythrocytes had risen to 3000000 and the Hæmoglobin to 35%, whereas the leucocyte count remained practically unaltered.

His general condition continued to improve; he took his food well, he became a better colour, his temperature steadied, and on October 14th his erythrocytes were 3,610,000; his hæmoglobin 65%; and his leucocytes - 2,800 per cubic millimetre. With this his weight had increased by another 2 lbs, to 10 st. 12 lbs. and he had not again vomited. At this time the arsenic given was increased to mxx ter in die, but as he went off his food, complained of griping pains in the abdomen, and his temperature took on a greater swing, it was stopped on October 17th.

Up to this time (Oct. 17th) patient seemed to be improving, though the leucocyte count remained below 3,000,there was no alteration in the size of the spleen and the aortic signs remained as on admission.

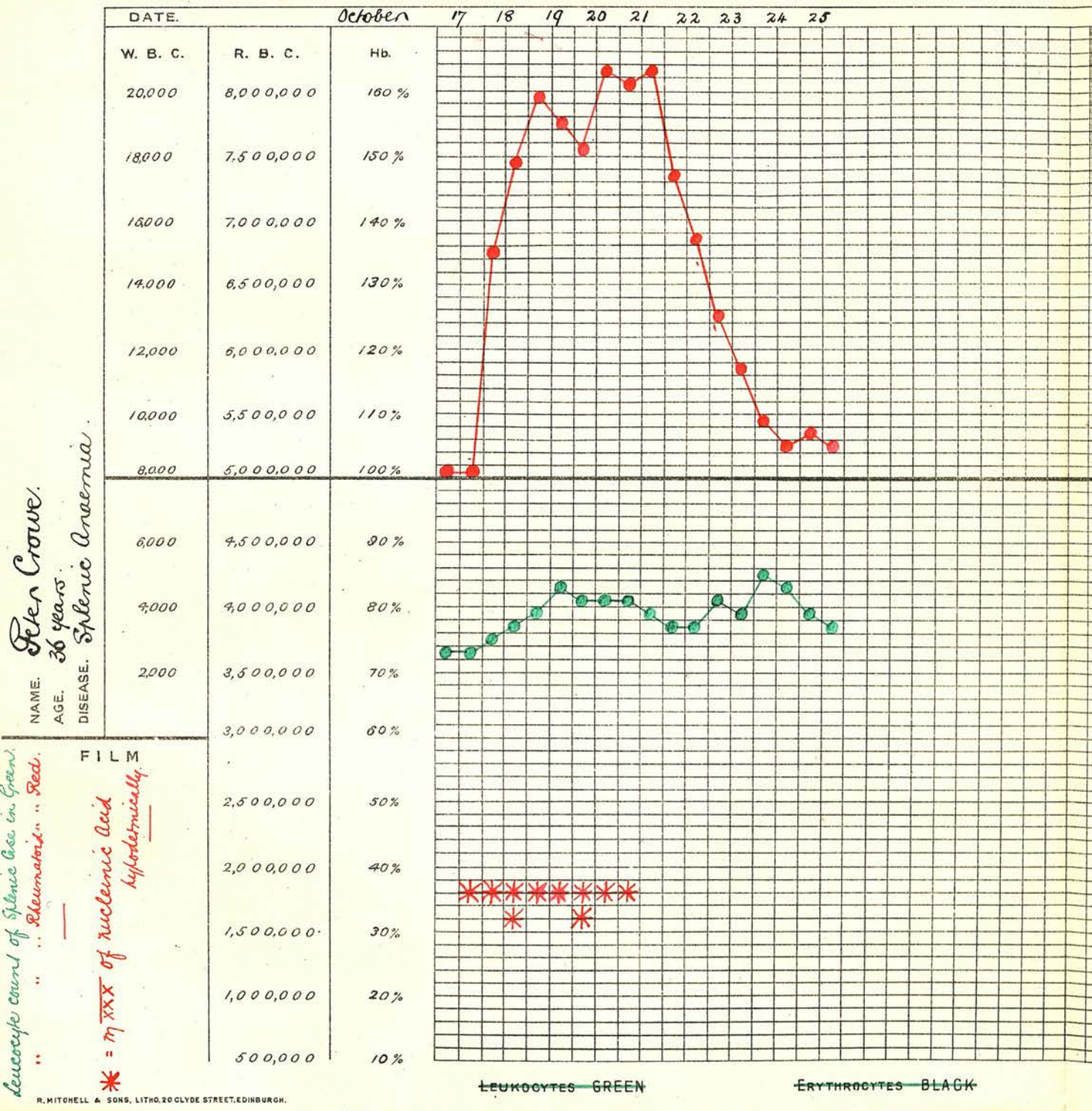


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Chart 1.

On October 17th we thought it would be of interest to know what the action of nucleinic acid on our patient's leucocyte count would be, and accordingly I decided to give him hypodermic injections of this drug, and in order that our observations might be of some value, I used the blood of another patient as a control. For this purpose I chose a man suffering from rheumatoid arthritis, and who had been in the ward, in bed for a fortnight. He was a very healthy man, and his blood was quite normal in every respect. His leucocytes, which had been counted on three occasions, numbered between 7,000 and 8,000.

Both patients were on a light diet, both of them were, and had, for some time, been lying in bed, and, in both cases, all other drugs were stopped.

At the time of the commencement of the administration of nucleinic acid the normal blood (A) showed a leucocyte count of 8,000, whereas the blood of the splenic patient (B) showed only 2,400 leucocytes per cubic millimetre.

The accompanying blood chart I. shows the course the W.B.C. count ran in both cases, the normal blood being figured in red, and the blood of the splenic case in green.

The leucocyte count, in this instance, was taken twice daily in both cases, at 10 a.m. and 10 p.m., so

that any dietetic influence might be at a minimum.

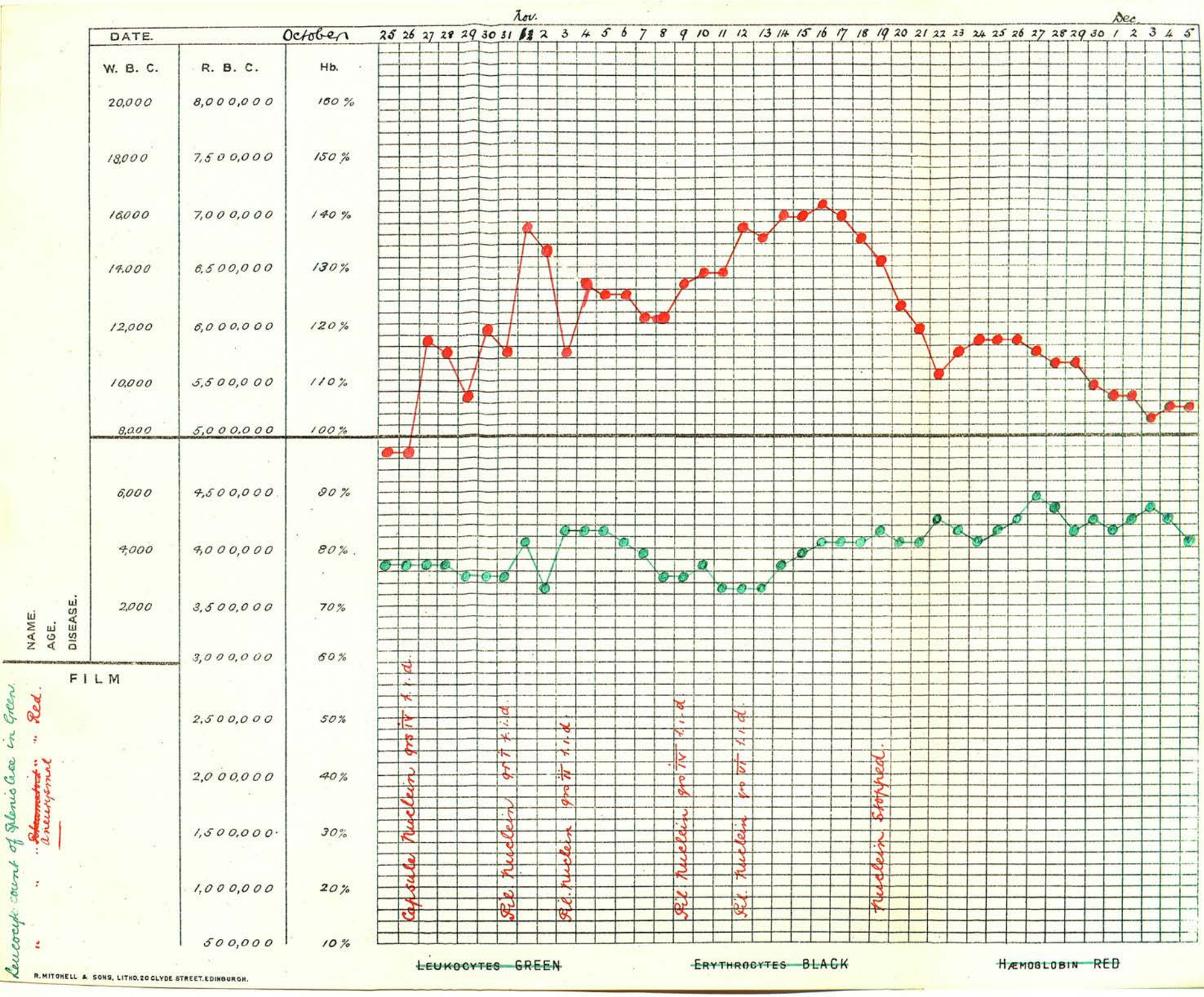
The preparation of nuclein given was a sterilized 5% solution of nucleinic acid, and it was given in hypodermic form. The amount given at a time was, in every case mɳ xxx, though, on two occasions, this amount was administered twice daily. The red stars at the foot of the chart each represent mɳ xxx of nucleinic acid.

The difference in the reaction of the two bloods to nuclein is clearly shown. In each case, the leucocytes started to increase in number within twelve hours of the first administration, but, whereas the normal blood attained a leucocyte count of 21,000, the leucocytes of our splenic patient did not increase beyond 4,800.

The hypodermic injections caused considerable discomfort, at the site of puncture, in B's. case, and therefore we thought it wise to discontinue the use of nuclein by hypodermic administration, the last injection being given on October 21st.

Hypodermic methods being, at any rate for the time, prohibitive, I thought it might be of use to attempt to obtain a reaction by giving nuclein by the mouth.

In this case, a different patient was used as a control. It was difficult to choose a patient on whom



Leucocyte Count of Glenic Case in Green
" " Rheumatic " Red.
" " Pneumonic "
" " Pneumonic "

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Chart 2.

the results would be reliable, and one who could be kept lying without further drug treatment. I chose a man who was suffering from an aneurysm of the abdominal aorta, and whose leucocytes, twice estimated, counted less than 8,000 per cubic millimetre. Chart II shows the reaction in the two cases.

Nuclein was given over a period of three weeks. At first, it was given in grs.iv doses in capsule form, but as this caused such a small reaction, after five days, it was given in gr. i doses made up in pill form, as it seemed possible that the capsules were not getting properly dissolved in the stomach. As the chart shows the amount of nuclein was increased till, on November 12th, both patients were getting grs. vi. 3 times daily.

A quite definite reaction was again given by the normal blood, although the leucocytes never rose beyond 16,200. The splenic blood, however, continued to show a leucocyte count of less than 4,000 till after the administration of nuclein had been stopped, on November 19th.

On November 24th I made another attempt to produce a leucocytosis by employing nucleinic acid in hypodermic form. On this occasion, I used a 2½% solution in m.xx doses in the hopes that this might cause less irritation. I took a gastric case with a

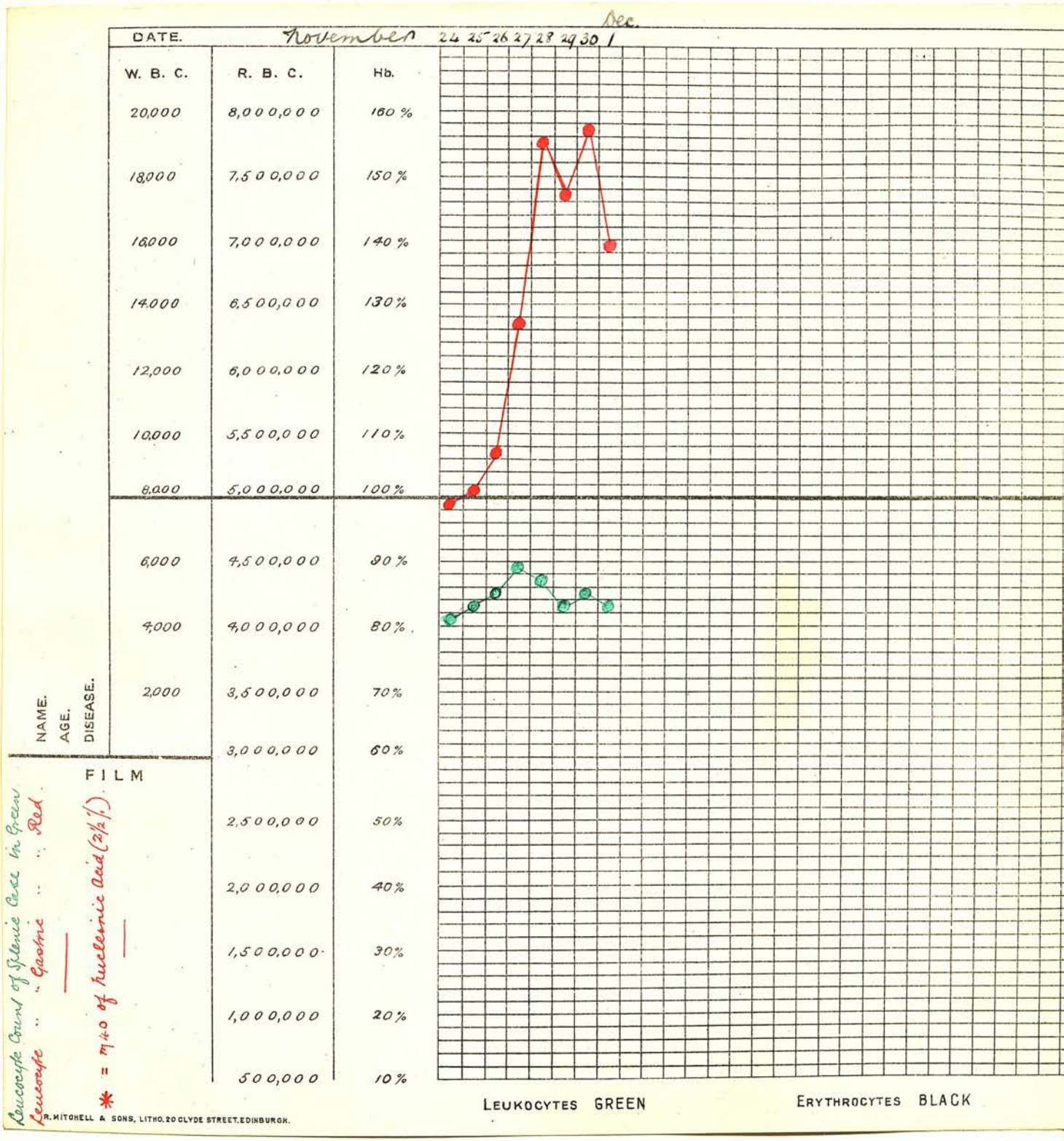
DATE.
November 24 25 26 27 28 29 30 Dec. 1
W. B. C.
R. B. C.
Hb.
20,000
8,000,000
160 %
18,000
7,500,000
150 %
16,000
7,000,000
140 %
14,000
6,500,000
130 %
12,000
6,000,000
120 %
10,000
5,500,000
110 %
8,000
5,000,000
100 %
6,000
4,500,000
90 %
4,000
4,000,000
80 %
2,000
3,500,000
70 %
3,000,000
60 %
2,500,000
50 %
2,000,000
40 %
1,500,000
30 %
1,000,000
20 %
500,000
10 %
NAME.
AGE.
DISEASE.
FILM
Leucocyte Count of Stevie Case in Green
Leucocyte " " Gastric " " Red.
* = m40 of Arsenic Acid (2½%)
LEUKOCYTES GREEN
ERYTHROCYTES BLACK
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Chart 3.

leucocyte count of less than 8,000, as a control. Chart III shows the leucocyte reaction in this case. The injections only extended over a week ɱ 40 being given daily over this period. At the end of this time, the splenic case was again complaining of pain, and also showed some redness and swelling at the sites of hypodermic punctures, and any attempt to raise his leucocyte count by means of the administration of nuclein was given up at that time. (Chart III).

Our patient appeared to make steady headway during the month of November. On November 7th, he complained of sharp attacks of pain in the left hypochondrium, which radiated through to the back, but he had no sickness or increase of pyrexia, and abdominal palpation caused him no discomfort. The pain subsided at the end of a week (by Nov. 15th), but, on November 22nd he complained of diarrhœa and heartburn, which, however, only lasted for 3 or 4 days.

His weight, during this month, showed considerable fluctuations, but, by the end of the month, he had gained $4\frac{3}{4}$ lbs since admission.

His blood showed great improvement, all the elements showing a marked increase.

A blood count on November showed:-

Erythrocytes	-	3,800,000 per cubic millimetre.
Hæmoglobin	-	70%
Leucocytes	-	4,200 - per cubic millimetre.

A blood film showed the leucocytes to be made up as follows:-

Polymorph. Neutrophils	-	63%
Lymphocytes	-	31%
Large Mononuclears	-	3%
Esinophils	-	2%
Mast Cells	-	1%

There was no poikilocytosis or polychromatophilia, and no erythroblasts were found.

By November 30th the spleen showed no alteration in size or position, and the patient had had no bleedings from any source.

At this time, seeing that the patient's general condition was fairly good, and that the tone of his circulatory system was as satisfactory as it was ever likely to be, the question of splenectomy had to be considered.

Removal of the spleen in parallel cases to this one, had met with such varying results, that we thought the prognosis of such a procedure might be largely dependant on the condition of the bone marrow.

The patient was quite willing to submit to any operation which we thought might help him, and we therefore asked Mr. Caird to remove some of the marrow from the upper part of the shaft of the tibia.

This was done on December 1st. Under chloroform, Mr. Caird trephined the inner surface of the shaft of the left tibia in its upper third, and picked out a cylinder of marrow, about 1½ inches long. The trephined bone was replaced, and the wound stitched up.

The marrow obtained showed an advanced degree of gelatinous degeneration. It will be more fully described later.

Under these circumstances we were disinclined to advise splenectomy, but as, from this date, there were fresh developments in the case, the patient's condition made any operative procedure practically impossible.

There were no ill effects following immediately on the operation, excepting that, for three nights, patient complained, a great deal, of pain in the leg at the site of the trephine. The wound looked clean, and although there was a blood effusion under the skin, it healed by first intention.

On December 4th the blood, which had, again, been gradually deteriorating showed:-

Erythrocytes	- 3,300,000	Colour Index = .93.
Haemoglobin	- 62%	
Leucocytes	- 5,000	

Film Examination showed:-

Polymorph. Neutrophils	-	54%
Lymphocytes	-	38%
Large Mononuclears	-	6%
Eosinophils	-	1%
Mast Cells	-	1%

The red cells showed nothing abnormal.

