I have to thank Professor W. T. Ritchie for the permission of writing these cases.

A series of cases on "Diseases of the Blood" written for the "Wightman Prize" June 1934.

Arrangement:

1. Case of "Pernicious Anaemia" (severe) ............ Page 1.

2. Case of "Subacute Combined Degeneration of the cord" and Pernicious Anaemia ............ " 10.

3. Case of "Pernicious Anaemia" (mild) ............ " 19.
   Discussion .............................................................. " 24.


5. Case of "Myeloid Leukaemia" ......................... " 36.

6. Case of "Lymphatic Leukaemia" ...................... " 46.
   Discussion
CASE I.

Name...Elizabeth Dippie.

Age. 52.

Admitted. 30th September 1933.

Discharged. 30th November 1933.

Complaint. 1. General weakness and extreme breathlessness.
2. Vomiting, flatulence and constipation.

History. During the last two months patient has not been feeling at all well. She felt weak and totally unable to carry out her household duties. This was accompanied by attacks of breathlessness on the slightest exertion. About a month ago, patient started vomiting a great deal, the vomit being a white frothy material. The vomiting was accompanied by a burning sensation in the chest, as well as a sour taste in the back of the throat. During this period too, patient was very greatly troubled with constipation and severe catching pains across the upper border of the abdomen, which did not bear any relation to the taking of food.

Previous History: Patient has not felt her usual self since her menopause in 1928. She has been of poor colour for several years. Insiduously she grew weaker and weaker, and when she later became breathless on the slightest exertion, she attended the Thistle Street Dispensary for some time, but her condition did not improve.

April 12, 1932, patient was taken to the Royal Infirmary, Edinburgh.

She was treated with Intra Venous injections of one of the new liver preparations for 10 days without any evident improvement.
Then put on to ventriculin with excellent results. Patient discharged from Royal Infirmary on 10th June 1932, and recommended to have 1 phial ventriculin daily. On admission into the Eastern General Hospital, patient was still on the ventriculin treatment.

**Family History:** Patient lives comfortably, and her habits are perfectly normal.

**Examination:** Patient admitted in an extremely debilitated condition. Breathless in the extreme and not even rest in bed seemed to give any relief. Patient so exhausted, that she became very restless during the night.

The whole surface of the body presented a lemon yellow tinge, smooth and waxy appearance. The lips and tongue seem bloodless, while patient is stout and flabby.

Mentally generally lethargic, somewhat restless and confused.

There was a marked puffyness under the eyes, as well as slight oedema of the ankles.

**Cardiovascular System:**

**Subjective phenomena.**

An uncomfortable feeling of faintness which increased with the slightest exertion, while the slightest excitement caused palpitation.

**Pulse.** 80 per minute, regular in time and force, full but soft and easily compressible, vessel wall faintly palpable. **B.P.** 120/60.

**Heart.** Apex beat is in the 5th interspace, just outside the
mid-clavicular line, faint and flabby in character with no thrill. The right border at the right of the sternal margin, and the upper border in the 2nd left intespace.

A soft blowing haemic murmer, systolic in time present in all the areas, followed by a weak second sound.

Haemopoietic System:-

The blood thin and distinctly watery, and showed a prolonged bleeding time. This was determined by pricking finger and removing blood at intervals of 30 seconds. Bleeding stopped after 15 minutes.

Haemoglobin 16%
Red Blood Cells 740,000
Colour Index 1.2

Microscopic Examination.

Films stained by (1) Jenner's solution.
(2) Giemsa.
(3) Leishman.
(4) Giemsa preceded by Jenner.

The blood film presented marked abnormalities. Anisocytosis present, but although microcytes are visible, the variation in size depended mainly on the large forms of corpuscles (Macrocytes). The average diameter of the corpuscles being distinctly greater than normal, in addition the cells also showed variation in size (poikilocytosis). Some of the red cells still retained their nuclei, while some of the cells assumed a faintly bluish colour, by taking on both the acid and the basic dye.
The differential blood count showed a slight relative lymphocytosis.

Leucocytes 6,000.
Neutrophiles 55%
Eosinophiles 1%
Monocytes 4%
Lymphocytes 40%

Blood Wasserman - Negative.

Blood gave an indirect Van den Berg reaction.

Alimentary System.

Subjective phenomena.

Appetite poor, and the taking of food accompanied by a feeling of nausea and discomfort, which was followed by prolonged vomiting.

Lips. Pale and bloodless, the secretions in the mouth scanty, while the tongue is flabby bloodless and dry.

Abdomen. Somewhat distended, with a well marked prominence in the epigastric region.

On palpation the abdominal wall found to be flaccid. The epigastrium was however definitely tender, and a well marked palpable mass about 3" in diameter found to be present.

Patient however was too ill at this stage to examine more fully the palpable mass which so closely simulated a carcinoma of the stomach.
On a later occasion when condition of patient had greatly improved, the abdomen was again carefully examined. Patient was asked to fold her arms and raise her shoulders from the bed. It was then found that the "palpable mass" was due to an epigastric hernia, as the result of divarication of the recti. The fingers was readily introduced between the recti, and the margins of the muscles distinctly felt.

The spleen not enlarged, while the lower border of the liver projected 1" below the costal margin.

Result of Test Meal.

![Graph showing results of test meal consumption.](image)

**Specimens withdrawn with great difficulty. Much mucus. Porridge visible to 3rd specimen. Then turbid fluid.**

**Total acidity low.**

**Absence of free HCl.**

**Respiratory System.**

Patient breathless, respirations rapid and shallow, but the chest movements normal and the breath sounds normal vesicular in character.
Urinary System.

Nil of note.

Nervous System.

Patient somewhat confused, and responded slow and rather incoherently to questions. She was however somewhat restless and slept very badly.

The fundusoculi of both eyes showed some congestion, but sight not impaired. The reflexes were unaffected, and there was no alteration in sensation.

Differential Diagnosis.

The diagnosis based on an accurate history, a careful clinical examination, supplemented by an adequate examination of the haemopoietic system, presented no difficulty in diagnosing this as a case of "Pernicious Anaemia".

In this case the malady was fully developed, and the appearance of patient, the peculiar waxy yellow colour, was practically diagnostic of the disease.

There are however no distinctive early signs of pernicious anaemia. Thus there is always a complaint of easy fatiguability, failing appetite, some form of digestive disturbance, weakness, palpitation and shortness of breath. Often however, there is one striking difference between pernicious anaemia, and the other forms of deficiency of red corpuscles. The latter usually are not indefinitely progressive, whereas the former intermittently becomes more severe until symptoms become so troublesome that
patient is forced to go to bed.

The disease often however has to be differentially diagnosed from Tuberculosis. Here however a careful examination of the respiratory and haemopoietic systems will establish the diagnosis beyond a doubt.

A sign of great importance is the character of the gastric juice.

The fractional Test Meal, showed an absence of free acid, while combined acid was present. The Test Meal curve simulates that of carcinoma of the stomach, which may co-exist with pernicious anaemia, owing to deficient gastric secretion. In such a case X-Ray as well as a full examination of the blood will be helpful.

In certain cases it is also necessary to exclude intestinal worms or sprue, this is done by a careful examination of the faeces.

The diagnosis of pernicious anaemia upon the typical changes in the blood, there is however considerable variation in the picture at different stages of the malady.

The essential features of the blood picture in pernicious anaemia are:-

1. The reduction in the number of red corpuscles together with decrease of haemoglobin, the former diminution being disproportionately great, so that the colour index is greater than 1.0.

2. A leucopenia with a relative lymphocytosis.

3. Reduction of blood platelets.

4. The stained red corpuscles show a large haemoglobin content, while the film shows anisocytes, poikilocytes,
polychromasia and punctate basophilia.

In summing up, the distinctive features of pernicious anaemia are the bile pigment in the serum which gives it its yellow colour, the typical blood picture and the achlorhydria, all of which serve to distinguish it from chlorosis and the other anaemias.

Aetiology.

Both sexes affected equally 85 per cent of cases over forty years of age.

The disease was first described by Combe of Edinburgh in 1822. Although incomplete, his suggestion as to the aetiology is well worthy or record:

"It is probably owing to some disorder of the digestive and assimilative organs that its characteristic symptoms have their origin".

Some thirty years later Addison published his classical account of the malady, which is now often named after him.

Treatment.

The condition of patient was such that the liver extract could not be administered by the oral route.

Patient was at once put on to campolon treatment. From the 3rd to the 11th of October patient was given 4cc of campolon intramuscularly daily.

