Observations on Myeloma with special reference to pathological conditions found in the leucocytes.

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Contents

Resumé of Subject of Myosotoma.  pag. 1.
   Case I.  .......................... 30
Clinical Cases
   Case II.  ......................... 32
   Case III.  ......................... 38
   Case IV.  .......................... 66

Examination of the Blood.
   Method of Examination  ......... 86
   Description of Elements. ...... 97
   Enumeration of Elements. ..... 115
   Conclusion  ........................ 121
Observations on Mynordema with special reference to pathological conditions found in the leucocytes.

The subject of Mynordema which I have ventured to bring before your notice has lately attracted much attention on account of the advances that have been made in its treatment. Having had rather exceptional opportunities of seeing cases both as a student in Edinburgh and whilst holding resident appointments in provincial hospitals, I have taken more than usual interest in the disease.

In my paper, I will attempt to give firstly a brief resume of the subject, secondly a clinical description of five cases and finally my observations on the leucocytes of the blood.
Myxodema was first recognised and described by Sir W. Peel [Clin. Soc. Trans. Vol VII. 1874] in a paper read before the Clinical Society of London as early as 1873. He describes it as a rare constitutional disorder without any internal visceral disease but characterized by great inconstancy to spontaneous elevation of both mind and body. The deposits of fat and changes in the connective tissue correspond to a languid condition of the nervous circulation but without any tendency to any phlegma or any signs of cardiac disease, and perceiving its similarity to the cretin state termed it tentatively rather than dogmatically a cretinoid condition.

First considering the whole of the symptoms were caused by or related to the jelly-like swelling of the connective tissue, proposed the term of Myxodema, as one
representing the condition, but not
an explanation of its cause.

Myxedema is a disease
affecting particularly, and for some
time thought exclusively, females,
but men are not altogether exempt,
and probably about 10% of the
cases occur amongst men.

Although it is most common
between the ages of 30 and 65, yet it
is by no means limited, and may
affect the young and aged.

Like other diseases it is no regarder
of persons, and as in many other
maladies, the poor are more often
affected than the well-to-do.

As to the Cause, little can
be definitely stated. It seems
to occur in more than one
member of a family, and some
claim heredity as a predisposing
cause, but whether it is handed
down by parent to offspring, or
whether the members of a family
are affected through being exposed
to the same surrounding conditions is still a matter of speculation. Several cases appeared to be hereditary. A certain number were preceded by hypertrophy of the thyroid, which disappeared later.


In some, the symptoms of myxodema have been preceded by enlargement of the thyroid, a case being recorded of myxodema consisting with syphilis and alcohol. [Med. Rec. New York, Sept. 13, 1890.]

Syphilis and alcohol may take a part in this, as in so many other diseases, but are probably not important factors in its cause. It has been found associated with tuberculosis.

Ammon used the cause suggested are - mental and emotional disturbances, frequent pregnancies, prolonged lactation.

Buzdilagian [Sapere 1892, Vol. IV, H.] recognizes a connection between the occurrence of myxodema and alterations in the
reproductive organs. Clarke [Edin. Med. Jbn. May 26, 91] reports the occurrence of Myxedema in hereditary insanity, and it is stated to have occurred after the long continued use of Peru cordials for another disease [St. John's Ld. 10, Jan. 1891].

Myxedema has been attributed to acute rheumatism, and is said to have followed excess in hemorrhage.

Myxedema is characterized by dilatations in the skin, hands, nose, and generally the mental condition. The face, in shape tends to be round rather than oval, is generally of a pale colour, with often a malar shade of a delicate rose-purple tint, contrasting with the surrounding pallor. The skin of the face is smooth, porcelainous in appearance, with soft fair complexion, and is often thrown into folds. The swelling of the face obliterate the
Tennis of expression.
The alar nasi broadened and flattened, causing the naris to appear wider apart than usual. The nostrils are swollen.
The maxillary sinus, thickened and bulging, translucent or waxy-looking, hanging down and almost covering the lips. The lower lid hanging down on to the cheek. They look redened and remind one very much of a case of renal dyspepsia, but do not pit on pressure.
The ephelides elevated so as to help support the ephelides.
The lips are thick, pendulous, flabby and swollen with often a blood colour. Sometimes allows escape of saliva.
The mouth expressionless, widened transversely, and slit-like, with lips parted together.
The general facial appearance is very characteristic. It is stupid, heavy, apathetic with total lack of
expression, the features appear coarse and sags and in fact cretinoid. There is often marked scantiness of the hair which is crisp dry and brittle. The scalp is scalp. Some cases (case 1) being almost completely bald. The head is sometimes hung down on the chin, and when elevated with difficulty, falls very much backward and to one side. 

There is usually blemish about the neck, and the skin is thrown into folds. The subcutaneous tissue and fat above the clavicle, seem to be increased. The thyroid is diminished in size, atrophied or completely wanting. 

The patients usually appear bulky massy. Their movements clumsy and awkward. Their weight is usually increased. The temperature is nearly always abnormal. 

The hands are described as pale.
like, but I fail to see how a thick broad hand resembles a glove.
The fingers are thick and awkward and ill fit for finer manipulation.
Their sense of touch is diminished; patients often say they cannot
see or execute finer movements as well as they could do. The whole
hand looks swollen and bulky and has lost much of its fine
comhens.
The nails are short and thick; sometimes however they are incurved.
One of the forefingers completely covering the bulbo. [Med. Chir. Trans. 1884]
The joint are also bulky and swollen and often cold.

**Integumentary System:**

The skin over the body generally
is dry, hard, showing tendency to
crack with little or no perspiration or
obscureous secretion. It is often covered
with scales or dryness due to
atmospheric conditions. To the touch it feels rough and con-
tinuous elastic. There is over the body
an increase in the amount of the subcutaneous tissue, and the skin is in folds. This is particularly the case above the clavicles in front and the neck behind.

The hair of the body is in apilla and on the pubis is diminished, and one case is recorded in which there was general alopecia.

Plethora is present, more or less over the whole of the body. It differs however from true plethora, in that it does not pit on pressure, and does not gravitate to dependent parts. It is more marked in the face and upper extremity than in the lower. True plethora may occur concomitantly but accidentally in the lower extremities, and does often present itself towards the end secondary to vascular changes.

The swelling of myxodema varies from time to time being most marked in cold weather. This I have noted particularly in Case iv.
Nervous System.

Sensor Functions.

Many of the patients complain of feeling cold. They say they never felt comfortably warm, and sit huddled themselves near the fire, or lie cuddled up in bed. This symptom was present in all the cases I have recorded.

Headache, both frontal and occipital, various pains in the extremities like rheumatism, occasional numbness or tingling are complained of.

Other complaints are weakness, fatigue on exertion, sadness.

Exceptional symptoms recorded by Hompelein [Sagous 1891 vol IV H] are anxiety, need of warmth and tremors (only one observed before). These symptoms he says occur also in Cachexia subphrenica and ophthalmic sore.

In a case recently recorded by Mr. Anderson, 'shivering of the inside' seemed a prominent and brought some symptoms. [Practitioner Jan 1893.]
Sensibility to touch may be and sometimes is slightly deficient, but more often it is retarded. This may be due to the sluggish, sleepy way in which patient responds to external stimuli of any description.

Notwithstanding the feeling of cold which made patients complain of, there seems to be a deficiency in the perception of external variations in temperature - many of them not opposed to draughts without taking any notice.

The special senses, on the whole may be said to be less acute than normal. Here is sometimes impaired vision and on account of this, and the watering of the eyes, case iv came under my notice.

Sensations of taste and smell may be diminished or prevented. One case had a peculiar sour taste in the mouth and foul smell in the nostrils. Oct. [Med. Chir. Trans. Vol. 61, 1878].

Hearing is often impaired.
Motor functions:
The superficial reflexes were in some cases diminished, in few absent, and the knee-jerk, though usually normal, may be diminished.
Slight partial paralysis of the muscles of the extremities and neck is sometimes observed.
The power of coordination is usually diminished, especially in the lower extremities, giving rise to a peculiar clumsy gait.
The walk is slow and awkward and is described as though the patient were deep in thought. Sometimes the gait is staggering, with a kind of sway for the knees to jut way unexpectedly.

Mental functions: There is marked slowness in perception, thought and action, but as Mr. Matthews once having started a line of thought they pursue it. They seem to be sluggish and dull, in a torpid condition and do not want to
engage in any active mental process. They may have in
the later stages delusions or
hallucinations, or are subjects of
insanity. They not infrequently
end their days in lunatic
asylums.
There is usually marked torpor
the patient appears drowsy. They
are always inclined to sleep during
the day as well as during the night,
and sleep is not infrequently
disturbed by unpleasant dreams.
Convulsions and coma are of
common occurrence (Whitwell).
His memory is usually impaired;
they may remember things that
happened sometime back but not
those of recent occurrence.
Their mode of Speech and the
intonation of the Voice is peculiar,
and though not easily defined is characteristic.
Remember hearing one of the
Edinburgh Professors says that
he could diagnose a case of Malaria by hearing the voice and seeing the hands. Ord [after C. T. Tran 1878] describes the mode of speech thus: "When about to speak, she closed her lips, stroking the under one forward, made a movement of swallowing, and then with much widened mouth commenced inhalation at the same time expelling air explosively through the nose. The speech is slow and monotonous, the voice dull and tedious with little or no intonation. It seems nasal and gruff and has been compared to that of quincy. The alteration in the voice is often noticed by the friends of the patient. The temperament varies, some are irritable and fretful, others placid. Alimentary System: The lips are thickened and pendulous; the jaws swollen.
The teeth tend to fall out or decay.
The tongue is often broad, thick, and swollen. It is protruded deeply. The tongue is too large for the mouth, so that false teeth cannot be worn (Sill). The fauces and uvula are swollen, and sometimes difficult to distinguish as such.
The appetite unimpaired. Nausea is frequent. The bowels usually constipated, in one case the act of defecation was attended with difficulty on account of the dilatation of the anus.
Not infrequently there is a tendency to digestive troubles.

