Six Cases

of

Macrocytic Anaemia.

Ronald H. Girdwood.

May 1939.

CONTENTS.

CASE A

PATIENT'S NAME: Grace Ganson (SINGLE)
AGE :- 33 years.
OCCUPATION :- Domestic Servant
ADDRESS :- 3, Tolbooth Wynd, Leith
RECOMMENDED BY :- Dr Cowan, Penicuik
DATE OF ADMISSION :- Dec 3rd, 1937.
DATE OF FIRST EXAMINATION :- Dec 5th, 1937.
WARD :- 30, R.I.E.

COMPLAINT.

Tiredness - six months' duration
Breathlessness - two months' duration.

HISTORY:-

THE ONSET --- From the beginning of the year (1937) the patient and her friends noticed that she was becoming PALER. At about the time when this was first noticed, she began, too, to feel a DISTASTE FOR FOOD. This distaste extended to all sorts of foodstuffs, and became more marked as the year progressed. Accompanying this symptom, there was felt a DULL ACHE in the epigastrium: this was constantly present, of a very vague character, and did not appear to be related to the taking of meals, or to be relieved by eating. Later in the year the patient VOMITED up her food on two or three occasions: she felt as if the material she had just eaten was lying unchanged in her stomach, then about two hours after taking it she vomited up lumps of undigested food material. About May, 1937, people first began to remark on the fact that her face was showing a slight YELLOWISH TINGE; while this was never very marked, it gradually increased in intensity as the year wore on,

and she began to notice a similar discolouration on her limbs and body.

GENERAL SYMPTOMS:

At the beginning of the year, too, she though she was becoming thinner, and her friends remarked on this fact. Her suspicions are borne out by the fact that in December, 1936, she weighed 8 st 10 lbs, whereas just before admission her weight was registered as 6 st. 10 lbs.

From about June, 1937, the patient found that it ~~she~~ was only with difficulty that she could carry out her duties as a domestic servant. This was because she felt very easily TIRED, and generally UNFIT. So bad was this feeling in October, that she was compelled to take to her bed for five days. She felt a little better with this rest, but was by no means fit when she returned to her work. Soon after this she began to feel rather BREATHLESS, especially with the taking of exercise, and on climbing stairs. About the same time, too, she commenced to be troubled with SLEEPLESSNESS. For no apparent reason she remained awake at nights.

LOCALISED SYMPTOMS In June, 1937, the patients' tongue became RED and SWOLLEN. She could not understand why this should occur. - The tongue was painful, and she had difficulty in eating, but she says that she gained some relief by removing her dentures. The patient did not find that this symptom was made worse by any particular articles of foodstuff: she says, however, that associated with these lingual symptoms she had what she describes as a 'continuous burning feeling in the back of the breast bone', which was present day and

night and was neither relieved nor made worse by the taking of food or by anything else. These symptoms in the tongue and thorax were most marked soon after their commencement, and although they were still present at the time of admission, they were not very marked.

During the month previous to admission she suffered from a dull PAIN in the NECK. This felt as though it were deeply situated: it started in the midline of the back of the neck, and passed up towards the vault of the skull. This symptom came on at various times during the day, but not during the night.

There was no history of tingling of the limbs, no oedema, and no giddiness. She noticed no abnormal cardiac symptoms such as palpitations: her bowels remained regular.

On the 30th of November, the patient felt so unfit that she went to bed, and a doctor was sent for. He estimated her haemoglobin percentage to be 30%, and arranged for her admission to Ward 30 of the R.I.E. She was admitted on the 3rd of December.

PREVIOUS HEALTH:-

The patient had never suffered from a serious illness or accident of any kind. She gave the usual history of colds, but could not recollect having had any of the common illnesses of childhood.

SOCIAL HISTORY

The patient had been in domestic service in various situations for about eighteen years.

She had always had plenty of food and regular meal hours. For about a year previous to admission she had been working in a moderate sized hotel in a country district, where her chief duties consisted of dusting and polishing. She felt, however, that the work was too much for her while she was feeling so unfit. She was allowed a fair proportion of hours off her work, and took walks for exercise. These walks became less extensive as her feeling of unfitness increased.

The patient was a non-smoker, who never took alcoholic refreshment.

FAMILY HISTORY.

Father - died aet 61 - diabetes mellitus
Mother - died aet 47 - drowned herself - she suffered from sleeping sickness.

The patient is the third member of a family of nineteen.

Eight are dead, most of them dying very young.

One sister, aet 30, the fourth in the family is anaemic.

One brother, aet 13, is 'troubled with his stomach' The other eight are alive and well.

(The patient did not appear to be capable of giving a reasonably intelligent description of her family's general health.

STATE ON EXAMINATION.

The patient was a small adult female, whose intelligence appeared to be rather low, and whose finger nails were almost completely bitten away. Her height was 4 stone 11 lbs, and her weight, on admission, 6 stone 10 lbs. Her standard weight, however, was 8 stone 8 lbs.

The patient was thin, but not emaciated; the iliac crests were prominent, but the ribs were not unduly prominent. The muscles were soft and flabby. The skin was not very dry, but had lost some of its elasticity.

The face and mucus membranes were very pale, and all parts of the skin had a distinct lemon-yellow tint. The patient appeared to be very weak and exhausted; she was propped up with one extra pillow, and lay back, indifferent to what was occurring, although still fully conscious of what went on around. There were no cutaneous eruptions, and no oedema could be demonstrated.

To summarise, it may be said that the patient was very weak, and appeared to be profoundly anaemic.

Temperature	97.1°.
Pulse Rate	88
Respiratory Rate	22.
Blood Pressure	120/70.

Last Menstrual Period. August, 1937.

HAEMOPOIETIC SYSTEM.

The symptoms that might be referred to this system have already been detailed. The chief features noticed by the patient and by her friends were:

Breathlessness: sleeplessness: tiredness: pallor of the face, and a tinge of jaundice.

THE BLOOD - (further findings given under Progress Notes)

5: XII: 37.

Haemoglobin	43%.
Erythrocytes	1,870,000.
Leucocytes	4,000.
Platelets	
Reticulocytes	very few
Bleeding Time	5 minutes
Colour Index.	1·15

43/37 = 1

Film.

The red blood cells exhibited anisocytosis and poikilocytosis: many of the cells were of large size, oval in shape, and well filled, the appearance being that of the megalocyte. No nucleated red cells were seen.

The spleen and liver were not enlarged. Two or three slightly enlarged lymph glands were palpable on each side of the neck: these were discrete, firm, and freely mobile.

ALIMENTARY SYSTEM.

SYMPTOMS. One of the patient's earliest complaints was of distaste for food of all sorts, becoming progressively worse: she had a feeling of fullness after food, and at a later date she vomited on two or three occasions; she felt as though the food were lying unchanged in her stomach, then about two hours after taking it, she vomited up undigested food material. Sometimes she was troubled with flatulence, but never with acid eructations.

A constant dull ache was present in the epigastrium for about a year prior to admission. It was of a vague character, did not radiate, and was not influenced in any way by the taking of meals.

About six months before admission, the patient states that her tongue became red and swollen, and was painful; she found that she had some difficulty in swallowing at this time: the symptoms subsided. At this time, too, there was felt what was described as 'a continuous burning feeling in the back of the breast bone' present day and night, and not related to the taking of meals.

The bowels were regular.

SIGNS.

The lips were pale: the teeth had been extracted, the patient wearing dentures.

The tongue was clean and moist. There was simple atrophy of the papillae, the

surface of the tongue being smooth, but there were no fissures or ulcers present.

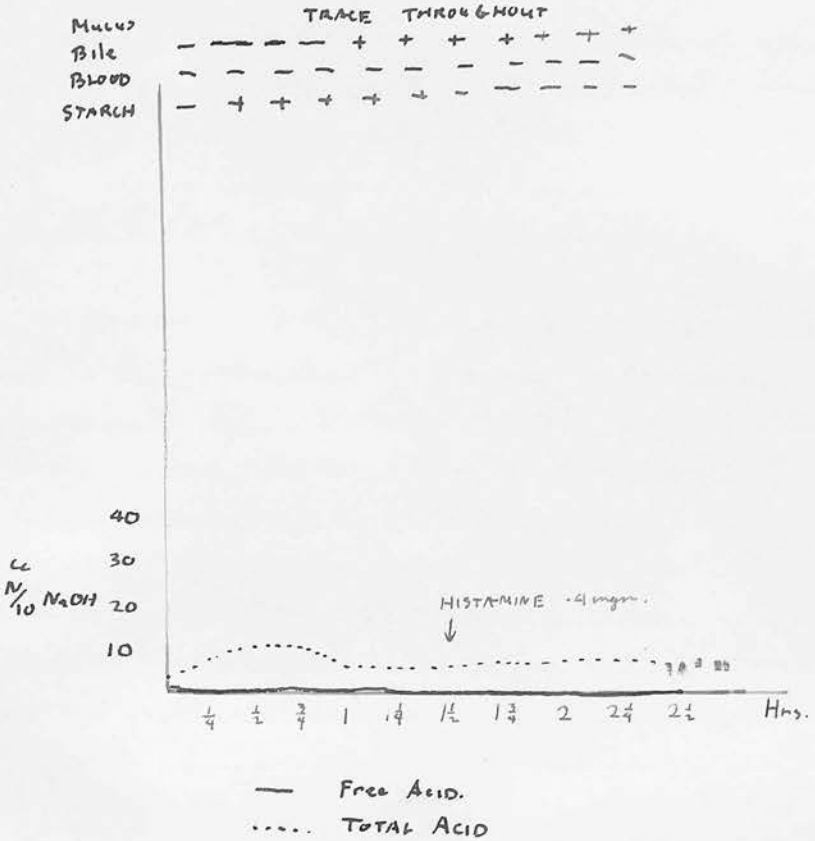
The abdomen was poorly covered, and the skin had an icterus tinge. The abdominal wall moved freely with respiration. There were no haemorrhages of the skin, and no other surface abnormalities. The symmetry of the abdomen was not impaired.

On palpation, the wall was found to be flaccid. There was no localised rigidity or tenderness, and no abnormal swellings could be palpated. The liver and spleen could not be palpated. The lower pole of the right kidney was palpable, but the organ was not enlarged.

Splashing was present in the stomach three hours after a meal. There was no free fluid in the abdomen.

The faeces showed no abnormality on naked eye examination.

Gastro Intestinal Analysis was carried out by means of a fractional test meal. The findings are given on the following page.


Mucus
Bile
Blood
Starch
TRACE THROUGHOUT
40
30
20
10
cc N/10 NaOH
HISTAMINE .4 mgm.
1/4 1/2 3/4 1 1 1/4 1 1/2 1 3/4 2 2 1/4 2 1/2 Hrs.
Free Acid.
Total Acid

CARDIO-VASCULAR SYSTEM

As already recorded, the patient suffered from breathlessness; she sometimes felt faint, especially on rising suddenly. There was no palpitation.

Arteries. The rate was 86/minute. The pulse was regular in time and force. The wave was of normal character, and the vessel wall was not palpable.

B.P. 110/64.

Veins: with the patient in the upright position, no pulsation was visible in the lower part of the neck. The external jugular vein was not engorged.

There was no hepatic enlargement detectable

Capillaries. The patient was pale, and had a jaundiced tinge. There was no cyanosis or oedema.

HEART.

There was visible pulsation that was fairly well localised, situated in the fifth space in the mid clavicular line. No pulsation was visible in other parts.

There were no palpable thrills. A well localised apex beat was felt in the fifth space in the mid clavicular line.

On percussion, the position of the heart was found to be such that it may be represented by the following formula $\frac{III}{1\,|\,4}$.

On auscultation, the sounds in the mitral and tricuspid areas were found to

be closed and of normal character. A soft, blowing systolic murmur was present in the second left space just at the edge of the sternum. This murmur was not propagated. A more rough systolic murmur was heard at the level of the fourth costal cartilage, half an inch to the left of the midline: this, too, was not propagated.

RESPIRATORY SYSTEM

Symptoms: There was no cough, or expectoration. The presence of breathlessness, and of substernal pain has already been recorded.

Respiration: The rate was 22/minute, and the breathing was abdomino-thoracic in character, with no abnormality of rhythm.

No pathological process was visible in the throat or on the tonsils.

THORAX.

The chest was rather flattened; and there was no evidence of previous rachitic processes. The ribs were visible through the skin but were not of the prominence that is seen in the very emaciated patient. There was some depression beneath the clavicles.

The spine was straight, and the scapulae not unduly prominent. There was no local chest retraction or bulging.

Movement was free on the two sides, and there was no localised lagging or diminution of movement.

On palpation, the symmetry of movement

was confirmed, and vocal fremitus was found to be equal on the two sides.

Percussion showed that resonance was good throughout the chest, and that there was no localised impairment. Tidal percussion indicated free diaphragmatic movement.

Breath sounds were vesicular in all areas, and no accompaniments were heard. Vocal resonance was equal on the two sides, and of average intensity.

URINARY SYSTEM.

There were no symptoms referrable to this system.

The lower pole of the right kidney was palpable.

Urine.

4/12/37. Was of straw colour, sp gr. 1024. ph. 8·5. Mucus deposit. No albumen or sugar was present. A few epithelial cells were seen on microscopic examination.

NERVOUS SYSTEM.

Mental Functions. The patient was of rather low intelligence, and was inclined to show excessive emotional reaction: she appeared to be very depressed, and said that she could not sleep. There was no abnormality of her speech, and no hallucinations or delusions. Memory for recent and for past events was good.

Cranial Nerves.

I No abnormality of the sense of smell

II Visual acuity in both eyes was good, and the fields of vision were not impaired. No retinal haemorrhages or other abnormalities were seen on ophthalmoscopic examination

III, IV, VI Both eyes moved freely in all directions: there was no diplopia or strabismus, and no nystagmus or ptosis.

The pupils were of average size for the conditions under which they were examined. They were round and equal. The direct and consensual reactions to light, and the reaction to accomodation were not impaired.

V Motor. Contraction of masseter and temporal muscles equal on the two sides. No deviation of the jaw on opening the mouth.

Sensory: Corneal reflex present: no impairment of sensation over the areas of distribution of any of the three branches of the nerves. There was no loss of taste sensation as regards salt in the anterior two thirds of the tongue. Other substances were not used.

VII There was no evidence either of supranuclear or of infranuclear paralysis, the facial muscles moving freely. There was no hyperacousis, and taste as already described was not impaired.

VIII No impairment of hearing. Air conduction was better than bone conduction.

On rising suddenly, the patient suffered from dizzyness, and she had had tinnitus for

some weeks.

IX The patient said that when her tongue became swollen there was difficulty in swallowing. There was no anaesthesia of the pharynx.

X The palate moved in the midline.

XI No impairment of movement in muscles supplied.

XII No deviation of the tongue and no tremor.

Summary - No impairment of cranial nerves.

CERVICAL SYMPATHETIC.

There was no recession of either eyeball, and no drooping of the upper lids. Pupil reactions were not impaired.

MOTOR FUNCTIONS.

There were no abnormal muscular movements. There was no impairment of movement in any of the muscles of the limbs or trunk, and no motor weakness.

The muscles were rather flabby as one might expect in a patient confined to bed. There was no true flaccidity and no spasticity to be detected in any muscles.

There was no inco-ordination in the upper or lower limbs.

REFLEXES.

Superficial. The conjunctival, palatal and abdominal jerks were not impaired. The plantar reflexes were bilaterally plantar-flexor.

Deep Reflexes.

Biceps present and equal on the two sides
Triceps " " on the two sides
Supinator " " on the two sides.
Jaw - present

Knee - Brish : more so on the right side
Ankle - Brish : more so on the right side.

No knee or ankle clonus was present.

SENSORY FUNCTIONS.

The presence of a dull pain in the neck has already been mentioned. Nothing was found in the neck that might give rise to this. The patient had always suffered from tingling of the fingers in cold weather. Otherwise there was no complaint of numbness, tingling, pain, or coldness of fingers or toes.

Objective:

Upper Limbs. There was no impairment of vibration sense, of sense of position, or of stereognostic senses. The sensations of touch, of pain, and of heat and cold were also unimpaired.

Lower Limbs. The findings here were similar, except that in the distal parts of both limbs, vibration sense was not apparent.

There was no difference of any of the sensations between the two sides.

There were no vasomotor or trophic changes.

INTEGUMENTARY SYSTEM.

No symptoms were present.
The skin was rather inelastic and was slightly dry, but not markedly so. The finger nails had been bitten almost completely away.

REPRODUCTIVE SYSTEM.

LAST MENSTRUAL PERIOD. August 1937. The periods had been of short duration for two or three months. Otherwise there was no abnormality.

LOCOMOTORY SYSTEM.

There was nothing to be noted as regards this system.

ENDOCRINE SYSTEM.

There was no enlargement of the thyroid gland, and nothing to suggest abnormal processes in this or in the other organs of the endocrine system.

Progress Notes.

In each case, these will be considered under the following headings.

1. Investigations carried out other than blood examinations
2. General Progress of the Patient
3. Treatment given.
4. Progress of the Blood picture, and treatment adopted to improve the blood picture.

1. Investigations.

3·XII·37. Height 4 feet 11"
Weight 6 stone 10 lb.
W R negative.

4·XII·37. Urine. Straw colour: sp gr 1024 : ph 8·5 : epithelial cells
6·XII·37 " Fractional Test Meal done. - see the case report.
7·XII·37. Icteric Index 16.
Van den Bergh Direct Reaction negative.
Indirect " positive.
12·XII·37. Urine - Pale lemon: sp gr. 1014. acid. mucus deposit.
13·XII·37. Weight 6 stone 13 lb.
20·XII·37. Weight 7 stone 4 lb.: BP 116/66
23·XII·37. Urine - straw colour: sp gr 1016. acid. mucus deposit.
27·XII·37. Weight 7 stone 1 lb.
3·1·38 Weight 6 stone 13 lb.
4·1·38 Blood pressure 120/65.

There were no significant changes of Temperature respiratory rate or pulse rate during the time in hospital

2. General Progress.

3·XII·37. Patient admitted.

5·XII·37. She feels rather miserable and is not sleeping well.

8·XII·37. Jaundice still present; patient depressed.

12·XII·37. Jaundice less noticeable. Patient said that she no longer had the epigastric pain.

15·XII·37. The jaundice could hardly be distinguished. The patient felt much more cheerful.

20·XII·37 The patient was allowed up. She was pale but no longer jaundiced. She felt weak on her feet.

23·XII·37. She feels very depressed and her appetite is poor. Breathlessness is now practically absent.

25·XII·37. The patient fainted to-day when she was up and listening to carol singers. She is off her food and is depressed.

27·XII·37. Patient still off her food.

29·XII·37. Patient is sleeping badly but says she 'feels fine': appetite is better.

31·XII·37. Patient received news of the death of a niece and was much upset.

1·I·38. She slept badly and collapsed on rising in the morning. – off her food and sobbing all day.

2·I·38. Even although morphia was given, the patient says she slept badly.

4·I·38 Still depressed and sleeping badly

5·I·38. Patient feeling much better – has decided not to worry, and is up and about.

3. Treatment other than that directed to the blood.

3·XII·37. Light diet. - ordinary diet on 16·12·37.

23·XII·37. Aspirin gr V
Phenacetin gr X } 1·15 am.
Caffein gr IV

24·XII·37. Nepenthe m. XXV 11·15 pm.

25·XII·37 " m XX 2·15 am.

25·XII·37. Aspirin gr X
Phenacetin gr X } 10 am.
Caffein gr IV

25·XII·37. Nepenthe m. XXX 10·5 pm

26·XII·37. Chloral Hydrate gr XX
Sod Bromide gr XX } 1·35 am.

28·XII·37. Acid Hydrochlor. 3 i ÷ tid.

28·XII·37. Chloral Hydrate gr XXV
Sod Bromide gr XXV } 11·45 pm.

30·XII·37. Chloral Hydrate gr XXV
Sod Bromide gr XXV } 1·45 am.

31·XII·37. H.i Morphine gr 1/6
Hyoscine gr 1/100 } 10·5 pm.

2·I·38. H.i Morphine gr 1/4
Hyoscine gr 1/100 } 8·30 am.

2·I·38. Nepenthe gr XXX - 10·5 pm.

FURTHER NOTES.

25/1/38.

Patient reported

Red cells 3,980,000

Haemoglobin 85%

Reticulocytes 1·5%.

4 cc Neo Hepaten given.

Further treatment to be given by patient's doctor.

4. The Blood -

(a) Treatment Given.

7·XII·37.	Neo Hepaten.	2cc daily
13·XII·37		Reduce to every other day
15·XII·37.		Stop.
28·XII·37.		2cc.
4·I·38.		4cc
8·I·38.		2cc.

(b) The Blood Picture.

Film on admission:

This showed anisocytosis and poikilocytosis. The cells were large, but comparatively poorly filled. There was evidence of polychromasia. No nucleated red cells were seen.

I Main blood counts

Day in Hospital	Rbc's	Hb.	Colour Index	Reticulocytes	Wbc.	Date.
1						3rd Dec.
2						4th ..
3	1,870,000	43%	1·2	Few.	4,000	5th ..
4	1,910,000	42%.	1·1	Few	5,800	6th .
5						7th ..
6	1,980,000	46%.	1·2	4·3%.	5,200	8th ..
7		48%.			5,000	9th .
8				5·2%.		10th ..
9	1,840,000	50%.	1·3	7·1%.	5,000	11th .
10						12th ..
11				13·5%.		13th ..
12	2,820,000	65%.	1·2	27·0%.	4,800	14th .
13				17·4%.		15th ..
14	3,120,000	65%.	1·0	15·0%.	3,800	16th ..
15				7·2%.		17th ..
16.	3,290,000.	68%.	1·0	3·1%.	3,800.	18th

Day	Rbc.	Hb	C.I	Reti	Wbc.	Date
17						14th Dec
18				2·4%		20
14	3,270,000	65%.	·99	3·4		21
20						22
21	3,850,000	67	·86	2·8	3,200	23
22				3·1		24
23						25
24	3,510,000	65	·92	2·0	4,000	26
25		65	·	2·0		27
26	3,460,000	70	·88	3·0	4,200	28
27	3,560,000	69	·97	2·4		29
28	3,570,000	70	·98	2·9		30
29				1·2		31
30	4,060,000	69	·85	1·6	5,600	1st Jan
31				2·2		2
32	3,800,000	76	1·0	2·2	4,200	3
33				2·1		4.
34	4,400,000	84	·95	1·4	5000.	

III	Differential White Count				
	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes
7/12/37	41%.	2%	0	44%	13%.
13/12/37	50%.	1%	0	41%.	8%.
20/12/37	53%	2%	0	34%	11%.
25/12/37	62%.	2%	2%.	31%.	3%.
27/12/37	61%	0%	0	35%.	4%
29/12/37	64%	2%	0	32%	2%
1/1/38	66%	1%	0	30%.	3%
5/1/38.	72%	1%.	1%	24%.	2%.

IV Arneth Count.

(Unfortunately this was not done at the time of the other counts, and the earlier slides were not kept, so that this count, and that of the relative size of erythrocytes, is incomplete.)

	Lobes. 1	2	3	4	5	6	7
23/XII/37.	8	20	30	28	10	4	—
26/XII/37.	5	19	36	22	12	3	
1/1/38.	10	24	28	20	14	2	
5/1/38.	8	24	32	20	12	4.	

V Indication of relative sizes of erythrocytes

(Note - this is not an accurate representation, as explained in the notes on Technique of investigation)

	Macrocytes	Microcytes	Poikilocytes
23/XII/37	3%.	1%.	4%.
26/XII/37	4%.	2%.	3%.
28/XII/37	6%.	2%.	2%.
1/1/38	3%.	1%.	1%.
5/1/38.	2%.	1%.	4%.

VI Special Cells

No nucleated red cells were found, and there were no unusual white cells.

VII Other Investigations

3/1/38 Platelets - 300,000.
Bleeding Time 3 minutes

CASE B

NAME :- Agnes Jack (SINGLE)
AGE :- 47 years.
OCCUPATION :- Waitress (Unemployed).
ADDRESS :- 233, Leith Walk, Edinburgh.
RECOMMENDED BY: Dr Johnstone, Dalziel Place
DATE OF ADMISSION :- 15th December, 1937.
DATE OF FIRST EXAMINATION 18th December, 1937.
WARD :- 25, RIE.

COMPLAINT :- General Unfitness - 2 years.
Palpatation on exertion - 1 year.
Sensation of heaviness in the legs - 9 months.

HISTORY :-

The patient considers that her trouble dates from December, 1935, when a submucous resection of her nose was done. She did not feel at all well after the operation, and left her job, where she was employed as a waitress. During 1936 she continued to feel GENERALLY UNFIT, without having any other definite symptoms. Her appetite had never been very good, but she did not notice any change for the worse at this time, and never noticed any feeling of breathlessness during the year 1936.

In December, 1936, the patient's mother developed a cerebral haemorrhage, and the patient was kept very busy attending to her mother. She felt more run down even than before, and began to be greatly troubled with BOILS in the neck and arms. Her mother died at the end of December, and shortly after this the patient developed a febrile illness with sudden onset, much coughing and sneezing, some

headache, and marked feeling of depression. This was diagnosed as INFLUENZA, and the patient was confined to bed for two weeks. When she was able to go about again, in the middle of January, 1937, she found that she felt very TIRED and was BREATHLESS on exertion. On walking uphill, or hurriedly on the level, she tended to develop PALPATATION. She felt her heart beating very forcibly and rapidly: associated with this, she experienced a mild PAIN in the EPIGASTRIUM. This symptom was related to the palpatation, and was proportional to it. There was no selective radiation. The discomfort was relieved by rest, and disappeared about half an hour after she stopped exercise.

About the same time she began to be troubled with headaches. These were of a vague character and appeared to her to 'fill her head'. They were present during the day and sometimes at night if she lay awake. Another very troublesome feature was a FEELING OF NUMBNESS and HEAVINESS in both legs. When she lay in bed with a hot water bottle, the latter might be so hot that she could not touch it with her hands, and yet her FEET DID NOT FEEL the HEAT. when they were brought into contact with the bottle. If she walked any distance, her LEGS felt SORE and WEAK. The pain was especially marked in the calf. If she stopped and stood for a minute or two, the symptoms practically disappeared again. Her limbs did not feel abnormally cold, but she was troubled a great deal with a feeling of 'PINS and NEEDLES' in her feet. The symptoms in her limbs ~~have~~ did not cleared up during the course

of the year, but they did not become progressively worse. They were still present at the time of admission.

About June, 1937, people first began to remark to the patient that her FACE had a YELLOWISH TINGE. She noticed, too, that she was becoming THINNER, and losing weight. In October, 1937 she weighed 9 stone 2½ lb. on automatic scales. At the beginning of December she weighed 8 stone 9 lb. This patient never suffered from giddyness, noises in the ears, oedema, or from lingual symptoms.

She first went to see her doctor in October, 1937, because of her palpation, general lassitude, and lower limb symptoms. He told her that she was "suffering from nerves". He advised rest, and gave her a drop bottle of what she said was digitalis. She did not improve with this treatment, and was sent to see Dr. Comrie, who admitted her to Ward 25 at once.

PREVIOUS HEALTH.

She had measles when a child.

A submucous resection of the nose was done in December, 1935.

Otherwise her health had been good.

SOCIAL HISTORY.

The patient was an unemployed waitress who left her job because she felt unfit. She had been employed in the same situation (an Edinburgh café) for a number of years and had quite enjoyed her work. She said that she took plenty exercise and plenty fresh air

but she lived alone in a very small, old house in a densely populated area, and during the year previous to admission she felt so unfit that she did bother very much about cooking for herself. Her diet consisted, to a large extent, of carbohydrates, and there does not appear to have been much in the way of fresh fruits and vegetables.

She was a non-smoker, and did not drink alcohol.

FAMILY HISTORY.

Father - died at the age of 69 from asthma and bronchitis

Mother died aged 80, of cerebral haemorhage.

A brother died aged 24 years, of pulmonary tuberculosis. Two sisters were alive and well.

STATE ON EXAMINATION.

The patient was a middle aged female of average intelligence. Her muscles were rather flabby, and she was thin, (the tendons at the wrist being prominent), but not emaciated; it did appear, however, as though she might have been losing weight recently. The face was pinched, and had a distinct pallor, with a marked tinge of jaundice. The mucous membranes of the lips, and the conjunctiva of the lower eyelids, too, were pale, and the icterus tinge was present in the sclera, but only to a very mild degree.

The patient appeared equally content to sit propped up or to lie down in her bed, and had a contented appearance. She did not appear to be in any way depressed by her illness

Temperature	98°
Pulse Rate	86
Respirations	22
Blood Pressure	125/75.
Height	5 feet 5½ inches
Weight	8 stone 7½ lbs.

HAEMOPOIETIC SYSTEM.

All the symptoms directly concerned with this system have already been described. Briefly, they were as follows:

Tiredness: breathlessness and palpitation: a yellow tinge of the face was noticed. It may be remarked that the patient did not complain of pallor of the face, but when asked, agreed that before the jaundice became marked, she had been becoming paler.

