Six Cases of Macrocytic Anaemia.

Ronald H. Girdwood.

May 1939.
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CASE A

Patient's Name: Grace Ganson (Single)
Age: 33 years
Occupation: Domestic Servant
Address: 3, Tolbooth Wynd, Leith
Recommended by: Dr. Conran, Penicuik
Date of Admission: Dec 3rd, 1937
Date of First Examination: Dec 5th, 1937
Ward: 30, R.E.

Complaint:
Tiredness - six months' duration
Breast lumps - 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 discoloration 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 8st 10lbs, whereas just before admission her weight was registered as 6st 10lbs.

From about June, 1937, the patient found that it was only with difficulty that she could carry out her duties as a domestic servant. This was because she felt very early 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 in 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 patient's 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 article 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 chill 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 nape of the neck. 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 bowel remained regular.

On the 30th of November, the patient felt so unwell 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 portion 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 at 61 - diabetes mellitus
- **Mother** - died at 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, aged 30, the fourth in the family, is anaemic.

One brother, aged 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 fingernails 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 ribs were not unduly 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 mucous 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 her friends were:

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

THE BLOOD - (Further findings given under Progress Note)

5: XII: 37.

Haemoglobin: 43%
Erythrocytes: 1,870,000
Leucocytes: 4,000
Platelets

Red cells: very few

Bleeding time: 5 minutes
Colour Index: 1.15

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

The abdomen was poorly covered, and the skin had an intense 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 for 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.

Gastrointestinal analysis was carried out by means of a fractional test meal. The findings are given on the following page.
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, but the vessel wall was not palpable.

T.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 thrill.

A well-localised apex beat was felt in the fifth space in the mid-clavicular line.

On percussion, the portion of the heart was found to be such that it may be represented by the following formula $\frac{117}{1 + \frac{4}{4}}$.

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 localized 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 localized 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 referable 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. Urine deposit. No albumen or sugar was present. A few epithelial cells were seen on microscopic examination.

NERVOUS SYSTEM.

Mental Function. 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.
Craniial 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 hemorrhages or other abnormalities were seen on ophthalmoscopic examination.

III. Both eyes moved freely in all directions. There was no diplopia or strabismus, and no nystagmus or pits.

IV. 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 accommodation 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.

VI. There was no evidence either of supranuclear or of infranuclear paralysis. The facial muscles moving freely. There was no hyperacusis, and taste as already described was not impaired.

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

On rising suddenly, the patient suffered from dizziness, and she had had dizziness for
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.
Sensory " " on the two sides.
Taw - present
Knee - brisk : more so on the right side.
Ankle - brisk : more so on the right side.
No knee or ankle clonus was present.

SENSORY FUNCTIONS.

The presence of a chill 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 sense. 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. Investigation 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. Investigation.
3. XII. 37. Weight 4 feet 11"
Weight 6 stone 10 lb.
WR negative.

4. XII. 37. Urine. Straw colour: sp gr. 1024; pH 8.5; specific activity.
6. XII. 37.
Fractional Test Meal done—see the case report.
7. XII. 37.
Fosreni Index 16.
Van den Bergh Direct Reaction negative.
Indirekt " positive.
12. XII. 37.
Urine—Pake Lemon; sp gr. 1014, acid.
mucus present.
13. XII. 37.
Weight 6 stone 13 lb.
20. XII. 37.
Weight 7 stone 4 lb.; BP 110/66
23. XII. 37.
Urine—straw colour; sp gr. 1016, acid.
mucus present.
27. XII. 37.
Weight 7 stone 1 lb.
3. I. 38.
Weight 6 stone 13 lb.
4. I. 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**


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


12. XII. 37. Jaundice less noticeable. Patient noted 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 in 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 cards being sung.

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. 1. 38. She sleeps badly and collapsed on rising in the morning. Very off her food and sobbing all day.

2. 1. 38. Even although morphine was given, the patient says she sleeps badly.

4. 1. 38. Still depressed and sleeping badly.

5. 1. 38. Patient feeling much better - has decided not to worry, and is up and about.
3. Treatment other than that directed to the fluid.


23. XII. 37.
Aspirin gr. X
Phenacetin gr. X
Caffeine gr. IV

24. XII. 37. Nepenthe m. XXX 11.15 pm.

25. XII. 37.
Aspirin gr. X
Phenacetin gr. X
Caffeine gr. IV

25. XII. 37. Nepenthe m. XXX 10.5 pm.

26. XII. 37.
Chloral Hydrate gr. XX
Sed. Bromide gr. XX 1.35 am.

28. XII. 37.
Acid Hydrochlor. 3.1 sid.

28. XII. 37.
Chloral Hydrate gr. XXX
Sed. Bromide gr. XXX 11.45 pm.

30. XII. 37.
Chloral Hydrate gr. XXX
Sed. Bromide gr. XXX 1.45 am.

31. XII. 37.
Hyoscine gr. t
Morphine gr. t

2.1. 38.
Hyoscine gr. t
Morphine gr. t 8.30 am.

2.1. 38.
Nepenthe gr. XXX - 10.5 pm.
Further Notes.
25/1/38.
Patient reported
Red cells 3,980,000
Hemoglobin 85%
Reticulocytes 1.5%
4 cc Neo Hepaton given

Further treatment to be given by patient's doctor.
### The Blood -

#### 2. Treatment Given.
- **New Hepaton.** 2cc daily
  - Reduce to every other day
  - Stop.
- 2cc
- 4cc
- 2cc

#### 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.

### Main Blood counts

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<th>Hb.</th>
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<th>Wbc.</th>
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**Different Leukocytes**

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<th>Lymphocytes</th>
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<td>41%</td>
<td>8%</td>
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<tr>
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<td>3%</td>
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<tr>
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<td>1%</td>
<td>1%</td>
<td>24%</td>
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</tr>
</tbody>
</table>
IV. Anneth 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.)

<table>
<thead>
<tr>
<th>Date</th>
<th>Lobe 1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<tbody>
<tr>
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<td>8</td>
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<td>4</td>
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<tr>
<td>26/11/37</td>
<td>8</td>
<td>19</td>
<td>36</td>
<td>22</td>
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<td></td>
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<tr>
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<tr>
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<td>32</td>
<td>20</td>
<td>12</td>
<td>4</td>
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V. Indication of relative sizes of erythrocytes

(Note: this is not an accurate representation, as explained in the notes on technique of investigation.)

