Thesis.

Clinical Observations on Pernicious Anaemia.

W. A. Simpson.
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Thesis
by
William Adamson Simpson MD 1926
THESIS.

Clinical Observations on Pernicious Anaemia.

By William Adamson, B.S.C. 1926.

Of late there have appeared in different medical periodicals, several communications on the subject of pernicious anaemia. In spite of these however the subject never seems to be trite; there is always something refreshing about it, although the subject matter may contain nothing new. Probably the main reasons for the continued interest are (1) that so little is known of the cause of the disease and (2) that, according to most authorities, it is invariably fatal, no definite case being known. As a student, I remember Professor Galland telling his class that a case of his had survived fifteen years.
I have never since heard of a case lasting so long.

From my own small experience and from conversation with other medical men, I should say that few cases survive more than five years from the onset of the disease, and that the more acute the onset, the shorter will be the patient's life.

In this thesis I intend largely to confine myself to fourteen cases I have actually seen or had under my care since September 1924, i.e., since I became a resident medical officer.

Eleven of these cases came under my observation in St. Luke's Hospital, Bradford, where about fifty per cent
Of the beds were medical. I am indebted to Dr. William Wrangham for permission to use these cases in my commentary.

One of the cases was allotted to me while sitting the M.D. Clinical Examination, and may with advantage be included.

Two of the cases occurred during my stay in Preston Royal Infirmary where only about ten per cent of the beds are medical.

When I come to the question of differential diagnosis I will be able to mention other cases from these Bradford and Preston hospitals which resembled pernicious anaemia but were not.

I have therefore only had
Fourteen hospital cases of what I think were genuine pernicious anaemia. Of these, eight were men and six women. I had as many as six cases under me in Bradford at one time, but this was of course exceptional.

Table of Cases.

<table>
<thead>
<tr>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>Age</td>
<td>Married</td>
</tr>
<tr>
<td>1</td>
<td>69</td>
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<tr>
<td>2</td>
<td>49</td>
</tr>
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<td>3</td>
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<td>7</td>
<td>55</td>
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<td>8</td>
<td>57</td>
</tr>
</tbody>
</table>

Average 59.5% 100% -
It will be seen from the foregoing table that the youngest patient under my care was a woman of 34 years, and the oldest a man of 69 years. I was on the lookout for cases in young persons, but could not find a marked anaemia in a young person to be idiopathic in origin.

Taken all over, in spite of the paucity of my cases, the occurrence of the disease in men being greater than in women, corresponds with the usual findings. Moreover, the average age in man is greater than in women -vide table - average age men 59.5 years, average age women 46.5 years.

I have always regretted that
These cases could only be
under my care for a few months
at the most. Under these circumstances,
it is difficult to trace progress.
I have visited Bradford several times
since leaving St. Luke's Hospital
and have attempted to keep
myself in touch with the progress
of the different patients, but this has
not always been possible.

As far as I know five
of my cases have died, but only
in one case was it practicable to
get a post-mortem examination. This
was greatly to be regretted, inasmuch
as it obliterated a likely field of
research: much we can see or find
in the dead, is often unsuspected
in the living.
I have been unable to trace any history of hereditary anaemia in parents or descendants of these cases. Still it is readily conceivable that over a longer space of time a family history might be established.

Addison's definition still holds good. He characterised the disease as "a general anaemia, occurring without any discoverable cause whatever, cases in which there had been no previous loss of blood, no exhausting disease, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, sthenic, or malignant disease."

Only two theories of any importance have been advanced to explain the origin of the disease—
I refer of course to

1. The theory of Haemolysis

2. The theory of a chronic septic

infection, often associated with a

specific glossitis, and oral, gastritic or

intestinal sepsis.

Each theory has its admirers,
each its abusers. I do not think any
good purpose can be served by

argument over these theories; much can

be said for both, and when all is

said and done, they are only

theories—it may be proved conclusively

some day that neither is right.

Here it may be remarked

that in all my cases no definite

cause could be found. The

majority showed alimentary disorders

such as pyorrhoea, glossitis, enteritis,
etc. Constipation was not a marked

feature.
Before giving a summary of the cases I will consider briefly the symptomatology.

Symptoms are usually insidious. Six of my patients gave a history of less than a year duration of illness— one went so far as to insist that she had been fit and at work till three weeks prior to admission, yet she had a red blood count of 980,000 and only 25% haemoglobin. No patient could state definitely when he or she began to be unwell.

The first symptom was usually loss of appetite, sometimes accompanied by nausea and occasionally by vomiting. Vomiting, as a rule, is rare. This was followed by a
feeling of tiredness, especially on slight exertion: rest in bed alleviated this tired feeling but never dispelled it. The lethargy was apparent in both mental and physical exertion.

Slight exertion also brought on palpitations, which might last for a few hours, and breathlessness, readily relieved by resting.

The ankles swelled if the patient walked or stood about too much; this was always relieved by resting in bed or raising the ankles above the level of the knees.

Symptoms resembling those of arteriosclerosis appear: headache, inability to concentrate, sleeplessness, worry, etc.

The patient usually does not lose weight. He looks stouter, but is
in reality more flabby and unhealthy looking; "the apparent gain in bulk is in striking contrast to the debility and exhaustion seen in the patient's general condition" (Osler).

Symptoms depend largely on the state of the disease. Hence no two patients exhibited the same symptoms although in many respects they were similar.

The more progressive a case was, the more pronounced were the mental symptoms. In the late stage, patients became very morose, and irritable and became not only a worry to themselves but a worry to those around them. This was especially the case in old men, but was not confined to them only.
Brief Notes on 14 Cases

Case 1.

Albert Mortimer aged 60. Labourer.

Admitted 8.8.24

Died 20.9.24.

Patient had had avarice ulcer for 30 yrs, sometimes healing but always relapsing again; occasionally he had slight superficial bleeding from the ulcer but this was never serious. The ulcer showed no signs of healing during his stay in hospital. His Wassermann report was negative 15.9.24. He was a lemon yellow colour and was complaining of weakness and dyspnoea.

R.B.C. 840,000 per c.m.

Hb. 20%

Color Index 1.2

W.B.C. 5,000 per c.mm.

Film showed marked poikilocytosis and anisocytosis; no megaloblasts; normoblasts and megalocytes present.
No free HCl was present in the Test Meal.