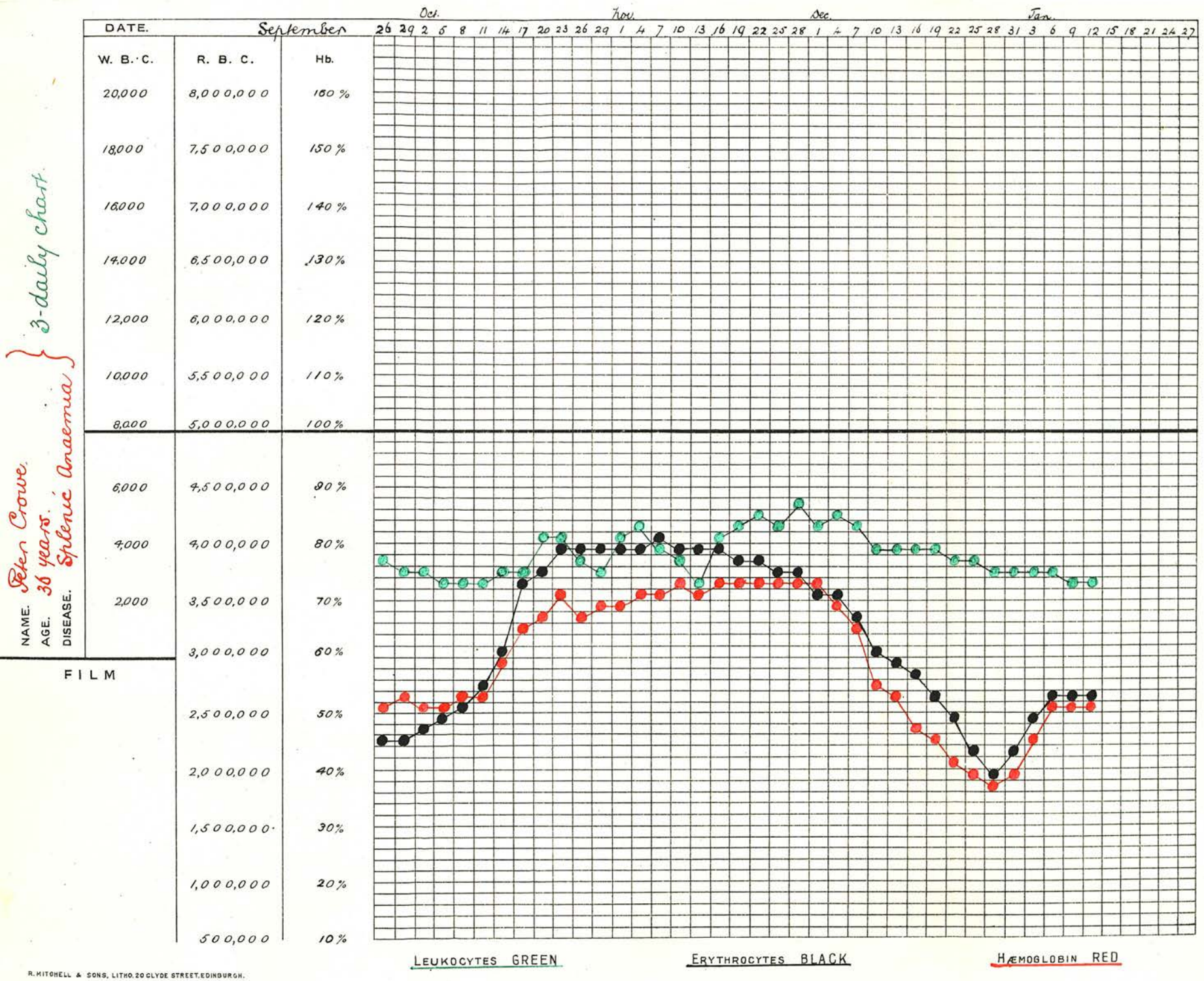
Patient was again started on arsenic in grs v doses three times daily.

Two days later, on December 6th, he had a slight epistaxis from the right nostril. This stopped by itself.

The following day, however (December 7th), the bleeding started again, this time from both nostrils. It was very profuse and only stopped by plugging both anterior and posterior nares with adrenalin gauze. At the same time pain was again complained of in the left hypochondrium, similar in character and position to that previously mentioned.

Another ophthalmoscopic examination was made at this time, but the discs and fundi were quite healthy and revealed no retinal hæmorrhages. Moreover, there had never been either hæmaturia or melæna.

On December 8th epistaxis again started, on this occasion from the right side only. It was again



R. MITCHELL & SONS, LITHO. 20 CLYDE STREET, EDINBURGH.

Chart 4.

profuse, and the nose was again plugged with adrenalin gauze.

From this time, calcium lactate was given with the arsenic thrice daily in grs xv doses.

On December 9th there was no more bleeding from the nose, though the urine showed a trace of blood.

As the blood chart shows, there was a continued decrease in all the blood elements, so that the hæmoglobin was now 55%, erythrocytes below 3,000,000, and leucocytes 4,000 per cub.mm. With this, patient was evincing less desire for his food, and looking paler and thinner. He still complained of occasional attacks of pain in the left hypochondrium, and also in the left leg.

On December 10th there was again a very profuse epistaxis from both nostrils, which was only stopped with difficulty by anterior and posterior plugging and ice bags. From this time onwards, adrenalin was applied three times daily to both nostrils, in the form of an ointment, and there was no more bleeding for some days.

On December 14th there was noticeable œdema of the feet and ankles, rather more marked on the left side, and the urine again contained blood in small quantities. This œdema rapidly became more evident and on December 16th extended almost up to the knees,

and was also present, to a slight extent, over the back. There was no ascites, and no apparent change in the size of the liver and spleen. A few crepitations (medium), were heard at the bases of both lungs, but there was no fresh dulness to percussion.

The heart showed further enlargement, and the apex now lay behind 7th rib, 5¼ inches to the left of midsternum. Pulsation was again more evident in all the vessels, which showed marked throbbing over the whole body. There was a long rough systolic murmur and a long soft diastolic blow in the aortic area, and the capillaries and retinal arteries could be seen to pulsate.

With this, patient was taking his food very poorly, and appeared much thinner, haggard and anxious.

The blood also was rapidly getting poorer, a count now showing:-

Erythrocytes	-	2,700,000	) Colour Index=
Hæmoglobin	-	40%	) .8.
Leucocytes	-	3,800	

The pulse frequency showed a tendency to increase, though the temperature did not alter its character.

On December 18th patient started to cough, the cough being hard and dry and unaccompanied by pain. No cause for this was found either in the throat or

lungs. He started to take his food more satisfactorily again, and the œdema became less marked.

There was no further hæmorrhage from any source till December 21st, when patient again had an epistaxis from the left side, this time not very profuse. Although the temperature had taken on a larger swing he looked a little better, showed increased desire for his food, and was more sanguine and cheerful.

As the cough irritated him considerably, he was given ℥ss of the Brompton Mixture night and morning, in addition to the arsenic and calcium lactate, which were still being continued in their original doses.

Another slight epistaxis took place on December 24th, the cough continued to trouble him, though there was no evident cause for it. There were still a few crepitations at the bases of both lungs, but there were no other physical signs, and the œdema in the back and limbs had almost disappeared.

The next day, December 25th, there was a copious bilateral epistaxis, which was again stopped by plugging. Diarrhœa also set in, and with this there was a large quantity of blood in the motions. The cough was still causing trouble, and patient complained of a dry, uncomfortable sensation in the throat.

Laryngoscopic Examination showed nothing abnormal

and on ophthalmoscopic examination there were no signs of retinal hæmorrhages. The Brompton Mixture was stopped and grs x doses of Pulv. Kino Co. were substituted, night and morning.

On December 26th the epistaxis and malæna continued though the diarrhœa was less severe.

The following day (December 27th), there was only a small amount of blood in the stools and no further bleeding from the nose. Patient was extremely pale and very thin, but the cough was less troublesome and he still remained cheerful. His pulse was weak and becoming more rapid, and the throbbing of the whole arterial system more and more evident.

Another blood count at this time showed:-

Hæmoglobin	- 35%	) Colour Index = 1.
Erythrocytes	- 1,850,000	)
Leucocytes	- 3,800.	

Film:-

Polymorph. Neutrophils	-	53%
Lymphocytes	-	40%
Large Mononuclears	-	4%
Eosinophils	-	2%
Mast Cells	-	1%

There was still no poikilocytosis or polychromatophilia and no sign of normoblasts or myelocytes.

Blood-platelets appeared to be present in normal amount, though no absolute estimation of them was made.

By December 29th patient was feeling and looking very much better, and had had no further bleeding from the nose or rectum and there had been no more blood in the urine. His pulse slowed down somewhat and his appetite improved. His cough still troubled him and his voice was very husky.

This improvement was maintained, and by December 31st his cough being much easier, his bowels again quite normal, and there being no more hæmorrhages, the Pulv. Kino Co. was stopped. His blood also was, at this time, showing marked improvement. He was able to partake liberally of his New Year's Dinner, which did not cause him any ill effects. As the motions were rather offensive, he was put on to salol grs x ter in die.

On January 5th he was again showing marked improvement. There had been no sign of further hæmorrhage, his cough and huskiness had quite disappeared and he was very bright and cheerful.

His blood showed marked improvement, as testified by the following blood count which was made at that time:-

Hb.	-	50%	) Colour Index = .96.
R.B.C.	-	2,600,000	)
W.B.C.	-	3,000	

Film:-

Polymorph. Neutrophils	-	54%
Lymphocytes		36%
Large Mononuclears		6%
Eosinophils		3%
Mast Cells.		1%

Patient continued to show progressive improvement till January 10th when he had another epistaxis and again commenced coughing. On this date, also, there was a re-appearance of the malæna, though the quantity of blood passed was small. He again went off his food, his pulse quickened, and his temperature showed greater irregularity.

The following day, January 11th in addition to epistaxis and malæna, he also coughed up a small quantity of bright frothy blood. There was now a larger area of dulness at the base of the left lung, the breathing was faint at this situation, and a few medium sized crepitations were scattered throughout the lower lobes of both lungs. No signs could, however, be found, suggesting the site of the hæmoptysis.

On January 12th bleedings from the above three sources continued, though the amount of blood lost was not great. Patient again looked haggard and anxious and lost all desire for food. He also

perspired freely at night and showed very marked pulsation all over the body.

There were now signs of fluid in the abdominal cavity, and abundant crepitations were heard at the bases of both lungs.

Systolic murmurs were heard in all the cardiac areas, and, in the aortic area, the previously mentioned diastolic blow was very evident.

The following day, January 13th, it became evident that he was rapidly losing strength. He had no recurrence of the epistaxis, but the hæmoptysis continued, and both the motions and urine contained blood. His temperature and pulse rate steadily increased and he looked deathly pale with a faint malar flush. His breathing also became distressed and though it was not rapid, the alæ nasi were working, and the sternomastoids and scalene muscles were brought into action.

The pulse, temperature and respirations progressively rose till, on the morning of January 14th his temperature reached 105.2° and his respirations 38 per minute. He again, at this time, coughed up a small quantity of bright blood and had another slight epistaxis. Stimulation and infusions of saline were of no avail, and he died on the evening of January 14th without showing any fresh symptoms.

A post mortem examniation was obtained and it was conducted by Dr. Carnegie Dickson on January 15th. The following is his rpport:-

"Body that of a fairly well developed middle aged male. Rigor mortis present in extremities, passing off in neck. Post mortem lividity present in dependent parts.

The abdomen shows distinct protruberance.

Pupils medium sized and equal.

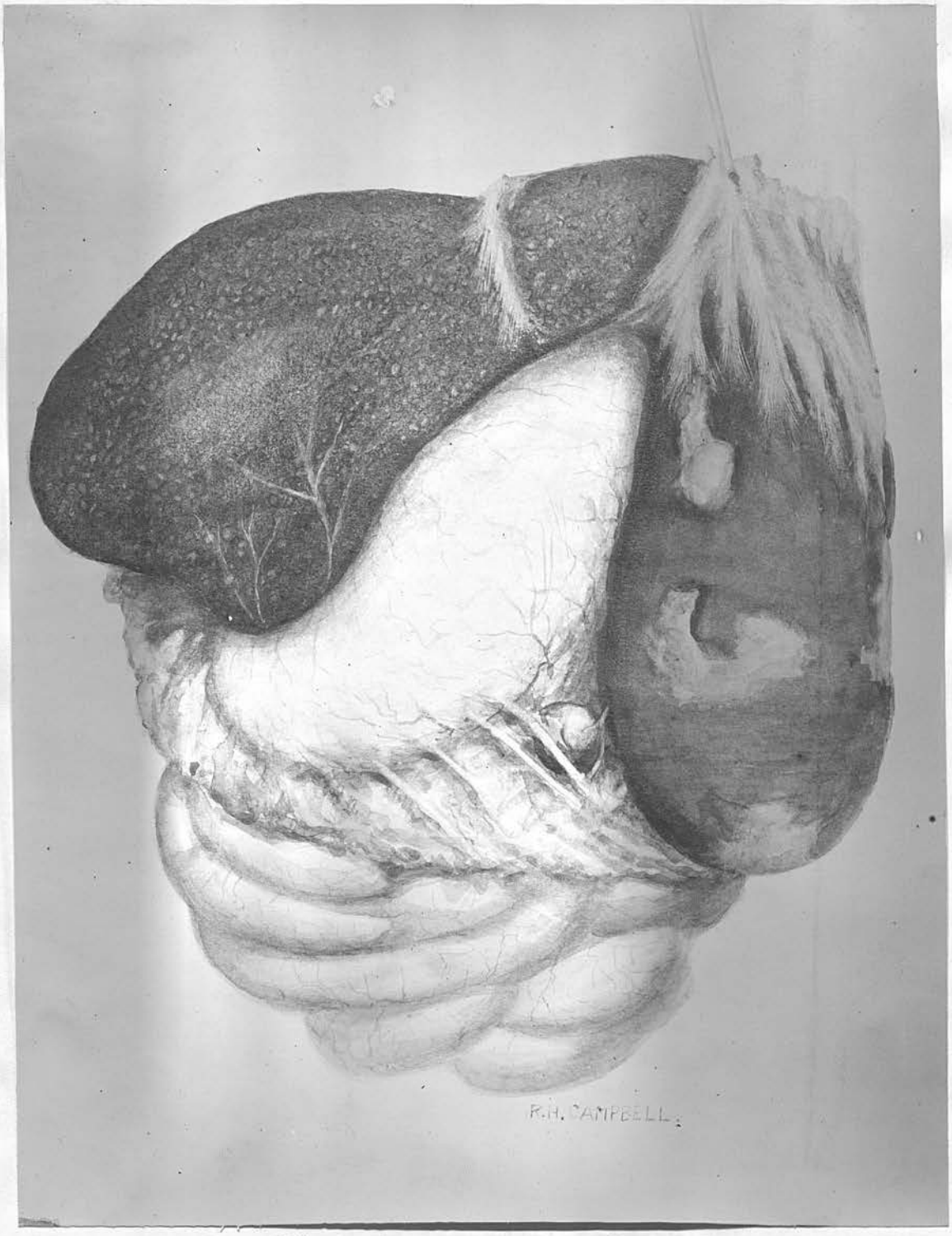
Subcutaneous fat somewhat scanty and shows a slightly orange tint. The muscles are very pale in colour.

Blood is fluid, and shows a somewhat crimson - lake colour resembling that seen in CO poisoning." This colour was, as nearly as possible, copied and represented in the left lower corner of Mr. Campbell's painting.

"The left pleural cavity:- No adhesions, contains a few ounces of fluid. Lung partially collapsed from pressure from below. Right pleural cavity contains about 6 oz of similar fluid. No adhesions.

Pericardium greatly distended, and contains about 15 oz of clear, pale lemon-yellow coloured fluid.

Peritoneal cavity contains about three pints of similar fluid. Slight general thickening of peritoneum.



From Case I. Photograph of the Abdominal Viscera.
(Photograph by Mr. Charles Geary).

Spleen greatly enlarged, lower pole reaching umbilicus and anterior margin reaching left nipple line (See Photograph).

Lower margin of liver lies half way between unbilicus and right costal margin in right nipple line. It reaches iliac crest in anterior axillary line.

Stomach considerably dilated and situated vertically between liver and spleen, the pylorus being situated at lower costal margin in right anterior axillary line.

The liver is pushed over to the right, and its lower surface is directed almost vertically to the left

The heart is considerably enlarged, the left ventricle being much hypertrophied and somewhat dilated and in systole. The right ventricle shows marked increase of subepicardial fat. There are thick œdematous "milk spots" over anterior aspect of the heart - (Apex of left ventricle, conus anteriosus and centre of anterior aspect of right ventricle - a similar one on centre of posterior aspect of left ventricle). Also well-marked thickening over vessels and over auricular appendices.

Right auricle is extremely dilated and thin-walled. Tricuspid orifice dilated, admitting six fingers. Right ventricle is dilated and shows a

moderate degree of hypertrophy. Cavity much encroached upon by bulging of septum. There is extreme fatty infiltration of muscle, especially towards apex. Pulmonary valve cusps dilated and show thickening most marked along attached margin. Pulmonary artery dilated. There are a few small white tags of fibrous tissue at one of the free margins of one of the cusps, probably due to old endocarditis. . Left auricle is moderately dilated and endocardium shows considerable thickening. Foramen ovale is closed.

Mitral valve is dilated, admitting five fingers. Aortic valve is markedly incompetent. Aorta is slightly dilated and shows slight patches of atheroma immediately above the valve. Sinuses of Valsalva greatly dilated.

Aortic cusps are dilated and show marked thickening along free margins and presence of numerous somewhat long, finger-like chronic vegetations at free margin, causing marked incompetence. The left ventricle is greatly hypertrophied and markedly dilated. Muscle is pale, firm and shows some evidence of slight fibrous change. The myocardium next to the cavity shows distinct fatty degeneration,,but not of "thrush-breast" variety.

Mitral orifice - anterior cusp shows marked thickening and the same evidence of old endocarditis.

Descending thoracic aorta comparatively healthy. Slight patches of atheroma.

Left Lung - No chronic pleurisy except slight patch of fibrous adhesion on posterior aspect of upper lobe. Very slight old tubercular scarring at apex.

On section, well marked chronic, venous congestion and slight œdema. Partial collapse of lower lobe.

Right Lung. Surface similar. On section - similar but more marked œdema. Also some collapse of lower lobe.

Spleen:- Length 12". Breadth at centre 7½" Weight 7 lbs.

There are old fibrous adhesions of upper pole to diaphragm. There are numerous old infarcts, the surfaces of which vary from ½" up to 2½" in diameter. These are situated both along anterior and posterior margins, and also over outer surface.

Over these there is chronic perisplenitis, most marked towards the upper pole where thickening is almost cartilaginous in consistence. Infarcts pale yellowish-white in colour (resembling fresh butter in colour). Older ones show absorption and fibrous

contraction at their margins; more recent ones show an area of congestion around them. At hilus there is a spleniculus which has become enlarged to size of pigeon's egg.

On section - the older infarcts, i.e. the majority, show a homogeneous yellowish-white caseous appearance (like fresh butter) surrounded by zone of fibrous tissue. Some of the oldest infarcts show almost complete transformation to fibrous tissue, and a few are more recent and are surrounded by a hæmorrhagic zone and no fibrous tissue.

Spleen pulp is dark purplish red in colour.

The Malpighian bodies being much separated and surrounded by dark zones of congestion and also apparently with hæmorrhage.

Liver. Is also considerably enlarged. Vertical diameter in anterior axillary line is 9½". Weight - 7½ lbs.

Surface shows a mottled dull brick-red appearance with small rounded and irregular palish brown areas scattered over it measuring up to ¼" in diameter, and giving a granite or pudding-stone like appearance to it. Small atrophic areas on lower surface corresponding to surface tributaries of the hepatic veins

and, at one part, a tag of liver substance on lower aspect of lower lobe about size of a pea and attached by a narrow peduncle of fibrous tissue.

On section:- A corresponding appearance was found, viz: numerous pale, brownish-yellow, rounded nodule-like areas, surrounded by a dull red congested area - (apparently advanced chronic venous congestion).

Stomach and duodenum show slight chronic catarrh and chronic venous congestion.

Intestine - Duodenum and jejunum show considerable œdema of mucous membrane with some patches of slight congestion in upper parts. The bowel is pale yellowish-white in colour. There are a few small submucous hæmorrhages towards the centre and lower end of ileum. No ulceration. Caecum and large intestine show no hæmorrhages or ulceration.

Left Kidney - is distinctly enlarged. Very soft in consistence. Capsule is thin and strips readily, leaving a smooth, pale yellowish-white mottled surface with congested vessels and small areas of hæmorrhage. At the lower pole there is the scarred remains of an old infarct of medium size.

On section - Cortex is distinctly reduced in superficial part, but there is marked mottled-yellow and white swelling of deeper parts, there being, in the organ a mixture of advanced fatty degeneration with chronic venous congestion and slight catarrh.

Right Kidney - Similar except for more marked chronic venous congestion.

Pancreas - Is pale in colour; lobules somewhat separated by œdematous fibrous tissue. Gland tissue pale and soft.

Bone-Marrow of Femur shows extreme gelatinous degeneration with scattered hæmorrhages.

The bone is dense and sclerosed.

Tibia is similar.

Rib Bone thick and sclerosed. Marrow fairly abundant, pale pinkish-red in colour and also somewhat gelatinous.

Head. Skull cap is thin, but bone dense and heavy. Dura not unduly adherent to bone. There is a

thin surface extravisation of blood on the extero-superior aspect of the right occipital lobe.

On section - the Pons, Medulla and Cord show no naked-eye abnormality except marked pallor.

Cerebrum and Cerebellum ditto, except for the recent effusion of blood into pia arachnoid, in the sulci on the outer aspect of the right occipital lobe, corresponding to area seen on surface.

Summary. Splenic Anæmia. Great enlargement of spleen with numerous infarctions. Extreme gelatinous degeneration of Bone-marrow. Enlargement and chronic venous congestion of Liver. Fatty degeneration and chronic venous congestion of Kidneys. Old Endocarditis of aortic and mitral valves. Hypertrophy and dilatation of left ventricle. Fatty Infiltration of Right Ventrical."