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<td>3%</td>
</tr>
<tr>
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<td>2%</td>
</tr>
<tr>
<td>1/1/38</td>
<td>3%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>5/1/38</td>
<td>2%</td>
<td>1%</td>
<td>4%</td>
</tr>
</tbody>
</table>

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 13
NAME: Agnes Jack (Single)
AGE: 47 years
OCCUPATION: Waitress (Unemployed)
ADDRESS: 233, Leith Walk, Edinburgh
RECOMMENDED BY: Dr. Johnston, Dalziel Place
DATE OF ADMISSION: 15th December, 1937
DATE OF FIRST EXAMINATION: 18th December, 1937
WARD: 25, RIE

COMplaint: General Unfitness - 2 years
Papillation on extensor - 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 PALPITATION. She felt her heart beating very forcibly and rapidly; associated with this, she experienced a mild PAIN in the EPICASTRIUM. This symptom was related to the palpitation, 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 in a great deal with a feeling of 'PINS and NEEDLES' in her feet. The symptoms in her limbs have 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 palpatory, general somnitude, 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. Bonnie, 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 cafe') 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 haemorrhage.

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 intercostal tinge was present in the sclera, but only to a very mild degree.

The patient appeared equally content to sit, sit 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
Respiration 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.

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<th>Value</th>
</tr>
</thead>
<tbody>
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<tr>
<td>Erythrocytes</td>
<td>1,140,000</td>
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<tr>
<td>Leucocytes</td>
<td>3,200</td>
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<tr>
<td>Reticulocytes</td>
<td>0.4%</td>
</tr>
<tr>
<td>Colour Index</td>
<td>1.5</td>
</tr>
</tbody>
</table>

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 liver edge of the liver was palpable three finger breadths below the costal margin.

Van den Berg. Delayed Direct Reaction
Icteru Index 12

ALIMENTARY SYSTEM.

Almost a year before admission, the patient was troubled with epigastric pain. This nausea 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 no 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 muscles of the abdominal wall were 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: Jack
Ward: 25
Bed: 16/12/37

1. FRACTIONAL TEST-MEAL

- Fasting Juice: 15cc
- 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 midline. 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 Report

16.XII.37

Central 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 (15 seconds 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.

7.1.38.

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

10.1.38.

"Electrocardiogram is completely normal, rate approximately 100.

Re-breathing experiment was carried through in closed system with CO₂ absorption in soda lime. Under condition of anaemia patient developed mild precordial pain. The experiment was
discontinued and the oxygen content of expired air estimated. This was found to be approximately 99%. Simultaneous electrocardiograph record shows little or no change.

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

13/1/38. "Breathing experiment repeated. Final oxygen concentration in inspired air = 7.5 vol.%. Patient complained of precordial 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 localized chest retraction or bulging. Movement was free and equal on the two sides, and there was no localized change.
In 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 referable to this system. The kidneys were not palpable.

Urine.
15 XII 37. Was of straw colour, specific gravity 1016. Acid reaction. 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.

- **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
Mystagmus or palsy. There was no diplopia or nystagmus. The pupils were round and equal. There was no impairment of direct or consensual reaction to light, or if the reaction to accommodation.

I 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.

II There was no evidence of supranuclear or infranuclear paralysis of either nerve, and no hyperacusis.

III No auditory impairment: air conduction was better than bone conduction. There was no tinnitus or dizziness.

IV There was no dysphagia, or anesthesia of the pharynx.

V The palate moved in the midline.

VI No muscular impairment.

VII 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.

Triceps: Equal and brisk.
Superfice: Equal and brisk.
Trapezius: Equal and brisk.
Knee: Present.
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 first 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 at 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. Investigation carried out.

Gestrin Index - 12.
Height 5 ft 5½" 
Weight 8 stone 7½ lb.
Pulse Rate 95.
Respiratory Rate 20.
Electrocardiograph report - already given.
Fractional Test Meal - ""

18.12.37. Pulse Rate 85.
Respiratory Rate 20.


31.12.37. orange colour 1025 acid
+ albumen
mucus deposits

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.
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.
25.12.37  The patient is very depressed, as there have been three deaths in the Ward.
29.12.37  Patient suffering from cataract.
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 precordial 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 precordial pain.
18.1.37  Discharged to Convalescent Home.
3. Treatment.
15. XII. 37  Triple Tab qd x 9 pm
17. XII. 37  Luminal qd + 11.30 pm
              Light diet.

Vegetable carotene were given throughout when required.

4. The Blood

(a) Treatment.
16. XII. 37  Campulan 5 cc daily
31. XII. 37  5 cc every three 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.

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<th>Rbc</th>
<th>Hb</th>
<th>CI</th>
<th>Reti</th>
<th>Wbc</th>
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**Differential White Counts**

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<th>Basophils</th>
<th>Lymphocytes</th>
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<tbody>
<tr>
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<td>1%</td>
<td>35%</td>
</tr>
<tr>
<td>22/11/37</td>
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<td>0%</td>
<td>0%</td>
<td>39%</td>
</tr>
<tr>
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<td>53%</td>
<td>0%</td>
<td>0%</td>
<td>38%</td>
</tr>
<tr>
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<td>55%</td>
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<td>2%</td>
<td>35%</td>
</tr>
<tr>
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<td>36%</td>
</tr>
<tr>
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<td>6%</td>
<td>1%</td>
<td>30%</td>
</tr>
<tr>
<td>14/12/38</td>
<td>65%</td>
<td>5%</td>
<td>0%</td>
<td>24%</td>
</tr>
<tr>
<td>16/12/38</td>
<td>60%</td>
<td>6%</td>
<td>1%</td>
<td>26%</td>
</tr>
</tbody>
</table>
ON ADMISSION.

DURING TREATMENT

ON DISCHARGE
IV. Arueh 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.