17.3.24. He had a very sudden attack of severe abdominal pain. Pain began in the epigastrium and an hour later had spread all over the abdomen. Rigidity was present in the epigastrium - not elsewhere. He was absolutely doubled up in agony and the pain was increased by the slightest movement. He had nausea but no vomiting. Knee Jerks were elicited and the pupils reacted to light. He became very collapsed and almost pulseless. The liver dullness was slightly diminished - no dilatation of the heart was found. Blood Pressure 90/62. Hot bottles were applied overnight and he was considerably easier in the morning.
19-9-24

R.B.C. 990,000
Hb. 22%
C.S. 1.2
W.B.C. 5,200

Film: very similar to the last
No megaloblast seen.


Post Mortem Findings

The body was not emaciated.
The skin showed a lemon-yellow tint.
No haemorrhages were seen in the skin or serous surfaces.
The heart was enlarged and flabby
and contained practically no blood;
the heart muscle was pale-yellow
in colour.
The stomach was only about
half the normal size and the
mucous membrane was shiny and
atrophied.
The liver was fatty but not
enlarged. The Russian blue reaction
was positive.
The spleen was smaller than usual.

The bone marrow of the left femur was reddish coloured and showed a marked excess of normoblasts and megaloblasts.

Case 2.

Ellen Osbaldstone aged 51. Housewife

Admitted 20-1-25

No history of previous illnesses.

Patient had been ill about one year. She complained of shortness of breath, heart burn, swelling of ankles and hands, coldness of feet, puffiness of face, inability to walk fifty yards without stopping, 'dyspepsia'. No history of haemorrhages. Menopause one year previously.
On admission she had a pulse rate of 100, temperature 97, respiration 20. She had a very seawor complexion.

The pulse was regular in time and force. The apex beat was 4½ inches from the mid-line and blowing systolic limits were heard in all areas.

She had had pyrvohea. The tongue was moist and clean, and the papillae could hardly be seen. The abdomen showed no abnormality.

The pupils were equal and reacted to light and to accommodation.

The knee-jerks were present and the plantar response on both sides was extensor. There was no disordered sensation and no marked loss of power.
The Wassermann report was negative.

Fest meal examination showed no
free HCl, lacthi acid present, and
Boca of this bacilli present.

21-1-28. R.B.C. 1,700,000 per cmm.
Hb. 35%
C. F. 103.
W.B.C. 5,600. per cmm.

Film - red cells increased in
size on an average.
Polychromatophil, anisoctyes,
and polyhromasia.
Megalocytes and normoblast.

She was put on LIq. Arsenical, m\(\text{m}^{11}\) t.i.d. and this was increased after a
week to m\(\text{m}^{2}\) t.i.d. and reduced to m\(\text{m}^{11}\)
a fortnight later. Acid Hydrochloric Bil
was given in 3\(\frac{1}{2}\) doses t.i.d. in
3\(\frac{1}{2}\) oz. warming with meals.

She did not appear to be
progressing with LIq. Arsenical, so
that was stopped and she was given
six weekly injections of sulfasemol in doses of 0.3 to 0.6 gm. The red count slowly improved. There was a considerable change for the better in her mentality and her colour began to improve. She often had attacks of nausea but no diarrhoea. She had all her teeth removed in two stages.

She had no numbness or tingling of the fingers. Her temperature was settled all the time.

She began to walk three months after admission, but could never do much without support.

Fig. 9. Arsenicals was stopped and restarted at intervals in doses of \( m \text{m} \) to \( m \text{iv} \) t.d. This was later combined with ferri et arsen. Cit. gr. 1 and to Nuci. Vom. \( m \text{x} \) to the 3p Ag. Chlophormis.
When last seen her condition was stationary and strongly suggested aplastic anaemia.

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C. S.</th>
</tr>
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<tbody>
<tr>
<td>21.1.25</td>
<td>1,170,000</td>
<td>35%</td>
<td>1.03</td>
</tr>
<tr>
<td>27.2.25</td>
<td>1,940,000</td>
<td>35%</td>
<td>.92</td>
</tr>
<tr>
<td>27.3.25</td>
<td>1,810,000</td>
<td>35%</td>
<td>.97</td>
</tr>
<tr>
<td>24.4.25</td>
<td>2,940,000</td>
<td>45%</td>
<td>.77</td>
</tr>
<tr>
<td>1.6.25</td>
<td>2,710,000</td>
<td>45%</td>
<td>.83</td>
</tr>
<tr>
<td>7.7.25</td>
<td>3,010,000</td>
<td>45%</td>
<td>.66</td>
</tr>
<tr>
<td>17.8.25</td>
<td>2,940,000</td>
<td>50%</td>
<td>.86</td>
</tr>
</tbody>
</table>

A film taken on the day of the last blood count showed poikilocytosis and anisocytosis, occasional megalocytes, no normoblasts.

When last heard of, this patient was getting worse. Her general condition was improved in a manner corresponding to the red cell count.
Case 3.

William Burgess aged 59 Labourer

Admitted 22.1.25
Discharged 16.5.25.

Patient gave a history of four months duration of symptoms; his main complaint was increasing weakness and shortness of breath.

On admission he was very pale but not lemon-yellow in colour.

He had a small, quick pulse regular in time and force. The apex beat was hardly visible or palpable. Heart sounds were heard in all areas.

He had very bad hypothena; the tongue was pale and smooth but showed no ulcers.

There was no complaint of tingling of the fingers.

The Wassermann report was negative.

A test meal showed no free HCl.
a very low total acidity, no lactic acid and no Bos. Ophii bacilli.

He was given 3 g. America; m. ii. for one week; m. iv. for three weeks; m. v. for one week (all t. i. d.) but as he showed signs of intolerance, the dose was reduced to m. iii. t. i. d., the dose being occasionally stopped for a week.

He gradually increased in strength; he had his bad stumps extracted under local anaesthetic.

Acid hydrochloric 3% was given in 3½ doses in 3vi. lemon water t. i. d. with meals, but the patient found this was rather too bitter for him.

On admission he showed

R. B. C. 1,100,000
Hb 30%
C. S. 1.3
W. B. C. 4,800.

The film was a very characteristic one.
The red cells were rather larger than normal; there was marked poikilocytosis and anisocytosis; some polychromasia, megaloblasts, normoblasts and megalocytes; granular degeneration was seen.

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C.S.</th>
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<tr>
<td>22.1.25</td>
<td>1,100,000</td>
<td>30%</td>
<td>1.3</td>
</tr>
<tr>
<td>4.3.25</td>
<td>2,200,000</td>
<td>45%</td>
<td>1.02</td>
</tr>
<tr>
<td>25.3.25</td>
<td>2,800,000</td>
<td>45%</td>
<td>.8</td>
</tr>
<tr>
<td>22.4.25</td>
<td>2,630,000</td>
<td>50%</td>
<td>.9</td>
</tr>
<tr>
<td>13.5.25</td>
<td>2,760,000</td>
<td>50%</td>
<td>.9</td>
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</table>

He did not show much improvement in the last two months, but he was very much better than on admission.