After this the campolon was cut down to 2cc daily.

The results were phenomenal, the breathlessness and restlessness disappeared the 3rd day after commencement of treatment.
Patient now slept well, and a cheerful disposition took the place of a previous general lethargy and mental confusion.

Rapid improvement followed, and patient is now in excellent condition, she has a satisfactory count, while the blood picture is practically normal.

The accompanying graph shows the progress made.

On discharge patient was recommended to have 2cc campolan intramuscularly at weekly intervals.
CASE 2.

Name: Alice Aitchison.
Age: 43.
Admitted: 26th October 1933.
Died: 24th November 1933.

Complaint:

Patient admitted in a prostrate and semi torpid state, and extremely debilitated.

History: (obtained from relatives was as follows)

Her present history is that of a prolonged sequence of events which came on insiduously and progressively grew worse and worse.

The first noticeable feature of patient's condition was a mental strangeness. This was noticed by her friends and relatives about 4 years ago. She seemed to loose all interest in her occupation, friends and surroundings. Patient was, however, very stout, she retained a good appetite, as a matter of fact she had a special craving for delicacies. She slept well and never complained. Gradually patient became pale, which was accompanied by a feeling of langour. At this stage, the Doctor was called in. She received "Iron" treatment, and there was an improvement in her condition which lasted about 6 months.

She relapsed, however, and improvement again followed after prolonged treatment with "iron".

About 4 months ago, the old condition returned with greater vehemance than ever before.

Patient/
Patient now not only showed mental and anaemic symptoms, but she progressively lost weight, became very breathless, and developed a decided weakness in her legs. Her legs became so weak that she could climb the one flight of stairs, with only the greatest difficulty. She often used to complain of a numb feeling in her hands and feet.

She vomited periodically while nausea and a sore tongue were common features. It was at this stage that patient had a very severe attack of diarrhoea, as well as acute cramp-like pains across the stomach.

For about a month prior to admission patient remained in bed for the greater part of the day, and often complained about her hands and feet being very cold.

Three weeks prior to admission she became bed-ridden, and it was then noticed that she could not walk. Soon patient became doubly incontinent and at this stage the relatives noticed that she had developed extensive bed sores.

On the evening of removal, patient did not seem to recognise anything not even her parents.

Previous History:

Patient always enjoyed excellent health, she lived comfortably and her habits were perfectly normal.

Examination:

Patient was in a state of feeble delirium, lethargy and complacency, and co-operation with patient totally inadequate.

Patient/
Patient was pale, the surface of the body blanched and smooth, while her lips seemed bloodless.

There was definite signs of emaciation. The legs were, however, oedematous, with extensive bed sores over the buttock and sacrum and the odour unbearable.

Debilitated in the extreme, with paroxysms of severe breathlessness.

Cardio vascular System:

Pulse: 135 beats per minute, shready irregular in time and force, not well sustained, easily compressible, of small dimensions, vessel wall faintly palpable B.P. $100/65$.

Heart: Normal in size and shape.

A faint blowing haemic murmur present over all the areas. A faint murmur also audible over the vessels in the neck.

Haemopoietic System:

Blood pale and watery looking, with prolonged bleeding time.

There was a reduction in the number of red corpuscles together with a decrease of the haemoglobin, [the former diminution being the haemoglobin], the former diminution being disproportionately great so that colour index was greater than 1.0.

There was a slight leucocytosis with a relative lymphocytosis.

The blood film showed well marked variation in size of the cells (anisocytosis) megalocytes in particular being a prominent feature, with diminution of microcytes.
The cells also showed polychromasia, poikilocytes and punctate basophilia.

Normoblasts present although scanty.

R. B. C. 1,423,000.

Haemoglobin 36%

Colour Index 1.4

W. B. C. 11,500 Polymorphs 32%

Lymphocytes 63%

Blood Wasserman negative.

Blood gave an indirect Van den Berg reaction.

Alimentary System:

Appetite very poor and the taking of food was accompanied by cramps over the abdomen and prolonged vomiting.

Lips: Pale and bloodless, mouth dry, tongue furred and dry, teeth carious.

Abdomen: Somewhat distended, but no tenderness anywhere, and the spleen not enlarged.

Result of Test Meal

[Graph showing the results of a test meal]
Respiratory System:

Patient breathless, respirations rapid and shallow. Movements normal, no impairment of percussion note. Breath sounds normal vesicular, with a few moist sounds over the bases posteriorly.

Urinary System:

Nothing abnormal in urine, but patient doubly incontinent.

Nervous System:

1. Mentally patient was greatly confused. Response to even the simplest of questions, elicited with the greatest difficulty.

2. The fundus oculi somewhat congested.

3. Very definite weakness of both upper and lower extremities.

4. Knee and ankle jerks absent, with extensor plantar responses.

5. Complete loss of cutaneous sensibility, both to pin prick and cotton wool in both extremities. In the hands it extended to just above the wrists, while in the lower extremities to just below the knees.

6. Also loss of sensation of position, passive movement and vibration in the extremities.

7. Sphincters affected and patient doubly incontinent.

Differential Diagnosis.

The differential diagnosis, based on a history obtained from the relatives, and an accurate physical examination, particularly of the "Central Nervous Systems" and "Haemopoietic Systems"/
Systems", would lead me to diagnose this as a case of "Subacute combined Degeneration of the Cord", with a blood picture that of "Pernicious Anaemia".

The nervous manifestations, however, has to be differentially diagnosed from "Polyneuritis".

The flaccid paralysis, the absent tendon jerks, and the peripheral anaesthesia, with absence of tenderness of the muscles is a useful point of distinction. The presence of extensor plantar responses, and sphincter disturbance, clinches the diagnosis in favour of a "Subacute Combined Degeneration of the Cord".

It is, however, very difficult to decide which of the two conditions manifested itself first, the "Anaemia" or the degenerative changes in the cord. It is probable that they arose concomitantly and that the same causal factor was responsible for both.

**Treatment:**

Patient put on a light, but nourishing diet. Composed mainly of milk, orange juice, eggs, benges food and marmite.

Patient further had intra muscular injections of 2 cc of "Campolon" t.i.d.

**Progress Notes:**

Patient had a sub normal temperature, but a week before she died she developed marked rigors and died during one of these rigors.

Soon after admission there was a very definite improvement in patient's condition. Mentally she became much more responsive, and/
and her colour and general health improved greatly.

Her blood picture showed a very definite response to treatment, and at one stage she had a reticulocyte response of 11%.

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>H.b.%</th>
<th>C.I.</th>
<th>W.B.C.</th>
<th>R.cs%</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.10.33</td>
<td>1,423,000</td>
<td>35</td>
<td>1.4</td>
<td>11,500</td>
<td>2.75</td>
</tr>
<tr>
<td>1.11.33</td>
<td>1,660,000</td>
<td>40</td>
<td>1.2</td>
<td></td>
<td>7.5</td>
</tr>
<tr>
<td>4.11.33</td>
<td>2,130,000</td>
<td>44</td>
<td>1.1</td>
<td></td>
<td>9.5</td>
</tr>
<tr>
<td>11.11.33</td>
<td>2,700,000</td>
<td>48</td>
<td>.9</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>15.11.33</td>
<td>3,000,000</td>
<td>51</td>
<td>.85</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>20.11.33</td>
<td>3,200,000</td>
<td>52</td>
<td>.8</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

Eventually patient developed a very severe cystitis. The bed sores became more extensive and septic, and patient also developed a moist gangrenous condition of both big toes.

Patient at this stage developed rigors, which was accompanied by acute attacks of paroxysmal breathlessness, and died during one of these attacks.

Cause of Death:

Pernicious Anaemia, and Toxaemia from bed sores.
POST-MORTEM REPORT.

Death: 24. 11. 33.
Section: 26. 11. 33.

General State: Slightly built emaciated female subject presenting on each gluteal region a large ulcerated area measuring 5" in diameter. On the left the tuberosity of the ischium has been exposed and the origin of the biceps and semi-tendinosis partially destroyed.

Limbs: Dry gangrene of both ankle joints, left great toe and pressure sores at each heel.

Cardiovascular System: Heart small, flabby and the myocardium pale. This being particularly well marked on the inner $\frac{2}{3}$ of the wall of the left ventricle. Several pale blood clots in the right side. The first part of the aorta, near the cusps showed commencing atheromatous changes.

Alimentary System: Teeth bad, gums very pale, tongue smooth.
Stomach: Small and atrophic.
Intestine: thin walled and dilated.

Serous Membranes: Firm old adhesions in right pleural sac.