<table>
<thead>
<tr>
<th>Date</th>
<th>Macrocytes</th>
<th>Microcytes</th>
<th>Polychromat.</th>
</tr>
</thead>
<tbody>
<tr>
<td>18/XII/37</td>
<td>16%</td>
<td>4%</td>
<td>11%</td>
</tr>
<tr>
<td>22/XII/37</td>
<td>12%</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>26/XII/37</td>
<td>14%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>30/XII/37</td>
<td>11%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>4/1/38</td>
<td>5%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>8/1/38</td>
<td>7%</td>
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<td>2%</td>
</tr>
<tr>
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<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>16/1/38</td>
<td>5%</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Date</th>
<th>Platelets</th>
<th>Bleeding Time</th>
</tr>
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<tbody>
<tr>
<td>20/XII/37</td>
<td>80,000</td>
<td>4 minutes</td>
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<tr>
<td>1/1/38</td>
<td></td>
<td>160,000</td>
</tr>
<tr>
<td>23/XII/37</td>
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<td></td>
</tr>
</tbody>
</table>
CASE C.
NAME: John MacIntosh (Married).
AGE: 46 years.
OCCUPATION: Policeman.
ADDRESS: c/o Wilson, 55 Restalrig Road, Edinburgh.
DATE OF ADMISSION: 29th November, 1937.
RECOMMENDED BY: Dr Butler, Charlotte Street, Leith.
DATE OF FIRST EXAMINATION: 18th December, 1937.
WARD: 31, O.I.E.

COMPLAINT.
- Bad taste in the mouth and distaste for food 6 months
- Sore tongue
- Loss of weight and tiredness
- Pain under right lower ribs
- Swelling around the eyes

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 other. The smoking of a cigarette aggravated this symptom. The unpleasant taste, loss of appetite and painful tongue were still present on admission.

Two months prior to admission, he started to feel listless and generally unwell. His bowels continued to move regularly.

Two months prior to admission,
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 ½ stone 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, aged 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 his 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 sclerae, too, had a tinge of icterus. The lips and the conjunctiva 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

HAEMOPOIEITIC SYSTEM.

The symptoms which may be referred directly to this system were:

Tiredness, Breathlessness, Giddiness.

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 Proper Note)

16. XII. 37

Haemoglobin 32% (Schli).
Erythrocytes 1,670,000.
Leucocytes 4,800.
Reticulocytes very few.
Colour Index 1.4

Neutrophiles 50%.
Eosinophiles 3%.
Lymphocytes 39%.
Monocytes 13%.

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 abdomen.
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 midline, 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, mouth, 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 and respiration was free. No peristaltic waves were visible.

On palpation, the wall was found to be rather flabby; in the left side of the abdomen, a firm tube about two inches long was felt. This appeared to be loaded colic. 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.

Upright films: at end of 19 hr., the density of the gall-bladder shadow may be regarded as being within normal limits.

15/12/37. Esophagus, stomach, and duodenum negative.
was pressed over the fundus of the gallbladder, and a deep breath elicit (Murphy's test); there was no hyperesthesia 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 dulness in the flanks or fluid thrill was detected.

On percusion of the liver, its lower margin was found to lie 1/2" 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 he was seized with acute pain under the right costal margin; this did not involve the pericardial 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.

Vessels. 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, the 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: \( \frac{11}{14} \frac{1}{2} \frac{1}{2} \frac{2}{2} \).

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 left lateral 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 abdominal-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 in both ribs, and there was no localised diminution of movement.
Vocal resonance 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. Visual percussion revealed free diaphragmatic movement.
On auscultation, breath sounds were vesicular, and there were no accompanying vocal resonance was equal and unimpaired on the two sides.

**URINARY SYSTEM**

Six weeks before admission, the patient had seen 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 loin or bladder.

The kidneys were not palpable.

**URINE**
(on admission)

Acid reaction: orange colour: no naked-eye deposit
Blood: negative: albumen negative: nitrogen - trace
Acetone: - nil: - trace: - urea - nil: - nil

Microscopic: Few amorphous urate crystals
NERVOUS SYSTEM

In June, 1937, the patient was much disturbed because his wife became 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 residual changes.
 III/IV/VI
 There was no impairment of ocular movements, and no nystagmus, piosis, or diplopia.
 Pupils were round and equal, and reacted well to light and accommodation.
 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.
Tongue was projected straight forward: 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: Present and equal
Sternocleidomastoid: Present and equal
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 abnormalities

**ENDOCRINE SYSTEM**

No abnormalities.
**Progress Notes**

1. **Investigations**
   
   2. X.11.37. WR - negative.
   4. X.11.37. X-ray of Gall Bladder region - already reported.
   7. X.11.37. Weight 12 stone 12 lb.
      
      Acid reaction: Orange: mucus deposit
      Albumen, blood and sugar negative
      No bile
      Microscopic: Amorphous crystals
   4. I.38. Weight 12 stone 1 lb.
      
      Acid reaction: Orange: mucus
      Albumen, blood and sugar negative
      No bile
      Microscopic: Few crystals: some debris.
   18. I.38. Weight 12 stone 2½ lb.
   25. I.38. Weight 12 stone 8 lb.

   *There was no pyrexial disturbance at any time.*

2. **General Progress**

   17. X.11.37. Still the same
   19. X.11.37. No change in condition.
   22. X.11.37. Patient feels a little better - is very interested in his trouble.
   25. X.11.37. Appetite improving; sleeping well.
   28. X.11.37. Patient quite bright and cheerful and anxious to talk about his illness - jaundice less marked.
   30. X.11.37. Says he feels fine. Appetite good, and sleeping well. Anxious to get up.
   2. I.38. Patient wants to get up. Jaundice practically
5.1.28. Patient says he is now alright, and was up: appetite good: jaundice disappeared.
10.1.28. Still improving.
16.1.28. Patient allound up - feels weak in legs, but otherwise fine.
20.1.28. Feels very much better than on admission. No heartless now: no subcutaneous pain and no edema of the ankles.
23.1.28. Progress still very satisfactory. No murmur.
28.1.28. Patient discharged.

3. Treatment other than that directed to the blood:

5.12.37 Luminal gr. 11 7pm
6.12.37
11.12.37
13.12.37
15.12.37
16.12.37
23.12.37
25.12.37
27.12.37
31.1.38
3.2.38

THE BLOOD

4. Further Notes - recorded with the blood curves, e.g.:

17/12/38
18/12/38
24/12/38
4/1/38
8/1/38
12/1/38
19/1/38
20/1/38

2cc Examens intravenously
2cc
2cc
2cc
2cc
2cc
5c Renamaen Forte intramuscularly
5c
5c
The blood picture:

Film on admission:

- Lymphocytes and polymorphonuclears were marked.
- Many cells were large, oval, and well filled.
- There was no purulent sanguineous: occasional megaloblasts were seen.

