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4

THESIS

For the Degree of DOCTOR of MEDICINE

of the UNIVERSITY of EDINBURGH.

" EFFECTS of the RÖNTGEN RAY
TREATMENT in LEUCOCYTHAEMIA and SPLENIC ANAEMIA"

Tendered by

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28th. April. 1906.

While acting as Clinical Assistant and as Resident House Physician to Dr Byrom Bramwell, I have had the opportunity of **studying** the effects of Rontgen Ray treatment in two cases of Lymphatic Leukaemia, two cases of Spleno-Medullary Leukaemia and one case of Splenic Anaemia. Dr Bramwell has kindly allowed me to use the notes of these cases taken while they were under treatment. I have collected other typical cases which show the effect of such treatment, and I have endeavoured to note the results of the researches which have been published by workers on this subject, and in the light of the most recent information to apply the knowledge which has been acquired to the cases which I had and those which I still have under observation. I have arranged the Thesis under the following heads :-

1. A Description of the five cases with their progress which I observed in the Royal

Infirmery, Edinburgh.

Page 4.

2. History and Results in other Typical Cases. Page 78.

3. How Rontgen Rays Act in Leucocythaemia. Page 117.

4. Technique and Dangers in the Use of Rontgen Rays in Leucocythaemia. Page 133.

5. Results of Rontgen Ray Treatment in Leukaemia upon Metabolism. Page 141.

6. General Conclusions. 180

The first of four cases of Leukaemia which have been treated in the Royal Infirmary, Edinburgh, by Rontgen Rays - in the order in which they were admitted to Dr Byrom Bramwell's Wards, was a case of Chronic Lymphatic Leukaemia.

J... H... a Schoolboy aged 15.

Admitted to Ward 28, on the 21st. February 1905

COMPLAINT:

- General Weakness.
- Dimness of Vision.
- Swollen Abdomen.

HISTORY:

The first thing the patient noticed seriously wrong was dimness of vision. That was three years ago. He then consulted an Oculist who

5

detected Double Optic Neuritis with marked enlargement of the Retinal Veins.

The patient says that at that time his abdomen was slightly swollen, and it was about t then that he began to feel weak and short of breath on exertion, and it was noticed that he was getting rather pale.

His weakness and breathlessness did not become marked till one or two years after that, i.e., ten months before admission, but then they caused him to give up games at School.

Nine months before admission he began to have trouble with his Stomach, retching and vomiting and pain within a few minutes of taking food. One morning at this time after he had been retching, he felt his eyes 'puffy' and found they were surrounded by dark rings which had not been there before.

During the next month his stomach symptoms increased, and he noticed the glands in

his axilla were swollen. At this time, too, he began to notice his feet and ankles swollen at night - the swelling would disappear before morning. This was in July. In September he first noticed areas of Eccymoses - similar to those around his eyes - over the front of his chest. The swelling in his A Abdomen was gradually increasing, and - though the vomiting had diminished - the pain in his Stomach immediately after food had increased, and he suffered greatly from heartburn and waterbrash two or three hours after food.

In October he had an attack of Diarrhoea of one week's duration.

He says he rapidly became weaker and thinner during the last five months; his weight (undressed) diminishing in that time from 7 st. 7 lbs to 6 st. 6 $\frac{3}{4}$ lbs.

He had never felt any pain nor dragging sensation in his left side.

7

PREVIOUS HEALTH:

Good up to three years ago.

Measles and Whooping Cough in infancy.

Patient says that three years ago his Doctor told him that his Kidneys were not quite right, and that he had Albumen and Blood in his Urine.

FAMILY HISTORY:

Father, aged 65, and Mother, aged 50, both alive and healthy.

Had two Sisters, eldest aged 13, alive and healthy. The youngest had died aged 7, of 'Valvular Disease' following Rheumatic Fever.

SOCIAL CONDITIONS:

Were extremely satisfactory.

STATE on ADMISSION.

Height 5 feet 7½ inches. Weight, 6 stones. 6¾ lbs. Pulse 100. Temperature 98. Respirations 28.

The patient was very intelligent, and

8

extremely anxious about his condition. His body and limbs were thin and emaciated.

There were dark areas of ecchymoses round both orbits.

His face was unduly broad in the temporal regions, and there was a bluish discolouration beneath the skin in these parts. Over the front of his chest, extending as low down as the nipples, and laterally to the armpits there were areas of bluish green discolouration indicating recent extravasations of blood which were being absorbed. There was a similar area about the size of a florin over the left Scapula. There were no signs of haemorrhages about his legs, but patient said they 'come in crops' and disappear again.

His mucous membranes were pale and anaemic looking.

HAEMOPOIETIC SYSTEM.

HAEMOPOIETIC SYSTEM.

BLOOD COUNT.

The drop of blood which exuded from a pin prick on thumb was paler than normal.

Reds.	2,000,000.
LEUCOCYTES.	340,000.
Hb.	38 %.

DIFFERENTIAL COUNT of LEUCOCYTES.

Small Lymphocytes.	69.2 %.
Large Lymphocytes.	23.8 %.
POLYMORPHS.	4.6 %.
Myelocytes.	2.4 %.

No Eosmophils were seen.

No Nucleated Reds were seen.

SPLEEN.

The Spleen was greatly enlarged, extending from the 8th Rib in the Midaxillary line to within 2 inches of the Pubis. It extended to the Right just to the Umbilicus at that level and filled up the whole of the Left of the Abdomen. The anterior border was distinctly notched to palpation.

GLANDS.

GLANDS.

There was a general enlargement of all the Lymphatic Glands in the body, Axillary, Submaxillary, Carotid, Inguinal, and Femoral.

The Glands were quite discrete, firm and elastic, not adherent to the skin, and not tender to pressure. The Glands varied in diameter from $\frac{1}{8}$ to 1 inch.

CIRCULATORY SYSTEM.

Dyspnoea and Oedema as in history. No Ascites. Pulse 100, regular in rate and rythm, force was fair, tension poor. No thickening of vessels.

HEART.

Diffuse pulsation was seen around the nipple and internal to it in the third and fourth interspaces, extending almost to the left margin of the Sternum. Apex beat was felt over area the size of a crown but it was most intense in the

//.

4th space, half an inch external to the Mammary Line. A thrill, systolic in time, was palpable on the right side of the Neck.

On Percussion the Right border was found $1\frac{1}{4}$ inches from the Mid Sternal Line.

The Left border $4\frac{1}{2}$ inches from the Mid Sternal Line in the 4th Space.

The Upper border reached the lower border of the 2nd Rib.

On Auscultation there was a well marked Mitral Systolic Murmur, blowing in character slightly propagated into the Axilla. This murmur was heard less distinctly in all the other Cardiac areas, but in the first right interspace and in the neck, there was a very loud, rough murmur - Systolic in time.

ALIMENTARY SYSTEM.

He often felt inclined to vomit without result. Lips and tongue were pale, not

swollen. Teeth very unsatisfactory, several missing. Most of those remaining, especially the Molars were decaying.

STOMACH.

The Stomach was not enlarged.

LIVER.

The Liver dulness extends in the Mammary Line from the 5th Rib to $\frac{3}{4}$ of an inch below the Costal Margin.

ABDOMEN.

On the left the Abdomen is filled with the Spleen which is hard, with sharp edges.

On the right the Abdomen is tense, giving a loud tympanic note on percussion.

RESPIRATORY SYSTEM.

His Respiratory System was normal.

URINE.

Passed 70 Ozs in the last 24 hours.
Light Straw coloured.
Slight mucous deposit.
Specific Gravity 1009.
Reaction, Acid.
Slight trace of Albumen.

URINE.

No Blood or Sugar.

A few Hyaline Casts.

NERVOUS SYSTEM.

There were no abnormal subjective symptoms except diminished Vision. His eyeballs were not prominent.

Ophthalmoscopic Examination shewed great enlargement of the Retinal Veins, and Double Optic Neuritis. The Discs were swollen, their edges badly defined, and the vessels which passed over the Disc were obscured by swelling and blood-extravasations. There were numerous haemorrhages and remains of former haemorrhages in the surrounding Retina.

TREATMENT and PROGRESS.

On February 24th Patient was put on

Liq: Arsenicalis, Mii, t.i.d.

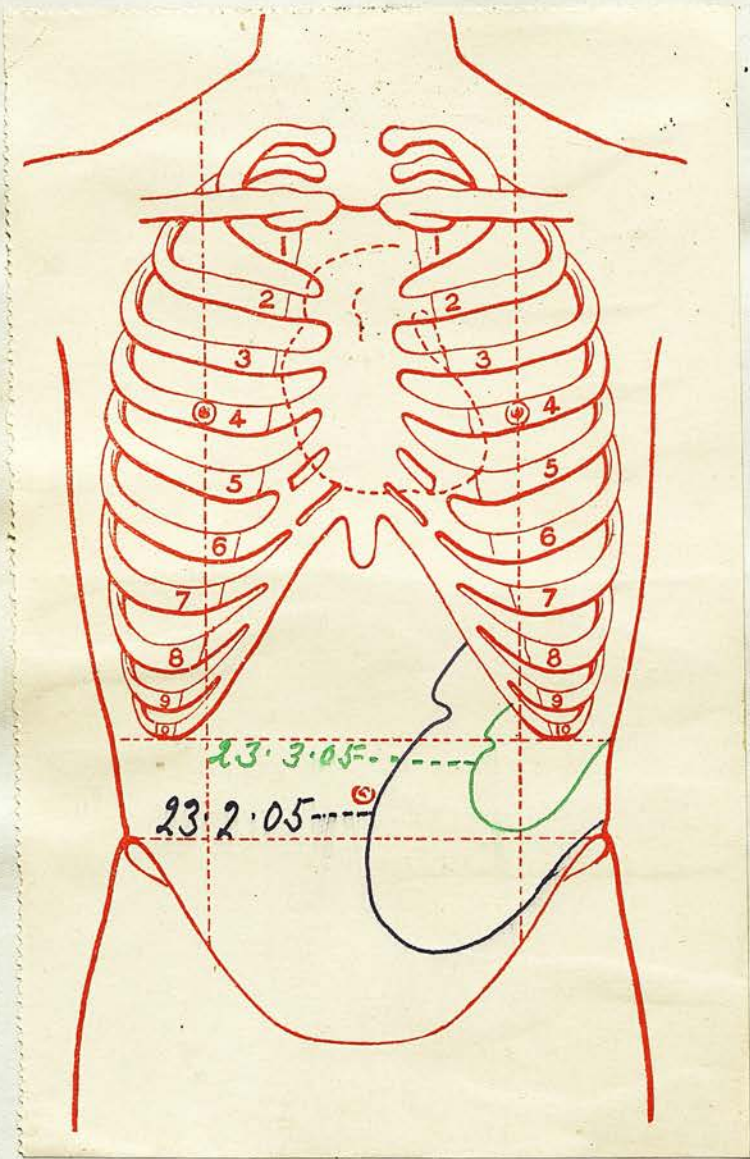
On February 27th. his Blood count

was:-

Reds.	1,600,000.
Whites.	230,000.
Hb.	33 %.

Rontgen Ray Treatment commenced.

The Treatment consisted in exposures of five minutes each. A fairly soft tube and an amperage of 5 was used. The Splenic region anteriorly, laterally and posteriorly, was treated in order at each sitting. He received 13 exposures on alternate days.



J. H. Chart of Spleen.

Showing diminution from Feb. 28rd to Mar. 23rd.

His temperature rose that night to 101.4, and was down next morning to 97.6, assuming a swinging type for some days. Gradually the Whites decreased in number. (See Table). The Spleen and Lymphatic Glands diminished in size, but the Reds did not increase in number, and the boy's general condition got gradually worse.

MARCH 1st.

Was sick and vomited just before getting the X Rays.

MARCH 23rd.

There was some Erythematous inflammation over the Spleen, some throbbing in his head, and palpitation. X Rays ceased.

Blood Count:- Reds 1,110,000; Whites 7,800; Hb. 34 %.

Spleen diminished as in ^{Diagram} ~~Photo~~ opposite. Spleen and Glands were very soft.

APRIL 3rd.

Patient had not been feeling well for some days. On this day a small (petechial)

purpuric rash appeared on his legs and arms both above and below the knee, and above and below the elbows. Chiefly on the extensor aspects of the shoulders, upper part of the arms and forearms and on the legs below the knees. None on the trunk nor face. None on interior of mouth.

No fresh extravasations around the eyes nor on conjunctivae, temples, nor front of chest.

In the evening he said he had felt faint all day and had a constant taste of blood in his mouth and there was slight bleeding from two molar teeth.

Temperature rose to 103. Pulse to 128.

APRIL 4th.

Patient said he felt better. Bleeding in Mouth had ceased. Headache gone. He looked more pallid than usual.

APRIL 7th.

17.
APRIL 7th.

Reds are down to 660,000, Hb to 20 %, and his Whites have risen again to 26,000.

There have been no fresh extravasations, but frequent attacks of Epistaxis.

Patient was evidently sinking fast and his friends took him home. He died 7 days later. The P.M., was refused.

I regret to say that I did not at this time know the value of examining the Urine to see the effect of the X Rays on Nitrogen Metabolism, and it was not done.

The Case shews how in Acute Lymphatic Leukaemia the X Ray treatment may reduce the Leucocyte count to normal and reduce the size of the Spleen and Glands, while at the same time the subjective symptoms may increase and the Patient die.

Following are the Temperature Charts, a Chart shewing the changes in the Blood Count,

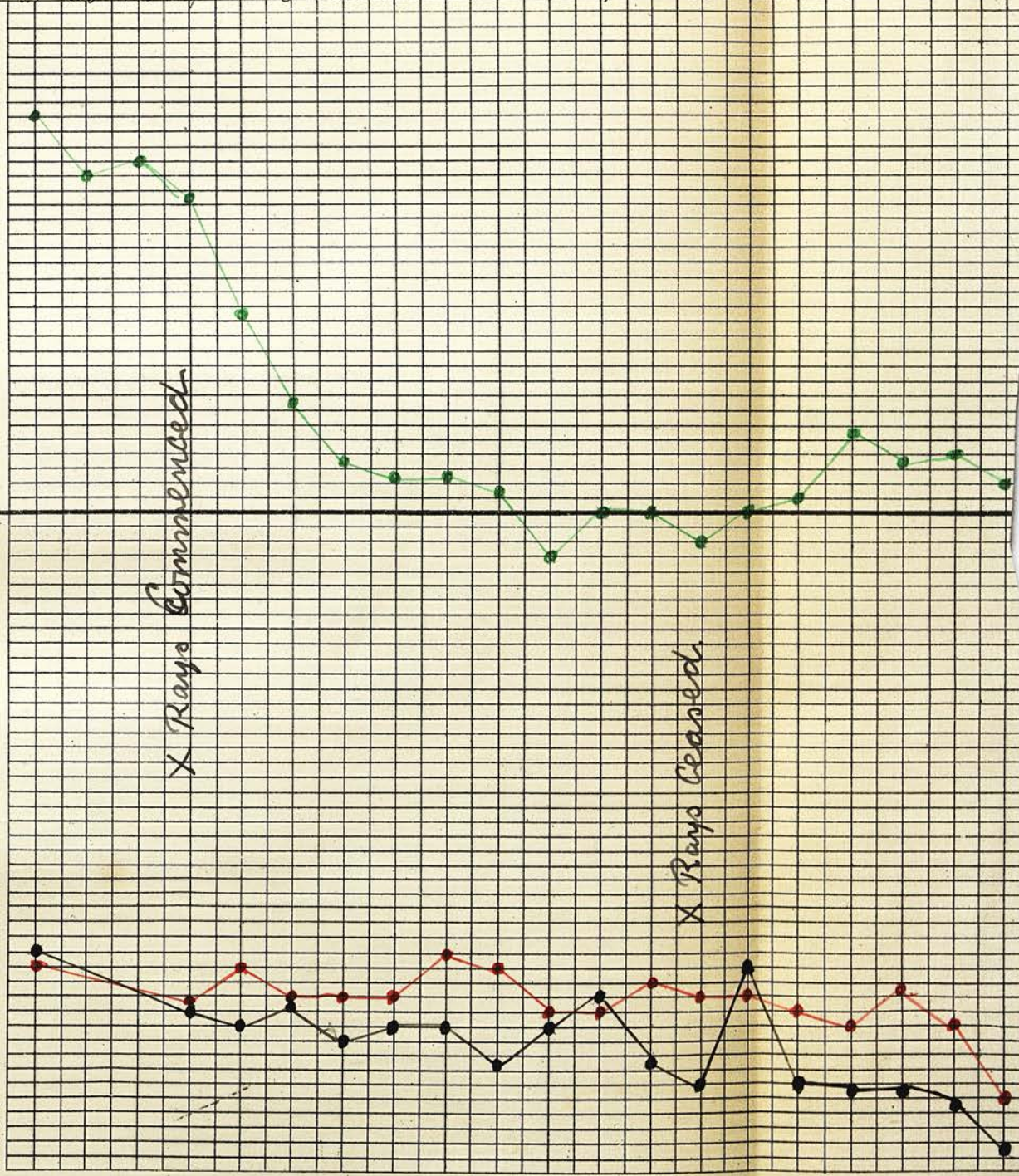
and a Table giving the Counts at different dates.

DATE. 1905.	Hb.	REDS.	WHITES.
Feb. 21st.	38 %.	2,000,000.	340,000.
Feb. 25th.			260,000.
Feb 26th.			280,000.
Feb. 27th.	33 %.	1,600,000.	230,000.
Rontgen Rays commenced.			
March 1st.	38 %.	1,510,000.	134,000.
March 3rd.	34 %.	1,650,000.	74,000.
March 6th.	34 %.	1,400,000.	32,000.
March 8th.	34 %.	1,500,000.	26,000.
March 10th.	40 %.	1,500,000.	28,000.
March 12th.	38 %.	1,280,000.	10,200.
March 15th.	32 %.	1,500,000.	7,000.
March 17th.	32 %.	1,700,000.	8,000.
March 20th.	36 %.	1,220,000.	8,000.
March 22nd.	34 %.	1,110,000.	7,800.
Rontgen Rays Discontinued.			
March 26th.	34 %.	1,920,000.	8,000.
April 1st.	32 %.	1,200,000.	14,000.
April 3rd.	30 %.	1,100,000.	56,000 .
April 5th.	35 %.	1,100,000.	34,000.
6th April.	30 %.	920,000.	39,000.
April 7th.	20 %.	660,000.	26,000.

NAME. J. 15.
 AGE. 15.
 DISEASE. Chronic Lymphatic Leukaemia.

DATE.	W. B. C.	R. B. C.	Hb.
Feb. 21	400,000	8,000,000	160%
25	300,000	7,500,000	150%
26	200,000	7,000,000	140%
27	150,000	6,500,000	130%
28	100,000	6,000,000	120%
1 March 1	50,000	5,500,000	110%
3	8,000	5,000,000	100%
6	6,000	4,500,000	90%
8	4,000	4,000,000	80%
10	2,000	3,500,000	70%
12	8,000	3,000,000	60%
15	6,000	2,500,000	50%
17	4,000	2,000,000	40%
20	2,000	1,500,000	30%
22	8,000	1,000,000	20%
26	6,000	800,000	18%
1 April 2	4,000	700,000	16%
5	2,000	600,000	14%
6	8,000	500,000	12%
7	6,000	400,000	10%

Feb. 21 25 26 27 1 March 3 6 8 10 12 15 17 20 22 26 1 April 2 5 6 7

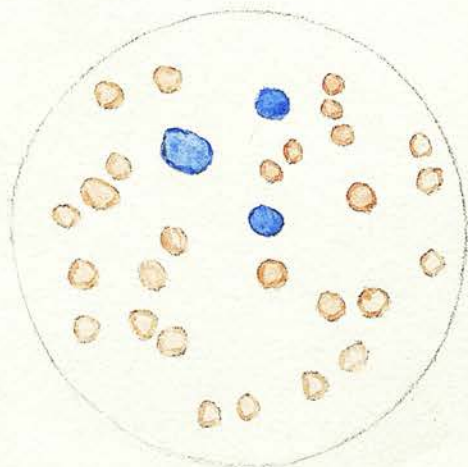
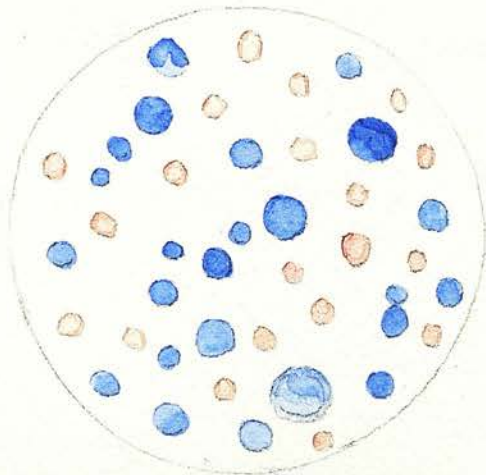


X Rays Commenced

X Rays Ceased

FILM percent
 Lymphocytes Sm 69.2
 " Large 23.8
 Polymorphs. 4.6
 Myelocytes 2.4

LEUKOCYTES GREEN ERYTHROCYTES BLACK HÆMOGLOBIN RED



BLOOD FILMS. J. H. (Lymphatic Leukaemia)

No 1. On Admission, 22 - 2 - 05.

Reds.	2,000,000.
Hb.	38 %.
Leucocytes.	340,000.
Small Lymphocytes.	69.2 %.
Large Lymphocytes.	23.8 %.
Polymorphs.	4.6 %.
Myelocytes.	2.4 %.
No Eosinophiles.	
No Nucleated Reds.	

No 2. On Discharge. 7 - 4 - 05.

Reds.	660,000.
Hb.	20 %.
Leucocytes.	26,000.
Small Lymphocytes.	58 %.
Large Lymphocytes	40 %.
Polymorphs.	2 %.

The next case is one of Chronic
Myeolog^einous Leukaemia.

J..L.., a single girl, aged 28, a Weaver, was admitted to Ward 30, on 22nd February, 1905, the day after the preceeding case was admitted to Ward 28.

The treatment by Rontgen Rays was commenced, in this case with success, while during the same time the Lymphatic Leukaemia got progressively worse.

COMPLAINT.

Swelling of Abdomen. Pain and hardness in left side. Amenorrhoea for ten months.

HISTORY.

In May 1904, she consulted her Doctor for a pain in her left side, which was diagnosed as Ovaritis. A constant feeling of dull soreness - never acute - has been present there ever since. She has not Menstruated since the pain appeared, but was quite regular before then.

In October last her Doctor told her

there was a 'lump' in her left side. She had been gradually getting weaker and more easily tired, and had been losing weight up to time of admission.

There had been no breathlessness nor Oedema. No Haemorrhages. No Stomach troubles. No Diarrhoea. No Subjective Nervous Symptoms.

PREVIOUS HEALTH.

Always Good.

FAMILY HISTORY.

Father 73. Mother 74. Both alive and well. There were nine in family.

SOCIAL CONDITIONS and HABITS.