Pathologic Section:
The thyroid has almost universally been found abnormal or absent, and as Cushing observed [Med. Chir. Trans. 15:48] that whilst jortic was more or less associated with impending asthenia, the thyroid was actually absent or
atrophied in sporadic cutisirius occurring in this country, and faits assumes the presence of jaule to be a safeguard against cutisirius.

A case is recorded in Brit. Med. Journal 1893 of the occurrence of Myxobolus with jaule. The lymphatics have been noted in some cases to be enlarged. The blood in both these cases was examined microscopically and found normal.

The Report of the Committee on Myxobolus [Med. Chir. Trans. 1878] states in the blood of 24 cases no characteristic change were observed. It was normal in 16 cases; in 8 it. The coloured corpuscles and the haemoglobin diminished. In one case the colourless corpuscles were increased in another they were diminished. I can find no other account of alteration in the blood.
Circulatory System:
There may be some of the subjective symptoms of chronic present.
The heart is usually normal, except towards the end, when kidney mischief has started and hypertension may be found. The heart's action is slow and the sounds often weak. The pulse is slow and weak. In some cases it may show signs of athroma. The capillaries of the face are dilated. There is a tendency to homnorrhagia.

Urinary System:
There may be frequency of micturition or occasionally incontinence of urine. The specific gravity of the urine is lower than usual. The quantity may be increased or diminished. Albumen is absent, but may
The disease is a slowly progressive one, and certainly shortens life. The actual cause of death may be pulmonary phthisis, renal or less frequently other complications. Some end their days as inmates of incurable asylums, succumbing to nervous exhaustion.

The symptoms vary from time to time, especially the bulk. The swelling of the skin and the nervous symptoms, a large proportion of patients actually losing the
Characteristic conformation before death. Prof. [Verh. des M. Verh. 5. Berlin Nat. Congress 1890].

Pathology.

The general belief now expressed is that Myxodema is due to destructive changes in the thyroid gland.

The thyroid has, in many post-mortem examinations, been found greatly diminished in size and of a yellowish colour.

Microscopically the changes in the gland seem to be at first a small cellular infiltration, which is followed by the substitution of fibrous tissue for the gland structure proper.

This fibrous invasion is seen also in the structure of the skin, the subcutaneous and subcutaneous glands, and the hair follicles are infiltrated with, and surrounded by, a number of small cells.

[Prof. explains [Med. Chir. Trans. 78] the
No. 2984
County Hospital
York

No. 27, 1898.

Dear Sir,

Enclosed please find cheque for £6.5.0 for my thesis (on "Myx-ridema") for the M.B.

I enclose also a declaration that the work has been entirely done by myself.

I have forwarded the thesis by this post.
The County Hospital
York.

April 27th 93

I hereby certify that the Thesis entitled "Observations on Myxodema with special reference to Pathological Conditions found in the Egg-stage" has been done and composed entirely by myself.

I further state that I have passed the subjects of Greek and Logic in the Preliminary Examinations at the University and that
I am 26½ years of age.

Alfred Charles Cole.
M.B. c.r. 1867.
B.S. de Public Health 1870.

"Rivoli"
Governer Rd.

Bournemouth.
Yours, Coln.

Command.

W. L.
action of the skin by the atrophy of the sweat glands and by the packing of the nerve terminations in the skin with the jelly-like substance, so that there is a loss of tonic influence.

These interstitial changes in the skin etc. occasionally seen in the viscera are probably of an inflammatory nature.

Harley [Med. Chir. Trans. 1844] noted in addition that the quantity of blood in the body was small and that the tissues were abnormally firm, and he defines his case as "a general febrile invasion producing a chronic cold debility." He thinks the myxoedemic and scleromic conditions in these patients were the result of some old inflammatory mischief, affecting, amongst others, the pleura, peritoneum and sympathetic.

Savage thinks [Journ. Prat. Science Jan 50] that the delusions arise from
primary brain changes, or at least changes in the nutrition of the brain, and that the cause - of nervous symptoms - is central rather than peripheral.

The great increase in the amount of mucin in the tissues, as recorded by Ord in his first cases, has not been generally found in subsequent cases, but this, as has been suggested, may be owing to the fact that the former cases died in the 'swollen' stage of the disease, whilst the latter died in the 'atrophic' stage, when the increase in the connective tissue, but the had very much diminished.

An increase in mucin has however been found in the tissues of animals after the removal of the thyroid.

The committee of the Clinical Soc. appointed to investigate the subject of Myxedema finally state that
There is strong evidence that myxoe
sporadic cataract, endemic cataract
 cachexia strumipriva--is the term
applied by Kocher to the condition
which develops after total
sterilization of the Thyroid--and the
operative myxedema of animals
are severally species of one genus:
and such clinical differences as
exist between them are due to causes
which can be explained. The one
pathological fact common to all
these conditions is the occurrence
of morbid processes--or of operation
involving the amnition of the
Thyroid body. [Chin Soc Trans., Suppl.,
1891]
What the cause of the destruction
of the Thyroid is seems as yet
undetermined.
Kocher reports some cases which
support the theory that the function
of the Thyroid is to prevent the
accumulation of mucin in the
tissues. [Centralblatt fur Chirurgie 1891, p. 204]
As regards the primary symptoms
e.g. changes in the skin, mucous membrane and nervous system depend on disturbance of the nutrition of the brain.

Bircher also noticed the watery condition of the blood, the diminution in the number of red blood corpuscles, and the increase in the amount of mucin in the tissues, and considers the thyroid is an organ necessary to life. [Lancet, Oct. 15. 92.].

Boyce and Beadles have recently noted [Journal of Pathology 93.] the occurrence of atrophy of the thyroid with enlargement of the pituitary body in two cases of myxoedema and one of sporadic cretinism.

The increase in the size of the pituitary body was due, for the most part, to an increase in the colloid substance within and around the acini, but also to the presence of dilated capillaries in the gland structure.

They however remark that S. Hadden...
never found the pituitary body enlaid in myxodema.

Treatment:

Till recently the treatment of myxodema has been very unsatisfactory, and the condition regarded as practically incurable. Tonics, especially iron, strychnine, quinine etc., have been used, but with little success.

In account of the condition of the skin, pilocarpin and jaborandi, and the frequent use of hot baths, have been of some service. The maintenance of warmth and the removal of the patient to a warmer climate during the winter appears to prolong life.

Prof. Granjeo Stewart reported at the Berlin Medical Congress [Aug. 90.] a case under his care, in which, on account of the presence of mitral stenosis, Turkish baths were impossible. She improved
The skin and relieved her other symptoms by rubbing the skin with a rough grater. This, in conjunction with a good diet, the administration of arsenic and tonics, was followed by marked improvement. Shortly the treatment of myxedema has taken new lines, and very remarkable results have been obtained with the thyroid treatment.

As had pointed out, the primary and constant condition present in myxedema was the disappearance or atrophy of the thyroid gland. A similar train of symptoms was produced by removal of the thyroid in man or animals. Prof. Schiff and others showed that the evil effects of hypothyroidism could be diminished by transplanting a thyroid gland from one to the other. Prof. Hooley suggested the transplanting of thyroid in
myxedema, and the beneficial results which followed were evidently due to the absorption of some substance in the gland.

Kassulé and Flügge showed that the injection of an extract made from the thyroid, removed the acute symptoms which followed thyroidectomy in dogs.

Brown-Squard and A.-Nonval suggested in 1891 that such an injection—subcutaneously—would prove successful in myxedema.

Previous to this, and quite independently of these observations, D. J. Murray of Newcastle had tried this method with good results, and afterwards Dr. Højris and others, published successful cases.

Murray’s method of preparing the extract was as follows [Braithwaite, Rep. Vol II. 1892]. The fresh gland is taken and each lobe minced, then bruised in a mortar. For each lobe he employed 1 c.c. of glycerine and 1 c.c.
of a 0.5% soln carbolic acid in boiled distilled water is added. The mixture is allowed to stand for 12 hours, and then squeezed through a cloth in a press, so as to obtain as much liquid as possible from the mixture.

About one-third of this extract are injected with antiseptic precautions subcutaneously, very slowly, in the interscapular region.

Bad symptoms are to some extent avoided by injecting slowly. The objections raised to this mode of treatment were: the liability to the recurrence of condurations or abscesses at the point of injection, the occasional appearance of alarming symptoms & the difficulty of preparing an antiseptic aqueous extract.

H.T. Fox and Mackenzie independently and about the same time suggested the administration of such thyroid gland by the mouth.
The freshly bruised glands is infused with
brandy or beef tea.
Mackenzie mashes the gland, adds
a few teaspoonfuls of water and allows
it to stand for 1/2 an hour. It is
then strained through linen or muslin
and the expressed juice added to
beef tea. He finds that one gland
or half a gland (or the extract made
from it) sufficient twice a week
and afterwards once a week.

The effects of the administration
of thyroid are almost immediate:
rise of temperature to the normal
or even above it — and a comfortable
feeling of warmth produced.
The pulse increases greatly in
frequency.

Occasionally the administration
of thyroid by the mouth causes
doombome vomiting, and not
infrequently nausea.
The alteration in the condition
of the patient is remarkable.
The swelling of first the face and
afterwards the hands and feet diminish. The hands and feet desquamate and the harsh rough skin is replaced by soft flesh skin. The hair begins to grow. There is a diminution in the bulk and weight of the patient and an improvement in the mental condition.

The medical journals daily contain accounts of the beneficial results obtained from the thyroid treatment and now reliable preparations of the extract and even of the tablets of thyroid gland can be procured.
Clinical Cases.

Case I. Whilst acting for a short time as visiting surgeon to the Chester Infirmary, I came across what I considered a fairly well marked case of myxœdema, but unfortunately I did not take full notes of the case.

A. B., female aged about 57, by birth a German, lived with her husband at a public house. She complained of debility and exhaustion on slight exertion. At a glance one noticed the peculiar configuration of the face which with the voice were quite characteristic.