Main blood counts:

<table>
<thead>
<tr>
<th>Day</th>
<th>Rbc's</th>
<th>Hb</th>
<th>Cl</th>
<th>Retic</th>
<th>Wbc</th>
</tr>
</thead>
<tbody>
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<td>1-17</td>
<td>Patient not diagnosed - no counts, made.</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>18</td>
<td>1.67 (1,670,000)</td>
<td>37%</td>
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<td>Few</td>
<td>4,800</td>
</tr>
<tr>
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<td>17</td>
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<tr>
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<td>1.4</td>
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<td></td>
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<tr>
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<td>1.3</td>
<td>1.2</td>
<td>6,200</td>
</tr>
<tr>
<td>37</td>
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<td>1.2</td>
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<tr>
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<td>2.31</td>
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<td>6,200</td>
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<tr>
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<td>2.31</td>
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<td>1.2</td>
<td>6,200</td>
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<td>1.2</td>
<td>6,200</td>
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<td>72</td>
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<td>5,600</td>
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**Progress - as an out-patient**

- Haemoglobin: 90%
- Pernicious Acid: 5cc imi

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### Differential White Blood Count

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<th>Basophils</th>
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<th>Monocytes</th>
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<td>-</td>
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### Arneal Count

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### Relative Sizes of Red Blood Cells

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<tr>
<th>Date</th>
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<th>Microcytes</th>
<th>Paichilocytes</th>
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<tr>
<td>18/11/37</td>
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<td>6</td>
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<td>5</td>
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<td>13/12/37</td>
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<td>4</td>
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<tr>
<td>19/12/37</td>
<td>4</td>
<td>3</td>
<td>2</td>
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<td>4</td>
<td>0</td>
</tr>
<tr>
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<td>4</td>
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</tr>
<tr>
<td>23/12/37</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>
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.

Further Investigations
23/12/37 Platelets 217,000.
27/1/38 Platelets 280,000.
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 assisting the patient from the dispensary. According to them, the patient suffered from:

- BREATHLESSNESS  18 months.
- LOSS OF WEIGHT  12 months.
- WEAKNESS  12 months.
- EPICASTRIC 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 this 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 growing PAIN in the EPICA STRIUM 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 stage of her illness, the patient became very weak in her legs; she lived four stairs up in a tenement house, and from September to the time of her admission 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 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 she 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 with great difficulty. However, the skin was dry and melaena, and there was putting oedema of the ankles.

Temperature 97.5.
T 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 palor of the skin, lips, and conjunctiva 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.

<p>| | |</p>
<table>
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<tr>
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<tr>
<td>Leucocytes</td>
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<tr>
<td>Platelets</td>
<td>None seen</td>
</tr>
<tr>
<td>Colour Index</td>
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</table>

Polymorph
Eosinophils
Basophils
Lymphocytes
Monocytes

Film. showed marked polymorph leucocytes and amorphous. Megalocytes were numerous - a few megaloblasts were seen. Polychromasia was not very marked
One normal sign was seen: there was no evidence of purpura hemorrhagica.

**ALIMENTARY SYSTEM**

The symptoms mentioned by the daughter were:
1. A growing 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 bony 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 and moaning 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
CARDIO- VASCULAR SYSTEM

For over a year the patient suffered from breathlessness. This was worse on exertion. For about three weeks a dull pain was present over the precordium, 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.

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 - putting oedema of the ankles was present. This was not looked for at the back as it was considered unnecessary 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 midclavicular line. It was well localized, and there were no thrills.

Percussion - the portion of the heart may be given thus: 
\[
\frac{11}{34}
\]

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 precordial 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.

Movement 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. As in both cases, however, there appeared to be some impairment of resonance.

On auscultation, both sounds were found to be vesicular, except in the base posteriorly where they were broncho-vesicular in character. Rhonchi and coarse crepitation were heard anteriorly, laterally and posteriorly, especially in the lower part of the chest. Vocal resonance was not investigated.

**URINARY SYSTEM.**

No symptoms were present.
The kidneys were not palpable.

**URINE:**

 Urine colour: acid reaction up to gr 10.26. Mucus, deposits
 Albumen: no sugar: no blaze: excess uric acid
 Microscopically: few pus cells: no reds.

**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 kept 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.**

1. Retinial hemorrhages were present in the region of the optic disc in both eyes. These
There was no squint in pupils. Both eyes moved freely in all directions. The pupils were round and equal and reacted to light.

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

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

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 plantarly planar flexor.

Deep:
- Brachial — 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, but was made for blood counts, and also felt pain when the stilette
was pulled 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.
1. Investigation
27 X11 37. Urine - orange: acid reaction: mucous deposit
+ albumen: no sugar: no blood. pp 1026
Microscopic - pus cells (few) excess uric acid
No Rbc.
31 X11 37. BP 102/48

2. General Progress
26 X11 37. Admitted - seriously ill.
27 X11 37. Patient shows no change in condition, and is not taking food. She whispered that she "felt fine".
No change.
25 X11 37. No change - patient very sleepy.
24 X11 37. Taking a little food: very sleepy, and doesn't know night from day.
30 X11 37. Marked improvement. Patient still very sleepy, but anxious to know when she will get up.
4.1 38. She is still very ill, but wants home.
5.1 38. Patient urateable and wants home. Taking food better. She announced today that she had "just about had enough o' this juggling."
A tinge of colour was seen in the cheeks.
7.1 38. Patient improving but has developed a persistent irritating cough.
9.1 38. Cough worse, but patient unable to bring up any mucus.
10.1 38. Patient very ill, with temperature of 101°.
11.1 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 summarize, 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:

Veralin, gr. V
Medinal, gr. V

H. i. Omnipan, gr. to - gr. t.

In addition, the following were given:

26. XII. 37. Chloro Ephedrine 37
12.1.38. Thyroid gr. 1 14.1.38.
15.1.38. Cocaine 1 cc at 7 am

1 pm
3 pm
11 pm.

H. i. Strychnia, gr. to as 11 am
7 pm
3 am.

18.1.38.

Soap and water enemas were given at frequent intervals.
4. **The Blood**

(a) **Treatment**

- 26.11.37: Percocet 4cc im.
- 27.11.37: Percocet 4cc im.
- 10.1.38: Percocet 4cc im.
- 17.1.38: Percocet 4cc im.

(b) **The Blood Picture**

I. **Film on Admission**

This showed marked polychromotysis and anisocytosis. Megablasts were numerous and there was polychromatophilia. The smaller cells were not well filled. Megablasts were present but not numerous. One normoblast was seen.