Quite Satisfactory,

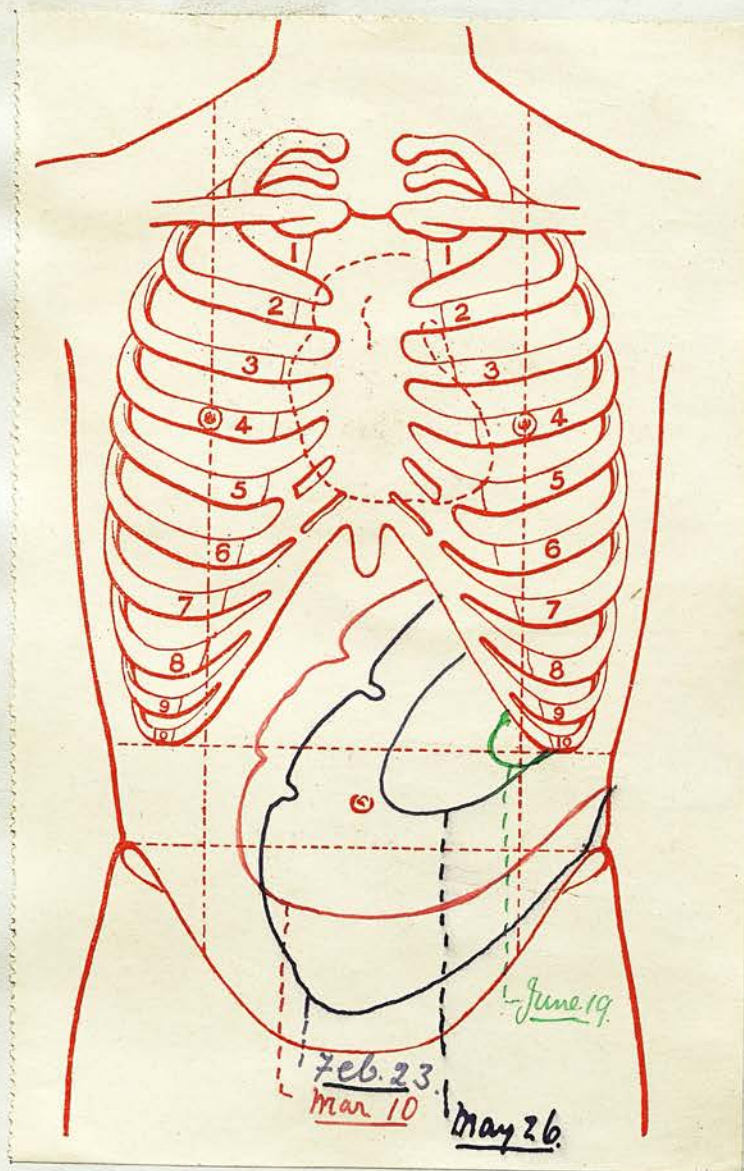
On ADMISSION.

Height 4 feet. 11½ inches.
Weight 6 st. 6 lbs.

She says her former weight - dressed - was 8 st. 4 lbs.

Pulse 104. Temperature 97.9. Respirations 24.

She was thin, general muscularity and nutrition poor. Complexion muddy. Mucous Membranes slightly Anaemic.



f--L. Chart of Spleen.

Showing progressive diminution

from Feb. 23¹⁹²¹ to June 19th

HAEMOPOIETIC SYSTEM.

BLOOD.

Reds	3,800,000.
Leucocytes.	540,000.
Hb.	69 %.

DIFFERENTIAL COUNT.

Myelocytes.	43.2 %.
Polymorphs.	41.4 %.
Lymphocytes.	4.4 %.
Eosinophile Myelocytes.	5.8 %.
Eosinophile Polymorphs.	2. %.
Basophiles.	3.2 %.

SPLEEN.

Greatly enlarged. Extended up to the Seventh Rib in the Mid Axillary Line; to the eighth rib in the line of the angle of the Scapula, to 5 inches below the Umbilicus and crossed the Middle Line at that level by about one inch.

The organ was hard, the edges quite distinct, and notches, as seen in diagram, were felt. No friction was elicited over the Spleen, but it was tender to pressure in its lower border.

GLANDS.

The only enlarged glands detected were a few small Femoral ones.

CIRCULATORY SYSTEM.

Pulsation over the Praecordia was diffuse. The apex beat was palpable in the 4th Interspace, five inches from Mid Sternal Line.

There was venous pulsation in the Neck.

The Pulmonary first sound was loud and a little blurred; the Second was accentuated.

Other Sounds were normal.

(Pressure of the Stethoscope over the Sternum caused marked tenderness)

ALIMENTARY SYSTEM.

Her tongue was clean but pale and slightly swollen. Her teeth were bad. Only one remained in the upper jaw and five in the lower. She had had bad teeth all her life. Her appetite was always good.

There were no marked disturbances in digestive functions. Never Epistaxis, haematemesis nor Melaena.

The Liver was not enlarged.

The skin over the Abdomen was darker than the rest of the body and dark brown pigmented spots were scattered about the lower part.

URINARY SYSTEM.

Never any Haematuria.

Urine pale straw colour.

Specific Gravity 1016.

Reaction Acid.

Deposit of Urates.

Albumen present in trace.

NERVOUS SYSTEM.

No Subjective Symptoms.

Eyeballs slightly prominent.

Vision quite good.

Optic Discs normal.

Retinal Veins slightly dilated.

TREATMENT and PROGRESS.

February 25th. Put on Liq: Arsenicalis,
M ii, t.i.d.

February 28th. Rontgen Ray Treatment
commenced as follows :-

The technique was the same as the previous
case, J.. H..

March 4th. For the last three days the
temperature has been swinging. Evening temperature
on this day was 101, Morning 98.4.

March 21st. Reds increased to 4,000,000;
Whites diminished to 70,000, and Hb. increased to
90 %. An Erythematous rash appeared over the Spleen.
There were no constitutional symptoms. Rontgen Rays
suspended.

April 11th. Whites have varied between
48,000 and 112,000. On this date they were 80,000.

There was a dark red discolouration
all over the Splenic region with slight dry feeling
of the Epidermis. Patient felt well and happy.

Rontgen Rays resumed.

May 20th. Reds increased to 5,200,000.
 Hb. increased to 82 %.
 Whites diminished to 34,800.

Patient looked rosy and well. She felt quite well and happy and was discharged.

There was no record of Nitrogen Metabolism.

The following are the Temperature Charts and Tables of Blood Counts at different dates.

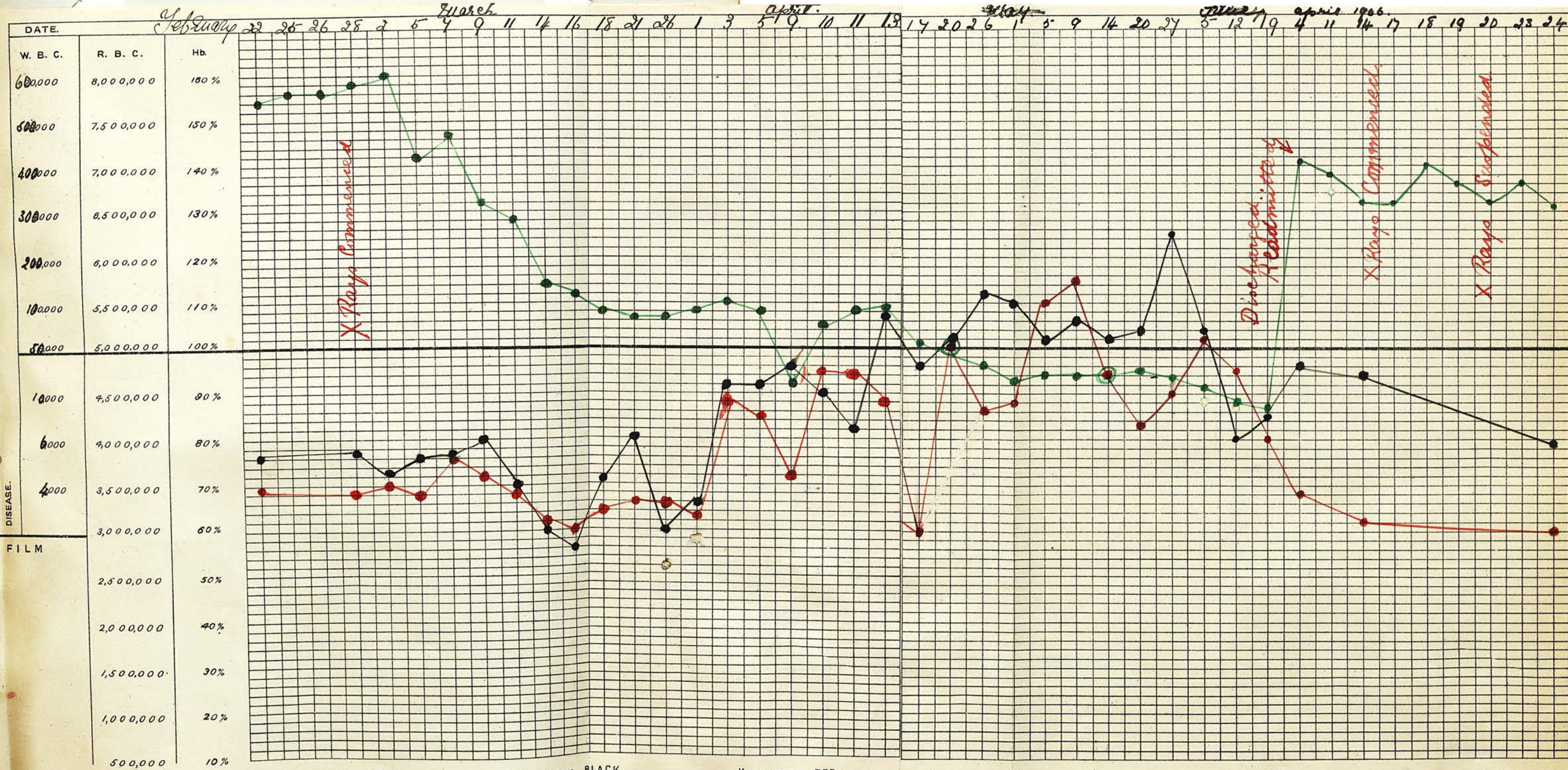
Table of Blood Counts. J... L...

Date.	Hb.	R. B. C.	W. B. C.
Feb. 22nd.	60 %.	3,800,000.	540,000.
Feb. 25th.			560,000.
Feb. 26th.			565,000.
X Feb. 28th.	68 %.	3,850,000.	590,000.
Mar. 2nd.	70 %.	3,650,000.	600,000.
Mar. 5th.	68 %.	3,800,000.	420,000.
Mar. 7th.	76 %.	3,850,000.	470,000.
Mar. 9th.	72 %.	4,000,000.	320,000.
Mar 11th.	68 %.	3,500,000.	300,000.
Mar. 14th.	62 %.	3,000,000.	148,000.
Mar. 16th.	60 %.	2,670,000.	118,000.
Mar. 18th.	46 %.	3,450,000.	84,000.

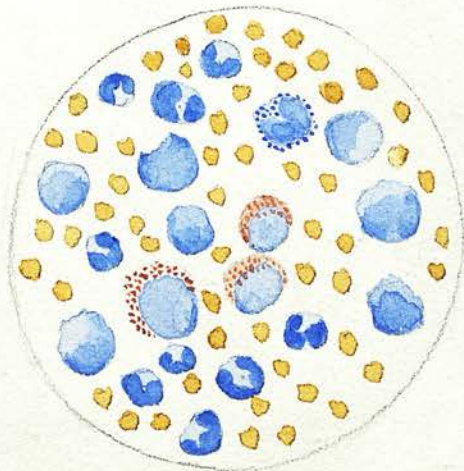
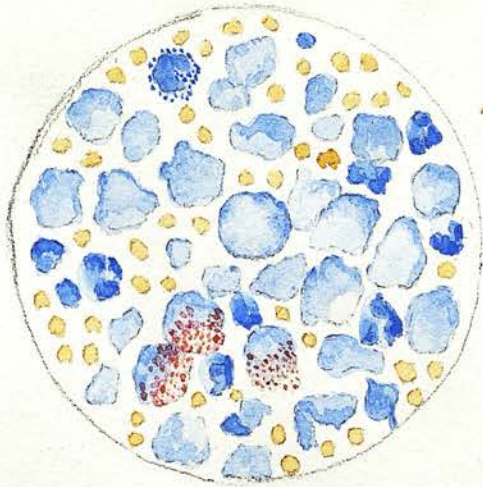
X. X Rays commenced.

Date.	Hb.	R. B. C.	W. B. C.
Mar 21st.	66 %.	4,000,000.	70,000.
Mar. 26th.	66 %.	3,050,000.	68,000
April 1st.	67 %.	3,300,000.	112,000.
April 3rd.	90 %.	4,600,000.	111,000.
April 5th.	85 %.	4,560,000.	107,000.
April 9th.	72 %.	4,800,000.	20,200.
April 10th.	95 %.	4,530,000.	65,800.
April 11th.	94 %.	4,080,000.	80,000.
April 13th.	88 %.	5,250,000.	84,200.
April 17th.	60 %.	4,808,000.	55,000.
April 20th.	100 %.	5,100,000.	50,000.
April 26th.	85 %.	5,610,000.	47,000.
May 1st.	88 %.	5,540,000.	28,000.
May 5th.	110 %.	5,120,000.	29,000.
May 9th.	115%.	5,350,000.	32,000.
May 14th.	95 %.	5,100,000.	30,000.
May 20th.	82 %.	5,200,000.	34,800.
May 27th.	90 %.	6,250,000.	31,000.
June 5th.	102 %.	5,200,000.	13,600.
June 12th.	95 %.	4,090,000.	9,800.
June 19th.	80 %.	4,240,000.	9,400.

NAME: J. L.
AGE:
DISEASE:



LEUKOCYTES GREEN ERYTHROCYTES BLACK HÆMOGLOBIN RED LEUKOCYTES GREEN ERYTHROCYTES BLACK HÆMOGLOBIN RED



BLOOD FILM. No 3. J..L.. (Spleno-Medullary Leukaemia)

On Admission. 22-2 - 05.

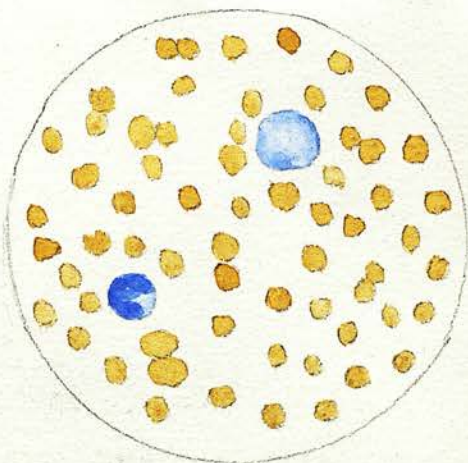
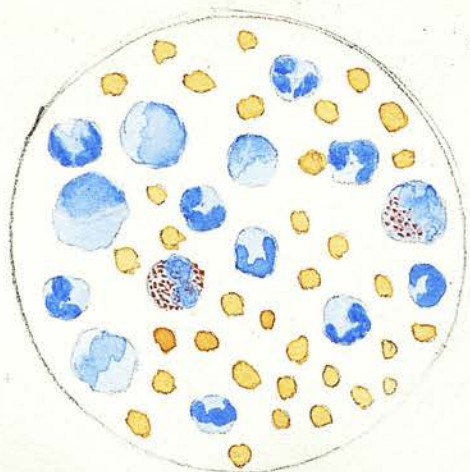
Reds.	3,800,000.
Leucocytes.	540,000.
Hb.	69 %.
Myelocytes.	43.2 %.
Polymorphs.	41.4 %.
Lymphocytes.	4.4 %.
Eosinophile Myelocytes.	5.8 %.
Eosinophile Polymorphs.	2 %.
Basophiles.	3.2 %.

The Film showed 3 Eosinophiles and 1 Basophile (Jenner)

No 4. J.. L.. 18 - 3 - 05.

Reds.	3,450,000.
Hb.	60 %.
Leucocytes.	118,000.
Myelocytes.	24.2 %.
Polymorphs.	70 %.
Lymphocytes.	2.6 %.
Eosinophiles.	5.8 %.
Basophiles.	2 %.

Film showed 3 Eosinophiles and 1 Basophile. Eosinophiles were always found in groups. (Jenner)



BLOOD FILM No 5. J. L. 3 - 4 - 05.

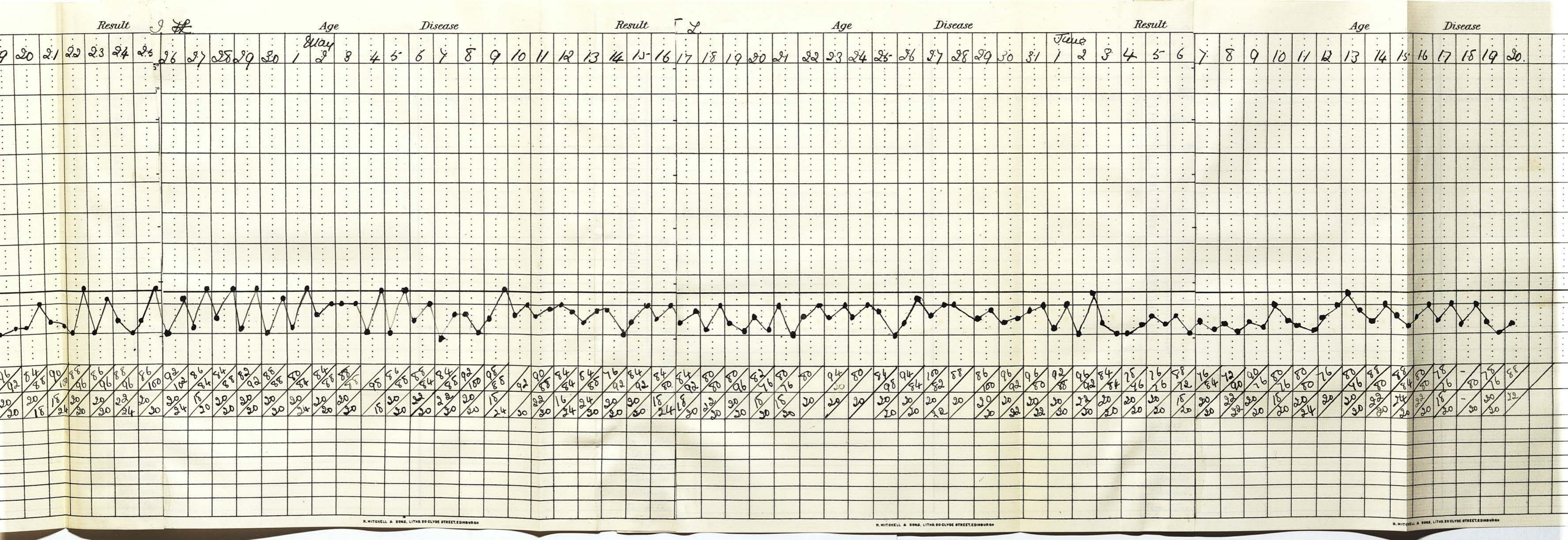
Reds.	4,600,000.	
Hb.	90 %.	
Leucocytes.	111,000.	
	Myelocytes.	41 %.
	Polymorphs.	37.5 %.
	Lymphocytes.	13.5 %.
	Eosinophiles.	7 %.
	Basophiles.	1 %.

Film shows 1 Eosinophile Polymorph and 1 Eosinophile Myelocyte (Jenner)

BLOOD FILM No 6. J. L. 9-5-05.

Reds.	5,350,000.	
Hb.	115 %.	
Leucocytes.	32,000.	
	Myelocytes.	17 %.
	Polymorphs.	65 %.
	Lymphocytes.	7 %.
	Eosinophiles.	7 %.
	Basophiles.	4 %.

Film showed Leucocytes more discrete than previously. 1 Myelocyte and 1 Polymorph in field. (Jenner)



On September 2nd she came to the Ward to show herself. She was looking very well and stout, and weighed 8 stones 2 lbs in her clothes, a gain of 2 lbs since her discharge in May. She said she Menstruated on June 1st, and had done so regularly every three weeks since.

The Spleen was smaller than on discharge and extended along the 10th Rib to the Mid-Axillary Line.

Her Blood Count was :-

Reds.	5,400,000.
Whites.	51,200.
Hb.	90 %.
Polymorphs.	77 %.
Lymphocytes.	5 %.
Large Mononuclears.	8 %.
Eosinophiles.	1 %.
Myelocytes.	9 %.

Since then she has been following her occupation as a Weaver, and feeling quite well and happy till six weeks ago, when she had an attack of Bronchitis, with a sharp, cutting pain between

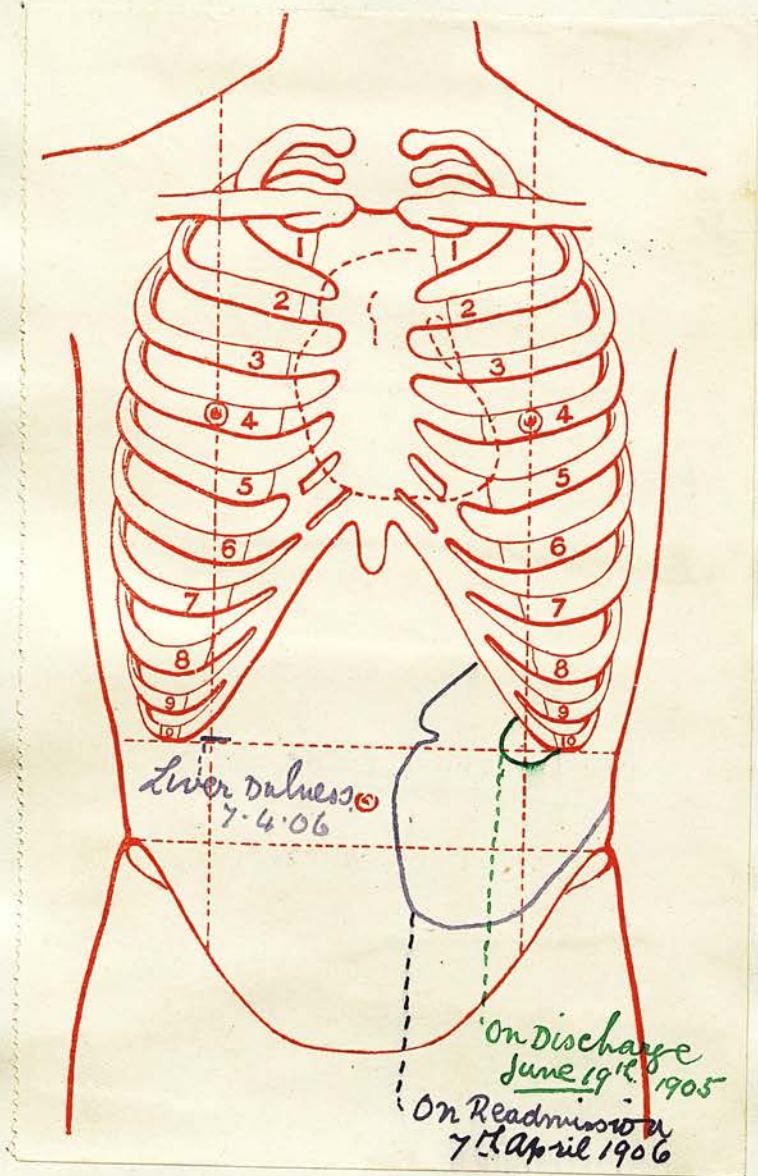
between the shoulders - worse on taking a breath.

This pain and cough lasted a week. Since then she has felt very tired on exertion and has had no appetite for food.

Her Menstruation continued to be regular till the last two occasions which were of the fortnightly type, and each lasted ten days. Her other periods never lasted more than four days. There have been no haemorrhages, Epistaxis nor Haematemesis.

She has been feeling sick occasionally after food with dyspeptic pains and a desire to vomit. She retched and vomited during the whole afternoon and evening of one day last week.

As there was evidently a relapse, she was re-admitted to Ward 30, for treatment, on April 7th 1906. Her weight was 7 stones $3\frac{1}{2}$ lbs, as compared with 8 stones when she left Hospital. She looks pale, the mucous linings are anaemic, and she complains of feeling languid and 'done'.