Liver: Markedly enlarged, well below costal margin, pale and yellow brown in colour.
Gall Bladder: Normal.
<table>
<thead>
<tr>
<th>Organ System</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spleen:</td>
<td>Normal in size and shape, soft friable and congested. Prussian Blue reaction absent.</td>
</tr>
<tr>
<td>Kidneys:</td>
<td>Pale, toxic and friable.</td>
</tr>
<tr>
<td>Genito-Urinary System:</td>
<td>Right ureter contained yellow pus, also bladder revealed early cystitis.</td>
</tr>
<tr>
<td>Reproductive System:</td>
<td>Uterus showed fibroid tumour 1 cm in diameter situated at fundus.</td>
</tr>
<tr>
<td>Bone Marrow:</td>
<td>Shaft of femur displayed considerable erythroblastic activity. All fat being replaced by red marrow tissue.Films made from bone marrow stained Leishman, Jenner, Jenner-Giemsa. The films showed a marked erythroblastic activity, the red cells showing evidence of active proliferation. Many of the cells being of the large nucleated type (megaloblasts). Myelocytes and lymphocytes also present, but owing to the preoccupation of the marrow with red cell formation, their members were insignificant.</td>
</tr>
<tr>
<td>Brain:</td>
<td>Not examined.</td>
</tr>
<tr>
<td>Spinal Column:</td>
<td>Portion of the thoracic part excised. The cord showed degenerative changes of the posterior and postero-lateral columns.</td>
</tr>
<tr>
<td>Summary:</td>
<td>Case of pernicious anaemia with degenerative changes in the cord.</td>
</tr>
</tbody>
</table>
CASE 3.

Name: Jessie Grossert or Conlon.
Age: 51.
Admitted: 9th November 1933.
Discharged: 16th November 1933.
Complaint:
1. General weakness.
2. Breathlessness followed by palpitation on the slightest exertion.
3. Indigestion and constipation.

History:
Patient had an uneventful history, always being in the prime of health, up to about 2 years ago. Her first complaints, however, were not very definite, she noticed she became very easily tired. Gradually but steadily the vague feeling of langour became more and more pronounced. Exertion made her breathless and this was accompanied by paroxysmal attacks of palpitation.

It was at this stage, that patient developed vague feelings of discomfort in her stomach after the taking of meals. Her appetite became poor and she became constipated, which was periodically followed by severe attacks of diarrhoea. There was however, never any history of glossitis or stomatitis.

Progressively patient became weaker, and eventually her friends told her she was jaundiced.

There was never any signs of loss of weight, and patient never confined to her bed prior to admission.
Family History:

Patient lives comfortably, has a daughter and four sons all alive and well, while in her habits she is perfectly normal.

Examination:

Patient presented a very characteristic appearance. This was so typical of her malady, that it was almost sufficient to diagnose the disease.

The face full and slightly swollen, with some puffyness under the eyes, while the skin had a peculiar waxy yellow tinge, the conjunctiva was definitely yellow, while the lips were pale.

Patient stout, with an abundance of sub cutaneous fat.

Mentally patient was somewhat dull and lethargic.

Oedema only slight, and most marked in the regions of the ankles.

Cardio Vascular System:

Pulse: 75 per minute, regular in time and force, full but flabby in character, easily compressed, vessel wall faintly palpable B.P. 120/65.

Heart: Normal in size and shape \[\text{1} \quad \text{1}\frac{1}{2}\]

Heart sounds equal and closed.

Haemopoietic System:

The blood pale and watery, with bleeding time prolonged.

Haemoglobin 31%

Red Blood Cells 1,360,000

Colour Index 1.3

White Blood cells 6,200

Polymorphs/
Polymorphs 32%
Lymphocytes
  Large 17 65%
  Small 48 48%
Eosinophiles 1%
The blood film was very distinctive. Anisocytosis definite, with the average diameter of the blood corpuscles greater than normal (megalocytes). Many of the cells showed irregularity of shape (poikilocytosis). Nucleated red blood corpuscles also present - megaloblasts. A few normoblasts and slight polychromasia.

Wasserman - negative.

Alimentary System:

Appetite poor, a feeling of discomfort after meals slight pains over epigastrium but no vomiting.

Lips pale, teeth dentures, tongue large flabby and dry but clean. The abdomen slightly distended but flabby. No tenderness on palpation while the abdominal muscles are somewhat atonic.

Spleen not enlarged, while the liver is normal in size.

Result of Test Meal:

![Graph showing acid levels](image-url)
The other systems, Respiratory, Renal and Central Nervous System showed nil of note.

Diagnosis:

The diagnosis presented practically no difficulty.

The long history, which progressively became more severe, and the typical appearance of the patient was practically diagnostic of the malady.

The typical blood picture, the absence of free hydrochloric acid with no loss of weight, clinched the diagnosis as that of "Pernicious Anaemia".

Treatment:

Patient put on a No.2 diet.

Received 2 cc Campolon daily.

Progress Notes:

Patient had a slight sub-normal temperature. The progress was rapid and uneventful, and patient was allowed out of bed after two weeks.
Progress in blood picture:

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>Hb%</th>
<th>C.I.</th>
<th>W.B.C.</th>
<th>Rcs%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.11.33</td>
<td>1,360,000</td>
<td>31</td>
<td>1.3</td>
<td>6,200</td>
<td>2.5</td>
</tr>
<tr>
<td>15.11.33</td>
<td>1,530,000</td>
<td>32</td>
<td>1.2</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>19.11.33</td>
<td>1,820,000</td>
<td>37</td>
<td>1.1</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>22.11.33</td>
<td>2,200,000</td>
<td>45</td>
<td>1</td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>25.11.33</td>
<td>2,780,000</td>
<td>51</td>
<td>.94</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>30.11.33</td>
<td>3,320,000</td>
<td>62</td>
<td>.9</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>5.12.33</td>
<td>3,870,000</td>
<td>71</td>
<td>.8</td>
<td></td>
<td>3.5</td>
</tr>
<tr>
<td>8.12.33</td>
<td>4,000,000</td>
<td>76</td>
<td>.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.12.33</td>
<td>4,230,000</td>
<td>81</td>
<td>.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.12.33</td>
<td>4,410,000</td>
<td>88</td>
<td>.99</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Reticulocytes estimated daily after the 2nd day.

The most outstanding feature about this case is the very late stage at which patient sought medical advice.
These are three cases of "Pernicious Anaemia" or "Addisonian Anaemia", showing marked differences in its manifestation.

The first case certainly was a very severe case, there were however, no complications and the patient had a perfect recovery. On her discharge, she had an almost perfectly normal blood picture. I examined her blood at monthly intervals after her discharge, my last examination being on the 12th May 1934, and found no alteration in her condition.

The second case was complicated by degenerative changes in the cord, a condition which often goes hand in hand with pernicious anaemia.

The third case a very mild case, which made a very rapid recovery.

History:

The disease was first described by Combe of Edinburgh in 1822.

Some thirty years later Addison published his classical account of the malady.

Symptomatology.

The onset of the malady is slow and insidious, but progressively becomes more severe, until patient is forced to seek medical advice.

There are definitely no distinctive early signs. A feeling of languor, which is accompanied by disturbances of the alimentary/
alimentary tract, such as glossitis, stomatitis, and digestive disturbances, are amongst the earliest complaints. Progressively the condition becomes more severe, and eventually anaemia becomes very marked.

The fully developed disease, presents a very characteristic appearance. There is generally no loss of weight. The face is usually slightly swollen, and the whole body presents a peculiar waxy yellow appearance.

Another feature of great importance, is the absence of free hydrochloric acid in the gastric juice.

The most outstanding feature, however, is the very distinctive blood picture. The final diagnosis of the disease, vesting with the full examination of the blood.

The typical blood picture being

1. The reduction of both haemoglobin and red blood corpuscles. But the latter is proportionately greater than the former giving a colour index of about 1.0.

2. Variation in size of the red corpuscles (anisocytosis). The average diameter of the red corpuscles being greater than normal (megalocytosis).

3. Polychromasia, poipilocytes, punctate basophilia, normoblasts and megaloblasts.

4. Reduction in number of platelets.

5. Leucopenia usually, with a relative lymphocytosis.

6. Bleeding time prolonged.

Treatment/
Treatment:

The modern treatment of Pernicious Anaemia with liver or liver extracts, was the outcome of the experimental work of Wipple and his co-workers in 1920 on post haemorrhagic anaemia in dogs.

In 1926 Minot and Murphy recorded cases of the successful treatment of Pernicious Anaemia, on a diet rich in liver and red meat.