Her face had a marked tinge of jaundice and underlying this it appeared pale, as already described.

THE BLOOD (further findings under Progress Notes)

18: XII: 37.

Haemoglobin	34%.
Erythrocytes	1,140,000.
Leucocytes	3,200.
Reticulocytes	.4%.
Colour Index	1.5.

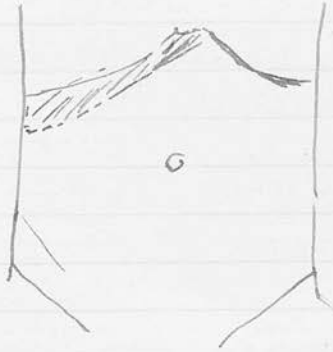
Film

Anisocytosis was marked, and there was some poikilocytosis: many cells were of large size, oval shape, and well filled. There was no punctate basophilia, and there were few nucleated red cells, but one or two megaloblasts could be seen

Differential White Count

Neutrophils	52 %
Eosinophils	2 %
Lymphocytes	34 %
Monocytes	12 %.

There were no palpable glands in the neck. The spleen was not enlarged. The smooth, regular lower edge of the liver was palpable three finger breadths below the costal margin



Van den Berg.	Delayed Direct Reaction
Icteric Index	12.

ALIMENTARY SYSTEM.

Almost a year before admission, the patient was troubled with epigastric pain. This, however, was associated with palpitation, and was relieved by rest, being in no way related to the taking of food. Her appetite had never been good, and she did not notice any change during the course of the present illness. There were no special food likes or dislikes

She did not suffer from flatulence, from attacks of vomiting, or from a feeling of weight in the epigastrium. There was thirst and no acid eructation.

There were no lingual symptoms.
The patient was inclined to be constipated, and took cascara to relieve this.

SIGNS

The lips were pale: the teeth were in good condition. There was no evidence of pathological change in the throat.

The tongue was clean and moist. The surface of the organ was smooth, without fissure, and there was atrophy of the papillae.

The abdomen moved freely with respiration: the muscle of the abdominal wall was flabby and lacking in tone, and the skin had a yellow tinge. The symmetry was not impaired, there being no local prominences.

On palpation, no points of tenderness could be found. The lower edge of the liver was palpable three finger breadths below the costal margin: the spleen and kidneys were not palpable. There was no splashing of the stomach three hours after a meal.

Percussion confirmed the hepatic enlargement, and revealed no other abnormality. There was no free fluid in the abdomen.

Investigation of the gastric contents by means of a test meal was carried out. The findings are given overleaf.

GASTRO-INTESTINAL ANALYSIS.

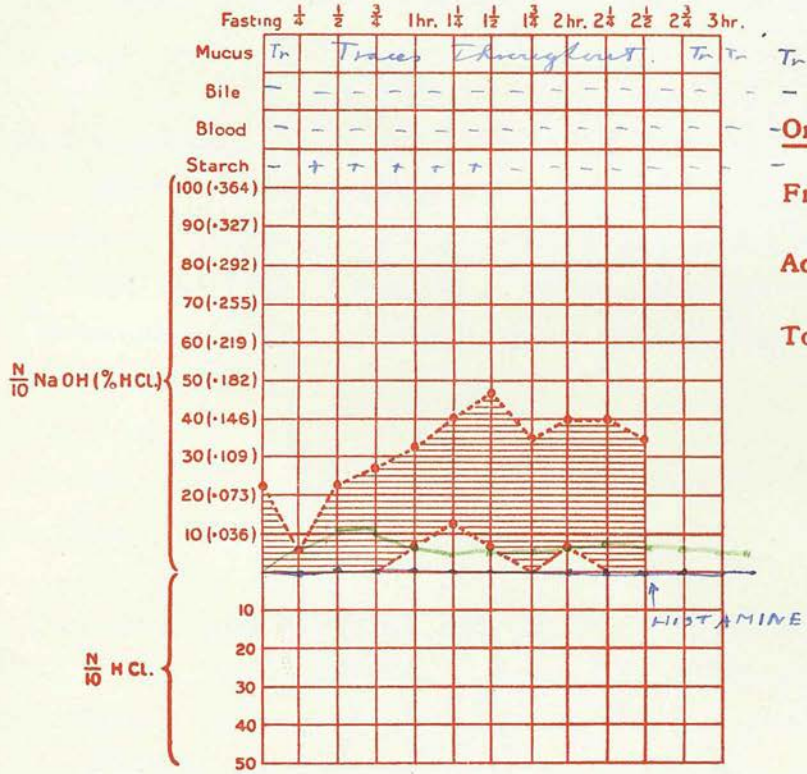
Name of Patient Miss Jack *Ward* 25 *Bed*

1. FRACTIONAL TEST-MEAL. Date. 16/12/37.

Fasting Juice.

Volume. 15cc

Cells.



The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——— represents free HCl.

..... represents total acidity.

Summary.

2. FÆCES.

CARDIO-VASCULAR SYSTEM.

After an attack of influenza eleven months before admission, the patient was breathless on exertion. On walking hurriedly she was troubled with palpitation, and associated with this there was mild epigastric pain, relieved by rest.

The pulse rate was 120. The pulse was regular in time and force, and the wave gave the impression that the pulse was of small volume. The vessel wall was palpable.
Blood Pressure. 120/60. There was no arterial pulsation visible in the neck.

There were no abnormally distended veins to be seen anywhere.

The apical impulse of the heart was not visible, and no pulsation was to be seen in other situations. The apex beat was palpable in the fifth space, four inches from the mid line. There were no palpable thrills On percussion, the left border was found to lie just within the midclavicular line, and the right border was not displaced.
In the mitral area, a blowing systolic murmur was heard, and it was propagated into the left axilla. A systolic murmur of similar quality was heard, too, in the aortic area and over the upper right half of the sternum. It was not heard in the arteries of the neck. The sounds were closed in the tricuspid and pulmonary areas.

Electrocardiograph Reports

16·XII·37

"Control records show normal rhythm with tachycardia (105/minute) T waves biphasic in lead I: negative in leads II and III. T waves low in chest leads.

After exercise (18 ascents in 1½ minutes, producing slight tightness across chest) standard lead shows some exaggeration of the negativity of T in leads II and III, and minor changes in chest leads.

Summary. Patient was unable for more than very mild exercises, and changes in cardiographs are inconclusive. The inversion of T in leads II and III, and biphasic T. in the resting cardiogram are significant, however, of myocardial damage - possibly due to anaemia."

7·I·38.

"Unfortunately only standard leads were taken at rest.

The record shows marked changes from that taken on 16/12/37. T waves are now positive in all leads, " and the cardiograms completely normal.

10·I·38.

"Electrocardiogram is completely normal, rate approximately 100

Rebreathing experiment was carried through in closed system with CO_2 absorption in soda lime. Under condition of anoxaemia patient developed mild praecordial pain. The experiment was

discontinued and the oxygen content of expired air estimated. This was found to be approximately 9%. Simultaneous electrocardiograph record shows little or no change."

12/1/38. "Resting electrocardiogram as on 7/1/38.
Exercise test: 41 ascents of steps in 3 minutes - slight pain developed after lying down on couch
No significant alteration in ST or T waves."

13/1/38. "Breathing experiment repeated. Final oxygen concentration in inspired air = 1·8 vols. %.
Patient complained of praecordial tightness and distress.

RESPIRATORY SYSTEM.

There was no cough, expectoration or pain in the chest. The occurrence of breathlessness has already been referred to.

The respiratory rate was 22/minute, and the breathing was of thoraco-abdominal type, with no abnormality of rhythm.
The fauces were healthy.

THORAX.

The chest was of the normal healthy shape and was symmetrical. There was no evidence of past rachitic change. The ribs were not unduly prominent. The spine was straight. There was no localised chest retraction or bulging.
Movement was free and equal on the two sides, and there was no localised change.

On palpation, it was found that vocal fremitus was unimpaired.

Percussion revealed normal resonance throughout the chest, and tidal percussion, too, was unimpaired.

Breath sounds were vesicular throughout, and there were no accompaniments. Vocal resonance was equal on the two sides.

URINARY SYSTEM.

There were no symptoms referrable to this system. The kidneys were not palpable.

Urine.

15·XII·37. Was of straw colour, specific gravity 1016. Acid reaction. Mucus deposit. No albumen or sugar was present. The test for excess of urobilinogen with aldehyde reagent gave a positive finding.

NERVOUS SYSTEM.

Mental Functions.

This patient was of average intelligence: she did not appear to be unduly emotional, and her memory for recent and for past events was good. She did suffer from sleeplessness, and her speech was not impaired.

Cranial Nerves. - SUMMARY - no abnormal findings.

I. No sensory disturbance.

II Visual acuity good, and fields of vision unimpaired. No retinal changes.

III: IV: VI Ocular movement was unimpaired in all directions, and there was no

nystagmus or ptosis. There was no diplopia or strabismus. The pupils were round and equal. There was no impairment of direct or consensual reaction to light, or of the reaction to accomodation.

V Motor. There was no impairment of movement in the muscles supplied.

Sensory: The corneal reflex was present: there was no impairment of sensation over any of the areas supplied by the nerve.

VII There was no evidence of supra- or infra-nuclear paralysis of either nerve, and no hyperacousis

VIII No auditory impairment: air conduction was better than bone conduction. There was no tinnitus or dizzyness.

IX There was no dysphagia, or anaesthesia of the pharynx

X The palate moved in the midline

XI No muscular impairment

XII No deviation of the tongue to either side and no tremor.

CERVICAL SYMPATHETIC.

There was no evidence of paralysis.

MOTOR FUNCTIONS

There were no abnormal movements, and no muscle weakness or impairment of movement

in any of the limbs. The muscles were soft, but were not hypotonic: nor was there any rigidity. Movements in the upper and lower limbs were co-ordinated.

REFLEXES.

Superficial. The conjunctival and palatal jerks were not impaired. The abdominal reflexes could not be elicited. The plantar reflexes were bilaterally plantar-flexor

Deep.

Biceps	Equal and brisk
Triceps	Equal and brisk
Supinator	Equal and brisk
Jaw.	Present.
Knee	Equal and very brisk
Ankle.	Equal and very brisk

No knee or ankle clonus was present.

SENSORY FUNCTIONS

Subjective sensations experienced by the patient were as follows.

1. Vague headaches
2. A feeling of numbness and heaviness in both legs.
3. A diminished sensation of heat in the lower limbs, so that she did not feel the heat of a hot water bottle in contact with her legs or feet.
4. A feeling of vague 'soreness', and weakness in her legs on walking any distance, the 'soreness' being most marked in the calf, and relieved by rest.
5. A feeling of 'pins and needles' in the

feet. There was no ataxia.

Objective.

Upper limbs: There was no loss of the sensations of touch, pain, pressure, heat and cold or of vibration sense, muscle and joint sense or stereognostic sense.

Lower limb. Vibration sense was lost in the foot and lower third of the leg on each side. Other sensations, including that of heat and cold, were not impaired.

There were no vasomotor or trophic changes.

INTEGUMENTARY SYSTEM.

No symptoms were present.

The skin had a tinge of jaundice. Apart from this, there were no changes of note.

REPRODUCTIVE SYSTEM.

Menopause aet. 45.

LOCOMOTORY SYSTEM.

When she walked any distance, the patient's legs felt sore and weak, the pain being most marked in the calves and relieved by rest.

ENDOCRINE SYSTEM

Nothing to be noted.

PROGRESS NOTES.

1. Investigations carried out.

17.12.37. Van den Bergh - Direct Reaction, delayed.
Icteric Index - 12.
Height 5 feet 5½"
Weight 8 stone 7½ lb.
Pulse Rate 95.
Respiratory Rate 20.
Electro cardiograph reports - already given.
Fractional Test Meal - " "

18.12.37. Pulse Rate 85
Respiratory Rate 20.

23.12.37. BP 108/60.

24.12.37 Urine - lemon colour: sp gr 1015: acid
+ albumen.

31.12.37 " orange colour 1025 acid
no albumen mucus deposit

1.1.38. Weight 8 stone 6 lb

8.1.38. 8 stone 8 lb. BP 125/65.

15.1.38. 8 stone 8½ lb.

After 18.12.37, the temperature varied between 96° and 98.1°, and the pulse rate between 70 and 92. Respiratory rate remained around 20/minute.

2. General Progress.

15.12.37 Admitted.

18.12.37 The patient was fairly cheerful. The jaundice and cardiac murmurs were still present.

20.12.37. She is now taking her food quite well, and is more cheerful.

24.12.37 She is now much better and less jaundiced. Food is taken much more readily, and she is already talking about getting out.

28.12.37. The patient is very depressed, as there have been three deaths in the ward.

29.12.37 Patient suffering from catarrh.

30.12.37 She is bright and cheerful, and taking her food and sleeping well.

31.12.37 She was allowed up - breathlessness is still present, but praecordial pain not noticed

1.1.37. Jaundice now practically absent.

4.1.37. Patient is bright and is sleeping and eating well. No abnormal sensation now felt in the lower limbs.

8.1.37. No cardiac murmurs now audible.

13.1.37. Patient transferred to side ward and 'feeling fine'.

15.1.37 Patient wants home. - sleeping and eating well. No breathlessness or praecordial pain

18.1.37. Discharged to Convalescent Home.

3. Treatment.

15·XII·37 Triple Tab gr X 9pm
Lumenal gr ¼ 11-30 pm

17·XII·37 Light diet.

Vegetable laxatives were given throughout, when required

4 The Blood

(a) Treatment.

16·XII·37 Campolon 5cc daily
31·XII·37 5cc thrice weekly

(b) Investigation.

1. Film on admission

This showed anisocytosis and poikilocytosis Many cells were of large size and well filled. A very small number of megaloblasts were present: polychromasia was not a marked feature.

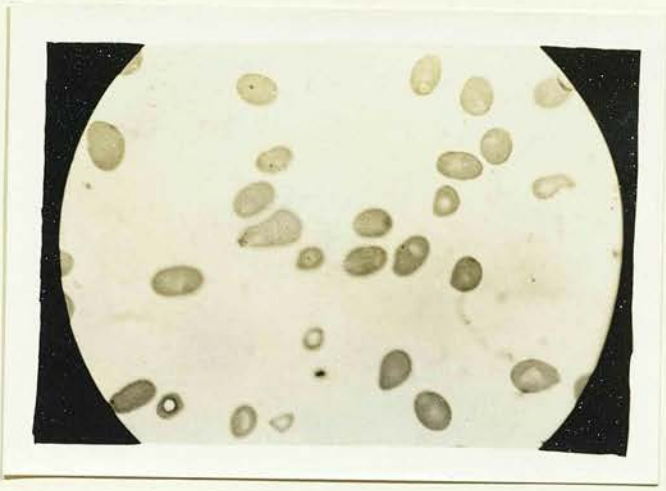
II Main blood counts.

Day in hospital	Rbc	Hb.	CI	Retic	Wbc.	Date.
1	1·14 (1,140,000)	34%.	1·5	Few	4,600	15th Dec
2						16
3	1·22	36%	1·5	4%.		17
4		38%				18
5	1·32	38%	1·4	10%.	4,800.	19
6	1·54	44%.	1·4	16%		20
7	1·72	46%.	1·3	24%		21
8				20%.		22
9	2·22	58%.	1·3	18·4%	5,000	23
10	2·31	54%.	1·1			24
11						25
12	2·49	50%.	1·0	10·6%	6,200	26

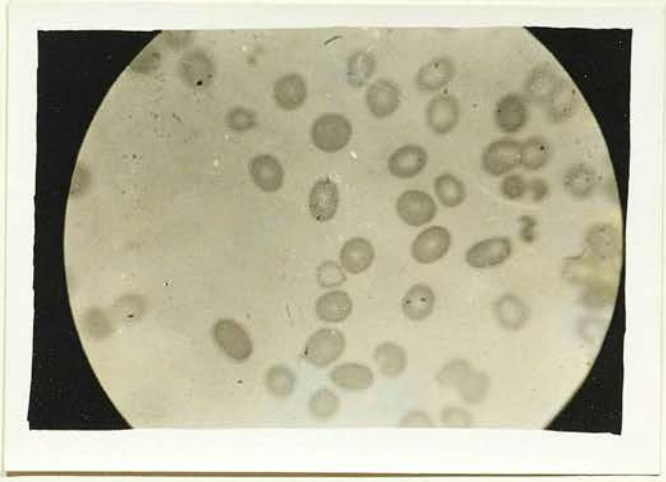
Day	Rbcs.	Hb	Cl.	Reti	Wbc.	Date
13	2·46 (2,460,000)	56%.	1·1	6·4%.		27th Dec
14						28th "
15	2·98	63%.	1·1	5·2%.	6,800	29 "
16	2·97.	62%.	1·1	4·8%.		30 "
17				2·8%.		31 "
18	2·98	64%.	1·1	2·8%.		1 Jan.
19				2·4%.		2
20	3·16	72%.	1·2	2·3%.	6,400	3
21	"			2·4%.		4
22	3·79	73%.	·96	2·1%		5
23	3·6	70%.	·97	1·0%.		6
24						7
25	3·49	71%.	1·0	1·0%.	5,600	8
26						9
27						10
28	3·52	70%.	·99	1·2%.		11
29						12
30						13
31	3·78	69%	·91	1·6%	4,400	14
32						15
33.	3·44.	73%.	·93	1·2%.	5,000.	16

III Differential White Counts

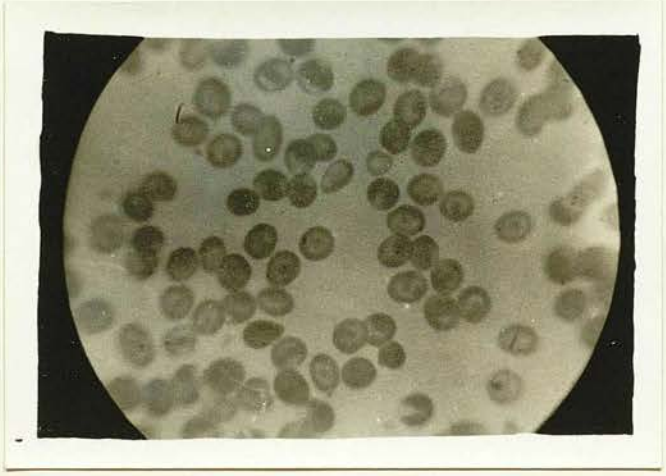
	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes
19/XII/37	50%	2%	1%.	35%.	12%.
22/XII/37	51%.	0%	0	39%.	10%.
26/XII/37	53%	0%	0	38%.	9%.
30/XII/37	55%	3%	2%.	35%.	5%.
3/1/38	54%.	6%	0	36%.	4%.
8/1/38	60%	6%	1%.	30%.	3%
14/1/38	65%	5%	0	24%.	6%
16/1/38.	60%	6%.	1%.	28%.	5%.



ON ADMISSION.



DURING TREATMENT



ON DISCHARGE

IV Arneth Count.

Unfortunately this was not done at the time of the other counts, and the stain had faded from the white cells in this patient's case alone.

V Relative Size of Red Cells.

	Macrocytes	Microcytes	Normocytes.
18/XII/37.	16%.	4%.	11%.
22/XII/37.	12%.	5%	10%.
26/XII/37.	14%.	4%.	4%
30/XII/37.	11%.	4%.	4%
4/I/38	5%	2%.	1%
8/I/38	7%	3%	2%
14/I/38	6%	2%	4%
16/I/38.	5%.	2%.	1%.

VI Special Cells.

Megaloblasts were present in films made on 15/XII/37, 17/XII/37, and 21/XII/37, but were not seen thereafter.

VII Other Investigations

20/XII/37	Platelets	80,000.
1/1/38	"	160,000.
23/XII/37	Bleeding Time	4 minutes.

CASE III

CASE C.

NAME :- JOHN MACINTOSH (Married).

AGE :- 46 years.

OCCUPATION :- Policeman.

ADDRESS :- c/o Wilson, 55 Restalrig Road, Edenburgh

DATE OF ADMISSION 29th November, 1937.

RECOMMENDED BY :- Dr Butler, Charlotte Street, Leith.

DATE OF FIRST EXAMINATION :- 18th December, 1937.

WARD - 31, R.I.E.

COMPLAINT.

Bad taste in the mouth and distaste for food	6 months.
Sore tongue	6 months
Loss of weight and Tiredness	2 months.
Pain under right lower ribs	6 weeks
Puffiness around the eyes	6 weeks.

HISTORY.

The patient considers that he was in perfect health until June, 1937, when his wife had a mental disturbance at the time of the menopause. The patient was greatly upset by the occurrence, and went into lodgings, which resulted in a change of food and surroundings. At that time he LOST HIS APPETITE, which had always been fairly good, and also was troubled with what he described as a "poisonous" TASTE that was constantly present in his mouth, and SORENESS of the TONGUE. It was sore all day long, and there were times when it was worse than others: the smoking of a cigarette aggravated this symptom. The unpleasant taste, loss of appetite and painful tongue were still present on admission. All this time he felt LISTLESS and generally UNFIT. His bowels continued to move regularly.

Two months prior to admission, he noticed

to LOSE FLESH and was more off his food than ever. The development of this thinness was noticed both by himself and by his friends. He went to see his doctor at this time: the latter tested his urine, then treated him with sodium bicarbonate and magnesium oxide. The doctor told him that he was suffering from gastritis due to his advancing years. No benefit was derived from this treatment.

About six weeks before admission, the patient began to suffer from BREATHLESSNESS on exertion. This did not trouble him very much, however. He noticed, too, that he was becoming PALER, and during the month prior to admission, both he and his friends noticed a YELLOWISH TINGE in his face. He gradually felt more and more exhausted, and thought that he would collapse if he carried on with his work. He lost 1½ stones weight in six months. About the time that the breathlessness commenced, the patient noticed a PUFFINESS around the eyes. This was present all day, and was not worse at any particular time of day.

Six weeks prior to admission, when he had just returned to Edinburgh after a journey, he was suddenly seized with an acute PAIN under his right costal margin, when in his own home. He cannot recollect what he was doing at the time. This pain was constantly present, not colicky, and was situated about three inches from the midline. He felt cold, and shivered, but did not vomit and had no respiratory distress. He went to bed, and the pain remained for two days, but did not

prevent him from sleeping. It went away gradually, but a dull ache remained in the same place for about four weeks. At the time of the pain, he had a little FREQUENCY of MICTURITION: he passed water four or five times per day when the pain was acute, but did not require to rise during the night. He thinks that his urine was a little darker in colour at this time. He resumed his work after a few days.

However, he began to feel even weaker than before, and during the three weeks before admission, he felt UNSTEADY on his legs. During this period, too, he felt even more breathless on exertion. About seven days prior to admission, he noticed slight SWELLING of his ANKLES at night. In the latter part of his illness, he felt slightly GIDDY, but had no noises in his ears. He was never troubled with palpitation.

Things became so bad that his doctor arranged for his admission to the R.I.E.. He entered Ward 31 on 29th November, 1937.

PREVIOUS HEALTH

He had never had any illness of note, having enjoyed perfect health throughout his life..

SOCIAL HISTORY.

The patient was a constable in the Edinburgh Police Force. Until June, 1937, he lived with his wife: at that

time she had a mental upset, and from that time the patient lived in lodgings. He was quite happy in his occupation, which he had held for twelve years. His meals were somewhat irregular, and he had to work out of doors in all sorts of weather. He was in a position to obtain plenty wholesome food: he was a moderate smoker who did not drink to excess, smoking five to ten cigarettes per day, and drinking two or three pints of beer each week.

FAMILY HISTORY.

His mother; aet. 70, was alive and healthy
His father; died at the age of 75- cause unknown.
He had one son, who died in infancy.

STATE ON EXAMINATION.

The patient was a man of average intelligence who appeared to be very depressed by his condition, and who wished to talk about nothing else. He lay quietly in bed with the bedclothes pulled well up, because he was feeling cold. He was a well developed man with a prominent jaw: he appeared, however, to be rather thin, but not wasted. The face had a yellow tinge with a malar flush. The sclera, too, had a tinge of icterus. The lips and the conjunctivae of the lower eyelids were pale.

Temperature	98·2°
Pulse Rate	80.
Respirations	20

Blood Pressure 116/50.
Height 5 feet 11 inches.
Weight 11 stone 10 lbs.
W R Negative

HAEMOPOIETIC SYSTEM.

The symptoms which may be referred directly to this system were:
Tiredness: breathlessness: giddyness:
He became paler, and a yellow tinge was noticed in his face. For seven days he noticed oedema of the ankles.

THE BLOOD - (further findings under Progress Notes)

16. XII. 37

Haemoglobin	32%. (Sahli).
Erythrocytes	1,670,000.
Leucocytes	4,800.
Reticulocytes	very few.
Colour Index.	1·4.
Neutrophils	50%
Eosinophils	3%
Lymphocytes	34%.
Monocytes	13%.

By Film

Anisocytosis and poikilocytosis were marked. Many of the cells were well filled, of large size and oval shape. There was no punctate basophilia, and no nucleated red cells were seen, other than a very occasional megaloblast.

There were no enlarged lymph glands. and the liver and spleen were not enlarged. There was no oedema of the ankles or sacrum

ALIMENTARY SYSTEM.

The first of the patient's complaints was of loss of appetite, with a "poisonous" taste in the mouth, and soreness of the tongue.

Six weeks before admission, he was suddenly seized with acute pain under the right costal margin: this was situated three inches from the median line, was constantly present, and lasted for two days, then gradually went away. There was some shivering associated, but no vomiting. At the time there was a little frequency of micturition.

There was no history of vomiting or of other gastric symptoms; the bowels moved regularly.

SIGNS.

The lips were pale, and the gums healthy. Teeth were all false.

The tongue was clean, smooth, red and moist: atrophy of the papillae was not a marked feature: there were no fissures or ulcers.

The abdominal wall was well covered, and the symmetry was not impaired. Movement with respiration was free. No peristaltic waves were visible.

On palpation, the wall was found to be rather flabby; in the left iliac fossa, a firm tube about two inches long was felt. This appeared to be loaded colon. No further masses were palpable, and the liver and spleen could not be felt.

No tenderness could be elicited at any point. No pain was experienced when the thumb

X ray Report.

4/12/37

Plain films of gall-bladder region : no calculi seen.

Opacol films - at end of 14 hrs. the density of the gall-bladder shadow may be regarded as being within normal limits

15/12/37. Oesophagus, stomach, and duodenum negative

was pressed over the fundus of the gallbladder, and a deep breath taken (Murphy's test): There was no hyperaesthesia over the right lower ribs posteriorly (Boas' test), and no tenderness over the costal cartilages. There was no splashing of the stomach three hours after a meal.

No dullness in the flanks or fluid thrill was detected.

On percussion of the liver, its lower margin was found to lie 1½" below the costal margin on expiration. The spleen was not enlarged.

The faeces were of normal appearance.

X-ray examination – recorded on opposite page.

Permission to do a test meal was not given.

CARDIO-VASCULAR SYSTEM.

The patient suffered from breathlessness on exertion, for six weeks, and slight oedema of the ankles for seven days. As already mentioned above, on one occasion she was seized with acute pain under the right costal margin: this did not involve the praecordial region, however. There was never any palpitation

The pulse was regular in time and force, rate 80/minute. The wave was of normal character, rising sharply, and falling away more gradually. The vessel wall was not palpable.

Blood Pressure 116/50.

Veins. The veins of the neck and chest were not distended, and there was no abnormal neck

pulsation. No cyanosis or oedema could be detected.

The apex beat of the heart was visible in the fourth space, very slightly outside the mid clavicular line. It was well localised in position. No abnormal pulsations were seen.

On palpation, this beat was felt just outside the mid clavicular line, well localised and not unduly forcible. No thrills were felt. The position of the heart as revealed by percussion may be indicated by the following formula. — $\frac{III}{\frac{1}{2}" \mid 4\frac{1}{2}"}$

On auscultation, the rhythm of the heart was found to be regular. A soft systolic murmur was present in all areas: the point of maximum intensity was in the mitral area, and from this point, it was propagated out to the left axilla. The second sound was closed and of good quality in all areas.

RESPIRATORY SYSTEM.

There was no cough, expectoration or pain in the chest.

The respiratory rate was 20/minute, and the breathing was of abdomino-thoracic type.

The throat was clean and healthy.

THORAX. The chest was fairly well covered, and was symmetrical. The spine was straight, and there were no localised changes of form. Movements were free on both sides, and there was no localised diminution of movement.

Vocal fremitus was equal on the two sides, and was not impaired

On percussion, it was found that resonance throughout the chest was unimpaired the note being of good quality. Tidal percussion revealed free diaphragmatic movement.

On auscultation, breath sounds were vesicular, and there were no accompaniments. Vocal resonance was equal and unimpaired on the two sides.

URINARY SYSTEM

Six weeks before admission, the patient had some frequency of micturition when the acute pain in his right side (under the costal margin) was severe. He had to pass water four or five times in the day, and as he had to do this urgently, the symptom was of the nature of urgency of micturition. After the pain went away there was no frequency, and no haematuria or dysuria. There was never any pain in the loins or bladder.