J-L. Chart of Spleen.

Showing increase between discharge on June 19th 1905.
and readmission on April 7th 1906.

BLOOD COUNT.

Reds.	4,800,000.
Whites.	401,000.
Hb.	68 %.

DIFFERENTIAL COUNT.

Myelocytes.	40 %.
Polymorphs.	31 %.
Lymphocytes.	4 %.
Eosinophiles.	4 %.
Transitionals.	21 %.

SPLEEN.

The Spleen which was just below the Costal Margin on her discharge, now extends 7 inches below it, and two inches to the left of the Umbilicus. (See Diagram). It is hard and firm, not freely movable and not tender to pressure. There are no enlarged glands beyond a few small ones in the groin which were previously noted. There is no Oedema, and there has not been any swelling of the feet since her discharge.

The venous pulsation in her neck is rather more marked than when she was in before,

but there are no Cardiac murmurs.

Her Bronchitis has quite cleared up, and there is nothing abnormal in her Respiratory System.

The Liver is a little larger than it was on her previous examination, the hepatic dulness now extending $\frac{3}{4}$ of an inch below the Costal Margin in the Mammary Line. She has been very constipated during the last few months. The Urine is free from abnormal constituents.

APRIL 11th. Patient who has been Menstruating since admission, ceased to-day. Rontgen Ray treatment is being postponed until I have had an opportunity of testing the Nitrogen Metabolism in the Urine.

April 16th. Since her admission the patients temperature has varied irregularly between 96.8 and 99.8. Rontgen Ray treatment has commenced to-day.

April 17th. It is interesting to note that the

Leucocyte Count has risen to-day from 325,000 to 426,000. This rise on the day following the first exposure has been noted by Auberdin and Beaujard, (see page 123).

April 18th. The Leucocyte Count, though it has fallen below yesterday's, is still higher than it was before Rontgen Rays commenced. It is 400,000 to-day.

April 20th. The patient has had no change in symptoms following exposures to Rontgen Rays. There is no feverishness, nor any appearances of Toxaemia, but her temperature has assumed a swinging type from 98 in the morning to 102.5 in the evening, Menstruation has commenced again to-day after a period of 9 days, and the Rontgen Rays have been discontinued. The Leucocytes have fallen to 323,000.

April 21st. Menstruation has ceased, lasting only one day. Patient complains of severe headache, and her evening temperature last night was 101.4. The

treatment is still suspended.

April 23rd. Although she has had no further exposures, the patients temperature has retained its swinging type (see Chart). Her headache has disappeared, and there have been no other symptoms. No increase in perspiration. A trace of Albumen appeared in the Urine 5 days ago and has persisted. Her appetite has increased. Her constipation is less obstinate and she says she feels much better than she did on admission. The Metabolism is dealt with on page

April 24th. Her Blood Count to-day is :-

Reds.	3,920,000.
Hb.	58 %.
Whites.	317,000.

DIFFERENTIAL COUNT.

Myelocytes.	45 %.
Polymorphs.	39 %.
Eosinophiles.	6 %.
Basophiles.	6 %.
Transitionals.	3 %.
Lymphocytes	1 %.

A reference to the Table following page 26, will show that in the ten days succeeding the commencement of Rontgen Rays treatment, last time the Leucocytes fell from 600,000 to 300,000, the Reds fell from 3,850,000 to 3,500,00 and Hb remained stationary.

It will be frequently observed in this thesis that the prognosis in Rontgen Ray treatment of Leukaemia is not good unless there is an increase in the Reds and Hb.

Following this fall in the Reds during the first ten days of treatment last time came a still further fall to 2,670,000, and then a gradual rise till 2 months later (May 27th), the Reds had reached 6,250,000, the Hb, 90 %., and the patient showed marked improvement.

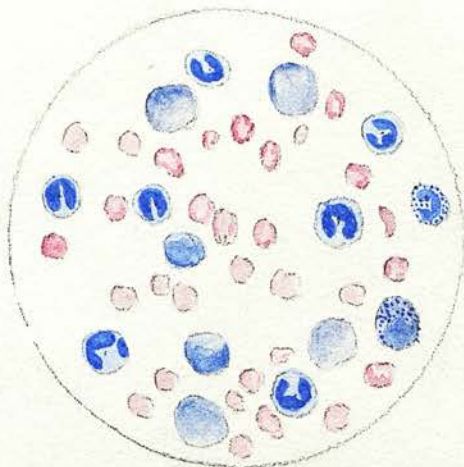
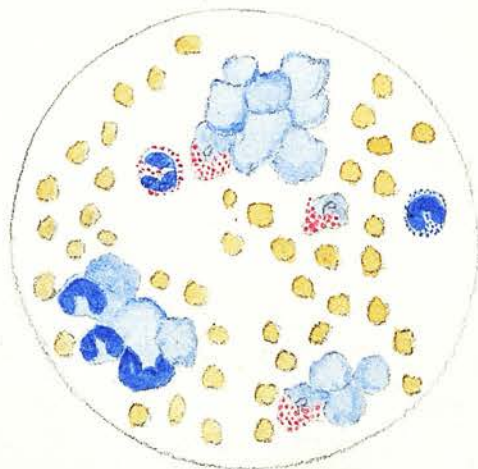
On this occasion also, the Reds and Hb are falling and at the same time there is not such a marked diminution in the Whites, but the general condition has improved and the prognosis not

justifiably be considered unfavourable, after such a short period of treatment.

The following are her Blood Tables and
x
Charts and Temperature Charts since her re-admission.

Date.	Hb.	R. B. C.	W. B. C.
April 4th.	68 %.	4,800,000.	401,000.
April 11th.			376,000.
April 14th.	62 %.	4,680,000.	325,000.
April 17th.		Rontgen Rays commenced.	426,000.
April 18th.			400,000.
April 19th.			358,000.
April 20th.			323,000.
Rontgen Rays Suspended.			
April 23rd.			360,000.
April 24th.	58 %.	3,920,000.	317,000.

x
For Blood Charts see Chart opposite page 27.



BLOOD FILM No 7. J. L.

On Re-Admission. 7-4-06.

Reds.	4,800,000.
Hb.	68 %.
Whites.	401,000.
Myelocytes.	40 %.
Polymorphs.	31 %.
Lymphocytes.	4 %.
Eosinophiles.	4 %.
Transitional.	21 %.

The Myelocytes were found in clusters in several films taken on this day. Film shows 3 Eosinophiles Myelocytes. 1 Eosinophile-Polymorph. 1 Basophile (Jenner)

FILM No 8. J. L. 24-4-06.

REDS.	3,920,000
Hb.	58 %.
Whites.	317,000.
Myelocytes.	45 %.
Polymorphs.	39 %.
Eosinophiles.	6 %.
Basophiles.	6 %.
Transitional.	3 %.
Lymphocytes.	1 %.

The Cells are quite discrete now. The Film shows 2 Basophiles.

The third case was one in which the effect of the Rontgen Rays was clearly to accelerate the disease and to excite reactions very like those of acute toxaemia. The case was one of Lymphatic Leukaemia.

The Patient was a boy, M... M....., a Greek, aged 8, and was admitted to Ward 28, on the 20th, January 1906.

COMPLAINT.

Swelling in the Neck with pain.

His parents were very unintelligent Greeks and could not speak English. Through an Interpreter, I made out that beyond the swelling in the neck and progressive weakness - both of one year's duration - they had observed nothing wrong with the boy.

STATE on ADMISSION.

Height 3 feet, 6½ inches.

Weight 3 st. 1½ lbs.

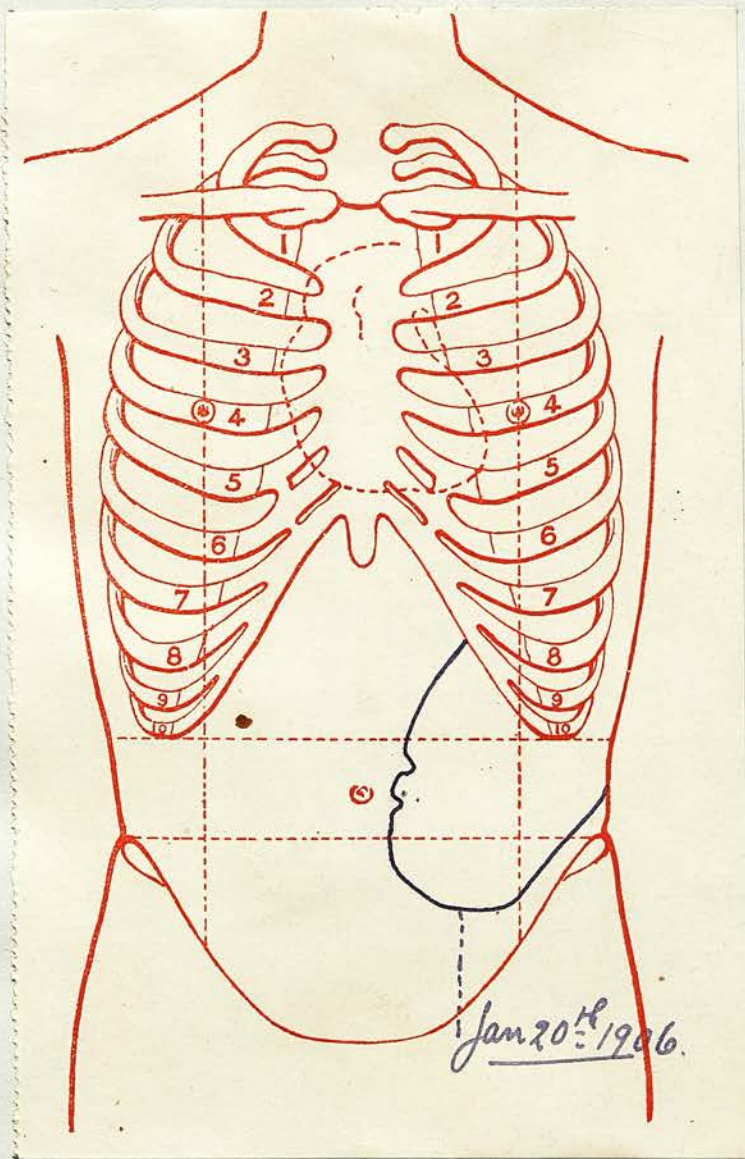
Pulse 150. Temperature 101. Respirations 42.

The Patient was fat in the face, with rather a large head. Complexion pale. Nutrition of trunk and limbs was fair. Eyelids were distinctly puffy.

The left side of his neck was occupied by several large glands, varying in size from $\frac{1}{2}$ an inch in diameter to the largest which was $2\frac{1}{2}$ inches in diameter, and situated immediately behind the lower part of the left ear. Several glands were felt deep beneath the angle of the left jaw and down the neck, the lowest being just below the lower border of the left clavicle.

The glands were freely movable beneath the skin, discrete, not hard, fairly elastic, and slightly tender to pressure.

No enlarged glands were discovered anywhere else. The did not appear to give rise to any pressure symptoms.



M—M—

Chart of Spleen.

On Admission Jan 20th

No perceptible diminution followed.
treatment.

STATE on ADMISSION.

ABDOMEN.

The Abdomen was very prominent and distended with gas.

SPLEEN.

The Spleen was palpable to within two inches of the Umbilicus. The enlargement was uniform, regular and smooth. Two notches could be felt in its anterior border. There was pain on pressure over it.

BLOOD.

Reds.	3,710, 000.
Leucocytes.	10,600.
Hb.	52 %.

DIFFERENTIAL COUNT.

Lymphocytes.	40 %.
Polymorphs.	57 %.
Eosinophiles.	3 %.

There were no Nucleated Reds.

CIRCULATORY SYSTEM.

There was nothing to note in his Circulatory System.

RESPIRATORY SYSTEM.

RESPIRATORY SYSTEM.

Respiration did not seem to be affected by the enlarged glands. His chest was full of ronchi and coarse crepitations, back and front.

Patient had a cough which was very frequent and moist. The Sputum was copious, white, frothy and contained several organisms among which were groups of Staphylococci, a few chains of Streptococci and several Diplococci.

URINE.

The Urine was very high coloured.

Specific Gravity 1017.

There was no Albumen, Sugar or Casts.

A copious deposit of dark red Urates.

ALIMENTARY SYSTEM.

His teeth were very decayed, and several were wanting. The Tongue was narrow pointed and thick, moist, clean and not pale.

The floor of the Mouth appeared raised and swollen.

There was no vomiting, nor Diarrhoea.

His appetite was poor, and his bowels were constipated.

His Liver was not enlarged.

NERVOUS SYSTEM.

There was nothing to note in regard to his Nervous System.

There were no Optic symptoms nor abnormal signs.

The Diagnosis lay between Lymphatic Leukaemia, Lympho-Sarcoma and Hodgkin's Disease.

Permission could not be obtained for the examination of one of his Glands.

Referring to this difficulty in Diagnosis the following note which appears on page 264 of Vol XLIII of the "Transactions of the Association of American Physicians"

" Dr Thayer said he remembered 2 cases which in the beginning shewed glandular enlargement suggestive of Hodgkin's Disease, with but little Anaemia; the blood showing nothing characteristic excepting a rather large relative proportion of

" of the smaller form of lymphocytes. Later on
 " however there developed the characteristic blood
 " picture of small celled Lymphatic Leukaemia.
 " Both of these instances were in adults."

Another instance of the difficulty of diagnosing such cases is reported on Page 254 of the same Volume by Dr John Lovett Morse.

The Patient was a Jewess, aged 3½, whose only complaint was a tired feeling and pain in the ears. She had been losing weight and strength for two months and had had occasional attacks of Abdominal pain, Nausea and Vomiting for some weeks. Puffiness of Face and swelling of Neck for 2 weeks before admission. No Haemorrhages.

The Blood Count showed

Reds.	1,765,000.
Whites.	19,000.
Hb.	41 %.
Small Mononuclear	58.
Large Mononuclear.	9.
Polymorphs.	32.8.
	0.2.

Considering the age of the child no

definite diagnosis could be made. In spite of treatment (drug), she grew rapidly worse. Petechial haemorrhages and Spongy Gums appeared. But the Blood showed nothing characteristic till 2 months after the first count, when it showed,

Reds.	3,216,000.
Whites.	30,000.
Hb.	55 %.

DIFFERENTIAL COUNT.

Lymphocytes.	91.4 %.
Polymorphs.	8 %.
Eosinophiles.	0.4 %.

The increase in Leucocytes from 19,000 to 30,000, with the large and increased percentage of Lymphocytes, enabled the Diagnosis of Lymphatic Leukaemia to be made. A Gland was excised and confirmed the Diagnosis. The Child died a month later. No Autopsy.

After a week's observation, Dr Bramwell pronounced the case I have described as M.. M.. M., to be one of Lymphatic Leukaemia.

For a week the patient was kept warm in bed. His temperature swung between 98 in the morning to 100. in the evening. During the week his Bronchitis almost entirely cleared up and his constipation and Flatulance yielded to treatment. He was put on Liq: Arsenicalis M ii, t.i.d.

On January 31st Rontgen Ray treatment was commenced. For two or three hours after, patient lay in a semi-exhausted condition, and refused his food. That night he perspired profusely, but there was no definite Rigor. His cough became very troublesome and his sputum at once became copious and frothy.

On the morning of the 1st February, he seemed well and bright again and was sent to the Rontgen Ray Department. On his return he was exhausted as on the previous day. He lay drowsily the whole afternoon, only rousing to cough. The perspiration was profuse and his expectoration was

copious. There was no alteration in the swinging temperature. The Rontgen Ray Treatment was suspended after two administrations.

After three days his symptoms had subsided - the perspiration had ceased, and the cough and spit much diminished.

On February the 5th, 6th, and 7th, he was again treated with Rontgen Rays.

The Glands in his neck during this time became distinctly larger and much softer. After each administration he was brought back to the Ward exhausted. His temperature now swung between 99 and 101.2. Perspiration became profuse and almost constant. Cough and Sputum much increased - one or two pints of the latter in 24 hours. He was very weak and refused food.

Rontgen Rays were now suspended and not resumed. The perspiration yielded to Quinine, Digitalis, and Opium, but the patient was obviously sinking, and his parents insisted on taking him

him home.

His Spleen on discharge was if any thing a little larger than on admission. It was also distinctly softer.

On making enquiries at the boy's home in Bonnyrigg, I learnt that he gradually sank and died 3 weeks after his discharge from Hospital.

Clinically the results following Rontgen Ray treatment in this case of Lymphatic Leukaemia may be put down as :-

1. A period of prostration, following immediately after receiving each exposure and lasting for from 2 to 4 hours.
2. Profuse perspiration, at first only in the evenings of the days on which he received exposures - later becoming almost constant.
3. Loss of appetite.
4. Recurrence of Bronchitis. Copious expectoration - which had almost ceased, began again in the evening of the day of his first

exposure. The Sputum was always increased in amount immediately after the exposures to Rontgen Rays.

5. The Glands in the Neck became softer and smaller.

6. The Spleen became softer and a little larger

This was a case in which no improvement in the blood condition followed Rontgen Ray treatment. On the contrary, the reds which had increased from 3,710,000 on January 20th to 3,990,000 on January 27th, fell, following the Rontgen Rays, during February to 3,360,000 and on March 5th, they were 2,180,000. The Leucocytes which were 14,000 (not an abnormal number for a boy of his age - 8 years) fell after treatment to 9,600 and later to 6,600, while the Hb. sank from 50 %, to 38 %.

The Kidneys did not appear to have been affected, and no Albumen appeared in the Urine.

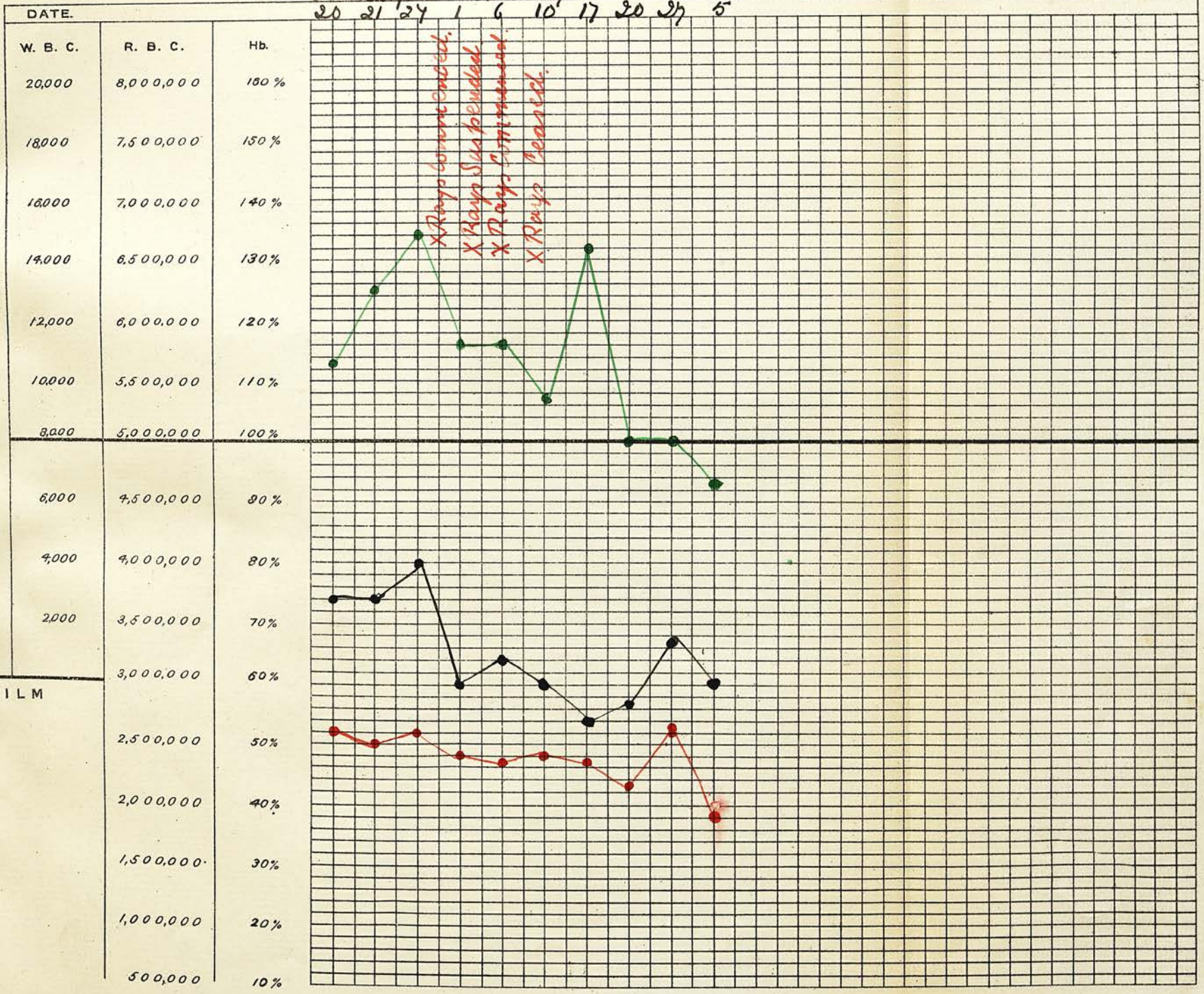
From the facts, and from the impression I got from watching the patient during the treatment, I am convinced that in his case, the

Rontgen Rays accelerated the Disease, and it adds another instance to those recorded of the failure of the Rontgen Rays to do any good in advanced cases of Lymphatic Leukaemia.

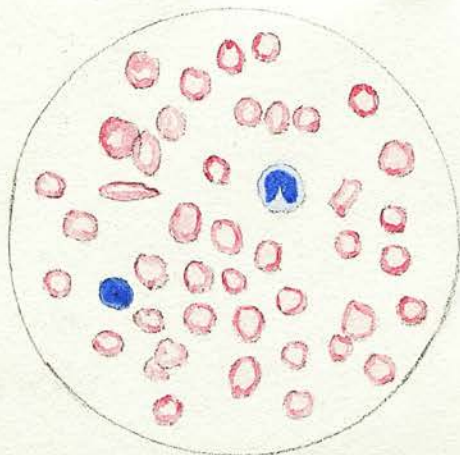
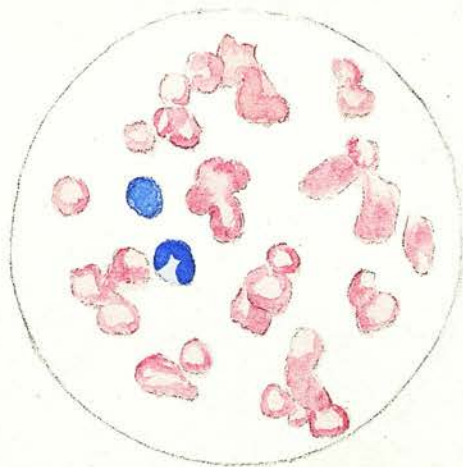
DATE	REDS.	WHITES.	Hb.
JANUARY.			
January. 20th.	3,710,000.	10,600.	52 %.
21st.	3,730,000.	13,000.	48 %.
27th.	3,990,000.	14,800.	50 %.
February			
February. 1st.	3,000,000.	11,200.	46 %.
6th.	3,290,000.	9,600.	47 %.
10th.	3,080,000.	9,600.	46 %.
17th.	2,710,000.	14,400.	47 %.
20th.	2,790,000.	8,000.	43 %.
27th.	3,360,000.	8,000.	53 %.
MARCH.			
March. 5th.	2,180,000.	6,600.	38 %.