The next advance was in 1928 when Cohn prepared a liver fraction which contained the essential anti-pernicious principle. Highly purified extracts are now available for intra muscular or intra venous infection.

More recently various stomach extracts have also been used with excellent results.

Etiology:

Several theories have been put forward as to the pathogenesis of Pernicious Anaemia, but the etiology is, however, still obscure.

1. Ehrlich applied the term "megaloblastic degeneration", and regarded it as one leading to imperfect blood formation. There is however, no evidence that the change is a primary one and the cause of the anaemia. In patients infected with bothriocephalus latus changes in the blood and marrow similar to those in Pernicious Anaemia occur, and recovery may take place when the paracites are got rid of. Showing that this megaloblastic change may be produced by toxic agencies.

2. Hunter again lays particular stress on the changes encountered in the alimentary system - atrophy of the gastric mucosa associated with the almost consistent absence of hydrochloric acid and pepsin from the gastric juice in pernicious anaemia.
It results, of course, in a loss of the normal antiseptic action of the gastric juice. In this way organism from the mouth may survive, and on the other hand there is also an extension of organisms from the large bowel to the stomach. In this way it is possible that some infective agent or poison may enter into circulation.

It must be borne in mind, that if the disease is due to an organism, the agent produces a toxin with action unlike that of known bacterial toxins.

3. Recently however the whole problem has been looked at from an all together different angle.

The work of Castle, of Boston, points to the presence in the gastric juice of a specific factor: In normal persons this factor reacts with another factor in the food, and this reaction is in some way connected with the formation of blood; in P.A. the gastric factor is absent. It is along these lines that the beneficial effect of Hog's stomach is explained.

Attempts have been made to isolate this intrinsic factor from normal gastric juice:- The British workers maintain that it is an enzyme like substance "haemopoietin", while the American investigators regard it as a hormone and call it "Addisin".

It is possible that both are the same substance, but in neither case has the actual principle been isolated. The extrinsic factor in the food has been said to be vitamin B2, but this has been questioned.

Pernicious Anaemia, is therefore, a deficiency disease conditioned/
conditioned by the lack of a specific intrinsic factor present in normal gastric juice. This factor is a heat labile substance, different from any digestive ferment, and its function is to interact with an extrinsic factor in the food to produce specific haemopoietic effects. The extrinsic factor appears to be vitamin B₂.

Pernicious Anaemia may occur in three ways:—

(1) Lack of intrinsic factor in stomach.

(2) Lack of extrinsic factor in diet.

(3) Failure to absorb or utilize the products of their interaction.

Certain macrocytic anaemias, such as occurring in Sprue and tropical anaemias, have been treated successfully with diets rich in vitamin B₂, which points to a lack of extrinsic factor in diet. Marmite—which is rich in vitamin B₂, has however, proved ineffective in P.A. but very effective in macrocytic anaemias.

An interesting point brought out by a German observer, is that since the great war nervous complications in P.A. has been on the increase, especially since the introduction of liver therapy.

The exact relationship between "sub-acute combined degeneration" and "pernicious anaemia" is at present far from clear.

It does not seem likely that the degenerative changes of the cord is due to the anaemia. This is shown by the absence of the necessarily relationship between degree of anaemia and the appearance of progressive nervous symptoms. Furthermore, nervous changes often manifest themselves even before obvious changes in the/
the blood. Then too treatment which will cure the P.A. conditions does not cure the nervous symptoms.

4. Seyderhelm (Frankfort-on-Main) maintains that pernicious anaemia is due to a combination of factors - chronic intoxication and a deficiency of the haemopoietic principle - and the therapeutic rational of liver is due to its vitamin B constituent.

The etiology is, however, still obscure, and once this has been definitely ascertained, prevention and cure should prove simple.
on exertion, and on occasions he bled profusely from his nose.

His stomach troubled him greatly, there always being a warm painful feeling in the region of the epigastrium, while his bowels were caustive, alternating with a frothy mucoid diarrhoea.

About a week prior to admission, he developed a rash on his legs, and his ankles became swollen, and since then patient has been confined to his bed.

**Family History:**

Patient married but lives apart. Is a heavy smoker and takes alcohol in moderation, mainly in form of spirits. Lives in a small room, which he shares with two other people, in the High Street.

**Examination:**

Patient has a pale, sallow, bloated expression, and markedly breathless. Mentally slow and generally apathetic, very obviously weak and tired, but not markedly wasted.

The eyes lustreless, the conjunctiva pale, with sub conjunctival ecchymosis of the inner aspect of the right eye.

**Alimentary System:**

**Subjective Phenomena:**

Appetite poor, warm burning pain across the upper border of the abdomen, bowels caustive alternating with diarrhoea.

Lips pale, while the tongue is large, flabby, thickly coated with small ulcerations on the sides.

Teeth filthy and carious, while the gums are swollen and spongy.
spongy. The spongyness is most marked round the teeth, which are carious. The gums bleed easily, while the teeth are loose. Patient has great difficulty in chewing his food, and his breath is foetid.

The abdomen showed some wasting, with a little tenderness across the epigastric region.

The stool - negative for blood.

Muscular and Integumentary System:

The muscles somewhat atonic, with definite signs of wasting.

The skin dry and pale, while petechiae seen over various areas stood out in marked contrast.

The medial aspect over the R. tibia had an extensive area of discolouration as if bruised. This was surrounded by numerous discrete reddish brown spots not raised above the skin surface.

The entire left leg was covered with small petechial haemorrhages. These petechiae were present round the hair follicles and were not raised above the skin surface.

Both ankles slightly swollen and painful.

Cardiovascular System:

Pulse: 70 per minute, regular in time and force, well sustained and vessel wall slightly thickened but not modular B.P. 130/80.

Heart: Normal in size and shape. Sounds equal and closed in all the areas.

Haemopoietic System:

The/
The bleeding time normal.

Red Blood cells 3,400,000
Haemoglobin 52%
Colour Index .75
White Blood Cells 9,500
Polymorphs 68%
Lymphocytes 26
Other Forms 4%
Eosinophiles 2%

Blood Film:

The red blood cells small and stained lightly. Some of the cells showed irregularity in shape (poikilocytes) while others stained a faintly bluish tinge (polychromasia) - these cells were however, not very numerous. A few punctate basophilia also present, while the polymorphs were the dominating type of the white corpuscles.

Blood Wasserman - negative.

Respiratory System:

Subjective Phenomena:

Patient very breathless, and exertion aggravated the condition.

The chest movement normal with no impairment of percussion note.

Respiratory rate slightly increased, but breath sounds normal vesicular, with a few coarse crepitations over the larger bronchi.

Urinary and Central Nervous System:

Nil of Note.

Differential/
Differential Diagnosis:

The long history, lacking in the essential factors (vitamins) of an adequate diet; the main symptoms of the malady, such as the general debility, the condition of the mouth particularly the gums, the petechiae on the skin, and the condition of the blood form the main clues in the diagnosis of the disease.

On admission the malady was well established, and really was well established, and really presented little difficulty in recognising this as a case of "Scurvy".

The disease however, has to be differentially diagnosed from "Acute Leukaemia" in which stomatitis and haemorrhage may be present, other cases of "purpuric" eruption and "syphilis".

The blood count and the differential count, at once distinguishes scurvy from Leukaemia.

The history, the spongy condition of the gums, and the response to adequate treatment are the main factors in diagnosing "scurvy" from "purpura".

The examination of the C.N.S. the blood Wasserman diagnosis scurvy from Syphilis.

Etiology:

In the history of medicine, the scourges caused by scurvy, and the various attempts which were made to combat the disease, affords very interesting reading.

It was one of the problems which baffled the explorers of the middle ages, and used to be the scourge of the British Navy for
a considerable time until the introduction of lemon juice as a prophylactic.

The Great War gave abundant opportunity for studying the disease. The research carried out at the Lister Institute by Dr Harriette Chick established the fact, that the antiscoreric vitamin is contained in large amount in lemon, oranges and fresh green vegetables.

The disease has practically been stamped out, but it still occurs as isolated cases amongst the poor living under unhygienic conditions.

It is one of the deficiency diseases, due to a too long continued diet, in which the water soluble "vitamin C" is absent.

Treatment:

Patient received a liberal diet, with plenty of fresh vegetables. In addition patient had one lemon and two oranges daily.

The symptomatic treatment was gargles with condys fluid, as well as Bismuth and opium for the diarrhoea.

Progress Notes:

As it was an uncomplicated case of scurvy, patient responded quickly and recovered completely.