The kidneys were not palpable.

URINE
(on admission)

Acid reaction : orange colour : no naked eye deposit
Blood - negative : albumen negative : sugar - trace.
Acetone - nil : bile - ? trace (HNO_3 test).
Pus - nil.

Microscopic Few amorphous urate crystals

NERVOUS SYSTEM

In June, 1937, the patient was much disturbed because his wife become temporarily upset mentally during the period of the menopause. The patient was troubled with sleeplessness after that time.

The patient was of average intelligence. He was depressed, but very anxious to talk about his illness. Speech was not disturbed, and there were no hallucinations or delusions.

Cranial Nerves.

I. No disturbance.

II. Visual acuity good: fields of vision not impaired: no retinal changes.

III, IV, VI. There was no impairment of ocular movements, and no nystagmus, ptosis or diplopia. Pupils were round and equal, and reacted well to light and accomodation.

V. Motor - no impairment of movement in the muscles supplied
Sensory - no impairment of sensation over the areas supplied by any of the three divisions of the nerve.

VII. There was no paralysis of the facial muscles, and no hyperacousis.

VIII. No auditory impairment. Air conduction was better than bone conduction. There was no tinnitus, but the patient felt slightly giddy just before admission

IX. No dysphagia, or anaesthesia of the pharynx.

X The palate moved in the midline

XI No muscular impairment

XII Tongue was projected straight forwards: no tremor.

CERVICAL SYMPATHETIC - No evidence of paralysis.

MOTOR FUNCTIONS.

There were no abnormal movements: there was no weakness of any muscles, or impairment of movement. The muscles were not hypotonic, nor was there any rigidity. Movements were co-ordinated in upper and lower limbs.

REFLEXES.

Superficial

The conjunctival, palatal and abdominal reflexes were not impaired. The plantar reflexes were bilaterally plantar flexor.

Deep.

Biceps	Present, rather sluggish, equal
Triceps	" " " "
Supinator	" " " "
Knee	Present and equal
Ankle.	Present and equal.

No knee or ankle clonus was present.

SENSORY FUNCTIONS.

There were no subjective phenomena of cold, numbness or tingling in the limbs. There was no headache.

Objective

Upper Limbs. There was no loss of sensation of pain, touch, pressure, heat

and cold, or vibration, muscle and joint or stereognostic sense.

Lower limbs - also no loss of sensation.

No vasomotor or trophic changes were present.

INTEGUMENTARY SYSTEM

The skin had a tinge of jaundice - otherwise there was no change.

LOCOMOTORY SYSTEM.

No abnormality

ENDOCRINE SYSTEM

No abnormality.

PROGRESS NOTES.

1. Investigations

2·XII·37. W R – negative.
4·XII·37. X ray of Gall Bladder region – already reported.
7·XII·37. Weight 11 stone 12 lb.
9·XII·37 Urine.
Acid reaction: orange: mucus deposit
Albumen, blood and sugar negative
No bile.
Microscopic – amorphous urates
15·XII·37. X ray. – Barium meal.
4·I·38. Weight 12 stone 1 lb.
10·I·38. Urine.
Acid reaction: orange: mucus
Albumen, blood and sugar negative
No bile
Microscopic: few urates: some debris
18·I·38. Weight 12 st. 2½ lb.
25·I·38. Weight 12 st 8 lb.

There was no pyrexial disturbance at any time.

2 General Progress.

16·XII·37. Patient feels much depressed.
17·XII·37 Still the same
19·XII·37. No change in condition
22·XII·37 Patient feels a little better – is very interested in his trouble.
25·XII·37. Appetite improving: sleeping well.
28·XII·37 Patient quite bright and cheerful and anxious to talk about his illness – jaundice less marked.
30·XII·37. Says he feels fine. Appetite good, and sleeping well. Anxious to get up
2·I·38 Patient wants to get up. Jaundice practically

gone now.

5.1.38. Patient says he is now alright, and wants up: appetite good: jaundice disappeared

10.1.38. Still improving

16.1.38 Patient allowed up - feels weak on legs, but otherwise fine

20.1.38. Feels very much better than on admission. Not breathless now: no subcostal pain and no oedema of the ankles.

23.1.38 Progress still very satisfactory. No murmur.

28.1.38 Patient discharged.

3. Treatment other than that directed to the blood.

5.12.37	Luminal gr II 7pm
6.12.37	Cascara
11.12.37	Mist carc. Co.
13.12.37	Ol. ricin
15.12.37	Ol ricin.
16.12.37	Soap Enema
23.12.37	Mist Carc. Co.
25.12.37	" " "
27.12.37	" " "
31.1.38	" " "
3.2.38	" " "

4. Further Notes - recorded with the blood counts - q.v.

THE BLOOD - (a) Treatment.

17/12/37	2cc	Examen intra-venously
18/12/37	2cc	" " "
24/12/37	2cc	" " "
1/1/38	2cc	" " "
4/1/38	2cc	" " "
8/1/38	2cc	" " "
12/1/38	5cc	Pernaemon Forte intramuscularly
14/1/38	5cc	" " "
20/1/38	5cc	" " "

(b) The blood picture.

I Film on admission

Anisocytosis and poikilocytosis were marked. Many cells were large, oval and well filled. There was no punctate basophilia: an occasional megaloblast was seen

II Main blood counts.

Day in Hospital	Rbc's	Hb	CI	Retic	Wbc.	Date.
1–17	Patient not diagnosed – no counts made.					29th Nov → 15th Dec.
18	1·67 (1,670,000)	37%.	1·1	Few	4,800	16
19	1·24	30%	1·2	1·2		17
20	1·01	29%	1·4	1·8		18
21	·97	24%.	1·5			19
22	1·13	32%.	1·4	6·5	5000	20
23	1·17	34%.	1·4	14·5		21
24						22
25	1·47	40%.	1·3	10·8		23
26	1·87	43%.	1·1	21·4	5,400.	24
27						25
28	1·80	46%	1·3	12·4.		26
29	2·19	44%.	1·0	7·2	6,000	27
30						28
31				4·2		29
32	1·98	46%.	1·2	4	6,200	30
33						31
34	2·6	53%.	1·0	2	6,000	1st Jan
35						2
36				2·2		3
37	1·89	45%.	1·2	·8	6,400	4
38						5
39						6
40	2·31	60%	1·3	1·2	6,200	7
41						8
42						9

Day	Rbcs.	Hb	C.I.	Retic	Wbc.	Date
43	2·52	56	1·1	1%	5,800	10th Feb
44						11
45						12
46	2·89	65	1·1	4·2	5,800	13
47						14
48	2·73	72	1·3	5·4	5,600	15
49						16
50	2·75	71	1·3	6·1		17
51						18
52	2·91.	75	1·3	3·5	5,200.	19
53						20
54						21
55	3·52	80	1·1	2·9	4,600.	22
56						23
57	3·42.	78	1·1	2·1	5,800.	24
58						25
59	3·59	77	1·1	1·8		26
60	3·51	80	1·1	1·6.	5,200.	27
61						28

Progress – as an out patient

2/2/38	Haemoglobin	90%.	Fernaemin Forte	5cc t.i.d.
10/2/38		100%.		5cc "
9/3/38		88%.		5cc "
16/3/38		40%		5cc "
30/3/38		120%		5cc "
20/4/38.		102%		5cc "
11/5/38		104%		5cc "
8/6/38		106%		5cc "
6/7/38		92%		5cc "
10/8/38		94%		5cc "
14/9/38		104%		5cc "
12/10/38		102%		5cc "
16/11/38		98%.		5cc "

III Differential White Count

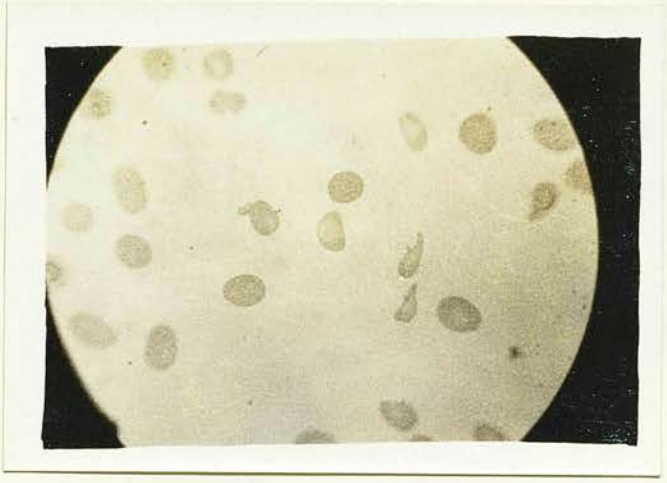
	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes.
18/12/37.	42%.	-	-	56%.	2%.
20/12/37.	40	3%	-	55%.	2%
22/12/37	46%	2	2	46%.	4%.
24/12/37.	43%.	5	-	42%.	5%.
27/12/37	45	6	1	44%	4
31/12/37.	49	6	-	43	2
4/1/38.	67	6	1	21	5
13/1/38.	64	8	1	22	5
19/1/38.	62	8	-	20	10
24/1/38	57	7	-	28	8
28/1/38.	52	6	2	34	6.

IV Arneth Count.

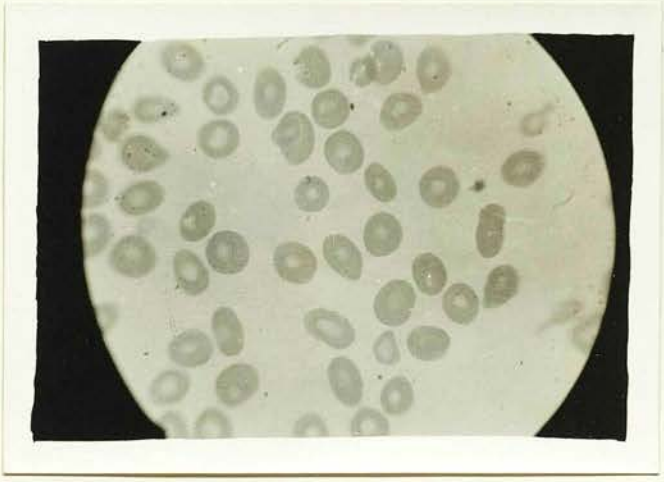
Lobes	1	2	3	4	5	6	7.
18/12/37.	4	30	32	16	14	2	2
27/12/37.							
4/1/38.	8	24	52	10	6		
13/1/38.	12	26	36	16	8	2	
19/1/38.	10	25	46	15	4		

V Relative Sizes of Red Cells.

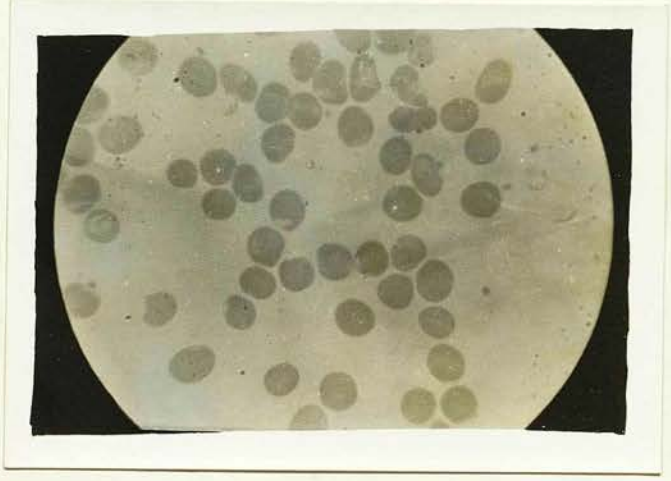
	Macrocytes	Microcytes	Poikilocytes.
18/12/37	17%.	5%.	23%
21/12/37.	23	6	16
27/12/37.	8	4	6
30/12/37.	10	5	9
4/1/38	12	3	5
13/1/38	8	2	5
19/1/38.	5	8	4
24/1/38	4	3	2
28/1/38.	5	4	0.



ON ADMISSION



DURING TREATMENT



ON DISCHARGE

VI Special Cells.

Megaloblasts were seen in the film on 16/12/37 and until 21/12/37, but were not seen after that.

Howell-Jolly bodies were seen in one cell - 4/1/38.

VII Further Investigations

23/12/37	Platelets	217,000.
22/1/38	Platelets	280,000.

Case IV

CASE D

NAME MRS. CATHERINE PROUDLOCK.
AGE 74
OCCUPATION Retired book
ADDRESS 19, Jamaica Street, Stockbridge.
REC. BY Dr Henderson, Thistle St. Dispensary
DATE of ADMISSION 26: XII: 37.
DATE of EXAMINATION 27: XII: 37.
WARD 28, R.I.E.

COMPLAINT. (The patient was too ill to answer questions. All information was obtained from her daughter and from the student who was visiting the patient from the dispensary. According to them, the patient suffered from :-

BREATHLESSNESS	18 months.
LOSS OF WEIGHT	12 months
WEAKNESS	12 months.
EPIGASTRIC PAIN	9 months)

HISTORY.

The daughter attributes the patient's illness to the fact that, three years before admission, the patient broke her right wrist. It was set in the R.I.E. without an anaesthetic and after that the patient never felt well. For over a year she suffered from BREATHLESSNESS which was made worse with exertion, and about twelve months before admission it was first noticed that she was becoming much THINNER: previously she had been very robust. During this period of twelve months, too, she frequently

felt FAINT, usually about one o'clock in the afternoon, after helping to get the meal ready, and she found she had to sit down to recover her strength. She lost interest in her food at the time when she broke her wrist and this symptom has continued, her most intense dislike being for tea. For about nine months prior to admission she complained of a gnawing PAIN in the EPIGASTRIUM which came on immediately after a meal: she said that she would rather do without food than have this pain. In the last month of her illness she was troubled with DIARRHOEA.

In the later stages of her illness, the patient became very weak on her legs: she lived four stairs up in a tenement house, and from September to the time of her admissio in December, she was never able to walk downstairs. The patient always refused to allow a doctor to attend her, but in the first week of December she had to take to her bed, and a student from the Thistle Street Dispensary attended her. Since that week, too, the patient ate practically no food.

About this time, also, the patient was first troubled with a dull PAIN in the PRAECORDIAL region. This was worse when she moved about in her bed: in addition, she became very much troubled with PALPITATION, a symptom which had troubled her to a lesser extent for about two years. The daughter stated here that the patient had had a weak heart

from the time when she suffered from pneumonia, twenty-six years previously, but could give no reasons for this statement.

The patient did not at any time suffer from a sore tongue or swelling of the ankles. The daughter had not noticed any change in the colour of the patient's skin, but agreed that it had become rather yellow when this was pointed out to her.

The student treated the patient for an organic heart lesion, but as this treatment did not appear to be producing very successful results, Dr. Henderson was called in from the Dispensary, and he diagnosed pernicious anaemia. It was arranged that the patient should spend Christmas day at home, and then be admitted to the Royal Infirmary. On Christmas day, however, the police telephoned for the student who was attending her, as it was thought that the patient was dying. It was found that the patient, who had been propped up in bed in the orthopnoea position, had fallen sideways, and was gasping for breath. She was admitted to Ward 28 early on the 26th December 1937.

PREVIOUS HEALTH.

In 1911, the patient suffered from double pneumonia which resolved satisfactorily. Ever since then the patient has suffered from palpitations.

At the end of 1934, the patient fell and broke her right wrist. She was very

much upset by this happening.
Otherwise this patient's general health always remained good.

SOCIAL HISTORY:-

Until the age of 70, this patient worked as a cook in an Edinburgh restaurant: she was discharged because of her age. From that time she stayed at home with her daughter who was unmarried, in the fourth floor of a Tenement house, situated in a somewhat congested part of the town. She never was in the habit of taking much exercise, and as this present illness progressed, she became unable to take any. Because of her occupation she knew how to provide satisfactory meals, and ~~has~~ never suffered from lack of good food, but with this illness, her appetite was lost.

FAMILY HISTORY.

One daughter - alive and perfectly healthy
Three sons - died in infancy.
Husband - died in his sixties - cause unknown

STATE ON EXAMINATION.

NOTE - The patient was too ill for a thorough systematic examination to be carried out.

The patient was a thin and emaciated elderly woman who was propped up in bed in the orthopnoeic position and who lay gasping for breath. The face was pale with a very slight yellow tinge. The eyes were sunken, and the expression was one of

apathy, the patient taking no interest in her surroundings, lying in a state almost of coma, from which she could be aroused without difficulty. however. The skin was dry and inelastic, and there was pitting oedema of the ankles.

Temperature 97.5.
Pulse Rate 110.
Respiratory Rate 24.

HAEMOPOIETIC SYSTEM.

The symptoms that might be referred directly to this system are.

Breathlessness, present for over a year
A feeling of faintness in the afternoon after helping to get the meal ready.
Weakness in the legs.

The extreme pallor of the skin, lips and conjunctivae of the lower eyelids were also due to anaemia.

No lymph glands were felt in the neck, and the spleen was not palpable or enlarged to percussion. The ankles were oedematous.

BLOOD.

Haemoglobin	25%.	Polymorphs
Erythrocytes	840,000.	Eosinophils
Leucocytes.	3,600.	Basophils
Reticulocytes.	None seen.	Lymphocytes
Colour Index.	1.5	Monocytes

Film. Showed marked ~~polych~~ poikilocytosis and anisocytosis. Megalocytes were numerous - a few megaloblasts were seen. Polychromasia was not very marked

One normoblast was seen: there was no evidence of punctate basophilia.

ALIMENTARY SYSTEM

The symptoms mentioned by the daughter were:

1. A gnawing epigastric pain, coming on just after a meal - present for nine months. This was not related to any special food.
2. Diarrhoea - this was present during the last month.

The lips were pale: the tongue was clean and moist, but not markedly atrophic. The teeth were false.

The abdominal wall was dry and inelastic, and the iliac crests were prominent. Movement with respiration was free. There was no impairment of symmetry.

On palpation, the muscle was found to be flabby. There was no localised resistance. There did not appear to be any tenderness, but the patient was not in a fit enough state to co-operate and appeared distressed when anyone approached her, groaning ~~aloud~~ no matter what part of the abdomen was touched. The liver and spleen could not be felt, and there were no palpable masses in the abdomen. The kidneys were not palpable.

There was no abnormal dullness in the flanks, and no fluid thrill.

The motions were of normal colour and

were quite firm.
A test meal was quite impossible here.

CARDIO - VASCULAR SYSTEM.

For over a year the patient suffered from breathlessness that was worse on exertion.
For about three weeks, a dull pain was present over the praecordium, worse with movement.
Palpitation, which had been present in a mild form for about two years became worse at this time.

The pulse rate was 110. There was no abnormality of rhythm. The pulse wave was of poor volume, and was difficult to feel. The vessel wall was palpable.
BP 105/60.

Veins. The external jugular veins were not visible. There was pulsation to be seen in the subclavian triangles, apparently of venous origin, with the patient propped up in the orthopnoea position.

There was no cyanosis - pitting oedema of the ankles was present: this was not looked for at the back as it was considered unwise to disturb the patient too much.

Heart.

The apex beat was not visible, and there was no visible extracardiac pulsation other than the venous neck pulsation mentioned above.

The apex beat was felt in the fifth space in the mediclavicular line. It was well localised, and there were no thrills.

Percussion - the position of the heart may be given thus $\frac{III}{1" | 3\frac{1}{2}"}$

On auscultation, soft systolic murmurs were heard in all areas, especially the pulmonary area. A systolic murmur was heard, too, in the left axilla, and in the neck.

The second sound was closed in pulmonary and aortic areas, and was of feeble intensity.

RESPIRATORY SYSTEM.

There was no cough or expectoration, and no pain in the chest, other than the praecordial ache already mentioned.

The respiratory rate was 24, and breathing was thoraco-abdominal in type. The accessory muscles of respiration were called into use. There was no Cheyne-Stokes breathing or other abnormality of rhythm.

The chest was poorly covered, and there was no impairment of symmetry. The spine was straight.

Movements of the chest were free, but it was evident that the patient having respiratory difficulty

Palpation confirmed that movements were symmetrical.

On percussion resonance was found to be unimpaired anteriorly and laterally.

and over the upper part of the surface of the lung posteriorly. At both bases, however, there appeared to be some impairment of resonan

On auscultation, breath sounds were found to be vesicular, except at the bases posteriorly where they were broncho-vesicular in character. Rhonchi and coarse crepitations were heard anteriorly, laterally and posteriorly, especially in the lower parts of the chest. Vocal resonance was not investigated.

URINARY SYSTEM.

No symptoms were present.

The kidneys were not palpable.

URINE:

Orange colour: alk reaction sp gr 1026. Mucus deposit + albumen: no sugar: no blood: excess urobilin

Microscopically - few pus cells: no rbcs.

NERVOUS SYSTEM.

The patient lay propped up in a bed in a state of drowsiness and apathy, verging upon coma. She made no remarks spontaneously and appeared to be too ill to answer when spoken to. With the aid of sedatives she slept quite well.

A complete examination of the nervous system was not carried out, because the patient was too ill, and, in any case, was not able to co-operate. The following list is of the findings revealed by a modified investigation.

CRANIAL NERVES.

II. Retinal haemorrhages were present in the region of the optic disc in both eyes. There

were of small size.

III, IV, VI — There was no squint or ptosis. Both eyes moved freely in all directions

The pupils were round and equal and reacted to light

V — There did not appear to be any impairment of movement of the jaw.

VII — There was no impairment of movement to be seen in the facial muscles.

XII — No paralysis or atrophy of the tongue.

MOTOR FUNCTIONS. There were no abnormal muscular movements.

Muscle power in the upper limbs was generally weak, but the patient was able to hold things in the hands, and to move the limbs. The patient was able to move her lower limbs.

REFLEXES.

The conjunctival reflex was present: the abdominal could not be elicited.

The plantar reflexes were bilaterally plantar flexor.

Deep.

Biceps - could not be elicited.
Knee - absent on both sides
Ankle - absent on both sides.

SENSORY FUNCTIONS.

A satisfactory examination could not be made: the patient felt the pain of the stab that was made for blood counts, and also felt pain when the stylette

was jabbed into the legs: the fact that the plantar reflexes were present indicates that the stimulus used to elicit them was felt in the soles of the feet.

PROGRESS NOTES.

1. Investigation

27·XII·37. Urine - orange: acid reaction: mucus deposit. + albumen. no sugar. no blood. sp gr 1026
Microscopic - pus cells (few) excess urobilin. no rbcs.

31·XII·37 BP 102/48.

2. General Progress.

26·XII·37 Admitted - seriously ill.

27·XII·37. Patient shows no change in condition, and is not taking food. She whispered that she "felt fine".

28·XII·37 No change.

29·XII·37. No change - patient very sleepy.

30·XII·37. Taking a little food: very sleepy, and doesn't know night from day.

2·I·38. Marked improvement. Patient still very sleepy, but anxious to know when she will get up.

4·I·38. She is still very ill, but wants home.

5·I·38. Patient irritable and wants home. Taking food better. She announced 80-day that she had "just about had enough o' this jaggin".
A tinge of colour was seen in the cheeks.

7·I·38. Patient improving but has developed a persistent irritating cough.

9·I·38. Cough worse, but patient unable to bring up any sputum.

10·I·38. Patient very ill, with temperature of 101°.

11·I·38. Still very ill with persistent cough - wants home.

13·1·38. No improvement. patient appears to be asleep all day.

15·1·38 No improvement. Cough still present. Patient does not know where she is, and is unable to answer questions.

18·1·38. Patient died this morning.

3. Treatment.

The list of sedatives given to the patient is so long that it would occupy several pages of this report. To summarise, it may be said that from 26/12/37 to 17/1/38, the patient had some such drug administered every few hours. These drugs included

Veronal. gr $\overline{V}$

Medinal. gr $\overline{V}$

H.i. Omnipon gr $\frac{1}{6}$ → gr $\frac{1}{2}$.

In addition the following were given

26·XII·37	Elixir Epiedrine $\overline{3i}$	
6·1·38.	Brandy $\overline{3ss}$ 4 hrly.	stopped 11·1·38.
8·1·38	Tinct Digitalis m $\overline{XX}$ tid.	" 12·1·38.
12·1·38.	Thyroid gr $\overline{i}$	" 14·1·38.
13·1·38	Ferri et ammoniae gr $\overline{XXX}$ tid	" 14·1·38.
15·1·38	Coramine 1cc at 7 am	
	1 pm	
	3 pm	
	11 pm.	
	Hi Strychnine gr $\frac{1}{60}$ at 11 am	
	7 pm	
16·1·38.	3 am.	

Soap and water enemata were given at frequent intervals.

4. The Blood

(a) Treatment.

26·XII·37	Pernaemon	4cc imi
27·XII·37	Pernaemon	4cc imi
3·I·38	Pernaemon	4cc imi
10·I·38	Pernaemon Forte	5cc imi
17·I·38.	Pernaemon Forte	5cc imi.

(b) The Blood Picture.

I Film on admission:

This showed marked poikilocytosis and anisocytosis. Megalocytes were numerous and there was polychromasia. The smaller cells were not well filled. Megaloblasts were present but not numerous. One normoblast was seen.

II Main blood counts

Day of Illness	Rbc.	Hb	CI	Retic	Wbc.	Date
1	·84 (840,000)	25%.	1·5	nil		27th Dec
2	·84	20%.	1·2	·01%	3,800	28
3	·75	20%	1·3	nil	3,400	29
4	·72	19%.	1·3	3%		30
5	·82	20%	1·2	3·7%	6,000	31
6	·94	20%	1·1	9·1%.	6,400	1 Jan
7	·84	24%	1·3	9·0%		2
8	1·08	24%.	1·0	15·6%.		3
9	1·10	24%	1·3	37·8%.	5,600	4
10	1·05	30%.	1·4	15·0%.		5
11	1·2	28%.	1·1	10%		6
12	1·84	32%.	·90	11%.		7
13	2·02	34%.	·89	10%		8
14				9%		9
15	1·65	34%.	1·0	6%		10
16						11
17				7%		12
18	1·32	39%.	1·4	6%.		13

Day	Rbcs	Hb	C.I.	Reta	Wbc	Date
19	1·44	42%.	1·4			14th Jan
20	1·83	41%.	1·1	25%.	9,200	15
21				22%.		16
22	1·40.	40%.	1·1	24%.		17
23						18.

III Differential White Counts.

	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes
29/12/37.	24%.			66%.	10%.
1/1/38	35%.			53%.	12%.
5/1/38	34%			65%.	1%.
10/1/38	42%.			54%	3%.
15/1/38	78%.			20%	2%.

IV Arneth Count.

29/12/37. - Polymorphs were very few, so that sufficient cells could not be found to give a reasonable count.

	1 lobe	2	3	4	5	6	7	8	9 lobes
2/1/38.	12%.	20%.	32%.	20%.	10%.	6%.			
15/1/38	0 %	7%	24%.	22	20	12	4		1

V Indication of relative sizes of Red cells.

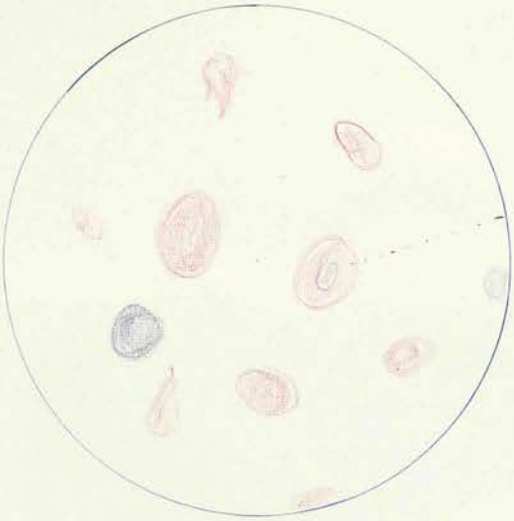
	Macrocytes	Microcytes	Poikilocytes
29/12/37	23%	13%	15%
1/1/38	22%	12%.	8%.
5/1/38.	14%.	3%.	2%.
10/1/38.	16%	5%.	4%
14/1/38.	12%	4%.	2%.

VI Special cells.

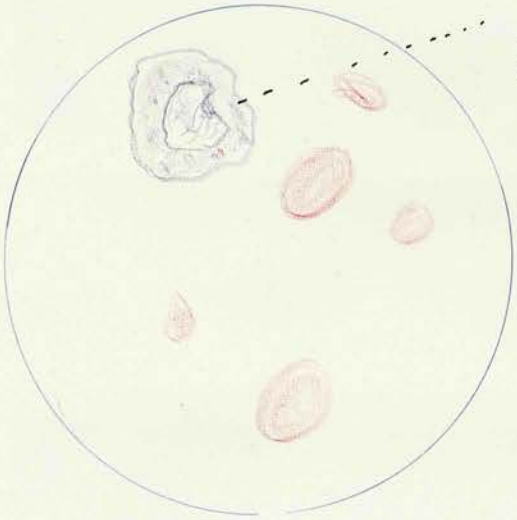
28/12/37 A search for the megakaryocyte

type of macropolyocyte revealed the presence of few cells that might come under this heading.