NAME. ~~H. R. M. M.~~ M.
 AGE.
 DISEASE.

January 20 21 27 1 6 10 17 20 27 5
 February
 March.



LEUKOCYTES GREEN ERYTHROCYTES BLACK HÆMOGLOBIN RED



BLOOD FILM No 9. M M. (Lymphatic Leukaemia)

On Admission 20-1-06

Reds.	3,710,000.
Hb.	52 %.
Leucocytes.	10,600.
Lymphocytes.	40 %.
Polymorphs.	57 %.
Eosinophiles.	3 %.

The Red Cells are clustered together in this Film, which Shows 1 Polymorph and 1 Lymphocyte.



Film No 10.

M. M.

On Discharge. 5 - 3 06.

Reds.	2,180,000.
Hb.	38 %.
Leucocytes.	6,600.
Lymphocytes.	44 %.
Polymorphs.	55 %.
Eosinophiles.	1 %.

The Cells are discrete and show marked Poikilocytosis.
Each Red Cell is markedly Anaemic.

The fourth of Dr Bramwell's cases is a girl who is at present under treatment in Ward 30.

She has Myelogenous Leukaemia.

M.. S., aged 27, single, and lives at home.

Admitted 3rd March 1906.

COMPLAINT. Pain and Swelling in left side.
Progressive Weakness.
Shortness of Breath.

HISTORY. She had a severe attack of Influenza in the beginning of October last. She was in bed for a fortnight during which she felt occasional sharp, cutting pains just under the left lower ribs. After being up for a week, she had a relapse. The influenza returned and she spent 2 months, November and December in bed. During this time the pain in left side was always present, sometimes very severe. It made her catch her breath and was worse when she coughed. She rose from her bed during New Year week, very weak and short of breath on exertion. The pain in her side became more severe and she had

had occasional pains in the small of her back.

It was then that she noticed her clothes were getting tight round her waist - due to a swelling in her left side. She has been up and about since New Year but has not regained her strength. Pain in her side had persisted till a fortnight before admission butv has been absent ever since. The swelling in her side persisted but she thinks it is less now than when it was first noticed.

PREVIOUS HEALTH. "Bloodlessness" 6 or 7 years ago from which she recovered after three months on "pills".

FAMILY HISTORY. Father alive, 53, healthy.
 Mother alive, 55, healthy.
 Seven in family, 5 boys and 2 girls, all alive and healthy. One sister aged 30, was treated for "bloodlessness" in the Royal Infirmary, Edinburgh, 7 years ago.

SOCIAL CONDITION and HABITS.

Very Satisfactory.

STATE on ADMISSION.

Height 5 feet 4½ inches. Weight 9 st. 7 lbs. Pulse 76. Temperature 98. Respirations 22.

Patient has a healthy appearance. Her development is good but muscles are rather soft and flabby. She perspires profusely, day and night. The mucous linings are rather anaemic. There is no visible swelling in the abdomen. On percussion and palpation the Spleen is found to extend 3 inches across the middle line at the level of the Umbilicus ~~in the middle line.~~ There is tenderness to pressure where the Spleen crosses the middle line, midway between the Umbilicus and Xiphisternum. No where else. There is ^{no} tenderness over ends of long bones nor over Sternum. Three small very hard glands are felt in the left groin. None on right side or any where else.

BLOOD COUNT.

Reds.	2,830,000,
Whites.	204,000.
Hb.	56 %.

DIFFERENTIAL COUNT.

Polymorphs.	45 %.
Myelocytes.	40.5 %.
Eosinophiles.	4 %.
Lymphocytes.	6.5 %.
Basophiles.	3 %.
Transitional.	1 %.

CIRCULATORY SYSTEM.

Pulse regular. Expansion full.

tension good.

HEART. Apex in 5th space, $\frac{1}{2}$ an inch internal to nipple line. Very faint soft Mitral Systolic. Rather louder Pulmonary Systolic. No other murmurs. Heart not enlarged.

MENSTRUATION.

Regular. 28 day type. Severe pre-menstrual pains for 1 day. Flow lasts 3 days. Lost an unusually large amount of blood at her last period three weeks ago.

OPTIC DISCS.

There was nothing abnormal in the Discs but the veins of the Fundus were slightly

dilated.

Dr Shennan's report of his examination of her blood for microorganisms is as follows :-

" 10 cc of blood taken on the 19th inst were
" distributed in ten tubes and one flask of
" Medium. Broth. Glucose Broth. Agar and Milk
" Broth, and no organism has so far developed
" in any. All are sterile. 24 -3 - 06."

URINE.

The Urine was neutral and contained no abnormal constituents.

TREATMENT and PROGRESS.

March 6th. She was put on Liq: Arsenicalis,
M ii, t.i.d, to increase M i every fourth day to
M viii.

MARCH 8th. Rontgen Ray treatment was commenced as follows :- Daily exposures, the splenic region anteriorly, laterally and posteriorly being treated in order, 5 minutes each. A soft tube with an amperage of 5 was used.

March 10th. Patient commenced to menstruate profusely and felt weak and rather prostrate. There had been no rise in temperature following the Rontgen Ray treatment, Rontgen Rays suspended temporarily. Her leucocyte count today is 254,000 an increase of 50,000 during the past week.

March 16th. Menstruation ceased. It had been more severe than patient remembered before.

Rontgen Rays resumed.

March 29th. Four days after Rontgen Ray treatment was recommenced, on the 16th, the temperature began to swing between 97 in the morning and 99 to 100.4 in the evening. After every exposure the patient feels rather prostrated for from two to three hours.

The Leucocyte count has fallen to 187,000 and there are fewer myelocytes proportionately but there is no apparent change in the size or consistency of the Spleen.

April 1st. Last night patient's temperature rose to 101.4. She is perspiring rather freely and

shows indications of a toxæmia. She complains of a general soreness over the front of the chest and there is slight pain on pressure over the sternum.

April 4th. Patient has been treated during the last 4 days with the Ward triple powder containing Salicylate of Soda, Quinine and Phenacetin. The temperature under this treatment has ranged between 96.4 and 99, but the sweatings have continued.

The patient's skin has a distinct yellowish hue and she looks more prostrated and ill than before. The Rontgen Ray treatment was to-day discontinued.

April 8th. Patient feeling and looking much better. Rontgen Rays recommenced.

April 10th. Temperature rose yesterday evening to 100.

April 11th. During the last few days the patient has been complaining of a pain in her left side which has been getting worse and which kept her awake last night. It is worse on taking a long

breath. On palpation, distinct friction can be made out over the anterior part of the enlarged Spleen, and this part is tender to pressure. Rontgen Rays suspended.

April 16th. Pain has disappeared and the feeling of prostration *and* mallaise has also disappeared.

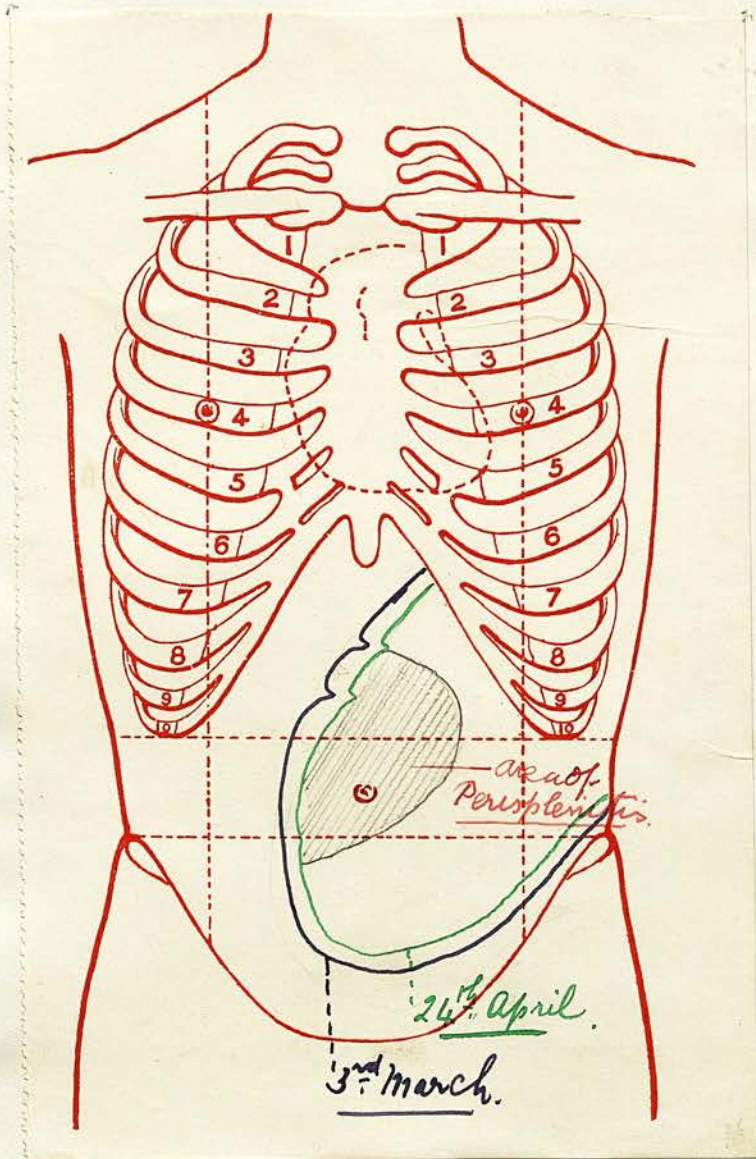
The Leucocytes have fallen from 120,000 to 60,000 during the last fortnight. The Spleen is softer and more freely movable, but the area of splenic dulness has not diminished. Rontgen Rays resumed.

April 24th. During the last week the patient has been steadily improving in every way, though during the last few days there has been a slight trace of Albumen in her Urine. The Blood Count to-day is

Reds.	3,730,000.
Hb.	52 %.
Whites.	29,800.

DIFFERENTIAL COUNT.

Polymorphs.	44 %.
Myelocytes.	34 %.
Leucocytes.	10 %.
Basophiles.	5 %.



M-S- Chart of Spleen.

Showing slight diminution
after 5½ weeks treatment.

Shaded area = Perisplenitis

Eosinophiles.	2 %.
Transitionals.	5 %.

This shows an increase since admission in Reds of 900,000, the Hb has been stationary and the Whites have diminished by 174,200. The Myelocytes have diminished from 40.5 % to 34 %, the Polymorphs have remained stationary, the Eosinophiles have diminished from 4 % to 2 %, while the Basophiles have increased from 3 % to 4 %. Except for the last point the blood picture offers a very hopeful prognosis though - as has been pointed out before - experience shows that the blood picture alone is not sufficient in itself to enable one to form a favourable prognosis.

The anterior border of the Spleen has retracted $\frac{1}{2}$ to 1 inch (see Chart). Her temperature has partly lost its swinging type and varies from 97 to 99. Her colour has improved, her perspiration has ceased and she says she feels better and stronger than she has done for some months. It will be

noted that in this case, while diminution in the Leucocyte Count commenced within 5 days after the commencement of Rontgen Ray treatment, general symptomatic improvement only began a week ago, that is 5½ weeks after the commencement of treatment, accompanied by distinct diminution in the size of the Spleen. I noticed to-day that the patient's hair was not so thick as it used to be and she told me that it has been coming out profusely during the last three weeks. It has never done this before. The metabolism of this patient before and after the commencement of Rontgen Ray treatment, is discussed under "Effects on Metabolism" on page 173.

The patient is still undergoing treatment in Ward 30.

The results following the Rontgen Ray treatment may be summarised in this case of Spleno-Medullary Leukaemia as follows:-

1. General improvement of blood picture,

increase of Reds, diminution of Whites and proportionate diminution in the leucocythaemic elements of the Whites.

2. Softening and diminution in size of the Spleen.
3. General symptomatic improvement (somewhat delayed in commencing).
4. Peri-Splenitis, which has become chronic.
5. Swinging temperature and occasional tox-aemic symptoms.
6. Increase in Menstrual flow.
7. Loss of hair (which may be due to an indirect action of Rontgen Rays - there is no other apparent cause.)
8. Appearance of Albumen in her Urine.

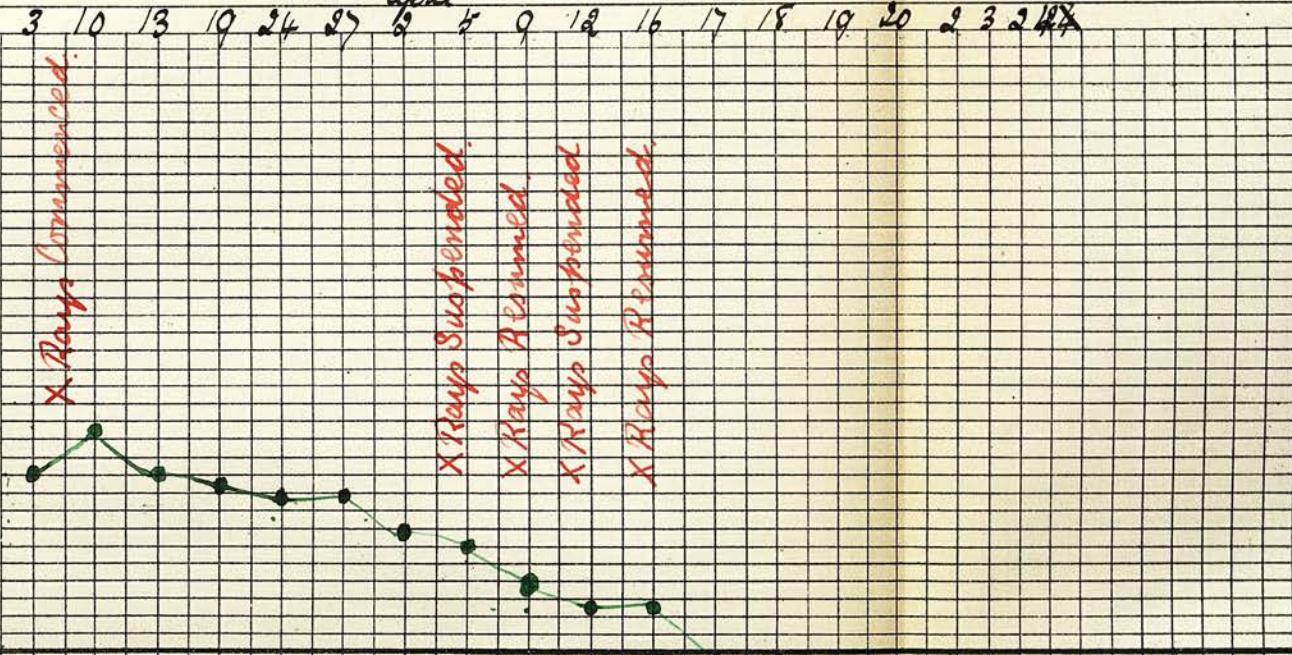
The following are her blood tables and charts.

Blood Tables and Charts. M.. S....

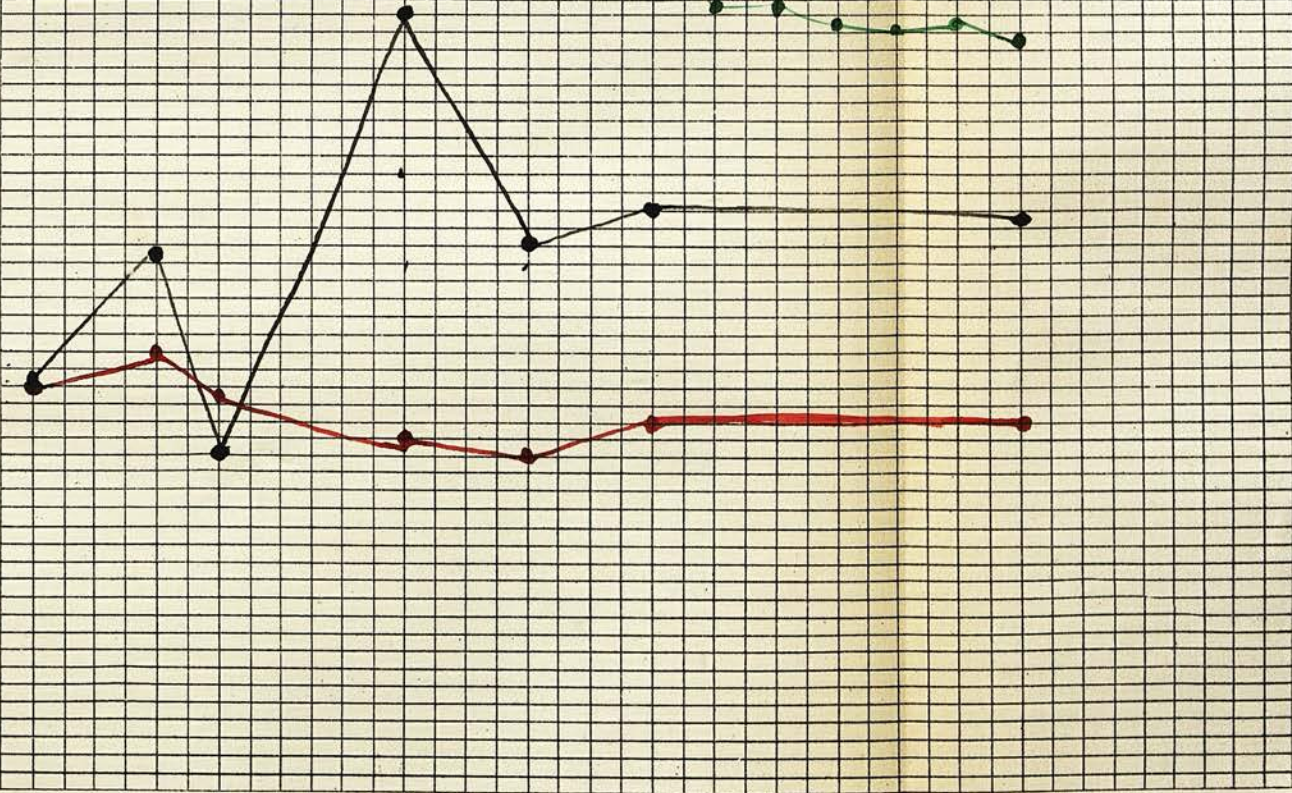
DATE.	Hb.	R. B. C.	W. B. C.
March 3rd.	56 %.	2,830,000.	204,000.
March 10th.			254,000.
March 13th.	60 %.	3,560,000.	204,000.
		Rontgen Rays commenced.	
March 19th.	55 %.	2,240,000.	194,000.
March 24th.			182,000.
March 27th			187,000.
April 2nd.	50 %.	4,900,000.	144,000
April 5th.			120,000
April 9th.	48 %.	3,600,000.	86,000.
April 12th.			58,000.
April 16th.	52 %.	3,800,000.	60,000
April 17th.			41,000.
April 18th.			46,000.
April 19th.			38,000.
April 20th.			34,000.
April 23rd.			37,000.
April 24th.	52 %.	3,730,000	29,800.

March 3 10 13 19 24 27 April 2 5 9 12 16 17 18 19 20 23 24

DATE.	W. B. C.	R. B. C.	Hb.
	600,000	8,000,000	160%
	500,000	7,500,000	150%
	400,000	7,000,000	140%
	300,000	6,500,000	130%
	200,000	6,000,000	120%
	100,000	5,500,000	110%
	50,000	5,000,000	100%



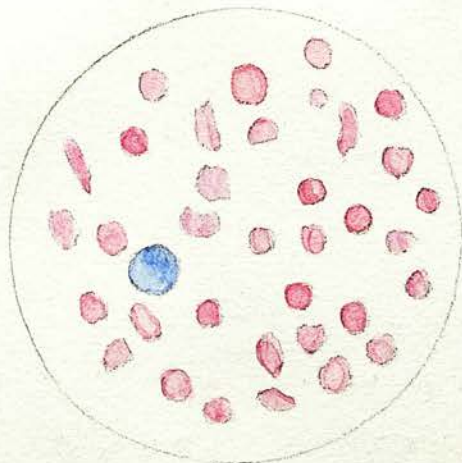
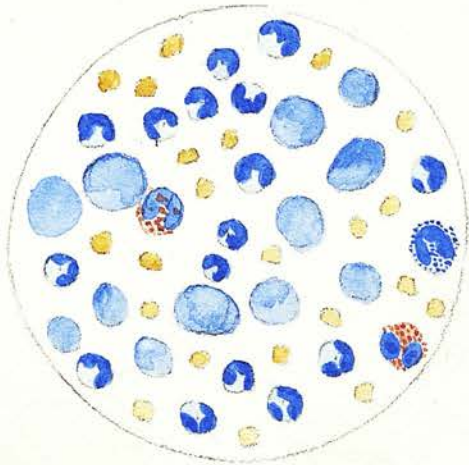
DISEASE.	FILM	LEUKOCYTES GREEN	ERYTHROCYTES BLACK	HÆMOGLOBIN RED
	10,000	9,500,000	90%	
	6,000	9,000,000	80%	
	4,000	3,500,000	70%	
		3,000,000	60%	
		2,500,000	50%	
		2,000,000	40%	
		1,500,000	30%	
		1,000,000	20%	
		500,000	10%	



LEUKOCYTES GREEN

ERYTHROCYTES BLACK

HÆMOGLOBIN RED



FILM No 11. M. S. (Spleno) Medullary Leukaemia)

On Admission, 3-3-06.

Reds.	2,830,000.
Leucocytes.	204,000.
Hb.	56 %.
Polymorphs.	45 %.
Myelocytes.	40.5 %.
Eosinophiles.	4 %.
Lymphocytes.	6.5 %.
Basophiles.	3 %.
Transitional.	1 %.

The Cells are well formed and discrete. 2 Eosinophiles and 1 basophile were in this field. (Jenner)

Film No 12. M. S.

After 6 weeks treatment. 24-3-06

Reds.	3,730,000.
Hb.	52 %.
Leucocytes.	29,800.
Polymorphs.	44 %.
Myelocytes	34 %.
	10 %.
Basophiles.	5 %.
Eosinophiles.	2 %.
Transitional.	5 %.

The Reds are rather Anaemic looking and there is some poikilocytosis. This field showed 1 Myelocyte

The next case is one of Splenic

Anaemia of three years duration, who, having been treated with Arsenic and Blaud's Pills for 4 weeks with increase in his symptoms, showed marked improvement under 5½ weeks Rontgen Ray treatment, his Haemoglobin recovering in that time from 25 % to 62 %, and his Reds from 2,810,000 to 4,260,000, with slight diminution in the size of his Spleen.

W... B..., aged 27, Single, an Engine Fitter. Admitted to Ward 28, May 21st. 1905.

COMPLAINT.

- Vomiting of Blood.
- General Weakness.

HISTORY.

Three years ago he suddenly felt a sharp pain in his left iliac region. Ten minutes later he felt faint and vomited a large amount of blood, bright red. He continued to vomit blood in smaller quantities for 18 hours. Since then he never regained his strength and worked off and on till

March 1904, when he again vomited blood. Since then had been much weaker but had not lost weight. His complexion had been yellowish for 3 years. He had never been abroad and denies Syphilis and Gonnorrhoea.

PREVIOUS HEALTH.

Pleurisy when aged 16.

Epistaxis at intervals prior to March 1902. None since.

FAMILY HISTORY.

Good.

SOCIAL CONDITIONS and HABITS.

His home was in a low lying part of Doncaster, near the river. His workshop was considered unhealthy owing to constant nasty smells from the engines.

He had always been Teetotal.

STATE ON ADMISSION.

Height 5 feet 6 $\frac{3}{4}$ inches.

Weight 10 stone, 7 $\frac{1}{2}$ lbs.