He went out at his own request, being able to walk about and do light work.
Case 4.

Elizabeth Thorpe aged 34, Metal-Worker.

Admitted 31.3.25


Patient had had influenza twice in the previous twelve months. No history of excessive loss of blood.

Two months prior to admission she had to give up her work owing to weakness of legs—there was no swelling of the legs. She went to Southport to convalesce but did not improve. She had become very pale the night prior to admission she complained of feeling queer, did not recognize her relatives and became gradually unconscious. There was no history of drug-taking.

On admission she had a pulse-rate of 92, a temperature of 99.5 and respiration 22. She was of a pale lemon yellow colour, had constant twitching of the
fingers and would not lie still. She threw her arms about and kept shouting
"Oh my God" Oh mamma", but would not answer questions.

The pulse was regular in time and force: systolic limits were heard
in all areas.

The tongue was pale, furry, not trembling, striated transversely. Both upper
and lower denture, more artificial.

Abdominal reflexes were not elicited but otherwise the reflexes were
normal. Plantar response was flexor.

The urine was pale and of a

low specific gravity

She had a rickety rt. knock-knee.

The Wassermann report was negative.

Test meal showed no free HCl, total acidity 2 c.c. 7/10 NaOH %. and

traces of lactic acid

2:425. She recovered her senses and

appeared rational - she complained of
much pain in the bottom of the back.

The R.B.C. was 1,120,000. p.c. cmm.

Hb. 30%  
C. F. 1:34.  
W.B.C. 5,600 p.c. cmm.

The film showed poorly-stained red cells, slightly bigger than normal, marked polikilocytosis and anisocytosis, normoblasts, megalocytes, but no megaloblasts. The white were well-stained and present in normal proportion.

She was given Fig. Arsenicalis miv t.i.d. and Acid Hydrochloric acid 3 1/2 in 3 1/2 fl. Ag. lemonis t.i.d. with meals. The arsenic was increased up to miv t.i.d. for one week. She then had a six weeks course of sulfanenol in doses of .24 gm. to .42 gm. The fig. Arsenicalis was restarted 26-5-25.

The temperature was unsettled for six weeks but thereafter was subnormal.
She had numbness and weakness of both hands, from the beginning; weakness of the legs gradually improved, so that by 25.8.25 she was walking with the aid of a stick, and could actually manage a few yards without a stick. The tongue occasionally became very tender — this symptom disappeared if the lig. arsenicalis was stopped.

R.B.C.  N.  C.  S.
2.4.25  1,120,000  30%  1.34.
12.5.25  1,690,000  45%  1.33.
9.6.25  3,070,000  55%  .90.
7.7.25  3,840,000  65%  .85.
25.8.25  4,460,000  75%  .86.

The film of 25.8.25 showed no trace of pernicious anaemia.

In the six months she was under observation, this patient improved amazingly — so much so that one almost doubted the diagnosis. However, she gradually weakened again and in
a few months was again profoundly anaemic. She lingered some months but was obviously becoming weaker.

When first seen she looked a typical case of pernicious anaemia.

Six months later, no one seeing her for the first time would have diagnosed her as pernicious anaemia. The mental and physical improvement had to be seen to be believed. The color of the skin became pinkish white.

At first she was thought to be a case of hysteria but the blood findings negatized that diagnosis.

I think that in conjunction with the pernicious anaemia there was present a subacute combined degeneration of the cords, improvement in the one condition being followed by improvement in the other.
Case 5.

Thos. Jottesley, aged 60. Woolpuller.

Admitted 23.4.25

Discharged 4.7.25.

Patient had twice previously been in hospital with chronic bronchitis.

He complained of rheumatism of the left shoulder, cough and expectoration, vague pains in the chest, tiredness on exertion. He had been getting much worse in the previous six months.

He had a very pallor complexion but it was not lemon yellow. His Wassermann report was negative. His mentality was sluggish; he had a double set of artificial teeth.

Fast meal showed no free HCl, a low total acidity, lactie acid present, no Box, of Leu. bacilli.

He was put on Lig. Americana.
in doses from m" to m" 3rd with an occasional week's rest, coupled with Acid Hydrochlor 8il 3 to 4th with meals, diluted with 3° Ag. hemorhous.

His colour definitely improved. He ceased to show tingling of the fingers and his appetite returned; his general condition became very much improved.

<table>
<thead>
<tr>
<th>Date</th>
<th>RBC</th>
<th>Hb</th>
<th>C. F.</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.4.25</td>
<td>2,140,000</td>
<td>50%</td>
<td>1.16</td>
</tr>
<tr>
<td>24.6.25</td>
<td>3,260,000</td>
<td>70%</td>
<td>1.08</td>
</tr>
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</table>

The blood film of 24.4.25 showed marked poikilocytosis and anisocytosis, with nucleated reds; megalocytes, but no megaloblasts, were present. The film of 24.6.25 showed great improvement in the shape of the red cells, and
no nucleated reds were seen.

I think this was an early case of pernicious anaemia.

Case 6.

Alice Kellett aged 46, housewife

Admitted 25.4.25

Discharged 8.5.25.

There was no history of previous illness.

Patient gave a history of tiredness, shortness of breath, numbness of fingers and four months anaesthesia.

Her pulse was rapid, temperature and respirations normal on admission. She appeared well-nourished but was in reality flabby - she was puffy under the eyes and of a distinctly lemon-yellow colour. There was no oedema.
Systolic bruits were heard in all areas; the apex beat was three inches from the mid-line.

She had a poor appetite. Her teeth had been artificial for twenty years. The tongue was moist, smooth and trembled considerably; there was no ulcer.

Tingling and numbness were felt in both sets of finger tips. The pupils reacted and the knee jerks were present.

The Wassermann report was negative. Fast meal showed no free HCl; a low total acidity; no lactic acid and no Baeillus Bacilli.

R.B.C. 1,440,000 per cmm.

Hb 40%

C. A. 1.39

W.B.C. 4,200 per cmm.
The blood film showed the red cells on an average to be somewhat larger than normal. Anisocytosis and poikilocytosis were marked: no polychromasia: normoblasts and megaloblasts were present, along with megalocytes. The white cells were well stained and present in normal proportions.

She was put on B. trivalent in 3/4 T.D., and acid hydrochloric 3 T.D., but insisted on going home, against medical advice.

I was unable to follow up his case, but she was almost certainly a case of pernicious anaemia.
Case 7.

Wm. Richardson, aged 57, labourer.
Admitted 9.3.25
Discharged 22.6.25

No history of previous illness was given.