Microscopic.

On microscopical examination of the bone-marrow, the following points were made out:-

A. Bone-Marrow from Tibia (ante-mortem).

The marrow is fatty and is undergoing gelatinous degeneration, a comparatively advanced degree of this

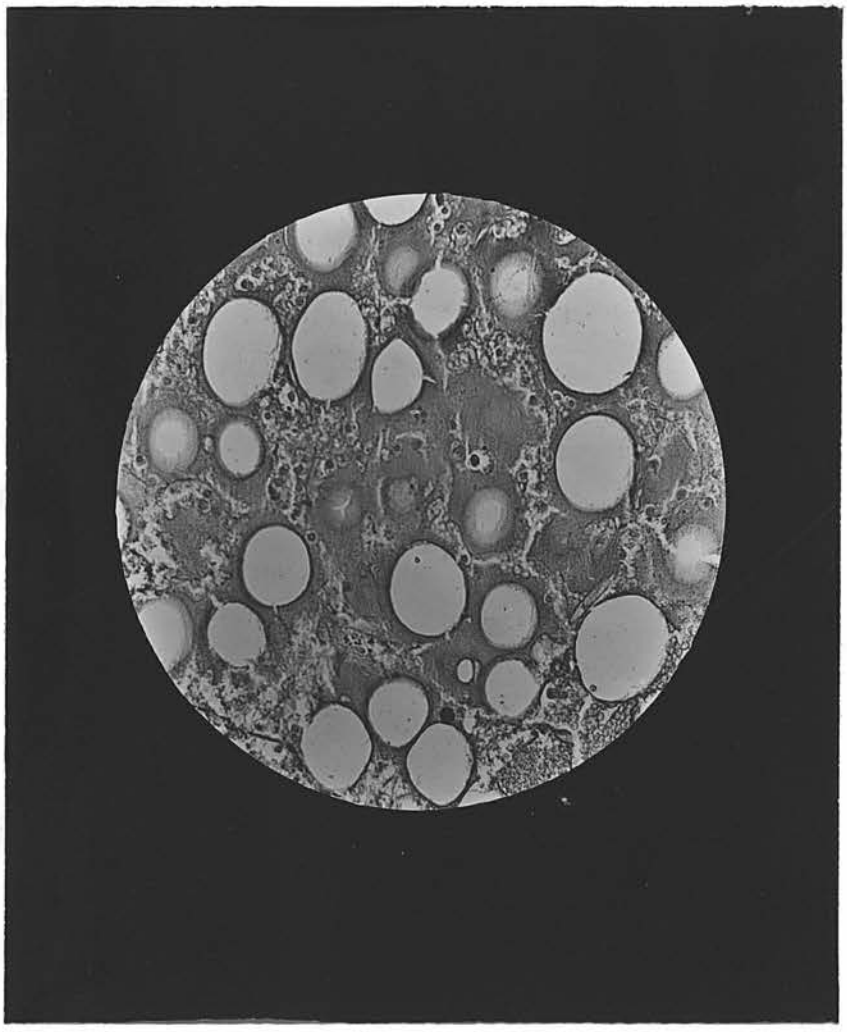


Figure 1. Photomicrograph of the bone-marrow taken from the tibia of Case I. Showing a high degree of gelatinous degeneration. X 250. (Photograph by Mr. Charles Geary).

change being present. The gelatinous change shows as a dense homogeneous appearance round the periphery of the fat cells, the fat globules having undergone partial absorption. Between these fat cells there is, at parts, a loose reticulum (in places somewhat granular), in which is embedded a very scanty number of blood-forming cells. (See Micro-photograph - Fig. I.)

Bony trabeculæ are very scanty, as are also hæmopoietic cells. The ratio between the red and white series of cells doesn't appear to be very much altered, but the nucleated red cells are, perhaps, rather more numerous in proportion. All are much diminished absolutely.

The eosinophil myelocytes form a large proportion of the white cells; more so than normal.

There is a wide-spread hæmorrhage at one part, but this is quite probably due to surgical manipulation.

No giant cells are seen.

There is no evidence of any local destruction of blood in the bone-marrow, in the shape of numerous phagocytic cells, such as are seen in pernicious anæmias, in sévere secondary anæmias generally, and in septicæmias.

No megaloblasts can be seen.

In the bone-marrow of the femur (post mortem). -

The appearances are very similar, the fat cells being surrounded by a ring of gelatinous change (Micro-photograph, Fig. i.).

The Spleen, on microscopical examination shows:- A marked increase of fibrous tissue. The Malpighian bodies are widely separated and are much atrophied (Micro-photograph Fig. ii). The vascular spaces are considerably dilated and congested with blood. There is slight thickening of the walls of the central arteries of the Malpighian bodies, apparently partly due to endothelial increase. There is evident proliferation of the endothelial cells lining the vascular spaces, and some of these cells and also a few giant cells which are present, can be seen to contain several disintegrated red blood corpuscles. The proliferation of the endothelial cells in this case gave the appearance seen in Micro-Photograph Fig.iii which is from Case III.

The liver, apart from the general appearance of chronic congestion, shows very little that is abnormal. There is no increase in fibrous tissue.

In a few places there is a slight degree of small round-celled infiltration. No blood pigment is seen.

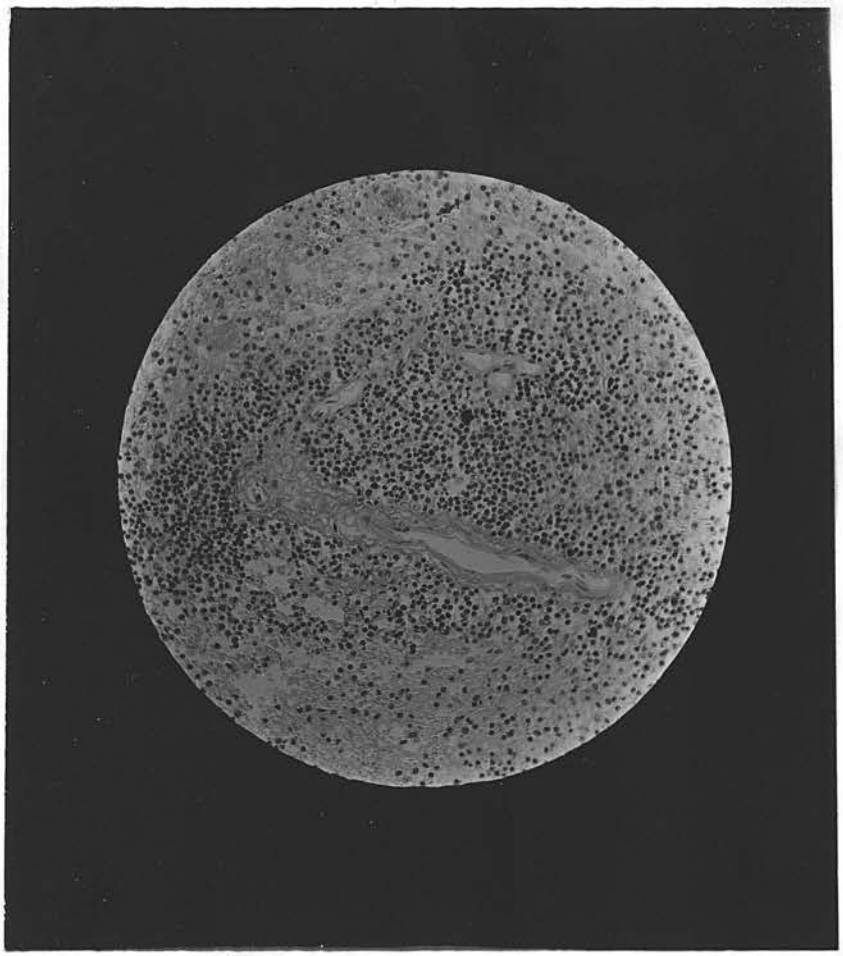


Figure 2. Microphotograph from Case I, showing an atrophied Malpighian Corpuscle, and an increase in thickness of the walls of the central vessel. × 200. (Photograph by Dr. Charles Geary).

The following case was not in Dr. Gibson's Ward while I was acting as his House Physician, but I was able to see him on several occasions.

CASE II.

Andrew A., aged 16 years; by occupation - a miner. He was born in Scotland, had lived all his life in that country and had never been abroad. He was admitted to the Edinburgh Royal Infirmary, under Dr. Gibson's care, on April 14th, 1908, complaining of breathlessness and weakness, and swelling of the feet.

History:

His Father died in middle age, probably as the result of a cerebral hæmorrhage. His mother, three brothers and one sister are alive and in good health. None have died.

He is accustomed to good food and lives in a dry, airy cottage, excellently situated in the country.

His work, as a coal miner, necessitates his going down into the pits, but, as pits go, this is a very healthy one.

He is teetotal, never smokes and gives no venereal history.

He had measles and whooping cough in infancy. He says he never had acute rheumatism, chorea, or skin rashes of any kind, but that he has occasionally been troubled with growing pains.

In January last, a beam hit him on the genitals

and cut him; he was, as a result, confined to bed for four weeks, has never felt well since, and dates his illness from this time. He felt breathless when he left his bed, and noticed, also, that he had a slight cough. His feet, also, almost immediately commenced to swell. He has suffered from no pain in any region, and thinks, that apart from his above-mentioned breathlessness and swelling of the feet, he is a perfectly healthy boy.

On Admission:

He is a moderately healthy-looking boy, excepting that he is pale and somewhat emaciated.

Circulatory System:

He has suffered from palpitation once during the last month. Otherwise he has had no subjective phenomena.

The pericardial region is well formed, though poorly covered with adipose and muscular tissue. The apex is diffuse, and only just visible in 4th and 5th left interspaces. Pulsation is to be felt all over the pericardial region.

On Percussion:

The upper limit of liver dulness is in the 4th interspace in the right mammary line. The apex of the heart lies in the 5th interspace, $3\frac{3}{4}$ inches to the left of midsternum.

The right border of the heart at the level of the 3rd and 4th ribs, lies $1\frac{1}{4}$ inches to the right of midsternum.

The upper border of the heart is at the level of the upper border of the 3rd rib in the left sternal line.

Auscultation:

In the mitral area, there is a well-marked rough presystolic murmur leading up to the first sound which is closed. The 2nd sound is accentuated.

In the tricuspid area, both sounds are closed. In the aortic area, both sounds are closed, but the 2nd sound is much accentuated, and is high-pitched and flapping in character.

In the pulmonary area, there is a soft, blowing systolic murmur which is followed by an accentuated 2nd sound. There is no evident venous pulsation in the neck.

The pulse shows no irregularity in time or force,

and there is no thickening of the vessel walls. The volume is good, and the frequency is 84 per minute.

Respiratory System:

There are no subjective symptoms.

The chest is well formed, but poorly covered with muscle and adipose tissue.

The respiratory movement is free and equal on the two sides.

On Palpation - there is no change in vocal fremitus.

Percussion yields a healthy lung note all over the chest.

On Auscultation - breathing is vesicular in all areas and free from any accompaniments or superadded sounds. The vocal resonance shows no departure from the normal.

Hæmopoietic System:

The spleen is much enlarged. It is easily palpable during ordinary respiration, and the lower pole reaches two inches below the costal margin.

From pole to pole, the spleen measures 7½ inches. There is no enlargement of any of the lymphatic glands.

The Blood:

The blood count is as follows:

Erythrocytes	-	4,410,000	) Per cubic millimetre.
Leucocytes	-	3.200	)
Hæmoglobin	-	70%	
Colour Index		.8	

A differential count of the leucocytes shows: -

Neutrophil Polymorphs	-	58%
Lymphocytes	-	28%
Large Mononuclears	-	12%
Eosinophils	-	1%
Mast cells	-	1%

Alimentary System.

The teeth are in a carious and septic condition.

The tongue is clean, but pale and flabby.

There is nothing subjective to note.

His appetite is good, and he has no pain or discomfort in connection with his food. He has not been troubled with vomiting. His bowels move regularly about once daily, and he has never noticed blood in his motions.

The abdomen moves freely and equally on both sides, nothing abnormal is noticed on inspection.

Palpation causes no discomfort in any area, and,

excepting for the splenic tumour already noted, reveals no undue resistance in any area.

The liver is not palpable.

On Percussion, the lower border of the liver is found to reach the costal margin in the left mammary line.

Urinary System:

There is nothing subjective to note.

The urine is clear, has a specific gravity of 1015, and is acid in reaction.

Examination of the urine shows it to contain nothing abnormal.

Nervous System:

Nothing is complained of as regards sensory phenomena.

Sensibility to touch, pain, heat, and cold are absolutely normal.

His sight is good, and the pupils react normally both to light and accommodation.

Well-marked nystagmus is present (he has worked in the pit for one year).

On Ophthalmoscopic Examination, the optic discs and the fundi appear quite healthy. There are no

retinal hæmorrhages.

The organic reflexes are healthy.

The superficial reflexes are all quite normal in quality and quantity.

The tendon reflexes are extremely active in all the limbs. No clonus is present.

Intelligence, memory, attention and speech are all unimpaired.

Bones and Joints: - There is no evidence of rickets about the chest, head or long bones.

The temperature is normal.

Progress.

By April 20th, all swelling of the feet had disappeared, and there had been no fresh disturbance of any kind.

The presystolic murmur was not always present, and the pulse was quite regular.

The blood showed no change, the leucocyte count remaining below 5.000

He continued to improve, and by the commencement of May had gained 3 lbs. in weight.

On May 3rd, he had an epistaxis, which, however, was not very severe, and stopped without special treatment. He had another epistaxis on May 12th,

very similar to the previous one. No local cause was found for the bleeding.

On May 18th, he was started on Liq. arsenicalis ♏ v. three times daily, and on the following day, May 19th, he complained of headache, did not wish for his food and started vomiting. With this, the temperature rose to 102.6, and the pulse and respiration rate rose proportionately.

Nothing was found to explain this disturbance excepting a pure gastric attack, and he was given ℥i of castor oil.

The castor oil had the desired effect, and the patient was apparently quite well next day. He had lost ¾ lb. in weight during the past week, but he made it up again during the following week, and by June 15th, having had no fresh trouble in the mean time, he had gained another 3¼ lbs.

The spleen, up to this time, showed no change in its size, and the blood count varied but little, the leucocytes still averaging about 4,000 per cubic millimetre.

Dr. Gibson regarded this as an early case of splenic anæmia, and, with a view to later splenectomy, the boy was, on June 24th, transferred to Mr. Caird's ward for the purpose of having his tibia trephined for

the sake of examination of his bone-marrow. Mr. Caird trephined the left tibia in its upper third the same day. There was no special tendency to hæmorrhage at the time of the operation, and the patient suffered no ill-effects. He returned to Dr. Gibson's ward the following day, June 25th.

To the naked eye, the appearance of the marrow was healthy.

On microscopical examination: - There are no advanced degenerative changes.

The hæmopoietic cells are fairly numerous, and appear practically normal in number, size and proportions. Nucleated red blood cells are present in about their normal proportions. A large hæmorrhage is present, undoubtedly due to the surgical manipulations.

Giant cells are small and extremely scanty.

There is no proliferation of the adenoid reticular cells.

The marrow, thus showing a fairly healthy condition and a satisfactory regenerative state, splenectomy was advised.

The patient has refused to submit to the operation for the present, and prefers to wait, at any rate, for a time, to see if his health improves with

rest in the country.

The wound on his leg healed up by first intention, and gave him no further trouble.

He left in the middle of July, having had two more attacks of epistaxis since his operation. His blood still remained as previously noted, and the leucocytes showed no tendency to increase.

I have been unable to get any news of him since he left the ward.

That this is a genuine early case of splenic anæmia seems very probable. The enlarged spleen and leucopenia without marked other blood changes favour this view. The heart condition cannot, in my opinion account for the size of the spleen in the absence of hepatic enlargement or other signs of backward pressure. If his condition becomes worse, he should be a good case for splenectomy.

CASE III.

Violet N. aged 14 months.

She was admitted to the Medical Wards of The Children's Hospital, Paddington Green under Dr. Sutherland's charge on October 6th 1908, the mother complaining of her yellow colour.

History:

She was born at full-term and the labour was normal and non-instrumental.

She was fed solely on the breast till she was 3 months old, and since this time she has also been getting Ridge's Food.

She was, to all appearance, a very healthy infant, and her mother noticed nothing wrong until she was 6 months old: at this time, the child's colour changed, the previous healthy tint being gradually replaced by a pale, faintly yellow hue. The degree of yellowness is said to vary, being sometimes deeper than at others. As she was yellower today than she previously has been, her mother brought her up to this hospital, and she was admitted to the ward. She has always taken her food eagerly and she has never vomited. The bowels have been regular, and the motions healthy in appearance, and the child has

not had hæmorrhages from any source. She has had no other illnesses, infectious or otherwise.

Family Health:

The father and mother are both alive and enjoy good health.

One other child, aged 3, living and healthy.

One child died within a few hours of birth,- cause unknown.

There have been no miscarriages or premature labours.

On Admission:

(Note. I didn't see the child at the time of admission, and the following notes were taken by my predecessor at this Hospital).

"The child is very pale, but fat and well-developed. She has 10 teeth. The tongue is clean and the throat healthy.

The face, and the skin all over the body is very pale, as also the lips and the conjunctivæ. The face has a faintly lemon-yellow tint.

There is no discharge from the ears or eyes, and the child has no snuffles.

The joints all appear normal.

Chest. Nothing abnormal to note. Lungs appear quite healthy.

Heart. Apparently healthy. Sounds are closed in all areas.

Abdomen. The spleen is considerably enlarged, extending 1 inch below the costal margin.

There is no liver enlargement.

No enlarged glands are palpable in any area.

The superficial and deep reflexes are all healthy."

The child was put onto a milk diet and raw meat juice, and given a mixture of castor oil and salol three times daily.

She was always ready for her food and was very bright and cheerful.

The pulse was rapid, averaging about 136 per min., and the temperature was swinging slightly, being usually about 100° at night and 98° in the mornings.

On October 13th, there is a note to the effect that the spleen is slightly increased in size, and,

on the evening of that day, the temperature rose to 103°, though no cause was found for this, and the child remained bright and happy.

The temperature again reached 103° the following evening (October 14th), and still no fresh signs were found and the child appeared quite comfortable.

Following this, there was no great fever, and the temperature resumed its previous characters. On October 16th, the blood was examined and charted as follows:-

Erythrocytes	4,290,000.
Hæmoglobin	65 %
Leucocytes	12,000.

No differential count was made.

I rather doubt the accuracy of the above blood count, as I saw the child shortly afterwards and repeatedly obtained very different results, although there was very little evident change in the child's appearance or condition. The child appeared to do very well, was always exceedingly bright, and her colour improved. The spleen showed no perceptible alteration in size. No further blood count was made at this time. By October 28th she seemed much improved and was sent to the Hospital's Convalescent Home, where she was given $\eta\frac{1}{2}$ of Liquor Arsenicalis

Photograph of the subject of Case 3, showing the outline of the spleen, also cardiac and hepatic dulness.

three times daily.

She was, at this time, diagnosed as a case of Splenic Anæmia.

I first saw the child a fortnight later, on November 13th at the Convalescent Home, but I was, at this time unable to examine her thoroughly.

She then looked exceedingly bright and happy, but was extremely pale and the skin had a faintly yellow tint. The mucous membranes were much blanched. The gums were quite healthy. There was an abundance of subcutaneous fat.

The head was square (see photograph) and the child's facies were rather suggestive of Mongolism, the child's bright, vivacious temperament rather adding to this suggestion. There was no bossing of the skull, and no signs suggesting either rickets or specific disease.

The lower pole of the spleen was easily palpable lying 1½ inches below the costal margin in the left parasternal line. It felt firm and moved with respiration, and palpation of the organ caused no discomfort. The liver was not enlarged.

The heart was slightly enlarged, but no murmurs were detected in any area.

The lungs showed nothing abnormal.

The motions were slightly undigested and offensive, and contained no blood.

She was feeding and sleeping satisfactorily, and had increased 1½ lbs. in weight since she left Paddington Green, her weight now being 18½ lbs.

The temperature, during the past fortnight, had been swinging slightly as before.

I saw the child again a fortnight later, on November 27th, and found that she had had a pyrexial attack continuing for the last 10 days, the temperature always being high at night, and, on three occasions, exceeding 104°. With this, the child had evidently suffered abdominal discomfort, and the pain seemed to be confined to the splenic region. There had been no vomiting and no diarrhœa.

The spleen now lay 2 inches below the costal margin in the left parasternal line.

I again examined the heart and lungs without finding fresh signs.

As the attack was now subsiding, I allowed the child to remain out at the Convalescent Home.

On December 11th I again saw the child. There was no appreciable change in her condition from my former visit. Her weight remained the same, she was

NAME. Violet Nutman.
AGE. 14 months.
DISEASE. Splenic Anaemia.