Pulse 84.

Temperature 97.

Respirations 24.

He was fairly well developed, and well nourished, but the muscles were soft. His skin was of a decided orange-yellowish colour, more marked on face and hands. His mucous membranes were very pale. His sclerotics were distinctly bluish. There was no Jaundice nor oedema.

HAEMOPOIETIC SYSTEM.

BLOOD. Reds 4,030,000, the Corpuscles were very pale.

Whites 3,800.

Hb. 48 %.

DIFFERENTIAL COUNT. 84.6 %.

Polymorphs.

Lymphocytes. 9.3 %.

Large Mononucleated 3.3 %.

Basophiles. 1 %.

Eosinophiles. 1.6 %.

There was some slight Poikilocytosis.

There were no nucleated Reds seen.

SPLEEN.

The Spleen was enlarged. It extended to within $1\frac{1}{4}$ inches of the Middle Line, midway

between the Umbilicus and Xiphisternum. While it extended $3\frac{1}{2}$ inches below the Costal Margin in the Left Mammary Line. The Spleen was hard and smooth to palpation, the edges were uniform, and there was no tenderness over it.

GLANDS.

There were a few enlarged glands about $\frac{1}{4}$ of an inch in diameter in the Axillae and along the posterior border of the Sterno Mastoid.

CIRCULATORY SYSTEM.

There was shortness of breath on exertion. The pulse was regular, of good force and moderate tension.

The Heart was slightly enlarged, and Systolic bruits were heard in all the areas and in the neck.

ALIMENTARY SYSTEM.

Teeth good. Tongue, pale, slightly furred and dry. Had been troubled with pain and feeling of discomfort in region of his Stomach as

long as he can remember. Always worse after meals. Had always been constipated. There was slight tumidity of the Abdomen, and on palpation there was a distinct, small area of tenderness, the size of half a crown, situated at the junction of the left midpoupart and intercostal lines.

Nothing else was made out.

URINE.

The Urine was dark amber in colour. There was a deposit of phosphates, and microscopically a few granular casts. Specific gravity 1010. Reaction, neutral. No Albumen, blood nor sugar.

DIAGNOSIS.

Several examinations of the Blood - as shown in table - showed constant diminution in Leucocytes, and absence of Myelocytes or of any special features - excluded Leucocythaemia.

The Liver was small, but he was a teetotal

The character of the Blood and the

Colour index excluded Pernicious Anaemia. There was no history of Malaria, and Dr Bramwell pronounced the case to be Splenic Anaemia.

TREATMENT and PROGRESS.

May 29th. Treatment commenced with Liquor

Arsenicalis in increasing doses.

May 30th. Patient had a severe haematemesis, 53

ozs of blood. No pain or discomfort.

June 6th. His Reds and Hb were rapidly

decreasing (see table). He was started on Blaud's

Capsules in addition to the Arsenic and kept strictly

in bed on a light diet. His temperature - except

when he had the haematemesis - swung between 98

and 99.

June 22nd. The diminution in Reds and Hb was

continuing. Rontgen Ray treatment was commenced

as in Dr Bramwell's other cases. Applications

being directed to the Spleen. After the second

day's application, his temperature remained

subnormal the whole of the remainder of the time he

71.

was under treatment.

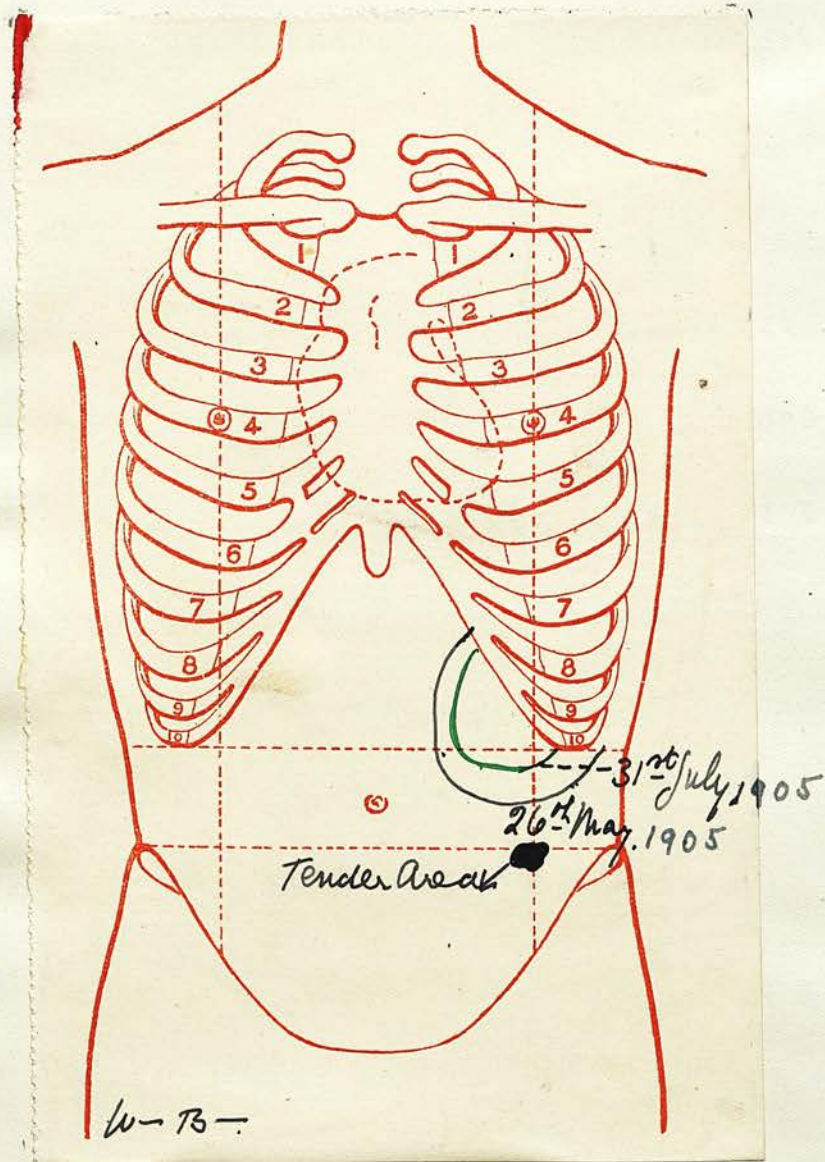
June 26th. After 4 days Rontgen Rays patient looks much better than he did on admission. He is less yellow and said he felt better and less tired out.

There was an increase in his Hb from 25 % to 35 %, but his Reds were still diminishing. (See Table). *Page 75.*

July 21st. There had been steady and continuous improvement with no toxaemic effects of the Rontgen Rays. Patient was now put to sleep in the open air and said he never felt better in his life. His weight which had dropped from 10 stones $7\frac{1}{2}$ lbs on May 24th to 9 stones $6\frac{1}{2}$ lbs, on June 23rd, the day after the Rontgen Rays commenced, had steadily risen to 9 stones $11\frac{1}{4}$ lbs.

July 30th. The yellowness in patients skin had almost disappeared. His Blood Count was:-

Reds.	4,260,000.
Whites.	4,200.



W.- B.- Splenic Anaemia. Chart of Spleen
Showing diminution in size
after 9½ weeks.

Hb. 62 % - an increase
after 5½ weeks Rontgen Rays of 37 %.

There had been no further dyspeptic
symptoms nor any more haematemesis.

His Spleen had diminished only
slightly as in Diagram.

In this case none but benign results
followed the administration of the Rontgen Rays,
and as the patient was getting worse under drug
treatment at the time when the exposures were
commenced, their beneficial action is particularly
well shown.

April 24th 1906. I wrote and asked W.. B.. to
come up from Darlington where he lives for
examination and he came today.

He says he has had no more haemorrhages of any description. His bowels have been quite regularly free. He has had no stomach troubles
His only complaint is that he "does not get as

strong/

strong as he should do and gets short of breath on exertion." He has not been getting weaker but he never regained his former strength.

He looks well, his complexion is healthy and clear. There is no appearance of the lemon yellow colour he had when he was in the Ward a year ago. There is a little anaemic pallor about his conjunctiva but his lips are red.

His weight is now 10 st. 4 lbs.

His Spleen reaches a hand's breadth below the costal margin. It is soft, movable, there is no pain nor tenderness on pressure. His Liver is normal.

His temperature is subnormal. Pulse 60, soft and irregular. Soft blowing systolic murmurs are heard in all the cardiac areas, most probably haemic.

His Blood Count is:-

Reds.	4,000,040.
Hb	72 %.
Leucocytes.	6,900.

The Differential Count is :-

Polymorphs.	70 %.
Myelocytes.	16 %.
Large Mononuclears	10 %.
Lymphocytes.	2 %.
Eosinophiles.	2 %.

The large single nucleated cells, which numbered 3.3 % of the White Cells 10 months ago have increased to 26 %, 16 % of which I have classed as Myelocytes and 10 % as large mononuclears but I found it difficult to decide into which group to place a large number of these cells.

It is evident that the improvement in his general condition which followed the Rontgen Ray treatment has been maintained during the past 9 months, while the only change in his blood is this increase in the large mononucleated white cells.

N.B. In all these five cases Dr Bramwell had the blood examined by the Infirmary Pathologist for microorganisms and in each case the Report was negative.

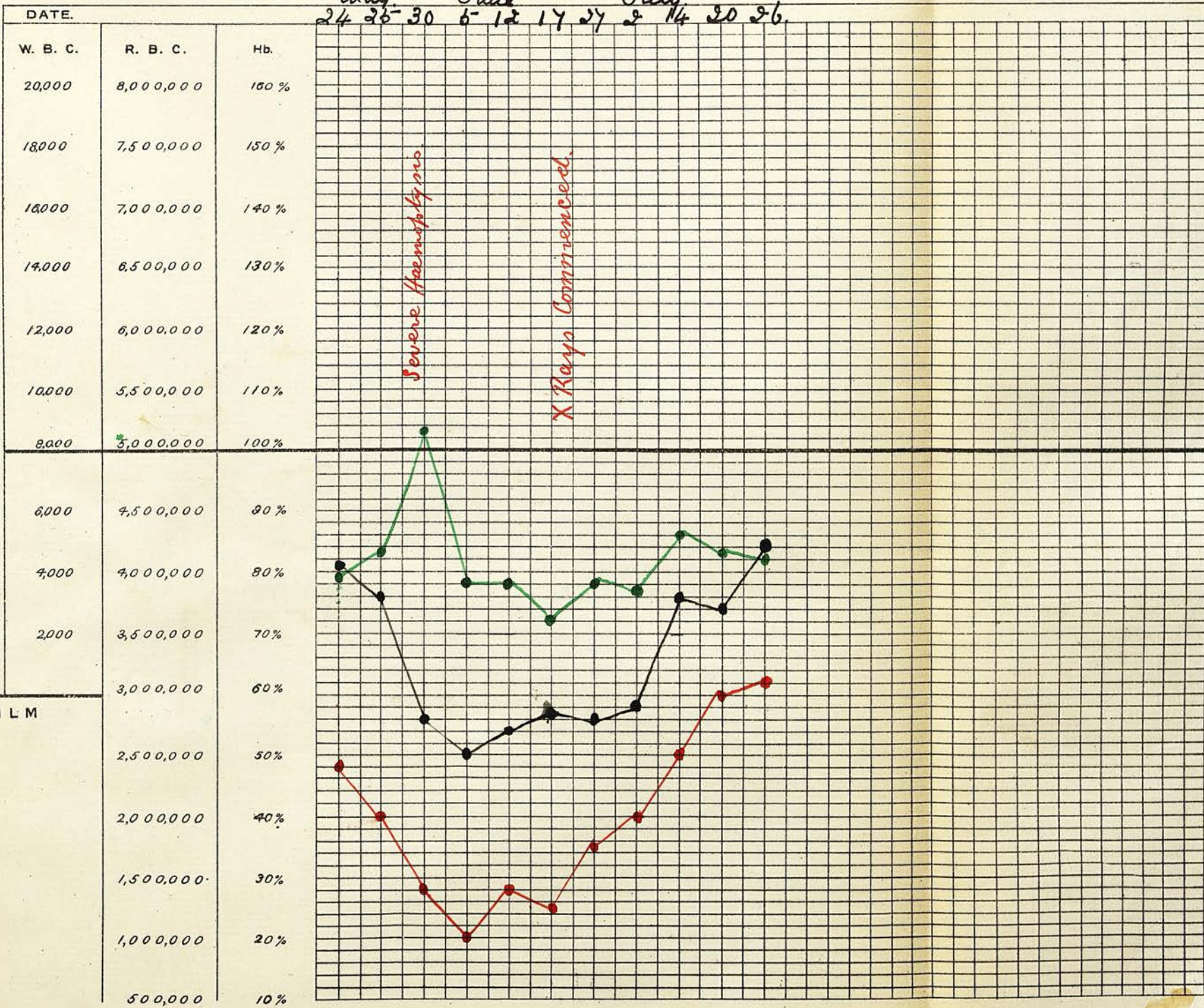
Blood Table. Splenic Anaemia. W... B...

Date.	Reds.	Whites.	Hb.
May 24th.	4,030,000.	3,800.	48 %.
May 25th.	3,790,000	4,400.	40 %.
May 30th.	2,800,000.	8,600.	28 % after haemorrhage.
June 5th.	2,440,000	3,600.	20 %.
June 12th.	2,690,000.	3,600.	28 %.
June 17th.	2,840,000.	2,400.	25 %.
Rontgen Rays commenced.			
June 27th.	2,810,000.	3,700.	35 %.
July 2nd.	2,890,000.	3,500.	40 %.
July 14th.	3,810,000.	5,200.	50 %.
July 20th.	3,700,000.	4,400.	60 %.
July 26th.	4,260,000.	4,200.	62 %.

On examination , 24th April 1906,

4,040,000. 6,900. 72 %.

May 24 25 30 June 6 12 17 27 July 2 14 20 26



Severe Haemoptysis

X Rays Commenced

W 13

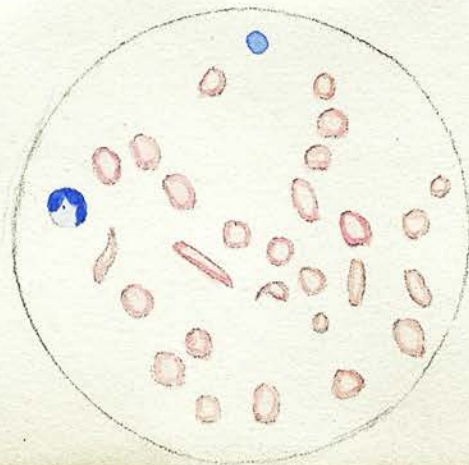
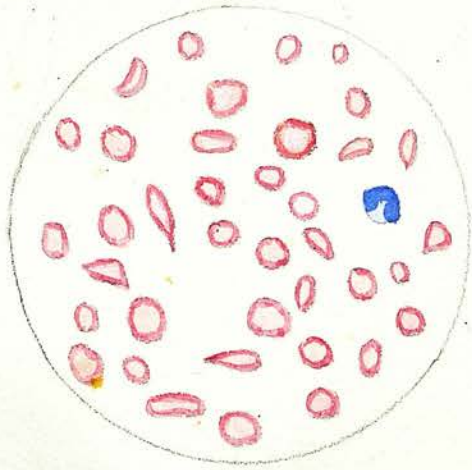
NAME.
AGE.
DISEASE.

F I L M

LEUKOCYTES GREEN

ERYTHROCYTES BLACK

HÆMOGLOBIN RED



FILM No 13. W. B. (Splenic Anaemia).

On Admission. 21 - 5 - 05.

Reds. 4,030,000.

Hb. 48 %.

Leucocytes. 3,800.

Polymorphs. 84.6 %.

Lymphocytes. 9.3 %.

Large Mononuclear. 3.3 %.

Basophiles. 1 %.

Eosinophiles. 1.6 %.

The film shows slight Poikilocytosis and Anaemia of the Reds .

FILM No 14. W. B.

After severe Haemorrhage, and 4 weeks treatment with Iron and Arsenic. 17 - 6 - 05.

Reds. 2,840,000.

Hb. 25 %.

Leucocytes. 2,400.

Polymorphs. 84.6 %.

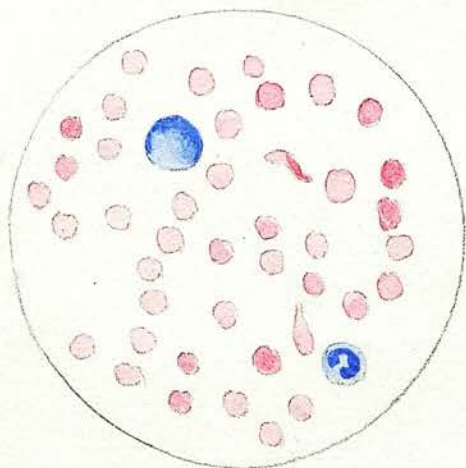
Lymphocytes. 9.3 %.

Large Mononuclear. 3.3 %.

Basophiles. 1 %.

Eosinophiles. 1.6 %.

Poikilocytosis has increased, and the Film shows great Anaemia of the Reds. I deeply regret that the slide showing the improvement in his blood following Rontgen Ray Treatment has disappeared from my collection.



FILM No 15. W. B. (Splenic Anaemia.)

Nine months after treatment had ceased.

24 - 4 - 06.

Reds.	4,040,000.	
Hb.	72 %.	
Leucocytes.	6,900.	
	Polymorphs.	70 %.
	Myelocytes.	16 %.
	Large Mononuclear.	10 %.
	Lymphocytes.	2 %.
	Eosinophiles.	2 %.

The Film shows slight Poikilocytosis, and one of that Group of Cells in which I have found much difficulty in differentiating between Myelocytes and Large Mononuclear Leucocytes.

HISTORY and RESULTS

in other

TYPICAL CASES.

----- 0 -----

The starting point in what has grown to be the almost universal treatment of Leukaemia by Rontgen Rays seems to have been a case that was reported 'Cured' by Senn, in the Medical Record, page 281, August 1903, though other Cases are reported as having been treated by Rontgen Rays prior to that. The first I can find are Pusey's.

William Allen Pusey. M.D., in his text book, "The Rontgen Rays in Therapeutics and Diagnosis" 1903, Page 552, records two Cases of Leukaemia treated by Rontgen Rays, one of which showed no improvement and the other died.

The first was a Myelogenous case.

BLOOD.

Reds. 3,000,000.

Whites. 300,000.

Hb. 50 %.

SPLEEN.

The Spleen filled the whole of the left side of the Abdomen. There were no enlarged glands. The patient was given exposures for a month with no effect. No subsequent history is given.

The Second Case was one of Lymphatic Leukaemia, and the following is a brief condensation of Pusey's Report.

The Patient was a man aged 44.

MARCH 1901. Present illness began with a chill, followed by a Fever lasting 3 days.

APRIL. Patient had an exactly similar attack.

JUNE 15th. 1901. A third similar attack, followed on the third day by a hard, red swelling in the left side of the neck, causing intense pain.

JUNE 20th. Swellings excised. No pus.

SEPTEMBER. Swelling, size of a fist, appeared in left Axilla. Removed surgically. Later swellings appeared in the left axilla and both groins.

MARCH 6th. 1902. Came under Dr Pusey's treatment.

In his right Axilla there was a mass of 5 or 6 glands varying in size from a walnut to a large egg. On the right side of the neck there was a very large mass of glands, 10 or 12 in number, the largest about the size of a small egg. All were freely movable, fairly hard and painless.

LIVER. The Liver was enlarged, the edges were sharp and the organ was not tender.

SPLEEN. The Spleen was palpable 8 c.m. below the Costal margin. The edge was hard and round but not tender. He was Cachectic.

Between March 1st and March 25th, he had 18 fairly vigorous exposures, with marked subsidence of the exposed glands. A few days after

the last exposure he was attacked with an acute illness resembling Acute Miliary Ruberculosis.

MAY 7th. 1902. He had recovered from illness. The

glands on the left side of the neck had entirely disappeared. A few other glands remained which were quite soft.

SPLEEN. The Spleen was softer and smaller.

LIVER. The Liver remained unchanged.

SEPTEMBER 6th. Returned with enlarged glands in the right axilla and right side of neck which disappeared after 4 strong exposures.

A few weeks later glands began to reappear rapidly.

NOVEMBER. 1902. The Patient Died.

BLOOD COUNTS were :-

	March.6.1902.	April 9.1902.	Sept. 6. 1902.
Reds.	2,678,000.	2,160,000.	2,480,000.
Whites.	74,300.	12,000.	102,7000.
Hb.	45 %.	43 %.	48 %.

Dr Pusey only gave this Case 22 exposures, which he described as "vigorous ones".

This Case and the Boy J.. H., of Ward 28, (Lymphatic Leukaemia)^{Page 4} are alike in the fact that in both, after The Rontgen Rays, the glands softened and disappeared - more so in the man's case than in the boy's- in both the Whites were considerably reduced in number, in both the Reds and Hb. failed to increase and both died.

Then in the Journal of the American Association for June 2nd. 1902, Drs Groosh and Stone report an interesting case of Myelogenous Leukaemia which improved up to a certain point under the Arsenic treatment and then the Disease began to advance in spite of the treatment.

Rontgen Rgys were used with marked diminution in Leucocyte count and size of Spleen, but the patient suddenly collapsed and died.

The following is a brief digest of

their Report.

The patient was a bricklayer, aged 44 and alcoholic. His illness began in June 1902 with pain in the back and diarrhoea, followed by shortness of breath and weakness.

On admission in June 1903 he is described as large framed but muscularly wasted and with brown pigmentation over neck , chest and Axillae. The Axillary Glands were enlarged to the size of a filbert. There was no oedema of the lower extremities.

ABDOMEN. The abdomen was tense, prominent, and tympanitic.

The Liver was felt below the Costal Margin with a sharp edge.

The Spleen was enormously enlarged, notched edge, firm consistency, and extended from the 7th Rib in Midaxillary line to the Umbilicus on the right, and almost to the Symphysis Pubis.

The Urine was Negative.

BLOOD. The Blood was yellowish red in colour

Reds.	2,100,000.
Whites.	960,000.
Hb.	45 %.

DIFFERENTIAL COUNT.

Polymorphs.	54.2 %.
Myelocytes.	34.1 %.
Lymphocytes.	7 %.
Transitionals.	3.3 %.
Large Mononuc	. 6 %.
Degenerates.	. 3 %.
Normoblasts	. 3 %.

Of the above 3.6 % were Eosinophiles

From June to December he was treated with Arsenic and Mercury. The Whites were reduced to 135,000; the Eosinophiles being reduced to 2.5 %.

The Spleen was reduced to extending to a hand's breadth below the Umbilicus and was soft to palpation.

During January and February the Whites steadily increased to 252,000.

The Patient was now treated with

daily applications of Rontgen Rays over the Spleen, Sternum and ends of the long bones for five minutes each. A medium hard vacuum tube being used at a distance of 6 to 8 inches.

By March 20th, after 20 treatments, a general rash developed, more marked over the chest, abdomen, face and left hand, resembling an Erythema Multiformis. The Spleen was somewhat smaller, being at the level of the Umbilicus.

The Rontgen Rays were stopped.

On March 26th. the Leucocytes were 11,360. The Spleen was harder than before treatment was begun. There were a few blisters over the Splenic area which ruptured showing a pink skin underneath.

On April 10th the Leucocytes were 10,600. The entire chest and abdomen raw, exfoliation of Epidermis only. General condition of Patient was fair.

In a few days the patient began to fail suddenly and died from asthenia. There was no evidence of any intoxication caused by the Rays at any time.