II. **Main Blood Counts**

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<th>Cl</th>
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<td>27° Dec</td>
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<tr>
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<td>84</td>
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<td>Rbc</td>
<td>Hb</td>
<td>CI</td>
<td>Ratio</td>
<td>Wbc</td>
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**II** Differential White Count:

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<th>Basophils</th>
<th>Lymphocytes</th>
<th>Monocytes</th>
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<td>66%</td>
<td>10%</td>
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<tr>
<td>1/1/38</td>
<td>35%</td>
<td>53%</td>
<td>12%</td>
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<td></td>
</tr>
<tr>
<td>5/1/38</td>
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<td>65%</td>
<td>1%</td>
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<tr>
<td>10/1/38</td>
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<td>59%</td>
<td>3%</td>
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<td>78%</td>
<td>20%</td>
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</table>

**IV** Arneath Count:

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

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<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
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<td>22</td>
<td>20</td>
<td>12</td>
<td>4</td>
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**V** Indication of relative size of Red Cells:

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<tr>
<th>Date</th>
<th>Macrocytes</th>
<th>Normocytes</th>
<th>Microcytes</th>
<th>Porphoblasts</th>
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<tr>
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<td>12%</td>
<td>8%</td>
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<td>19%</td>
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<td>10/1/38</td>
<td>16%</td>
<td>5%</td>
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<tr>
<td>14/1/38</td>
<td>12%</td>
<td>4%</td>
<td>2%</td>
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</tbody>
</table>

**VI** Special cells:

28/12/37 - A search for the megakaryocyte
type of macropolyocyte revealed the presence of the 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 Macrophage

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 jaundice.

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 knees. 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 thirst - heart.


Appearance of severe anaemia.
Slight dilatation of both ventricles.
Coronary vessels - were not underly atheromatous for the age of the patient.
Aorta - was the rest of moderate atheromatous change.

RESPIRATORY
Darynx, trachea, and Bronchi:
...contain 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 rest of emphysema. The lower lobe showed widespread patchy consolidation and softening and multiple aloes 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 - no extension 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 x 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, the body was found to be a cholesteric substance around which a foetal 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 bili 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 fuscous material as well as considerable numbers of pigment stones varying from grains of sand up to 1 cm in diameter. The common bile duct and gall bladder likewise contained gallstones of somewhat larger size.

Spleen. Slightly congested. Weighed under 300 gm. It was firm in consistency, and on section, deep red, 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.

Peleus, 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: Mucosa from the stomach wall has the structure of a carcinoma, and infiltration through the muscle coat is present in the section.
Case E

Name: Catherine Dunlop - Single

Age: 58

Occupation: Cook

Address: St. Margaret's, Loanhead

Rel. 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 foodstuffs 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 lightly breathing 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. McBride. 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 giddiness or noises in the ear, 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 'rheumaticy' 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 1935, 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 these family members 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 at 82 - old age.
- **Mother**: died at 54 - pneumonia.
STATE ON EXAMINATION.

The patient was of average intelligence.
She was well developed and quite well nourished.
There was very distant 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 97.9°
Respiration 20
Pulse Rate 65
B. P. 126/76
W. R. negative
Height 5 feet 4½"
Weight 145 lbs.

HAEMOPOETIC SYSTEM.

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

Waller 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 spleen 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 3,726,000.
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 amicrocytes, 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 hyper.
ALIMENTARY SYSTEM.

1. The symptoms, already described, were as follows. For over three months, less 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 fat. 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 color than usual, and that just before admission the motion 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 external tinge was present in the mucous membranes. 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 symometry 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 epulping 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 follow.

**CARDIO-VASCULAR SYSTEM.**

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

Arteries
Pulse Rate 65
BP \(126/76\).

There was no abnormality of cardiac rhythm; the pulse wave rise was with normal sharpness, pulling 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 position of the heart on percussion was as follows:

\[ \frac{1}{3} \]

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

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2 1/2 hours).

---

One Hour Fraction.

Free HCl.

Active HCl.

Total Chloride: 14

2. FÆCES.
the wounds were closed, and of normal intensity

RESPIRATORY SYSTEM.
There was no cough or expectoration at any point. 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. Tidal percussion 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 present.
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 Movement of the eyes were unimpaired.

IV There was no nystagmus, ptosis, or diplia. The pupils were circular and equal, and reacted at once to light and accommodation.

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.

VI There was no impairment of muscular movement, and no hyperacusis.

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

VIII There was no anaesthesia of the pharynx and no dysphagia.
The palate moved in the median.
No muscular abnormality
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.

Deep.

- Biceps: Present and equal
- Triceps: Present and equal
- Supinator: Could not be elicited.
- Knee: Present and equal but sluggish.
- Ankle: Present and equal.
- Apogee: No impairment.
There was no clonus.

SENSORY FUNCTIONS.
The patient's 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 color, there was no abnormality.

**ENDOCRINE SYSTEM**

No abnormality.

**LOCOMOTOR SYSTEM**

No abnormality.
Progress Notes

1. Investigations

14. XII. '37  BP 126/76
20. XII. '37  Van den Bergh  Direct Reaction
21. XII. '37  Weak
22. XII. '37  Recti Index 27
28. XII. '37  Urine
24. XII. '37  Blood WR  normal

Weight 9st 5½ lb.
Weight 9st 5 lb.
Weight 9st 5½ lb.

2. 1. '38  BP 126/80
3. 1. '38  Recti Index 12

Urine

Semen: alkaline. sp. gr. 1.015.
No albumen, sugar or bile. no excess urobilin.
Barium meal.

4. 1. '38  Weight 9st 6 lb.
5. 1. '38  BP 122/78
11. 1. '38  Weight 9st 5 lb.
15. 1. '38  9st 6½ lb.
23. 1. '38  BP 112/74
2. 2. '38  Urine

Semen: weak reaction. sp. gr. 1020.
No albumen, sugar, bile, no excess urobilin.
Nuclear deposit. Debris and mucus seen on microscopic examination.

Weight 9st 6 lb.

1. 2. '38  Fractional Feeding Meal

4. 2. '38  BP 100/66
8. 2. '38  Weight 9st 8½ lb.
15.2.38  Weight 9st. 9lb.
16.2.38  Throat swab.

The specimen contained Strep. pyogenes 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 65, and the respiration rate between 20 and 22.

On the 15th February, lowering the temperature rose thus:

15.2.38  Temp. 100°
         Pulse 78
         Resp. 24

16.2.38  Temperature 97.8

17.2.38  Temperature 97.2

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.
13.1.38. 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. Today she developed a cold in the head and her temperature rose slightly.
18.2.38. Cold now disappeared - patient discharged.