Megaloblasts were seen in most films, but only after a careful search. A normoblast was seen in the first film examined, but none were seen after that.

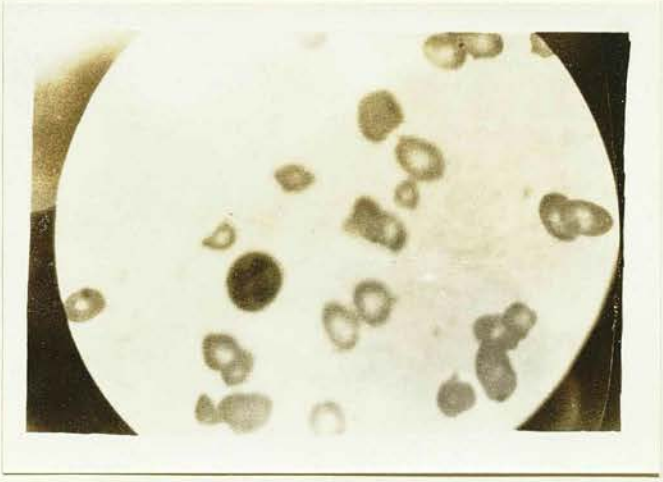


MEGALOBLAST

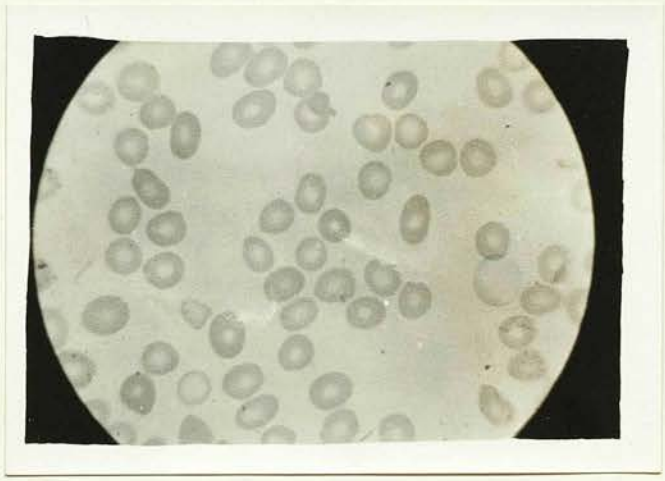


MEGAKARYOCYTIC TYPE OF MACROPOLYOCYTE

RETICULOCYTES



ON ADMISSION.



JUST BEFORE DEATH

POST MORTEM REPORT. 18/1/38.

SUMMARY

Hyperchromic megalocytic anaemia, with poikilocytosis and anisocytosis.

Profound anaemia with bone marrow reaction and iron deposits in liver and spleen, together with mild icterus.

Confluent broncho-pneumonia of right lower lobe. Bronchopneumonia of left lower lobe with multiple abscess formation.

Old standing cholecystitis and cholelithiasis with ulceration of gall stone into duodenum: generalised dilatation of bile ducts, and multiple gallstones throughout the bile passages.

? Infiltration by carcinoma of stomach wall.

DETAILS.

GENERAL The body was that of a well developed, well nourished elderly female. Post mortem rigidity and lividity present. There was considerable pitting oedema of the lower extremities as far as the knee. Generalised lemon-yellow icterus.

SEROUS SACS Peritoneal and pericardial sacs - healthy.

Pleural sacs - both showed extensive adhesions of a fibrous nature but apparently of recent date and easily divided

CIRCULATORY. Heart was of average size and shape. Endocardium throughout was healthy. The muscle was very pale in colour, but did not display the typical "knife-edge" heart

appearance of severe anaemia.

Slight dilatation of both ventricles.

Coronary vessels - were not unduly atheromatous for the age of the patient.

Aorta. Was the seat of moderate atheromatous changes.

RESPIRATORY Larynx, Trachea, and Bronchi. Contained quantities of thin greenish pus.

Lungs: Both somewhat reduced in size, but of average shape.

Left Lung: Lower lobe of the lung was heavy in consistence and irregularly consolidated. Upper lobe was emphysematous. On section, the upper lobe was pale in colour, and the seat of emphysema. The lower lobe shewed widespread patchy consolidation and softening and multiple abscess formation.

Right Lung: Externally this lung corresponded closely to the left lung, with the exception that the lower lobe was more definitely consolidated. On section, this lobe was found to be the seat of a confluent bronchopneumonia - so extensive that the consolidation involved practically the whole of the lower lobe.

ALIMENTARY. Oesophagus - healthy.

Stomach - was of average size and shape. On opening the stomach, the wall was seen to be thin and atrophied.

There was a curious raised and discoloured area, approximately 3×4 cm. in diameter, a short distance from the cardiac orifice

The mucous membrane over this swelling, which was raised about 3 mm. above the surface of the stomach, was purplish in colour.

The appearances were those of an infiltrative process, possibly early carcinoma, but the exact nature will remain doubtful until microscopic examination

Close to the pylorus there was a small circular patch about 3 mm. in diameter, slightly raised above the stomach wall, sharply demarcated and purplish black in colour.

The appearance was that of a circumscribed submucous haemorrhage.

Duodenum. Was closely adherent to the undersurface of the liver. On opening the duodenum, an ovoid concretion the size of a pigeon's egg was found lying in a recess of the wall in its first part.

On section, this body was found to be a cholesterol solitaire around which a faecal or pigmented concretion had formed. It was obviously a gall stone and appeared to have entered the duodenum from a communication which was found between the duodenum and gallbladder. The opening of the common bile duct into the duodenum was grossly dilated, and admitted the tip of the little finger.

The intestines otherwise were healthy.

LIVER. Was of average size, shape, and consistence. It was light brown, on the surface and on section

The liver gave a definite reaction for iron with the ferrocyanide test.

The bile ducts in the substance of the liver were considerably dilated, and contained gritty light brown feculant material. as well as considerable numbers of pigment stones varying from grains of sand up to ½ cm in diameter. The common bile duct and gall bladder likewise contained gallstones of somewhat larger size.

SPLEEN. Slightly congested. Weighed under 300 gms. It was firm in consistence, and on section, deep red It gave a marked iron reaction

KIDNEYS.

Were of average size and shape: pale in colour. On section, the cortex and medulla were well differentiated. The capsules stripped readily leaving a smooth, pale surface

The kidneys gave a doubtful reaction for iron.

Pelves, Ureters, Bladder etc. were normal.

Uterus and appendages - senile and normal

BONE MARROW. Marrow from the middle of the shaft of the femur showed an intense erythroblastic reaction

Microscopic

Bone Marrow: Shows intense reaction, with islands of primitive (megaloblastic) red cell formation. The appearances are consistent with pernicious anaemia under treatment with a potent preparation of iron

Liver: Shows intense and widespread fatty degeneration. There is marked increase in fibrous tissue around the portal tracts, and even the smaller bile ducts are surrounded by dense collars of scar tissue. There is no true cirrhosis, however.

The appearances are due to peri-portal fibrosis secondary to the cholecystitis described with the naked-eye report

Stomach - Nodule from the stomach wall has the the structure of a carcinoma, and infiltration through the muscle coat is present in the section.

CASE V

CASE E

NAME Catherine Dunlop - Single

AGE 58

OCCUPATION Cook

ADDRESS St. Margaret's, Loanhead.

REC. BY Dr. Hamilton, Loanhead.

DATE OF ADMISSION 18.12.37.

DATE OF EXAMINATION 29.12.37.

WARD. 28

COMPLAINTS

Loss of appetite	4 months
Loss of energy	4 months
Loss of weight	3 months
Jaundice	3 months.

HISTORY

In the middle of September, 1937, the patient first noticed that she had lost interest in the taking of her food, and that she had developed an actual distaste for eggs, an article of foodstuff that she had previously enjoyed. She had also developed a dislike for tea, and there was no food that she really felt she was anxious to eat.

At this time, too, the patient found that it was only with a struggle that she could carry out her duties as a cook: she felt that she had no energy left. She noticed that, when she climbed a certain hill of moderate steepness, which had previously given her no trouble, she felt very BREATHLESS, and had a sensation as if she were choking. It took several hours before she felt that she had completely recovered

from such an attack. Moreover, she was now slightly breathless when she climbed the stairs in the house where she was employed. About the end of September, people began to say to her that her FACE was becoming YELLOW, but she herself only thought that it was PALER than usual.

She struggled on with her work, feeling less and less capable of fulfilling her duties satisfactorily, until the end of October, when she went to see her doctor. She asked him if he thought she were jaundiced and he answered in the negative. However, he asked for a specimen of her urine, which he tested, and then told her that she was jaundiced. He sent the patient up to the M.O.P.D of the Royal Infirmary, where she was examined by Dr. McCrie. It was considered there that her jaundice was possibly of the catarrhal type, and that her condition was not sufficiently serious for her to require admission to the R.I.E.

The patient therefore returned home, where she was fed on a diet low in fat. Her jaundice became worse, and for five weeks she was confined to bed: at the end of this time she felt very well, but the yellow colour, although less intense than it had been, was still present. Her appetite was still very poor, the only foodstuffs that she felt she could eat being a little piece of chicken or some toast. Nothing else interested her. She did not want to eat sweet things, and the thought of fatty foods, which she had never cared for, gave her a

feeling of nausea. As things were not progressing as he would have wished, her doctor sent the patient back to the R.I.E. with a request for a more detailed examination. She was admitted at once to the ward.

At no time did this patient suffer from giddyness or noises in the ears, nor were there any lingual symptoms. In winter, her finger tips felt cold and numb, but there were no other sensory disturbances in the limbs.

The patient was not in the habit of weighing herself, but thought it possible that she might have been becoming THINNER during the six or seven months prior to admission.

A fortnight had elapsed between the day of admission and the writing of this history. From the second day in the ward, she felt a definite improvement in her appetite: she was now willing to eat sweet things, and to partake of larger quantities of foodstuffs. The thought of fats was still nauseating to her, but fatty things were not included in her diet. During these two weeks, there had been no improvement in the colour of her skin.

PREVIOUS HEALTH

Prior to 1930, the patient enjoyed perfect health. In that year, she had pains in the region of the ankles, which she said was due to neuritis. Treatment was given in the massage department of the R.I.E., and then she had to lie up in the Western General Hospital for 3 weeks. Her pains had vanished when

was discharged. From that time, she suffered from 'rheumatichy' pains in her joints, which were more marked in damp weather.

In May, 1935, she had a chill with severe tonsillitis: she was off her work for three months, three weeks of this time being spent in bed. From that time until October 1934, she was able to continue at her job. In November 1935, she had an acute pain under the right costal margin: she could remember no details.

SOCIAL HISTORY

The patient was a cook who held a good post in a private house. She was not overworked and remained quite happy in her job. She was well fed and had a generous amount of spare time. The patient had always felt distaste for fatty foods, which made her sick - otherwise she had no dislikes: she said that she took no alcohol.

She intended to live with a niece after her discharge from the Infirmary.

FAMILY HISTORY.

The patient was one of a family of seventeen: she came in about the middle of the family. Three of this family had died from accidental causes - the others were all alive and healthy, with the exception of one sister who died of jaundice: the patient stated that she had diabetes and kidney trouble for years, but was unable to supply particulars of the illness.

Father died aet 82 - old age.
Mother died aet 54 - pneumonia.

STATE ON EXAMINATION.

The patient was of average intelligence. She was well developed and quite well nourished. There was very distinct jaundice present in the skin and in the buccal mucous membrane and in the sclerae. The lips were pale, and the conjunctivae of the lower eyelids were also less red than in the normal person. There was no cyanosis or oedema.

The patient was not unduly depressed by her condition: she was able to sit up or lie down without distress. There was no cyanosis or oedema.

Temperature	97.4°
Respirations	20
Pulse Rate	65.
B.P.	126/76.
W.R.	negative
Height	5 feet 4½"
Weight	9st. 5 lb.

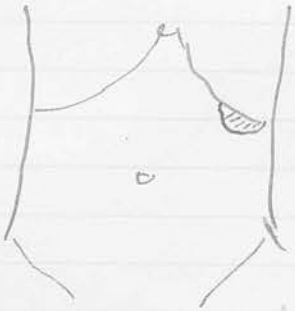
HAEMO POIETIC SYSTEM.

Symptoms that may be referred to this system are of breathlessness and of loss of energy.

Pallor of the face was noticed three months before admission, also jaundice, but the yellow colour was more intense than one would expect from disorder of this system alone.

The anterior border of the spleen was palpable just below the costal margin on the left, on deep inspiration. On percussion,

the presence of splenic enlargement was confirmed



No lymph glands were felt in the neck or axillae.

THE BLOOD.

NOTE - Unfortunately, the patient had been in hospital over a week before this investigation was begun. A detailed examination of the blood was not done during this period, but the following figures were supplied

21/12/37.	Red blood cells	3,720,000.
	Haemoglobin	69%.
	Reticulocytes	3·6%.
	Colour Index.	·93.

These figures may, however, be inaccurate. Further estimations are given with the progress notes.

At this time, the film showed - some anisocytosis, a few poikilocytes, a fair number of larger oval, well filled cells, and no nucleated red cells.

Icteric Index 27

Van den Bergh Direct reaction, weak biphasic.

ALIMENTARY SYSTEM.

1. The symptoms, already described, were as follows. For over three months - loss of appetite, with distaste especially for eggs and for tea; at this time, too, she began to take even less fatty things than before, but she had always had a distaste for fats. There was no pain.
2. For about the same period, the patient's skin had a marked yellow tinge, which progressed, and then became less, but did not disappear.
3. During this period, she considers that her urine was darker in colour than usual, and that just before admission the motions became paler. She had been constipated for two months.
4. At this time she was troubled with flatulence and vomiting after meals.

The lips were rather pale and the teeth were false. An icteric tinge was present in the buccal mucous membrane. The tongue was clean and moist, but not atrophied. The throat was healthy.

The abdomen was well covered, and movement was free with respiration. The symmetry was not impaired.

On palpation, there was no rigidity or tenderness to be found. The spleen was found to be enlarged as already described, but there was no enlargement of the liver. The gallbladder was not palpable. There was no splashing of the stomach three hours after a meal.

There was no tenderness over the region of the gallbladder, over the costal cartilages, or half way between the umbilicus

and the gallbladder point. No abnormal masses were palpable, and there was no evidence of free fluid.

The stools were pale at the time of admission, but not at the time when this investigation was begun.

X ray examination - noted opposite: Test meal follows.

CARDIO-VASCULAR SYSTEM.

The patient suffered from breathlessness on exertion for about three months. There was no palpitation or praecordial distress.

Arteries

Pulse Rate 65

BP 126/76.

There was no abnormality of cardiac rhythm; the pulse wave rose with normal sharpness, falling away more slowly. The vessel wall was not palpable.

Veins - There was no abnormal distension of the veins of the chest, abdomen, or neck.

Heart - The apex beat was not visible, and there was no extra cardiac pulsation.

The apex beat was palpable in the fifth space, within the midclavicular line. The beat was well localised. There were no palpable thrills.

The portion of the heart on percussion was as follows: $\frac{\text{III}}{1''|3''}$

On auscultation, a soft systolic murmur was heard in the mitral area, and it was not propagated. In the other areas,

GASTRO-INTESTINAL ANALYSIS.

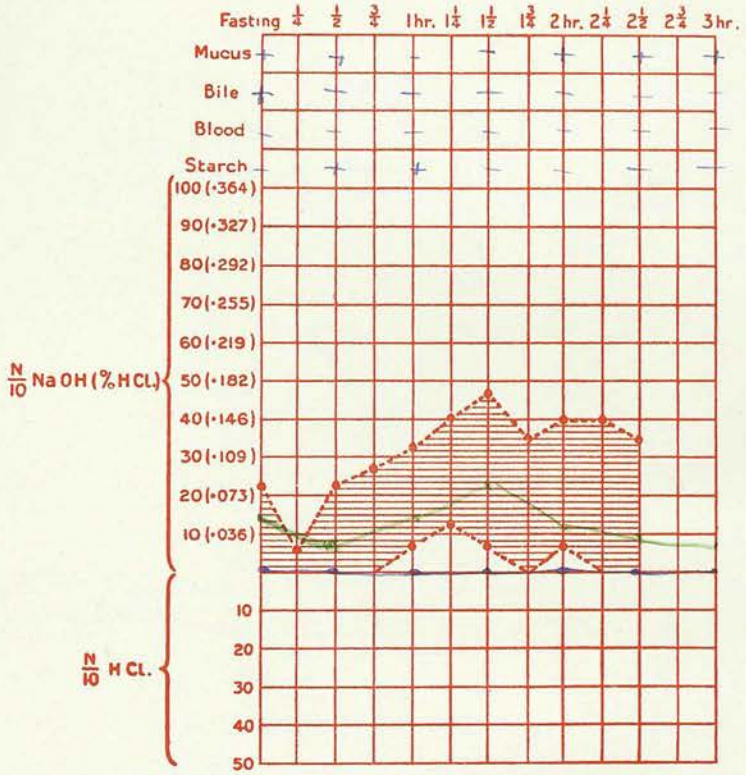
Name of Patient Miss Catherine Dunlop **Ward** 28 **Bed**

1. FRACTIONAL TEST-MEAL. Date. 1/2/38.

Fasting Juice.

Volume. 20cc

Cells.



One Hour Fraction.

Free HCl. —

Active HCl.

Total Chloride.. 14.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

represents free HCl.

represents total acidity.

Summary.

2. FÆCES.

the sounds were closed, and of normal intensity

RESPIRATORY SYSTEM.

There was no cough or expectoration or pain. The presence of breathlessness has already been referred to.

Breathing was thoraco-abdominal in type, with no alteration of rhythm. The chest was of healthy shape, and was well covered. There was no localised disturbance of symmetry and the spine was straight. Movements were free, with no localised impairment.

On palpation the symmetry of movement was confirmed. Vocal fremitus was equal on the two sides and unimpaired.

On percussion, the lungs were found to exhibit good resonance throughout and diaphragmatic movement was shown by tidal percussion to be free.

Breath sounds were vesicular in character with no accompaniments, and vocal resonance was equal and unimpaired on the two sides.

URINARY SYSTEM.

There were no symptoms referable to this system; there was no tenderness in the renal angle

URINE.

Alkaline. sp gr. 1022. Mucus deposit.
Albumin - nil. Sugar - nil.
No bile, and no excess of urobilin

Microscopically, an occasional pus cell was found.

NERVOUS SYSTEM.

The patient was of average intelligence. There was no emotional upset, and no disturbance of memory. She slept well, and had no hallucinations, delusions, or disturbance of speech.

CRANIAL NERVES.

I No abnormality

II Visual acuity in the two eyes was good, and the visual fields unimpaired. On ophthalmoscopic examination, the fundi appeared rather pale, but otherwise there was no change.

III, IV, VI } Movements of the eyes were unimpaired. There was no nystagmus, ptosis or diplopia. The pupils were circular and equal, and reacted at once to light and accomodation.

V. Contraction of the masseter and temporal muscles was equal on the two sides.

The corneal reflex was present. There was no impairment of sensation over the areas supplied by any of the divisions of the two nerves.

VII There was no impairment of muscular movement, and no hyperacousis.

VIII No auditory impairment. Air conduction was better than bone conduction. There was no tinnitus or vertigo.

IX There was no anaesthesia of the pharynx and no dysphagia.

X The palate moved in the midline
XI. No muscular abnormality
XII No impairment of lingual movement, and no atrophy.

CERVICAL SYMPATHETIC. No impairment.

MOTOR FUNCTIONS.

There were no abnormal movements. There was no paralysis, and no impairment of the power of any of the muscles. Co-ordination was not impaired, and there was no muscle wasting or changes in tone.

REFLEXES.

Superficial The conjunctival and palatal reflexes were present, and the abdominal reflexes absent.

The plantar reflexes were bilaterally plantar flexor.

Deep.

Biceps	Present and equal
Triceps	Present and equal
Supinator	Could not be elicited.
Knee	Present and equal but sluggish
Ankle.	Present and equal
Organic	- No impairment.

There was no clonus.

SENSORY FUNCTIONS.

The patients fingers and toes were cold in winter. Otherwise there was no sensory disturbance.

Objective.

There was no disturbance of the sensations

of touch, pain, heat and cold., or of vibration sense, muscle and joint or stereognostic senses.

There were no vasomotor or Trophic disturbances

INTEGUMENTARY SYSTEM.

Apart from the jaundiced colour, there was no abnormality

ENDOCRINE SYSTEM

No abnormality

LOCOMOTORY SYSTEM

No abnormality.

PROGRESS NOTES.

1. Investigations

14·XII·37 BP 126/76.

20·XII·37. Van den Bergh Direct Reaction
Weak Biphasic.
Icteric Index. 27.
Blood WR negative

21·XII·37. Weight 9 st. 5½ lb.

28·XII·37. Weight 9 st 5 lb.

29·XII·37. Urine.
Lemon: alkaline: sp gr 1018.
No albumen, sugar or bile: no excess urobilin
Barium meal.

2·1·38. BP 126/80

3·1·38. Icteric Index 12.
Urine.
Straw: alkaline sp gr 1020.
No albumen, sugar or bile: no excess urobilin. Debris and a trace of phosphates present on microscopic examination

4·1·38. Weight 9 st. 6 lb.

6·1·38. BP 122/78.

11·1·38. Weight 9 st 5 lb.

18·1·38 " 9 st 6½ lb.

23·1·38. BP 112/74.

25·1·38. Urine
Straw: acid reaction: sp gr 1022.
No albumen, sugar, bile, or excess urobilin
Mucus deposit. Debris and urates seen on microscopic examination.
Weight 9 st. 6 lb.

1·2·38 Fractional Test Meal
Weight 9 st. 7 lb.

4·2·38 BP 100/66.

8·2·38 Weight 9 st 8½ lb.

15.2.38 Weight 9 st. 9 lb.

16.2.38. Throat swab-

The specimen contained Strep viridans and micrococcus catarrhalis.

From the time of admission, until 14/2/38, the temperature was between 96.2 and 98.5°, the pulse rate between 58 and 85, and the respiratory rate between 20 and 22.

On the 15th February, however the temperature rose thus

15.2.38. Temp. 100°
Pulse 78.
Resp. 24

16.2.38 Temperature 97.8 Pulse 80 Respirations 24

17.2.38 Temperature 97.2 Pulse 72 Respirations 20.

2. General Progress.

As already mentioned, this patient had been in hospital for some time before the investigation was begun.

·XII.37 Patient admitted.

28.XII.37. Patient feels much the same as when admitted and feels rather depressed.

31.XII.37. She still is not anxious to eat, and feels rather depressed. She sleeps well, however

4.1.38. She is rather brighter, and more willing to eat.

7.1.38. Patient is still jaundiced and the cardiac murmur is still present. She is sleeping well and is more willing to eat.

10.1.38. No change in condition

17.1.38. Still sleeping well and eating fairly well.
16.1.38. Feels fine - jaundice still present, but the cardiac murmur was not heard.
14.1.38. Patient very bright having been told she would soon get home. Jaundice still present but less intense.
23.1.38. Told that she would have to remain in the ward as her jaundice was not clearing up satisfactorily.
26.1.38. Appetite still quite good, and sleeping well.
29.1.38. Much depressed as a result of a clinical lecture about the patient which gave her the impression she might die at any minute. - she now is convinced that she has cancer.
31.1.38 Patient still depressed. Yellow tinge still present, but less marked.
3.2.38. No change in her condition
6.2.38. Patient more cheerful, and wants to get home.
9.2.38. No change in condition
15.2.38. To day she developed a cold in the head and her temperature rose slightly
18.2.38. Cold now disappeared. - patient discharged.

3. Treatment given.

19.12.37. Glucose and orange juice
light diet.
21.12.37. S and W Enema.
22.12.37. Aloin pill
23.12.37. Calomel gr i
28.12.37. S and W Enema.
15.2.38. Dover's Powder gr X at 8 pm.
16.2.38 Dover's Powder gr X at 7 pm.

FURTHER PROGRESS.

4/3/38. Patient Reported - looks and feels well.
Rbc. 4,240,000
Hb. 75%.
Wbc. 5,200.
Weight (with clothes on) 10 st. 2 lb.
5cc Pernaemon given

25/3/38. Weight 10 st. 4 lb
5cc Pernaemon given.

3/4/38. Readmitted. Jaundice has become deeper: she complains of no pain, just the jaundice and tiredness
She was seen by Mr. Paterson Brown, who thought that an exploratory laparotomy should be done.

5/4/38. Rbc 4,750,000
Hb 95%
C. Index 1.

Ammon chloride gr XV
Mandelic acid gr XLV } t.i.d. stopped 13.4.38

11/4/38. Icterus Index 54
13/4/38 Glucose drip set up.
Pot citrate gr XX
Tinc thyroxymus m X } 4 hrly stopped 14.4.38.

No liver injections given during the week.

15/4/38 OPERATION.
Revealed a grossly diseased liver, small and contracted, and markedly nodular, suggestive of a cirrhotic condition, although the presence of carcinoma

could not be excluded. No evidence of obliteration of the common bile duct. The abdomen was closed as no further surgical interference was possible.

27/4/38.

Readmitted for convalescence. The scar had healed nicely. The jaundice is not so marked now. She complains of pain occasionally across the gallbladder region, and between the shoulders.

Weight 9 st. 1 lb.

Kept comfortable by nepenthe mXX sos.

13/5/38.

"Allowed up. Able to walk about the ward. Feels much better, but the prognosis is hopeless, and nothing further can be done for the patient. It was suggested to the doctor that should she require further hospital treatment at a later date, she might be sent to one of the municipal hospitals."

28/5/38. Discharged.

(No liver injections were given during the stay in hospital)

Diagnosis – carcinoma of liver.

4. The Blood

(a) Treatment.

24/12/37.	Pernaemon "Forte"		5cc i.m.i
30/12/37.	"	"	5cc.
6/1/38.	"	"	5cc
13/1/38.	"	"	5cc
20/1/38.	"	"	5cc
27/1/38.	"	"	5cc
3/2/38.	"	"	5cc
9/2/38.	"	"	5cc
17/2/38.	"	"	5cc.

22/1/38. Ferri et Ammon Cit gr XXX t.i.d

(b) The Blood Picture

I "Film on admission

This showed a slight degree of anisocytosis, a few poikilocytes, and a number of larger, oval cells. There were no nucleated red cells.

II Main Blood Counts.

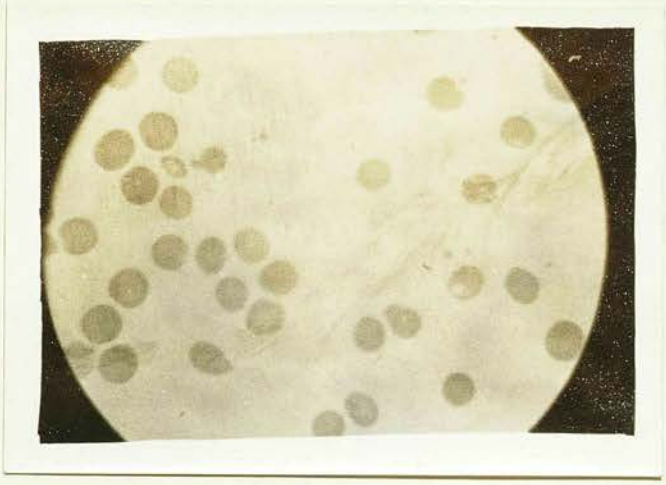
Day in Hospital	Rbc	Hb	CI	Retic	WbC	Date
1						18th Dec
2						19
3						20
4	3·72	69%	·93	3·6%.		21
5						22
6						23
7						24
8						25
9	Case not diagnosed as P. A before this					26
10	24th Dec. Unfortunately no counts had been made at this time					27
11	3·54	68%.	·96	1·8%.		28
12	3·51	72%.	1·02	2·3%	3,400	29

Day	Rbc	Hb.	CI.	Retic	Wbc	Date
13	3·					30th De
14	3·51	71%	·99	2·9%		31st
15				4·0		1 Jan
16	3·72	69	·93	3·6	3,600	2
17				5·0		3
18	3·74	74	·99	2·7	3,800	4
19				2·3		5
20						6
21	4·19	86	1·02	1·6		7
22	4·32	80	·90	1·3	3,600	8
23						9
24	4·08	80	·98	1·0		10
25	4·58	86	·94	1·0	3,800	11
26						12
27	4·00	80	1·0	1·2		13
28						14
29	3·93	79	1·0	1·5	4,000	15
30						16
31	3·64	80	1·1	1·6	4,400	17
32						18
33	3·78	73	·97	1·5	3,000	19
34						20
35	4·06	80	1·0	1·3	3,400.	21
36	4·23	78	·92	2·7		22
37						23
38	4·56	82	·90	2·3	3,200	24
39						25
40	4·42	79	·90	2·1	3,000	26
41						27
42	4·10	76	·92	1·8	4,200	28
43	4·39	78	·89	2·5	4,600	29
44						30
45	3·90.	78.	1·0	2·8.	5,000.	31
46.						1st Feb

Day	Rbc.	Hb %	CI	Retic	Wbc.	Date
47	4·12	77	·83	2·5%	5,800	2nd Feb
48						3
49	4·60	77	·80	2·5%	5,600	4
50	4·79	80	·83	2·7%.		5
51						6
52	4·57	76	·83	3·0%.	6,200	7
53						8
54	4·45	78	·88	2·3%	6,400	9
55						10
56	4·19	80	·95	1·3%	6,200	11
57	4·61	78	·84			12
58						13
59	4·42	78	·88	2·1%	5,000	14
60						15
61	4·39	80	·88	1·6%	8,000	16
62						17
63	4·45	78	·88.		7,000	18.