The face was very much swollen of a pale colour, with dilated vessels over the cheeks. The nose was broadened and thickened, the lines of expression lost. The lips were bulbous, swollen and wrinkled especially the lower. The eyelids swollen...
but did not put on pressure
She hands were thick, swollen
and awkward
Her tongue was lazy and thick
It was protruded slowly, its size seemed to interfere with her speech.
She spoke imperfect English, very slowly. Her voice being monotonous
and drawling, had a peculiar thick nasal character.
Her movements (she was at the time able to be up) were very slow and awkward. She walked slowly, tending to drag her leg
after her with the head bent forward.
She stein was very dry, while dry
and harsh. The substantious tissue thickened. Her figure
was bulky.
When questioned - and it was no easy matter to make her understand - she said her face had increased in size, and the voice
had attended much in character.
She always felt cold.
Her hair was scanty especially at the back of the head.
I looked for but could not make out the presence of the thyroid gland.
The treatment adopted in this case was such as to improve the general circulation, digitalis, and tonics.

Case II.

I saw this case at the East Suffolk Hospital, Ipswich, in June 1891. She was chiefly probably on account of the condition of the hair looked upon and treated as a case of syphilis. All I was struck by her peculiar shyness. All the medical men who saw her agreed in my diagnosis. It was the most
advanced of any of the cases I have seen.

C. G. aged 37, came into the hospital complaining of weakness which she had noticed for the last six years.

**History:**

- Family history on both paternal and maternal sides good. No history of any previous illness or accident.
- History as to syphilis and alcohol was negative.

**Surroundings at home good.**

She had "good food" and health till the last child was born some 8 years ago, since when she has been getting gradually weaker.

She complains of her weakness particularly in walking and in ascending stairs. She notices that her weakness is much greater in the lower extremities — especially in the knees, than in
The upper part of the body. Patient noticed that since she has been losing strength, she has become gradually fatter especially in the hands and face. She tells me she has altered very much in the face, as much as that her brother after three years absence could not recognize her. She complains that many of her friends and relatives have commented upon the change in her voice, face and walk, and "on this account" she says many of them do not seem to know me now.

State on Examination:

Her face is swollen and looks very much, at first, like that of Chronic Bright's disease. If is expressionless. The features blunted and coarse. The nasolabial furrow etc. are completely obscured by the general swelling. The face looks pale and anaemic.
but there is at times a well-marked localized malar flush. The skin of the face is smooth and dry, fluffy, and transparent looking. The eyelids, especially the lower, are swollen and look edematous. The lips are thickened, willcoloured and somewhat pendulous. The nose is broadened and flattened causing the eyes to appear far apart, and the whole face looks as if it were flattened and had spread out laterally. But what is more striking than almost anything is the nearly total baldness. The whole of the back of the head, the posterior part of the crown and laterally, as far as the ears, are demided of hair, beyond a few short stumps. It is not so clean or shiny as in abtuscin arctata, but the skin has an atrophic dry scaly appearance. The hair over the fore-part of the
head is thin and scraggly, the scalp dry and thrown into folds. The patient says the hair began to come out about the same time that she noticed the weakness, and has continued to fall off. So noticeable a feature was the baldness that the case had been regarded as one of tertiary syphilis. The eyebrows are thin and scaly. The tongue is swollen and indurated and this was commented upon by the patient. Her speech is slow, monotonous and dragging. The voice is thick, guttural and somewhat indistinct. Her thought seemed slow. When asked a question, it takes her some time to realize what is said and is a long time in answering. Her movements are stiffish and awkward. The memory seems fairly good. She says she always feels cold, and has great difficulty in keeping warm, even in bed.
This she has noticed for some time. Her temperature is subnormal, averaging about 97.5°F. She walked with difficulty, and her gait was uncertain. She attributes this to weakness, and says she feels as though the knees would give way. The urine, which was examined frequently, showed no trace of albumen. There was no edema of the lower extremities.

I had an opportunity of watching this case for about a month or five weeks. She was at first treated with Pot. iodide and Hyp. perchloride, afterwards with arsenic and tonics, and was kept in bed. There was only slight improvement. Recently I have written to the present house-surgeon concerning her present condition, but she has seen last sight of.
Photograph of S.S. Case III. taking some time after treatment had commenced.
Case III.

E.S. widow aged 53 living at Clifton, near York. Admitted into County Hospital Nov. 21st 1872. Was sent into hospital as probable commence malaria.

Complains chiefly of weakness, headache, occassional headache and nausea.

History

Permitatory Tendencin.

Mother died at the age of 63 from apoplexy, having lost the use of the whole of the use of the left side.

Patient was the fourth child of his father's second marriage. The other three died in childhood, but does not know the cause of death.

Father died at the age of 60 from old age.

Patient married at age of 27 and had six children. Two second died in infancy, the other members of the family are in good health.
The oldest being 23 or 24 years of age. Her husband was killed in an accident at the age of 44.

Habits as to food and drink. The patient says she was not addicted to alcohol, but the eldest sister informs me that she was rather in the habit of taking it.

Surroundings at home. Patient was a milk-seller, but did not go out to work. Her occupation—besides domestic duties—consisted in milking the cows in the morning and taking the milk and farm produce into York—a distance of about a mile and half. She was exposed to all weathers.

Previous Illness.

Patient had measles when a child and—says—scarlet fever at the age of 30, having to keep in her bed for 7 to 8 weeks.

No history of syphilis. Has had one miscarriage.

She has never had any accident.
Present Illness: -

Little could be learned from the patient as to the time and mode of origin of the present illness. She complained of dizziness which has lasted for a year, of lassitude and headache. She has always been the subject of sick headaches.

She says she was in good health 12 months ago, but was in reality an invalid at the hospital and regarded then as a case of Mphiomia.

From the oldest daughter I ascertained that her mother came to the hospital on account of swelling, particularly of the spheno and to a less extent of the body. She says her mother's face was always small and it is now much larger than it used to be. She cannot, however, describe what changes have taken place in the face, beyond that of
swelling. The patient has altered much in her manner. He last 3 years, and her speech has changed. "Mother," she says, "does not get out her words distinctly and is so long in getting them out." She recognizes people but cannot recall their names, and her memory is not as good as it was.

She says the hands are thicker than they used to be, she cannot pick up any small object, and takes a long time to dress herself. She is dizzy and has a tendency to fall forwards.

State on Admission:

The medical man who went in the case informed me that when he visited the patient, he found her in bed all in a heap, muttering and groaning—looking rather like a case of approaching madness and adrenal...
her removal to the hospital.
On looking at the case, I thought it to be either one of Bright's disease of pyrexia, and when in answer to a question, she very slowly turned in bed, slowly opened (or partially opened) her eyes, and spoke with such a characteristic slow monotonous voice, it left little doubt that the case was that of the latter. As soon as possible, the urine was examined and found copious deposit of pus and a little albumen, such as would be accounted for by the presence of the pus. Never since that day, however, has any albumen been found.
She was lying cuddled up in bed, with the knees flexed on the abdomen, the shoulders and head bent forward and seemed very drowsy. The position was exactly that which would be taken to keep the body warm.
She is rather a small woman weighing on admission only about 100 lbs. slightly built, and very muscular about 5' in height. The face is pale and somewhat sallow in appearance. The skin of the face is dry, smooth and velvety to the touch. It is very loose and is drawn into folds on the forehead. It feels thickened. There is at times a slight delicate rose coloured malar flush, and what is rather noticeable is that occasionally on speaking to her a delicate blush appears on the forehead and cheek - as if the vasomotor nerves were in abeyance. The nose is broadened and thickened. The eyelids are swollen translucent and oedematous looking. At first there was a distinct bug of oedema on the right upper eyelid but on pricking it
with a needle no serum came out. Both upper lids hang down very much low over the eyes, due probably to the relaxed and atonic condition of the textures. In fact, at first, she could only just open the eyes and could not look upwards at all. Even now, when she looks at any object above the level of the eyes, she has to throw back the head to counteract the drooping of the lids.

There is a tendency to cataract condition of the conjunctiva. Eyebrows appear very high up and the growth of hair short and scanty.

The eyeballs are sunken.
The lips are not very much thickened, but the whole of the mouth is widened transversely and the lips pressed together.

The subcutaneous tissue under the jaw is increased in quantity, loose and pendulous.
The expression of the face generally is certainly culminoid, and the obliteration of the lines of expression gives it a vacant placid appearance. The hair on the head is of a dark brown colour, crisp and dry with a tendency to scaliness of the scalp. It is unusually thin and scanty, but at the occipital and posticus parietal regions it is particularly thin and has the appearance of commencing baldness. The scalp and skin over the forehead is thickened, thrown into folds and feels soft and bony. The neck is thickened, especially at the posterior part. The hands are dry, smooth, with an atrophic look of the skin which is shining more particularly at the finger tips. The hand is somewhat thickened. The fingers taper off at the extremity with their pulps of the finger tips.
diminished in size. The nails tend to curve over the ends of the fingers. They are not clumsy looking, the hand having rather a sharp pointed appearance.

Integumentary system:

The skin of the body is dry, harsh, and scaly. There is no perspiration.

The subcutaneous tissue over the trunk seems to be increased over the whole of the chest and upper part of the abdomen. The skin can be pressed in handfuls. There is no true osseous of the lower extremities. Upon the lower extremities it was noticed that the tissues seemed very thick, and on prolonged deep pressure one could feel a peculiar fusing which had never seen before: the fusing persisted longer than a quarter of any hour, and had a hard ridge round it, very much like the fusing one can obtain.
in a fat cadaver, as if the subcutaneous tissue were setting.
The patient complains of the difficulty she experiences in keeping warm, and says when she is always sitting over the fire, the pigmentation of the skin of the lips attesting to the truth of this statement.
The temperature is subnormal, the average of the first three weeks being 96.5° fahr. The lowest was 96° fahr. The highest 97.4° fahr. After this time it gradually rose till it reached the normal where it remained for some little time (probably due to treatment) but occasionally falling a little.
The administration of thyroid by the mouth was followed by an immediate rise in the temp.
Nervous System:
Sensory Functions:
Patient complains chiefly of piddliness. She says that if
she walks about, she feels ready to fall at any time.
She always feels chilly.
Sometimes she has tingling sensations in the lower extremity
and pains and aches in the feet,
and says she feels stiff all over.
Sensibility to touch seems normal in all parts - that to pain, tested
by prickig with pin - somewhat slower response than usual.
She distinguishes easily between hot and cold hot tubs.
Vision somewhat impaired.
She very marked drooping of both upper lids gives her a peculiar appearance and allows of only a small vertical visual field.
The optic discs are normal.
The pupils are equal, of medium size, and react to light and accommodation.
Hearing is somewhat impaired.
Taste and smell natural, and having always been so.
Motor Functions:

Organic reflexes normal, except for the first two days in hospital when she had incontinence of urine.