For a month prior to admission he had complained of weakness, loss of appetite, loss of weight, oedema of ankles, constipation; no vomiting and no tingling of the fingers.

On admission the pulse, temperature and respirations were normal. The skin was dry and very lemon yellow.

Haematochromatosis was present in all areas. The tongue was coated, moist, not tremulous and showed no ulcers. Pyorrhea was very marked. There was
cutaneous hyperesthesia in the right hypochondrium.

The pupils reacted to light and the knee-jerks were present but sluggish.

The Wassermann report was strongly positive.

There was no occult blood in the stools.

Test meal showed no free HCl and no B. Opper. Bacilli.

The temperature varied from 98° to 100°.

He was given Acid Hydrochlor.

kil 3½ H.R. and sulfasoxazole 4.5gm. weekly intramuscularly.

<table>
<thead>
<tr>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C. I.</th>
<th>W.B.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.5.25</td>
<td>1,825,000</td>
<td>40%</td>
<td>1.1</td>
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<tr>
<td>19.6.25</td>
<td>2,520,000</td>
<td>55%</td>
<td>1.08</td>
</tr>
</tbody>
</table>

Blood films of 9.5.25 showed red cells somewhat larger than normal. The cells were poorly stained. There was...
matured amicrocytes but not
matured poikilocytes; normoblasts and
megablasts were seen but no
megablasts.

He was discharged at his
own request, and I was unable to
follow his progress.

He was thought at first to be
an example of specific secondary
anaemia, but the blood examination
was against this, and strongly in favour
of pernicious anaemia.

Case 8.


Admitted 14.5.25

Died 3.6.25.

He gave a vague history of gastritis,
twelve months before admission.
The patient gave a six weeks' history of vomiting and loss of appetite. The vomit was never coffee-ground and always painless. There was no jaundice and no constipation.

On admission, his pulse, temperature, and respirations were normal. His skin was very lemon-yellow in colour and showed old scarring round the knees.

There were no haemorrhoids.

The tongue was dry and pale but not tremulous and showed no ulcers. Pectoriloquy was bad. There was some tenderness in epigastrium, but no abnormal swelling could be felt. The pupils were equal and reacted to light and to accommodation. The knee jerks were sluggish.

The Wassermann was strongly positive.
Test meal showed no free HCl and no Boas typhoid bacilli.

<table>
<thead>
<tr>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C.S.</th>
<th>W.B.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-8-25</td>
<td>1,720,000</td>
<td>40%</td>
<td>1-2</td>
</tr>
</tbody>
</table>

Blood films showed large poorly-stained red cells, marked poikilocytosis, and anisocytosis, normoblasts and megaloblasts but no megaloblasts.

Vomiting ceased after admission but there was no general response to Acid Hydrochloric Oil and Pot. Iodid in gr. 3 doses t.i.d.

In this case specific secondary anaemia and carcinoma of the stomach were excluded by the findings in the blood. These were not typical, but sufficiently characteristic to warrant a diagnosis.
Case 9.

Elizabeth Jagger aged 68. Housewife.

Admitted 27.5.25

Discharged 8.8.25.

Patient gave a history of asthenics twenty years ago.

Present symptoms had lasted for four months. She had vomiting, flatulence, constipation, weakness, swelling of ankles on exertion: she had lost four stones in weight: there was no tingling of the fingers or toes.

On admission the pulse, temperature and respirations were normal. Skin was very lemon yellow.

Systolic bruits were heard in all areas; the apex beat was not displaced outward.

The tongue was clean, pale and moist. Of the teeth, only one natural stump was left. There was
slight tenderness-and deep resistance in epigastrium. The lower border of the stomach was two inches below the umbilicus.

There was no difficulty in walking and no abnormality in the reflexes.

The urine was pale and of low specific gravity.

The Wassermann report was negative.

Feast meal showed no free HCl.

A Bismuth meal was given and, apart from spasticity of the small bowel, no abnormality was observed.

The temperature remained settled.

She was put on increasing dose of Hyd. Arsenicalis up to \( \text{miv} \) tid, then reduced to \( \text{miv} \) tid.

with occasional rest of one week. The Acid Hydrochloric Sul was given concurrently.
With the increase in the red count the condition of the skin gradually became normal and no discharge she had quite a definite malar flush. Her appetite improved, she did not vomit after admission. She was discharged at her own request.

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C. I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.5.25</td>
<td>1,380,000</td>
<td>35%</td>
<td>1.3</td>
</tr>
<tr>
<td>20.6.25</td>
<td>1,810,000</td>
<td>55%</td>
<td>1.5</td>
</tr>
<tr>
<td>25.7.25</td>
<td>2,660,000</td>
<td>55%</td>
<td>1.04</td>
</tr>
</tbody>
</table>

Blood films of 28.5.25 showed fairly well stained large reds, polychromasia, well marked poikilocytosis and anisocytosis; occasional megaloblasts; normoblasts and megalocytes common. The white cells were well stained and present in normal proportions.
Case 10.

George aged 49. Lead worker.

Admitted 3-6-25
Discharged 18-8-25

Patient gave no history of previous illness.

He had not walked for ten weeks.

One day while picking up lead ingots he suddenly felt faint — he did not lose consciousness — he felt his legs numb, and felt as if he were walking on broken bottles.

He had constipation for a week before admission; he had no increased frequency of, or pain on, micturition.

On admission he complained of numbness and tingling of the soles.

He had partial impairment of sense of touch, and power of discriminating between heat and cold. There was no wasting and no hypesthesia. The
Impairment of touch was most marked on the outer aspects of both legs below the knees. The abdominal reflexes were lost, the knee jerk was exaggerated, and the pupillary reactions were normal.

The heart and lungs were normal.

There was a marked itchy discoloration in perineum — the skin here was almost black.

The Wassermann was negative.

Radiograph of the long spine, processes, and vertebrae showed no evidence of tumor or other abnormality.

No lead was found in a chemical analysis of the urine.

The cerebrospinal fluid showed less than 5 cells per cmm, the globulin content normal, and the Wassermann negative.
Test meal showed no free HCl, very low total acidity, lactic acid present and Buns off pH Bacilli absent.

R.B.C. Hb. C.S. W.B.C.
3,180,000 70% .9 3,200.

Blood films showed slight poikilocytosis and anisocytosis and relative lymphocytosis.
He was given Acid Hydrochlor. B12 i/p t.d. with meals and a mixture containing Hg Amebicis, Feri et Amnon Cit, and Fr Nucie Yon.

He went home at his own request feeling very much better and able to walk about with the aid of a stick.

This was, I think, a case of subacute combined degeneration of the cord with early symptoms and signs of pernicious anaemia.
Case II.