III Differential White Count

	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes
28/XII/37	59%.	2%	0	34%	5%
1/1/38	62%	7%	0	28%	3%.
5/1/38	60%.	3%.	0	31%.	6%
9/1/38	57%	4%	0	33%.	6%.
15/1/38	53%.	7%	1	36%	9%.
20/1/38	57%.	2%	0	35%.	6%.
24/1/38	60%	2%.	0	33%	5%
29/1/38	62%	1%	1%	28%.	8%
5/2/38	60%	5%	2%	30%	3%
11/2/38	65%	5%	1%	25%	4%
16/2/38	64%	1%	0	25%	5%



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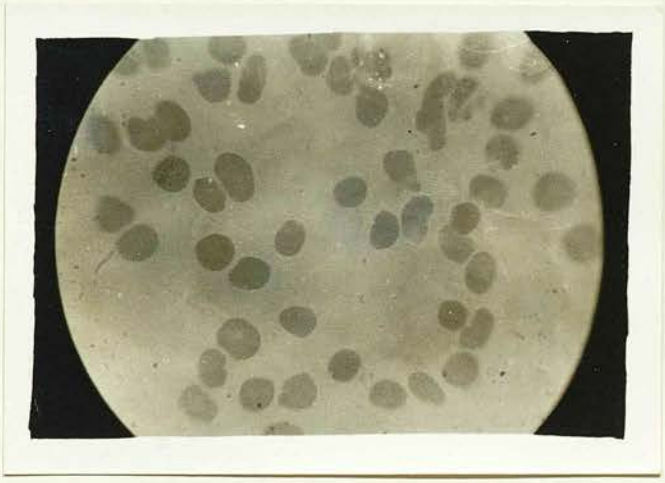
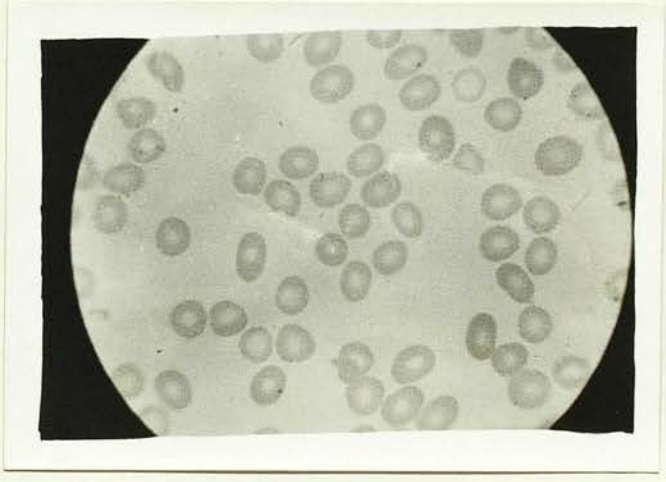


UNDER TREATMENT



AT DISCHARGE

IV Arneth Count

	1	2	3	4	5	6 Lobes
30/XII/37	10	24	40	20	6	
7/I/38	12	22	45	16	5	
11/I/38	8	28	43	16	4	1
9/2/38	12	28	36	20	4	

V Estimation of Relative sizes of erythrocytes

Although there was some evidence of macrocytosis and poikilocytosis, the condition was not sufficiently marked for an estimation of the numbers being of any value.

VI Special Cells.

No nucleated red cells were seen

VII Other Investigations

29/XII/37 Fragility Normal

4/1/38 Bleeding Time 4½ minutes

15/1/38 Platelets 430,000

CASE F

NAME Mrs. JEAN HUTCHISON

AGE 64

OCCUPATION Housewife

ADDRESS 8, East Cottages, Granton

DATE OF ADMISSION 25th December, 1937.

RECOMMENDED BY Dr Munro, Sea View, Granton Place

DATE OF EXAMINATION 27th December, 1937

COMPLAINT

General weakness 6 months

Breathlessness - had been troubling her for 2 years but had been more marked for 3 months.

HISTORY

In September, 1935 the patient first began to feel FAINT and BREATHLESS. The feeling was worse in the mornings, when she had more housework to do, or when she exerted herself physically. When she experienced those symptoms she sat down until she had recovered. There was no praecordial pain, but there was at this time a vague pain over the left scapula: this, however, was not related to her other symptoms, being present at various times of day and night.

She visited her doctor, who said that her heart was not too sound, and told her to do less housework: in addition, a bottle was prescribed. Gradually the patient's condition became worse: she felt easily TIRED: her rosy cheeks became PALER, so much so that she was afraid to look at herself in the glass: and

then, in the early part of 1937, people drew her attention to a YELLOWISH TINGE in her complexion. She found, too, that she was LOSING WEIGHT. In 1934, the last occasion on which she was weighed, she was 11½ stone: in July, 1937, she was only 10½ stone.

In June, 1937, she felt that her condition was really becoming much worse. Her breathlessness was much more troublesome: now she could only climb a few steps at a time when going up stairs. Between the steps she had to pause to get breath, and then she was able to advance again: such exertion gave her severe PALPATATION, lasting for about fifteen minutes after the task was completed, and distressing her greatly: She noticed, too, that she now obtained no pleasure from eating her food, and that her chief dislikes were for tea, for eggs, and for fatty foodstuffs, all of which gave her a feeling of NAUSEA: Moreover, she suffered from flatulence in the stomach just after taking meals - there was no gastric pain, and, at this time, no vomiting. A further symptom that troubled the patient was constipation, which she relieved with Epsom salts. This CONSTIPATION was present throughout 1937, especially in the later months. Further disturbances which troubled the patient during the year were PRURITIS VULVAE, which disappeared six weeks before admission, and FREQUENCY OF MICTURITION, both diurnal and nocturnal, which had been present for several years.

At the end of November, 1937, the

patient consulted her doctor because of her breathlessness and general weakness. He advised her to rest, and she agreed to spend each afternoon in bed However, she began to feel worse, and had to spend the whole day in bed.

At this time, when she was first confined to bed all day, the patient developed symptoms which her doctor diagnosed as being due to influenza. She had pains in her ears, and tinnitus: pains were present in the joints and calf muscles: she felt sick, and vomited on one occasion: her appetite was completely lost and she could not sleep: there was what she described as a "nippy" feeling in her tongue. The patient said that during this time she was not fevered. and had no cough

For four weeks she remained in bed. Her feeling of weakness became more pronounced, and she vomited on three occasions: her doctor prescribed a bottle which did not relieve this sickness A week before admission, she got up- she felt exhausted and quite unable to stand: arrangements were made for admission to the R.I.E.

When admitted, the patient was still suffering from weakness and breathlessness, a nippy feeling of the tongue, palpitation and dullness of hearing with tinnitus.

PREVIOUS HEALTH.

Scarlatina - at age of ten.
Varicose Veins - on both legs, especially the left, for many years. Injection

were given on two occasions, once leading to phlebitis of the left leg, which laid the patient up for six weeks. Associated with the varicosity there was oedema of the legs. for several years.

SOCIAL HISTORY.

The patient lived in a house on the sea shore: she got plenty fresh air and good food. She did not smoke, and took no alcohol, and had plenty of time for out door walks. Her husband was a mason, still in employment.

FAMILY HISTORY.

She had six children, including twins who died in infancy. The other four were alive and healthy.

2 brothers. - one alive and well - the other died, aet. 65, of pneumonia
2 sisters. one alive and well - the other died at 59 of pernicious anaemia - twelve years before this history was taken.
Father and mother both dead.

STATE ON EXAMINATION.

The patient was of average intelligence. She was well developed and quite well nourished, and was equally comfortable sitting propped up or lying down in bed. She was rather depressed by her illness, and appeared exhausted.

The face was pale and had a tinge of jaundice. The lips and conjunctivae of the lower eyelids were pale. On the cheeks, the spidery lines of vessels were seen

under the pale yellow skin, suggesting that the patient had once had rosy cheeks.
Oedema was present in both lower limbs, but was associated with varicose veins.

Temperature	97°
Pulse	92.
Respirations	22.
Weight	8 st. 10 lbs.
Height	4 ft 11½"
Blood Pressure.	122/56.

HAEMOPOIETIC SYSTEM.

The patient was troubled with breathlessness and a feeling of faintness. Her cheeks became pale and developed a yellow tinge. Palpitation and tinnitus were also present.

There were no palpable glands in the neck, and the spleen was not enlarged.

BLOOD.
25/12/39.

Erythrocytes.	2,420,000.
Haemoglobin	45%.
Leucocytes	5,200.
Reticulocytes	.2%.
Colour Index.	.93.

This is the count on admission before this investigation was commenced. Its accuracy cannot, therefore, be vouched for.

ALIMENTARY SYSTEM.

Symptoms

1. Seven months before admission, the patient began to dislike her food, especially tea, eggs and fatty foodstuffs. These gave her a feeling of nausea.
2. At this time there was flatulence just after the taking of meals.
3. Constipation was present for about a year, and was relieved with Epsom salts.
4. About ~~three~~ six weeks before admission, she had an illness that was diagnosed as influenza, and vomiting occured on four occasions. The vomit had a greenish colour.
5. At this time she first felt a 'nippy' feeling in the tongue, still present on admission.

The lips were pale, and the teeth were false. The mouth and throat were healthy. The tongue was clean and moist. There was definite atrophy of the papillae, but no fissures or ulcers were present.

The abdomen was well covered, and the abdominal wall moved freely with respiration. There were no localised changes of contour.

There was no rigidity or tenderness of the abdomen. The liver and spleen were not palpable. No abnormal masses were felt. There was no splashing of the stomach two and a half hours after a meal, and there was no evidence of free fluid in the abdomen.

Test Meal - on following page.

GASTRO-INTESTINAL ANALYSIS.

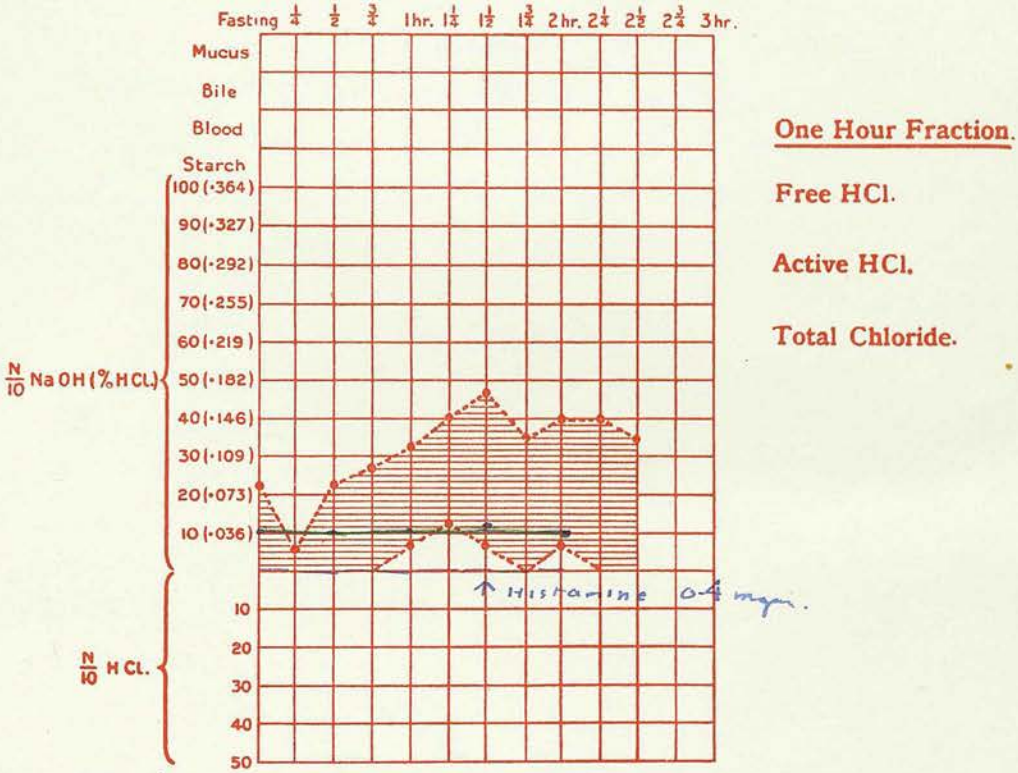
Name of Patient Mrs. Jean Hutchison *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date. 27/12/37.

'asting Juice.

'olume. 10c

'ells.



One Hour Fraction.

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——— represents free HCl.

····· represents total acidity.

ummary.

2. FÆCES.

Faeces - no abnormality was seen on naked eye examination.

CIRCULATORY SYSTEM.

As already described in the history the patient suffered from breathlessness and for about six months she suffered from severe palpitation with even mild exertion. There was no praecordial distress.

Arteries: The pulse rate was 92. There was no abnormality of rhythm.

The pulse wave was of poor volume, and the vessel wall was not palpable at the wrist.

BP 122/56.

Veins.

No abnormality of the veins of the neck, chest or abdomen was present. The condition of the veins of the legs is described later.

Oedema of the legs was present, but this was of the non-pitting variety, and was associated with varicose veins

Heart.

The apex beat was not visible, and there was no extracardiac pulsation.

On palpation, the apical impulse was found to be well localised, in the fifth space.

internal to the midclavicular line. There were no palpable thrills.

The formula as found by percussion was $\frac{III}{1''/3\frac{1}{2}''}$

On auscultation, blowing systolic murmurs were heard in all areas and in the neck. They were most intense at the mitral and pulmonary areas, and least intense in the aortic area. The second sound was closed and of normal intensity in all areas.

RESPIRATORY SYSTEM.

There was no cough or expectoration. The presence of breathlessness has already been recorded.

The throat was healthy.

The respiratory rate was 22. Breathing was thoraco-abdominal in type with no change of rhythm.

The chest was of a rather flat shape and was well covered. Movements were free, and there was no localised changes in symmetry or in movement. The spine was straight

On palpation, the symmetry of movement was confirmed, and vocal fremitus was found to be equal and unimpaired on the two sides

A good, resonant percussion note was present throughout the chest on both sides, and tidal percussion revealed free movement of the diaphragm.

The breath sounds were vesicular in character and there were no accompaniments. Vocal Resonance was not impaired.

URINARY SYSTEM.

During 1937, the patient suffered from pruritis vulvae, that disappeared six weeks before admission. Diurnal and nocturnal frequency of micturition was present for many years.

There was no tenderness in the loins, and the kidneys were not palpable.

URINE

Lemon colour. Sp gr 1020. Neutral to litmus
Mucus Deposit No albumin or sugar,
and no casts of urobilin.
Microscopic - phosphates.

REPRODUCTIVE SYSTEM.

Menopause aet 39.
No vaginal discharge.

NERVOUS SYSTEM.

The patient was a woman of average intelligence, who was rather depressed by her illness. She did not sleep too well. Her memory was good, and there were no hallucinations or delusions, and no speech abnormalities.

CRANIAL NERVES.

I No disturbance
II Visual acuity good in both eyes: fields of vision not impaired: there was no abnormality to be seen on ophthalmoscopic examination.

III, IV, VI } The eyes moved freely, and there was no strabismus, nystagmus or ptosis. The pupils were round and equal, and reacted briskly to light and to accomodation.

V Motor. There was no impairment of the power of the masseter or temporal muscles.
Sensation. The corneal reflexes were present: there was no impairment of sensation over the areas supplied by this nerve.

VII No impairment of movement of the facial muscles: no hyperacousis

VIII There was tinnitus present in both ears, but no vertigo. The patient had not been able to hear as well as formerly after a febrile illness that was diagnosed as influenza. Bone conduction was better than air conduction on the right side, but not on the left.

IX. There was no dysphagia or pharyngeal anaesthesia.

X The palate moved in the midline

XI No impairment of muscles supplied.

XII No paralysis of the tongue.

CERVICAL SYMPATHETIC No abnormality

MOTOR FUNCTIONS. There were no abnormal movements, and no paralysis or muscular weakness. There was no inco-ordination, and no muscular atrophy. The muscle tone showed no changes.

REFLEXES.

Superficial The conjunctival, palatal, and abdominal reflexes were present. The plantar reflexes were plantarflexor.

Deep.

Jaw	present
Biceps	present and equal.
Triceps	could not be elicited
Supinator	present and equal.
Ankle	present and equal - of normal intensity
Knee.	present and equal - of normal intensity
Organic	No changes.

There was no knee or ankle clonus.

SENSORY FUNCTIONS.

In this case, there were no abnormal subjective sensations, and there was no headaches.

Objective disturbances.

There were no changes in the sensations of touch or pain, or of vibration sense, muscle and joint sense or stereognostic senses.

No vasomotor or trophic disturbances.

LOCOMOTORY SYSTEM. and INTEGUMENTARY SYSTEM

An icterus tinge was present in the skin. In both legs, oedema of the non pitting type was present., associated with varicosity of the saphenous veins on the medial sides of the limbs. There was varicose dermatitis, and pigmentation. In the left calf there was a tender swelling

that was very painful in the region of the small saphenous vein - This was apparently due to the presence of phlebitis

ENDOCRINE SYSTEM.

No abnormality.

PROGRESS NOTES.

1. Investigations.

27·12·37. Test Meal.

2·1·38. BP 122/56.

6·1·38. Faecal Benzidene - weak +ve.

8·1·38. Urine: Straw colour: sp gr 1018: alkaline: mucus. No albumin or sugar., and no excess urobilin. Microscopic - phosphates.

17·1·38. Urine: Orange colour: sp gr 1016: acid: mucus and urates deposit: No albumin, sugar, or excess urobilin.

26·1·38. BP 132/76.

8·2·38. Weight 8 stone 10 lb. BP 112/76.

15·2·38. Weight. 8 stone 9 lb. BP 124/80.

During the first week, the pulse rate fell from 110 to 80, and then varied between 60 and 80 till 11/2/38. Meanwhile the temperature remained between 96·5° and 98·3° On 11/2/38 the patient developed a cold.

11/2/38	Temperature 100·8°	Pulse 88	Respirations	24
12/2/38	" 98·2°	80		22
13/2/38	" 97·4°	86		20
14/2/38.	" 97°	78.		20

2. General Progress.

27/XII/37. Patient still depressed, and anxious to know when treatment will start.

28/XII/37. Appetite good and sleeping fairly well.

31/XII/37. Patient more cheerful.

1/1/38. Patient says she is a little better.

4/1/38. Says she feels much better. - sleeping well and appetite good.

7/1/38. Jaundice and systolic murmurs still present, but patient improving

11/1/38 Appetite good; sleeping well.

15/1/38. Patient's legs very tender and painful; she appears to have mild phlebitis: jaundice now slight.

15/1/38. Feels very well, but legs painful, and upsetting her sleep.

20/1/38. Gauzdie now absent.
The patient feels well, but her legs are painful.

23/1/38. Systolic murmurs now absent.

29/1/38. Still improving, but legs still painful.
Patient is depressed as a result of a Clinical lecture in which her case was discussed.

4/2/38. Patient allowed up. She feels shaky and her legs are still sore, but otherwise she is feeling alright.

7/2/38. Appetite good, sleeping well, and feels very much better when she is up than before admission. There is now no palpitation, breathlessness or faintness.

11/2/38. Patient has coryza and a sore throat. with a Temperature of 100.8°. She was therefore not allowed up.

16/2/38 She has now recovered. allowed up.

18/2/38. Patient discharged.

3. Treatment.

25/12/38. Aloin pill.
26/12/38. S & W Enema.
30/12/38. Phenolain pill
31/12/38 S & W Enema.
1/1/38. Luminal gr ī nocte
2/1/38. Luminal gr ī nocte
S and W Enema.
Aloin Pill
4/1/38. Aloin Pill
7/1/38 Aloin Pill
8/1/38. Petrolagar 3ī ter die.
14/1/38. Legs bound with wool and supported.

4 The Blood

(a) Treatment.

1/1/38.	Binaemon Tablets	- 4 t.i.d.
24/1/38.	" "	stopped
18/1/38	2cc anahaemin	i.m.i
25/1/38	2cc "	i.m.i
1/2/38.	2cc "	i.m.i
8/2/38	2cc. "	i.m.i
15/2/38.	2cc "	i.m.i.

(b) The Blood Picture.

I Film on admission

Showed anisocytosis, poikilocytosis, and a very few cells showed polychromasia. There were no nucleated red cells to be seen

II Main blood counts.

Day in Hospital	RbC	Hb	CI.	Retic.	Wbc.	Date.
1	2·42.	45%	·93	Few.		25th Dec
2						26
3	2·14.	43%.	1·0	Few		27
4	1·55	40%.	1·3	·5%.	4,600	28
5	1·61	40%.	1·2			29
6						30
7	1·57	39%	1·2	1·7%.	5,400	31
8				1·8%.		1
9	1·59	38%.	1·2	2·8%.		2
10				5·9%		3
11	1·42	34%	1·4	4·5%.		4
12				4·3%.		5
13	1·45	38%.	1·3	4·8%.	4,200	6
14				9·8%		7
15	1·35	35%.	1·3.	8·7%.		8

Day	Rbc	Hb	CIndex.	Retic	Wbc	Date
16				35.0%.		9th Jan
17	1·76	37%	1·0	13·5	3,800	10
18	1·82	39	1·1	6		11
19						12
20	1·55	30	·97	5·3	3,800	13
21	1·51	33	1·1			14
22	1·76	35	1·0	7·2	3,600	15
23						16
24	1·92	38	·99	17%.	3,600	17
25						18
26	2-31	42	·91	18·5		19
27				14·0		20
28	2·44	47	·94	10·3	3,200	21
29				6·5		22
30						23
31	2·22	51	·90	8·0	4,800	24
32						25
33	3·13	56	·89	6·4	4,800	26
34						27
35	2·92	57	·98	7·6	5,400	28
36	3·30	61	·92	7·8	5,600	29
37						30
38	3·34	70	1·0	5·9	4,000	31
39						1st Feb
40	3·52	74	1·1	4·8	4,600	2
41						3
42	3·48	74	1·1	4·6	5,200	4
43	3·56	75	1·1	2·5	6,000	5
44						6
45	3·99	79	·99	3·0	6,400	7
46						8
47	4·22	81	·96	3·2	6,800	9
48						10
49	4·02.	81	1·0.	1·8	7,200.	11

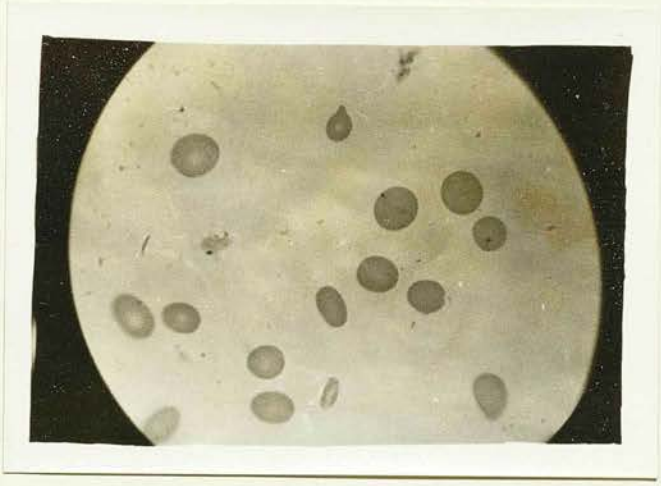
Day	Rbc	Hb	C. Index.	Retic	Wbc.	Date
50	4.41	78%	.89	3.1%	7,800	12th Feb
51						13
52	4.42	79	.89	1.8	5,200	14
53						15
54	4.41	78	.88	1.9	5,800	16
55						17
56	4.40.	82	.84		6,600.	18.

III Differential White cell counts.

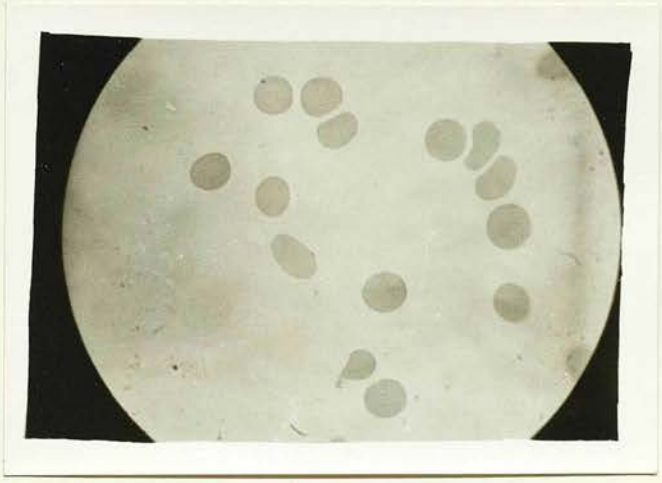
	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes.
28/XII/37.	42%.	6%	–	40%.	12%.
2/1/38.	52%.	4%	2%.	34%.	8%.
8/1/38.	50%.	2%	1%.	42%.	5%.
14/1/38.	54%.	4%.	–	36%.	6%.
21/1/38.	54%.	3%	3%.	36%	4%.
31/1/38.	56%.	0	1%.	35%.	8%.
4/2/38.	60%.	3%	–	33%.	4%.
11/2/38.	74%.	4%.	–	14%.	3%.
14/2/38.	68%.	3%.	1%.	23%.	5%.

IV Arneth count.

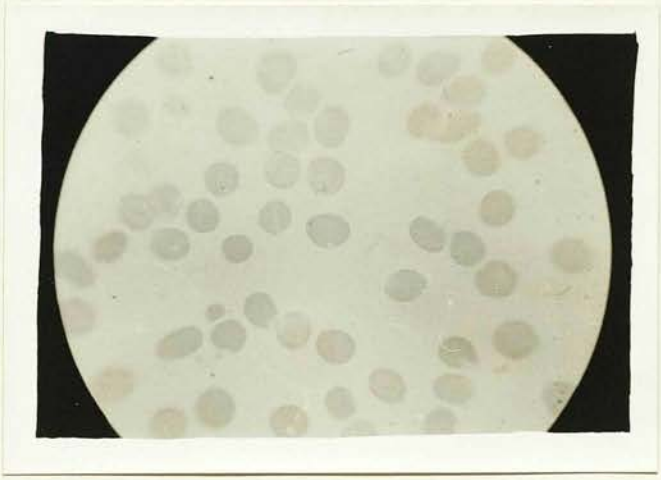
Lobes	1	2	3	4	5	6	7.
28/XI/37.	12%.	22%.	35%.	19%.	10%.	2%.	
2/1/38.	8%.	20%.	42%.	17%.	8%.	5%.	
9/1/38	10%.	21%.	32%.	27%.	9%.	1%.	
14/1/38.	12%.	19%.	41%.	22%.	5%.		1%.
21/1/38.	9%.	24%.	33%.	22%.	9%.	3%.	
31/1/38	8%	25%.	47%.	17%.	3%.		
4/2/38	10%	14%.	40%	25%.	5%.	1%.	
11/2/38	12%.	24%.	51%.	19%.	4%		
15/2/38.	10%.	25%.	47%.	13%.	5%.		



ON ADMISSION



DURING TREATMENT.



ON DISCHARGE

TECHNIQUE OF INVESTIGATION.

Haemoglobin

This was investigated in each case by means of the Sahli haemoglobinometer. In certain cases, estimation was being made for ward purposes using other instruments. In these cases a separate estimation was made with the Sahli instrument.

Films

These were stained Leishmann

Blood Counts - were always made at the same time of day.

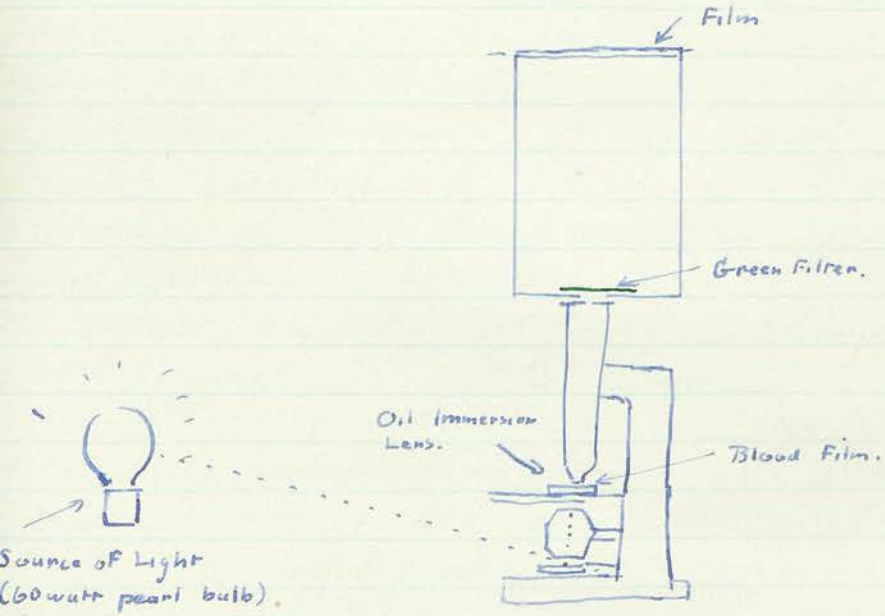
Reticulocyte counts - a drop of alcoholic cresyl blue was allowed to dry on a slide: a drop of blood was put on to the slide and mixed with the cresyl blue, using a glass rod: the film was then made and stained Leishmann.