The plantar, syringestic, Babin reflexes normal—so is also the knee-jerk, which is if anything rather increased.

Coordination—She cannot stand with feet together and eyes shut; she sways forward and backward and would fall but for support.

Other movements such as touching the tip of the nose with the forefinger—the eyes being closed—or describing a circle on the floor with the toe, are performed irregularly.

Mental Functions:

Her intellectual processes are sluggish and once or twice since admission she has been delirious. There is marked slowness in her thought and motion.
At first she did little but sleep and resented any interference. She slept much during the day. She often complains of headaches—chiefly frontal though sometimes occipital. Her memory is impaired. She speaks very slowly, in a monotonous dull somewhat squeaky voice.
She was at first very apathetic, with placid temper, but is at times inclined to be fretful and pernickety.

**Stomachary System:**

The lips are dry, not anaemic. There is a tendency to erosion of the lower lip which is somewhat thickened. The teeth, especially those of the upper jaw, are very decayed and many are wanting. The gums are somewhat spongy. The tongue is protruded very slowly. It is not very much enlarged and is always covered with a thin layer of fur. The odour of the breath
is always offensive.
She eats very little, and complains
much of nausea. There is no pain
after food, but has usually, as
she describes, a very weak languid
feeling after a meal.
She has, for the past few months,
felt sick particularly before break-
fast. She bowels constipated, the
motions natural in appearance.
The abdomen is not prominent.
The abdominal walls are extremely
flaccid and apparently well
filled with subcutaneous fat.
No dilated vessels seen.
On palpating the abdominal wall
thickened, and one is able to
take up handfuls of the loose
tissue. The skin in this region
is dry, harsh and very mobile.
The abdominal contents are
apparently normal. The dress
on percussion, of the liver in the
upper line is somewhat diminished.
No tenderness over the abdomen.
Except on deep pressure over the hepatic and splenic regions.

Circulatory System: -

No breathlessness or palpitation on exertion, but says she cannot hurry as it gives her headache all the day. She feels dizzy and has occasional attacks of sickness when going about the house. Has had only one fainting fit, and that three months ago.

Examination:

Inspection: a large dilated vein is seen running up the sternum and over the base of the left breast. The junction of the 2nd (costal) cartilage with the sternum is very prominent, but there is no history of any injury to that part. The apex beat is not visible.

On palpation: the apex beat is only just felt, as a diffuse faint sinking rather than an impulse at a point ½ inch below the left nipple, in the nipple line.
The outline of cardiac area by percussion seems fairly normal.

Inspection: Over the whole of the cardiac area, little beyond the 2nd sound is audible—while at the aortic area, is short, sharp, almost musical, and although distant, is very clear.

At the apex, the 2nd sound is heard, rather longer, less pure and still distant. No murmur.

The 1st sound is only heard at a faint, almost imaginary sound.

The heart sounds slow, but regular are about 60 per minute.

I noted that some time after admission, and whilst on digitalis, the 1st sound became distinctly audible over the whole of the chest cardiac area.

The pulse is infrequent, averaging about 60 beats per minute, regular in rhythm and force.

The mouth is somewhat small. The tension of the pulse, as tested by
rolling it transversely under the finger is normal.
The strength, as measured by the compliance, is somewhat diminished. No atheroma or tortuosity of vessel wall.

Respiratory System:
The breathing is slow and deliberate, range about 14-16 per minute, quiet. There is no cough or expectoration. Respiration more abdominal than thoracic. There is only partial expansion of chest wall on both sides.

On palpation: The vocal fremitus and vocal resonance are very indistinct, no increase on either side, except at the right apex where it is much more pronounced than at the corresponding position on the left side. Percussion, however, reveals no difference at either apex.

Resonation: The normal resonator breathing heard over the chest is very distant. At the right apex there is
marked prolongation of expiration, in fact the expiratory sound is of longer duration and more marked than the inspiratory.

At the left stethome there was less, but perceptible prolongation of expiration. No jerky character of the breath sounds, and no accompaniments.

I paid especial attention to the examination of the spicis, knowing the susceptibility of such cases to phthisis.

Urinary System:

Patient on admission passed most of her urine in bed whilst asleep. About two ounces were however saved. The urine was acid in reaction - pale straw colour with a thick yellowish white sediment. In this specimen albumen was detected with nitric acid in the cold, and by heat, but not much only about 1/50. No blood was found by the jussicum test.

On microscopical examination it
was seen that the sediment consisted of pus, and several varieties of epithelial cells from the urinary tract. There were flakes of squamous epithelium in clusters, probably from the vagina.

In the evening, i.e. the day after admission, there was no albumen by heat or nitric acid.

It is probable that the albumen found on the first day was due to the admixture of vaginal discharge with the urine, as it has never been detected since.

Examination of the Urine:

The quantity of urine passed in the twenty-four hours was very small, measuring only 20 ounces, the lowest being 14 ounces. It was of a pale straw colour with a florid-like yellowish-white deposit. No odour was present. The specific gravity was on an average 1022.
The reaction was constantly faintly acid.

There was no albumin present.

The quantity of urea was greatly diminished—only 90 grains being ejected in 24 hours.

No sugar or bile was detected.

On microscopic examination the deposit was seen to consist of mucus, and a peculiar precipitate of phosphate of lime, with a few crystals of ammonium-magnesin phosphate. No tubal casts were detected.

**Reproductive System:**

Stimulation began with the patient was 15 years of age. The period of discharge was two or three days, the quantity was always very small. It ceased at the age of 43.

There has been no intermenstrual discharge.

The patient has had six pregnancies.

The first at the age of 25, the
last at 43 years. The labours have always been normal, with no excessive haemorrhage. She has had one miscarriage.

Hæmorrhagic System:

The Thyroid seems to be entirely absent. There is no enlargement of the lymphatic glands. Repeated careful examination reveals no enlargement of the spleen.

Enumeration of the blood with the Thomas-Tina apparatus gave 4,000,000 red blood corpuscles in the cubic millimetre of the blood. There was no increase in the number of the leucocytes.

[For further description of the examination of the blood—see below.]

Somatic System:

At first the patient was quite unable to stand alone, and could only lately has she been able to walk without support. Today she walked down the ward, touching the beds when she
felt herself falling.

The walk is irregular, the legs are drawn after her in a trailing manner, and she tends to fall forward.

The joints are normal, except the x-ray of the knee, in both of which the patella is rotated upwards, and the whole of the knee invaginated. The labia having, as to squeak, a compensatory curve on them.

Treatment and Progress.

On admission, Nov. 22, the case was put on digitalis and iron, and milk diet, simple appetites being given almost every day.

From November 22 to Dec. 12 the temperature remained subnormal, at an average of 96.5°F. The pulse 61, and inspiration 15 per minute. Then the temperature rose a little and remained at about 97.4°F for a month.

A mixture of soda, janthin and
arsenic was then given and quinine sulphate for the headache. Food was changed to fish and later mutton.

Jan 19th. Bismuth, soda and arsenic were given. The temperature remained at about 97.2°F. Generally, she was brighter, not so lethargic, but no very pronounced improvement.

Feb 8th. We commenced treatment by the administration of thyroid by the mouth, but found that in all probability it was a piece of muscle and not thyroid which she had received as there was no reaction.

Feb 14th. A whole thyroid gland was given, minced, as a sandwich. The temperature rose from 96.7°F on the 14th to 99.6°F on the 15th and to 100.5°F on the 16th. The pulse being 82 and the respiration 16 per minute. Patient immediately complained of headache and nausea.
The face on the 16th was flushed. The skin hot. She says she feels ill. The temperature in evening reaching 101.2°. The pulse 99.
She vomited twice.
Feb. 16th. Still feels ill. Complains very much of frontal headache, and at times, is very cold. Generally she feels as if to use her own expression funny.
Tongue is not altered. She feels very sick and frequently fidgety.
The eyeballs seem sunken.
In the morning she wandered a little, and seemed very excited for about an hour. In the evening chills and forehead flushed. Temperature 100.
Vomited once, the ejected being bile stained.
Feb. 17th. Today the speech is very slow and plaintive. She is tired and keeps continually vomited once. She asks vacantly and repeatedly for a drink. Says her first hurt her.
The first sound of the heart is now
heard very distinctly. The temperature is normal, but the pulse remains at about 90 per minute, the respiration being 22.

In a few days she felt all right again. The temperature remained normal till March 7th when it again became subnormal. The pulse however kept at about 80 but now it is normal again. (It for her 60 per minute.) The temperature being subnormal.

Some days after she had recovered from the effects of the first attack, we tried to give her half a small piece of hypodrined mince, in a sandwich, in broth tea and in brandy but much as she herself said she could not keep it down.

We were therefore compelled to give up for a time at least. The administration of raw thyroid by the mouth.

March 31st: The legs and feet became very swollen. After she had been
ups. This is the first time that there has been any swelling of the lower extremities, although she had regularly got up during the day.
She became very drowsy, and spoke with difficulty. The temperature rose to 100° F at 6pm. The urine increased from 12 to 56 ounces in the 24 hours.
April 1st. Slept all night and day and complained whenroused. Very much of his throat, had difficulty in swallowing, and took very little milk. Throat on examination showed injection of the fauces, some enlargement of the tonsils, and marked oedema of the uvula. Temperature 102.4° at 10am.
She urined decreased to 14 ounces
She kept normal in eyes.
Temperature was 102° F at 6pm.
April 2nd. Vomitted bile stained, green liquid. She has been quiet and sleepy all day. Took her milk better. Temperature 100° F at 10am.
April 3. Complains very much of headache. Had three attacks of delirium - was very frantic and troublesome - screamed and fought. In the intervals was quite sensible and quiet. She seemed conscious of having had the attack but said it was due to her head being so painful.