James Smith, aged 69, Hawker.
Admitted 1-9-25
Died 12-9-25.

Patient had been in hospital three times in the two preceding years, being treated for bronchitis, ulcerated legs and anaemia. He had had a rodent ulcer of the left cheek which had healed with repeated applications of X-ray treatment.

When admitted he had severe diarrhoea and was getting weaker each day. The Widal reaction was negative.

<table>
<thead>
<tr>
<th>Date</th>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-4-25</td>
<td>1,930,000</td>
<td>40%</td>
<td>1.05</td>
</tr>
<tr>
<td>2-9-25</td>
<td>1,540,000</td>
<td>40%</td>
<td>1.29</td>
</tr>
</tbody>
</table>

Blood films showed a typical pernicious anaemic appearance.
Case 12.  

Annie Lambert, aged 43, Weaver.

Patient is at present under observation, she gave no history of previous illness. She was very well and at work till three weeks ago when she began to complain of tingling of fingers, but not of the toes. She noticed herself getting pallid and felt very weak—she had only been in bed the previous two weeks.

On admission she had an evening rise of temperature, the pulse was rather rapid, the respirations normal. Breath murmurs were heard all over the heart.

She was lemon-yellow in colour and had somewhat swollen legs. The tongue was pale and moist but no ulcers were seen. The speech was very monosyllabic.
The Wassermann reaction was negative.

Test meal showed no free HCl.

<table>
<thead>
<tr>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C.S.</th>
<th>W.B.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>980,000</td>
<td>25%</td>
<td>1:3</td>
<td>5,300</td>
</tr>
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</table>

Blood films showed the most typical appearance of pernicious anaemia I have seen. Megaloblasts were common as also were megalocytes.

She was put on Ag. arsenicæ mii t.i.d., increased daily to miv t.i.d., and reduced to miv t.i.d.

The acid hydrochloric oil in 37½ dose diluted with 3/1 Ag. Leucon was given concurrently.

The patient is at present in a convalescent home and is improving, both mentally and physically.
Case 13.

George Owen 68 Railwayman

No history of previous illness was forthcoming.

Patient had been feeling out of sorts for the last four months. At first he began to get tired easily and his ankles swelled on slight exertion. He had occasional vomiting and vague pains in the epigastrium accompanied by flatulence. He had no tingling of the fingers or toes.

The pulse, temperature and respirations were normal. His pallor became more marked.

The Wassermann report was negative.

Test meal showed no free HCl and a very low total acidity.
R. B. C.  Hb.  C. S.  W. B. C.
960,000  28%  1.5  4,400.

Blood films were again very typical of pernicious anaemia - megaloblasts were fairly common.

Treatment by big Amanichi and Acid Hydrochloric Oil produced no response - the patient was obviously dying - he became gradually weaker and was dead within a month of being seen.
Case 14.

Woman aged 37. Housewife.

Patient stated she had been in poor health for five years. Four years previously she had been in the R.I.E. for one month with symptoms of breathlessness, loss of weight, swelling of ankles and tiredness on exertion.

These symptoms had all recurred and in addition she had pigmentation of the back of the hand and on the face but not inside the mouth.

The Wassermann report was negative.

Test meal showed no free HCl.

The blood pressure was 96 - 64. but the pulse rate was not abnormally rapid.

<table>
<thead>
<tr>
<th>R.R.C.</th>
<th>Hb.</th>
<th>C.F.</th>
<th>W.R.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,300,000</td>
<td>20%</td>
<td>1.2</td>
<td>5,000</td>
</tr>
</tbody>
</table>
Blood films showed a fairly typical appearance of pernicious anaemia except that no megaloblasts were seen.

The differential diagnosis, which will be discussed later, lay between Addison's Anaemia, Addison's Disease, Secondary Anaemia and Pellagra.

System affected by Pernicious Anaemia

Digestive System

The lips are always pale and smooth and usually dry. The gums are always pale, smooth, and moist. No stomatitis is seen and no history of stomatitis given.

Seven of my cases showed marked photophobia, or had bad stumps.
Generally speaking the teeth were not suitable for mastication.

The tongue was always pale, flabby, trembling, very sensitive and occasionally fissured. The epithelium was atrophied and devoid of papillae. No ulcers were seen at edges of tongue.

Apart from the appearance of ulcers, the tongue has a similar appearance in all cases of prolonged anaemia. I saw the "anaemic" tongue very well-marked in a lad of nineteen, who had had repeated attacks of haematemesis, bringing his red cells down to 920,000 per cmm., and haemoglobin to 20%.

Vomiting is not a common symptom, but on the other hand may be one of the first symptoms. It is associated with nausea and a
vague feeling of being unwell. It usually occurs shortly after taking food, and is almost entirely undigested food plus gastric juices.

No haematemesis occurred in my series of cases.

Flatulence is never troublesome.

Pain in abdomen frequently occurs, preparatory to vomiting. Three of my cases complained of pain in the epigastrium and rt. hypochondrium but it was usually vague and with no definite relation to the taking of food.

Case 1. had an attack of pain in the epigastrium which closely resembled perforation of a gastric ulcer. The latter was however, negativised by a post-mortem examination a few days after the attack when nothing was found to
account for the pain. No textbook on the subject records the occurrence of such attacks (as far as I know) nor have I heard of a similar attack described elsewhere.

No fractional test meals were done — these were not the facilities.

Every case of pernicious anaemia shows no free HCl in the stomach contents, and the total acidity is always low. This was borne out in all my cases. Several showed Boro-Offler bacilli but the finding of these is not regarded nowadays as of much importance in diagnosing carcinoma of the stomach.

The weight usually remains fairly constant. Pernicious anaemia does not produce cachexia.

Diarrhoea is occasionally a
prominent symptom and is very difficult to stop - a case I had showed no response to Bismuth and Catechu.

Constipation is not a marked symptom.

Melaena occurs very seldom and makes one naturally doubtful about the diagnosis. Case 12. had two attacks of slight melaena; yet I am convinced she has pernicious anaemia.

None of my cases showed tarry - red stools; I think these are the exception rather than the rule. No parasites (tape - worms etc...) were found.
Cardiovascular System

Osler described the pulse as usually full and bounding. In my cases it was always easily compressible and regular in time and force.

Generally the apex beat was normal in position and was localized. No thrill was felt: there was no precordial or anginosus pain. Haemie bruits were heard best at the base—no diastolic bruit, were heard.

Oedema of the ankles was only present if the patient had been walking about.

There was often dyspnoea, worse at night, but no cyanosis.

The superficial veins were prominent.

Repeated haemorrhages are incompatible with the disease.