The great majority of estimations were made personally: in the early stages of the illness, (before this investigation was commenced) in a few cases, the counts of others were accepted.

5. Microphotographs.

Admittedly these are rather unsatisfactory, but they serve to give some indication of the progress of the blood picture in each case: the apparatus was simple - a box camera without a lens. The film used was Agfa 155. Panchromatic cut film - exposure

about 15 seconds: the somewhat crude apparatus was used thus:



6. Relative sizes of red cells.

The original intention was to measure the cells in the photographs, but as this would have necessitated the taking of several hundred pictures, the idea was abandoned. Instead a rough idea was made by judging unduly large cells with the eye, comparing the slide against a normal blood film.

DISCUSSION

We have here a group of six cases of macrocytic anaemia, in five of which it may be accepted that the patient is suffering from what is commonly known as 'pernicious' anaemia, but in one of which the diagnosis is not quite so evident. The more doubtful case is that of Miss Dunlop, who was shown at operation to be suffering from cirrhosis of liver. Doubts as to the accuracy of a diagnosis of pernicious anaemia were present, however, from the very first. It was realised that there was something pathological in the liver or its connections, and the problem was whether this was the sole condition present, or whether pernicious anaemia was also a feature of the case.

It is proposed to consider the cases system by system and to compare the findings in each as they are reached, because otherwise such a discussion is apt to become rather unwieldy and involved. The points about Miss Dunlop's case will thus be considered one at a time rather than all at once, and will later be summarised. We may take it, then, that we are dealing with five cases of pernicious anaemia, and one more doubtful case, and we shall postpone special consideration of this case till later. The differential diagnosis of the other five may be dismissed in a few sentences - each patient arrived with very severe anaemia, the severity of which alone suggested the diagnosis, because pernicious anaemia alone is likely to give such a severe degree of

bloodlessness developed so insidiously and with so little real general upset. Blood examination revealed that it was a macrocytic anaemia: there was no suggestion of any of the cases being of the other types of macrocytic anaemia, such as malaria, cancer, sprue, severe sepsis, or bothriocephalus latus infection.: the case was therefore one of pernicious anaemia. Put that way, it would appear that a case of pernicious anaemia could scarcely be missed: actually, as we have seen, the diagnosis was a difficult matter that was made at a late stage in every patient.

We may start by considering the patients themselves, realising of course that nothing can be said about such matters as age or sex incidence on six cases alone. It is said that eighty per cent of cases occur between the ages of 40 and 70 years, and we see that our youngest (Grace Ganson) is aged 33, and our oldest (Mrs. Proudlock), is aged 74. Five of the cases are females. The disease is not recognised as having any occupational incidence, but it may be noted that we have a housewife, a policeman, two cooks, a domestic servant, and an unemployed waitress. Draper suggests that the condition tends to occur in persons whose measurements tend to approach those of the acromegalic. This is, perhaps, suggested in the frame of our policeman, who is well built, with a broad chest and square jaw, but the females tend rather to be small. With regard to the question of familial incidence, we may note that Mrs. Hutchison had a sister who died of pernicious anaemia. Whether

MISS

JACK

MRS

PROUDLOCK

MISS

GANSON

BEFORE TREATMENT AFTER TREATMENT

MISS DUNLOP

JOHN MACINTOSH

MRS HUTCHISON

any of the others had relatives with achlorhydria, a fact that is sometimes demonstrable, we cannot, of course, tell.

The etiology of the condition hardly comes into this discussion which must be aimed rather at the six patients this at pernicious anaemia in general. To make the picture a little more complete, however, it may be mentioned that the accepted view is that maturation of the red cells is stimulated by the haemopoietic factor which is derived from

a) an extrinsic factor, occurring in the protein of meat.

with b) an intrinsic factor, secreted by the stomach.

This haemopoietic factor is stored in the liver: in pernicious anaemia there is an absence of free hydrochloric acid in the stomach and associated with this, there is deficiency of the intrinsic factor. Moreover, changes of the nature of subacute combined degeneration occur in the spinal cord, but whether this is due to deficiency of the same factor or not, has not been decided.

As a result of the deficiency of haemopoietic factor, megaloblastic reaction, rather than normoblastic hyperplasia occurs in the bone marrow. We do not, however, know why this happens.

There is a view that a constitutional factor is responsible in the production of pernicious anaemia, and that a "releasing factor" may precipitate an attack of the disease., the constitutional factor being lack of the intrinsic factor that is normally secreted by the stomach

All of this, however, is tending to be too theoretical for this discussion, because no contribution to such investigations may be attempted from the study of only six cases. Enough has been said to indicate that the clinical features we should look for are

a) those of anaemia
b). those of changes in the alimentary tract
c) those of changes in the central nervous system.

We may notice, first of all, that the onset was insidious in each case, and that the very first symptoms were general ones; in each, such phrases as "feeling generally unfit", "faint and breathless", or "loss of appetite" may be seen. The duration of symptoms and the degree of anaemia may be compared thus:

Grace Gunson:	Duration 6 months	: RBC's on admission 1,870,000.
Agnes Tach.	2 years	: 1,140,000.
John MacIntosh	6 months	1,670,000
Mrs. Priedlock.	18 months	840,000
Miss Dunlop	4 months	3,720,000.
Mrs. Hutchison	2 years.	2,420,000.

There is, therefore, no very definite correlation between the time of onset and the severity of the anaemia, but, of course, the disease is one that has remissions and relapses, so that we cannot say, in any of the cases, that the blood figures are at the lowest point that they have reached, although admittedly all the histories are of progressive increase of debility without evidence of remission.

We have, therefore, symptoms such as tiredness, breathlessness, and tinnitus, which can be explained away by the fact that there is

marked anaemia present. Then there are alimentary symptoms, of loss of appetite for all sorts of foodstuffs, the only one that two or three of the patients mentioned specifically being tea. Lingual symptoms, too, figured prominently in some cases; these will be referred to again, but it may be noted that two patients had rather severe lingual symptoms: one patient had slight "pippyness": and the other three had no abnormal sensation at all.

No case commenced with symptoms referable to the nervous system; Agnes Jack had definite sensory disturbance in her lower limbs for about a year, with a feeling of 'pins and needles', some loss of sensation, and also intermittent claudication. Mrs Prendloch was found on examination to have definite loss of sensation and evidence of changes in the spinal cord, but there is no history of abnormal sensations being felt. The other four patients have no symptoms to suggest involvement of the spinal cord.

These, then were the first symptoms: it is true that there were other features which cannot be placed under the above headings, such as pain under the costal margin - these things will be considered later. The first signs, as noticed by the patients' friends, were of pallor or of a yellow colour of the face, or, on the other hand, of development of redness in the patient. No useful purpose would be served by discussing how early it was before such signs were noticed in each case, as such changes are not noticed by those who see a person from day to day: whereas a friend who returned to see the patient after a short interval would spot any difference

at once. We may remark, however, on the fact that the yellowish tinge was noticed in practically every case, sometimes before the pallor, and that loss of weight was present in most, but was not very severe in some. It may be mentioned here, that in Miss Dunlop's case, the period of onset was of shorter duration, the blood count much higher on admission than in the others, and the yellow colour more pronounced.

It is usual for patients to date any illness from some important event in their lives, such as an acute disturbance of health, or from an accident or a period of worry. We find that such is the case in some of our six patients. Agnes Jack dated her troubles from the performance of a nasal operation: John MacIntosh dated his from the time when he was worried by his wife's mental condition: and Mrs. Proudlock's daughter was quite convinced that if her mother had not broken her wrist three years before, her health would have remained unimpaired.

The next point for consideration is the diagnosis of each patient's case by the doctor in charge. It has been suggested above that there should be no difficulty in diagnosing the disease - but there is, indeed, a very real difficulty in coming to a decision when faced with such a vague illness, with no localising symptoms, occurring at a time when a person is becoming older and a less fit, and characterised by spontaneous periods of remissions and relapse. If every doctor were to make blood films and do blood counts

every time he was confronted with a middle aged patient who felt tired and generally unfit, then he would require to employ an assistant or to reduce the number of patients in his practice. However, it should be possible to recognise the presence of anaemia before the blood count is down in the region of 1,500,000, and then an investigation of the blood picture is a necessity, not a luxury. Briefly, it may be recalled that the diagnosis in each case was as follows.

Grace Ganson :- did not call in the doctor till her haemoglobin was 30%. He diagnosed anaemia

Agnes Jack :- Was treated with small quantities of digitalis for three months because she was 'suffering from nerves'.

John MacIntosh :- Attention was focussed on the occurrence of acute pain in the right costal margin, of sudden onset. He was admitted to the Royal Infirmary, and was not diagnosed for some time.

Mrs. Proudlock :- Was treated for three weeks by a student as a case of mitral stenosis on the strength of a systolic murmur.

Miss Dunlop :- Was referred to the R.I.E. by her doctor as a case of possible catarrhal jaundice: the doctor was not satisfied as to this being an accurate diagnosis

Mrs. Hutcheson :- Was considered by her doctor for two years to be a case of breathlessness due to early cardiac failure.

Now that the true condition present is recognised some of these diagnoses may appear very badly wrong, but in actual fact most

of them are quite understandable.

Having thus considered the onset of the condition, the next step is to compare the various objective findings, system by system, and to mention, at the same time, any atypical symptoms present in any of the cases.

On general examination, we have six adults, all very pale, all rather breathless, and all with a yellow tinge of the facies. The egregious Miss Dunlop is less pale and more jaundiced. The patients are rather thin, but, except in the case of Mrs Proudlock, there is no emaciation. Mrs. Proudlock, however, had been eating practically no food, so that wasting was inevitable. In this patient, too, oedema of the ankles was present: MacIntosh also had noticed this for a few days, but no swelling was found on examination. Mrs Hutchison had oedema but this was associated with varicose veins. No patient showed subcutaneous haemorrhages.

All except Miss Dunlop, whose blood count was at a higher level, appeared to be in a state of exhaustion when admitted. The improvement brought about by liver injections was a truly remarkable one. Only a few days elapsed before these people, who had lain back against the pillows all day, were sitting up once more, evidently much brighter and anxious to recover. Unfortunately Mrs Proudlock, whose case was of a much more severe nature, never reached this happy state.

Finally, it may be remarked that there was a tendency for the pulse rate to be raised,

the blood pressure and temperature to be rather low, and the respirations to be, if anything, rather quick.

We ought, perhaps, to consider next the findings obtained on examination of the blood, but as these are of supreme importance it is probably better to dispose of other matters first, so we may conveniently begin by consideration of the alementary system.

Not one of the patients had a good appetite. Miss Dunlop disliked eggs and fatty things, but the others had no special dislikes, except that some of them first noticed a distaste for tea. Vomiting was not a prominent feature in any, although Grace Ganson and Mrs. Hutchison vomited on two or three occasions. As one would expect, none suffered from acid eructations, but several complained of flatulence or a feeling of weight in the epigastrium. The fact that Grace Ganson brought up undigested food about two hours after taking it and that she felt that it lay undigested in her stomach may be remarked upon, because the stomach usually empties fairly rapidly in pernicious anaemia, and this type of symptom is not very common. Miss Dunlop had been troubled with flatulence and vomiting after meals for some three months, and, as we have seen, associated with this there was jaundice and possibly some darkening of the urine. This would suggest that she had jaundice of the catarrhal or obstructive type, but bile was not found in the urine, and the motions were not pale until just before admission. We will discuss this below, but meantime it is sufficient to say that the flatulence and vomiting must not be regarded from

the point of view of pernicious anaemia.

One does not as a rule associate epigastric pain with this disease, but Grace Ganson had a constant dull ache for about a year, which cleared up with treatment. If it really existed, it must have been related to the condition of the stomach but it is at least possible that there was some psychological element present and that her attention was directed to the stomach by the feeling of fullness. If not, the flatulence itself may be a sufficient explanation.

MacIntosh was admitted because of pain under the right costal margin of sudden onset, but not of a true colicky nature. The sudden onset and the site of the pain are very suggestive of impaction of a stone in the cystic duct: as there was no jaundice with this pain it could not have been a stone blocking the bile duct. However, no stone was revealed by X ray examination, so that if it were due to the presence of stone, then either the X ray failed somehow to show it up, or it was passed into the duodenum, without causing the usual colicky pain during its passage. Another, perhaps rather theoretical possibility is that there was a small stone that was large enough to cause pain in passing along the cystic duct but small enough to remain in the bile duct without giving rise to symptoms. Such considerations are however, rather outside the confines of this discussion, because nobody can say definitely what did cause the pain, but it was almost certainly not due to pernicious anaemia so that its only value to us is that it led to the patient's major illness being

discovered earlier that might otherwise have been the case.

Mrs Proudlock, too, had a gnawing epigastric pain.

The next consideration is the very important one of the state of the tongue. It is said that the tongue in pernicious anaemia is clean and moist and that if this is not the case, the diagnosis must be reconsidered. All our cases had clean moist tongues. One may expect either signs or symptoms referrable to the tongue, or both. For clarity the cases may be listed as follows.

Garson:- Pain in the tongue was an early symptom, and the patient said it was red and swollen, but this subsided. The tongue was smooth, and showed simple atrophy of the papillae.

Guch:- There were no symptoms. The tongue showed atrophy of the papillae.

MacIntosh:- Soreness of the tongue was an early symptom: the surface was rather smooth, but not markedly atrophic.

Proudlock. No signs or symptoms

Dunlop. No signs or symptoms.

Hutchison A 'nippy' feeling of the tongue was a late symptom. Atrophy of the papillae was seen.

Thus we see that none of the patients showed the more severe changes such as fissuring or ulceration of the tongue, and that none had the more acute type of glositis when admitted, although Grace Garson may have had this at an earlier period.

Examination of the abdomen gave purely negative findings in all cases except that of Miss Dunlop. There was no evidence to support any diagnosis such as cholecystitis in the case of Mac Intosh.

We may take this opportunity to dispose of the matter of Miss Dunlop's jaundice. To summarise what has been mentioned several times already, it may be recalled that

1. The first symptoms of breathlessness was followed in a week or so by yellowness of the skin
2. At this time she thought her urine was darker but her doctor could find no bile present
3. The motions were not pale either at this time or when admitted, but she thinks that they were paler just before admission
4. There was flatulence and vomiting with distaste for food.
5. On admission there was no bile in the urine and no excess urobilin, and the icteric index was 27. The Van den Bergh test gave a direct reaction, weak biphasic.
6. There was enlargement of the spleen, but no enlargement of the liver.
7. There was anaemia, and the blood picture suggested pernicious anaemia
8. Operation at a later date revealed the presence of cirrhosis of the liver.
9. X ray examination on first admission revealed a calcified gall stone in the gallbladder.
10. Two years before admission the patient had an acute pain under the right costal margin: there was no jaundice, but she could not remember details.

This last pain may have been due to the stone seen in the X ray blocking the cystic duct. There was obviously something definitely wrong with the liver and its connections on admission, and it might be that the symptoms were all due to cirrhosis: the fact that there was no bile in the urine is explained by the fact that the jaundice, as estimated by blood examination, was not of sufficiently severe degree to cause bile to appear in the urine. The presence of a direct Van den Bergh reaction would fit in too, because of obstruction of the bile ducts by the proliferating connective tissue within the liver.

There must be consideration, however, of the fact that the jaundice certainly cleared up to a great extent while the patient was in hospital. This can hardly be explained away as being due to treatment with liver injections, but possibly there was a catarrhal condition superimposed upon the cirrhotic process. There was also the possibility of the jaundice being due to some such process as carcinoma of the head of the pancreas, but the disease was not as progressive as one would expect with this, and the general condition of the patient's health was not so poor as one would find. The presence of a stone in the common bile duct was also a distinct possibility, that could not be excluded with any definite certainty without operative investigation. Such investigation revealed that there was no stone, and so the surgeon was able to tell the physician that there was present cirrhosis of the liver.

The next question that arises is whether

pernicious anaemia was present as well, and if not, whether another explanation can be put forward to explain the bloodless state. Those treating the case were satisfied that pernicious anaemia was indeed present, and suggestions that there was some doubt about the matter were not regarded seriously. Nevertheless it must be argued that only on two occasions was the colour index greater than 1: that response to liver injections was unsatisfactory - eg., on the fourth day in hospital the red count was 3,720,000; on the 33rd day, 3,780,000: and the 45th day 3,400,000: that the blood film never showed very definite megalocytosis: and that, although the test meal showed absence of free HCl, histamine was not injected, so the test was valueless. Against this view it may be said that these findings are explained by the fact that the anaemia had not reached a stage of great severity, and the picture would correspond to that of any other of the patients whose count had risen to such a relatively high level. Such an argument is quite sound, and cannot be roughly brushed aside.

If the case is not one of pernicious anaemia, then we must try to decide what it really is, and here it may be recollected that there was definite enlargement of the spleen. Now, not only is such a finding sometimes present in pernicious anaemia, but slight enlargement is very commonly associated with cirrhosis, which was proved to be present in our patient's liver.

However, the combination of enlarged spleen with anaemia suggests that we should bear in mind the possibility of a diagnosis of splenic anaemia: we may first decide what is meant by the term "splenic anaemia". Six conditions have been put under

leading. There are as follows.

1. Acholuric jaundice. - in this condition one would not find hepatic cirrhosis, and there would be an indirect Van den Bergh reaction. It is therefore excluded.
2. Pure splenic hypertrophy, leading to anaemia from increased blood destruction. - out of the question in this case.
3. Splenomegaly associated with thrombosis of the splenic or portal veins - also out of the question.
4. Splenomegaly with peri-ellipsoidal haemorrhages and nodular siderosis - this is a pathological entity, not a clinical one.
5. Banti's disease, in which the splenic enlargement is associated with portal cirrhosis. In this condition one usually finds haemorrhages occurring into the stomach and elsewhere, but the same thing is true of cirrhosis itself, without splenic change, and here we have definite cirrhosis without such haemorrhage. We cannot exclude Banti's disease on these grounds, therefore. In Banti's disease one finds a microcytic anaemia, with low colour index, and our case was more like a case of macrocytic anaemia. This is a serious objection that can only be circumvented by a confession of error: however, it has never been claimed that our patient had a high colour index, and the enclosed photographs of typical fields show that the tendency to megalocytosis is not marked. It might be argued, too, that the marked jaundice indicates that we are dealing with a case of biliary cirrhosis rather than one of portal cirrhosis. However, no person can say definitely where

portal cirrhosis ends and biliary cirrhosis begins, so that such an argument is perhaps rather theoretical. The important practical point is that jaundice is not usually very marked in Banti's disease, especially with a blood count. That is as high as 3,700,000. This condition, then, is one that must be borne in mind, but it is most unlikely that a diagnosis of Banti's disease would be a correct one in this case.

6. Reticulo-endothelial hypertrophy of the spleen: this is another pathological entity, in which large endothelial cells are scattered through the pulp and venous sinuses. It is not a condition that one would diagnose clinically.

To summarise, therefore, we may say that not one of the recognised forms of splenic anaemia furnishes us with a satisfactory diagnosis of Miss Dunlop's case.

The condition of biliary cirrhosis is mentioned above; primary biliary hypertrophic (Hanot's) cirrhosis might, at first sight, be thought of in the diagnosis. In such a condition, jaundice is a marked feature and ascites is absent until late. But Hanot's cirrhosis is a rare disease, and in it, not only is the spleen enlarged, but there is generally considerable enlargement of the liver, which was not present here. Moreover, the liver of

Hanot's cirrhosis is smooth, and the liver in this case was shown at operation to be very nodular.

So, one by one, the more unlikely possibilities have been eliminated, and it remains for us to discuss the more likely ones. As already explained, enlargement of the spleen is not uncommon either in pernicious anaemia or in hepatic cirrhosis, so we need no longer search for further explanations of this physical sign. The outstanding fact that remains is that the liver is cirrhotic, and anaemia is present. Now it is very common for a microcytic anaemia to accompany cirrhosis, possibly due mainly to the accompanying deficiency of free hydrochloric and leading to defective absorption of iron. We have already considered the possibility of Miss Dunlop having, not a megalocytic anaemia as was at first suspected, but rather a microcytic form: and it was decided that, although the colour index was not very high, it was on the other hand, not very low, and that the appearance of the film did suggest rather a macrocytic than a microcytic anaemia. But, less commonly, a macrocytic anaemia accompanies cirrhosis, and is said to be due to failure of the liver to complete the metabolism of the absorbed specific anti-anaemic factor. There is, again, no reason why a person with cirrhosis should not suffer from the more common type of hyperchromic macrocytic anaemia due to lack of secretion

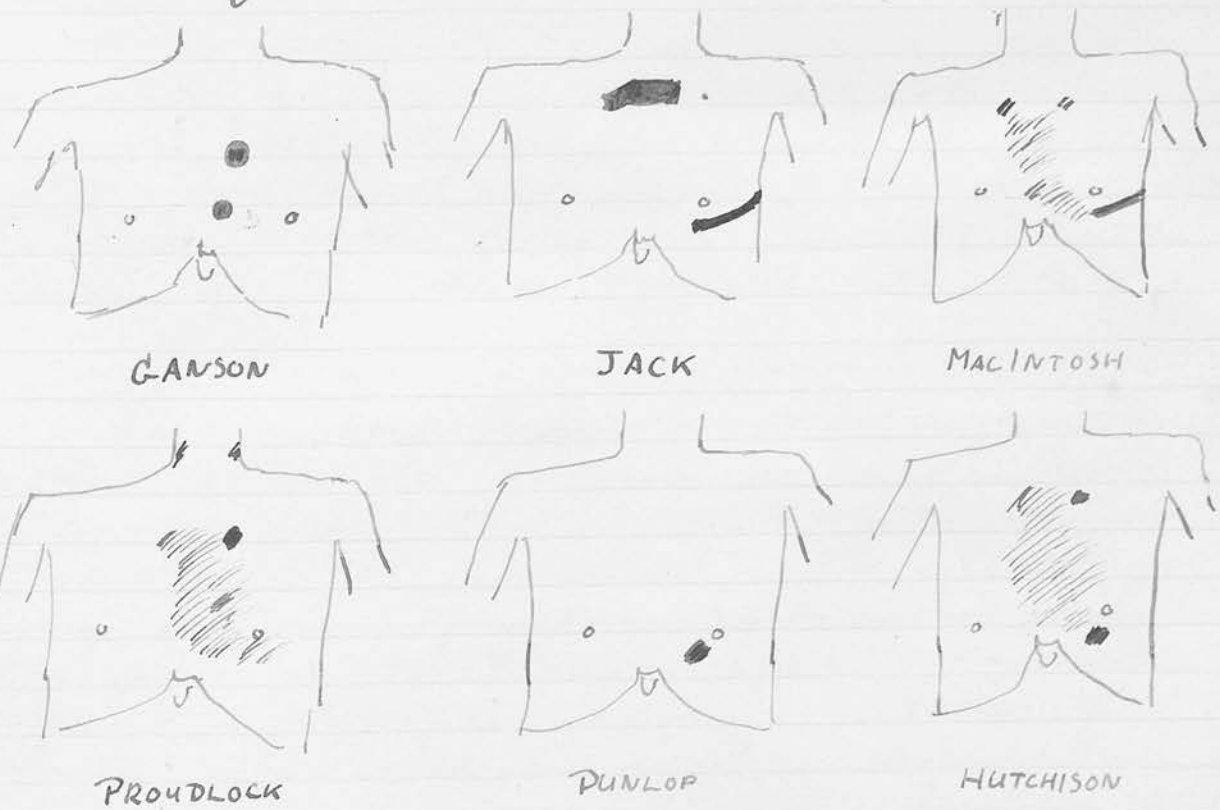
of intrinsic factor, and it might be that such a patient would be more likely to have deficiency of such secretion in a similar way to her deficient secretion of hydrochloric acid.

To summarise, therefore, it may be said that, although there appears at first sight to be some doubt as to Miss Dunlop's true condition, nevertheless she does seem to have a macrocytic anaemia. Whether this is due to deficient metabolism or to deficient secretion is hard to say, but is of more than academic interest, because in the former case one would not expect such favourable results from liver therapy as in the latter: the rather poor response in this case might indicate that the defect was a metabolic one.

Lastly, as regards the alimentary system, one would look for complete achylia gastrica in any case of pernicious anaemia, and if it were not present one would reconsider the diagnosis. We have seen that it was present in Grace Ganson, Mrs. Hutchison and Miss Gash, and that Miss Dunlop had achlorhydria. Investigation was not made in the other two.

We may next glance at the findings revealed by examination of the circulatory system. Every patient complained of breathlessness, and in most this was an early feature. Three of them suffered from palpitation. These symptoms are, of course, such as one would expect in the presence of any severe type of anaemia. Miss Gash and Mrs. Pendlock both had some praecordial pain which, too, may be considered due to the anaemia, so that the heart muscle was not gaining sufficient nourishment.

In all cases there was low blood pressure. There a rather slow pulse (rate 65) in the case of Miss Dunlop, which may have been a result of jaundice. The pulse rate was increased in the others, reaching a rate of 120 with Miss Jack, and 110 with Mrs. Proudlock. This, too, may be explained as being due to the anaemia. The only other positive findings were those of systolic murmurs which were found in every case. As we have seen, the site and direction of propagation of these murmurs varied in each, and they may be summarised in the following diagrams.



■ = site of murmur.

Thus we see that such haemic murmurs tend to be very inconstant as regards their situation. It is generally said that they tend to occur in the pulmonary area but here we have them in all areas. Moreover these diagrams only show the rates of murmurs at the time of admission. They tended to change as the disease progressed towards relief under the influence of liver therapy. It may of some interest to note the level of the blood count when systolic murmurs ceased to be heard.

Jack.	Red cells	3,490,000	Haemoglobin 71%.
MacIntosh		3,520,000	80%.
Hutchison		2,440,000	50%.

Such murmurs cannot, obviously, be related accurately to the number of cells present, and, indeed, one would not expect this because so many other factors are concerned in the hearing of any sound connected with the heart.

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The conditions present in the respiratory systems may be dismissed in a few words. We have seen that in all cases except that of Mrs. Proudlock, the findings were entirely negative. In her case, the signs at the bases suggested hypostatic congestion or hypostatic pneumonia; when first admitted she had no cough or expectoration, but evidence of bronchitis soon developed and the broncho-pneumonia that was revealed by post mortem examination was undoubtedly a major factor in bringing her life to its end

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On examination of the urine one expects to find excess of urobilen in a severe case, and we see that such was the case in none of the patients. Otherwise there is nothing to note in the urinary system.

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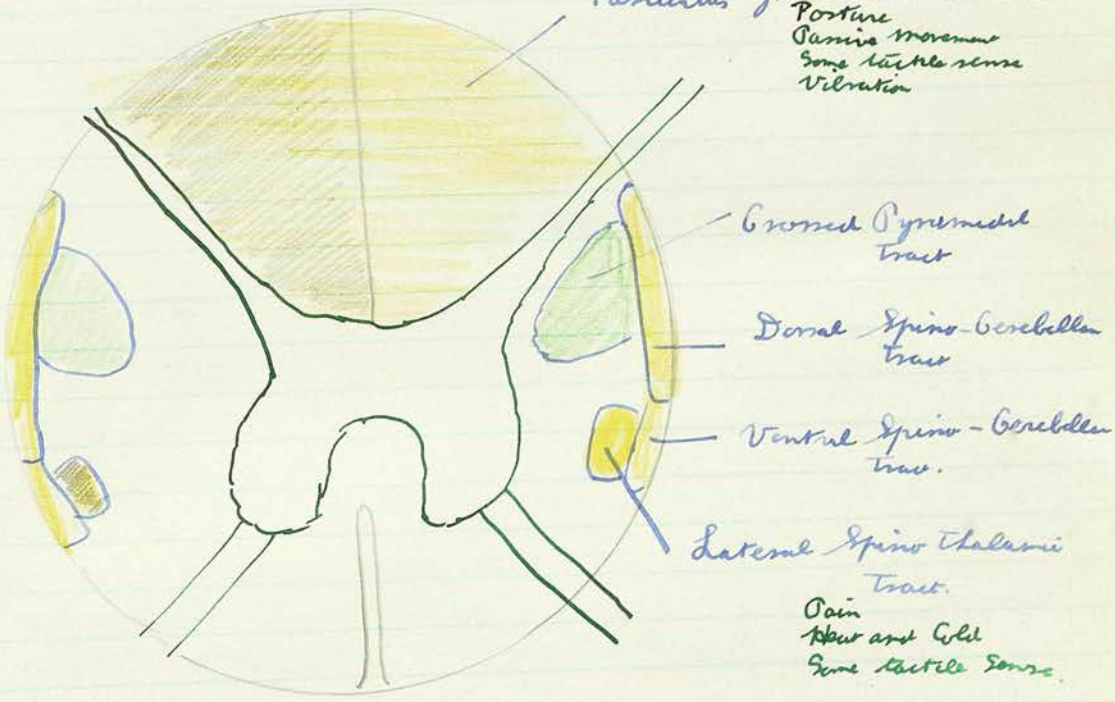
Examination of the nervous system showed that in most of our six cases, there was no evidence of any pathological process. It is sometimes said that 80% of pernicious anaemia cases have symptoms, but against this it is argued that early tingling and similar sensory changes are due to severe anaemia and cardiac weakness and are peripheral in origin. This may well have been the chief trouble with Miss Jack. It may be recalled that fairly early in her illness, she had a feeling of numbness and heaviness in both legs with this was a feeling of 'pins and needles', soreness of the calf on walking any distance, and a diminished sensation of heat so that she did not feel a hot water bottle touching the feet.