W. B. C.	R. B. C.	Hb.
20,000	8,000,000	160 %
18,000	7,500,000	150 %
16,000	7,000,000	140 %
14,000	6,500,000	130 %
12,000	6,000,000	120 %
10,000	5,500,000	110 %
8,000	5,000,000	100 %
6,000	4,500,000	90 %
4,000	4,000,000	80 %
2,000	3,500,000	70 %
	3,000,000	60 %
	2,500,000	50 %
	2,000,000	40 %
	1,500,000	30 %
	1,000,000	20 %
	500,000	10 %

FILM

See Diet Sheet.

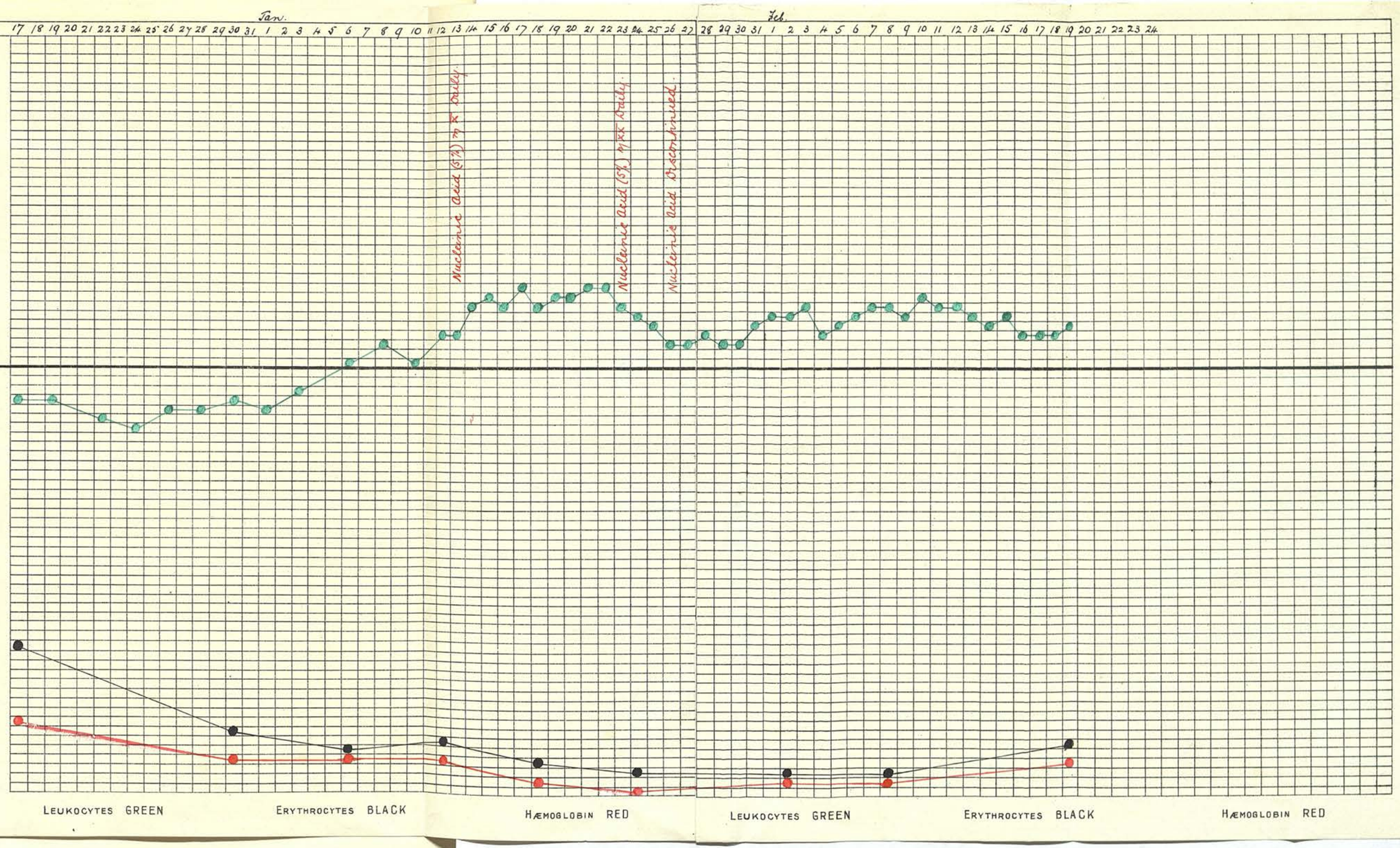


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Chart 5.

very bright and taking her food well. She had apparently had no more abdominal discomfort, and the spleen remained the same size. The temperature had continued to swing up to about 101° nightly.

As she was showing no improvement and I wanted to have her blood thoroughly examined, I had her sent back to Paddington Green on December 17th.

The blood now showed a great change from the first count already given and my first blood examination (on December 17th) gave the following result:-

Erythrocytes	2,010,000	Colour Index = ·63
Hæmoglobin	25 %	
Leucocytes	6,600	

Examination of a film showed:-

Polymorphonuclear Neutrophils	29 %
Lymphocytes	65 %
Large Mononuclears	1 %
Eosinophils	1 %
Transitional Cells	4 %

No myelocytes were seen.

An average of 4 normoblasts were found for every 100 white cells counted.

There was a slight degree of Polychromatophilia and Poikilocytosis (Chart V).

The accompanying diet sheets, which I devised for use in the wards, shows how the differential count varied after this date, and the blood chart shows the course taken by the red and white cells and hæmoglobin.

At this time (Dec. 17th), the lower pole of the spleen could be palpated 1¾ inches below the costal margin in the left parasternal line. The spleen felt of firm consistence, had a smooth surface and was movable with respiration.

The liver was also now slightly enlarged, the lower margin extending ¾ inch below the costal margin in the right mammary line. No enlarged lymphatic glands were palpable.

The heart showed slight enlargement, but the sounds were closed in all areas.

No abnormal signs were found in the lungs.

The motions were green, undigested and offensive, and I therefore stopped the arsenic at this time and again gave the child a mixture containing castor oil and salol.

During the following week, there was no evident change in the child's condition excepting that she appeared more and more pasty. She took her food well and was always hungry. The motions were still very

offensive. She was therefore given Hydrarg. cum Creta with Bicarbonate of Soda, and put onto a diet of milk, soup and rice.

The urine was quite normal and contained no albumen.

On December 25th there was noticeable œdema below the eyes, most marked on the right side. There was no œdema elsewhere. There was still no albuminuria. The œdema gradually disappeared, and by Dec. 28th, there was no trace of it. The following day, the temperature, which had, as before, been swinging up in the evenings to about 100°, rose to 103°. It quickly settled again. The spleen remained the same size and no cause was found for this temperature. The next day, another examination of the blood showed that it had deteriorated considerably during the past 10 days, the red cells now numbering only 1,120,000 per cub. mm., and the Hæmoglobin 15 %. The white cells remained much as previously - see diet sheet and blood chart. On December 31st, I gave her 2½ grs. of Thymol, and examined the faeces for ova. The examination proved negative. As the motions were still very offensive, I gave her gr. ½ of Thymol three times daily, and raw meat juice was added to her diet.

Name Case 3. Age ..... Clinical Clerks { .....

Blood. Date.	17·12·08	30·12·08	6·1·09.	12·1·09.	18·1·09.	24·1·09.	Start.	Treatment.	Stop.	Diet.
R.B.C.	2·010·000	1·120·000	960·000	1·020·000	860·000	780·000				
Hb.	25%	15%	15%	15%	12%	10%				
W.B.C.	6·600	6·800	8·200	9·800	11·600	10·200				
Film :—		Film :—	Film :—	Film :—	Film :—	Film :—				
Polymorphs	29%	16%	14%	21%	42%	38%				
Lymphocytes	65%	71%	69%	60%	48%	47%				
Large Monos	1%	4%	5%	6%	3%	4%				
Eosinophils	1%	2%	3%	2%	2%	2%				
Mast Cells	-	1%	1%	3%	1%	1%				
Comments :—										
Transitional 4%		6%	8%	8%	4%	7%				
Normoblasts 4% glWBC		2% glWBC	} As before	} As before	} As before	} As before				
Slight poikelocytosis		} As before								
No myelocytes.										

Date.	Urine.	Blood Pressure.	Sputum.	Gastric Contents.	Additional Facts.

Diet Sheet 2.

showing the differential blood counts at different dates.

On January 1st 1909, a finely rough bruit was present in the mitral area, preceding the first sound. It was heard most intensely at the apex, and was carried out into the axilla and upwards to the 3rd left rib, and could be heard in the tricuspid area.

The child at this time was extremely pale, and hadn't a vestige of colour about her, but she was still as bright and happy as before.

The lungs appeared healthy, there was no ascites nor œdema in any area, and there were no skin hæmorrhages.

On January 6th, the blood count had again fallen, the red cells numbering less than a million with the hæmoglobin still standing at 15 % (see diet sheet).

Four days later, I was struck with the alteration in the character of the child's pulse. The wave now had a very quick rise and fall, and its apex was poorly maintained. It very much suggested the pulse of aortic regurgitation. I could not find a capillary pulse, but the child was too anæmic to demonstrate this if it had been present.

All the vessels, especially those in the neck, showed marked throbbing.

On examination of the heart:-

Pulsation is seen to be diffuse over the

præcordia. A soft thrill is felt in all parts of the præcordia, but it can't be accurately timed.

The apex lies ½ inch outside the left mammary line, and the right border of the heart extends ¾ inch to the right of midsternum.

On Auscultation:-

In the mitral area, there is a long, blowing systolic murmur. No trace of the previously-mentioned presystolic murmur is now found. This systolic murmur is faintly heard in the axilla, but is not propagated inwards.

In the aortic area, a rough systolic bruit is heard, propagated into the vessels of the neck, and there is a long, faint blowing systolic murmur heard best over the sternum at the level of the 3rd interspace, and audible down to the level of 4th rib.

In the tricuspid area, distinct presystolic and systolic murmurs are audible. Their area of propagation is very limited.

In the pulmonary area a soft, blowing murmur is distinctly heard.

This sudden alteration in the heart sounds and accompaniments came as a surprise, for the child had shown no fresh manifestations, the temperature had shown no unusual swing, the pulse rate was unaltered

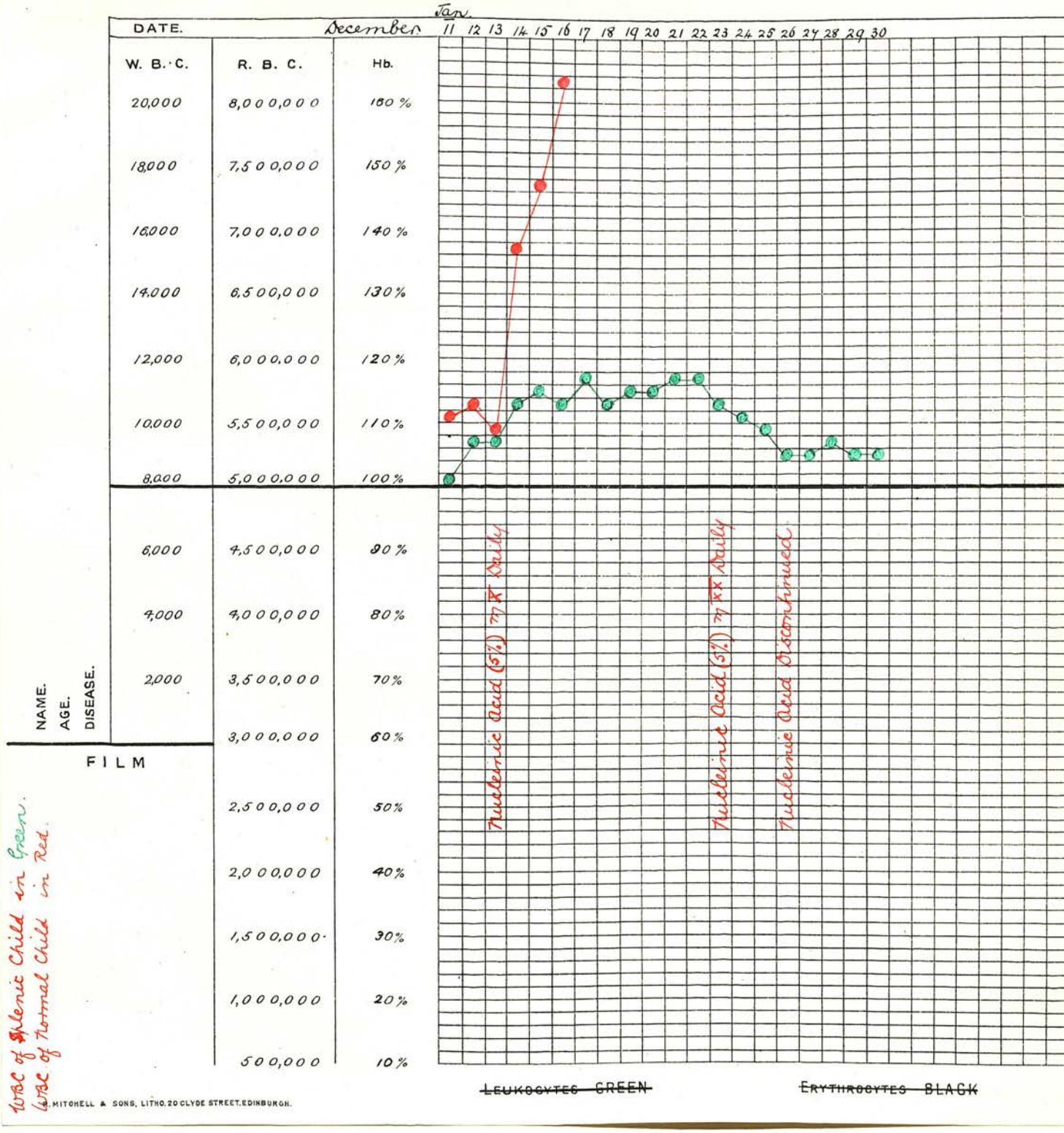
and the fact that the child's heart was auscultated practically daily, and often by 2, 3 or 4 observers, left no doubt that these findings were really new, and not due to want of or faulty previous observations.

As chart V shows, the blood was still in practically the same condition, all the elements having increased slightly.

Following this, there was no change in the child's condition, the cardiac murmurs remained constantly as just reported, and the spleen showed no variation in size.

On January 13th, I decided to try the effect of nucleinic acid on the leucocyte count of this child, in the same way as in Case I reported above. The amount given was $\eta\overline{x}$ of a 5 % solution once daily, and this was given by hypodermic method.

As chart VI shows, there was practically no reaction of the leucocytes to the nucleinic acid although it was, on January 23rd increased to $\eta\overline{xx}$ daily. A few days after the commencement of these injections, the temperature took on a greater swing and finally, on January 25th rose to 104·6. With this the child became so ill, that I had to discontinue the drug. I may say that nucleinic acid was not looked on with much favour at this Hospital, and



WBC of Splenic Child in Green.
WBC of Normal Child in Red.

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Chart 6.

consequently I was unable to make the controls I would have wished. I gave a few injections, however, to a child 18 months, in the ward on account of previous improper feeding, and I got a very prompt and marked result, and felt bound to discontinue it in this case also. As before, both bloods were counted as nearly simultaneously as possible, and at the same time daily.

On January 19th and 20th temperature rose to 103° and 103·4° in the evenings, and the child seemed to be losing her strength and cheerfulness. The spleen, at this time, appeared a little reduced in size, the lower pole lying 1¼ inches below the costal margin in the left parasternal line. The respirations were now very hurried and reached 72 per minute, and there were many catarrhal sounds throughout both lungs, though there was no dulness to percussion, and no bronchial breathing was heard. The heart sounds were masked by the pulmonary accompaniments, but, as far as could be made out, they remained very much as previously noted.

The temperature steadied for 2 days after this, but then took on a large daily swing as before, and on January 25th reached 104·6° and remained at this height for 24 hours. As previously noted, the

nucleinic acid was stopped at this time.

The child, all this time, never ceased to take her food heartily and to sleep abundantly. The respirations were always very rapid, but she showed no distress with them.

On January 23rd, the pulmonary sounds having largely disappeared, the heart sounds and murmurs could again be heard with some certainty. The aortic murmurs were now less evident, but were still present in the same sites as before. The presystolic tricuspid murmur was much louder than previously, and there appeared to be a return of the presystolic bruit in the mitral area, whilst a blowing systolic murmur in the pulmonary area was very evident.

The blood, at this time gave an extremely low count of red cells and hæmoglobin (see chart and diet sheet), but a film showed very little change in the characters of the cells. The slight increase in leucocytes which occurred with the administration of nucleinic acid, seems to have been due to augmentation of polymorphonuclear cells, as it will be noticed that their ratio has increased at the expense of the lymphocytes.

The motions had, all along, continued to be green, undigested and offensive, and, at this time,

the abdomen showed considerable distension which was apparently of intestinal origin.

On the evening of January 24th, though the child had been quite merry all day, she suddenly became much distressed, coughing and spluttering, and gasping for her breath, and with this, she seemed to be in pain, again locating this pain in her left side. At the same time, the legs became œdematous, and the abdomen greatly distended, presumably with gas. The temperature rose to 104, and the pulse was feeble and running at 168 per minute. The bowels were moving freely, and there was no vomiting. She was given Liq. Strychninæ $\mathfrak{m}\overline{\text{iii}}$ hypodermically and nepenthe $\mathfrak{m}\overline{\text{v}}$ by the mouth. She was quiet and slept well after this, and the following day, although, as previously stated, the temperature was above 104°, she seemed very much better, being again cheery and bright and showing no uneasiness. The abdominal distension also and the œdema of the lower limbs were much less marked.

This improvement was continued on Jan. 26th, by which time, the abdominal distension and œdema of the limbs had practically disappeared. There were now certainly separate presystolic bruits in both the mitral and tricuspid areas, and a loud systolic murmur

in the aortic and pulmonary regions.

During the next few days the child appeared to be gradually going downhill. She seemed to be losing weight, her features looked drawn, and her vigour was deserting her.

On January 29th the pulse was weak and 160 per minute and her respirations reached 74 per minute. She was restless, but although her respirations were so rapid, she continued to take her food well, and didn't appear to be suffering. At night, she seemed so weak that we didn't expect her to live many hours.

She rallied a little next day, and, from this time, started to improve.

On February 2nd, on being weighed, she was found to have lost 26 oz. in weight during the past fortnight. She was, at this time, again looking brighter, but her features still looked drawn. There was no recurrence of œdema, and no change in the size of the spleen or liver. The blood also had altered very little (see chart).

By February 5th, she had improved very markedly. She looked rather a better colour, and was merrier than she had been for 3 weeks. With this, the blood showed a slight tendency to improve, though the red cells were still below one million per cub. mm., and

the spleen was a little reduced in size and felt softer. The temperature also, had settled, and was keeping between 98° and 101°.

This improvement was maintained, and by February 13th the child had gained 1 lb. in weight, and the temperature for the last week had been practically normal, never rising above 100°. The spleen again seemed a little smaller, the lower pole being palpable 1¼ inches below the costal margin.

The pulse was slower and stronger, though it still had the aortic characters previously mentioned, and there was no change in the heart. There was, however, a slight degree of dulness to percussion over the upper lobe of the right lung, and over this area, the breath sounds were exceedingly harsh and vocal resonance considerably increased.

The lower border of the liver lay 1 inch below the costal margin in the right mammary line. There was no ascites and no œdema in any area.

The urine contained, from time to time, a slight trace of albumen, but there was never any blood, and no casts were, at any time found in it. Neither was there ever any blood in the motions.

On February 19th the child still seemed to be improving,and the blood showed another slight increase

of all its elements.

The white blood corpuscles, which had been examined every day up till this time, had remained slightly elevated ever since the administration of nucleinic acid, though they were, all along, rather below the normal average for a child of this age.

Unfortunately, I was, on account of illness, forced to leave the Hospital on this date, and no further blood examinations were made. She died quite suddenly, 5 days later (on February 24th), when she was apparently progressing favourably. No fresh signs were found during her last few days, and she appeared to be doing well until a few hours before her death, when she became languid and drowsy, and died quite suddenly on the afternoon of February 24th. The spleen, examined on the day of her death, still remained the same size as last described by me.

I was unable to be present at the autopsy, but the following is the report of the post-mortem examination which was made by Dr. Emery.

Post Mortem Report:-

"Pleuræ - healthy.

Right Lung. Patches of collapse in the lower lobe; otherwise healthy.

Left Lung. Upper lobe completely collapsed, probably from pressure by the heart. Lower lobe shows patches of collapse.

Bronchial Glands. Slightly enlarged and congested. Not caseous.