She vomited three times to-day. The vomit was very clear, hardly any mucus. Said her throat was very painful.

Gave physostigmine. Chlorate of potash was given on April 2 and hot fomentations applied to the neck.

Face flushed. Respiration 14, pulse 88. Temperature normal.

April 4. Still continuing with these attacks. Her sickness has stopped and the throat is better. Takes her food and feels better. Temperature normal. Wine decreased to six ounces.
April 5th 6 1/2. Patient greatly improved — quite sensible. Bowen's very constipated and urine decreased.

Finding it impossible to get her fresh thyroid, we have commenced the administration of tartaric of thyroid, each said to contain 1/2 of thyroid gland.
Photograph of H. A. Case IV.
Case IV.

Mrs. H., 52, a domestic servant. Born at Rochlington near York, resident in York.

The patient came as an outpatient to the Ophthalmic department of the County Hospital in Nov. 92, complaining of failing sight and expressing a wish to be fitted with glasses.

The surgeon in attendance passed her on to me, in order that I might estimate her refraction.

I was at once struck by her appearance and voice, and examining the urine found, as suspected, no albumen.

On a little further examination, I satisfied myself that this was certainly a case of Myelosma, a diagnosis with which several medical men— all who have seen her — agreed.

She was in Nov. 92, and although much interested in her case. 
Last night of her life January of this year.

**History.**

(a) **Family History:**

The patient states that her grandmother, on maternal side, enjoyed good health and lived to be 86. Her grandfather was always thin; he suffered much from cough and shortness of breath and died at the age of 65, "choked with blood."

There was no history of the grandparents on the father's side. Her mother enjoyed good health till her marriage, after which she was never quite as robust. She suffered from a long illness after the birth of the last—the eleventh—child, which was delivered with instruments.

Her illness was attended with great weakness and she became very emaciated. Somewhat was the
The patient says, that in tearing a piece of cloth, the sudden jerking at the hem caused a dislocation of both shoulders. Her mother complained of the movement of something in her chest, and expressed a wish that she should be examined after death.

She did not suffer from heart disease or dropsy.

All her labours—except that of the last—were normal, and there is no history of flooding.

She died at the age of 49.

Patient's father died of consumption aged 60.

There were seven born of the marriage—six females, five males.

The eldest—male—died at 55 from heart disease. The eldest sister at 54 from cancer of the womb.

Another sister died at 56 from debility. She had been an invalid for 8 years, suffering from asthma and heart disease. She had
swelling of the body - particularly in the neck. Patient says his sister was very like her in appearance, especially in the swelling under the jaw and in the neck, which also varied from time to time.

This is the only member of the family who had anything which might be termed dropsy. Another sister died aged 50 from consumption. Another from injury to the hip - a result of an accident; and the other three boys died in infancy, but does not know the cause of death.

Two sisters are living - one aged 53 married with seven children. The other single, aged 63, both of whom are in good health.

Patient is the ninth in the family.

(β) Personal History:
Patient lived at home till 16 years of age, in a healthy country market town near York.
After that age, she went into service in various parts of the country. She has always had plenty of food, wholesome food, and is not addicted to alcohol. Her surroundings have always been good.

Previous Illnesses:

She had measles when 6 or 7 years of age, and when 14 Typhoid Fever, of which her uncle and aunt died, and which was raging at the time in Brockton.

Whilst a child, she had quinsy.

She then remained in good health until 27 or 28 years of age, when she had Rheumatic Fever and was unable to resume her work for several months.

In the same year, she had another fever, which the doctors said was a low, and which the patient stated was a very high fever. It was not attended with any rash, there was no sore throat, and she did not feel
after it, and she does not think it was scarlet fever. It was characterized by head symptoms and delirium. This fever lasted some time, and when she got up, found that she could not put her clothes on from the great increase in size. The swelling was fairly universal, but most marked in the face and trunk, and, to use her own expression, she was "ballooned up." The swelling lasted about one or two months, but a squint, which resulted from the fever, remained for a year.

Since that time she has remained in excellent health, with the exception of occasional attacks of rheumatism in the shoulder, thumb, and to a less extent, other joints, till 1846. There is no history of syphilis. Patient says she has never sustained any accident.
Time and Mode of Origin of Present Illness:

Patient attributes the origin of the present illness to overwork whilst nursing a sister who died of phthisis in 1866. A little before the death of her sister, she noticed that her face was getting larger, and her body and hands began to swell.

The swelling came on very gradually; she never noticed any enlargement of the legs, but felt stiffness in the knees.

Her friends noticed the alteration in her face, and remarked that she was getting fat, and from the thickening and alteration of her voice, thought that she had always a cold.

She can walk fairly well, but has some difficulty when going up stairs. Her hands feel stiff, especially the knees.

On account of the weakness of the lower extremities, she cannot rise
from a low chair, except by pulling herself up by the hands.
She is sometimes stumble, especially on looking upwards, but she can walk in the dark quite well.
Subjective Phenomena: She complains of weakness of sight, and occasionally of a burning pain below the breast. She never suffers from headache.

State on Admission:

Patient is 5 ft. 5 in. in height and weighs 10½ stones.
She is well developed and looks muscular, but in reality the muscles are flabby. She has the general appearance of being bulgy.
The face is swollen and blooded.
The skin is smooth, clear and pale. There is occasionally a malar flush. The lines of expression are obliterated.
The eyelids are swollen and puffy and somewhat translucent in appearance. The eyebrows are elevated
The base of the nose is thickened and broadened; the alae nasi are swollen. The lips are thick and large, the lower one being somewhat squared. They are of a bright red colour and contrast greatly with the pallor of the face. The tongue is very much swollen and can only be partially protruded.

The hair on the head is scanty, of a dark colour turning grey. The scalp is dry and scaly. The patient says that the hair has been getting much thinner lately. The subcutaneous tissue, under the jaw, hangs in thick folds, giving the face a very peculiar expression. The skin of the forehead is thick and dry. The eyes look watery and there is profuse lacrimation. The tears running down the cheeks. The neck is very full and measures 14 inches in circumference.
The general expression of the face is dull and heavy, and she looks typically cli
tuboid.
There is no marked increase in the supra-clavicular fat, but posteriorly, over the spines of the lower cervical and upper dorsal vertebrae, and in the supra scapular regions. The tissues are very much thickened, giving almost the appearance of a fatty tumour in this locality.

The hands are thickened and gnarled like, the skin being rough and hard. The patient compares the condition to the skin of a salmon. She says that sometimes they are very scaly, as if they had been plunged in flour. The swelling of the hands varies from time to time. Consequently she is unable to wear kid gloves. She is totally unable to do much washing, as this causes the hands to increase in bulk and gives
about a feeling of stiffness and numbness. When the hands are at their worst, she can see or use her fingers to pick up small objects, and at such times, she experiences difficulty in writing.

**Integumentary System**

The skin over the body generally and of the hands particularly, is always dry. There is also much itching of the skin. She says the body and hands occasionally feel stiff.

On examination, the skin feels dry and harsh with a tendency to scale, and the formation of folds.

The subcutaneous tissue of the body is very much thickened, and that over the chest and abdomen is easily grasped in the hand.

The body is subcutaneous, the upper arms are 10½, and the forearms 8½ inches in circumference.

The chest, at the level of the 3rd
coup-ternal articulation, measures 33½ inch in circumference, at the
level of the epaulette cartilage 28½ inches; the abdomen at the level
of the umbilicus 33½ inches.

The tissues of the back are thick-
ened, but there is not putting on
pressure either in the lumbar
region or in the lower extremities.

After a hot bath, the whole
of the body swells up very much.

The swelling has been confined
almost exclusively to the face,
hands, neck, and body. The lower
extremities have never been
involved.

The patient states that the swelling
of the body varies very much from
home to home, and one day she has
to let out, and the next to take
in her clothes. This almost
diurnal variation in size seems
rather exceptional.

There is practically no perspiration
or serous secretion.
The patient has always a feeling of coldness. Her temperature is abnormal and averages 97° F.

Nervous System:

Sensory Functions:
She has a feeling of chilliness, especially in the toes. She has had numbness in the toes and fingers, and was unable to pick up pins, see, or even fasten her buttons.

She has also pricking sensation in the fingers. Occasionally patient has a sensation of burning heat all over the body, this is accompanied by flushing of the face, and is very quickly followed by a sensation of cold and sometimes of chilliness.

The sensibility to touch, heat etc. is normal. The muscular sense as tested by lifting both of the same size but of different
weights, is not impaired in the slightest.

The pupils are equal, of moderate size and react to light and accommodation.

Patient complains of impaired sight and particularly of watering of the eyes, which is very troublesome when in the cold air.

Distant vision tested by Snellen type showed $R = \frac{15}{40}$ and $L = \frac{15}{20}$.

Retinoscopy revealed hypermetropia to the extent of Right = +4 D. Left = +3 D.

With glasses +4 Doph. for the right and +5 Doph for the left eye, vision is brought up to standard.

By the indirect and direct ophthalmoscopic examination, the fundus was seen to be normal.

Hearing: She had a purulent discharge from the right ear about 25 years ago, which lasted about six weeks, since then she has not heard as well with the right ear. The hearing is easily affected.
by cold. His sense of taste is normal.

**Motor Functions:**

The organic, skin and tendon reflexes are normal. Coordination is somewhat impaired in the lower extremity, especially the left leg. The patient notices that when walking down stairs, the left leg appears sometimes to catch and the easily trips over a slight obstacle.

**Vasomotor functions:**

There is pallor of the face, with a variable malar flush. Perpiration is absent. There is no true oedema.