3. Treatment given.
15.2.38. Dover's Powder grt at 8 pm.
16.2.38. Dover's Powder grt at 7 pm.
FURTHER PROGRESS.
Rbc. 4,240,000
Hb. 75%
Wbc. 5,200
Weight (with clothes on) 10 st. 2 lb.
5 cc Pernasenon given.
25/3/38. Weight 10 st. 4 lb
5 cc Pernasenon given.

3/4/38. Readmitted. Jaundice has become deeper. The complaints 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

Common chloride gr \( \frac{XV}{X} \)
Mandelur acid g \( \frac{XLV}{XX} \) t.d. stopped 13/4/38

11/4/38. Lister's Index 54
13/4/38 Glucose drip set up.
(atc est, ete gxx \( \frac{XX}{XX} \) 4 hrs
This Mycogerm n X) stopped 14/4/38.

No liver injection given during the week.

15/4/38 OPERATION.
Revealed a grossly discolored liver, small and contracted, and markedly nodular, suggestive of a cirrhotic condition, although the presence of carcinoma
could not be excluded. No evidence of obstruction 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 gall-bladder region, and between the shoulders.

Weight 9st. 1lb.

Keeps comfortable by nephrite in RX 503.

13/5/38.

"Alloued up. Able to walk about the ward. Feels much better, but the prognoz 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 - Cirrhosis of liver.
4. **The Blood**

   **Treatment.**

   24/12/37. *Penicillin forte* 5 ce i.m.
   30/12/37. "  " 5 ce
   6/1/38. "  " 5 ce
   13/1/38. "  " 5 ce
   20/1/38. "  " 5 ce
   27/1/38. "  " 5 ce
   3/2/38. "  " 5 ce
   9/2/38. "  " 5 ce
   17/2/38. "  " 5 ce

   22/1/38. *Ferri et Ammon lft* gr. XXX 10 id

5. **The Blood Picture**

I. **Film on admission.**

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

II. **Main Blood Counts.**

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*Case not diagnosed as P. A before this.*

24th Dec. Unfortunately no urine had been made at this time.
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### Differential White Count

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V. Indication of Relative size of erythrocytes.

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

VI. Special Cells.

No nucleated red cells were seen.

VII. Other Investigations

- 29/11/37: Fragility Normal
- 4/1/38: Bleeding time 4½ minutes
- 15/1/38: Platelets 430,000
Case F

Name  Mrs. Jean Hutchinson
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 precordial 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 tincture was prescribed. Gradually the patient's condition became worse: she felt easily tired; her ruddy 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. Much exertion gave her severe palpitation, 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, she
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 a tenderness 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 dulness 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 this was oedema of the legs for several years.

**SOCIAL HISTORY.**

The patient lived in a house on the sea shore. She got plenty of fresh air and good food. She did not smoke, and took no alcohol, and had plenty of time for outdoor 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, aged 65, of pneumonia.

2 sisters: one alive and well. The other died at 59 of pneumonia.

Anemia - 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 up or lying down in bed. She was not too depressed by her illness, and appeared exhausted.

The face was pale and had a tinge of jaundice. The lips and conjunctiva of the lower eyelids were pale. On the cheek, the spider-like lines of veins were seen...
under the pale yellow skin, suggesting that the patient had one had very cheeks. Oedema was present in both lower limbs, but was associated with varicose veins.

Temperature 97°

Pulse 92

Respirations 22

Weight 8st. 10lbs.

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 the 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. There 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 six weeks before admission, she had an illness that was diagnosed as influenza, and vomiting occurred 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 centrum. 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 Hutchinson
Ward
Bed

1. FRACTIONAL TEST-MEAL.

Date: 27/12/37

Fasting Juice.

Volume: 104

Mucus
Bile
Blood
Starch

100 (-364)
90 (-327)
80 (-292)
70 (-255)
60 (-219)
50 (-182)
40 (-146)
30 (-109)
20 (-073)
10 (-038)

\[ \frac{N}{10} \text{NaOH (9.6 HCl)} \]

\[ \frac{N}{10} \text{HCl} \]

One Hour Fraction.
Free HCl.
Active HCl.
Total Chloride.

The shaded area represents the limits for free HCl. in 90% of normal people, and average rate of emptying (2-2.5 hours).

represents free HCl.
represents total acidity.

2. FÆCES.
Faces - 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 precordial 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.

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

Aortic: 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

\[
\frac{1}{11/3}\text{.}
\]

On auscultation, blurring systolic murmurs were heard in all areas and in the neck. These were most intense in the mediastinal and pulmonary areas, and less intense in the costal 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 voice 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 total 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
private urinai, that disappeared six weeks
before admission. Diurnal and nocturnal
frequency of micturition was present for many
years.

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

URINE

Mucus, Deposit: No albumin or sugar,
and no traces of uric acid.
Microscopic: Phosphate.

REPRODUCTIVE SYSTEM.

Menopause at 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.
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 accommodation.

Motor. There was no impairment of the power of the muscles of the temporal muscles.

Sensation. The corneal reflexes were present. There was no impairment of sensation over the area supplied by this nerve.

No impairment of movement of the facial muscles; no hyperacusis.

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.

There was no hypophagia or pharyngeal anesthesia.

The palate moved in the midline.

No impairment of muscles supplied.

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 change.
REFLEXES.
Superficial. The conjunctival, palatal, and abdominal reflexes were present. The plantar reflexes were plantar flexor.
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 headache.

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

No vasomotor or trophic disturbances.

LOCOMOTOR SYSTEM AND INTEGUMENTARY SYSTEM
An eczematous type was present in the skin. In both legs, edema of the non-pitting type was present, associated with varicosity of the superficial veins on the medial side 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. Investigation.

27/12/37. Test Meal.
BP 122/56.
6/1/38. Facial Benignes - weak +ve.
Microscopic: phosphates.
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.

12/2/38 " 98.2° 80 22.
13/2/38 " 97.4° 86 20.
14/2/38 " 97° 78 20.

2. General Progress.

27/1/37. Patient still depressed, and anxious to know when treatment will start.
28/1/37. Appetite good and sleeping fairly well.
31/1/37. 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. Gastric and systolic murmurs still present. Our 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. Gastric now slight.
5/1/38. Feels very well, but legs painful, and upsetting her sleep.
20/1/38. Gastricine now absent.
23/1/38. Lungs murmur 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.
16/2/38. She has now recovered. allowed up.
19/2/38. Patient discharged.