Pericardium - contains about 2 ounces of clear fluid.

Heart. Considerably enlarged, chiefly on the left side. It extends, on the right side, one inch to the right of the middle line. It extends up to the 2nd rib.

Right auricle and ventricle distended by a large amount of red currant jelly-like clot.

Tricuspid valve incompetent - about one inch in diameter. Cusps healthy.

Left auricle and ventricle contracted and empty.

Foramen Ovale not completely closed.

Mitral valve slightly dilated, cusps healthy.

Aortic orifice dilated. Semilunar cusps, both aortic and pulmonary, healthy.

No patent ductus arteriosus.

Thymus not abnormally large.

Stomach and Intestines - healthy.

Suprarenal Glands - healthy.

Lymphatic Glands - mesenteric and retro-peritoneal glands are not enlarged.

Kidneys - somewhat pale. Not otherwise abnormal. Microscopically, the kidneys appear perfectly healthy.

Liver - Slightly enlarged. Not obviously abnormal to the naked eye.

Spleen - Shows moderate enlargement. It reaches one inch below the costal margin. On section - slightly congested. Not otherwise abnormal.

Bone-marrow - appears normal as regards colour and consistency."

Microscopical Examination.

Spleen. There is a slight increase of fibrous tissue throughout the spleen substance. The Malpighian bodies show no signs of atrophy. The vas-

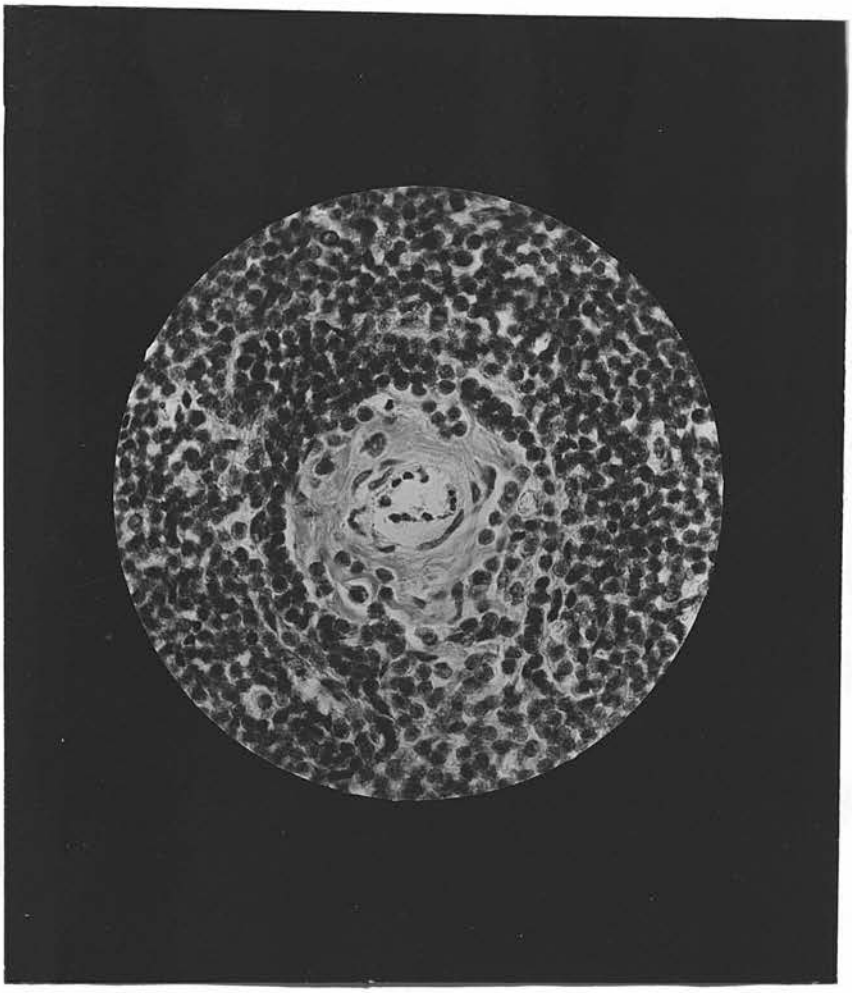


Figure 4. Microphotograph from Case 3, showing proliferation of the walls of the central artery of a Malpighian Corpuscle. × 450.
(Photograph by W. Charles Geary).

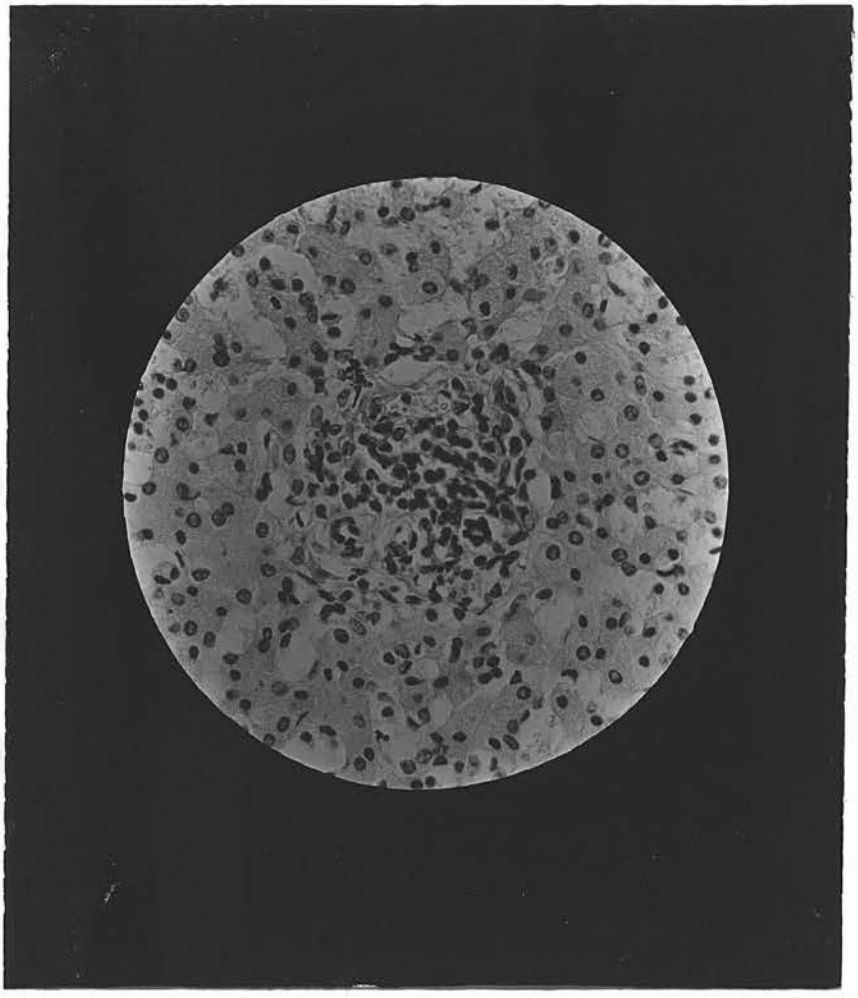


Figure 5. Microphotograph from Case 3. Showing an increase of lymphoid cells about a portal space. X 350. (Photograph by Mr. Charles Geary).

cular spaces are somewhat congested with blood.

The most marked change is in the central arteries of the Malpighian bodies. These are extremely small, due to proliferation of their walls. This proliferation is largely fibrous, but there is a very marked increase in the endothelial elements also. Some of the lumina of the vessels are almost occluded (see Micro-photográph, Fig. iv).

There is also marked increase in the endothelial cells lining the vascular spaces, and there are a few giant cells, but I have not detected any definite phagocytosis (See Micro-Photograph, Fig. iii).

Liver. There is a very slight increase in fibrous tissue. No blood pigment is seen.

In a few places, there is a slight increase of lymphoid cells in the portal canals. Otherwise, the liver appears normal (Micro-Photograph, Fig.v).

Bone-Marrow. To the naked eye appears healthy. On examination of a film of the marrow obtained from a rib, there is a very striking increase in the number of eosinophil myelocytes present. Nucleated red cells are extremely scanty. No gelatinous changes are observed in this marrow (Micro-Photograph, Fig.vi).

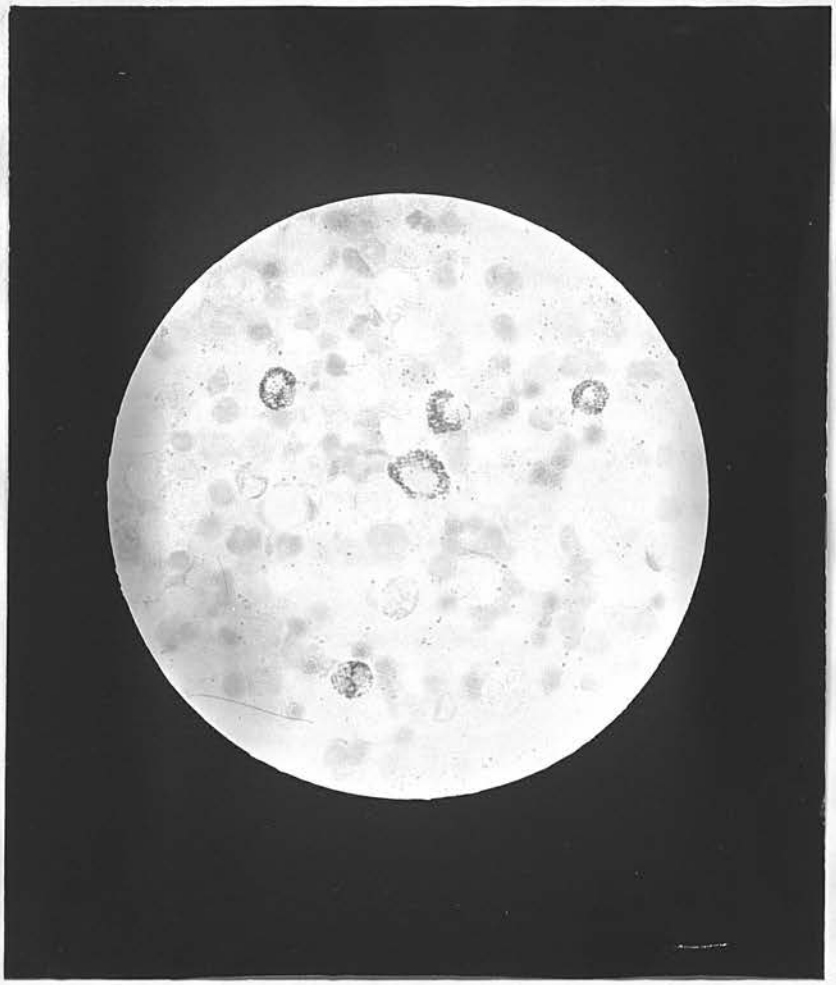


Figure 6. Microphotograph from Case 3, showing the large proportion of eosinophil myelocytes in a bone-marrow film. × 650. (Photograph by Mr. Charles Geary).

CASE IV.

This case was under Dr. Sutherland's care at Paddington Green Children's Hospital, three years ago, and as it illustrates, in an excellent manner, the benefit that may be derived from Splenectomy, and as it has never before been reported, I have asked Dr. Sutherland's permission to allow me to make use of it:-

Rose H., aged 12 years.

Admitted on April 24th 1906, complaining of pains in the stomach and all over the body.

History:

She was a very healthy child till two years ago, when she evidently had an attack of acute rheumatism. Since this time, she has been subject to pains in and swellingsof the joints. More latterly, she has complained of pains in her stomach, usually coming on shortly after the taking of food, and with this, she has been getting paler. She has not had bleedings from any source. No swelling of the abdomen has been noticed.

Family Health:

Her parents are both in good health. The maternal grandmother was consumptive.

She has four brothers alive and strong. Four sisters all dead: one of them died in Guy's Hospital with Splenic Anæmia.

On Admission:

She is a well-developed child and shows no emaciation. She is, however, very pale, and the skin all over the body has a sub-icteric hue, excepting in parts where there has been pressure (e.g. from garters etc.), where there is distinct brownish pigmentation. The gums and tongue are very pale, and the conjunctivæ much blanched, but not yellow.

There is an enlarged cervical gland on the right side, and also one slightly enlarged gland in the right axilla. Elsewhere, the lymphatic glands appear normal.

The heart shows some enlargement, the apex lying in the 5th left interspace, one inch external to the mammary line.

A musical systolic murmur is present in the mitral area, conducted outwards into the left axilla,

but not heard in the back. Elsewhere the sounds are closed.

The lungs appear healthy.

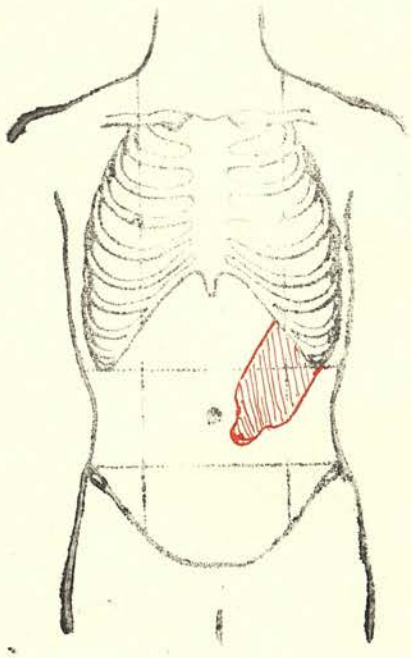
The tongue is clean but pale.

She complains that she frequently has pain of a sharp character in her stomach after taking food, and localises this pain to the left hypochondrium.

The abdomen shows some general distension, but its walls move satisfactorily with respiration.

On palpation of the abdomen, a large, firm mass is felt projecting from below the left costal margin (see chart) downwards and inwards, and reaching just below the umbilicus in the middle line. It has a short, finger-like projection at its lower pole. This tumour appears to have a smooth surface and is not tender on pressure. It measures $7\frac{1}{2}$ inches in length and $6\frac{1}{4}$ inches at its greatest diameter (i.e. one inch above the umbilicus).

The lower border of the liver reaches one inch below the costal margin in the right mammary line.



Chart

Showing the outline and position of the Spleen in Case 4.

The optic discs and fundi show nothing abnormal. The knee jerks are exaggerated.

The blood - examined the following day (April 25th) shows:-

Erythrocytes	3,000,000	))Colour Index - ·9.
Hæmoglobin	55 %	)
Leucocytes	9,400	

Film:-

Polymorphonuclear Neutrophils	68 %
Mononuclears	30 %
Eosinophils	·5 %
Mast Cells	1·5 %

There was no change in the child's condition. She was very comfortable, bright and happy, and, excepting for an occasional headache, complained of no pain. The urine was healthy, and the motions contained no blood.

On May 12th, the blood was again examined, and showed practically no change, either quantitatively or qualitatively, from the previous count. A few normoblasts were seen.

On May 18th she complained of pain in the eyes and of seeing double. No cause was found for this; it soon passed off and didn't again trouble her.

Another examination of the blood by Dr. Emery on May 30th showed:-

Erythrocytes	2,416,000
Leucocytes	3,400

Film:-

Polymorphonuclears	49·2 %
Mononuclears	48·8 %
Eosinophils	2 %

The child was given arsenic and sent to the Convalescent Home at Slough, where she remained for a month without showing any improvement.

On July 3rd, the blood, again examined, gave the following count:-

Erythrocytes	2,200,000	)
Hæmoglobin	48 %	)Colour Index = 1·1.
Leucocytes	10,000	

Film:-

Polymorphonuclear Neutrophils	51 %
Mononuclears	49 %

There was marked polychromatophilia and a few normoblasts were seen.

The spleen, at this time, still remained the same size, and the child's pallor and general appearance showed no appreciable change from the time of her admission. She had no discomfort and there was no

fresh glandular enlargement. The musical mitral systolic murmur persisted. She was always in good spirits, took her food heartily and slept well.

She had had no definite pyrexial attacks, but the temperature was often elevated to 100°, or a little higher, in the evenings.

On July 19th, a blood count showed:-

Erythrocytes	2,548,000	)
Hæmoglobin	40 %	)Colour Index = ·8.
Leucocytes	12,000	

A diagnosis of Splenic Anæmia had been arrived at, and it was decided to perform Splenectomy. This was done the following day - July 20th - by Mr. Burghard. The pedicle was found to be very difficult to clamp, and was tied off in sections along with the peritoneal ligaments.

The child stood the operation extremely well, and her pallor seemed to be leaving her before she left the operating table. She vomited a little that evening and the following day, but suffered practically no pain. The pulse remained at 120 per minute after the operation, and the temperature never rose to 101°.

The urine, examined the following day (July 21st), showed:-

A specific gravity of 1026.

An acid reaction.

A scant trace of albumen.

A copious deposit of urates.

There was no sugar or acetone present in it.

The tongue was moist and thinly coated.

She was very comfortable all day.

On July 22nd, she was evidently very much better. Had no pain and was not, in the least, restless. Her face appeared a little flushed and she looked very well. The pulse rate was 96, and the pulse full and regular.

The following day, July 23rd, the improvement was maintained and she was anxious for more food. The bowels were acting normally. The blood, again examined now, three days after the operation, gave the following count:-

Erythrocytes	4,704,000	)
		)Colour Index = ·8.
Hæmoglobin	76 %	)
Leucocytes	15,600	

It will be seen how, so soon after the operation, there was a very marked increase in all the blood elements. From the counts taken during the next few days, it appears as though there may have been a greater leucocytosis sooner after the operation. The

counts given for the next three days were:-

July 24th:-

Erythrocytes	4,092,000	))Colour Index = ·85.
Hæmoglobin	68 %	)
Leucocytes	12,000	

July 25th:-

Erythrocytes	4,584,000	))Colour Index = ·8.
Hæmoglobin	74 %	)
Leucocytes	9,200	

July 27th:-

Erythrocytes	4,456,000	))Colour Index = ·86.
Hæmoglobin	76 %	)
Leucocytes	6,400	

On July 28th, the sutures were removed from the abdominal wall. The wound had healed by first intention.

On July 30th, a small, but quite palpable and slightly tender gland was found in the left axilla. The blood showed renewed increase in its elements as follows:-

Erythrocytes	5,080,000
Hæmoglobin	76 %
Leucocytes	11,600.

On August 2nd, more palpable glands were noticed in the left cervical region. There were none in the right axilla or in the groins .

The blood - again counted showed:-

Erythrocytes	5,312,000	))Colour Index = ·73.
Hæmoglobin	78 %	)
Leucocytes	9,000	

A full examination of the blood was made on August 5th, and gave the following result:-

Erythrocytes	4,952,000	))Colour Index = ·79.
Hæmoglobin	78 %	)
Leucocytes	18,000	

Film:-

Polymorphonuclear Neutrophils	66 %
Lymphocytes	29·75 %
Large Mononuclears	1·5 %
Eosinophils	2 %
Mast Cells	·75 %

No normoblasts or polychromatophilia.

This may, therefore, be considered a very normal blood count for a child of this age, the leucocytes being slightly increased in numbers.

On August 9th, 13th and 16th, the following were the blood counts:-

On 9th:-

Erythrocytes	5,232,000	))Colour Index = ·82.
Hæmoglobin	86 %	)
Leucocytes	29,800	

On 13th:-

Erythrocytes	5,400,000	))Colour Index = ·8.
Hæmoglobin	86 %	)
Leucocytes	32,400	

On 16th:-

Erythrocytes	5,440,000	))Colour Index = 8.
Hæmoglobin	86 %	)
Leucocytes	23,200	

It will be noticed that a marked leucocytosis had suddenly developed. As it was ascertained that the child had contracted scarlet fever in the Hospital, the leucocyte count can probably be explained by that fact. She was removed, at this time, to the Fever Hospital.

The child got comfortably over her scarlet fever, and came up to Paddington Green for inspection on

December 1st 1906, 5 months after the operation. She looked extremely robust and well, and her skin and mucous membranes were a healthy colour. She had nothing to complain of excepting occasional rheumatic pains in her joints. There were no enlarged lymphatic glands, and the liver showed no enlargement.

The blood, on December 1st, showed:-

Erythrocytes	4,580,000
Hæmoglobin	90 %
Leucocytes	16,400.

The child still comes up to the Hospital occasionally on account of rheumatism, but excepting on this account, she has no distress, and is still in good health.

The spleen, on microscopical examination, showed a state of congestion. There was a slight increase in fibrous tissue and in the endothelial elements. Apart from this, the only striking feature was the enormous increase in the thickness of the walls of the central arteries of the Malpighian bodies, an endarteritis obliterans. The changes in the spleen in this case therefore conform very nearly to those in Case III, but in that case the proliferation of the elements of the vessel walls was less marked (See Micro-photograph Fig. iv).