In ten examinations no retinal haemorrhages were seen.
**Respiratory System.**

No signs of pulmonary disease, except chronic bronchitis, were found during the illness.

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**Genito-Urinary System.**

The urine was pale and of a low specific gravity. With rises of temperature there were often deposits of urates. Many of the cases were on a very meagre diet, yet showed no acetone in the urine.

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**Vaso. Motor System.**

No trophic sores were found. In every well-made case the temperature was unsettle: it never went above 101° and as a rule
varied between 97° and 99.5°. This was particularly true in cases of recent onset. The elevation of temperature was usually only observed at night and was generally accompanied by slight sweating.

\[\text{Integumentary System}\]

In a typical case the lemon-yellow tint of the skin is most characteristic. Conditions simulating this colour are (1) a mild or disappearing obstructive jaundice, (2) acholic jaundice and (3) Addison's Disease. These will be discussed later under "Differential Diagnosis".

The skin changes gradually from its normal pinkish-white colour to a faint yellow, and ultimately a lemon-yellow with a blanched, smooth, and
Waxy appearance: as a rule the skin is moist.

The whites of the eyes become pearly, and the lips, gums, and tongue are bloodless.

Cases have been described in which there is pallor without lemon yellow pigmentation—these cases strongly resemble cancerous cachexia.

If the patient improves under treatment, the skin shows it by becoming more natural in colour: the colour of the skin is frequently taken as an index of progress.

No typical lemon-yellow colour is seen unless the red cells are less than 2,000,000 per cmm; but the colour may be suspicious with a count of 3,000,000 per cmm.
Nervous System.

The memory is always good for recent events, but often poor for less recent. Sleeplessness is always complained of; patient usually state that they are "too tired to sleep."

Speech is usually slow and syllabic just like in disseminated sclerosis - this is very interesting in view of the association of subacute combined degeneration of the cord with pernicious anaemia.

Here is usually no abnormality of smell.

Many patients have muscle volitantes - little specks floating before the eyes, but as this is common in most severe anaemia it is of no real significance.

No retinal haemorrhages were seen in this examination. Pallor of the optic discs was observed.
As estimated by the dynamometers and exercises there was muscular weakness in all patients. Paresis may occur but not paralysis.

The tongue is very sensitive to hot drinks and to painful stimuli. Tingling and numbness of the fingers is a common complaint—it is only very occasionally that one gets tingling of the toes.

Pain is usually only felt in the abdomen; it has already been discussed under the heading of "Digestive System."

The reflexes are generally present but sluggish.

A positive Wassermann was found in two cases; but the blood count in these cases was that of a pernicious anaemia, not the secondary anaemia of syphilis. As a
general rule pernicious anaemia is not associated with syphilis, but it is quite possible that syphilis may be present prior to, and concurrent with pernicious anaemia. It has never been held that syphilis is a cause of pernicious anaemia.

The association of pernicious anaemia with subacute combined degeneration of the spinal cord will be dealt with later, under the heading of "differential diagnosis."

Haemopoietic System

Before patients come under observation the disease is so far advanced that the red blood count is very much below normal.

Apart from the case of subacute combined degeneration the highest count on admission was 7,140,000 per cu. mm. and the lowest 840,000 per cu. mm.
In typical cases the red blood count was always under 1,500,000 per cmm. and the haemoglobin percentage sufficient to make the color index between 1.0 and 1.6. As improvement set in, the red blood count gradually increased, and the haemoglobin increased, but not in the same proportion as the red cells so that the color index fell to 1.0 or below it.

In Case 4. compare

<table>
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<tr>
<th>R.B.C.</th>
<th>Hb.</th>
<th>C.I.</th>
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<tbody>
<tr>
<td>1,120,000</td>
<td>30%</td>
<td>1.34</td>
</tr>
</tbody>
</table>

and 4,460,000 | 75% | 0.86 |

An improvement in the blood is always followed by an improvement in the general condition, which manifest itself objectively by a healthier skin, more rational mentality, and a greater aptitude for work.
The white cell count can never be regarded as of much significance in pernicious anaemia. It is always low in marked cases of secondary anaemia or pernicious anaemia—anything from 3,500 to 8,500 per cu. mm. is met with in severe anaemias. The differential count is of some significance since the small lymphocytes frequently number as many as 70% of the total white cells, the remainder being largely polymorphs. I have never seen any myelocytes in a pernicious anaemia film.

In staining thin blood films I always used one of two stains

1. Leishman—as recommended by Leishman.

2. Jenner-Giemsa—one minute of Jenner stain followed by fifteen minutes 10% Giemsa stain. Two minutes
immersion in distilled water; dry with filter paper.

Of the two stains I prefer the leishman—
it has always been very satisfactory.
The Jenner-Giemsa stain stains the
white cells relatively better than the
red cells, and is consequently more
use in a leukaemia.

A characteristic leucemic anaemia
film shows:
(1) red cells on an average larger than normal
(2) marked anisocytosis
(3) marked poikilocytosis
(4) polychromasia
(5) granular degeneration of red cells
(6) megalocytes from 12–18 μ in diameter
(7) nucleated reds
(8) absence or diminution of blood platelet

In many cases, even after frequent
examinations, no nucleated reds can be seen.
(like tubercle bacilli in the sputum)
Sometimes they only appear during blood crises i.e. a throwing into the blood stream of numbers of nucleated reds followed by an increased red cell count. Blood crises are seldom seen and are generally of bad prognostic significance—frequently they occur within a few hours of death.

I have not seen nucleated reds with a count of 2,000,000 per cmm or over, but they have been described as occurring.

Nucleated reds when present occur in one of two forms—normoblasts and megaloblasts. In some cases there appears to be a cell almost intermediate in size. A normoblast is usually somewhat larger than an erythrocyte and oval shaped, with a rounded homogeneous nucleus.
A megaloblast on the other hand is usually rounded, averages 15-20 μ in diameter, and contains a nucleus which is rounded but not necessarily homogeneous in nature - it very often shows karyokinesis.

A bad prognosis is always associated with the presence of a relatively large number of megaloblasts, particularly if these exhibit karyokinetic nuclei.

Megaloblasts are not seen if normoblasts are not seen.

Blood platelets are much diminished in number and poorly-stained.

None of my cases showed any pathological enlargement of lymph glands or spleen. Case 16 was suspected of having an enlarged spleen but the edge was not definitely palpated.
Course and Prognosis.

If the patient had been longer under observation one would have been able to see the relapses and remissions so common in the disease before the fatal termination. That the condition is fatal I have not the slightest doubt. Great expectations are often raised by a apparent improvement but this is always only temporary; a sudden improvement is often followed by a sudden relapse, and each relapse is generally worse than the preceding one.