The blood picture practically normal, the condition of the gums had cleared up, while patient felt vigorous and energetic.
Name: John Boswell.
Age: 66.
Admitted: 12. 4.34.
Discharged: 28. 4.34

Complaint:
1. Lassitude and breathlessness on exertion.
2. Loss of weight.
3. Disability due to large swelling in the abdomen.

History:
Patient was not in a position to give the exact time of the onset of his complaint. For the last year, however, patient has been feeling generally debilitated.

He always felt tired, and became very breathless on the slightest exertion. Insidiously but progressively, his condition became more and more severe, this being accompanied by a very marked loss in weight.

His appetite became poor, his bowels were always regular, but he was greatly troubled with a feeling of fullness over the upper border of the abdomen especially after his meals.

Occasionally he had dull pains in the epigastric region, which did not bear any direct relation to the taking of food, and about 8 weeks ago he vomited undigested food which was mixed with streaks of blood.

Patient/
Patient noticed the swelling in his abdomen, which progressively became larger and larger, and caused great discomfort in walking.

In addition, patient was severely troubled with dizziness, and maddening bussing noises in his head, and periodically he bled profusely from his nose.

**Previous History:**

Patient enjoyed excellent health, up to about a year ago. He has, however, a history of having had malarial fever during the Boer War - but suffered no ill after effects.

**Social History:**

There is no history of a similar condition in the family. Patient lives in the country, his wife and six children are all alive and well. He lives comfortably, works in the open air, and his habits leave nothing to be desired.

**Examination:**

Patient propped up in bed. Facial features pinched, while patient looks tired, and the respirations somewhat laboured. There is marked anaemia, which even extends to the ears. The lips, are covered with thin brown scabs, but they look obviously bloodless.

The eyes are somewhat lustreless, while the conjunctiva shows marked anaemia. There is a slight puffyness under the eyes, which is most marked at the nasae angle.

On the right cheek are a few scabs surrounded by a zone of congestion.
The Blood Film showing myelocytes
The hands are pale, the skin atrophic and dry, while the finger tips are congested, and the nails soft and brittle, showing well marked arterial pulsations. There is, however, no clubbing of the fingers.

**Haemopoietic System:**

Patient bleeds easily, and the bleeding time is prolonged.

<table>
<thead>
<tr>
<th>Red Blood Cells</th>
<th>3,500,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>50%</td>
</tr>
<tr>
<td>Colour Index.</td>
<td>.7</td>
</tr>
<tr>
<td>White blood Cells</td>
<td>14,300</td>
</tr>
</tbody>
</table>

**Examination of Blood Film:**

**Red Blood Corpuscles:**

There was a slight irregularity in the size of these cells (anisocytosis) with a few poikilocytes, while some of the cells retained both the basic and the acid stains (chromatophilia).

**White Blood Corpuscles:**

The presentation of these cells was complicated, and the differential count achieved with no mean difficulty.

The various types of cells varied greatly in form and size. The outstanding feature being, that the leucocytes appeared in the various stages of their phylogeny. But the leucocytic picture was even more complicated than this; it was not a mere flooding of the circulation with immature cells of the neutrophyllic granular series, but the various cells in the different stages of their development, manifested great variation. For instance, even the fully/
**Blood Film**

Showing oxydase granules. A method which distinguishes myeloid from lymphatic cells.
fully matured polymorphs exhibited a very obvious variation in size. Some were small, while others were unduly large, but the nuclear lobulation were within the limits of normal.

There was a large majority of pre-myelocytes. These varied in size, the majority however, being large, while the myelocytes were scanty, these being neutrophilic eosinophilic or basophilic, many of these, however, appeared in the transitional stage between the immature and the mature cell.

The percentage of myeloblasts were fairly high and they too showed variation in size.

<table>
<thead>
<tr>
<th>Polymorphs</th>
<th>22%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes</td>
<td>4%</td>
</tr>
<tr>
<td>Pre-Myelocytes</td>
<td>44%</td>
</tr>
<tr>
<td>Myelocytes.</td>
<td></td>
</tr>
<tr>
<td>&quot; Neutrophils</td>
<td>16%</td>
</tr>
<tr>
<td>&quot; Eosinophils</td>
<td>3%</td>
</tr>
<tr>
<td>&quot; Basophils</td>
<td>2%</td>
</tr>
<tr>
<td>Myeloblasts</td>
<td>5%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>4%</td>
</tr>
</tbody>
</table>

The outstanding feature of the film is, the great variety of cell forms, the majority belonging to the neutrophilic granular series.

At arriving at the above observations it is, however, that I give a scheme of the cell classification adopted.

Primitive/
Cardio Vascular System:

Pulse: 75 per minute, regular in time and force, full pulse but flabby in character and easily compressible. Vessel wall thickened but not modular.

Heart: Normal in size and shape. Heaving pulsations over apex, but no thrill present.

Soft blowing murmur, systolic in time heard over mitral area. Sounds closed over other areas, with accentuation of second sound over pulmonary area.

Respiratory System:

Respirations slightly embarrassed. The chest flattened anterior posterior, with the lower end of the sternum depressed.

Chest wall moves freely and equally with respirations.

Percussion note normal, but a little hyper-resonant over base of left lung posteriorly. Vocal fremitus and vocal resonance decreased/
decreased over this area.

Breath sounds normal vesicular all over, but diminished over base of left lung.

**Alimentary System:**

Appetite poor, but bowels regular. Lips pale, teeth dirty and carious, tongue coated with whitish brown fur, but moist.

The abdomen is distended, but the distension is unequal, being most marked on the left side.

No tenderness on palpation, and in the left abdominal half, a large mobile swelling palpable, which extends from the costal margin down to the left iliac fossa.

The liver enlarged to about 3" below the costal margin, edge of liver smooth. A small swelling in the R. inguinal region, found to be an inguinal hernia.

The kidneys not palpable.

On percussion the spleen found to be greatly enlarged, splenic notch palpable. There was a dull percussion note over the whole of the left side of the abdomen, while the percussion note on the R. side was hyper-resonant.

**Urinary System:** Nil of note.

No involvement of central nervous system.

**Lymphatic and Integumentary System:**

No enlargement of any of the lymphatic glands.

The skin is generally dry and atrophic, no history of pruritis, but the skin over the abdomen particularly, is covered with/
with small brown spots not raised above the surface.

There is, however, an infection of the skin over the R. cheek, as well as on the dorsum of the left foot. The latter is in the form of small discrete haemorrhagic spots, while the surrounding area is red and congested.

Sense Organs:

Auditory System:

Patient very deaf, and according to him this came on about six months ago.

Patient has a history of bussing noises in his head (Meniers Syndrome), more adequately expressed in patient's own words. "I had bussing noises in my head, until I thought I was going mad".

On examination, however, this syndrome had disappeared.

Nose: Patient has a history of paroxysmal epistaxis, which was found very difficult to control.

On examination, however, the nose revealed nothing abnormal.

Ocular Changes:

No involvement of the optic nerves. The optic discs of both eyes are congested, with pale white spots.

Differential Diagnosis.

The two most important factors in determining the diagnosis, is the enlargement of the spleen, and the careful examination of the blood.

The history plays a relatively minor role in determining the diagnosis.
The essential point in the diagnosis, is the occurrence of an increase in the normal number of leucocytes.

There are indeed a great number of conditions which causes a leucocytosis, but, an increase of the leucocytes, concomitant with a massively enlarged spleen, limits the differential diagnosis to about half a dozen maladies.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Enlarged Spleen</th>
<th>Enlarged glands</th>
<th>Leucocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloid Leukaemia</td>
<td>Massive</td>
<td>Usually none</td>
<td>x x x</td>
</tr>
<tr>
<td>Lymphatic Leukaemia</td>
<td>usually slight</td>
<td>Moderate</td>
<td>x x</td>
</tr>
<tr>
<td>Hodgkins Disease</td>
<td>slight</td>
<td>marked and hard</td>
<td>slight</td>
</tr>
<tr>
<td>Splenic Anaemia</td>
<td>massive</td>
<td>none</td>
<td>Leucopenia</td>
</tr>
<tr>
<td>Gaucher Splenomegaly</td>
<td>massive</td>
<td>none</td>
<td>Leucopenia</td>
</tr>
<tr>
<td>Acholuric Jaundice</td>
<td>massive</td>
<td>none</td>
<td>slight</td>
</tr>
</tbody>
</table>

The differential count, however, leaves no doubt as to the condition of the malady. The presence of the large number of premyelocytes, with the consequence, that there is a relative diminution of the other varieties of white cells, diagnosis this as a case of "Myeloid Leukaemia".