3. Treatment
25/12/38. Alcein Pill
26/12/38. St W Cream
30/12/38. Phenol pill
31/12/38. St W Cream
1/1/38. Luminal gr 1 orally
2/1/38. Luminal gr 1 orally
St and W Cream
Alcein Pill
4/1/38. Alcein Pill
7/1/38. Alcein Pill
8/1/38. Petroglasin 3 1/2 ml
19/1/38. Legs combed with wool and supported.
The Blood

- Treatment:
  1/1/38:  Binaemon tablets - 4 tid.
  24/1/38:  stopped
  18/1/38:  2cc anaemia
  25/1/38:  2cc
  1/2/38:  2cc
  8/2/38:  2cc
  15/2/38:  2cc

The Blood Picture.

- Film on admission:
  Showing anisocytes, pochilocytes, and a very few cells showed polychromasia. There were no nucleated red cells to be seen.

- Main blood counts:

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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.

Film

These were stained Leishmann

Blood counts were always made as 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.

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, Panochromatic cut film — exposure
about 15 seconds. The somewhat crude apparatus was used thus:

![Diagram of apparatus with labeled parts: Source of Light (60 watt pearl bulb), Oil Immersion Lens, Blood Film, Green Filter, Film.]

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, under a large cells with the eye, comparing the slide against a normal blood film.
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 as suffering from carcinoma of the 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 connection, 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 systematically 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 summarised 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...
Blood loss was developed 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, spore, severe皮革 or enteric anaemia. The case was therefore one of pernicious anaemia. But 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 percent 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. Pardoe) 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 woman. 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. Hutchinson had a sister who died of pernicious anaemia. Whether
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 than 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.

and

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 nucleoside 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 "healing 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 unwell,” “faint and breathless,” or “loss of appetite” may be read. The duration of symptoms and the degree of anaemia may be compared thus:

Grace Gerson: Duration 6 months; RBC’s on admission 1,870,000.
Agnes Sack: 2 years: 1,140,000.
John MacIntosh: 6 months: 1,670,000.
Mrs. Prueckl: 18 months: 840,000.
Mrs. Dunlop: 4 months: 3,720,000.
Mrs. Hutchinson: 2 years: 2,420,000.

There, 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 anaemia, 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 foodstuff, the only one that live on three or four of the patients mentioned specifically being tea. Lingual symptoms, too, figured prominently in some cases; there will be referred to again, but it may be noted that two patients had rather severe lingual symptoms: one patient had right "poppyness" 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 limb for about a year, with a feeling of "pins and needles", some loss of sensation, and also intermittent claudication. Mrs. Bouldock 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 corneal 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 weakness in the patient. No useful purpose would be served by discussing how long it was before such signs were noticed in each case, as such change are not noticed by those who see a person from day to day. Whereas a friend who returns 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 less 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 was 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 nine patients. Agera 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 localizing symptoms occurring at a time when a person is becoming older and a less fit, and characterized by spontaneous periods of remission 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 done 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 such cases 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 focused 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. Brandlock: 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 A.I.E. by her doctor as a case of possible cardiac failure. The doctor was not satisfied as to this being an accurate diagnosis.

Mrs. Hutchison: was considered by her doctor for two years to be a case of osteoarthritis due to early cardiac failure.

Now that the true condition present is recognised, none 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 Mrs. Dunlop is less pale and more jaundiced. The patients are rather thin, but, except in the case of Mrs. Poullock, there is no emaciation. Mrs. Poullock, however, had been eating practically no food, so that wasting was inevitable. In this patient, no oedema of the ankles was present. Mrs. Hutchins had noticed this for a few days, but no swelling was found on examination. Mrs. Hutchins had oedema, but this was associated with varicose veins. No patient showed subcutaneous haemorrhages. All except Mrs. 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. Poullock, 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 rapid,
the blood pressure and temperature to be rather low, and the respirations to be of anything, rather quick. We ought, perhaps, to consider near 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 any consideration of the alimentary 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 none of them first noticed a desire for tea. Vomiting was not a prominent feature in any, although Grace Gannon and Mrs. Hutchinson vomited in two or three occasions. As one would expect, none suffered from acid Flatulences, but several complained of Flatulence or a feeling of weight in the epigastrium. The fact that Grace Gannon 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 anemia 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 been, associated with this there was Jaundice and possibly some darkening of the urine. This would suggest that she had jaundice of the Catarchel 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 later, 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 Yarrow had a constant chill 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.

MacNutt 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 impact of a stone in the cystic duct: as there was no jaundice with this pain it could not have been a stone clicking 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. Proudlack, too, had a growing epigastric pain.

The next consideration is the very important one of the state of the tongue. It is said that the tongue in pernicious anemia 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 referable to the tongue on both. For clarity the cases may be listed as follows:

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

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

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

Proudlack: No signs or symptoms.

Dunkin: 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 glossitis when admitted although Gane Gannon may have had it as 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 Miss Inish.

We may take this opportunity to dispose of the matter of Miss Dunlop’s jaundice.

To summarize what has been mentioned several times already, it may be recalled that
1. The first symptoms of jaundice were 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 motion were not paler 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 urobilin index was 27. The Van den Berghe test gave a direct reaction weakly positive.
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 Beryt reaction would fit in too, because of obstruction of the bile ducts by the proliferating connective tissue within the liver.

These must be considered, 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 injection, but possibly there was a cutaneous 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 until any definite certainty without operative investigation revealed that there was no stone, and so the surgeon was able to tell the physician that there was present cancer of the liver.

The next question that arises is whether...
pernicious anaemia was present as well, and if not, whether another explanation could 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 - e.g. on the fourth day in hospital the red cell count was 3,720,000; on the 33rd day 3,780,000; and the 45th day 3,100,000, that the blood film never showed very definite megaloblasts; and that although the test meal showed absence of free HCl, histamine was not injected, so the test was worthless. 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 whom could have 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 recalled 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...
Reading. There are as follows.