The Autopsy showed both Liver and Spleen to be in a condition of Chronic hyperplasia - the general fibrous tissue hyperplasia being well marked.

Drs Groosh and Stone end their Report as follows :-

" In the later stages of the Disease "this early passive enlargement has become an " active late hypertrophy (true), due to the " proliferation of the fibrous tissue elements; in " reality a true fibrosis.

Such was present in the Case under consideration. It would seem therefore that the greatest good may be hoped for in those cases where the Rontgen Ray applications are begun early in the course, before the hyperplasia of the cellular

constituents of the bone marrow becomes a chronic process; and in the case of parenchymatous organs, spleen and liver, before the resulting fibrous tissue proliferation has progressed so far as to perhaps seriously interfere with the functions of the organs in question.

Senn's Case was that of a Female aged 29, reported in the Medical Record page 281, August 1903.

Fourteen months before admission she became conscious of increasing weakness. Three months later her abdomen was noticed to be enlarged. It increased gradually.

Pain appeared occasionally in the left hypochondrium, lower end of Sternum and the epipheseal ends of the long bones.

On admission she was emaciated and profoundly anaemic.

The Spleen reached nearly to the

Pubis two inches across the Middle Line.

The Liver was enlarged.

The junction of the Gladiolus and
Ensiform Cartilages was exquisitely tender.

The Urine contained a slight quantity
of Albumen.

The temperature rose in the evening
to 100. The Pulse varied from 90 to 100.

She was treated with Arsenic for
three weeks without result. Then the Rontgen Ray
treatment was commenced over the Spleen, Sternum and
ends of the long bones daily for 10 to 20 minutes.

At the commencement the Blood Count
was:-

Reds.	3, 500,000
Whites.	64,800.
Hb.	56 %.
Numerous Eosinophiles.	

Occasionally during treatment the
Rontgen Rays had to be suspended for a day or two
owing to high temperature and other symptoms of

intoxication, which Senn ascribed to the absorption of broken down cellular constituents of Spleen and Blood.

Three weeks after beginning the treatment of Rontgen Rays, constitutional symptoms became marked, and the Spleen began at the same time to decrease. The blood kept improving.

The first change was a gradual disappearance of Myelocytes and Eosinophiles and the return of Erythrocytes to their normal shape.

April. 12. (Rontgen Rays began February 3rd.)

- No Myelocytes.
- A few Eosinophiles.
- No Poikilocytosis.

Treatment continued till 2nd week in June. Patient sent home "cured".

Menstruation which had been suspended for over a year, returned.

Senn said this was the first of the many cases of Leukaemia he had seen that

"recovered".

In a letter dated March 20th 1904, to Dr William J. Stone, Senn says, referring to this case that "The case of Myelo Splenic Leukaemia that had made such an excellent recovery, has returned with a moderate relapse and is again under Rontgen Ray treatment."

In this, the case resembles the case of J.. L., in my series, ^(Page 20) and also in the fact that Menstruation, which had ceased in both cases for over twelve months, became regular after treatment by Rontgen Rays had been followed for a few weeks.

This case attracted much attention both in America and in this Country, and on the Continent.

The year 1904 saw several cases treated on the same lines as Senn's. The following are the chief points in the more typical, and more fully reported of them.

Dr E. J. Brown, in the Journal of American Medical Association, March 26th, 1904, reports a Case of Myelogenous Leukaemia, symptomatically cured by Rontgen Ray treatment.

BLOOD EXAMINATION at beginning of TREATMENT.

Reds.	2,600,000.
Whites.	800,000.
Polymorphs.	40 %.
Myelocytes.	40 %.
Eosinophiles.	8 %.
Hb.	65 %.

SPLEEN.

The Spleen extended from the 7th Rib in the Midaxillary line to two fingers breadth below the Umbilicus in the left Mammary line; to the right it extended one finger's breadth across the middle line.

Treatment consisted in the use of Arsenic and Iron, internally, and Rontgen Ray applications to the Splenic region twice weekly.

After two months the Leucocytes

numbered 280,000 . After this the Rontgen Rays were applied daily to the Splenic region, ends of long bones and over the Sternum. The Iron and Arsenic was suspended. Two months later the Leucocytes numbered 129,000, Polymorphs 60 %., Myelocytes 25 %., and Eosinophiles 5 %.

The Blood formula showed a constantly decreasing number of Leucocytes, the Myelocytes also relatively decreasing with reduction in the size of the Spleen.

Three months later :-

Whites.	7, 894.
Reds.	4, 690, 000.
Hb.	95 %.

During the treatment there were no toxæmic symptoms, nor rise of temperature, though there was a little Dermatitis over the Spleen.

The treatment extended over 7½ months and improvement took place after the Iron and Arsenic were stopped.

Of other Cases recorded by Americans

George Dock M.D., in "American Medicine" for

December 24th 1904, gives an interesting analysis of 29 Cases of Leukaemia which were treated by the Rontgen Rays.

Acute Lymphatic form, two cases, both of which died.

Sub Acute Lymphatic form, three cases, two of which died and one improved.

Splenomedullary form, twenty one cases, ten of which are not sufficiently reported and in eleven the Leucocytes fell to normal.

His technique was to give exposures over the Spleen, the Epiphyseal ends and shafts of long bones and over the Sternum.

He found it impossible to estimate the dosage as the terms used by different operators vary. The time of exposures varied from 10 to 20 minutes.

EFFECT on DISEASED ORGANS.

In all chronic cases the glands were diminished.

The effects on the Spleen were not uniform, complete reduction not always being obtained. This may be due to the Connective Tissue overgrowth.

The Subjective symptoms were improved in most cases and the Oedema very often disappeared.

The improvement so often observed offers a striking contrast to the fact that relapses and even deaths have occurred among patients apparently most improved, not only generally but as regards the blood.

Toxic symptoms were noticed in several cases, some due to Rontgen Rays.

He considers this toxaemia one of the dangers of Rontgen Ray treatment.

Another important case is reported

by Dr J. T. Dunn in "The American Practitioner and News", July 15th, 1904.

The Patient was a female aged 26, a primipara. Her weight was 110 lbs. Her face and limbs were thin. Her complexion was muddy. She exhibited great debility. Her abdomen was as large as full term. She suffered from heavy and offensive sweats and amenorrhoea. The urine was negative. Her abdomen was filled to within two inches of the pubic bone, by a mass which was very hard, slightly movable, not painful nor tender to touch. She was given exposures almost daily of ten minutes duration. A hard tube was used 8 inches from the skin.

After two weeks the appetite began to improve and the sweats to diminish. After 36 treatments the appetite was splendid, the sweats were gone and the Spleen much diminished in size and quite soft.

After 75 treatments in 91 days, the Spleen could hardly be detected. The skin was a normal colour. The lips which had been pale were rosy. The weight had increased by $9\frac{1}{2}$ lbs, in spite of the diminution of the Spleen. The improvement in her blood is shown in the following tables.

The persistent presence of 15 % of Myelocytes and 5 % of Eosinophiles after ten months treatment does not coincide with their earlier disappearance in most of the cases recorded in this thesis.

BLOOD.

October 6th. 1903.

Reds.	4,600,000.
	128,000.
Hb.	60 %.
Reds irregular in shape and size.	
No	

Whites.

Large Lymphocytes.	8 $\frac{1}{3}$ %.
Small Lymphocytes.	2 $\frac{2}{3}$ %.
Polymorphs.	39.

Eosinophils.	7 2/3
Myelocytes.	38.

June 10th. 1904.

Reds.	5,544,000.
Whites.	37,000.
Hb.	65 %.
Reds same as before.	

Whites.

Large Lymphocytes	5 %.
Small Lymphocytes	10 %.
Polymorphs.	65 %.
Eosinophiles.	5. %.
Myelocytes.	15. %.

Doctors Bryant and Crane in "The

Medical Record" 1904, page 574, record a case of Splenomedullary Leukaemia treated by Rontgen Rays, which they class as "recovered". It was a woman aged 33 in whom the 1st symptoms of the disease had appeared one year previously.

They saw her first on September 29th 1903. Her Spleen was greatly enlarged, her Leucocytes numbered 176,000, the Myelocytes predominating

predominating. Eosinophiles were greatly increased, there was Poikilocytosis, and there were a few nucleated Reds.

Treatment with Arsenic, iron and Rontgen Rays was at once commenced. In two weeks the Leucocytes numbered 55,700, the Polymorphs were now predominating. Treatment had to be suspended for a few days on several occasions, on account of fever and intoxication.

On November 1st the Leucocytes numbered 4,500 in normal proportions and the Spleen was nearly normal in size and there was marked general improvement.

On November 27th the Patient was discharged "cured".

Doctors Bryant and Crane did not then know what experience has since taught us, that these so called "cured" cases almost inevitably at a later date suffer relapses and return for

further treatment.

In the "Journal of the American Medical Association", March 25th, 1905 Doctors Brown and Jack report a case of Splenomedullary Leukaemia in which the treatment by the Rontgen Rays was followed first by improvement and then by death. The Leucocytes had diminished under treatment from 800,000 to 7,000 and the case was discharged, but a few months later there was a relapse and in spite of the Rontgen Rays the patient became progressively worse, and died 16 months after first coming under observation.

They give no information as to differential blood count nor as to the presence or absence of symptoms of intoxication.

Of the Cases recorded by Continental observers I have selected a few of those in which the details of the results following Rontgen Ray treatment are more fully given.

Edward Schenck in the "Munchener Medicinische Wochenschrift, 1904 part 40, reports a Case of a woman aged 53, in whom the Rontgen Rays produced distinct lessening of the Spleen, great diminution in the Leucocytes, constant increase in the Reds and Hb, and a marked improvement in her general condition.

He reports another case of Spleno-Medullary Leukaemia which proved fatal. In this case which had been treated by Rontgen Rays for some weeks, the Whites fell from 76,000 to 3,000 in the week before death.

In these cases the Rontgen Rays were only applied over the Spleen, and he recommends that they should be applied to the Bone Marrow as

as well.

In the same Journal Fried reports two cases of Leukaemia in both of which the Rontgen Rays led to an increase of Reds and Hb., and a diminution in Leucocytes, lessening the Spleen, and causing a marked improvement in the general condition.

Cahen also, in the same magazine, No 48, records a man aged 47, who had shown symptoms of Spleno-Medullary Leukaemia for over a year. After 40 exposures of the Rontgen Rays, his Spleen had markedly diminished, his Reds had had increased, his whites had diminished, his weight had increased and his general condition shewed marked improvement.

Bozzolo in the Giornale della R. Acad di Medici di Tornio, 1904, No 7 and 8, records a patient who came with a huge splenic tumour and haemorrhagic Pleurisy.

Reds 2,800,000; Hb. 35 %., Leucocytes 140,000, of which 14 %., were Myelocytes, and Fever.

After 18 days, Temperature was normal. Tumour came down, and in five months was normal.

Leucocytes at first fell rapidly and sank to 10,000 after three months, but rose again till after five months they were 40,000. Rontgen Rays had been continued all the time. He questions whether at any time Rontgen Rays cause more than a temporary improvement.

Einor Rohde, in the "Nordisk Tidskift" for terapi, November 1904, reports a case which is remarkable for the rapidity and the extent with which improvement followed Rontgen Ray Treatment.

The case was a woman, aged 34, with Spleno-Medullary Leukaemia. The Spleen filled the whole of the left half of the abdomen. After two

months treatment:-

The Reds increased from 2,500,000 to 4,320,000.
The Hb., increased from 40 %., to 70 %.
The Leucocytes diminished from 23,600 to 4,000.
The Myelocytes diminished from 47 %., to Nil.
The Polymorphs increased from 40 %., to 90 %.
The Eosinophiles diminished from 1 %., to a few.

In the Munch Med Woch

1905, No 8, Schleip and Hildebrandt report a case which exemplifies the fact that in some cases treatment by Rontgen Rays is followed at first by an increase in the number of Leucocytes and then by a diminution. The case is also remarkable for the severity of the pressure symptoms caused by the enlarged Spleen. The patient who was treated in the Frei-bergerClinique, had been ill for 2½ years with Leukaemia. The Spleen was so big that it displaced the Heart to the right and pressing on the left Lung caused severe dyspnoea.

There was no glandular enlargement.

The Retinal Veins were white. Erythrocytes shewed great differences. The Reds were seldom seen and there was an enormous number of blood plates.

Reds.	3,000,000.
Hb.	72 %.
Leucocytes	280,000.

Properly formed Myelocytes were rare, but cells with round nucleus and strongly basophyle protoplasm were found, which he terms promyelocytes.

In the first three weeks the Leucocytes mounted to 350,000, while Reds diminished to 2,500,000.

A few weeks later the Reds were 3,600000, Hb. 80 % and the Whites 28,600.

Doctors Shleip and Hildebrandt are the only Continental workers who have, as far as I can find, given a record of the Nitrogen Metabolism in Leukaemia during Rontgen Ray Treatment.

They gave the following table:-

SCHLEIP and HILDEBRANDT'S TABLE.

	Amount.	Specific Gravity.	P O	Nitrogen.	Purin Bases.
September 2.	1900.c.c.	1019.	3153.	15.7322	28 mg.
November 22.	1450. c c.	1019.	-----	15.225.	25.72 mg.

The table shews a diminution in both the excretion of Nitrogen and of Purin bases.

The observation is taken on November 22nd and the treatment began on September 20th, 32 days before. Musser and Edsall show in "Transactions of the Association of American Physicians", Vol 20, page 299, that a marked increase in excretion of both Nitrogen and Purin Bases follows immediately on the commencement of Rontgen Ray Treatment.

Tedingham and McKarron, of Aberdeen, give very full notes of the first case of Leukaemia treated by Rontgen Rays in the Royal Hospital for Sick Children, Aberdeen.

The Patient, aged 11 years, was admitted on November 19th 1902. He was emaciated and weak and there was enormous enlargement of the Spleen. The examination of the Blood showed

Reds.	3,570,000.
Whites.	234,000.
Hb.	80 %.

The Myelocytes were numerous. The temperature at first rose in the evening from 100 to 101, becoming normal after a few days in bed, and rising to 102 or 103 whenever he was allowed up. He was treated with rest, dieting, and Arsenic for 1½ years, during which time the condition advanced.

Rontgen Ray treatment was commenced on May 19th, 1904., the Blood then being :-

Reds.	2,560,000.
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Whites.	188,000.
Hb.	46 %.

DIFFERENTIAL COUNT of LEUCOCYTES.

Small Lymphocytes	9 %.
Large Lymphocytes.	12 %.
Myelocytes.	44 %.
Eosinophiles.	2 %.
Polymorphs.	22 %.
Mast Cells.	8 %.
Neucleated Reds	8 per 100

White Cells.

Rontgen Rays were applied over the Spleen and the Knees, 20 to 15 minutes, every other day. No constitutional effects.

In six weeks the Leucocytes had diminished from 188,000 to 23,000, and until the middle of August when the Rontgen Rays were discontinued, the Leucocyte count oscillated round a mean of 80,000. Once they dropped to 17,880, but they never reached the normal, the Reds and Hb had increased but the Myelocytes never quite disappeared.

In discussing the case they give one fact which offers a striking contrast to the

results of the treatment in the four cases I have observed in the Royal Infirmary, Edinburgh.

In their case, previously to Rontgen Ray treatment, the patient was more or less bed ridden, owing to the invariable rises of temperature that were produced whenever he got up, while breathlessness and face flushings always followed an attempt to walk about the Ward. These symptoms disappeared after the commencement of the Rontgen Rays, the boy never having a rise of temperature after an exposure. In all my four cases and in most of the cases I have quoted, the exposures were frequently followed by a rise in temperature and toxaemic symptoms, the treatment having sometimes to be suspended for a few days to allow this to subside.

Charles H. Melland M.D. (Lond),

Senior Honorary Physician in Aucoats Hospital, Manchester, in the British Medical Joirnal for July 1905, gives a preliminary report of 4 cases of

Leukaemia, treated by Rontgen Rays, but as in one of them, Tuberculous infection supervened, affecting the blood count and followed by death, I shall only briefly refer to the other three.

The first was a married woman, aged 57. Pain in the left side of the Abdomen commenced in the middle of 1903. In January 1904, she had an attack of vomiting, continued with intermissions, for 9 or 10 weeks, and on one occasion she vomited blood. She had been losing flesh since then. In the middle of May she first noticed swelling of Abdomen. On July 11th, the blood showed the

Characteristic changes of Spleno-Medullary Leukaemia

Reds 3,360,000; Hb. 61 %.; Leucocytes ~~2~~,261,000.

A large proportion of the Leucocytes were typical Myelocytes. Her most marked symptoms were weakness and pain in the left side.

Rontgen Ray treatment began June 30th, 1904. She had applications regularly twice

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a week to the Spleen, average duration 20 minutes,
the tube being 4 inches from the abdominal wall.

The first change noticed in the Spleen was increased mobility, and this was followed by a gradual shrinkage. Marked improvement in general condition and in the blood count followed.

On January 27, 1905, the treatment was also applied to the knees.

The last blood count was on April 14th :-

Reds, 4,500,000; Leucocytes 19,000; Hb. 95 %.,
Myelocytes were still present to the extent of 10.8 per cent of the Leucocytes. The Spleen had diminished from within three inches of the pubic bone, to $4\frac{1}{2}$ inches below the costal margin.

Although the blood had not completely lost its Leucocythemic type, she had regained her former weight, and her general condition was excellent.

In this Case the treatment was

absolutely confined to Rontgen Rays, no drugs having been given at all, and so the improvement, as it followed immediately on Rontgen Ray exposures, can be credited justly to Radio-Therapy.

His third Case was a man aged 43, in whom also the first symptom was a pain in the left side. In addition he had a haemorrhagic rash on the legs and chest during November 1903.

He was admitted to the Manchester Royal Infirmary, August 19th. 1904, presenting the characters of a typical case of Spleno Medullary Leucocythemia. For 2 months the patient was treated with Fowler's Solution. As he was getting weaker and his Spleen was increasing, Rontgen Ray treatment was commenced on October 25th 1904. The blood count of that date shewed an increase since admission of nearly 200,000 in the white cells.

The Blood Count was:-

Reds.	3,570,000.
Leucocytes	548,000.
Polymorphs	36 %.

Myelocytes.	38 %.
Lymphocytes.	13.6 %.
Eosinophiles.	7 %.
Mast Cells.	4 %.

Applications were given regularly twice a week to the Spleen. Instead of going gradually down hill, as he had been doing under the Arsenic, his general condition rapidly improved and he put on weight. The Spleen, however, only became a little smaller.

The Blood Count on April, 9th, 1905, was :-

Reds.	5,000,000.
Leucocytes.	198,000.
Polymorphs.	50 %.
Myelocytes.	29 %.
Lymphocytes.	15.2 %.
Eosinophiles.	4 %.
Mast Cells.	2 %.

Nucleated Reds were still present.

The 4th Case was a married woman, aged 43, who first noticed abdominal swelling about June 1904. She had been living in Cape Town, but

had never had Malaria.

On admission she had an enormous Splenic tumour, extending $10\frac{1}{2}$ inches beyond the Costal margin. It was hard, firm, and almost immovable. It was not tender to pressure, but caused pain down the thighs and swelling of the feet.

Rontgen Ray treatment was commenced on February 10th. 1905, and was applied both to the Spleen and the Knees.

Within a few weeks the Spleen became soft and mobile, though it showed little diminution in size. She was put upon Arsenic also, but this had to be stopped owing to severe abdominal symptoms.

After three months treatment her condition was described as 'very satisfactory'. Her Spleen had been reduced by about 3 inches, her pressure symptoms had disappeared, she had put on

weight, and was quite cheerful.

The alteration in the Blood was as follows :-

Reds.	3,460,000 to 4,660,000.	
Leucocytes.	542,000 to 190,000.	
Hb.	70 %.	90 %.
Polymorphs.	44 %.	69 %.
Myelocytes.	34.8 %.	2 3.4 %.
Lymphocytes.	15.6 %.	4.8 %.
Eosinophiles.	3.6 %.	.8 %.
Mast Cells.	3 %.	2 %.

Nucleated Reds though much diminished, were still present.

In all these cases Rontgen Ray treatment was followed by marked improvement in the general condition of the patient; in none of the cases did the condition of the blood or the Spleen return to normal, but the improvement was marked in these organs by diminution in the size of the latter and in the former by diminution in the number of Myelocytes, Mast Cells, Eosinophiles and Nucleated Reds, with increase in the Polymorphs and

by constant, steady increase in the Hb carrying part of the Blood.

The cases are only given to show the immediate results of such treatment and it is not expected that the improvement was sustained.

HOW RONTGEN RAYS ACT IN LEUCOCYTHAEMIA.

It will be impossible to state definitely how the Rontgen Rays produce the effects they do in the treatment of Leukaemia until the Pathology of that condition is more thoroughly understood than it is at present. But since it has been shown that Radio Therapy has a beneficial action in this disease, many workers have endeavoured to prove which tissues are affected and in what manner.

Attention has been mostly directed to the Spleen, Lymphatic Tissues, and the Blood, and to the effect of the Rontgen Rays on the general metabolism.

SPLEEN and LYMPHATIC TISSUES.

In almost all recorded cases which have improved under treatment, exposure to the Rontgen Rays has been followed by marked gross

changes in the Spleen and Lymphatic Glands. The first becomes softer and less dense. This is soon followed by increased mobility. These changes indicate a diminution in the bulk of the Spleen which can be demonstrated Clinically if one assumes that the increased nitrogen excretion, which is generally synchronous with the changes, has its source in the broken-down Spleen tissue. Later in periods varying from 1 to 5 or 6 weeks, the Spleen becomes noticeably diminished in size, though in no recorded case of either Lymphatic or Spleno - Medullary Leukaemia, has the Spleen tumour entirely disappeared. Occasionally in Chronic cases, diminution in the size of the Spleen, has ceased while it still extends 3 or 4 inches below the Costal Margin, and while improvement in the Blood and in the general condition was continuing. This has been generally ascribed to the fact that a Fibroses has taken place in the Splenic tissue upon which the Rontgen Rays have no effect.

While the Spleen is disappearing, the enlarged Lymphatic Glands, though not necessarily directly exposed to the Rontgen Rays, also soften, diminish in size, and in some cases entirely disappear.

The minute changes have not yet been satisfactorily described.

Pusey, Professor of Dermatology, in the University of Illinois, in his " Therapeutic Action of Rontgen Rays ", 1903, page 239, points out that there is a marked difference in the way in which the tissues of different individuals react to the influence of Rontgen Rays. It has been his constant experience to see variations in the susceptibility of the tissues of different individuals. These variations seem to be purely a matter of personal equation of the tissues, without discoverable characteristics upon which increased susceptibility or decreased susceptibility may be predicated.

In had been suggested that in those cases in which Rontgen Rays had apparently ceased to act - as shown by the rise of the Leucocyte curve, this cessation was due to the patient having become immune to the action of Rontgen Rays.

Pusey has seen nothing in his experience to give colour to this opinion, that immunity is likely to develop, but he thinks rather that increased susceptibility is developed. He found it much easier to produce Dermatitis after a previous Dermatitis had occurred.

This was demonstrated in my case of the girl J.. L..., in whom Dermatitis, once having appeared, it was only by careful watching and occasional suspension of the Rontgen Rays, that its recurrence was prevented.