The blood picture is, however, never a stationary one, variations/
variations occur as time goes on. There is usually an increase in the number of leucocytes as time goes on.

The very high percentage of immature cells especially the pre-myelocytes makes the outlook worse.

Treatment:

So relatively little is known about the pathogenesis of this most vexed disease, that it is not surprising that no cure has yet been recorded.

The general principles of treating any form of anaemia must be observed. If patient is ill, rest in bed is essential; if discomfort is only slight, patient may be allowed up but kept quiet.

The cahexia can be postponed by giving ample and easily digestable food.

Various forms of therapeutic measures are adopted, but the only forms which show any signs of response are the "chronic leucoses".

Exposure to heat, has met with well marked temporary improvement.

Arsenic is commonly employed, this may be given by mouth, or subcutaneous injections of arsenical preparations.

Artificial induction of malaria has been tried, but no good results were obtained.

Benzol definitely is of some value, the danger, however, being chronic benzol poisoning. Benzol is a leucocytotoxic substance which has a greater effect on myeloid than on lymphatic tissue.
It causes a reduction in leucocytes, the number of red blood corpuscles rises, while the splenic and hepatic enlargements may diminish.

Surgery plays a relatively small part. There is the risk of haemorrhage, and it is doubtful whether splenectomy is really advisable.

The best results have been obtained by X-Ray therapy. This therapeutic measure was first used by Pusey in America 1902. Since then X-Rays has been used extensively although the technique has varied greatly from time to time.

Every case is treated on its merits. The technique consists of exposing the long bones of the body as well as the spleen to X-Rays.

The usual course is 150r. to each area, with a voltage of 140 K V. The best results are obtained by giving the whole course of treatment within a few days.

The rational of this therapy being that the immature cells are very sensitive to X-irradiation.

**Progress Notes:**

There was no rise of temperature. Patient was comfortable in bed, and during his stay there was no change in his condition.
CASE 6.

Name: Mrs Stewart.
Age: 48.
Admitted: 12th March
Died: 26.5.34

Complaint:
1. Palpitation and dyspnoea on the slightest exertion.
2. Extreme weakness and marked loss of weight.
3. Sleeplessness.
4. Dryness of mouth.

History:
Patient had an uneventful history, always being in the prime of health, upto her menopause two years ago.

Since then patient has suffered vague ill health, which insidiously but progressively became worse. She became breathless on the slightest exertion, while the least excitement brought on palpitation. Concomitant with this, she experienced a generalised loss of vitality and lost a great deal of weight.

About three months ago, patient had an accident, and fell on her head. This shocked her severely, and since then patient has been confined to her bed.

Her condition did not improve, but progressively became worse. Her appetite became poor, her mouth very dry, while she developed small sores on the side of her tongue, and gums.

Patient was troubled with indigestion felt like vomiting but/
but never actually vomited while her bowels became very caustive.

At nights she slept badly, patient ascribing this to the troublesome bussing noises which she had in her ears.

About a week prior to admission patient had a very severe attack of epistaxis, and had great difficulty in stopping the bleeding.

**Family History:**

No history of a similar condition in the family. Patient lives comfortably and perfectly normal in her habits.

**Examination:**

Patient debilitated in the extreme. Propped up in bed, facial features pinched, with an expression of profound exhaustion.

The hands and face, show marked signs of wasting, while patient was anaemic, with a generalised dull yellow tinge of the entire body surface.

The eyes lustreless, while the lips were pale and bloodless and respiration somewhat rapid and shallow.

**Cardio-Vascular System:**

**Subjective Phenomena**

An uncomfortable feeling of faintness which increased with the slightest exertion, while the least excitement caused palpitation.

**Pulse:** 90 per minute, regular in time and force, flabby in character, not sustained, easily compressible, vessel wall faintly palpable. B.P. 110/70.

**Heart:** Apex beat in 5th interspace, just outside the mid clavicular line; right border at right of sternal margin.
Apex beat diffuse, with well marked pulsations in vessels of the neck and epigastrium.

A faint soft blowing haemic murmur systolic in time over mitral area. Sounds equal and closed over other areas.

Soft blowing murmur also heard over vessels of the neck.

**Haemopoietic System:**

Blood pale and watery looking. Patient bleeds easily and bleeding time prolonged, to six minutes.

- Red Blood Cells 1,010,000
- Haemoglobin 15%
- Colour Index .75
- White Blood Cells 3,900

**Blood Film:**

The red blood cells showed slight irregularity in size (anisocytosis) while a few pear shaped cells were also present (poikilocytes), and some of the cells stained a slightly bluish tinge (polychromasia)

On the whole the cells were small. The average diameter slightly less than normal. A few megalocytes present but on the whole cells were hypochromatic.

**Differential Count:**

This did not reveal very much. Some of the lymphocytes were peculiarly shaped, and the film revealed a relative lymphocytosis.

- Polymorphs 38%
- Lymphocytes
  - Small 38.5% 52%
  - Large 14% 52%
- Monocytes 6%
- Eosinophiles 3%
Basophiles 6%
Myelocytes 2%
Blood Wasserman negative.

Respiratory System:

Patient breathless and the respirations rapid and shallow.
Chest poorly developed, but moved equally with respirations.
No impairment of percussion note, and breath sounds vesicular with a few crepitations over the large bronchi.

Alimentary System:

Subjective Phenomena:

Appetite poor, mouth very dry, cramp like pains across the upper border of the abdomen, bowels very constipated.

Examination:

Lips pale, tongue flabby and very dry, thickly furred with a few ulcerations on the sides of the tongue.
Abdomen slightly distended, abdominal wall atonic and showing signs of wasting.
Epigastric area tender, and the muscles showed some guarding, but nothing abnormal palpable on deep palpation.
The liver enlarged to about 3 finger breadths below the right costal margin, the edge smooth and rounded.
Kidneys not palpable, and the spleen not enlarged.
The superficial vessels over the epigastrium and lower border of the chest engorged and distended.
Result of Test Meal.

Specimens withdrawn with ease. Clear colourless supernatant fluid. Porridge visible up to two hours.

Central Nervous System:

No involvement of this system.

Integumentary and Skeletal Systems:

No history of pruritis. Skin dry and atonic, with small brown spots distributed over the abdomen and the lower part of the chest.

No involvement of the skeleton on palpation, but definite tenderness elicited by slight pressure on the anterior aspects of both tibia.

There was also very definite tenderness over the lower part/
part of the sternum on percussion (moslers sign).

**Lymphatic System:**

The only glands enlarged, were the glands in the left axilla and in both inguinal regions. The glands were, however, not very much enlarged discrete, firm and not painful.

**Sense Organs:**

**Auditory System**

Patient slightly deaf, with a definite history of Meniers Syndrome.

**Olfactory System**

History of epistaxis, nothing abnormal found on examination, of the nose.

**Ocular Changes**

The fundus congested, the retina dull with white patches, while the vessels were congested and tortuous.

**Diagnosis:**

At this stage it was very difficult to arrive at a definite diagnosis. The physical signs and symptoms were that which could accompany any form of anaemia. Neither was the blood picture very distinctive, but the leucopenia accompanied by a relative lymphocytosis rather suggested a condition of "Aleukemic Lymphadenosis", while the enlargement of the glands of the axillary and inguinal regions was suggestive of "Hodgkin's disease".

**Treatment:**

In addition to the general hygienic measures, careful nursing/
nursing and careful attention to the general comfort of the patient, the following medical measures were also adopted.

- **Campolon** 1 c.c. daily I.M.
- **Mist Ferri Ammon Cit** ½ oz. t.i.d. (30 grns.)
- **Petrol Agar** ½ oz nocte

In addition a soap and water enema was administered every third day.

**Diet:** Patient was put on a very light diet, as well as fluids given freely. In addition patient was given plenty of fresh fruit, oranges, grapes, and apples, as well as orange and lemon drinks.

**Progress Notes:**

Throughout the course of her illness patient always had a slightly swinging temperature. But there definitely was no Pel Ebstein Syndrome manifestation in the swinging temperature.

There was, however, such a marked variation in the condition of the patient from time to time, that a symptomatic representation of the progress is far more adequate.

The comparison of the varied clinical picture, with the changes in the blood observed every 4th day, as well as the differential counts performed at various stages of the illness is indeed very striking.

**March 12th - 15th:** Patient very tired and breathless, extremely caustive, slept badly and complained about ringing noises in her head.