1. Acholic 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 vein. - Also out of the question.

4. Splenomegaly with peri-ellipsoidal haemorrhage and nodular addisoni. - 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 haemorrhage 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 in 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 photograph of typical fields show that the tendency to macrocytosis is not marked. It might be argued too, that the marked jaundice indicates that we are dealing with a case of bilary 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 leukocyte 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. Periculoc-centro-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 hyper trophy (Hannot's) cirrhosis might at first sight be thought of in the diagnosis. In such a condition, jaundice is a marked feature and anaemia is absent until late. But Hannot's cirrhosis is a rare disease, and its 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
Hannot's carbonicis 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 claim the more likely ones. As already explained, enlargement of the spleen is not uncommon either in pernicious anaemia or in hepatic carbonis, so we need no longer seek for further explanation of this physical sign. The outstanding fact that remains is that the liver is carbonic, and anaemia is present. Now it is very common for a macrocytic anaemia to accompany carbonis, possibly due mainly to the accompanying deficiency of free hydrochloric acid and leading to defective absorption of iron. We have already considered the possibility of Miss Dunlop having not a megaloblastic anaemia as was at first suspected, but rather a macrocytic 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 carbonis, 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 carbonis should not suffer from the more common type of hypercholestemic macrocytic anaemia due to lack of secretion...
The intrinsic factor, and it might be that such a patient would more likely to have deficiency of such secretion in a similar way to her deficient secretion of hydrochloric acid.

To summarize, therefore, it may be said that, although there appears at first sight to be some doubt as to Miss Dunlop's final 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 much favourable results from liver therapy as in the latter: the latter's 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 Gason, Mrs. Hutchinson, and Miss Jack, 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 Jack and Mrs. Drummond both had some precordial pain which, too, may be considered due to the anaemia, as that the heart muscle was not gaining sufficient nourishment.
In all cases there was low blood pressure. There was 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 chart.
Thus we see that such haemorrhagic murmurs tend to be very inconstant in regards to 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 systemic murmurs ceased to be heard.

Jack: Red cells 3,490,000 Haemoglobin 11%
Max Intest: 3,520,000 80%
Hutchinson: 2,990,000 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 discussed in a few words. We have seen that in all cases except that of Mrs. Broadbend, the findings were entirely negative. In her case the signs at the bases suggested hyperaemic congestion or hypertensive 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.
On examination of the urine one expects to find excess of urobilin in a severe case, and we see that such was the case in some of the patients. Otherwise there is nothing to note in the urinary system.

Examination of the nervous systems showed that in most of our 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 foot. 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 ventricular alone, 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 unreasonable to look for evidence of pyramidal tract involvement. It 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 posterior columns were involved one would look for ataxia due to loss of sense of position. This we have seen, was not present.

Fasciculus gracilis and cuneatus
Posterior \ Ganglia Medullares
Sensory tactile sense

Cranial Pyramidal Tract
Dorsal Spino-Cerebellar Tract
Ventral Spino-Cerebellar Tract
Lateral Spino-thalamic Tract
Pain
Heat and Cold
Sensate tactile Sense

If, then, the symptoms are to be regarded as being due to cord lesions, then these must be situated in stenosis 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
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 ataxia; moreover, the loss of vibration sense was of the 'stocking,' type of distribution, a fact 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. Crosslock's 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
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 summarized 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 paresthesia.

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 atrophy 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 as he has loss of knee and ankle jerks, which is explained by posterior column involvement.

[Sketch of brain with shaded areas in pencil]
In acute combined degeneration, loss of reflexes is indeed due to such a condition, 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 neuropathy. If it were due to cord pathology, then one might expect to find that change had occurred in the lateral columns too. But we see here that we have no evidence of such change - the plantar responses were plantar flexion - 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 any marked change in the posterior columns.

It may therefore be said that we have absolutely no evidence of posterior 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 neuropathy, 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 such explanation is indeed the correct one.

The last consideration as regards the nervous system is that of the mental condition of the patient. A word or two must suffice - Mrs. O'Neill had been in a state of complete apathy - there was no special tendency in the other, except that she was 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. Anerytros and pochilocytes
3. Megalocytes
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 lymphocyte
9. A shift to the right in the leucocyte curve
10. Thrombocytopenia, with large platelets
11. The presence of macrocytocytes in the blood - i.e., unusually large polymorphs with hypersegmentation of the nucleus
12. A raised reticule 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 anerytros and pochilocytes, and the presence of polychromasia and of cells of the megalocyte type; in no case was polychromasia marked, however. Megaloblasts were seen in the case of

John Macintosh (1.67)
Mrs. Marrach (1.84)
Mrs. Jack (1.14)

They were not seen in the case of

* Denotes red cell count on admission. 1.67 = 1,670,000.
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.
MRS. PROUDLOCK

↑ PERNAEMON 4 cc imi
↑ PERNAEMON FORTE 5 cc imi
↑ THYROID gr. 1

MISS DUNLOP

↑ PERNAEMON FORTE - 5 cc imi
(NOTE: One injection had been given before this investigation began)

MRS. HUTCHISON

↑ = BINAEMON tablets 4 Hid. orally.
↑ = 2 cc ANAHAEMIN imi
MRS HUTCHISON (CONTIN.)

↑ = 2cc ANAHAEMIN ini
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% reticuloocyte response was obtained with the giving of Benaemon tablets by mouth. The results in this case (Mrs. Hutchison) were very gratifying, and this response was equalled only in the case of Mrs. Prudie, who was being given injections of Benaemon.

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 μc in diameter, and would show a shift to the right, because although an increased number of macrocytes are present, the percentage of these cells is not so large as the percentage of macrocytes. The crude cell distribution counts reveal further, that in the patient’s condition
improves, the cells approach normal dimensions, and poikilocytosis disappears.

Type of curves thus obtained (e.g. J. MacInness)

In admission

\[
\begin{array}{c|c|c}
\text{Macrocytic} & \text{Approx Normal} & \text{Macrocytic} \\
100 & 0 & 100
\end{array}
\]

In discharge

\[
\begin{array}{c|c|c}
\text{Macrocytic} & \text{Normal} & \text{Macrocytic} \\
100 & 0 & 100
\end{array}
\]

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.
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. Poulton, 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. Poulton 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 unusually 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 Amneth 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 the time later, and many cells had faded. The following graphs may be constructed from the data recorded.

**CHANSON**

![Graph 1](image1)

![Graph 2](image2)

**MAC INTOSH**
The Arnold Curve. Then, show a definite tendency towards a shift to the right, becoming less marked as the condition improves. As may be noticed that in Mrs. Brown'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. Pellett. 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 pain 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 blueness 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 erythropoietic 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 erythropoietic tissue is normally absent.

These findings may be correlated with the clinical picture thus.
had been under treatment with liver preparations. In 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.