The diagnosis of the anæmias of infants is fraught with more difficulty than is the case in adults. It is usually considered that the splenic anæmias of infants bear no relation to those of older people.
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Dr. Hutchison says that a distinction between the two is the constant presence of a marked leucocytosis in the cases affecting infants. He also says that, excepting for the finding of a fibrosis in the spleen there is no relation between the splenic anæmia of
71
infancy and that of adults. Dr. Hunter supports Dr. Hutchison's views.

The Splenic Anæmia of infants, often also termed Pseudo-leukæmia infantum of von Jaksch is said to be either due to rickets or syphilis. Other features usually given as belonging to this disease, besides the leucocytosis are - Enlargement of the liver and often, also, of the lymphatic glands, the presence of a large proportion of normoblasts and myelocytes in the blood and the absence of hæmorrhages.

That rickets and congenital syphilis may offer us a clinical picture which gives us nearly the signs of splenic anæmia I do not dispute, but I think that cases do exist in infants which are inseparable from splenic anæmia in more advanced life, both clinically and pathologically, and I put forward Case III. to support

my statement. I obtained an autopsy in this case, and both from this and the clinical course the disease ran, I am unable to separate it from the adult disease. My case, in contrast to the statements of other observers showed a leucopenia, and the leucocyte count, as in Case I. could not be materially altered by the administration of nucleins. The liver showed very little enlargement, there were no indications of either rickets or congenital syphilis, and the findings at the post-mortem agreed very closely with those in Case I.

The child's bone-marrow in Case III. did not show the gelatinous degeneration found in Case I, but it did show very markedly diminished formative power. The marrow in a child can more easily take on regenerative functions than is the case in later life, and I think this explains the fact that a higher leucocyte count may be found in the early stages of splenic anæmia in infants than in adults, and also, that a gelatinous condition of the marrow is less likely to be found in the former cases.

I am, therefore, of opinion that there are cases of the disease occurring in infants which should be classed as identical with the cases described in later life.

Note on Nucleinic Acid.

The germicidal power of the blood is not due to the leucocytes, but to a substance present in the blood plasma.

Vaughan[70] says:-

1. "That serum-albumin, as described by Buchner, is not the germicidal substance in blood serum since it is readily converted into peptone by peptic digestion, and that, after this, the germicidal properties of the blood are still unaltered. Further, peptone is favourable to the growth of bacteria and is used in preparing nutrient media."
2. "That the germicidal substance must belong to the proteids, otherwise it would be difficult to explain the fact that a temperature of 55° C. renders blood serum inactive."
3. "That the only proteid likely to be present in blood serum, and which is not destroyed by peptic digestion is nuclein."

Vaughan isolated from the blood a substance which is undoubtedly a nuclein, and he and others demonstrated that it had very decided germicidal properties.

From a physiologic standpoint, nucleins form the greater part of the chemic substances in the nuclei of all cells - i.e. chromatin. It is that constituent of the cell by virtue of which the histologic unit grows, develops and reproduces itself.

Nucleinic acid can be prepared from any form of nuclear material and plus some proteid matter forms a nuclein. It is most easily prepared from yeast cells, and contains about 9% of Phosphorus.

It is now well known that, by the administration to patients of the nucleins or nucleinic acid, the amount of leucocytes circulating, at any rate, in the peripheral blood can be considerably and rapidly increased.

Reeder and Wells believe that the increase in leucocytes is only apparent, being entirely peripheral at the expense of central paucity.

Most observers, however, including Ames and Huntley, are agreed that there is an actual total increase in circulating white corpuscles, and these last-named writers state that, within a few minutes of the injection of nucleinic acid, the blood shows an increase in small mononuclear cells, which, however, in the course of an hour or two, becomes changed into an increase in the polymorphonuclear elements. They con-

sider that the small mononuclear cell is the early stage of the development of the polymorphonuclear leucocyte, and that consequently, when the blood forming organs are suddenly stimulated to the throwing out of more white corpuscles, an increase in the mononuclear elements is first observed.

I think there is now no doubt that there is a total increase in leucocytes as the result of nuclein administration, though how this is brought about is uncertain. It seems probable that, when nucleinic acid is given, it finds the necessary proteid to form a nuclein, which stimulates the blood-forming organs to produce more leucocytes, though how this stimulation is actually produced is not clear.

Some writers state that part of the proliferation takes place in the circulation. I cannot say, from my own experience, whether or not there is, at first, an increase in the mononuclear forms of leucocyte, as my counts have practically all been made a considerable time after the administration of the nucleins; but my observations certainly show that, later, the increase is almost entirely one of polymorphonuclear leucocytes. The nucleins have been largely given before surgical operations, with a view to increasing the patient's resistance, but, so far as I can learn, they have not,

in this faculty, proved a marked success.

I thought it would be of interest to ascertain whether or not an artificial leucocytosis could be produced in these cases of Splenic Anæmia, and as my results show, the reaction to the nucleins has been very slight, especially in the adult case. My charts also point out that the response given by a normal blood is very much greater when the drug is administered hypodermically, and that the patient soon shows a tolerance to it.

Although I have not been able to use nucleinic acid on sufficient cases of splenic anæmia, in consequence of their rarity, I am inclined to think that a negative reaction to nucleinic acid may be of use in the diagnosis of these cases, at any rate when advanced, and that it may also help us in the prognosis of splenectomy in splenic anæmia, as it would suggest a degenerated bone-marrow incapable of further production.

Nomenclature.

The disease under discussion has been called by a great many different names:-

"Pseudoleukæmia," "Splenic Cachexia," "Primitive Splenomegaly," "Banti's Disease," "Splenic Pseudoleukæmia," "the Splenic Form of Hodgkin's Disease," "Lymphadénie Splénique"and"Anæmia Splenica."

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Cabot considers that the best terminology would be "Anæmia with Splenic Enlargement," and that, failing this, we should speak of "Splenic Pseudoleukæmia." He states that, if we talk of 'Splenic Anæmia' as indicating enlargement of the spleen with anæmia, to be consistent, we should apply the term "Lymphatic Anæmia" as applied to the association of lymphatic enlargements with impoverished blood.

32
Sippy says:- "If the ordinary forms of Hodgkin's Disease were described as 'Anæmia Lymphatica' and 'Anæmia Splenolymphatica', it would be consistent to apply the term 'Anæmia Splenica' to the rare cases under consideration. However, since the term 'Pseudoleukæmia' is more often applied to such conditions, I believe the appropriate name for this form of the disease is Splenic Pseudoleukæmia."

34
Osler quotes Socrates who says "Now, I have no objection to your giving names any significance you

please, if you will only tell me what you mean by them."

He (Osler) prefers to keep to the term "Splenic Anæmia" in preference to any of the other names under which this disease has been labelled. In support of this he says:- "If our knowledge does not permit us to give a name according with the ætiology of the disease, the rule should be to pick the one which seems least objectionable, taking priority and usage into account.....The name certainly expresses the two most constant features of the affection.....Usage, too, should count, and it is something that the name should have been introduced by such men as Strümpell, Senator, Coupland, Rolleston and others."

The name 'Splenic Anæmia' was first used by Gretzel[20] in 1866, in describing a case from Greisinger's clinique, and it is under this heading that the disease is now best known in English speaking countries.

Duration of the Disease.

The disease, in most cases, runs a prolonged course, though different authors show much disagreement as to its average duration.

From reports of cases occurring up to the present time, it seems evident that the length of the disease may vary within extremely wide limits.

Thus, most cases reported previous to Osler's

paper have been of short duration, two to four years, and Samuel West, in the article on "Anæmia Splenica" in Allbutt's System, states that the disease is not of long duration - six months to two years.

30
Bruhl says:- The duration of the trouble has been differently stated by different authors. Muller insists on its slow progression, which may last four and a half years. However, it is difficult to assign a precise duration to this trouble, if one takes into account the long latent period which constitutes the commencement, and if one remembers, that, sometimes complications come and shorten the duration. In some cases the duration is short."

Osler, on the other hand, is impressed by the long duration of the disease and by the frequency and duration of the intermissions. He divides the cases into acute and chronic, including under the former, cases under one year's duration, and placing in the latter category, cases which have been known to have differed from enlarged spleen with anæmia for one year or over.

Amongst his own cases, he reports one of fourteen years duration, several of over ten years duration, and the majority have had the condition over five years. In 7 of his 15 cases first reported, the disease has lasted more than ten years, and in 11 of them, more

than four years. Beyond this, he has collected 44 cases by other observers, and places 12 of these under the Acute Form, and the remaining 26, he classifies as Chronic. The acute cases varied in duration from 11 weeks to 12 months, and the chronic cases varied as under:-

11	years	duration	-	1 case
8	"	"	-	1 "
7	"	"	-	3 cases
6	"	"	-	2 "
5	"	"	-	1 "
4	"	"	-	1 "
3	"	"	-	2 "
2	"	"	-	3 "
Between 1 and 2	"	"	-	3 "

In one case, the duration was doubtful. Probably it lasted many years. Thus in nine of the cases the disease had lasted more than five years. In seven cases, the duration was unknown.

Professor Cowan[37] reports two cases in which the symptoms had existed for 12 and 14 years respectively, and he says:- "This is in accordance with the general results, death rarely ensuing early unless from accidental complications."

Dr. James[38] and Gaucher[39] report cases living for twenty five years after the splenic enlargement was

first observed, and [40] Wilson records a case living for thirty years. Rolleston reports a case of twelve years duration, beginning [41] in 11th year.

Age of Onset.

There is much lack of uniformity in the opinions given by different authors as to the average age at which symptoms commence in this disease.

Splenic Anæmia is met with frequently in infancy, most usually between the ages of 1 and 2 years. But most writers deny that there is any link between splenic anæmia in infancy (or Von Jacksch's Anæmia) and the splenic anæmia of adults. Allowing this to be the case the age of onset in cases they have observed is put at:-

2	years	by [42] Collier.
3	"	" [43] Bovaird and Brill.
3-6	"	" [40] Wilson.
6	"	" [44] Collier and Hamill.
7	"	" [39] Gaucher, [45] Williamson, [46] Springthorpe and Wilson. (2 cases).
8	"	" Wilson.
10 and 11	"	" Springthorpe (2 cases).
12 " 13	"	" [47] Scott.
14	"	" [48] Summons.
15	"	" [49] Michell Clarke.

In [41] Rolleston's collection of 35 cases, the average age (when seen?) was 32 years.

In [33] Osler's series of 15 cases, the average age of onset was 32-5 years.

It is, therefore, quite impossible to arrive at any age, or even decade, which may seem to favour the onset of symptoms, as observations, up to the present time, have shown such tremendous variation.

AEtiology.

The ætiology of this disease is still in a state of great confusion.

Apparently, males are affected more often than females. Out of 18 cases of Osler's, 14 were in the male sex.

Bruhl [30] collects 14 cases only 2 of which occurred in the female.

From cases at present on record, it seems probable that man is victimised about five times as frequently as woman.

The age of onset has already been referred to. Climate apparently has no influence on the disease as isolated cases have been noted in many different parts of the world.

Doubtless a great many cases have been reported in which the enlarged spleen has been of malarial

origin, but if we decide, as seems just, to exclude cases from the category of splenic anæmia in which there is a possibility of specific or malarial influence, locality does not seem to be an important factor in the disease.

More cases have been recognised in Italy than in any other section, probably, partially on account of the interest taken in this subject by Italian workers, headed by Banti. But, wherever there has been thorough clinical investigation, cases of splenic anæmia have been met with.

If rickets, malaria and syphilis be disallowed as causal agents, the trouble seems to arise independently of all constitutional disturbances.

An hereditary tendency to the disease has been recorded by several observers. It played no part in the cases reported by Osler.

Brill[50] has reported three cases in one family, one child dying aged 9 years with an enlarged spleen, and a brother and sister being still alive, aged 34 and 30 years respectively, and both of them suffering from the disease under discussion.

Bovaird[43] describes a similar condition in two sisters - aged 16 and 6 years.

Collier[42] reports two cases of this disease in

the one family, while Claude Wilson has reported a family in which, in three generations, six members had an enlarged spleen.

In New York in 1904, Libman exhibited a spleen from a case of splenic anæmia, in whose family several other children had the same disease.

Case IV of my series illustrates the hereditary tendency, as the patient's sister also died in Guy's Hospital with splenic anæmia.

Morbid Anatomy.

Before discussing the morbid anatomy of Splenic Anæmia, it will be wise to mention, briefly, our present ideas as to (1) the origin of the various cells found in the blood, and also (2) the functions of the blood forming organs and tissues.

(1) In adult life, the majority of blood cells originate in the bone marrow. It is practically certain that all the hæmoglobin-carrying cells are formed in the marrow, and it is extremely improbable that any of the granular series of leucocytes are formed elsewhere. There is more doubt as to the sites of origin of the non-granular leucocytes.

Small, non-granular leucocytes (lymphocytes) appear to be chiefly formed in the lymphatic glands

and spleen. But probably they originate from lymphoid tissue wherever it may occur, e.g. intestine, omentum and bone-marrow.

51
Dr. Dickson in his work on 'The Bone Marrow' says:- "Lymphoid patches ..... are usually somewhat scanty in normal marrow, throughout which these lymphocyte-like cells are generally scattered irregularly; but in certain pathological conditions they may be found in much greater numbers ..... or may even be found replacing almost entirely all the other varieties of marrow cell. These facts seem to lend colour to the assertions of Dominici, who holds that the hæmopoietic tissues are "built on a plan represented by a combination of two great varieties of tissue, lymphoid and myeloid, intermingled in one histological complex, the hæmopoietic tissue proper." Dr. Dickson then says:- "Both of these types of tissue occur side by side or mingled with one another in the marrow, but whether the same holds true of the spleen and lymphatic glands is doubtful."

The large mononuclear non-granular cells of the blood may be partially formed in the marrow, but they probably largely originate from the endothelial cells lining lymphatics, vascular channels and serous surfaces."

Thus it appears that the bone-marrow is the most important of the blood-forming tissues.

(2) Two varieties of marrow are physiologically found in the bones of adults - red and yellow.

Dr. Dickson says:- [51] "The Red, Lymphoid or Formative Bone-marrow Proper is found in the short and flat bones, sternum, ribs, vertebræ etc., and also to a varying extent at the ends of the long bones of the extremities in the adult. In the young child, it also fills the medullary cavity of the diaphyses of the last named variety of bone, but as age advances, it is in this situation gradually transformed into yellow or fatty marrow. It is in this red bone-marrow that the hæmoglobin-holding elements of the blood are developed, as are also the granular and perhaps some of the other forms of leucocyte; and according as the number of cellular elements which go respectively to form the red or white blood cells may happen to preponderate in the tissue, the marrow may ... be classified as erythroblastic or leucoblastic in type, a varying admixture of these two conditions being generally found present."

With regard to the Yellow or Fatty Marrow, Dr. Dickson says:- [51] "This variety of Marrow is as far

at all events as the formation of the cellular elements of the blood is concerned, an inert tissue. In relation, however, to the general nutrition of the organism, it may possibly be regarded as being of considerable importance, as it is exceedingly well supplied with blood vessels, and is capable of undergoing very rapid alterations in disease. It is probable that such fatty tissue should be looked upon.... rather as a storehouse where anabolic and katabolic processes are constantly at work, storing up and dealing out nutritive material, in accordance with the requirements of the organism."

This yellow marrow, in disease, has the capacity of becoming transformed into red marrow, a defensive action on the part of the organism.

The Lymphatic Glands and Lymphadenoid Tissue, wherever they may occur, e.g. Peyer's Patches, the solitary follicles of the intestine, the lymphoid tissue of the tonsils and pharynx, the lymphoid tissue of the spleen, the omenta and the bone-marrow, are the source of the small mononucleated white corpuscle of the blood (lymphocyte). Apart from this productive power, the lymphatic glands also act as filters for the lymph as it passes through them.

The Spleen, as I have already stated, has a certain rôle in blood formation, chiefly on account of the lymphoid tissue it contains (Malpighian Bodies). The idea, held until recently, that it formed erythrocytes, excepting during fœtal life, is almost certainly erroneous, the lymphocyte and probably also a few large mononuclear cells being the only corpuscles formed in this organ.

The functions of the spleen are not fully known, but, as the results of splenectomy have shown, it is not an organ necessary to life.

Quoting from [52] Beattie and Dickson:-

"Amongst other activities, it (the spleen) appears to act as a filter for the blood which passes through it, and serves to sift out damaged and effete blood corpuscles as well as bacteria and other organisms. Active phagocytosis on the part of the endothelial cells of the pulp proceeds in health, and may occur to a very exaggerated degree in disease.

Various processes carried out by ferments or enzymes occur in the organ, but are, as yet, only imperfectly understood. ..... Its anatomical relations to the portal circulation are important, and the organ probably aids the flow of blood through the liver ... . It is therefore especially affected by diseases which interfere with the hepatic circulation."

The Morbid Anatomy of the disease furnishes us with information of considerable importance.

As in other anæmias, the degree of muscular emaciation is in marked contrast to the abundance of subcutaneous fat usually found present at the autopsy.

Banti, Bruhl, Muller and Sippy comment on œdema of the tissues and the presence of fluid in the serous cavities being frequent features. The findings in my autopsies agree with this.[30] Bruhl and[32] Sippy also mention hæmorrhages in the serous membranes and under the capsules of the viscera as being usually present. No such hæmorrhages were observed in my cases.

Usually, thereis no enlargement of the lymphatic glands, and these, on section, appear perfectly normal. Occasionally, however, enlargement of some of these glands has been described with, on microscopical examination, an increase in fibrous tissue and rarely, also, gelatinous degeneration. The heart is usually dilated and frequently presents signs of fatty and granular degeneration of its muscle.

Pleurisy and congestion at the base of the left lung are not uncommon, and when the spleen is much enlarged, there may be atalectasis of the lower lobe of the left lung (See Case I).

32
Sippy says:- "Although nausea, vomiting and diarrhœa may be prominent symptoms throughout the course of the disease, the gastro-intestinal tract does not present serious alterations."

In the cases I have reported, the appetite was almost always good, vomiting and diarrhœa were never prominent features, and excepting for the perisplenitic pains and, in Case I, slight malæna and hæmatemesis towards the end of the illness, alimentary symptoms were practically absent.

The liver is almost always enlarged, though often only to a slight extent, and its capsule is frequently somewhat thickened. In one of Sippy's cases the liver weighed 2,800 grammes, the size here being very exceptional. Usually no hepatic cirrhosis is present, and my cases showed no trace of it, but in a few cases which have been of long duration, there has been a definite cirrhotic process, this constituting what is known as 'Banti's Disease'. The cirrhosis is sometimes very marked, and may cause atrophy of the liver.

The hepatic enlargement in my cases, as in the majority of others reported, was almost entirely due to chronic venous congestion.

In one of my cases, on microscopical examination, there was in places a slight increase in the amount of

interlobular connective tissue, but the only general change noticeable was an increase in the numbers of lymphoid cells about the portal spaces and between the liver lobules.

Strumpell[24] noticed an increased amount of blood pigment in the liver, and therefore supposed that the liver was the site of an exaggerated destruction of erythrocytes.

The Spleen being considered the probable causal agent of the disease, most interest centres around the pathological changes taking place in this organ.

Microscopically it is always enlarged, and usually very much so. In Case I, it weighed 7½ pounds, and in one case I have already mentioned its weight was recorded as 12½ pounds. It usually retains its shape, but in my cases, the notches were almost obliterated. There is often thickening of the capsule and there may be adhesions to the diaphragm and adjacent organs as the result of previous perisplenitis. (See Case I).

The surface of the organ is usually smooth excepting for areas of infarction or hæmorrhage which are frequently noted. In one of my cases there were numerous infarctions, chiefly on the anterior surface. The majority of them were old, and some of them cartilaginous in consistence. These older infarcts were

depressed, owing to fibrous contraction. Some of them were very large, and ranged up to 2¼ inches in diameter. (See accompanying painting).

On Microscopical Examination:- Normally in the spleen pulp there exist open blood spaces, these are formed by connective tissue fibres and cells. Split arterial capillaries and small arteries pour their blood into the lymph clefts of the pulp. The blood here mixes with the lymph and the mixture is carried away by venous capillaries and veins.

Gaucher, in 1882, described a proliferation of these endothelial cells, and since this time, other observers, amongst them being Bruhl,[30] Picou and Bovaird, have noted the same condition, the two latter of these describing it as an epithelioma or an endothelioma of the spleen.

Recently the majority of writers, including Osler,[34] Sippy,[53] Harris and Herzog,[35] have been impressed with this endothelial proliferation, and it is certainly most marked in both my cases.

Banti[26] summarised his findings in the spleen as:-

1. Atrophy and sclerosis of the Malpighian Bodies.
2. The substitution of an irregular and fibrous reticulum for the normal fine reticulum of the splenic pulp.

West reported the same changes.