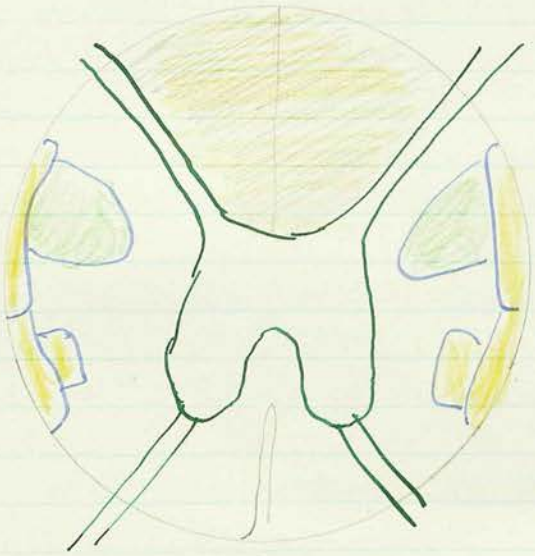
The soreness of the calf is suggestive of intermittent claudication. This is not usually due to anaemia alone, but there may have been an element of arterial spasm. The numbness, 'pins and needles' and loss of sensation may have been due to peripheral factors as mentioned above, the loss of heat sense being due to the legs being too cold to feel a hot water bottle touching them. Alternatively, they may indicate that changes had commenced in the posterior columns of the cord, but one would then have to postulate changes

in the lateral columns to explain loss of temperature sense. Usually, however, changes in the lateral columns first affect the descending tracts so that it would be reasonable to look for evidence of pyramidal tract involvement. So is true that the reflexes are recorded as having been brisk, but the Babinski sign is absent, and there is no evidence of spasticity in the limbs. Again, if the portion columns were involved one would look for ataxy due to loss of sense of position. This, we have seen, was not present.



If, then, the symptoms are to be regarded as being due to cord lesions, then there must be situated as shown in the above diagram. (shaded in pencil on one side only) These sites certainly do become involved in subacute combined degeneration but as already mentioned, the crossed pyramidal tracts would probably be involved as soon as, or earlier than, the

spino thalamic tracts. Moreover, no loss of temperature sense was found on clinical examination. There was, however, loss of vibration sense in the distal parts of the lower limbs. The examination of the nervous system would therefore suggest that any lesions are situated thus: (shaded in pencil)



However, the other senses conveyed by the posterior columns were not impaired, and there was no ataxy: moreover, the loss of vibration sense was of the 'stocking' type of distribution, a facts of less importance because of the difficulty of deciding very accurately the areas that have lost vibration sense in a limb. It may be said however, that there was no definite evidence of involvement of the spinal cord, and most probably any sensory changes were of peripheral origin.

Mrs. O'Sullocks' case, on the other hand, gives us a more suggestive picture. (It may be remarked in passing that the upper limit of age of onset of subacute combined degeneration is said by Taylor to be 70

years, while Mrs Pinedock is aged 74.)
In her case, great difficulty was experienced in making any investigation of her nervous system, because she was too ill to co-operate. The features present may be summarised thus:

1. For three months, the patient was unable to walk owing to weakness of the legs.
2. There was neither spastic nor flaccid paralysis of the limbs.
3. Knee and ankle jerks were absent, and the plantar reflexes were plantar flexor.
4. The sensation of pain was present in upper and lower limbs: other sensations were not investigated
5. There was no history of paraesthesiae.

Although the investigations are admittedly incomplete, they do furnish us with a fair amount of information. Thus, although the weakness of the lower limbs may have been due to old age and general debility it is quite likely that the symptoms were rather due to ataxy because of loss of position sense. We might then look for evidence of loss of vibration and allied senses: here the patient was in no condition for such investigation, but we have loss of knee and ankle jerks which is explained by posterior column involvement.

Lesions would therefore be in the areas shaded in pencil in the sketch.

Subacute combined degeneration can take on so many different types of clinical picture that the diagnosis of such a condition may be a very difficult matter. If the loss of deep reflexes is, indeed, due to such a condition, then there must be some involvement of the posterior columns: on the other hand, such loss may be due, not to cord disease at all, but to peripheral neuritis. If it were due to cord pathology, then one might expect to find that changes had occured in the lateral columns too. But we see here that we have no evidence of such change - the plantar responses were plantar flexor - there is no evidence of spastic paralysis. Again, there does not appear to be a flaccid paralysis present, as one would expect if there were very marked changes in the posterior columns.

It may therefore be said that we have absolutely no evidence of ~~posterior~~ lateral column degeneration. We do have certain changes which might be due to posterior column involvement, but there is not sufficient evidence for us to say definitely that such is present. These changes might equally well be caused by peripheral neuritis, and although it is probable that this last explanation is the true one, our evidence is not sufficient for us to be able to say definitely that this explanation is indeed the correct one.

The last consideration as regards the nervous system is that of the mental condition of the patients. A word or two must suffice - Mrs. Pendlock was in a state of complete apathy - there was no special tendency in the others, except that some were rather depressed

THE BLOOD.

We may commence what might otherwise become a most involved discussion by making a list of the features that one expects to find in a case of pernicious anaemia.

1. A very low red cell count, with high colour index
2. Anisocytosis and poikilocytosis
3. Megalocytosis
4. The presence of megaloblasts in a severe case
5. Polychromasia and possibly punctate basophilia
6. A relatively large percentage of reticulocytes
7. Flattening of the Price-Jones curve with a shift to the right.
8. Polymorph Leucopenia with a diminished white cell count and relative lymphocytosis
9. A shift to the right in the Arneth counts.
10. Thrombocytopenia, with large platelets.
11. The presence of macropolycytes in the blood - ie. unusually large polymorphs with hypersegmentation of the nucleus.
12. A raised icteric index

The red cell count and picture.

We have already seen that, in every case, with the possible exception of Miss Dunlop, the film at the time of admission showed anisocytosis and poikilocytosis, and the presence of polychromasia and of cells of the megalocytic type: in no case was polychromasia marked, however.

Megaloblasts were seen in the case of

John MacIntosh (*1·67)
Mrs. Proudlock (·84).
Miss Jack (1·14)

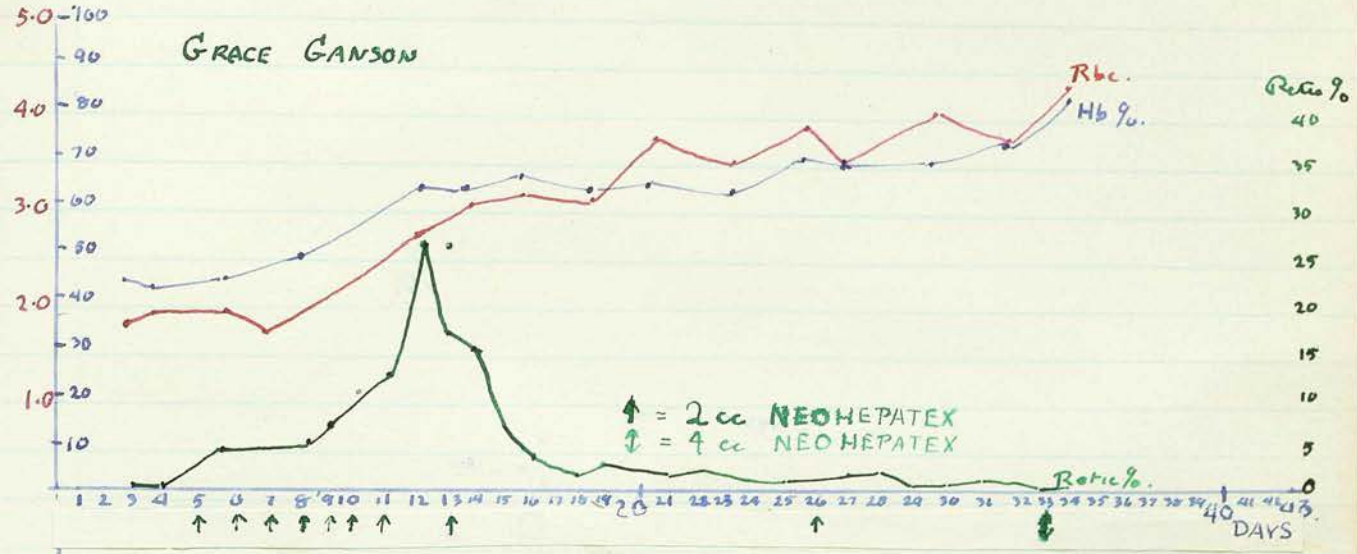
They were not seen in the case of

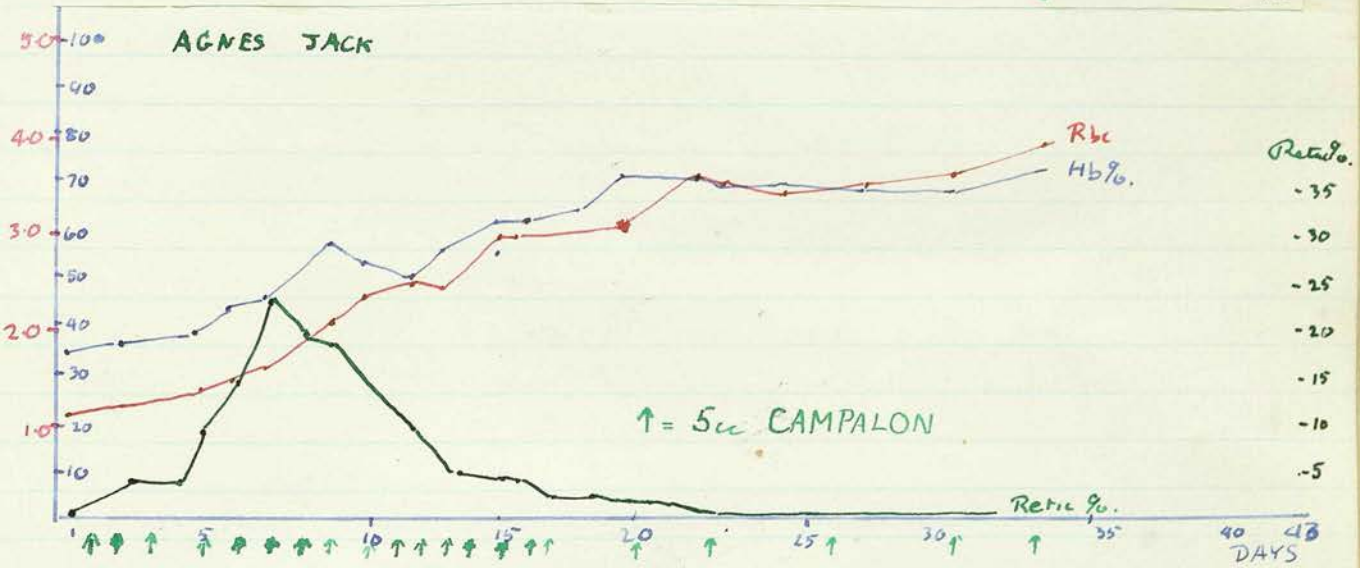
*Denotes red cell count on admission. 1·67 = 1,670,000.

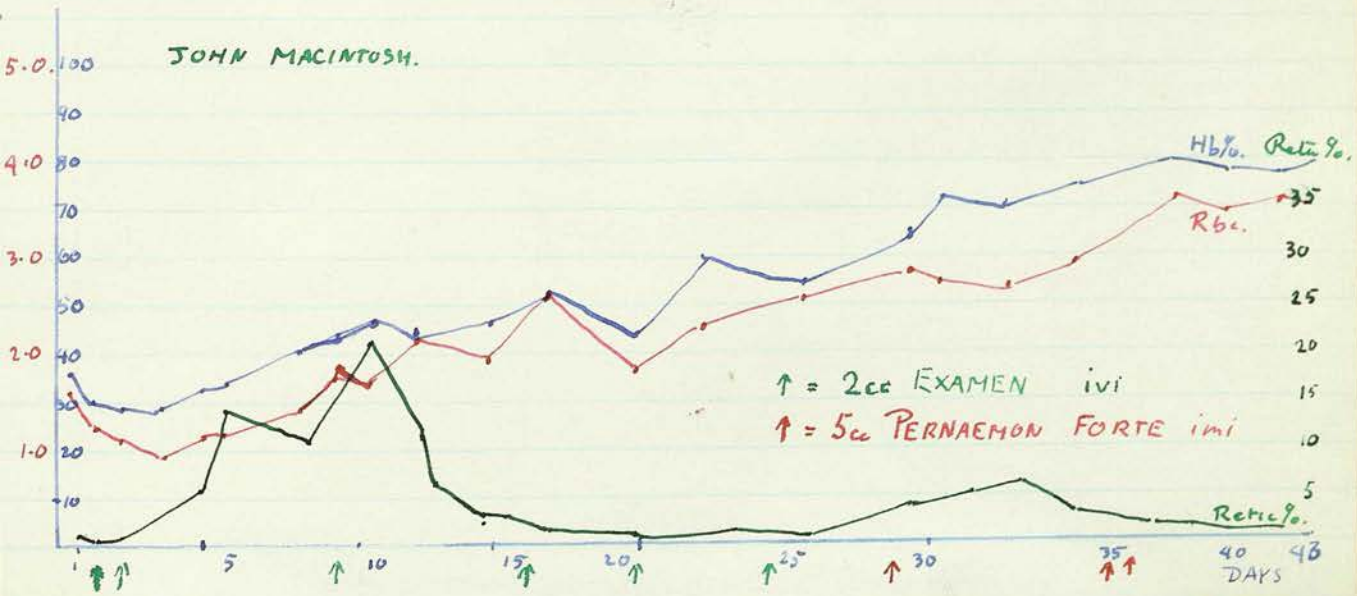
Miss Garson (1·81)
Miss Dunlop (3·72)
Mrs Hutchison (2·42 : this count later fell to 1·35, but megaloblasts were still not visible)

There is no evidence of a high percentage of reticulocytes at the time of admission in any of the cases (it may be noted that the first counts in each case were done by the doctors in charge of the wards, and are therefore probably reliable)

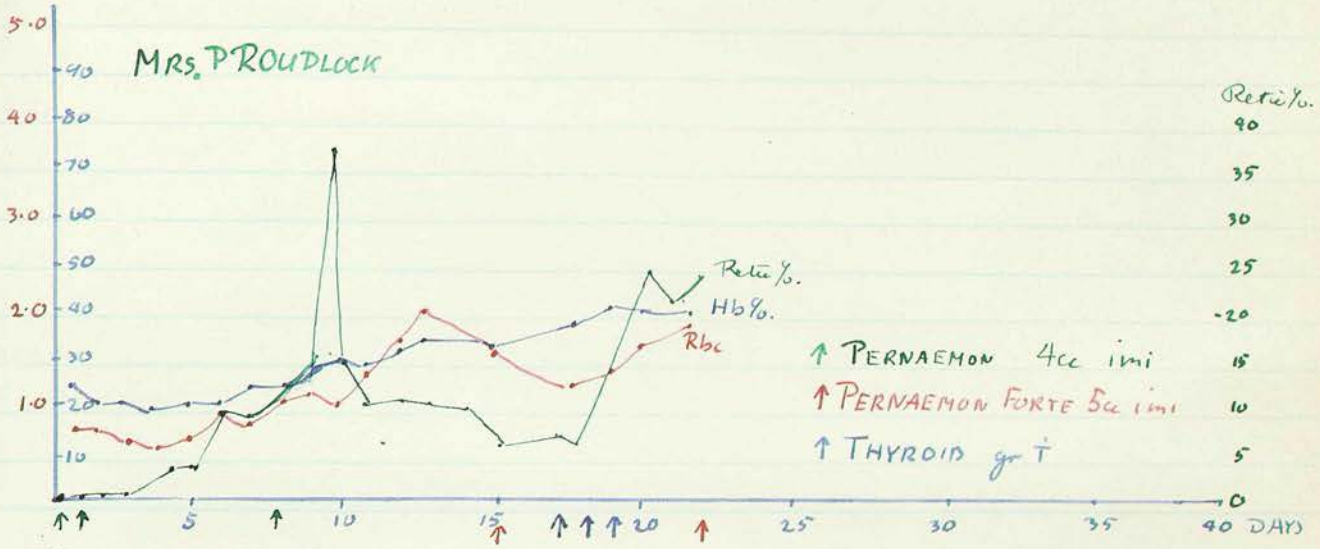
As lists of the blood counts have already occupied many pages, it would be profitless and wearisome to repeat the lists, but they are recorded below in graphic manner for purposes of comparison. The first six graphs show the progress of the individual patient. The following ones are composite and show the relative progress of the six.


GRACE GANSON
Rbc.
Hb %.
Retic %
↑ = 2cc NEOHEPATEX
↕ = 4 cc NEOHEPATEX
Retic %.
DAYS

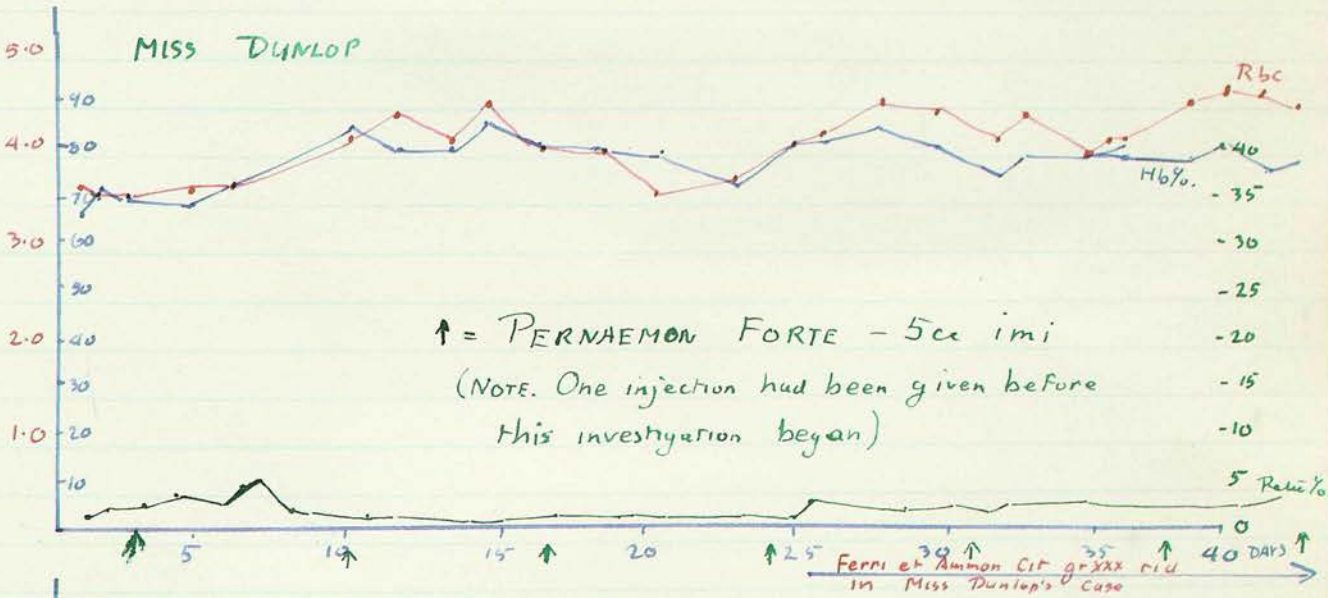

AGNES JACK
Rbc
Hb%.
Retic %.
↑ = 5cc CAMPALON
Retic %.
DAYS


JOHN MACINTOSH.
Hb%. Retic %.
Rbc.
↑ = 2cc EXAMEN ivi
↑ = 5cc PERNAEMON FORTE imi
Retic %.
DAYS

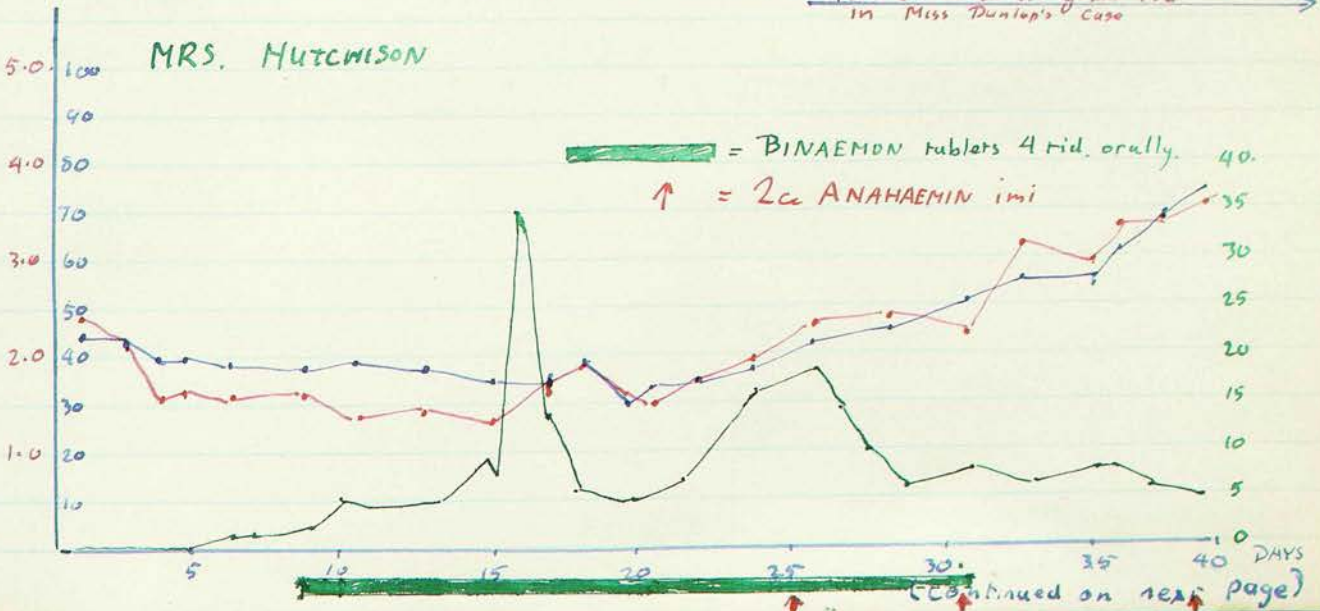
MRS. PROUDLOCK



MISS DUNLOP



MRS. HUTCHISON



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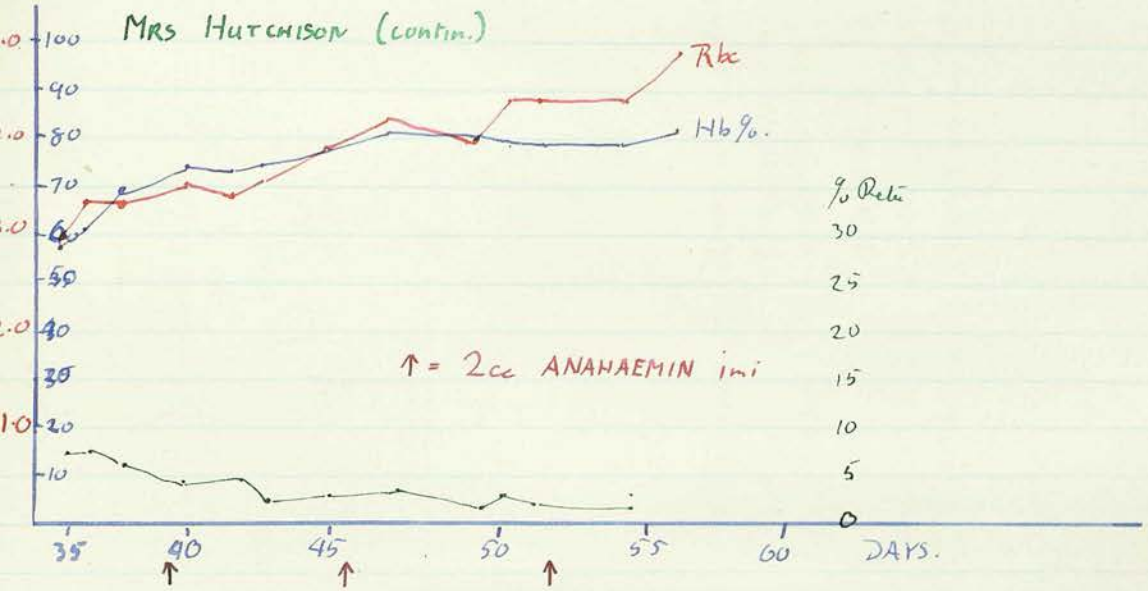
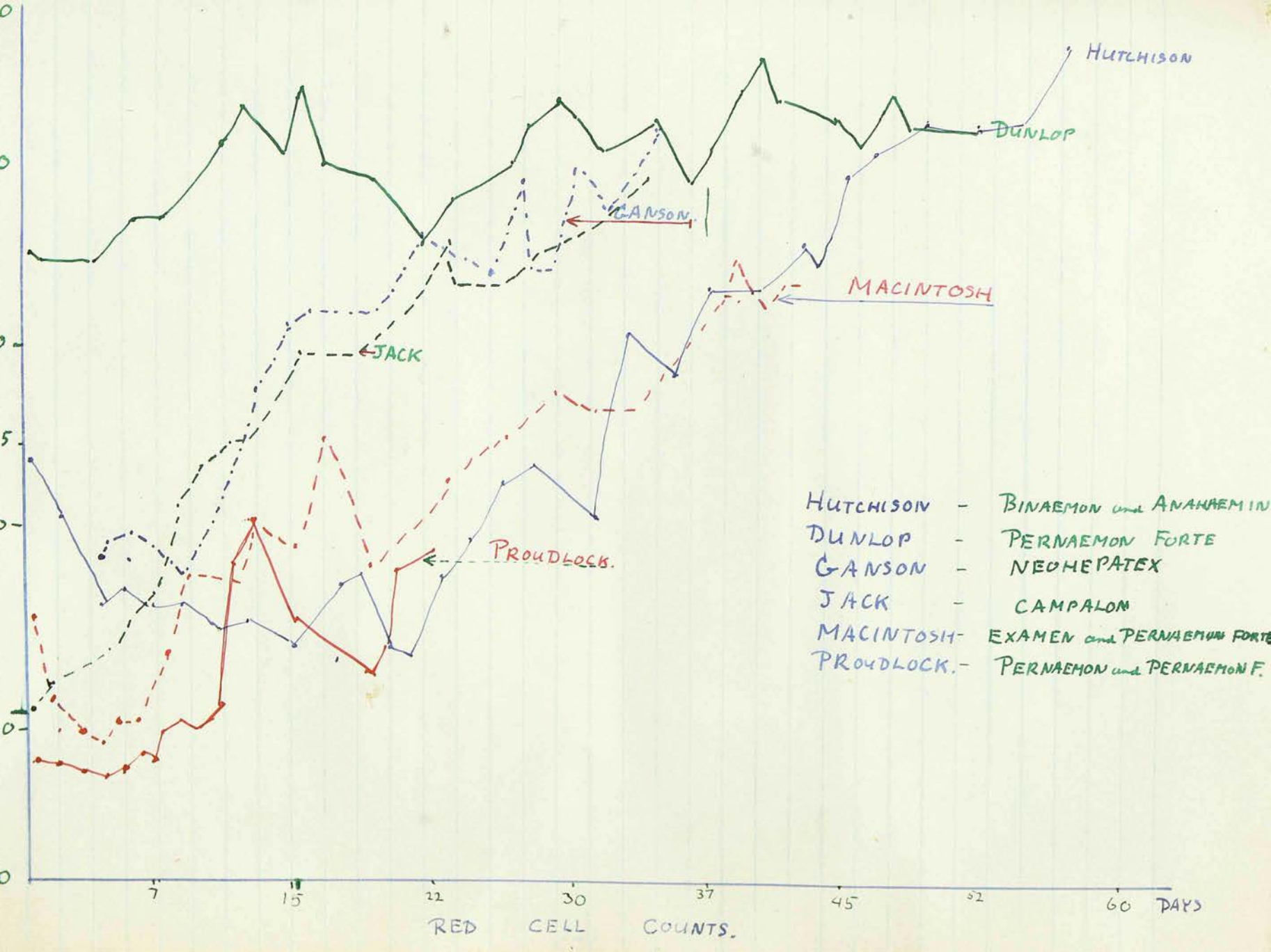

MRS HUTCHISON (contin.)
Rbc
Hb%.
% Reti
↑ = 2cc ANAHAEMIN im
100
40
80
70
60
50
40
30
20
10
30
25
20
15
10
5
0
35
40
45
50
55
60
DAYS.