My cases were unfortunately not long enough under observation to make the study of their progress of much practical value.
At least five of the cases have died. Four of these five showed no attempt at improvement, but case 4 showed very marked improvement up to the time she was last seen.

<table>
<thead>
<tr>
<th>Course</th>
<th>Case Number.</th>
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</tr>
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<tbody>
<tr>
<td>Stationary</td>
<td>2. 6. 7.</td>
<td>3</td>
</tr>
<tr>
<td>Bette</td>
<td>10. 12. 14.</td>
<td>3</td>
</tr>
<tr>
<td>Much Bette</td>
<td>3. 5. 9.</td>
<td>3</td>
</tr>
<tr>
<td>None</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Died</td>
<td>1. 4. 8. 11. 13.</td>
<td>5</td>
</tr>
</tbody>
</table>

Of the stationary cases Case 2 improved up to a point, but her red cell count seldom exceeded 3,000,000 per cmm. She had developed aplastic anaemia and her marrow
could not respond to treatment.

Case 13 had only a white cell count of 4,400 but the differential count showed 85% small lymphocytes; he was dead in a month.

Case 1 had severe epigastri pain and died three days later. Case 8 had marked vomiting; Case 11 had severe diarrhoea.

From personal observations I consider a bad prognosis justifiable in cases where any of the following are found:

(a) Acute onset of illness
(b) Red cell count below 1,000,000 per cmm
(c) Presence of many megaloblasts
(d) A colour index of 1.5 or over
(e) Differential white cell count showing 80% or more small lymphocytes
(f) Blood crises
(g) Patient showing intolerance to arsenic
(h) Severe gastro-intestinal symptoms
Differential Diagnosis

The common conditions which may simulate pernicious anaemia are:

1. **Secondary Anaemia** (e.g. from haemorrhages, suppurations, tuberculosis, syphilis, etc.)

2. **Chronic Nephritis**

3. **Carcinoma of the Stomach**

4. **Mild or Early Jaundice**

5. **Heart Disease**

6. **Pregnancy - Jaundice**

7. **Parasitic Infections**

The uncommon conditions which may simulate pernicious anaemia include:

1. **Addison's Disease**

2. **Acholuric Jaundice**

3. **Subacute Combined Degeneration of the Cord**
I should think that there are at least ten cases of secondary marked anaemia to every one case of pernicious anaemia.

A patient with secondary anaemia usually can give a causal history e.g. menorrhagia, haematemesis, injury etc. In appearance he is pallid but not yellowish; his symptoms are almost exactly those of pernicious anaemia—tiredness, sleeplessness, headaches, palpitations, inability to concentrate, swelling of the ankles etc.

In the absence of any definite history of haemorrhages it is often difficult to differentiate between the two conditions without doing a blood count. The haemoglobin percentage is of tremendous importance in making a diagnosis — it is relatively high in
hemonicous anaemia, and relatively low in secondary anaemia, so that a high colour index is got in the former and a low colour index in the latter. Secondary anaemia responds well to treatment with iron; hemonicous anaemia does not respond well to treatment with iron unless it is combined with arsenic, and then it is probably the arsenic which causes the improvement.

Poikilocytosis and anisocytosis are common in marked cases of secondary anaemia - they were very marked in the case of a boy with repeated haemorrhages from a gastric ulcer - but polychromasia is not as a rule seen. No granular degeneration of the red cells is seen. Hromoblasts are sometimes seen in secondary anaemia but I have not yet seen megaloblasts.
The white cell count in secondary anaemia varies according to the cause. In cases of chronic suppuration it is usually increased with a relative increase of the polymorphs. Generally speaking when the white cell count is normal or low in secondary anaemia there is a relative lymphocytosis.

The blood platelets are not scanty in secondary anaemia.

Chronic Nephritis.

Many cases of chronic anaemia show albuminuria and puffiness of face, hands, and abdomen. None of the present series of cases showed albuminuria.

Carcinoma of Stomach.

Cases of carcinoma ventriculi are frequently almost indistinguishable
From pernicious anaemia till a blood examination has been done. I had two cases in Bradford who both resembled pernicious anaemia very much. Each had marked pallor, no free HCl, and Boas apple bacilli in the gastric contents. (The latter are frequently found in pernicious anaemia.) The blood picture however was that of a secondary anaemia.

Three of my patients had pain in the epigastrum and at hypochondrium, but this did not come on after taking food. None of these cases showed haematemesis.

Cases of pernicious anaemia do not show wasting; the course is entirely different—remissions and relapses in pernicious anaemia, and a steady decline in carcinoma of the stomach.
Mild or Early Jaundice.

Mild or early cases are sometimes difficult to distinguish from pernicious anaemia without examining the blood. Usually the history of relatively acute onset in jaundice is helpful. Cases of obstructive jaundice can be separated from cases of haemolytic jaundice by means of the Van den Bergh reaction.

The predominance of gastrointestinal symptoms and signs (e.g. flatulence, constipation, clay stools etc.) over cardiovascular symptoms and signs points to a condition other than pernicious anaemia.

The examination of the blood clinches the diagnosis.

Heart Disease

Heart disease often simulates...
premieric anaemia because of dyspnoea, palpitation, and oedema. Cases are always against premature anaemia unless in a very advanced stage prior to death.

The Premenier

Since taking charge of the Maternity Ward at Bexton Royal Infirmary I have been struck by the apparent resemblance of some women in the premenierium to premieric anaemia. They often showed a suspicious lemon-yellow colour but the blood picture was always that of a secondary anaemia. After a few weeks they lost their anaemic appearance.
Parasitic Anaemia

I believe the occurrence of parasites, and particularly tape-worms in the intestines is a common cause of anaemia, which may easily be overlooked or unsuspected. None of my patients showed parasites in the stool.

Addison's Disease

A typical case of Addison's disease is readily distinguishable from Addison's anaemia, but border-line cases present some difficulty. Case 14 was a case of this kind - she had obvious anaemia but also dark brownish patchy pigmentation of the back of the hands, forearms and face, but not inside the mouth. In Addison's disease the pigmentation is usually present on the mucous membrane of the mouth and
vagina.

The blood pressure was systolic 96 mm.
and diastolic 64 mm, but the pulse was
not unduly rapid.

Muscular fatigue is more marked
in Addison's Disease, and wasting is a
prominent sign, as opposed to the
apparent gain in bulk seen in
pernicious anaemia.