The Malpighian corpuscles have usually been described as atrophied, and Bruhl[30] says:- "The chief lesion is in the Malpighian bodies, in which the texture is so much altered that they can hardly be recognised. The central artery presents a noticeable fibrous thickening; the dividing trabeculæ are likewise thickened, so much so, that the meshwork which they surround in the middle of the glomerulus is very narrow, and sometimes reduced to a mere speck ..... In some places, there is an almost complete sclerosis of the glomerulus, which ends in atrophy."

In case I of my series the Malpighian bodies were much separated and atrophied, and in the three of my cases in which the spleen was examined, I have also noted the great amount of thickening of the central arteries and the general fibrous increase, whereas in Cases I and III, endothelial proliferation was also very evident. Moreover, the pulp spaces were widened out and showed a proliferation of the endothelial cells lining them. In some of these cells and also in a few giant cells, disintegrated erythrocytes were clearly seen.

My findings are therefore much in accordance with the descriptions given by several authors. Professor Osler's cases showed a fibrous hyperplasia with atrophy

of the pulp and a gelatinous degeneration of the Malpighian corpuscles. He (Professor Osler) does not seem to have been struck by the endothelial proliferation described by Gaucher, Picon, Bovaird, Harris and Herzog and Rolleston, and shown also in my specimens.

In two of my cases a few giant cells were seen.
43
Bovaird has suggested that the endothelial cells finally form fibrous tissue, but it seems more probable that the proliferation of both these elements is due to some common cause, for instance, the production of a toxin in the spleen.

Symptoms.

Splenic Anæmia is described as commencing in various ways, but the early symptoms are usually simply those of a chlorosis, viz. palpitation, headache, breathlessness and a feeling of unusual muscular fatigue, With this, there may be a slight pallor of the
30
mucous membranes, and the patient looks pale. Bruhl considers this commencement of the trouble as being very like that seen in Addison's Disease.

On the other hand, the splenic tumour may be the first thing noticed, causing a feeling of abdominal weight and distension. This tumour may be present for a year or more before other symptoms set in and

without causing any discomfort. In several of Osler's cases, the patients were able to lead an active business life, without discomfort, for considerable periods after the splenomegaly was first noticed.

In other cases, the commencement has been marked by attacks of severe pain in the left hypochondrium, due either to perisplenitis or to pushing aside of the peritoneum by the enlarged organ, and this may be accompanied by a pleurisy at the left base. This pain may be very severe, resembling intestinal colic, and radiating to the left shoulder, and to the lumbar region. It is usually accompanied by a distinct rise in temperature, and often, also, by nausea, vomiting and almost uncontrollable diarrhœa. In these cases, although such an attack first draws the individual's attention to his condition of health, on careful enquiry, it can usually be ascertained that he has been in an unsatisfactory state of health, compatible with a moderate degree of anæmia for some time previously.

Usually, until late in the disease there is no lack of appetite, and, as in chlorosis, there is no marked emaciation, the subcutaneous fat often being very evident.

In cases starting in the most usual way, with the ordinary signs of anæmia, enlargement of the spleen is

noticed often in from three weeks to three months. It is seldom painful or tender to palpation, and chiefly disturbs the patient by its sense of weight.

Epistaxis is often an early symptom, and vomiting and persistent diarrhœa may trouble the patient before the disease is far advenced.

After a few months, whatever the mode of commencement may have been, the clinical picture presents the same essential features:-

1. Hypertrophy of the Spleen.
2. Weakness.
3. Progressive anæmia.
4. Absence of marked enlargement of the lymphatic glands.

By this time, there have probably been attacks of pain in the left hypochondrium, or these may be absent during the entire course of the disease. There will probably have been some gastro-intestinal disturbance, manifested by indigestion, vomiting or diarrhœa. Oedema of the limbs, face or body may have put in an appearance. Almost certainly, the temperature will have shown some irregularity, usually being at its height in the evening.

Later, at a period from the commencement of the disease showing very wide variations in different

cases, the anæmia and all symptoms become far more marked, and the patient reaches what has often been termed the third and cachectic stage. In this stage, the patient emaciates, the anæmia becomes more evident and it is often accompanied by a yellowish or brownish pigmentation of the skin. Oedema becomes permanent, and is often associated with fluid in the abdomen or thorax. Bleedings may occur from any channel, and petechial hæmorrhages are often noticed. The blood becomes more and more impoverished, and shows the characteristics of the blood in profound chlorosis plus a leucopenia, which latter has been present from an early period. The weakness becomes more and more extreme, and hæmorrhages increasingly liable to occur until the patient succumbs to sheer exhaustion.

The size of the spleen has been noted to vary considerably during the course of the disease, increasing size usually accompanying increasing anæmia and vice versa.

Although the disease is progressive from the start it has been generally noticed that there are periods of quiescence followed by relapse, and that during the quiescent periods the spleen tends to diminish in size and the blood to improve.

Special Symptoms.

1. The Splenomegaly: - The enlargement of the spleen is usually very marked as in Case 1 reported by me, where the organ weighed 7½ lbs. The enlargement of the organ is uniformly general. In a great number of reported cases, the spleen has not approached this size, an approximate average weight probably being about 3 lbs., and several writers, Sippy amongst them, state that although there is marked splenomegaly, that it is not very great. Osler is more impressed with the very large spleen found in splenic anæmia which, he says, is unequalled in any other disease, excepting, perhaps, leukæmia.[43] Bovaird reports a case in which the spleen weighed 12½ lbs. In 12 cases collected by[41] Rolleston, the average weight was 3 lbs. 13 oz.

In Case 1 of my series, the spleen was larger than abdominal examination alone would have suggested, as the upper pole of the organ had pushed the diaphragm upwards and was encroaching on the thoracic cavity.

The spleen, in this disease, usually enlarges very gradually, and is not subject to marked fluctuations in size, though Sippy mentions a case in which, during a period of diarrhœa, the size of the spleen diminished by fully 2 inches.

In some cases, friction rubs, due to perisplenitis have been heard.

The spleen is but rarely tender to palpation. In a few cases, severe paroxysms of pain over the splenic region have been early manifestations. Though these may often be due to attacks of perisplenitis, they are known to have occurred where no such perisplenitis was present. In these cases, the pain may have been caused by the organ dragging on to or stretching the peritoneum.

The spleen is usually firm and has a smooth surface, though, as in my Case I, irregularities due to infarcts may be palpable.

2. Anæmia:- In cases where the patient has been carefully observed from the commencement of the trouble, the anæmia has always been found to be secondary to the splenic enlargement.[53] Sippy points out that, so far as can be made out, the splenic hypertrophy precedes, or, at least develops contemporaneously with the anæmia; and he states that in no case of splenic anæmia can he find the anæmia preceding the splenic hypertrophy.

The salient features of the anæmia are:-

1. A diminished number of erythrocytes.
2. A relatively low percentage of hæmoglobin,

giving a colour index of from .4 to .7.

3. A diminished number of leucocytes.

The change in the red elements does not differ from that seen in chlorosis. Although in my cases, the red cells are present in much diminished quantities, Professor Osler's cases give an average erythrocyte count of 3,336, 357, and he comments on the relatively high erythrocyte count. Very much, of course, depends on the period of the disease at which the blood counts noted were made.

The hæmoglobin is usually diminished relatively, as in chlorosis. Osler's series of cases gives an average colour index of about .65.

The leucocytes are diminished in number. Many cases have been reported as splenic anæmia in which there has been a very marked leucocytosis, but, undoubtedly, several of these cases should have been classed as leukæmia, and, in the light of our present knowledge, I think we should only include cases under the term 'Splenic Anæmia' in which there is regularly a leucopenia.

Professor Osler's cases show an average leucocyte count of 4,500, and Case I of my series agrees with this very closely.

On film examination of the blood, it is not usual

to find abnormal cells in any quantity. Thus, nucleated red cells are either absent or very scanty, and, when present, they are almost always normoblasts. Myelocytes also are rarely seen, showing that the blood forming organs have very little regenerative power.

Poikilocytosis and polychromatophilia are conditions which are atypical of this disease, and, if present, are not marked.

The reports of differential blood counts are so scanty at present, that it is difficult to say whether or not the leucopenia is due especially to a diminished number of one particular variety of leucocyte. From my own observations, and a few other cases fully reported, it appears that all varieties of white cells are absolutely affected, but that the polymorphonuclear leucocyte is the variety chiefly affected.

3. Lymphatic Glands:- Enlargement of the lymphatic glands is not a feature of this disease. Enlargement of the retroperitoneal and bronchial glands has been noted, but if present, has always been moderate

4. Hæmorrhages: - Hæmorrhages may occur, and have been recorded from practically every source. Case I of my series had, at different times, epistaxis,

hæmatemesis, hæmoptysis, hæmaturia and melæna. Purpuric attacks, bleedings from the gums and retinal hæmorrhages have also been observed.

30 Bruhl considered that hæmorrhages were rare in cases of splenic anæmia. He says that epistaxis is not infrequent, but that it is very rarely intense. He also says that hæmatemesis is very rare. 54 Osler, on the other hand, is much impressed by the frequency of hæmatemesis, which was present in eight of his series, and by the fact that it is often an early symptom. Not infrequently, hæmatemesis has been the first symptom complained of, and a mistaken diagnosis of gastric ulcer made in consequence.

According to recent literature, hæmorrhages in one form or another are very frequent. Epistaxis is probably that most commonly seen, and it is often an early sign. Hæmatemesis and bleeding from the gums are reported in many cases, whereas, melæna, hæmaturia, retinal and purpuric hæmorrhages are noted comparitively rarely.

55 Watson's explanation of the frequency of hæmatemesis in cases of enlarged spleen is as follows:-

"The stress of the congestion is continually felt in the submucous capillary system, and the hæmorrhage which is apt, in such cases, to occur from the loaded

membrane receives a simple solution upon principles almost entirely mechanical."

5. Pigmentation: - Various degrees of pigmentation of the skin are noted in connection with splenic anæmia.

Usually, the patients show a pale yellow or sallow colouration, but deeper tints are noted, especially in cases of long duration.

In some cases, the skin has been bronzed, resembling the colouration of Addison's Disease. In other cases the skin has had more the tint seen in sufferers from Argyria. There are also reports of patchy pigmentation, and of this plus areas of leucoderma.

My cases showed nothing more than the very pale and faintly yellow colour of skin, and I saw in none of them any appearance of bronzing. The pigmentation in some of the cases reported has probably been due to the large doses of arsenic which have been previously administered.

Jaundice has been noted in the terminal stages in a few cases in which cirrhosis of the liver has been found at the autopsy.

6. Hepatic Enlargement. Enlargement of the liver is a sign frequently found in the terminal stages of splenic anæmia. It is not always present, and the liver is sometimes even reduced in size.

Increase in the size of the liver is noted in about 50% of cases. In a great number of these, as in my cases, it was chiefly due to venous congestion. In others, it was largely influenced by a cirrhotic process.

Splenic anæmia with enlargement of the liver was originally described by Banti[56] as a distinct clinical entity, and this condition was, till recently, termed Banti's Disease. It is now, however, considered simply as the terminal stage of splenic anæmia.

7. Ascites and Oedema. Ascites, hydrothorax and general œdema are, as might be expected, signs frequently met with in the late stages of the disease. In my own cases, and doubtless in many others reported, they have been influenced largely by the state of the heart. They may be seen in any grave anæmia, and it is therefore not surprising to find them in the affection under discussion. The ascites is, doubtless, sometimes to be attributed to hepatic cirrhosis. This is borne out by the fact that in several of the re-

ported cases of ascites in this affection, jaundice has also been present.

8. Fever is very frequently present, as is the case in most severe anæmias, be they primary or secondary.

In splenic anæmia there is usually a marked degree of fever occurring at infrequent intervals from an early stage of the disease, and often lasting for three or four days, before again settling to the normal. In the later stages, fever not infrequently becomes more regular, the temperature swinging up to 102° or more at nights.

All my cases showed this fever, though it was more pronounced in the infants than the adults.

I do not see any adequate explanation of these remissions of temperature which are common to all severe anæmias. In the disease under discussion they are doubtless due, occasionally, to attacks of perisplenitis, but they certainly cannot all be explained in this way.

9. Alimentary Symptoms. Apart from the hæmatemesis already discussed, gastric and intestinal disturbances are to be expected due to pressure from the enlarged spleen, and probably, also, to involvement

of the sympathetic.

Usually, the appetite is good until the later stages, but nausea and vomiting may be distressful at the times of the perisplenic pains.

Diarrhœa may occur at an early stage, and may be very persistent. More frequently, diarrhœa alternates with constipation.

Malæna is sometimes present, even when the liver is fairly healthy. The large size of the spleen coupled with frequent cardiac insufficiency, the frequency of intestinal irregularity, and the impoverished blood are sufficient to explain this.

10. Circulatory Symptoms. It is curious that in two of my cases the cardiac signs should have been so prominent, notwithstanding the fact that previously to the origin of the anæmia there had been no suspicions of cardiac involvement. In the infantile case the murmurs which appeared quite suddenly late in the disease, and without unusual disturbance of temperature, I think may all be of hæmic origin. In Case I, however, there was positive valvular disease. The heart is often somewhat dilated, and hæmic murmurs are sure to be present, at any rate in the advanced stages of the disease. According to [32] Sippy

"The carotids and other large arteries throb visibly, and the capillary pulse is not infrequently noted. The pulse is full and frequent, and may approach the 'water-hammer' type. The veins are often prominent, and the 'bruit de diable' may be present in the neck".

11. Pulmonary Symptoms. Dyspnœa, a feature of all anæmias, is usually present, due to deficiency of hæmoglobin and consequently of circulating oxygen. It is sometimes, as is well seen in my Case I added to by the enlarged spleen pressing upwards on to the diaphragm and consequently encroaching on the thoracic cavity. For the same reason there may be a pleurisy at the left base. Crepitations may be present at the base of the left lung as another result of splenic pressure, and when the trouble is advanced, and the patient has been lying for a considerable period, râles may be heard throughout both lungs, as in any prolonged illness.

In the terminal stages, there may also be a hydrothorax.

Hæmorrhage from the lower respiratory tract is occasionally seen, and was present in one of my cases.

Pulmonary congestion and pneumonia, consequent on prolonged lying may be present as terminal affections.

12. The Nervous System may show the symptoms common to any anæmia:- headache, vertigo and lassitude. There are no nervous signs peculiar to this disease, and even these already mentioned are rarely as marked in splenic anæmia as they are in chlorosis and the secondary anæmias. The mind is usually quite clear till the termination.

13. The Urinary System. Excepting that there may, from time to time, be the presence of blood in the urine, as seen in one of my cases, the urinary system shows nothing pathognomonic of splenic anæmia.

Diagnosis.

As we have seen, there is still much want of harmony amongst different opinions as to what symptoms are necessary to a diagnosis of splenic anæmia; and this is especially the case amongst the infantile cases.

Some observers, amongst them Emery, will not allow that such a disease exists as a separate entity, and they state that cases placed under the heading of 'Splenic Anæmia' could all be included under the Leukæmias, Pernicious Anæmia, Hepatic Cirrhosis, or, occasionally, other disorders.

Diseases of the blood and blood-forming organs are being studied more carefully and are consequently becoming more thoroughly recognised every day, and there is no doubt that the opinion that a separate disease, now generally known as 'Splenic Anæmia', and having signs and symptoms incompatible with any other known disorder, does exist, and is rapidly gaining ground.

The other maladies which may most closely simulate the disease under discussion are: -

1. Pernicious Anæmia.
2. Idiopathic Enlargement of the Spleen.
3. Cirrhosis of the Liver with enlarged Spleen.
4. Chronic Malaria.
5. Leukæmia.
6. Waxy Disease of the Spleen.
7. Hodgkin's Disease.
8. Essential Anæmia.

The majority of these diseases above mentioned offer but little resistance to the diagnosis of a case of splenic anæmia, but I mention them all, because all cases are not so typical as literature would lead us to believe, and some of them appear to lie on the borderland of two or more different diagnoses. Also

when a case is seen in an early stage it may, for a time, be impossible to say what its later development is to be.

Differential diagnosis from:-

1. Pernicious Anæmia. There is a good deal of difference of opinion as to the typical size of the spleen in pernicious anæmia.[34] Osler says that it is usually small: on the other hand,[36] Cabot states that splenic enlargement is the rule, and that it may be very considerable.

It is certain that the spleen may be enlarged in pernicious anæmia, but it is very rare to find this enlargement marked, and it probably never reaches the size found in splenic anæmia.

More important than the size of the spleen is the result of blood examination. In pernicious anæmia the colour index is almost invariably high (1 or over), a marked degree of poikilocytosis and polychromatophilia is usually seen, and nucleated red cells are almost constantly present in considerable amount, megaloblasts being often seen. In splenic anæmia, the colour index is low (.6 to .7 or lower); there is usually but little change in the shape of the red cells and polychromatophilia is rarely seen. Erythroblasts have been noted in several cases, but are

usually absent, and, if present, rarely take the form of megaloblasts.

In both diseases the leucocyte count is often low, but I have found an artificial leucocytosis to be obtained far more readily in cases of pernicious anæmia.

In splenic anæmia the liver is often enlarged. In pernicious anæmia hepatic enlargement is the exception.

2. Idiopathic Enlargement of the Spleen. It is not uncommon to find an enlargement of the spleen in an individual apparently in perfect health. The absence of symptoms and a normal blood count clinch the diagnosis.

3. Cirrhosis of the Liver with Enlarged Spleen. We have already allowed that, in the terminal stages of splenic anæmia, the liver may become cirrhotic, constituting 'Banti's Disease'. There may be much difficulty in deciding whether a case is one of advanced splenic anæmia, or whether it is a case of cirrhotic liver with enlarged spleen: that is to say, whether the enlarged spleen is secondary or primary to the cirrhotic liver, the more especially, as the blood may be of very little help to us here, being

of much the same nature in either affection. In hepatic cirrhosis, a leucopenia would be less likely than in splenic anæmia, and I believe, though I have been unable to put it to the test, that a leucocytosis could be more easily induced than in splenic anæmia.

The spleen of splenic anæmia is larger than that usually found secondary to hepatic cirrhosis, though in cases of alcoholic cirrhosis, the spleen may be very large. The history will often be of much assistance in arriving at a correct conclusion. A strong alcoholic history may be of help. Or the patient may give a history of syphilis, and with this we may feel that the liver has a very irregular surface. These facts coupled with a moderately enlarged spleen would suggest a diagnosis of hepatic cirrhosis. In this latter case also, irregularities on the surface of the spleen, which do not usually occur in splenic anæmia, may aid in the diagnosis.

The association of anæmia, splenomegaly, enlargement of the liver, ascites, and hæmorrhages from the stomach may be found in either case, and the differential diagnosis between these two affections is sometimes very difficult.

4. Chronic Malaria. Malaria must be excluded before a diagnosis of splenic anæmia is made, but a patient may suffer from malaria without being aware that such is the case. In such cases, the temperature may suggest the diagnosis; plasmodia in the blood or pigment in the leucocytes or plasma may negative a diagnosis of splenic anæmia. Beyond this, the case may prove its malarial origin by improvement under quinine, which has no good effect on splenic anæmia.

Nephritis is a complication often seen with malaria; this is not the case with splenic anæmia.

In cases of splenic anæmia, the colour of the skin is not of the slaty or dirty yellow colour peculiar to malaria, but rather a subicteric pallor.

5. Leukæmia. The diagnosis is made certain by blood examination, or rather, by examination of the white cells of the blood.

In lymphatic leukæmia, a leucocytosis is present; this is usually great in amount, but even though it should be only moderate, the quality of the leucocytes present would determine the diagnosis. Thus we would find a very high percentage of lymphocytes, and the leucocytes in general would usually show degenerative changes.

In splenic anæmia, the relationship of the different varieties of leucocytes found in the blood is disturbed only slightly if at all.

In a few cases of myelogenous leukæmia, though the leucocytes may not be increased in number, and are, sometimes, even diminished, the presence of a considerable number of myelocytes will usually point to the true nature of the case.

6. Waxy Disease. Acquired syphilis rarely produces any great enlargement of the spleen in the early stages, and still more rarely as a tertiary manifestation unless there is also amyloid degeneration. Waxy disease quite commonly affects the spleen before other organs, but before it could cause considerable enlargement of the spleen, we would expect to find the same condition in other organs - e.g. liver, kidneys and intestines, as evidenced by diarrhœa, albuminuria and the microscopic characters of the urine. We should also, in all probability, find an obvious cause for this amyloid disease, by way of bone suppurations, phthisis or protracted syphilis. Furthermore, examination of the blood of a patient suffering from waxy disease, should show that there is a moderate degree of leucocytosis, though the red ele-

ments may vary very little from those seen in splenic anæmia.