Several observers have found that the action of Rontgen Rays on healthy animals causes the formation of Myelocytes and Lymphoid Cells by the

Bone Marrow to cease. For instance Heineke, in the Deutsche Zeitschr f. Chir, Vol 78, Page 197, finds in healthy guineapigs, that during prolonged exposure to Rontgen Rays, the Bone Marrow ceases to produce Myelocytes and Lymphoid Cells. But these cells again proliferate when the exposure is withdrawn. Hence he concludes that the Rays form merely a symptomatic means of treating Leukaemia, and do not affect the unknown etiological agent, and therefore that they play only a temporary role in the Therapeutics of Leucocythaemia.

Heineke also in the Munchener Medicinische Wochenschrift, May 3rd, 1904, describes the action of Rontgen Rays on the Spleen. Small animals which were exposed to the Rays for a number of hours died in from 7 to 14 days. He found in the Spleen excessive increase in the pigment, disappearance of follicles and destruction of Splenic pulp.

The nuclei of the Lymphocytes in the follicles disintegrated within a few hours, and the remnants were taken up by the Phagocytes which shortly disappeared from the Spleen.

Analagous processes took place in all the Lymphoid structures of the body and in the Bone Marrow.

Heineke thinks that similar processes take place in man, and that the Lymphoid structures are affected without there being any reaction in the skin.

These changes, as has been shown by numerous cases in this thesis, have been frequently accompanied by symptoms of toxaemia. This will be referred to again under "Metabolism Effects".

BLOOD.

It is in the blood that we find the most marked changes following Rontgen Ray treatment. In all those cases in which improvement follows

exposures to the Rays, the Leukaemic blood picture disappears, more or less. In the Lymphatic form the number of lymphocytes is reduced - generally to normal - though it must be noted that, even when this occurs, the patient may die of the disease - as did my case J.. H.. In all cases which improve, the Reds and Hb, increase. In the Spleno-Medullary type, the Myelocytes gradually give way to the Polymorphs, the Mast Cells generally entirely disappear, and the Red Cells and Haemoglobin percentage increase. Improvement is always accompanied by a great fall in the Leucocyte count.

Some observers have noticed that the fall of Leucocytes is preceded by a rise.

Auberquin and Beaujard, in the Comp^t
Rend. Soc de Biolog. No 21, 1904, describe a case of Myelocytic Leukaemia in which the Rontgen Rays caused the number of Leucocytes to diminish, but the diminution was not regularly progressive. At first

each sitting was followed by a sharp increase in the number of Leucocytes which during the day fell again to their former number, and after the first 2 or 3 days, gradually fell below that number.

After the first few sittings, this augmentation was almost immediate, but as the patient got accustomed to the treatment, it became less intense and came later and later, until the diminution became progressive.

Auberdin and Beaujard noted the same thing in two cases which they record in the Soc. de Biologie, 20th Jan. 1905.

They had treated with equal doses of Rontgen Rays applied over the Spleen, a case of Myeloid and of Lymphatic Leukaemia which presented in addition to glandular enlargement, large Spleno Megally.

In the Myeloid case, they saw after 2 sittings, oscillations in the number of Leucocytes,

with augmentation of the Leucocytosis and here the augmentation chiefly affected the polynuclears, and only affected the Myelocytes a little.

The definite diminution in the number of Leucocytes did not commence till towards the 18th day, i.e., after the 3rd sitting.

The total number of Leucocytes which before treatment had been 308,000, and which after the first sitting had risen to 462,000, eventually fell to 244,000.

In the case of the Lymphatic Leukaemia, the diminution in Leucocytes showed feeble oscillations, the curve was almost uniformly downwards, and there was not after a period of some months, any modification of percentage.

Referring to the changes in the Blood in these two cases, the Authors say that in both, but particularly in the Lymphatic case, they observed a Leucolysis of the Nucleus and Protoplasm in the

Cells. The Rontgen Rays did not appear to them to act in the same manner in the two forms of Chronic Leukaemia. In the Spleno-Medullary form, they thought the action of the Rays was to cause an emigration in which the Polymorphs predeominated and a destruction in which the Myelocytes predominated. In the Lymphatic form, the proportion of Lymphocytes showing Histolysis and variations appeared to them to show a similitude to the process in the Spleno-Medullary form.

The observation referred to above of Leucolysis of the Nucleus and Protoplasm, has been supported by the results of experiments on healthy rats, rabbits and dogs, as reported by Hellier and Linser, in the Munchener Medicinsche Wochenschrift, No 15, 1905.

They found that the Rontgen Rays have an elective action on the Leucocytes, acting in the first place on the nuclear substance which is injured by the Rays.

The Lymphocytes were first affected and to the greatest degree. The destroying action on the white cells was to be sought, they considered, not so much in the blood-building organs, as in the circulating blood.

This observation of the action on the Lymphocytes, has been to a certain extent supported by an experiment which Lefmann (34, Kongr. d. deutch Ges. f. Chir.) conducted. He produced a lymphocytosis in rabbits by injections of 2 m.m. of Pilocarpine. He found that the number returned to normal after 15 minutes exposure to Rontgen Rays, but on stopping the Rays the Lymphocytosis returned.

Hirschfield, who is of the opinion that the seat of the disease - at least in the Myeloid form of Leucocythaemia - is to be found not in the Spleen or Glands, but in the Bone Marrow, (because, as I have pointed out above, it has been definitely shown that Rontgen Rays check the

m ?

formation of Bone Marrow of Myeloid Cells.)

In the Berlin Klin.Woch., No 48, 1904, he describes a case of mixed celled Leukaemia in which the Spleen had undergone not only myeloid transformation but was rich in normoblastic elements, while the Bone Marrow was only poor in these elements. Here the Spleen had undergone a vicarious compensatory change, not only as regards Leucocyte, but erythrocyte production.

From this he concludes that in such cases Rontgen Ray therapy of the Spleen may have a deleterious influence because by it the compensatory erythrocyte formation may be checked. Against this may be given all the clinical evidence which I have accumulated, that in improving cases the Red cells and Haemoglobin invariably increase under Rontgen Rays.

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Moreover Mosse and Milchner, in No 49 of the same Journal, report that they found on experimenting with animals that Rontgen Rays do not

destroy the Haemoglobin carrying elements of the blood, but that they do cause a partial destruction of Leucocytes.

Against Hirschfield's theory that treatment should be directed only to the Bone Marrow in order to effect a cessation in the formation of Myeloid elements, should be considered certain experiments which were very recently reported in the "Archives of the Rontgen Ray. No 68. March 1906." They tend to show that the reduction of the Leucocytes may be due to a Leucotoxin which is set free in the Serum under the influence of Rontgen Rays, and which destroys Leucocytes.

Hellier and Linser, while experimenting on the action of Rontgen Rays on normal blood in vitro, found that a Leucotoxin is set free from the Leucocytes contained in the Serum. The Leucotoxin destroying the Leucocytes is thereby rendered inactive and is found in solution in the Serum.

These experiments were followed up by Curshmann and Gaupp by investigations on animals. They injected the blood serum from a Leukaemic patient into a rabbit without producing any effect on its blood count. After the patient had been irradiated with successful results, the experiment was repeated and four hours later a considerable fall in the number of Leucocytes in the blood of the rabbit was observed. This artificial Leukaemia was evidently due to the presence of a leucotoxin which had been formed in the blood of the Leukaemic patient by the action of the Rontgen Rays.

A similar leucotoxic effect was observed when the serum from the patient was added to human leucocytes suspended in a Saline Solution. Heating the Blood Serum to 60 for half an hour completely destroyed its toxic action both in the circulation and in vitro.

In view of the fact that the fundamental cause of Leucocythaemia is as yet

unknown - (in some cases micro-organisms have been detected in the blood)- the disease may be due to some form of intoxication which has a special and specific irritating influence upon the organs in which White Blood Corpuscles are formed, the following experiment showing the influence which Rontgen Rays exert on living tissues in promoting the formation of a body which is antagonistic to Micro-organisms, is of great interest.

In Semaine Medicale, 1896, XVI, Page 266, Lorted and Genoud, report the results of the following experiment.

They inoculated in the inguinal region, 8 guinea pigs of the same size and weight, with material from the Spleen of a Tuberculous guinea pig. Of these 8, three were chosen at random and given Rontgen Ray exposures daily over the inguinal region. The three remained well, showing only small nodules at the point of injection, which

gradually disappeared, while in the 5 unexposed pigs, Tuberculous Ulcers developed at the points of inoculation, and the pigs became thin. They also found that Rontgen Ray exposures had no effect on Tubercle Bacilli in inert cultures.

Pusey argues from this (page 284, Rontgen Rays in Therapeutics), that the fact that organisms in living tissues can be destroyed by exposure to Rontgen Rays, while the same organism in inert cultures are uninfluenced by Rontgen Ray exposures, proves positively, that it is not the influence of the Rontgen Rays per se that causes the destruction, but that the tissues themselves, doubtless under conditions of activity excited by the Rontgen Rays, play the important role in the germicidal process.

and ?

Technique and Dangers in the use of the Rontgen
Rays in Leucocythaemia.

In the Royal Infirmary, Edinburgh, it has been the custom hitherto to expose the Spleen only, and not the Sternum nor ends of long bones, to the direct influence of the Rontgen Rays. The patient is seated with the skin over the Splenic Region exposed. The Vacuum Tube is usually fixed from 4 to 6 inches distant from the skin. Coils of 18 and 20 inch spark-gap are used. The exposure is seldom more than 5 minutes in duration, though in the London Hospitals, exposures of 15 to 20 minutes duration are common. It is found in the Royal Infirmary, Edinburgh, that with a short exposure, treatment can be carried on at shorter intervals with less risk of setting up Dermatitis.

In the "American Medical Record", 1902, LXI, Page 83, Carl Beck of New York says " In regard

" to the technique of irradiation for therapeutic
" purposes, careful individualization is the
condition sine qua non..... At first it is best
" to expose for a short time and at long intervals
" until the individuality of the patient studied. ?
" Some patients react soon, some after many exposures
" and some do not react at all. It should be
" regarded as an ironclad rule to stop the exposures
" as soon as the patient feels a burning sensation
" in the irradiated area..... As a rule, tubes
" of low vacuum (soft tubes) should be used for
" therapeutic purposes".

Several writers refer to this
"individualism" in response to Rontgen Rays.

Musser in his paper in the "Transactions of

American Physicians " referred to above, says "This
" dependence of the favourable effect of Rontgen
Rays upon individual reaction helps largely to
explain the difference in the results in different
" cases, and these differences are apparently due

not so much to mere stubborn progress of the disease as they are to lack of that power in the *individual* which makes him capable of controlling the disease by responding to the stimulating action of the Rontgen Ray."

Pusey in his text book on "The Rontgen Ray in Therapeutics", page 309, treats of the difficulty of estimating the dosage used by different workers, owing to the difficulties in standardization. He points out that although the effect upon the tissues varies directly with the length of exposure, the quality of the Rays and their intensity vary greatly according to the quality of the vacuum in the tube and this is an unstable factor. The mode of treatment which his experience has led him to pursue is the one in use in the Royal Infirmary, Edinburgh, namely, the repeated use of a small quantity of light rather than the use of more powerful exposures less frequently. Of dangers which are common to all classes of cases therapeut-

frequent?

therapeutically treated by Rontgen Rays, the principal ones are skin burns and Dermatitis, and Sterility. Most observers who have had much experience in Rontgen Ray work have referred to Sterility as a real danger and advise special precautions in the way of lead shields to protect the parts both of the patient and of the operator and methods of confining the action of the Rays to the part exposed for treatment. The special dangers of Rontgen Ray treatment in Leukaemia are due to the excessive metabolism which is already present in that disease, being suddenly increased - as has been shown - after exposures. As Musser points out, any method of treatment that may cause a patient to double his tissue break down requires care in its treatment. The excretion of the end products of this tissue disintegration may prove to be a severe tax upon many of the organs concerned in metabolism, and upon the excretory organs,

especially the kidneys. So that in Leukaemics, whose kidneys are already working at high pressure, care must be taken that the sudden application of Rontgen Rays with the consequent sudden increase in metabolic processes, does not overtax the already overworked organ, and the appearance of albumen in the urine should be a danger signal, and may possibly indicate a diminution in the dosage.

In Leukaemias, more than in other diseases, exposure to Rontgen Rays has been found to produce more or less severe and sometimes even dangerous febrile reaction - chills, vomiting, prostration and other pronounced general symptoms that have the appearance of being caused by an intoxication, a sudden flooding of the organism with products of tissue breakdown may readily be sufficient in itself to cause intoxication. This danger was exemplified in more or less all the cases, which I have described, in the Royal Infirmary, Edinburgh, more particularly in the Lymphatic

Leukaemia, mM. M... (page 39), and it should be insisted on that patients going from Wards to the Electrical Department for treatment, should be well wrapped up for the return journey to the Wards and go straight to bed - if there are the slightest indications of intoxication.

Many observers have noted in cases of Leukaemia which, having been treated by Rontgen Rays, have died and been ~~examined~~ (post mortem) - wide spread necrosis in the lymphatic tissues. Heineke also found this in his animal experiments which have already been referred to, but he detected no noteworthy symptoms that were evidently due to the destruction of lymphatic tissue, while later, when extensive bone marrow changes occurred as a result of prolonged exposures, he did see very severe symptoms that resulted in death. How far lymphatic tissue necrosis is a danger to the patient has yet to be determined.

Referring to the possibility of bad

results following Rontgen Ray treatment which have not yet been detected, Musser says on page 311 of the "Transactions of American Physicians " Vol XX, 1905, " It should be kept clearly in mind that an effect so profound and unfortunate as is sterility may apparently occur readily, and yet the evidence that it has occurred appears only when deliberate investigations are undertaken to demonstrate that it has resulted, and this makes one at once consider the possibility that other similarly unfortunate effects that are at present obscure may result".

From the above list of dangers I think it is clear that a patient who is under Rontgen Ray treatment - especially a Leukaemic - should be watched carefully by his Physician as well as by the Rontgen Ray operator, and my own experience as Resident House Physician in the Royal Infirmary, Edinburgh, induces me to point out r respectfully that in my opinion it would be to the advantage of the patient and would lead to an

increase of knowledge, both in the Physician and the Electrical expert, if they saw the patient together frequently during treatment and discussed the progress of the case from the point of view of of the Clinician and the Electrician.

To summarise the principal dangers to be guarded against in Rontgen Ray Treatment of Leucocythemia are :-

- 1 . Skin Burns and Dermatitis.
- 2 . Sterility.
- 3 . Toxaemia.
- 4 . Nephritis.

Results of Rontgen Ray Treatment in Leukaemia

upon Metabolism.

In "The Transactions of the Association of American Physicians" Vol 20. 1905, there two valuable papers on this subject - one by

David L. Edsall M.D., Assistant Professor of

Medicine in the University of Pennsylvania, and the

other by John H. Musser M.D., of Philadelphia, and

Edsall.

They describe at length the Metabolism

of Leukaemics, acute and chronic, before and after

treatment by Rontgen Rays. *They* compare their results

with the effect of Rontgen Rays upon normal persons

and ^{upon} ~~with~~ people with gout and diabetes. I have

endeavoured to follow their methods in examining

the Metabolism in the two chronic cases of Spleno

Medullary Leukaemia, J.. L.. and M.. S.., pages 4

and 53. I shall at first give a short account of

their work and the results they arrived at and then

give my own results.

In a case of acute Leukaemia which died $2\frac{1}{2}$ days after he first saw him, Edsall had an opportunity of estimating the balance between the intake of Nitrogen and the outgo in the Urine. He found a loss in this source alone of 22.28 grammes of Nitrogen in 24 hours. There was also a loss of phosphates equal to about 2 grammes.

in Wh. Direction?

He The compares these metabolic conditions to those found in Acute Yellow Atrophy of the Liver, and in Pneumonia at the time of the crisis. In these diseases sudden and very extensive autolytic tissue destruction occurs and he believes that the metabolic disturbance in Acute Leukaemia is alsoa disturbance of autolysis.

In a case of Chronic Leukaemia; which he successfully treated by Radio-therapy, he found immediately upon the use of the Rontgen Ray a most astonishing increase in the excretion of Nitrogen, Uric Acid, Purin Bases and Phosphates.

The excretion was on the whole fully doubled and that of Uric Acid, purin bases and phosphates was ultimately much more than doubled. On the other hand, a case of Chronic Leukaemia that was unsuccessfully treated with the Rontgen Rays showed almost no change in the metabolism as a result of this treatment.

Hellicor and Linser in the "Munch Med. Woch" 1904. No 23., have shown that the Nitrogen metabolism of normal persons is decidedly increased by the Rontgen Rays. This fact and the fact that the Leukaemic whom Edsall successfully treated, showed a striking response to the Rontgen Rays by increase in metabolism, while the Leukaemic who was unsuccessfully treated showed no noteworthy alteration, led Edsall to conclude that the changes in Metabolism that occur as a result of exposure to Rontgen Rays are due to some response in the individual, and not due to any direct physical or other effect of the Rontgen Rays upon the tissues.

He considers that the Rontgen Rays act in some way in increasing the ferment-like metabolic processes that are normal in the body, in other words in stimulating autolysis. That other authorities have held this view, I have shown on pages 121, 5 131.

Edsall also considers that the rapid tissue destruction which takes place normally in acute Leukaemia and that which can be excited by the Rontgen Rays on chronic Leukaemia are analagous.

In the latter this rapid destruction is benign in its influence upon the organism, and it seems possible to him that the destruction occurs in acute Leukaemia is a response on the part of the organism to the Leukaemic tissue hyperplasia and an attempt to control this, and to destroy the Leukaemic tissue.

stat/

Musser and Edsall, in their paper, say that their observations have indicated to them clearly that tissue destruction is in Leukaemia evidence of a favourable action, whereas when the Rontgen Rays fail to act, this tissue break down does not occur.

Heineke in the " Mittheilungenans

dem Greenzgebiete der Medizin und Chirugie"

Bd XL, Heft 1 and 2., showed by a series of experiments that the tissue destruction produced by the Rays is limited to the Lymphatic Tissues and the Bone Marrow, and as these tissues are the seat of the disease in Leukaemia, the symptomatic improvement that is coincident with tissue destruction may be due to the limitation of the disintegration to these tissues.

Musser and Edsall worked out their metabolism results in two cases which were treated almost simultaneously, one of which died and the other temporarily recovered.

The fatal case was a man aged 44, a Spleno-Myelogenous Leukaemia, whose symptoms commenced seven months before he came under observation. The Spleen was greatly enlarged and the inguinal and axillary glands were palpable.

The Blood Count was :-

Reds.	4,280,000.
Hb.	38 %.
Whites.	407,500.

The Differential Count was :-

Myelocytes.	49 %.
Polymorphs.	27.1 %.
Transitionals.	21.6 %.
Eosinophiles.	1 %.
Lymphocytes.	0.2 %.

There were 0.8 % of Nucleated Reds.

He was at once treated with Rontgen Rays and in the period from September 15th 1904 to February 1905, his Leucocyte Count fell from 407,500 to 35,000, and his Spleen became about normal in size. He then left for business reasons and was re-admitted on March 12th. 1905, much worse, with pain and soreness in his muscles, fever, and considerable weakness. His Spleen had reached his Umbilicus again, and his Leucocyte Count was 180,400. the Differential Count being:-

Basophils.	4 %.
Lymphocytes.	4 %.
Polymorphs.	18 %.

147

Eosinophiles.	2.5 %.
<i>Neutrophyle</i> Myelocytes.	71.5 %.

He grew rapidly worse and on the 21st day, the observation of metabolism stated [~]his ~~his~~ Leucocyte Count was 304,000. The preliminary observation of metabolism was continued for ~~two~~ days and Rontgen Ray treatment started on the 23rd. For several days he appeared better, though there was no fall in the Leucocytes, which, on the contrary became more numerous, the Count having risen to 496,000 on the 29th. He went into a sudden temporary collapse on the 31st day and died 2 days later.

The successful case was a woman aged 42, who was admitted on March 10th 1905. Her symptoms having first appeared in October 1903. She presented marked features of Leukaemia. The Spleen extended ~~out~~ to within an inch of Poupart's Ligament and across the Middle Line. No glandular enlargement.

BLOOD COUNT was :-

Reds.	3,410,000.
Hb.	68 %.
Whites.	245,000.

DIFFERENTIAL COUNT.

Myelocytes	45 %.
Basophite Myelocytes.	16 %.
Eosinophiles.	3 %.
Polymorphs.	26 %.
Lymphocytes.	9 %.

She was very weak and pallid and appeared emaciated. She became worse during the next few days. On the 26th when Rontgen Rays commenced after 2 days metabolic observations, her Leucocyte Count was 304,000. Continuous improvement began immediately after the first exposure to Rontgen Rays. The Spleen steadily decreased in size and there was a constant fall in the Leucocyte Count. (It may be noted in passing that while their first case presented a rise in leucocyte count immediately after Rontgen Rays, the first time he was treated, in the second case the Leucocytes fell at once. This is of interest when the observations of *Auberdin, and Beaujard*

are remembered, on page 123

149

By April 20th, the Leucocyte Count was 15,000.

For the study of metabolism each patient was put upon a diet of milk, bread, and butter, eggs, sugar, rice, steak, baked potato, and the amount was kept as nearly as possible the same on each day. To summarise their observations, the principal points they give of the metabolism before the Rontgen Rays commenced are :-

1. Both patients were very ill and were rapidly growing worse.
2. In the fatal case their results showed no evidence of rapid tissue destruction - altho' there were marked toxæmic symptoms. In the other case there was marked nitrogen retention, most of which they say was used in making leukaemic tissue and it is noteworthy that altho' she was retaining Nitrogen she showed symptoms of toxæmia and was growing worse; a fact which proves that toxæmia in

Leucocythaemia is not ^{necessarily} due to tissue disintegration.

3. There was in both cases a marked retention of Phosphorus which they explain by the statement that Leukaemic tissue is particularly rich in Phosphorus.

Their metabolism estimations following Rontgen Ray Treatment are briefly summarised as follows :-

In the fatal case there was no noteworthy change.

In the case that improved the changes in the average daily excretion in the urine were as follows :-

- The Nitrogen rose from 8.7456 grms. to 14.7933 gm
- The Uric Acid rose from 1.0545 grms to 1.6246 grm
- The Purin Bases from 0.0441 grms to 0.1543 grm.
- The phosphates from 1.3323 grms to 3.0793 grms.

The average increase therefore was as follows :-

<u>Nitrogen</u>	6.3477 grms.
<u>Uric Acid.</u>	0.5698 grms.
<u>Purin Bases</u>	0.1072 grms

Phosphates.

1.7469 grms.

Adding to the above the Nitrogen which they estimated was excreted in the faeces, and taking the balance, they estimated that the total tissue breakdown was increased more than 100 % in the 3 days immediately following the institution of Rontgen Ray treatment. In drawing their observations on this last case they say :-

" Results as striking as these, are, so far as
 " we know, not produced by any other therapeutic
 " agent unless the dose used is such as to give rise
 " to acute toxic effects. In this Leukaemic not only
 " was the effect of the Rontgen Rays ^{not} ~~most~~ damaging,
 " but it was profoundly benign. There was a rapid
 " tissue destruction as is seen in severe intoxicat-
 " -ions caused by infections, and by many direct
 " chemical poisons, and occasionally in constitutional
 " diseases, but instead of increasing the evidences of
 " intoxication that were already present in this case,
 " the process that produced the tissue destruction

" caused the appearances of intoxication to vanish
 " rapidly and the patient began rapidly to regain
 " symptomatic health."

C. Quadrone in the Zentralbl f innere

^M
 Medizin, No 21. 1905, found Rontgen Rays in Leukaemia

caused increased output of Uric Acid and Phosphoric
 Acid through the Kidneys even after the first ex-
 posure. After the first exposure there was often a
 definite but slight increase in the total number of
 leucocytes, but when qualitative and quantitative
 alterations in leucocytes had been brought about, he
 noted an increase in the Uric and Phosphoric output, b
 but the curves as regards the two acids were not
 quite parallel.