**Mental functions:**

The attention is more than usually acute. Memory for recent events impaired! She can recall the occurrence of the members of the family with great readiness but forgets what happened yesterday, day or the day before.
She sleeps well at night and frequently during the day. She constantly feels sleepy and disinclined to exert herself. She can write at times very well but experiences great difficulty when the fingers are numb. Her speech is slow and deliberate. Her voice is hoarse and thickened and somewhat monotonous. Her walk is slow, as if engrossed in thought. Her movements about the house are slow and clumsy.

**Alimentary System:**

The teeth are mostly absent and what few remain decayed. The gums are rather ulcerated. The appetite is somewhat impaired. The tongue is thickened, clean, rather flaccid. She has lately complained much of thirst. She has a few symptoms of dyspepsia, e.g., feeling of distension after a meal, and flatulence.
The bowels are constipated, the motion natural in appearance.
The abdomen. The abdomen is humid, the walls flaccid and thickened. The umbilicus not depressed. There were linear abbreviations at the lower part.
Palpation and percussion showed no alteration in the size of the liver or spleen.

Hematopoietic System:

The thyroid gland is absent.

There is no enlargement of the lymphatic glands or spleen.

Enumeration of the red blood corpuscles with the Thoma-Leitz apparatus gave as an average 4,880,000 per cubic millimetre of blood—With Gross hematocritometer, the red cells numbered on an average 4,900,000 per cubic millimetre.

The leukocytes showed no marked increase. [For further description of the leukocytes see below.]
Circulatory System.

There is occasional palpitation on exertion.

In inspection - no cardiac impulse is visible. There is heaving pulsation in the right side of the chest and neck.

In palpation, the apex beat is felt as a diffused, somewhat weak and indistinct impulse, displaced downwards and outwards.

Percussion reveals slight increase in the area of cardiac dulness to the right of the middle line.

Auscultation - The 1st sound of the heart is short and sharp in all areas. The 2nd sound is heard distinctly but somewhat distant. The pulse is infrequent, averaging about 66 per minute. It is regular. The vessel is of moderate size, of low tension. The pulse is fairly easily compressible. There is no thickening of the vessel wall.
Respiratory System:
Patient suffers from shortness of breath after taking food, going upstairs or hurrying.
The expansion of the chest is equal, but somewhat diminished, on both sides. Vocal resonance and resonance are normal. There is no alteration in percussive note and the breath sounds are normal.

Urinary System:
There are no subjective phenomena.

The Urine: is diminished in quantity, measuring on an average 26 to 30 ounces in the twenty-four hours.
It is of a pale straw colour, with a slight deposit on standing.
The reaction is acid.
The specific gravity about 1010.
There was (and is) no albumen either with nitric acid in the cold, or with heat.
Its area measured about 350
fever in the 24 hours.

For microscopic examination, the deposit was seen to consist of mucus. No tubercle were seen.

Reproductive System:

Menstruation began early, at the age of 12. It has always been excessive. It sometimes came on every week — and the discharge was always bright in colour. Menstruation ceased nine years ago. There was no pain at the change. She says she has increased in size since then.

Treatment:

The patient has, after trying tonic medicines — eg arsenic — nux vomica etc., as an out-patient, at last consented to come in for the thyroid treatment.
The Examination of the Blood.

The Methods used in the Examination of the Blood in the above Cases.

The Blood was examined:
1. In the fresh condition.
2. With the aid of some preservative.

In the Examination of fresh Blood, one simply has to place a drop of blood on a slide, cover with a coverslip and avoid, as much as possible, any delay or undue pressure as the former allows the corpuscles to clump, the latter distorts them and increases their diameter.

If a ring of Canada balsam be run round the slide, it will retard evaporation and preserve the specimen for some time.

To prevent alteration, and to preserve the corpuscles in their
natural condition, some form of
Preservation fluid may be used.
Of these, Tryon's solution, which
consists of Sodic Chloride 1. Sodi sulph.
5. Hydrarg. perchloride 1/2. and distilled
water 200 parts is extremely useful.
Bijogoss methyl violet salt solution
is 0.5% Sodi Chloride tinted with
methyl violet may be used, or
a solution of Sodi sulphate of the
parity 1022 coloured with methyl
violet.

To use any of these, a drop
of the fluid is laid on the finger,
and a prick made through it so
that blood at once flows into, and
is mixed with it.

3rd Blood Film Method.

The method of making dry
films on cover-slip, suggested by
Ehrlich, for the examination of
bacillus in liquids, has also been
applied to the examination of the
blood.
The natural description [Muir, Journal of
Anat. v. Phys. Jan 1891] is that a drop of blood of suitable size is allowed to spread itself out into a thin film between two cover glasses, which must be scrupulously clean. The two cover glasses are then separated by a sliding movement, and the films dried by a rapid to and fro motion in the air. These films are afterwards to be kept for some time on copper plates at a temperature of 180°C. This seems necessary to fix the elements in position and to allow the corpuscles to retain the haemoglobin.

Now, the difficulty of manipulating the cover glasses, either between the fingers or in forceps, I have adopted a method of spreading the films on the slide itself, a method which I have used for several years in the examination of opium for tubulae bacilli. Making films on slides is much easier than on
covered. It is not easy to clean up these covered places without breaking them, and when clean it is extremely difficult to spread a film of blood uniformly on them, without getting the outer side greasy, and besides, the process has to be performed rapidly or the blood begins to coagulate, or the corpuscles to erinate.

The hole of the ear, or the tip of the finger, which, we may be most convenient, is chosen as the point from which the blood is to be withdrawn. The part is washed—not with any antiseptic, as this may coagulate the blood—to remove any fatty matter on the surface, and then pricked with a needle. After trying several shapes of needle points, I have found that the triangular pointed one gives the largest drop of blood with the least pain. It facilitates matters, if the hole of
The ear is rubbed a little between the finger and thumb, before the puncture is made, so as to produce a slight amount of hyperaemia. The ear is pricked with one sharp, quick movement. The pain is practically nil, and immediately two clean slides are passed at their extremities. On one, the blood is allowed to touch near the passed end, and the other is used in one of two ways—either both slides laid flat or and then gently slid apart, or, as Whitby found better, the bottom slide held horizontally, and the tips moved along its surface, without any pressure, at an angle of about 30°, scraping as it were the blood before it.

It would seem that the tips slide would scrape all the blood off, but if carefully done, and if the slides are perfectly flat, it saves
a thin, almost invisible film on
the surface of the lower slide.

Microscopic examination
shows that this method of spreading
blood does not tend to distort the
form of its elements.

The slide is now removed to
and set in the air to dry as quickly
as possible the thin film.

The thinner the film, the more
uniformly spread, and the quicker
the manipulation, the better the
results obtained. Rapidity of
manipulation is necessary to
prevent crenation of the blood
corpuscles.

Having obtained two or three film
of blood, the slides are placed
film upwards, under a bell jar,
or better, back to back in a
wide mouth stoppered bottle, to
prevent the access of dust.

So far the method has been
entirely clinical, and has only
taken a few minutes.
One or two films so prepared may be examined to see if the corpuscles are uniformly spread out, and in manipulating the slide with the film, on the stage of a microscope, it is important that the finger should come in contact as little as possible with it, or otherwise the heat and moisture from the hand tends to disintegrate the film.

When examined thus, the corpuscles appear fainter and have less of the yellow colour ordinarily seen in fresh blood.

Next, and to me at first the most difficult part, is to fix the film. As in the slides so prepared a drop of stain is added, it will be found that the whole film has disappeared, and what remains is a mass of stained granular matter. To keep these slides at a temperature of 120° Cent. for several hours, as recommended
By Ehrlich, requires more time and apparatus than was at my command.

Many writers, especially those in the Brit. Med. Journal, recommend allowing the wet film to dry over acetic acid—1% solution, or of making the puncture through a drop of acetic acid solution, the blood being allowed to mix with it, and the film spread and dried.

Muir [Journal Med. 9 Thos. 1892] quite recently suggested placing the films downwards before any drying can occur on the surface of a saturated solution of corrosive sublimate. 34% with 34% solution of soda chloride added, put to a temperature of about 50°, and allowing them to remain for about half an hour. They are then washed thoroughly in a 34% solution of common salt, taken through successive strengths...
of alcohol, and then stained in the same way as sections.

After numerous failures at fixing the films, I have found that the only method which gives satisfactory results, is to further dry the slide film superficially over the flame of a spirit lamp, heating gradually, and setting nearer the flame till the slide feels hot even a the extremity held by the finger and thumb. How much heat a film will stand without spoiling, or how little will be sufficient to fix the film, time and experience alone will determine.

After moderate heating, usually examine under the microscope, to see if any change has been produced in the corpuscular elements, and then possibly heat again a little more.

Staining: -

The stain which is most easily manipulated, very quick in its
action, and sure good results is

method that is a saturated alcoholic
solution. It is only necessary to stain
for about \( \frac{1}{2} \)-\( \frac{1}{2} \) minute. The nuclei
of the leukocytes are stained blue.
The protoplasm and red blood cells
are unstained.

It has one advantage, that being
an alcoholic solution, it tends
rather to fix than to dissolve off the
films, and I easily obtained very
good specimens with it, but found
a difficulty in using contrast stains
with it. Tuchin 5% alcoholic
solutions is recommended as
a good contrast stain.

In my hands the double
stain of Hematoxylin and Eosin
has proved the most useful and
given the best results.

Also the leukocytes with eosinophile
granules are of most importance
in pathological conditions, we have
in this Hematoxylin and Eosin a very
useful stain for clinical diagnosis.
The double staining is better performed in two steps than using the stains in combination.

The haematoxylin stains are numerous, and after trying several, I prefer Starlich's Acid Haematoxylin Solution.

**Method of Staining:**

As I was using slide methods of coverglass films, the slide was placed in wide-mouthed two or three ounce bottles with stoppers, and the slides put in back to back, and left the desired time. This is no trouble, and loses very little stain, which can occasionally be filtered to prevent any deposit. The time necessary for staining with the acid haematoxylin stain seems to vary from one to two hours. The object in view is to obtain a purely nuclear staining reaction, and any excessive stain can be removed by treating the specimen, for a few minutes, with
Acidulated alcohol.