HUTCHISON
DUNLOP
GANSON.
MACINTOSH
JACK
PROUDLOCK.
HUTCHISON - BINAEMON and ANAHAEMIN
DUNLOP - PERNAEMON FORTE
GANSON - NEOHEPATEX
JACK - CAMPALON
MACINTOSH - EXAMEN and PERNAEMON FORTE
PROUDLOCK. - PERNAEMON and PERNAEMON F.
7
15
22
30
37
45
52
60
DAYS
RED CELL COUNTS.

These charts are of some interest, but they cannot, of course, be used to estimate the relative value of the various liver extracts used in treatment. A very much larger number of investigations would be necessary before any conclusion could be drawn. It may be noted, however, that a 35% reticulocyte response was obtained with the giving of Bencemon tablets by mouth. The results in this case (Mrs. Hutchison) were very gratifying, and this response was equalled only in the case of Mrs. Proudlock, who was being given injections of Pernaemon.

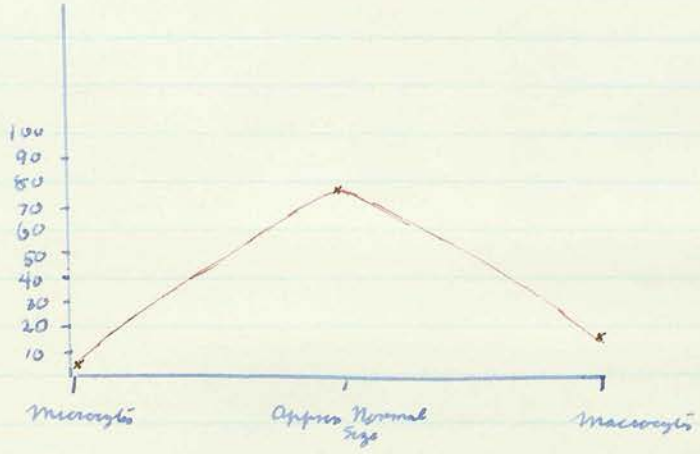
Unfortunately, we cannot construct a Price-Jones curve, as apparatus for measuring the size of the red cells was not available, and the efforts to give a suggestion of the relative shapes of the cells were made by such crude methods that they are of no value. It can only be said that these counts revealed that there was a tendency to macrocytosis, without a equally marked tendency to the formation of microcytes. This, therefore means that the cell distribution curve would be flattened, because a smaller number of cells would be around 7-2 μ in diameter, and would show a shift to the right, because although an increased number of microcytes are present, the percentage of these cells is not so large as the percentage of macrocytes.

The crude "cell distribution counts" reveal, further, that as the patient's condition

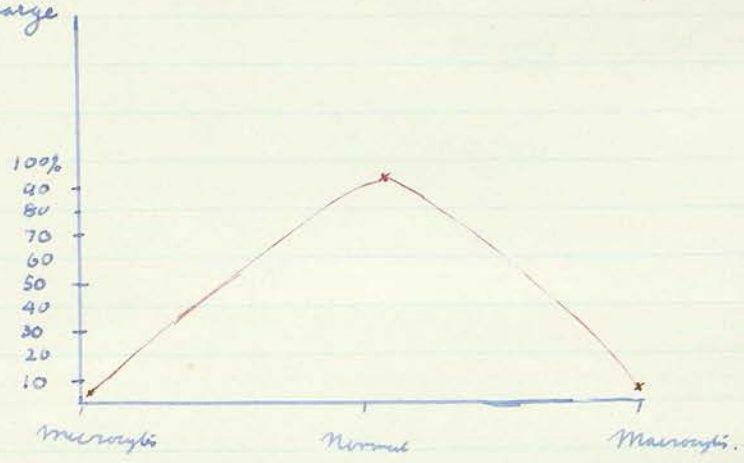
improves, the cells approach normal dimensions, and poikilocytosis disappears.

Type of curves thus obtained (eg. J. MACINTOSH)

On admission.



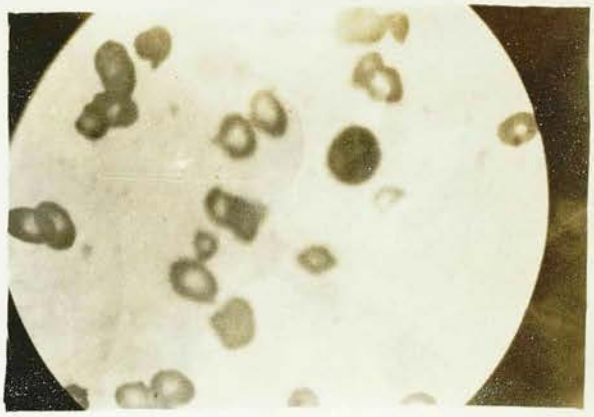
On discharge



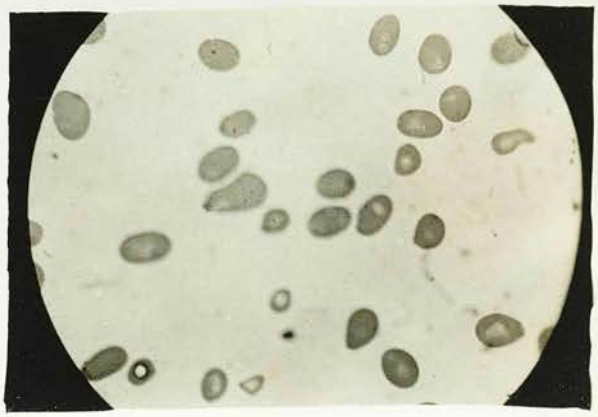
Such curves are, however, very crude, and of no practical value, so that they will not be constructed for each patient. It may be noted that the anisocytosis and poikilocytosis was most marked in those patients with the most severe degree of anaemia.

BEFORE TREATMENT

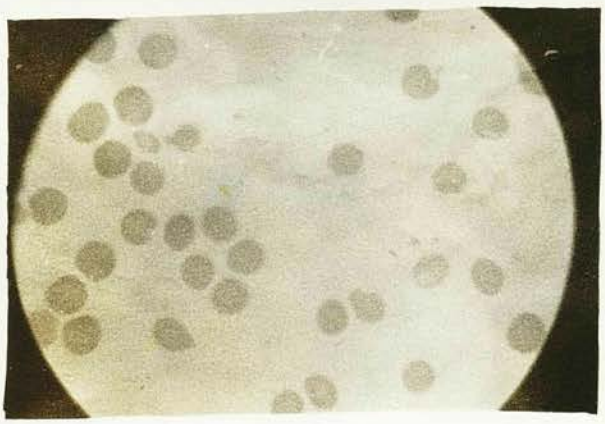
MACINTOSH



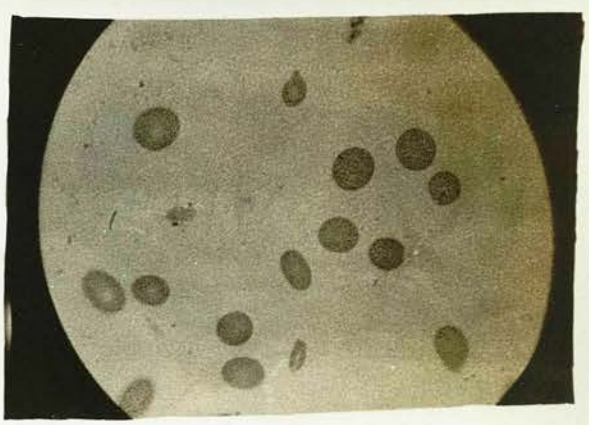
PROUDLOCK



JACK

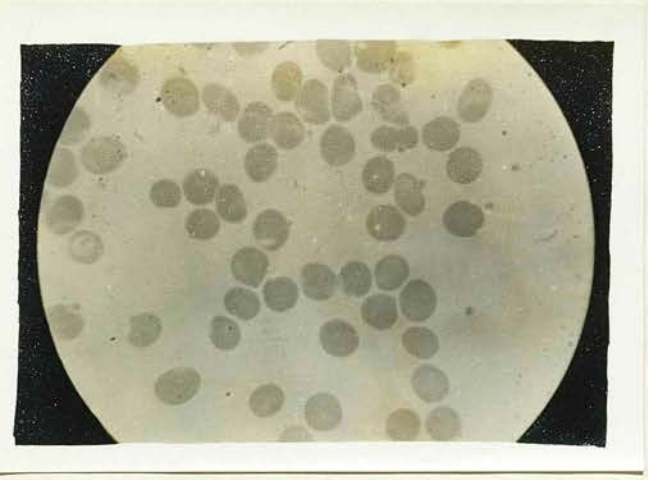


DUNLOP

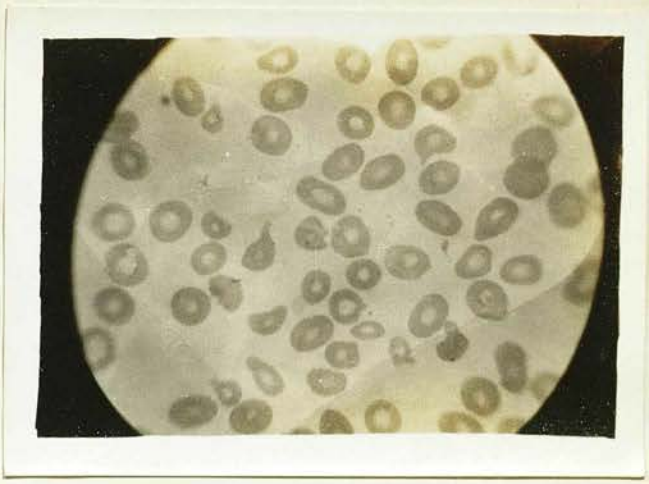


HUTCHISON

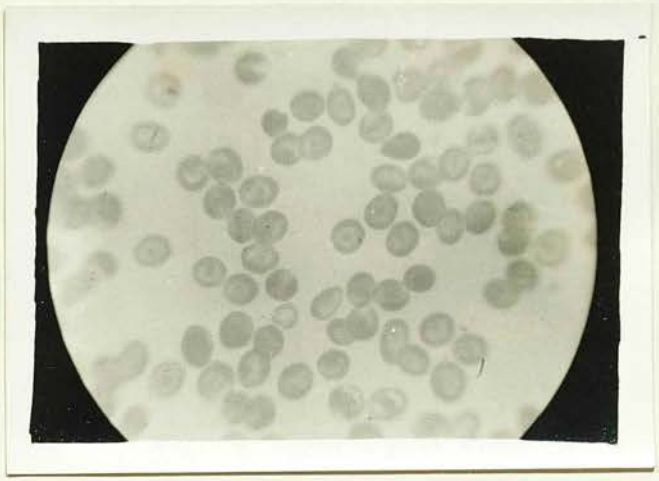
AFTER TREATMENT.



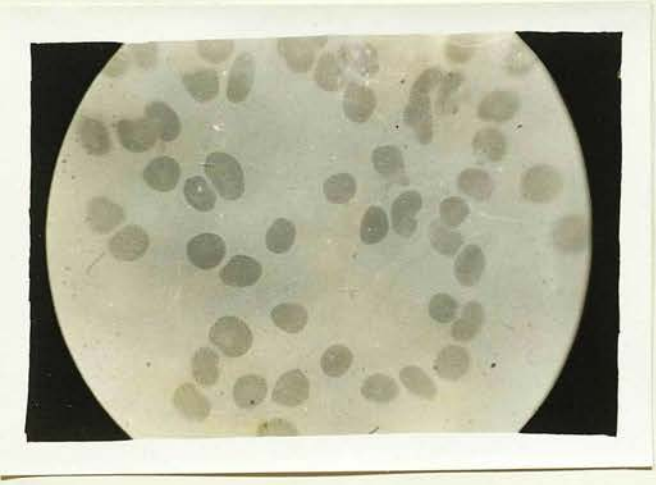
MACINTOSH



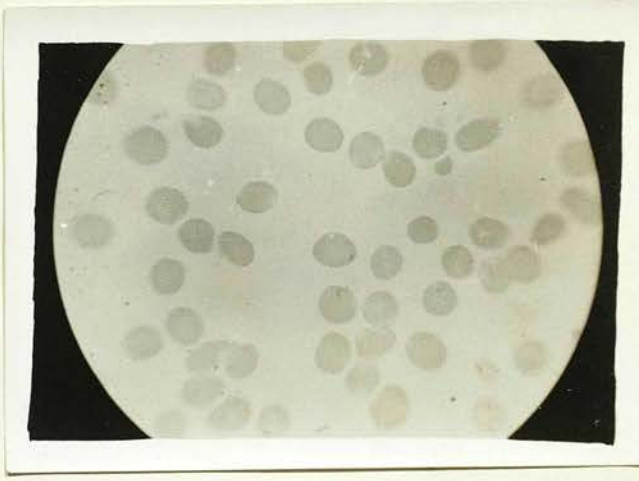
PROUDLOCK



JACK



DUNLOP



HUTCHISON

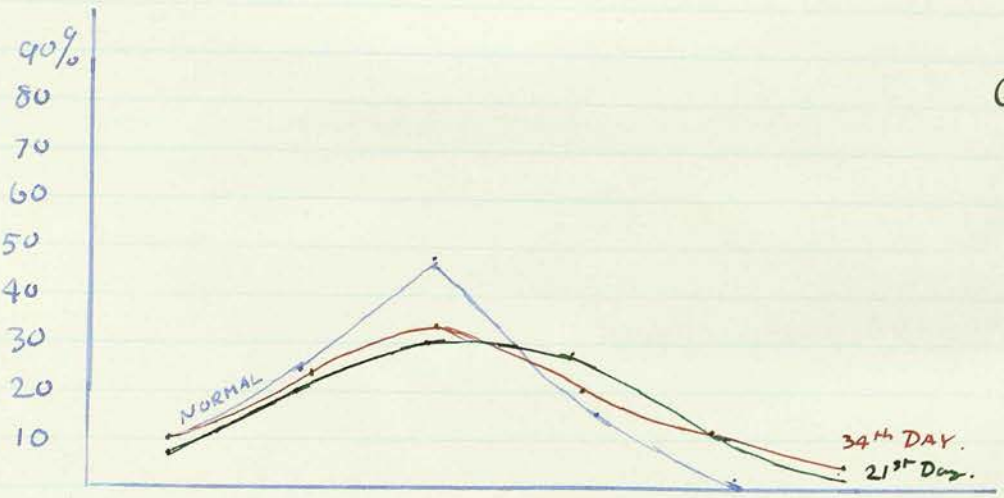
White Cells.

In pernicious anaemia one looks for a leucopenia with relative lymphocytosis, and in our cases it may be seen that such a condition was present. Thus in MacIntosh's case, the white count on admission was 4,800 with 42% Polymorphs. (neutrophils): with Mrs Proudlock, the total count was 3,800, with only 24% neutrophils.

It is not possible to draw up graphs relating these figures, because the normal total white count and neutrophil percentage vary within relatively large limits: thus the limits for the white cell count (as measured in the morning) is given as 9,000 maximum and 4,000 minimum, while the neutrophil percentage should be between 55% and 70%. Mrs. Proudlock has a total count of 3,800 with 24% of neutrophils. This is a very low percentage, and it may be that a true lymphocytosis was present. However, this is not usually seen in pernicious anaemia, and it is just possible to correlate these figures with relative, rather than true, lymphocytosis by mathematical calculation. Certainly in the other cases the fall in the total number of white cells can be explained by a diminution in the number of polymorphs alone. It is seen, too, that as the patient's condition improves, the differential white count approaches the normal limits, although it must be admitted that in some of the cases the rise of the total number of white cells does not exactly correspond. This may be explained away by the fact that the limits of normality are fairly wide

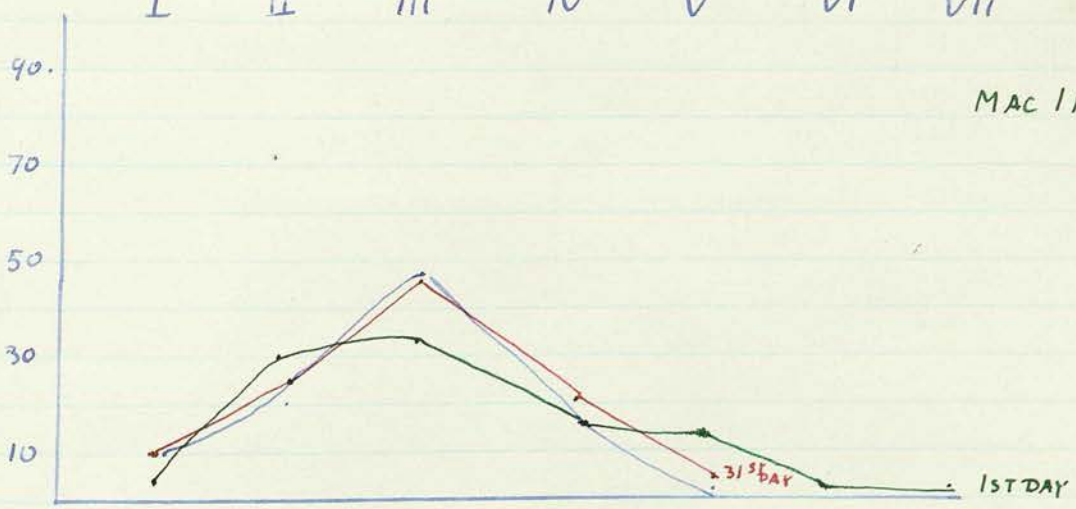
The Arneth counts, too, are interesting, in that a definite tendency towards a shift to the right is seen. Unfortunately the series is not complete, because the counts were not done till some time later, and many cells had faded. The following graphs may be constructed from the data recorded.

I II III IV V VI VII Lobes.



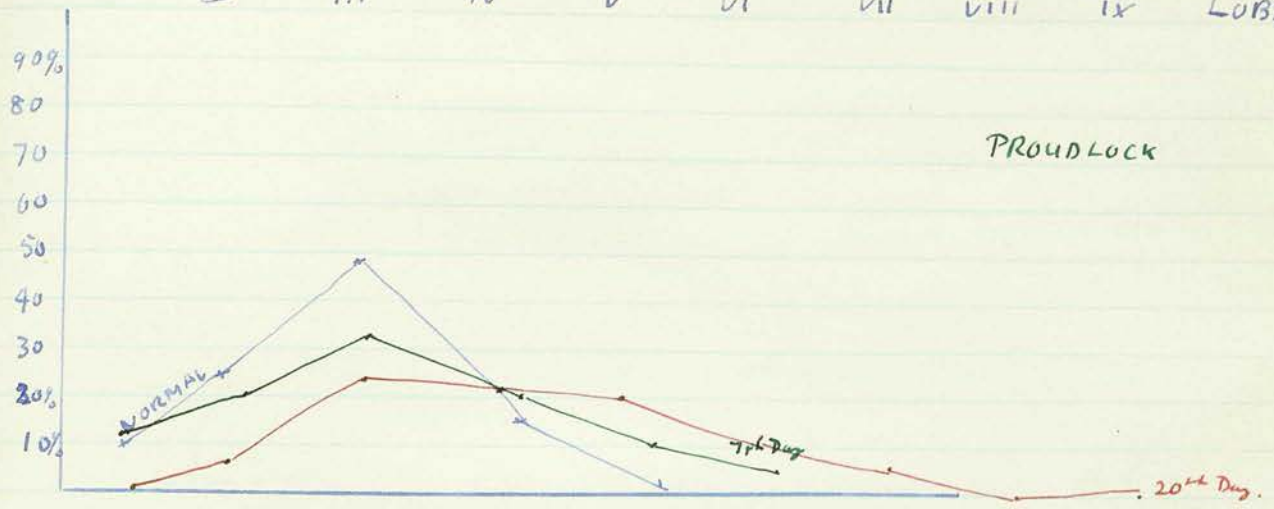
GANSON

I II III IV V VI VII

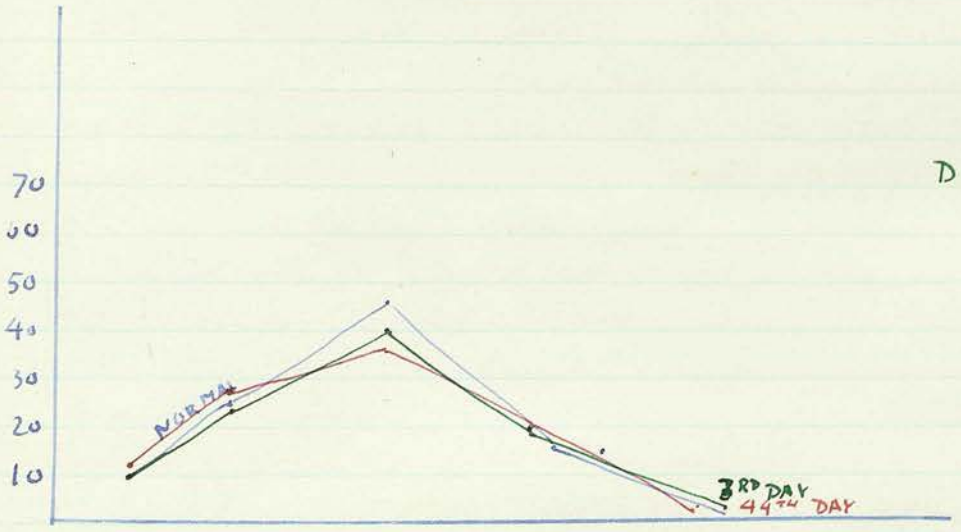


MACINTOSH.

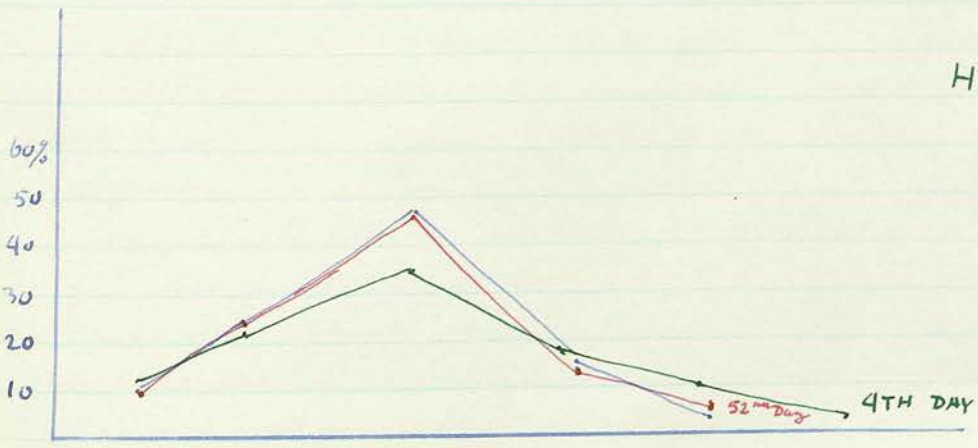
I II III IV V VI VII VIII IX LOBES.



PROUDLOCK



DUNLOP



HUTCHISON

The Arneth counts, then, show a definite tendency towards a shift to the right, becoming less marked as the condition improves. It may be noticed that in Mrs. Proudlock's case, the shift to the right was more pronounced at the 20th day, although her red cell count was improving

Our last consideration must be that of the condition found on post mortem examination of Mrs. Proudlock.

The less essential features may first be disposed of. Bronchopneumonia was present, with multiple abscess formation at the left lower lobe, and there was a pneumonic process at the corresponding lobe of the opposite side. This can easily be understood when one considers that this old woman had been lying propped up in bed for a considerable time, in a state of great weakness. The fact that a gallstone had ulcerated into the duodenum is of great pathological importance, but can hardly be considered as an essential part of the main condition. The biliary tract as a whole appears to have been in a highly pathological condition, but again this does not appear to be of very great significance from the pernicious anaemia point of view.

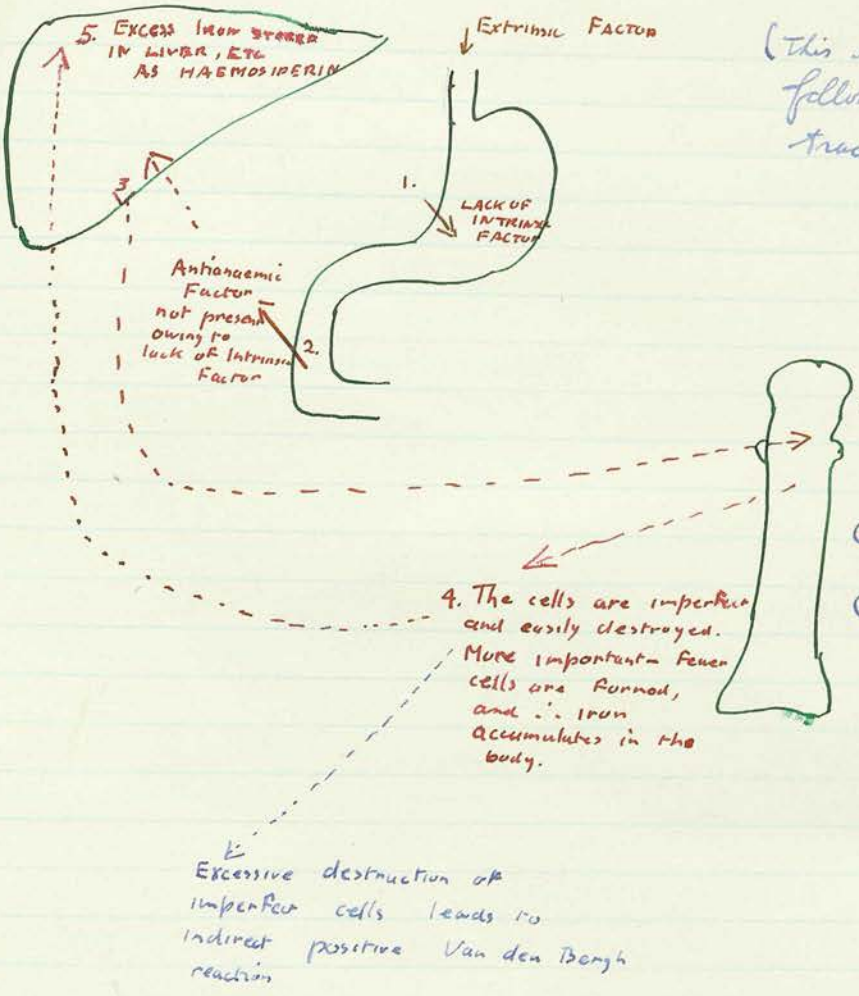
The same must be said of the patch of carcinoma present at the pylorus. If late carcinoma had been present, one might have considered it conceivable that the hyperchromic anaemia was of the type associated with such a

condition, but there again one would not expect the bluelessness to be so pronounced. It may be that the achlorhydric state of the stomach that is always associated with pernicious anaemia may have been a factor in the development of the cancer, although it must be said that a combination of carcinoma and pernicious anaemia is uncommon.

The rest of the picture fits in with the clinical diagnosis very well. There are, first of all, the changes associated with anaemia, such as fatty degeneration of the liver. Then there were the changes due to pernicious anaemia, the most important of which were seen in the bone marrow and in the liver. In the liver there was a very definite Prussian blue reaction. This reaction is, of course, not found only in pernicious anaemia, but in this case there is no doubt as to the condition present. From this reaction we know that the iron containing pigment, haemosiderin is being stored in the liver, and there was evidence of similar storage in the kidney.

The second very important finding is of intense erythroblastic reaction in the bone marrow, and the fact that islands of megaloblasts were present. This reaction was in the middle of the shaft of the femur, a place where erythroblastic tissue is usually absent.

These findings may be correlated with the clinical picture thus.



The above is not intended to represent all the changes that occur in pernicious anaemia, but is included to show the relationship between some of the clinical findings, and the post mortem report in Mrs. Priddle's case. From this it is easy to understand the relationship between the megaloblastic picture in the marrow, and the haemosiderosis of the liver: this is based on the more generally accepted theory, but it is true that other theories exist. The microscopic picture of the bone marrow was not purely that of a marrow packed with megaloblasts, but this is because the patient

had been under treatment with liver preparations. On the whole, this post mortem report may be considered as a most instructive document that may be used to correlate the findings of the clinical examination, not only in this one case, but in the whole group of patients.