Different observers seem to get
 directly opposite results as to the output of Uric
 Acid in Leucocythaemia following Rontgen Ray treat-
 ment. Musser, Edsall and Quadrone find the output
 is increased, while Rosenberger, Lessen and Morawitz
 and Joachim and Kurpjuwert find a diminution, and as

I shall show presently, my results also showed a definite and steady diminution in both cases in the excretion of Uric Acid.

F. Rosenberger in the same periodical as above, No 40. 1905, found in 2 cases of Leukaemia one of which was severe and the other mild, and both were treated by Rontgen Rays, that with the onset of improvement there was a lessening and with the onset of regression, an increase of the Uric Acid substances in the urine. On the ground of this observation he opposes the view that the frequent increase of Uric Acid is to be explained by the destruction of ripe leucocytes.

11 R

Lossen and Morawitz, Deutch Arch: f Klin. Med. 83, 3 and 4, say that "In myeloc~~y~~thaemia Rontgen Rays can cause a return of the white cells to normal and can reduce the Uric Acid output to normal, although it sometimes remains high in spite of extreme leucopenia."

Society, March 1905, Joachim and Kurpjuwert, report a case of Leukaemia which improved under treatment by Rontgen Rays, and in which the Uric Acid ~~presented~~ excretion diminished.

The patient was a woman, aged 39, presented a great leukaemic enlargement of the Spleen, It extended down to the Pubic Symphysis and crossed the middle line to the right. Her blood was characteristic of Spleno Medullary Leukaemia. The duration of her illness was 12 months. It had been aggravated by childbearing. Arsenic was first tried, but feverish ~~exacerbations~~ of general characters caused the Arsenic to be suspended in favour of Rontgen Rays. At first the exposures were given over the Spleen but she developed Dermatitis. Then the Rontgen Rays were applied to the epiphyseal ends of the long bones. The Blood Count improved. The excretion of Uric Acid which had been very high fell to normal. The Spleen diminished and her general health improved. No other details are given

The two cases in which I tested the metabolic changes (after Musser and Edsall in the Transactions of the Society of American Physicians. Vol XX, 1905. Page 297.) are both cases of Chronic Myelogenous Leukaemia.

The one, J.. L..., details of whose case and progress are given from page 4 to page 20 was a strong and well built single girl, aged 28, who had been treated with Rontgen Rays from February 28th 1905 to June 19th 1905, during which period her enlarged Spleen had contracted almost to normal and her leucocytes had diminished from 68,000 to 9,400, and she was discharged on that date looking and feeling quite well. She suffered a relapse and was readmitted to Ward 30 on April 7th 1906 (see page 31) with a Leucocyte Count of 401,000 and a Spleen extending 7 inches below the Costal margin. Her metabolism estimation was commenced on 12th April, and Rontgen Ray treatment on the 16th. For 2 days the leucocytes rose and then began to fall gradually. On the 20th, they were 323,000. Her temper-

temperature had assumed a swinging type and menstruation commenced after an interval of 9 days. The next day there was headache and symptoms of slight toxæmia. The headache became severe and the Rontgen Rays were suspended. On April 24th, all toxæmic symptoms had disappeared, her menstruation only lasted one day, but her temperature had retained the swinging type - between 97.8 and 101.2.

The other case M.. S..., the description of which commences on page 53, was also a single girl, aged 27, who was admitted on March 3rd, with a very enlarged, hard Spleen and a leucocyte count of 204,000 and in whom the symptoms of leucocythaemia commenced five months before admission. She was a strong girl and had a healthy, well set up appearance. In her case Rontgen Ray treatment was commenced on March 8th and was followed in a few days by a rise of temperature which assumed a swinging type like the last case, but her maximum temperature was not so high being 100.4. By April 4th, her leucocytes had fallen to 144,000, but there was no symptomatic improvement. On the contrary

each exposure was followed by a period of semi-prostration and she felt tired and ill continually. Her skin became of a yellowish hue. On April 11th, she showed marked signs of perisplenitis and Rontgen Rays were suspended. On April 12th, the metabolism estimation was commenced, and as her symptoms had disappeared by April 16th, Rontgen Rays were renewed, and she and J.. L., who commenced Rontgen Ray treatment on that day, were treated together.

They were both placed upon a diet which allowed them meat only once a day, and tea and coffee were struck out, as they interfere with the estimation of purin bases. The daily diet consisted bread 6 ozs, porridge 5 ozs, meat 5 ozs, milk 2½ pints, potatoes 3 ozs, milk pudding 2 ozs.

The following table gives an approximate

diet :-

	<u>Proteid</u>	<u>Fat.</u>	<u>Carbohydrates.</u>
<u>Bread</u>	6 ozs. 15.	2.2	90.
<u>Porridge.</u>	5 ozs. 72.	10.30.	96.

Table continued from page 157.

158.

		Proteid	Fat.	Carbohydrate
Meat.	5 ozs.	32.	32.	
Milk.	2½ pints	66.	80.	100.
Potatoes.	3 ozs.	1.5.	0.075.	4.
Milk Pudding	2 ozs.	4.	0.15	40.
		140.5.	124.825	330.

Calories. 574. 1153. 1353.

This gives an energy value in their daily diet of 3,080 calories, that is the nitrogen intake was 22.3 grammes per diem.

These figures have been calculated from Atwater's Tables in "American Food Materials", Atwater and Bryant, Bulletin, 28, U.S. Department of Agriculture. 1899.

The Methods I used in working out the changes in Metabolism following exposures to Rontgen Rays as shown in the Urine are as follows :-

TOTAL NITROGEN.

By the Kjeldahl Method, 5 cc of Urine are taken; to it 20 cc of Strong Sulphuric Acid and a small globule of Mercury are added in a conical flask. This is now heated over an oxidising flame till the fluid is colourless and colourless crystals of Ammonium Sulphate are formed. After cooling, these crystals are dissolved in water and transferred to a large distillation flask. 100 cc of Saturated Solution of Caustic Soda are added, and the flask is filled three quarters full of ordinary tap water. The flask is now connected with a distillation apparatus and 30 cc of Saturated Solution of Sulphide of Potash added through the thistle funnel of the apparatus. Heat is applied to the flask. Ammonia is distilled over and is received in 50 cc of

Decinormal Acid. This is titrated against
Decinormal Soda Solution. The calculation was was
as follows :-

50 c c's of Acid used - Burette reading
of the Decinormal Soda Solution = X.

(X X .0014) - .0004 (for the 20 c c's
of strong Sulphuric Acid used in process)=grammes
of Nitrogen in the 5 c c's of Urine taken, and
knowing the whole amount of Urine passed per diem,
one gets the total Nitrogen passed per diem.

AMMONIA NITROGEN.

The Ammonia Nitrogen was estimated by Schloesings

Method.

50 c,c's of Urine were placed in a porcelain
dish, and the dish was filled with Saturated
solution of Lime. The dish was now placed on a
glass triangle in a vessel containing 30 c c's of
Decinormal Acid Solution and the whole placed under
an air tight jar and left for three days. By that

time the Ammonia had been liberated and caught in the Decinormal Acid Solution which was titrated against Decinormal Soda Solution.

The calculation was :-

30 c c's (acid taken) - The Burette reading of the Decinormal Soda Solution \equiv X.

X x .0014 = Amount of Ammonia Nitrogen in the 50 c c's of Urine taken.

UREA NITROGEN.

Morner and Sjoquist's Method.

5 c c's of Urine were taken and placed in a 200 c c Bohemian flask. To it was added 5 c c's of Barium Solution containing,

- Baryta Hydrate. 5 0 grms.
- Barium Chloride. 250 grms.
- Water. to 1000 c c.

100 c c's of Alcohol Solution was added.

(Alcohol Solution was 2 parts Alcohol to 1 part of Ether.)

This was left to stand for 24 hours. By

this time all the Nitrogen which is not Urea Nitrogen was precipitated.

The fluid was filtered into a 500 c c porcelain basin and a pinch of Magnesium Oxide added to liberate any free Ammonia that may be present. This fluid was evaporated down to 20 c c's, and then transferred to a conical oxidising flask and treated by the Kjeldahl Method as above. The calculation is the same as in that Method.

URIC ACID.

Uric Acid estimation was carried out by Otto Folins Method, as given in the American Journal of Physiology, Vol XlIII, Feb 1st. 1905. No 1. as follows :-

200 c c's of Urine was measured into a narrow beaker and 50 c c's of the reagent containing,

- Ammonium Sulphate 500 grms.
- Uranium Acetate 5 grms.
- 10 % Acetic Acid. 60 c.c's.
- Water. 650 c c's.

The mixture is allowed to stand without stirring for about half an hour. The Uranium precipitate has then settled down and the clear supernatant liquid is removed by decantation.

125 c c's of this liquid is measured into another beaker, 5 c c's of strong Ammonia added and the mixture set aside till the following day. The precipitate is then filtered off, washed with 10 % Ammonium Sulphate Solution until the filtrate is quite free from Chlorides. The filter is removed from the funnel, opened, and the precipitate rinsed back into the beaker. Enough water to make 100 c c's is added and finally the precipitate is dissolved by means of 15 c c's of strong Sulphuric Acid and at once titrated with N/20 Permanganate Potassium Solution, each c C of which corresponds to 3.75 m g of Uric Acid. A correction of 3 m g, due to the solubility of the Ammonia Sulphate is added to the result. The very first pink colouration extending through the entire fluid from the addition of two

drops of Permanganate Solution while stirring with a glass rod, marks the end of the titration.

CREATININ ESTIMATION.

Creatinin was estimated by Otto Folin's Method, using Duboscq's Colorimeter.

10 cc of Urine were measured into a 500 cc Volumetric flask, 15 cc Picric Acid and 5 cc Sodic Hydrate were then added and the whole mixture allowed to stand for 5 minutes and then diluted with tap water to the 500 cc mark.

Colorimeter readings were then taken with the Instrument.

PURIN BODIES.

Purin Bodies were estimated by means of Walker Hall's Purinometer, instructions for the use of which are given in his "Purin Bodies of Food Stuffs." Manchester. 1902.

PHOSPHATES.

Phosphates were estimated by Hallibur-
ton's Uranic Acid Method.

The following tables (1 and 2)
show the Metabolism as indicated by the Urine,

1. Case of J.. L..

Date	Amount.	Sp. Gr.	Total Nitrogen.	Ammonia Nitrogen.	Urea Nitrogen.	Purin Bases.	Uric Acid.	Creatinin	P O
12 April	690	1025	8.43 grms.	.302 grms	7.48 grms	.0669.	.4209	.7984 grms	.88
Ap. 13th.	750	1020	7.36 "	.162 "	6.93 "	.0727	.5625	.6075 "	.89
Total	1440		15.79 "	.464. "	14.41 "	.1396	.9834	1.4059 "	1.77
Average	720.		7.89 "	.232 "	7.20	.0698	.4917	.7029	.885
(Rontgen Rays commenced on 16th.)									
April 17.	705	1024.	9.47 "	.257 "	8.65 "	.0958	.1982	.8158 "	1.9
18.	580	1023	7.76 "	.196 "	6.64 "	.1595	.0116	.5220 "	1.0
Total	1285		17.23 "	.453 "	15.29 "	.2553	.2098	1.3378 "	2.9
Average	642		8.61 "	.226 "	7.64 "	.1276	.1049	.6689.	1.45.

2. Case of M.. S..

Date	Amount.	Sp. Gr.	Total Nitrogen,	Ammonia Nitrogen	Urea Nitrogen	Purin Bases	Uric Acid	Creatinin	P O
			Before Rontgen Rays commenced.						
April 12.	705	1027	10.16 grm.	.322 grm	7.732	.0824	.6471	.6173 grm	3.85 grm
April 13	1200	1026.	15.27 "	.218	lost	.1164	.6727	1.0920 "	2.9 "
Total	1905		25.43 "	.540		.1988	1.3198	1.7093 "	6.75 "
Average.	952.		12.71. "	.270	7.732	.0994	.6599	.8546 "	3.37 "
			Rontgen Rays commenced on 16th.						
April 17.	850.	1023.	9.84 grm.	.196 grms	9.328	.1156	.6450	.6557 grm	1.9 grms
April 18	800.	1028	11.87 "	.134 "	8.376	.2313	.3900	.6280 "	2.4 "
Total	1650.		21.71 "	.330 "	17.704	.3469	1.0350	1.3377 "	4.3 "
Average	825		10.85 "	.165 "	8.852	.1734	.5175	.6688	2.1 "

167

Besides estimating the total nitrogen, I have estimated the Ammonia Nitrogen and the Urea Nitrogen, but the results I have obtained do not give any information which is not given by the total nitrogen results, though the per centage of Ammonia Nitrogen to the total Nitrogen is rather lower than normal.

In the case of J.. L.., who responded to the Rontgen Ray treatment well, the changes in the average daily secretion in the urine before and after Rontgen Rays commenced were as follows:-

- The total Nitrogen rose from 7.89 grm to 8.61 gr
- The Purin Bases rose from .0698 to .1276 grms.
- The Uric Acid fell from .4917 to .1049 grms.
- The Creatinin was practically unaltered.
- The Phosphates rose from .885 grms to 1.45 grms
- The average daily increase in Total Nitrogen was .72 grms.
- The average daily increase in ~~total~~ Purin Bases was .0578 grms.
- The diminution in Uric Acid was .3868 grms.
- The increase in Phosphates was .565 grms.

These results coincide with what one was led to expect from studying the results in

Musser and Edsall's successful case, except as regards the Uric Acid.

The increase in Nitrogen, Purin Bases, and Phosphates was not nearly so marked as it was in Musser and Edsall's case. It is possible that this may be due to the fact that the Americans are in the habit of giving stronger and longer exposures than is the custom in the Royal Infirmary, Edinburgh

The contrast between their results and mine as regards Uric Acid is difficult to explain. I took care to have my methods and figures carefully checked by an assistant in the Laboratory in which I worked, who is a duly qualified Analytic Chemist well accustomed to his work, and while an error might very easily have crept in to one or two estimations, I can hardly conceive that the steady diminution in Uric Acid excretion shown by the results in both my cases can all be wrong.

Moreover as I have noted on page 153 and page 154, a diminution in Uric Acid following the

Rontgen Ray Treatment was observed by Rosenberger;

Lossen and Morawitz; and Joachim and Kurpjuwert.

The following table is given to show the c̄ontinuat-

ion of the estimation in metabolism up to the

23 rd inst.

Table of Estimation of Metabolism. Case of J. L.

Date.	Amount.	Sp Gr.	Nitrogen	Purin Bases	Phosphates.
April 12.	690 cc	1025	8.43 grms	.0669 grms	.88 grms
13.	750 cc	1020	7.36 "	.0727	.89
14.	lost				
15.	610 cc	1022	6.52."	.1372	1 .11
Total	2050.		22.31	.2768	2.88
Average.	683		7.43	.0922	.96
April 16.	260 cc	1026	2.10	.0203	0.3
			Rontgen Rays	commenced.	
April 17.	705 cc	1024	9.47.	.0958	1.9
18.	580 cc	1023	7.76	.1595.	1.0
19.	505 cc	1023	6.19	.1257	1.0
20.	790 cc	1026	11.79	.0924	1.8
21.	340 cc	1035	Rontgen Rays 5.13	discontinued. .0595	0.9
22.	260 cc	1026	4.80	.1868	0.9
23	625 cc	1025	9.02	.1768	1.7
Total	3805		54.16	.8965	9.20
Average.	543		7,73	.1280	1.3

As Rontgen Rays commenced on the 16th the metabolism of the urine for that day does not enter into the calculation. The Rontgen Rays had to be suspended after the 20th owing to menstruation and intense headache, but I continued the metabolism estimation. The table shows an average daily increase in the nitrogen, purin bases and phosphates for the 7 days succeeding the first administration of the Rontgen Rays, *as compared with the three days preceding it,* as follows :-

Nitrogen 7.43 grms to 7.73 grms, increase of .30 grms
Purin Bases .0922 grms to .1280 grms increase of .0358 grms.
Phosphates .96 grms to 1.3 increase of .34 grms.

These figures when compared with the figures showing the average increase for the two days succeeding the Rontgen Ray treatment indicate that the increase in metabolism is greatest immediately after the Rontgen Ray treatment commences.

In the second case, M.. S.., the total Nitrogen and phosphates both diminished during the 2 days succeeding the commencement of Rontgen Rays, the Uric Acid also diminished as in the case of J.. L.., and the purin bases increased.

The increase and diminution were as follows :-

The total nitrogen fell from 12.71 to 10.85.

The purin bases increased from .0994 to .1734

The uric acid fell from .6599 to .5175

The creatinin fell from .8546 to .6688

The phosphates fell from 3.37 to 2.1

The average daily diminution in nitrogen was 1.86

The average daily increase in purin bases was .0740

The average daily diminution in uric acid was .1424

The average daily diminution in creatinin was .1858

The average daily diminution in Phosphates was 1.27.

If, as I think is the case, the beneficial action of Rontgen Rays in Leukaemia can be estimated by the increase in metabolism, then these results show that in this case there was no benefit.

The clinical evidence bears the

metabolic results out in this, because as the description of the patient's case on page 379 shews, although the leucocyte count had been falling since March 10th. There was no symptomatic improvement (indeed the patient's condition as regards toxaemic symptoms and shortness of breath was increasing) till after the 16th instant, the date on which the Rontgen Ray treatment was resumed, after suspension for a few days owing to Perisplenitis, and although the Spleen was a little softer, no diminution in its size could be detected until the 24th inst.

Referring to the theories of Carl Beck page 133, and others which have been quoted in this thesis regarding the individualisation of different patients in the response of their tissues to the action of Rontgen Rays, it may be possible that the dosage which was sufficient in the case of the girl J. L., to cause increased metabolism and give general improvement, was only sufficient in this case to excite a slight leucotoxic action in

the blood,(see Experiments by Hellier and Linser, page 129.) with corresponding Toxaemic symptoms without being sufficient to produce the more marked change that occurred in J.. L..

This theory, is I think, to a certain extent borne out by the fact that general symptomatic improvement with commencing diminution in the size of the Spleen appeared on the 24th inst., after a comparatively prolonged period of Rontgen Ray treatment lasting since March 8th; that is that the small dosage has done in a long time what a larger dosage would have done in a corresponding shorter time.

The following table shows the Meta-
bolic estimation extended for seven days after . re-
-commencement of treatment.

Date	Amount	Sp.Gr.	Nitrogen.	Purin Bases.	Phosphates.
April 12.	705 cc	1027	10.16	.0824	3.85 grms.
13.	1200 cc	1026	15.17	.1164	2.9 "
14.	lost				
15.	1100 cc	1028	14.44	.2739	2.75 "
Total.	3,005 cc		39.87	.4727	9.50 "
Average.	1,002 cc		13.29	.1575	3.16 "
April 16.	1030 cc	1027	7.98	.0810	1.4
17.	850. cc	1023.	9.84	.1156	1.9
18.	800. cc	1028	11.87	.2313.	2.4
19	1060. cc	1028	7.0	.1961	1.7
20.	1550. cc	1028	8.54	.0533	1.9
21.	1075. cc	1026	6.45	.1043	1.5
22.	1305. cc	1023	6.64	.1925	1.5
23.	1100. cc	1020	7.08	.3113	2.4
Total.	6740.		57.42	1.2044	13.3
Average.	963.		8.20.	.1920	1.9

Rontgen Rays Commenced.

177

This table shows the average daily excretion for the 7 days succeeding the Rontgen Rays and this is compared with the average excretion for the three days preceeding it.

The Nitrogen and Phosphates are still less than before the treatment, and the Purin Bases are still increased as follows :-

Nitrogen 13.29 grm to 8.20 grms, diminution of 5.09 grm
Purin Bases .1575 grms to .1720 grms, increase of .0145 grms.
Phosphates 3.16 grms to 1.9 grms, diminution of 1.26 grms.

I shall now shortly discuss these estimations generally.

NITROGEN. The increase in the excretion of Nitrogen is what one expects whenever tissue breakdown of any kind is occurring in the body. One got a definite though not marked increase in the first case, J. L., who is improving quickly. I cannot account for the fall in Nitrogen excretion in the second case M..S.

PURIN BASES. The Purin Bases include substances which contain the nucleus $C_5 N_4$ and those principally met with in the urine are Uric Acid and the

Xanthine bases. The quantity of Purin Bodies in the Urine bears a direct relation to the amount of the Purin contained in the food eaten and to the extent of nuclein cleavage during the metabolic processes of the body. As far as possible the food given to these two patients while observations were being taken was constant, so that the steady increase which the tables show must have been due to the nuclein cleavage which necessarily accompanies a break down of white blood corpuscles and spleen tissue. Both cases showed that the white blood corpuscles were diminishing and in both the purin bases excreted were increased.

PHOSPHATES. Leukaemic tissue is rich in phosphates and one would expect a marked increase in the excretion of this substance. In the first case an increase has been obtained, but in the second there is a diminution. Musser and Edsall obtained an increase of 0.7048 to 1.1050 grms, even in the patient who died shortly after treatment commenced

and I have failed to account for this diminution in
my second case.

CONCLUSIONS.

The conclusions I have come to while studying the subject of Rontgen Ray Treatment in Leucocythaemia are :-

1. That in Chronic Spleno-Medullary Leukaemia, Rontgen Ray Treatment is distinctly beneficial, in reducing the size of the Spleen and enlarged Glands - returning the blood to normal and in removing symptoms of the Disease, but the improvement is merely temporary, and sooner or later, the signs and symptoms of the Disease will return.

2. That in cases of recurrence after a period following Rontgen Ray Treatment in which signs and symptoms of the Disease have been absent, Rontgen

Rays appear to have the same power to temporarily restore the patient to symptomatic health as they had on the first occasion, though there has not yet been time to establish this fact.

3. That in Chronic Lymphatic Leukaemia, Rontgen

Ray Treatment can reduce the size of the Spleen and cause enlarged Glands to disappear, and at the same time reduce the Lymphocyte Count to normal without restoring the patient to symptomatic health or preventing death from the Disease.

4. That an increase in the number of Red Cells and in the percentage of Haemoglobin is as important a factor in judging the favourable progress of a case under Rontgen Ray Treatment, as is a fall in the Leucocyte Count.

5. That death may take place when the Glands and Spleen are quite small and when the White Count has been reduced to normal.

6. That Acute cases, Lymphatic or Spleno-Medullary, receive no benefit from Rontgen Ray Treatment.

7. That during Rontgen Ray Treatment, a rise of temperature and the exhibition of toxæmic symptoms, do not necessarily indicate a suspension of the treatment, as long as the excretory organs

are in good working order, but that the Urine should be carefully watched for Albumin, the appearance of which will indicate that the Kidneys are being overworked in disposing of the products of increased Metabolism.

8. That in those cases in which the Rontgen Ray Treatment is doing the patient any good, there is an increased secretion of products of metabolism in the Urine.

9. That in two individuals in apparently the same stage of the disease, judged clinically, who have been given equal exposures, under exactly similar conditions, the metabolic changes as shown by the Urine, may differ widely.

10. That some individuals respond more readily and more completely to the action of Rontgen Rays than others.

11. That it may be possible by further investigations, to fix a ratio between the purin bases excreted in the urine and the dosage necessary to

produce the best possible effect in the individual.

12. That in Splenic Anaemia, the Röntgen Rays have the power to improve the condition of the blood, and the general health, and to reduce in size the enlarged spleen; and that this improvement has been maintained after a period of nine months.

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