**March 15th - April 1st:** A very definite improvement in condition of patient. Her colour was better, she slept better and generally much more comfortable. During this stage too, the blood picture showed considerable/
Blood Film of Lymphatic Leukaemia.
considerable improvement.

April 2nd - 5th: Patient suddenly became very ill. Developed sudden acute cramp like pains over the abdomen and vomited repeatedly. In addition patient complained about very severe pains in the back. After a few days, however, the pains settled down.

April 5th - 12th: Patient again more comfortable, but perspired most profusely.

April 12th - 20th: It was during this period that the spleen was palpable for the first time. Simultaneously a round swelling was palpable in the right lumbar area. At the same time a modular infiltration of the skin was noticed over the left cheek, gradually spreading down to the chin and up to the hair. There was no discolouration of the skin.

The changes in the blood picture at this stage was rather striking. There was a very definite drop in the haemoglobin content of the blood, accompanied by a very marked leucocytosis.

April 20th - 1st May: Progressive enlargement of the spleen, palpable about four finger breadth below the costal margin. The swelling on the R. side a large slightly mobile mass about 3" in diameter. It was during this period that patient first complained about frequency of micturition and difficulty of retaining her water. Another distressing feature was, that at this stage patient developed acute attacks of breathlessness especially during the nights.

May 1st: Patient very very weak, progressively but steadily she/
she went downhill. Wasting in the extreme, while difficulty in breathing became more and more pronounced.

During this stage, the infiltration of the face which was first noticed on the 20th April, became discoloured into reddish brown indurated areas.

May 13.

The anaemia became more and more severe, patient debilitated in the extreme, the temperature more and more irregular, while the glands and the swellings in the abdomen became progressively larger, and patient died in an exhausted exanguinated state.

An attempt was made to give patient a blood transfusion, but as she agglutinated all types, the procedure was impossible.
## Variations of the Blood Picture

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>W.B.C.</th>
<th>Hb</th>
<th>CI</th>
<th>Blood Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. 3.34</td>
<td>1,010,000</td>
<td>3,900</td>
<td>15</td>
<td>.75</td>
<td>Slight anisocytosis, and polychromasia. Few poikilocytes. Cells hypochromatic and small. Differential Count - 12. 3.34. Polymorphs 38.2% Lymphocytes Small 38.5% Large 14%</td>
</tr>
<tr>
<td>16. 3.34</td>
<td>1,010,000</td>
<td>3,900</td>
<td>15</td>
<td>.75</td>
<td>Lymphoblast 4% Monocytes 4% Eosinophils 3% Basophils 2%</td>
</tr>
<tr>
<td>22. 2.34</td>
<td>1,030,000</td>
<td></td>
<td>18</td>
<td>1</td>
<td>W.B.C. 19. 4.34. Polymorphs 31% Lymphocytes Small 41% Large 9.5%</td>
</tr>
<tr>
<td>28. 3.34</td>
<td>1,060,000</td>
<td></td>
<td>20</td>
<td>1.25</td>
<td>Lymphoblasts 7.5% Eosinophils 4% Basophils 3% Myelocytes 3%</td>
</tr>
<tr>
<td>1. 4.34</td>
<td>1,150,000</td>
<td></td>
<td>28</td>
<td>1.26</td>
<td>W.B.C. 25. 4.34. Polymorphs 25% Lymphocytes Small 70% Myelocytes 3% Lymphoblasts 2%</td>
</tr>
<tr>
<td>4. 4.34</td>
<td>1,550,000</td>
<td></td>
<td>35</td>
<td>1.25</td>
<td>W.B.C. 6. 5.34. Polymorphs 12% Myelocytes 4% Lymphocytes Small 80% Lymphoblasts 4%</td>
</tr>
<tr>
<td>9. 4.34</td>
<td>1,600,000</td>
<td></td>
<td>37</td>
<td>1.13</td>
<td>W.B.C. 14. 5.34. Lymphocytes Small 92%</td>
</tr>
<tr>
<td>12. 4.34</td>
<td>2,910,000</td>
<td></td>
<td>43</td>
<td>1</td>
<td>Lymphoblasts 4% Myelocytes 3% Lymphoblasts 2%</td>
</tr>
<tr>
<td>16. 4.34</td>
<td>2,200,000</td>
<td>18,000</td>
<td>44</td>
<td>.9</td>
<td>Myelocytes 3% Lymphoblasts 2%</td>
</tr>
<tr>
<td>20. 4.34</td>
<td>2,190,000</td>
<td>25,000</td>
<td>41</td>
<td>.9</td>
<td>W.B.C. 19. 4.34. Polymorphs 31% Lymphocytes Small 41% Large 9.5%</td>
</tr>
<tr>
<td>24. 4.34</td>
<td>1,930,000</td>
<td>31,400</td>
<td>35</td>
<td>.9</td>
<td>Lymphoblasts 7.5% Eosinophils 4% Basophils 3% Myelocytes 3%</td>
</tr>
<tr>
<td>28. 4.34</td>
<td>1,580,000</td>
<td>32,600</td>
<td>23</td>
<td>.9</td>
<td>W.B.C. 25. 4.34. Polymorphs 25% Lymphocytes Small 70% Myelocytes 3% Lymphoblasts 2%</td>
</tr>
<tr>
<td>2. 5.34</td>
<td>1,420,000</td>
<td>32,900</td>
<td>26</td>
<td>.9</td>
<td>W.B.C. 6. 5.34. Polymorphs 12% Myelocytes 4% Lymphocytes Small 80% Lymphoblasts 4%</td>
</tr>
<tr>
<td>6. 5.34</td>
<td>1,320,000</td>
<td>33,200</td>
<td>24</td>
<td>.9</td>
<td>W.B.C. 14. 5.34. Lymphocytes Small 92%</td>
</tr>
<tr>
<td>13. 5.34</td>
<td>1,200,000</td>
<td>34,000</td>
<td>23</td>
<td>.9</td>
<td></td>
</tr>
<tr>
<td>20. 5.34</td>
<td>930,000</td>
<td>53,000</td>
<td>17</td>
<td>.9</td>
<td></td>
</tr>
</tbody>
</table>
During her illness the blood was carefully examined at various stages. The most striking feature is undoubtedly the marked variation of the leucocytes, not only in number but also in the composition of the cells at various stages.

At the beginning, there was a very definite diminution in the number of leucocytes. The differential count at this stage was of little value, except that the count revealed a relative lymphocytosis, while some of the lymphocytes revealed some abnormality which was not very definite.

The blood picture, however, did not remain constant. The leucopenia rather abruptly made way for a very definite leucocytosis.

The lymphocytosis still remain only relative, but there was a very marked increase in lymphoblasts, while a small percentage of immature polymorphs also appeared in circulation. This in all probability occurred as the result of some irritation of the marrow.

Progressively, however, the lymphocytes increased at the expense of all other forms of leucocytes, thus giving a very definite lymphocytosis.

The lymphocytes were predominantly of the small type. There was, however, no unanimity about their structure. Some of the cells resembled large lymphocytes, while the nuclei of the cells also showed abnormality in structure.

The presence of the immature (lymphoblasts) cells in circulation, is indicative of the acuteness of the disease.

The most interesting feature about the systematic examination of the blood, was that patient became progressively weaker/
weaker as the number of lymphocytes increased.

Differential Diagnosis.

In arriving at a diagnosis in this case, the cardinal considerations are; (1) The anaemic condition of patient (2) The enlarged glands in axilla and inguinal regions (3) The spleen which enlarged rather abruptly (4) Above all a careful and repeated examination of the blood.

Taking into consideration the relatively long history of 3 years, the enlargement of the glands, the definite leucopenia with a relative lymphocytosis on primary examination, would lead me to diagnose this as a case of "Chronic Aleukaemic Lymphadenosis", which became frankly "Leukaemic" towards the end.

The disease, however, must be differentiated from other causes of glandular and splenic enlargement.

Splenic enlargement may be found in cases of infection such as septic endocarditis, Banti's Disease, Congenital syphilis, Haemolytic jaundice, Acute gas poisoning (sometimes) Pernicious Anaemia and Myeloid Leukaemia.

While chronic glandular enlargement may be due to Hodgkin's disease, Tuberculosis and syphilis.

All these conditions can, however, be ruled out, with a careful routine examination of the blood.

In this case, the diagnosis towards the end presented no difficulty whatsoever.

The leucocytosis, with a 90% lymphocytes, established the/
the diagnosis.

The appearance of lymphoblasts, and myelocytes in circulation was indicative of marrow stimulation and an acute termination.