When stained sufficiently, the slide is washed with distilled water, and transferred to the contrast stain, an aqueous solution of Eosin about 1 in 2000, in which it is allowed to remain an hour or so. There also adopt the method of staining the slide in a bottle.

After staining in Eosin, the preparation is again thoroughly washed in distilled water, allowed to dry, cleaned with xylol, and mounted in Canada balsam.

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Examination of the Blood of Myxadisma.

Although it is now acknowledged that the Thyroid gland has not the blood-forming properties once attributed to it, it still is thought it extremely possible that in this disease some changes might be found, either in
The formation or nutrition of the blood cells. That my surmise was not altogether inaccurate. The following observations will show.

Case III. E.S. aged 53.

The Red Blood Corpuscles:

There were few pathological conditions observable in the red cells. They formed rouleaux, and did not tend to crenate sooner than those of normal blood.

The corpuscles however showed considerable variation in size, some being about 8 or 9 μ in diameter. Myelocytes, others not more than 4 or 5 μ. Microcystic.

Eerhorst's deeply stained red cells were not seen at any time.

The alteration in shape. Poikilocytosis was not as conspicuous as that of sogs, but a few showed variations in their outline. Many were oval, some pear-shaped, a few triangular, and still fewer
fragments.

The corpuscles were certainly paler than normal, and occasionally, one saw what has been termed a 'ghost red cell,' i.e., one with no colouring matter present, being as it were, a mere shell of a red cell.

These appearances were confirmed by the examination made with preservative fluids. I used Hayem's untinted solution, and in this the blood platelets were seen better and did not tend to run into groups and become granular as they quickly did in their fresh condition, but no other pathological state was noted.

The Lymphocytes.

These have been divided by several observers, into different classes, either according to the number and condition of their nuclei, the age of their cell, or the appearance of their protoplasm.
Shave, for the purpose of enumeration and description of the white blood cells, classified them into the easily recognisable and distinctive groups of:

1st. Unimncleated Lueocytes. Those possessing a single nucleus, and of which a large and a small variety is to be seen.

2nd. Multinucleated Lueocytes. Those with more than one nucleus, and have included, not only those in which the nuclei are quite distinct and separable one from another, but also those in which the nuclei though closely more or less together, might be correctly termed lueocytes with multibasite nucleus.

3rd. Eosinophile Cells. Lueocytes, the protoplasm of which contains granules which stain deeply with acid aniline dyes e.g. eosin and auranti.

4th. Large Unimncleated Cells formed by Enucleated Marrow Cells, and by Magnocncleated Hypertrophics.
The following water-coloured drawings by R. Calthorpe Esq. illustrate exactly the microscopic appearance of the various elements.

Varieties of Unimulsid Sineopto Dry Film Preparation.  Barn & Humate.
Uninucleated Leucocytes.

The most common form of this variety is a small, perfectly spherical cell. The nucleus is deeply stained with haematoxylin, is round, and occupies the greater part of the cell, having only a ring of protoplasm around it, which is usually thicker at one side.

The nucleus is distinctly localized. It is seen to have granules which are probably nodes of the intranuclear network.

In preparations stained only with Methyl blue, the small uninucleated leucocytes are deeply stained with little differentiation between nucleus and protoplasm. The surrounding protoplasm is small in amount and stains dark. Sometimes, however, none is to be seen.

The small uninucleated cells vary somewhat in size, some are but
slightly larger than the red blood corpuscles - others not so large.

The large uninnucleated cells were not so conspicuous in any of the preparations, but in those seen, the surrounding protoplasm was greater in amount, and the whole cell did not stain quite so deeply as the smaller variety.

A few oval leucocytes, about one and half times the size of a red blood corpuscle were seen.

Several measurements of the size of the leucocytes were made with the eye-piece micrometer, and although absolute measurement of cells is only reliable in the fresh blood, or that in preservative liquids, yet fairly accurate relative results were obtained. I found that the small uninnucleated leucocyte measured about 6-7½ µ in diameter and the large, about 9 µ in diameter.
Case III.

Varistiss of Multinucleated Leucocytes.

Dry Film Preparation. Stained with Eosin Haematoxylin.
Multinucleated Syncytia.

These vary in size, they are larger than the uninucleated, but not as large as either the roundshaped or marrow cells.

From a large number of measurements made, I found them generally about 10μ in diameter.

In shape they are generally spherical, occasionally oval, much more rarely irregular.

The cell wall is distinct and in films stained with Methylene blue.

The nuclei and cell wall only are stained, the former deeply, the latter faintly, the protoplasm of the cell being unstained.

The protoplasm is large in amount and has a finely granular appearance, resembling ground glass. Vacuoles are seen in some of the cells.

The nuclei vary greatly as to their number and arrangement, sometimes a number of separate oval or round nuclei are seen in a cell,
as many as four or six being in some cases counted—and there is usually some attempt at arrangement, but if there are two nuclei, they are often at opposite ends, if three, in the form of a triangle, four tending up the corners of a square and five with an additional one in the centre.

More often the nuclei are quite not separate, but connected by bands or threads of nuclear structure, constituting a multipartite nucleus. These threads of nuclei are generally so arranged as to give the appearance of an irregularly braided cord coiled up within the cell, the nuclei being connected to adjacent ones and the terminal nuclei free.

The strands connecting the nuclei are seen in some cases to be very fine, in others broad bands. The nuclear braided cord forms various shapes, the most common
The most common being that of a horseshoe, surrounded by, and encircling, more or less protoplasmic figures like 2.5. S or Z are often seen.

The nuclei are all darkly stained by methyl blue or haematoxylin, and show distinctly well their intranuclear structure. The chromatic nuclear wall with intranuclear ramifications are well seen.

Rarely, the protoplasm of the cells is not stained with eosin and in these cases it is finely granular with a distinct cell wall.

**Eosinophile Cells:**

Von Jekoch and Leopold has shown that the leukocytes can be variously classified according to the staining reaction of the granules within their protoplasm.

Other cells containing granules which stain with acid aniline dyes.
aurantia, as in the case of Agarophyllum or Oxyphillus.
Basophilies granules are those which stain with basic aniline dyes of:
dahlia, fuchsin, etc.
Neutrophilies granules, those staining with neutral dye of methyl blue and
acid fuchsin.
The eosinophilous cells have
assumed great importance of late in
the differential diagnosis of leuco-
cytosis and early leucocysthemia,
and in the past they play in the
role of phagocytosis.
They are somewhat larger than
the multinucleated leucocyte, but
not as large as the marrow cells.
The average diameter, according
to measurements made was about
11 and 12 μ.
They are usually round or oval
in shape, and have in some,
a distinct, in others an indistinct
cell wall. Even with a low power
of 40 with objective these cells are
Case III

Varieties of Eosinophils Cells.  
Dry Film Preparation, stained for Staining.
easily recognized by their being much more deeply stained with eosin.

The protoplasm stains with eosin, forming a background in which several spherical, highly refractile granules appear, arranged as a number of shot. Sometimes one or more granules are larger and more easily seen than the rest.

Most of the granules are small, but in all a few very large granules are conspicuous. The granules may be very dark and less refractile than normal, this gives the appearance of a cell with deeply stained protoplasm and dark, almost reddish brown granules.

The nuclei are often two in number and are found at the periphery of the cell. By far the greater part of the leukocyte's body occupied by granular protoplasm. In some the granules are mostly collected at one end, the nucleus being at the other, surrounded by non-granular.
protoplasm. The two nuclei are often connected by a structure which
stains like the nucleus but faintly, and therefore probably nuclear in
structure. Most frequently they are separate and unconnected.
Sometimes the nuclei are horseshoe-shaped, and, unlike the
nucliei of the multineucleated
leucocytes, occupy a peripheral and
not a central position.
The nucleus stains of a lighter
colour with haematoxylin than that
of the unineucleated or multineucleated
cell, but frequently one can see dark
fornules in the nucleus, stained
very deeply.
Between the eosinophile fornules one
occasionally comes across vacuoles,
or rather, unstained portions of the
background.
In those cells in which a nuclear
network is seen, the substance in
the network is of a pinkish colour,
especially so this noticeable towards
The periphery of the nuclei. Bright eosinophile granules are found occasionally lying in or upon the nucleus, and in these eosinophile leucocytes in which no cell wall is observable the granules are seen lying round the cell, as if in the preparation the wall had been ruptured and the contents allowed to escape.

They occur and attempted to draw various other modifications. In specimens stained with Methyl blue alone, without stain, I was able to identify one or two eosinophile cells by their peculiar shape, the arrangement of their nuclei, the granular highly refractive appearance of their protoplasm, and the peculiar tint with which they are stained.

Favors Uninucleated Leucocytes. Harrow Cells of Thrich or formed by Hayman "Leucocytes Hypertrrophic"
Case III

Varieties of Marrow Cells.
Dried Film preparation. Stained with Ehrlich’s Hematoxylin.
In my examination of several films of blood stained with haematoxylin and eosin from Myelodema Case III, I was struck by the presence of a number of very large leucocytes, having a single large nucleus and protoplasm, which stained in a peculiar manner with haematoxylin.

Whilst the nuclei only of the multi-nucleated and uninnucleated cells stain with haematoxylin, in these, both the nuclei and protoplasm are stained, and therefore, at first, in my examination, I thought of a better name called them "all blue" leucocytes.

These cells appeared to me at first to be merely a mass of protoplasm stained blue, but on further examination I recognised a nucleus surrounded by very faintly stained protoplasm.