**Acholuric Jaundice.**

While in Bradford I had
under observation a nurse with the
recognised type of acholuric jaundice.
About a year before she had had a
splenectomy performed - the spleen was six
times the normal weight. Temporary
improvement followed, but she returned
to hospital during my term of
residency looking like a case of
pernicious anaemia. She was markedly
deleter yellow in colour, flabby, and
suffered from dyspnoea, palpitations
and swelling of the ankles. The blood
films were typical of pernicious anaemia
-all the characteristics described on page
64—were seen. The red cell count varied
between 1,000,000 and 1,500,000 with a
colour index of 1.3 to 1.6; the red cells
were found to be abnormally fragile.

It was thought that she might
have developed an auxiliary spleen;
a laparotomy was performed but no
auxiliary spleen was found; there was
generalised tuberculous peritonitis; she
died a few months later.

If I had seen this patient
for the first time with no knowledge
of her previous history I should have
diagnosed her as a definite Addison's Anaemia.
Subacute Combined Regeneration of the Cord.

Cases 4 and 10 were both examples of this disease; both came directly under observation for their nervous symptoms. No patient under observation for anaemia, developed symptoms of subacute combined degeneration; according to Rice this latter is never seen.

Case 4 had a typical pernicious anaemia blood count and appearance. Case 10 had a count of 3,180,000 per cmm, Hb 9 70%, and a color index of 0.9. The white cell count was only 5,200 per cmm but showed a relative lymphocytosis.

I have been unable to trace the progress of Case 10. Case 4 died.

A typical case looks anaemic - a biscuit coloured skin is often
described - the same colour of skin as improving cases of anaemic anaemia show. This colour, in association with peripheral subjective sensations, slight spastic ataxy followed by flaccid ataxy, loss of muscular power, the appearance of the blood, a negative Wassermann, and the absence of free HCl from the stomach contents, usually makes a diagnosis fairly secure.

Such authorities as Galland, Collie, Hurst, and Price are agreed that there is a definite relationship between subacute combined degeneration - the anaemic spinal disease - and Addison's Anaemia. The progress and prognosis of the two conditions are alike, and the treatment of the anaemia is practically the treatment of the degeneration.
Treatment.

The treatment which was adopted as a routine with the cases was:

1. Rest in bed
2. Light nourishing digestible diet
3. Arsenic
4. Acid Hydrochloric acid
5. Attention to teeth

(1) Rest:

The rest in bed was of very great importance, particularly if the patient happened to be running a temperature. I always tried to keep patients in bed till the red cell count was at least 2,000,000 per cmm, but several objected, on the ground that they had walked in, and were therefore fit to walk about.
In one case the rest in bed was continued for about five months it was noticeable that no patient, in spite of his or her weakened state, developed bed-sores.

(2) Diet

On admission the patient found it difficult or impossible to take even a light diet. After giving Acid Hydrochloric Oil, it was found that they tolerated toast, eggs, tomatoes, fish, chicken, rabbit, tripe and vegetables very well indeed.

I found it of the utmost importance to keep the patient’s bowels moving; while constipation was complained of, I gave calomel gr. ii in four gr. i doses at night, followed by a saline (Mag. Sulph. 3p) in the
morning.

The patient was encouraged to drink with their meals.

(3) Arsenic.

Arsenic is still considered the sheet-anchor drug in chronic anaemia. I found (using the Hig. Arsenicalis) that it worked best starting with m i or m iii doses thrice daily, increasing m i thrice daily weekly till a limit of tolerance had been reached. No patient ever received more than m ix thrice daily. When signs of overdosage appeared the dose was reduced to three-quarters of the limit dose thrice daily.

The Hig. Arsenicalis was stopped at intervals for a week at a time.
Occasionally it was observed that
the patient's condition was more or less
at a standstill. Under these
circumstances the big. Arsenicalis was
stopped and sulfasemol given in
.24 to .6 gm weekly intramuscular
injections.

I have been struck by the
improvement which follows these
injections; while I do not believe
that sulfasemol can entirely replace
big. Arsenicalis, I do believe that it
is of great help in stationary cases.

I have no experience of
sodium arsenate, novarsenobillon or
other arsenical preparations.

A patient benefit considerably
if the big. Arsenicalis is combined
with iron, e.g. in the form of
Jeni et Amman Cat, Mr Bland etc.
The iron increases the haemoglobin percentage, the arsenic acts directly on the bone
marrow of the long bones, stimulating it to increased blood forming activities.
I have used extract of bone marrow,
robolene, and Ovaltine, but have never
seen any marked benefit derived therefrom.

(4) Dilute Hydrochloric Acid.

Authorities differ as to the
dosage of Acid Hydrochloric. Dr. Hirst
recommended 3½p three daily diluted
with 3½q. Lemon, and taken with
meals. I have followed this
recommendation, routine. I have been
struck by the increased appetite of
a patient who had no Acid Hydrochloric
Oil formerly. This increase of appetite is
only to be expected when the absent
free hydrochloric acid is replaced by
hydrochloric acid in a concentration
conelponding to normality at mea1
times

In my opinion, Acid Hydrochloric
Dil is almost as important as
arsenic in the treatment of pernicious
anaemia. The patient is able to take
and assimilate more food and
develops an increased feeling of
well-being therafrom.

In three cases I found that
the concentration of hydrochloric acid
was too acid-tasting—under these
circumstances I diluted the hydrochloric
acid with 3 x Ap. lemonis and
obtained the desired effect.
(5) **Attention to Teeth.**

In a condition like precarious anaemia where the cause is unknown, any likely source of the disease should be thoroughly investigated, and if possible, eradicated. It is quite natural to suppose that pyorrhoea alveolaris, by reason of septic absorption, which reacts on the bone-marrow, may produce an anaemia. Whether one believes in this theory or not, pyorrhoea should be corrected or general principles in all cases — if necessary all teeth should be removed and artificial teeth used.

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**Special Treatment.**

None of my patients had splenectomy performed — only one case
showed a doubtful enlargement, so that
there was no apparent call for removal.

No transfusion was done.
Although we had two professional
donors in Bradford, I never recommended
transfusions, because I believe that
the improvement which follows is only
temporary, in some cases lasting
only a few weeks. At the same
time one must realise the value
of transfusion to a patient when it
is particularly important to keep
him alive a little longer.

In cases of subacute combined
degeneration, in addition to the routine
treatment already described I have
used such intestinal antiseptics as
naphthalene, dimol, and hexamin, plus
education of muscles, massage and galvanism.
Conclusions from these Observations

The cause of the disease is unknown.
The case of the disease is unknown.
An "acute" case means a bad prognosis
The diagnosis depends entirely on the examination of the blood.
A positive Wessermann does not negative
a diagnosis of pernicious anaemia.
The disease is most amenable to treatment in the early stages.
Arsenic must be combined with Acid Hydrochloric Acid to produce the maximum benefit.
I could find no evidence of hereditary transmission.

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