7. Hodgkin's Disease. The spleen may be enlarged in Hodgkin's Disease, but it very rarely attains a large size and does not, per se, cause special symptoms. It is also distinguished from splenic anæmia by the fact that, in the latter disease, the lymphatic glands are never generally enlarged.

A leucopenia is not to be expected in cases of Hodgkin's Disease.

8. Essential Anæmias. In chlorosis and the secondary anæmias the blood findings and general appearance of the patient may closely simulate those of splenic anæmia. The history will usually form a fairly certain guide, however, informing us of blood loss or some definite cause for the anæmia. The spleen in the secondary anæmias is either not enlarged or very slightly so. I wish here to emphasize the importance of examination of the fæces in doubtful cases, as I well remember a child aged 14 years who had a moderately enlarged spleen, and a high degree of anæmia in which all the blood elements partook. There was much difficulty in coming to a dia-

gnosis in this case until I examined the stools and found the ova of ankylostoma duodenale abundant.

In children anæmia, whatever its cause, seems to be almost always accompanied by splenic enlargement to a degree that is not seen in the adult , and in them a diagnosis is always more difficult. In fact, at the present day, the anæmias of children seem to be known very little about and their whole comprehension is in a very unsatisfactory state.

I have reported two cases of anæmia in children which seem to conform so entirely to the type I have taken in the adult, that I have called them splenic anæmia, and considered them as identical with the adult cases.

Treatment.

Up to the present time medical treatment, in the form of drugs and electricity in its various branches has had no lasting benefit in this disease. Further than this I cannot find any record of an undoubted case of splenic anæmia recovering under other than surgical treatment.

Nearly all writers advise the administration of the usual blood tonics, arsenic being the drug in most universal favour.

Bruhl[30] says "Arsenical preparations are the best".[32] Sippy advises the administration of iron and arsenic.

Other drugs to find favour have been the sulphate of Quinine, Potassium Iodide and Mercurial preparations.

Billroth[18] stated that he had very good results from injections of arsenic into the spleen, and following him other observers, notably amongst them being Mosler,[57] state that they have caused much benefit by this procedure. These injections have caused fatal results, often from hæmorrhage, and Bruhl states that they should only be resorted to when dealing with a firm spleen. In order to avoid danger from hæmorrhage during these injections, Mosler advised the application of an ice-bag over the spleen for one hour before and one hour following the injection. Injections of 20% carbolic acid in this way have also been tried.

Faradism and electro-puncture were recommended twenty years ago. X-ray treatment seems to have caused temporary benefit in some cases.

It seems fairly clear that the disease can be only temporarily modified by other than surgical treatment, be it medical or electrical.

Special symptoms have to be medically treated as they arise, - the nausea and vomiting, the diarrhœa, the perisplenitic pains and the hæmorrhages.

Surgical Treatment. If, as I think, and as I have tried to show, the spleen is the primary cause of the trouble in splenic anæmia, it is only natural that we should consider the possibilities of removal of this organ and the benefits to be expected therefrom. We know that the spleen is not an organ which is necessary to life.

The fact that the lower animals could live after extirpation of the spleen was first shown by Bardeleben[58] in 1841, and he also reported certain changes in the blood and lymphatic glands after this procedure. Zegas[59], after splenectomy, also found enlargement of the lymphatic glands, and Winogradoff[60] an increase in the volume of all the glands.

Vulpius[61] first studied the changes in the blood following extirpation of the spleen in animals, and he summarizes his results as follows: -

1. Transitory decrease in erythrocytes and increase in leucocytes.
2. Lymphatic glands and bone-marrow show increased blood-forming activity.

It was shown, at this time, that animals could survive extirpation of the spleen without permanent injury.

Shortly after this, it was determined that man could also withstand removal of the spleen, but that he reacted much more vigorously to splenectomy than the lower animals.

Splenic anæmia is a disease in which very favourable results have been obtained by total removal of the spleen, and I certainly think that this procedure should be resorted to immediately a diagnosis is made, provided the disease is not advanced to a stage of marked cachexia, as being the only chance of saving the patient's life.

From what I have, so far, seen, I think that examination of the bone-marrow (ante-mortem), and the effect of the administration of nucleinic acid on the number of leucocytes may furnish an indication as to the probable result of splenectomy. I mean that the finding of a gelatinous marrow and the fact of a negative reaction to nucleinic acid would both augur ill for recovery; but, at the same time, the fact that removal of the spleen would furnish the only chance of saving the patient's life should make us recommend this procedure in almost all cases.

Results show that the prognosis of splenectomy gets worse as the disease advances, and the best results have been obtained in cases where the spleen has not been excessively enlarged.

The dangers of the operation are: -

1. Hæmorrhage. This is the most serious danger, and deaths after splenectomy have usually been the result of this. The causes of the hæmorrhage are various, chief amongst them being: -

(a) Adhesions. There are often adhesions of the spleen to the parietes and surrounding tissues, and separation of these is apt to cause surface bleeding which is very difficult or impossible to control.

(b) Bleeding from the vessels of the spleen and the gastro-splenic ligament which encloses them. The number of vessels to be ligated is very great, and unless they are tied one by one as they are met with, it may be a very difficult matter to catch them again after removal of the spleen.

(c) Post-operative hæmorrhage. A great deal of traction on the vessels is often necessary during removal of the spleen, and thus bleeding from damaged vessel walls is apt to occur after the completion of the operation.

(d) Owing to the impoverished state of the blood in advanced cases , and consequent malnutrition

of the vessel walls, another cause for danger from hæmorrhage is superadded.

(e) Hæmorrhage from vessels other than those of the spleen may result from splenectomy. The reason for this is that the spleen in enlarging causes displacement of other organs and consequent torsion and traction upon their vessels. Moreover, the large spleen, owing to its size and weight, may have compressed vessels, thus damaging their walls, and rendering them, in places, fragile.

(f) After splenectomy, the blood-pressure in the abdominal vessels is altered, and this + fragile vessels, renders hæmorrhage a possibility.

2. A spleen, and especially a much enlarged one contains a great quantity of blood, and the sudden removal of this furnishes a post-operative danger.

3. Shock. This may occur after any serious operation, but it is especially liable to occur when any large mass is removed from a body cavity, be it fluid (ascitic or pleuritic fluid) or otherwise.

We cannot state statistically what the results of splenectomies in splenic anæmia have been. The

results reported at different times are extremely gratifying, but so many of these cases have been backed up by such a small amount of clinical evidence, the majority of them never having had a blood examination, that we can pick out comparatively few, in which a diagnosis of splenic anæmia was justifiable.

[53] Sippy, in 1902, finds only seven cases of splenectomy done in cases which he considers to have been, without doubt, splenic anæmia. Recovery took place in five of these cases, and in not one of these five cases was the operation performed early in the disease. In one of the cases, the spleen was very large and cachexia extreme.

[62] Armstrong, in 1906, collected from the literature 32 cases of splenectomy in splenic anæmia with nine deaths - a mortality of only 28%.

Case IV of mine (v.s.), not previously reported, furnishes an extremely good example of the benefits of splenectomy.

Results of and changes after splenectomy: - When an organ such as the spleen is removed from the body, an organ which, if it only has limited blood forming capabilities plays an important part in blood scavenging and filtering, it would not be surprising to find changes in other blood-forming tissues and organs.

Various changes of these tissues are described, but no constant alterations have yet been found.

Observations by Mosler[63] and Neumann[64] seem to prove that the bone-marrow can perform the functions of the spleen after the removal of the latter, and that it can acquire increased blood-forming properties.

In a case of splenectomy reported by Riegner[65] in which the bone-marrow was examined four weeks later, processes of active new formation were found in the marrow.

Pouchet[66] said that both the spleen and bone-marrow could be absent without disturbing blood formation. His experiments were only carried out on fish.

Simon,[67] Zezas,[59] Bardeleban[58] and others state that the thyroid gland acts vicariously after removal of the spleen. There is, however, no proof of this, and hyperplasia of the spleen following splenectomy has only been observed on very rare occasions. Animal experiments, also, show that both the thyroid gland and the spleen can be removed without a fatal issue.

Occasionally, slight enlargement of the lymphatic glands has been noticed following splenectomy, and there was a certain indication of this in the case I

reported (Case 4), but here it was very transient and only affected isolated glands.

There is more uniformity about the statements made in regard to blood changes following splenectomy in splenic anæmia. The few cases fully recorded point to a very rapid increase in both red and white corpuscles after the spleen has been removed. In a case reported by Harris and Herzog[35], the blood which had, previous to operation, showed:-

Erythrocytes - 2,631,000

Leucocytes - 2,650

at the end of twenty four hours showed:-

Erythrocytes - 4,037,000

Leucocytes - 23,600

My Case IV shows this rapid improvement in the blood very beautifully. Unfortunately, there is no record of a blood examination till three days after the operation, but after this, the blood count remained constantly high.

Harris and Herzog[35] report a large increase in the percentage of eosinophils following splenectomy. I cannot see this confirmed by other observers, and it was not found in the case I have reported.

Pathogenesis.

Although of late years, much attention has been given to Splenic Anæmia, our knowledge of the origin and nature of the disease has been advanced but little, and remains much in the same obscurity as it did twenty years ago.

That the disease is primarily one of the spleen is now acknowledged by most authorities. Banti[26] and Muller[16] believed this to be the case, and Bruhl[30] was of the same opinion, supporting his view on the benefits occurring from splenectomy, and also on the fact that the splenic enlargement usually appeared at a considerable period previous to the first signs of anæmia or systemic disturbance.

Bruhl, however, believing that the red blood corpuscles are chiefly formed in the spleen, goes on to say that the diminution in their numbers, and in the amount of hæmoglobin in splenic anæmia is due to the cessation of the creative function of the spleen.

I certainly believe that the disease is primarily one of the spleen. If this were not the case, either we must look upon the splenic changes and the anæmia as due to some common cause, or else we must consider the splenic enlargement secondary to the anæmia. If this last were the case, the disease would be a primary

anæmia. This probability is discounted by the regular appearance of marked splenic enlargement for varying periods before the first sign of blood alteration. In the same way, the favourable results of splenectomy, one instance of which I have been able here to report, make it extremely unlikely that the cause of the affection is to be found outside the spleen.

From my own observations both ante and post mortem I am led to the belief that the nature of the change in the spleen is one of increased phagocytic action. As I have previously stated under Morbid Anatomy, my specimens showed abundant evidence of proliferation and increased phagocytic activity of the endothelial cells lining the vascular spaces in the spleen. The reason for this increased destructive power is very difficult to ascertain.

Some investigators attribute it to an infective agent - e.g. a micro-organism, and [68] Delbet claims to have cultivated a bacillus from the spleen which, when inoculated into dogs resulted in the production of glandular swelling. Experiments have not supported this theory, and [53] Sippy, who worked carefully at the subject, was unable to show evidence of micro-organisms.

Banti (in 1898) regarded the cause of the condition as being due to the production of some toxin by

the enlarged spleen. This, he said, resulted in anæmia. The toxic substance, in its passage through the spleen and portal veins to the liver, induced an intimal sclerosis and atheromatosis, sometimes even with calcareous deposits. If the disease lasted long enough, the toxæmia finally resulted in a cirrhotic condition of the liver resembling multilobular atrophic cirrhosis. This theory does not account for the enlargement of the spleen, the toxin, according to Banti, only being produced by the organ as the result of its enlargement.

Various bacteria and cocci have been described as being found in the spleen and bone-marrow of patients, the victims of splenic anæmia, but these have probably always been due to post mortem inclusion. I can only suggest that the disease originates from the production of a toxin or of toxins in the spleen or elsewhere, which toxin or toxins stimulate the normal phagocytic action of the spleen to increased activity.

The fact that I have found the bone-marrow in my cases to show a state of gelatinous degeneration does not appear to me to complicate the above theory of the nature of the disease. It is probable that, if the marrow could be examined at a sufficiently early stage of the disease, it would be found in a state of increased activity.

I assume therefore:-

1. That the increased destruction of blood in the spleen calls for increased activity on the parts of the marrow and other blood forming organs.
2. That this increased activity occurs early in the disease.
3. That the hæmatogenitic organs and tissues being kept in a condition of continuous hyper-stimulation in order to antagonise the destructive influence of the spleen, and that this hyper-stimulation, acting throughout a lengthened period, results, in the later stages of the disease, in exhaustion of these organs and tissues; the evidence of this, in the bone-marrow, being a condition of gelatinous degeneration.

Conclusions.

On taking into consideration the nature of the work I have done and the subject I have chosen for my thesis I have considered it wise only to make records of cases which I have been able to observe myself throughout prolonged periods.

I do not think that I should either have helped my own ideas of Splenic Anæmia or made my discussion any the more valuable by a report on and a comparison of isolated cases noted by isolated observers, such as might have been found in hospital reports.

With one exception, therefore, the cases I have recorded are all cases which I was able to watch and make clinical observations on during a considerable length of time. In two instances, I have also been enabled to give a full post-mortem report.

The one exception is Case IV, and I have included this as it was under my present chief's care in the wards in which I am now working, and because it gives a very good illustration of the benefits which may result from Splenectomy in the disease under discussion.

A total of four cases is not a very convincing number from which to gather one's conclusions; but Splenic Anæmia is a comparatively rare disease, and consequently very few examples of it are met with by

one individual. I consider that I have been fortunate in obtaining so many opportunities of studying this affection, the rarity of which is undoubtedly largely accountable for our incomprehension of it.

As the result of the work I have done and the literature I have perused on the subject of Splenic Anæmia I have drawn the following conclusions:-

1. That the disease does exist as a separate entity, and that it cannot be regarded, as some suggest, as resulting from some other disease either of the spleen, liver or general system.

2. That the essential feature of the disease is the destruction of all the formed elements of the blood.

3. That this destruction takes place in the spleen, and is brought about, possibly, by the production of a toxin either in the spleen or elsewhere.

4. That this toxin, by stimulation, causes proliferation of the endothelial and other phagocytic cells in the spleen, and by this means

increasesthe normal hæmolytic power of that organ.

5. That, early in the disease, there is probably a compensatory reaction on the part of the hæmatogenetic organs to keep pace with the increased hæmolytic action of the spleen, but that the prolonged demands on these organs end, finally, in exhaustion of their powers, as evidenced, histologically, by their gelatinous and fibroid degeneration.

6. That without a leucopenia in any but the early stages of the disease, a diagnosis of Splenic Anæmia is probably incorrect.

7. That, in doubtful cases, the effects on the numbers of leucocytes in the circulating blood of the administration of nucleinic acid, may furnish us with a clue to the correct diagnosis; and that the same proceeding may give us an indication of the condition of the bone-marrow and consequently help us in determining the results which are likely to accrue from Splenectomy.

8. That a prognostic idea of Splenectomy may be obtained by an examination of the bone-marrow

this being a measure which is easily carried out without endangering the patient's health.

9. That cases of Splenic Anæmia occur in children, which both from the clinical picture and also from the pathological findings, cannot be differentiated from cases of the disease occurring in later life.

10. That Splenectomy is the only treatment yet attempted which offers a chance of recovery.

11. That Splenectomy should be performed as soon as a definite diagnosis is arrived at, as the fact that it may be successful, even when the patient has reached the late stages of the disease, has been shown us on several occasions.

Alfred I. Stephen & Scholefield.

REFERENCES.

1. HIPPOCRATES.)
2. GALEN.)
3. MALPIGHI) From Sippy (Reference No 32)
4. MORGAGNI.)
5. NIVET.)

6. HODGKIN. Med. Chir. Transactions XVI, 1832. (From Bruhl - Reference 30).

7. BENNET.)
8. VIRCHOW.) From Sippy (Reference 32).
9. NEUMANN and BIZZOZERO.)

10. BONFILS. Receuil des trav. de la Soc. Méd. d'observations, t. I. (From Reference 30).

11. TROUSSEAU. (From Reference 32).

12. WOILLEZ. Bull. de la Soc. Méd. des hôpitaux, 1856. (From Ref. 30).

13. COLLIN. Bull. de la Soc. Méd. des hôpitaux. 1852. (From Reference 30)

14. WUNDERLICH. Arch. der Heilkunde, 1866. (From Reference 30).

15. GREISSINGER. (From References 30, 32 and 34).

16. MULLER. Berl. Klin. Wochenschr., 1867. (From Reference 30).

17. WILKES.)
18. BILLROTH.) From Reference 32.
19. COHNHEIM.)

20. GRETZEL. Ein Fall von Anemia Splenica. Berlin Klin. Wochenschrift 1866. (From Reference 32).

21. VON JAKSCH. From Ewing on 'The Blood'.

22. LANDOUZY. Bull. de la Soc. Anat. 1873. (From Reference 30).

23. PYE SMITH. Transactions of the Path. Soc. of London.

24. STRUMPELL. Arch. der Heilkunde.

25. Dr. H. C. WOOD. From References 34 and 36.

26. BANTI. Dell' Anæmia Splenica. Archivo della Scuola d'anat pathologica, Florence, 1883. (From References 30, 32 and 34).

27. PEL. Berlin Klin Wochenschr. 1885 and 1887.

28. RENVERS. Deutsche Med. Wochenschr. 1888.

29. EBSTEIN. Deut. Arch. f. klin. Med. t. XLIII.

(27, 28, 29: From Reference 30.)

30. BRUHL. De La Splénomégalie Primitive. Archives Générales de Medicine, 1891.

31. BANTI. La Splenomegalie avec cirrhosis du foie. Semaine Med., 1894 (From Reference 32).

32. SIPPY. A Critical Summary of the Literature of Splenic Pseudoleukæmia. (American Journal of Science, 1899. Vol. 118).

33. PROFESSOR OSLER. Amer. Journ. Med. Sci. 1900, p. 54.

34. PROFESSOR OSLER. Transactions of the Association of American Physicians 1902, p. 429.

35. HARRIS & HERZOG. Annals of Surgery, 1901, p. 111.

36. CABOT. Splenic Pseudoleukæmia. Historical Sketch, 1900.

37. COWAN. Anæmia with Enlargement of the Spleen. Quarterly Journal of Medicine, Oct. 1907.

38. Dr. JAMES. (From Reference 34).

39. GAUCHER. Thèse de Doctorat, Paris, 1892. (From Reference 37).

40. WILSON. Trans. Clin. Soc. London 1890, Vol.XXIII, p. 162; ibid, 1893, Vol.XXVI,p.163 (From Reference 37).

41. ROLLESTON. Clin. Journ., London 1902. Vol. XIX, p. 401.

42. COLLIER. Trans. Path. Soc. London, 1895, Vol. XLVI, p. 148.

43. BOVAIRD. Amer. Journ. Med. Sci. 1900, Vol. CXX, p. 377.

44. HAMILL. Arch. of Ped. N.Y. 1902, Vol. XIX, p. 641. (From Reference 37).

45. WILLIAMSON. Med. Chron. Manchester, 1893. Vol. XVIII, p. 103.) From Ref. 37.

46. SPRINGTHORPE. Lancet, London, 1904, Vol.II p. 1013.)

47. SCOTT. Amer. Journ. Med. Sci. 1903. Vol. CXXVI. p. 856.

48. SUMMONS. Lancet, London, 1904, Vol. II, p.1017. (From Reference 37).

49. MICHELL CLARKE. Bristol Med. Chir. Journ, 1903, Vol. XXI, p. 14.

50. BRILL. Amer. Journ. Med. Sci., 1901, Vol. CXXI, p. 375.

51. Dr. W. E. CARNEGIE DICKSON. The Bone-Marrow. A Cytological Study.

52. (PROFESSOR BEATTIE &) (Dr. W.E.CARNEGIE DICKSON. A text-book of Special Pathology.

53. SIPPY. Splenic Pseudoleukæmia with the report of a case, 1902.

54. PROFESSOR OSLER. Canada Medical and Surg. Journ. Vol.XI; and Ed.Med.Journal, May 1899.

55. WATSON. (From Reference 34).

56. Banti. Splenomegalie mit Lebercirrhose. Beitrage zur pathologischen anatomie und zur allgemeinen Pathologie. Band XXIV Heft. 1. (From Reference 32).

57. MOSLER. Arch. de Virchow (1888). (From Reference 30).

58. BARDELEBEN.)
59. ZEZAS.) From Nothnagel's Encyclopædia of Practical Medicine, 1905
60. WINOGRADOFF.)
61. VULPIUS.)

62. ARMSTRONG. B.M.J. - Nov. 1906.

63. MOSLER.)
64. NEUMANN.)
65. RIEGNER.) From Reference 35.
66. POUCHET.)
67. SIMON.)
68. DELBET.)

69. Dr. ROBERT HUTCHISON. B.M.J. - Oct 17th 1908.

70. VAUGHAN, AMES & HUNTLEY. Journ. Amer. Med. Assoc. Chicago, XXIX. 472 - 478.

71. Dr. HUNTER. Lancet. - Jan 23rd. 1909.