In shape they are generally round or ovoid, but are not do regular as the somniphile cells.
They are larger than any other variety, and in size contrast markedly with the small round cells. Their average measurement proved them to be about 15 to 16 µ in diameter. The cell wall is sharply defined but extremely thin. They are chiefly uninucleated, with the nucleus occupying more than half the cell. The nucleus is of a pale Cambridge blue color, which is totally different from the violet nuclei of the multinucleated cell. Its nuclear wall is not very definite, and the nucleus tends to merge into the protoplasm. The chromatin threads, nuclear in structure, are very fine, and only slightly darker in color than the general nuclear substance. The nucleus often shows indentations and is very like that of the intermediate variety of keycyst. The surrounding protoplasm is of
a still paler blue, of the same tint, often almost colourless and glassy.

In one noticed faint filaments of red extending from the cell wall to and surrounding the nucleus. In some a number of minute vacuoles are seen both in the protoplasm and nucleus.

A similar difference in the colour of these cells is noticed in preparations stained with methyl blue.

Examination of the Blood of Nyxordina

Case IV.

The Red Blood Corpuscles:—showed greater alteration in shape and size than in the previous case.

The Leucocytes:—

The changes in the appearance of the white cells were very similar to those found in the former case.
Case IV.

Varieties of Multinucleated Lymphocytes.
Dry Film Preparation, stain with Romanowsky.
The Uninucleated Leucocytes:

There was a great proportion of large to small uninucleated cells. Many of the large forms were as large, if not larger, than the ordinary multinucleated leucocytes.

The nuclei of both the large and small variety showed particularly well the familiar intranuclear structure, and stain deeply with haematoxylin. The surrounding protoplasm in some cases being faintly, in others deeply, stained with eosin.

Multinucleated Leucocytes:

These varied more in size than those of the former case, and even in the same part of the film, a large multinucleate leucocyte may often be seen along side of a small one.

In both cases I noted that the size of any variety of leucocyte, varied much according to the
Position and condition of the film.
In parts in which the film was thick and the red blood corpuscles much run together, all varieties of leucocytes appeared smaller, whilst where the film was uniformly thin, spread, and the red blood corpuscles distinct and some distance apart, the white cells were larger.

The nuclei are more fragmentary and often show complete division. They are more granular and show the intra-nuclear network better.

In one case the nuclei assumed the form of a branch, and in some appeared surrounded by a halo of unstained protoplasma.

The protoplasma is, on the whole, more granular. There were a few forms of leucocytes intermediate between the ordinary multinucleated and the typical eosinophile cell, in which the protoplasma was granular and stained deeply with eosin, but did not contain
Case IV.

Varieties of Eosinophils Cells.
Dry Film Preparation, Stained with Hematoxylin.

Case IV.

Varieties of Myeloid Cells.
Druid Film Preparation, Stained with Hematoxylin.
definite spherical granules.

Little alteration was noted in the appearance of the Eosinophile Cells.
The Uninucleated or Marrow Cells, or as I have termed them, "all the
leucocytes" were seen in this as in the former case, and in size, shape, and staining reaction agreed entirely with the description given
above.

An Enumeration of the Varieties of
Leucocytes found in
Cases III and IV.

I have made frequent enumeration
of the different forms of Leucocytes
seen in these two cases of
Malignancy, and found that haemo-
phile and safrin were the most
useful double staines for this purpose.
By counting a large number on
the mechanical stage of a microscope
using an ¼ objective fairly constant results were obtained.

It proved necessary to count those in the uniformly thin parts of the film only. My results were very interesting and the cases closely coincide.

**CASE III**

<table>
<thead>
<tr>
<th>Total Counted</th>
<th>Multinuclei</th>
<th>Uninucleated Marrow Cell</th>
<th>Eosinophile</th>
</tr>
</thead>
<tbody>
<tr>
<td>112</td>
<td>72</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>164</td>
<td>140</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>219</td>
<td>143</td>
<td>57</td>
<td>15</td>
</tr>
<tr>
<td>244</td>
<td>175</td>
<td>38</td>
<td>13</td>
</tr>
<tr>
<td>141</td>
<td>103</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>165</td>
<td>117</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>1045</td>
<td>750</td>
<td>176</td>
<td>61</td>
</tr>
<tr>
<td>Percentage</td>
<td>71%</td>
<td>16%</td>
<td>6%</td>
</tr>
</tbody>
</table>

**CASE IV**

<table>
<thead>
<tr>
<th>Total Counted</th>
<th>Multinuclei</th>
<th>Uninucleated Marrow Cell</th>
<th>Large Marrow</th>
<th>Eosinophile</th>
</tr>
</thead>
<tbody>
<tr>
<td>456</td>
<td>360</td>
<td>45</td>
<td>20</td>
<td>23</td>
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<tr>
<td>342</td>
<td>260</td>
<td>38</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>566</td>
<td>400</td>
<td>66</td>
<td>53</td>
<td>33</td>
</tr>
<tr>
<td>532</td>
<td>375</td>
<td>77</td>
<td>31</td>
<td>36</td>
</tr>
<tr>
<td>1496</td>
<td>1395</td>
<td>226</td>
<td>125</td>
<td>107</td>
</tr>
<tr>
<td>Percentage</td>
<td>74%</td>
<td>12%</td>
<td>6.5%</td>
<td>5.6%</td>
</tr>
</tbody>
</table>
Comparing and contrasting the results obtained in the two cases, I found that in the most important points they closely resembled each other.

Amongst minor differences, I noted that the eosinophile cells were more numerous in Case II than in Case I. They numbered about 6% in the former and only 2.2% in the latter.

Ehrlich finds the eosinophile cells to be 25-4% in health, and according to the increase in (former) case it is distinctly pathological.

From measurements I made of the size of the eosinophile cells in this case, I found the average was 12 μ in diameter. Muir says it is rare to find even the largest leucocyte exceeding 10 μ in health.

Amongst other still less important differences, I noted in the second case that:

1. The nuclei of the small un- nucleated leucocytes showed more
nuclear structure.
i. The nuclei of the multinucleated leucocytes were more fragmentary and often separate.
ii. The occurrence of cells intermediate between the ordinary multi and the typical eosinophil cells.
iv. A larger number of the large variety of the ordinary uni-nucleated leucocytes.

The most noticeable features in both cases were:
1. An increase in the relative number of the multinucleated leucocytes. In case iii. they reached 71%, in case iv. 74%.

In health, the proportion of uni-nucleated to multinucleated leucocytes is as 1 to 2, but in pathological conditions this ratio may be considerably altered.
2. The presence in both cases of distinctly pathological elements
viz. "Marrow cells" or myelocytes.

Uninucleated Leucocytes.

In the former case they numbered 6% in the latter 5.6%.

These leucocytes I had never seen in any of the cases of anaemia
which I had examined.

Mr. H. in an article on Leuco-
cysticemia [Journal of Pathology, Part 2, 1893]
describes the appearance of these
uninucleated corpuscles in the spleen-medullary variety of that
disease, as corpuscles sometimes
reaching 16m in diameter, possessing
a single large nucleus, which is
sometimes indented at one side
or may even be horse-shoe shaped,
but never showing the complicated
multipartite character seen in
many of the ordinary leucocytes.

The nucleus, in sections of these,
is poor in chromatin, staining
much less deeply than the nuclei
of the multinucleated leucocyte.

It has a distinct membrane, and
shows in its interior little masses of chromatin, with a few fine threads suggesting the presence of a very open intranuclear network.

In dried film preparations, the nuclei of these cells are more difficultly stained, but in some of them a nuclear network may be made out with fair distinctness.

They bear a marked similarity to the so-called "marrow cells" and Muir, and many others believe them to be identical.

He says they were associated with an increase in the number of the ordinary multinucleated leukocytes.

There is a general agreement amongst observers—Ehrlich, Muller, v. Einthoven etc.—that lymphocytomaemia is the only disease in which these large neutrophile uninnucleated corpuscles or marrow cells are present.
I am convinced that the corpuscles which I at first termed "all blue leucocytes," and of which I have given a description and drawings above, are identical with these "Marrow Cells" or "Neutrophile unimembranated Leucocytes." I have come to this conclusion after reference to drawings and literature on the subject from:

1. The peculiar manner in which they react with staining reagents.
2. Ordinary multinucleated or unimembranated leucocytes when stained with eosin and haematoxylin, show the nucleus or nuclei, with the intranuclear structure, deeply stained of a violet blue with haematoxylin, and the surrounding protoplasm stained of a pink colour with eosin.

These marrow cells, however, show with the same stains, the nucleus of a pale Cambridge blue, with the intranuclear structure hardly
visible. The surrounding protoplasm is stained of a still paler blue.

Secondly, from their size.

Ordinary leucocytes of normal blood seldom exceed 10μ in diameter. The cells in question measured fully 15μ, and in some cases 16μ.

Thirdly, from the shape of their Nucleus, which is generally oval and often shows an indentation at one side.

The pathological conditions met with in these two cases of Myosodema, in one, an increase in the number of eosinophile cells and in both, the presence of Marrow Cells associated with an increase in the ordinary multinucleated leucocytes, resemble Leucocraecemia more than any other blood disease.
Competent observers—Schürch etc.—have stated that the marrow cells occur only in leucocythaemia, stating in fact that they are diagnostic of it.

They say they originate from the bone marrow, as exactly the same form of leucocytes are seen in the marrow of bones.

So far as I am aware these marrow cells have never before been recognised in Myxodema, and at first one is inclined to attribute their presence in this disease, as having some immediate relation to the artery or absence of the thyroid gland.

In favour of this view is Koch's statement that after excision of the thyroid for disease anaemia followed, and he suggested that this might lend support to the theory of Cade and Ziege that the thyroid gland has blood-forming functions, but
on careful examination, he found no entanglement of the spleen.

Lockhart Rixon [Journal of Anatomy Phys. Vol. xx. 1846] has however shown that
the blood possesses no such power,
and is not compensatory to the spleen.

Think, on careful consideration,
that in Myxedema there is, as
in leucocysthemia, a pathological
condition of the bone marrow,
whereby these cells pass into the
general circulation, and this is
probably accounted for by the
influence the atrophy of the thyroid
gland has on the cerebral centres
and particularly the sympathetic
nervous system.

Whether my views on the subject
are correct, further observation and
more particularly, examination of
the bone marrow in Myxedema
after death, will prove.