Prognosis:

The expectation of lymphadenosis in general is ultimately bad, because no method of treatment results in a cure for the disease. Nevertheless patients may live for long periods if the glandular enlargements be not too great, and if the anaemia remain within reasonable limits.

Treatment:

In addition to general hygienic measures, treatment is directed towards combating the anaemia, while arsenic either intramuscular or by mouth or X-Ray therapy may be tried.
Report on Mrs Stewart.

Died: 26.5.34

Autopsy: 26.5.34

GENERAL:

The body was that of an elderly female. Rigidity present. Over the face, brow and neck were numerous purpuric eruptions.

SEROUS CAVITIES:

The pericardium contained a considerable quantity of clear, yellowish fluid. The left pleural cavity contained a small amount of similar fluid. The parietal pleura on both sides showed numerous petechial haemorrhages. Peritoneal cavity - N.A.D.

On incision the subcutaneous tissues were slightly oedematous. The flow of blood from the smaller vessels was rather more free than usual.

All tissues and organs showed evidence of marked anaemia.

LYMPHATIC AND HAEMOPOIETIC SYSTEM:

There was some enlargement of the cervical axillary and inguinal lymph glands, some of them being as large as large beans. They were all of firm consistence and pale in colour. Occupying the anterior mediastinum was a large mass of glands. This was adherent to the pericardium and continuous with enlarged glands round the hilum of each lung. The mass was firm in consistence and pale lemon-yellow in colour.

There was no enlargement of the abdominal lymph glands.

Spleen/
Spleen:

Was of normal size and firm in consistence. On section it was rather pale and the Malpighian bodies were very prominent.

Bone marrow:

Showed evidence of an active mixed leucoblastic reaction, the reddish-white marrow extending the whole length of both femora. Blood films stained Leishman revealed a very large number of small lymphocytes, forming 70-80%, together with lymphoblasts, myeloblasts and lymphocytes, of the total white cell count.

CARDIO-VASCULAR SYSTEM:

Heart:

There was no increase in pericardial fat. The myocardium was pale but otherwise appeared healthy. The valves were all competent and appeared healthy on macroscopic examination.

Aorta:

Healthy.

Lungs:

Were pale, both externally and on section. Neither lung was completely collapsed, both being rather voluminous. This was most marked in the lower lobes, which were pale, somewhat mottled, and on section were rather firmer in consistence than normal, though there was no increase in weight. Both upper lobes were emphysematous.

ALIMENTARY SYSTEM:

Stomach/
Stomach and small intestine showed no pathological changes on naked-eye inspection. Large intestine was loaded with faeces from caecum to anus.

Liver:
Was not enlarged. The parenchyma was pale and showed evidence of advanced fatty degeneration.

Pancreas:
N.A.D.

Kidneys:
Both kidneys were very markedly, though symmetrically, enlarged, being at least 3 to 4 times their normal size.

On section they were firm and pale in colour, showing marked infiltration with the lymphoid tissue. The cortex was clearly demarcated from the medulla, and was definitely paler than the latter. In one or two places the cortex was flecked with a golden-yellow substance and in at least one place this material had caused a small infarct under the capsule. Small deposits of the same substance were found in the calyces, forming small calculi. It was probably a deposit of urates.

The capsule stripped fairly easily in both kidneys.
The suprarenals appeared normal on gross examination.
The uterus and adnexa appeared normal.

CONCLUSION: The condition is a typical example of lymphatic leukaemia.
Kidneys:

Showing extensive lymphocytic infiltration. Both cortex and medulla being affected.

Bone Marrow:

Almost the whole of the myeloid tissue is replaced by typical small lymphocytes. A small percentage of immature myeloid leucocytes are however, also present, probably as the result of irritation by the masses of lymphocytes.

Thyroid Gland:

Packed with lymphocytic cells.
Liver:

In addition to degenerative changes, the most outstanding feature is the infiltration of the portal tracts with lymphocytes. The extension of the infiltration into the lobule is only slight.

Lungs:

The lungs show slight congestion, with the alveoli filled with exudate, while the alveolar walls show slight lymphocytic cellular invasion.

Intestine:

The intestinal tract also shows extensive cellular infiltration.
Skin:

The thickening of skin on side of face, due to diffuse infiltration of subcutaneous tissue with lymphocytic cells.

Lymphatic Glands:

Shows marked histological changes. There is a complete disappearance of normal structure. The bilum has the lymph channels obliterated, while even the capsule reveals the extensive infiltration of lymphocytes.

Spleen:

Impossible to distinguish between pulp and follicles, due to extensive infiltration of lymphocytes.
ETIOLOGY of the LEUCOSES.

The pathogenesis of "myeloid Leukaemia" as well as the other "Leucoses", is still very far from being complete.

Innumerable theories has been put forward as to the causes of Leucoses, but only a few of the outstanding theories will be given here.

(1) Leucoses regarded as an Infective Malady.

It seems very reasonable to assume this, especially if one bears in mind, that it is the leucocytes which react most intensely to many infections.

Another view of this kind is, that the leucosis results as a post infective condition, and it is held that malaria and syphilis are predisposing factors, although this has not definitely been proved.

It is true, that no micro-organism capable of causing any form of leucosis, has been isolated yet, therefore the theory of an unknown filterable virus has been postulated.

All experiments designed to transmit human leucosis to lower animals, whether blood, tissue or bacteria, has been unsuccessful.

In a recent article of the B.M.T. observations are made which seems rather to support the "Infective Theory".

In the Aetiology of Hodgkin's disease, Gordon (1933) found that rabbits injected intracerebrally with lymphadenomatous tissue, frequently developed highly characteristic nervous lesions.

This /
This reaction applied as a biological test has proved valuable in the differentiation of Hodgkin's disease from other forms of lymphatic hyperplasia.

Recently Friedmann and Elkeles have reported that the intracerebral inoculation of rabbits with bone marrow derived from cases of acute leukaemia and Pernicious Anaemia produces effects very similar to those described by Gordon.

A series of experiments were carried out, in which rabbits 2,000 grams in weight received intrathecally 0.4 cm of leucocyte suspension - the suspension previously having been subjected to the "Jochmann - Lockemann method of extraction.

The animals developed a progressive and fatal disturbance of the nervous system, paralysis of the hind legs being a characteristic feature of the late stages.

From these experiments he concludes that the agent which is present in human bone marrow, spleen and leucocytes which is pathogenic to rabbits cannot be a virus, as it could not survive the drastic treatment demanded by the Jochmann - Lockemann method of extraction.

Although satisfied that the pathogenic agent is not a virus, the effects of intracerebral infections in rabbits differ from the known effects of chemical substances - except those toxins like diphtheria and tetanus - in that they are progressive in character. In this progressive character following an incubation period of 4 days, there is a close resemblance to infectious diseases.

(British Medical Journal March 24 - 1934)
Furthermore, a disease has been recognised in fowels and mice which is very similar to the Leukaemia of the human being. This leukaemic condition is transmissible to other animals, but along very obvious specific lines. It is therefore reasonable to ascertain that the Leucoses is infectious, but transmission is along strictly specific lines.

(2) Leucoses are true Neoplasms.

The main supporters of this hypothesis are Sternberg and Banti. They both contend that the leucosis are essentially sarcomata, and that the deposits outside the haemopoietic organs are in the nature of metastases.

The great overgrowth of myeloid tissue itself, is to be interpreted as reactive hyperplasia.

This theory is substantiated by the fact that in the peripheal blood in cases with metastases of carcinoma or sarcoma in the bone marrow, immature leucocytes and nucleated red cells may be numerous.

(3) Leucoses the result of some disturbance of co-ordination in the body.

Ziegler, by a long series of experiments, subjected a variety of animals to X-Rays. He found that irradiation of the spleen was followed by atrophy of the malpighian bodies, myeloid metaplasia of the pulp and the appearance of immature granulocytes in the blood.

He concluded that "myeloid Leukaemia is, therefore, the expression/
expression of peculiar hyperplastic process in myeloid tissue, arising on account of a disturbance of the normal relationships between the lymphatic and the myeloid apparatus. This leads to myeloid metaplasia of spleen tissue, and to flooding of the blood with myeloid cells. The disturbance consists of a failure of spleen function due to destruction of its lymphatic components".

This theory cannot be accepted, because irradiation of the bone marrow does not lead to identical changes in the blood.

Furthermore removal of the spleen does not lead to myelosis, as one would expect if this theory were true.

(4) Disturbance of Endocrine balance.

This assumption has been put forward by Naegeli - but it has found very little favour.