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Observations on Myxoedema with special reference to Pathological Conditions found in the Leucocytes.

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Contents.

Resumé of Subject of Myxoedema. page 1.

Clinical Cases

- Case. I. 30
- 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 Myxœdema with special reference to Pathological Conditions found in the Leucocytes.

The subject of Myxœdema which I have ventured to bring before your notice has latterly 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 resumé of the subject - secondly a clinical description of four cases and finally my observations on the leucocytes of the blood.

Myxoedema was first recognised and described by Sir Wm Gull [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 inaptitude to spontaneous exertion of both mind and body.
The deposit of fat and changes in the connective tissue correspond to a languid condition of the venous circulation but without any tendency to any oedema or any signs of cardiac disease, and perceiving its similarity to the cretin state termed it tentatively rather than dogmatically a cretinoid condition.
He considering the whole of the symptoms were caused by or related to the jelly like swelling of the connective tissue, proposed the term of Myxoedema, as one

representing the condition, but not an explanation of its cause.

Myxoedema 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 though 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. [Med: Rec: New York. Sept. 13. 1890.]

In some, the symptoms of myxoedema have been preceded by enlargement of the thyroid, a case being recorded of myxoedema occurring with goitre & Exophthalmos. [Ord. Brit Med Congress. V. 132.]

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 tubercle.

Amongst other causes suggested are - mental and menstrual disturbances, frequent pregnancies, prolonged lactation.

Buzdygan [Sajous 1892. Vol iv H.] recognises a connection between the occurrence of myxoedema and alterations in the

reproductive organs. Clarke [Edin Med. Jour. May 36. 91.] reports the disappearance of Myxoedema in hereditary insanity; and it is stated to have occurred after the long continued use of Potas. iodide for another disease [Stalker Lancet. 10. Jan. 1891.]

Myxoedema has been attributed to acute rheumatism, and is said to have followed Excess in haemorrhage.

Myxoedema is characterised by alterations in the skin, hands, voice, 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 flush 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 obliterates the

lines of expression.
The alae nasi broadened and flatt-
-ened, causing the eyes to appear
wider apart than usual. The
nostrils are swollen.
The Eyelids - swollen, thickened and
rolled, - translucent or waxy looking
hanging down and almost covering
the eyes - the lower lid hanging
down on to the cheek. They look
oedematous, and remind one very
much of a case of renal dropsy,
but do not pit on pressure.
The Eyebrows elevated so as to help
support the eyelids.
Lips are thick, pendulous, blubbery
and everted with often a livid
colour. Sometimes allow escape of
the saliva.
The mouth expressionless, widened
transversely, and slit like, with
lips pressed together.
The general facial appearance is
very characteristic. It is stolid,
heavy, apathetic with total lack of

expression; the features appear coarse and large and in fact cretinoid. There is often marked scantiness of the hair which is crisp dry and brittle - the scalp is scaly, some cases (cf Case I.) being almost completely bald.

The head is sometimes hung down on the chin, and when elevated with difficulty, falls very much backwards and to one side Ord. [Med. Chirurg. 78]

There is usually fulness about the neck, and the skin is thrown into folds. The subcutaneous tissue and fat above the clavicles seem to be increased.

The thyroid is diminished in size, atrophied or completely wanting.

The patients usually appear bulky massive - their movements clumsy and awkward. Their weight is usually increased.

The temperature is nearly always subnormal.

The hands are described as spatu-

like, but I fail to see how a thick broad hand resembles a spade.
The fingers are thick and awkward and less fit for finer manipulation.
Their sense of touch is diminished, patients often saying they cannot sew or execute finer movements as well as they could do. The whole hand looks swollen and bulky, and has lost much of its former comeliness.
The nails are short and thick: sometimes however they are incurved, those of the fingers completely covering the pulp. Harley. [Med. Chir Trans 1884].
The feet are also bulky and swollen and often cold.

Integumentary System:-

The skin over the body generally is dry, harsh, showing tendency to crack - with little or no perspiration or sebaceous secretion. It is often covered with scales or branny desquamation. To the touch it feels rough and sometimes elastic. There is over the body

an increase in the amount of the subcutaneous tissue, and the skin has in folds, this is particularly the case about the clavicles in front and the neck behind.

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

Oedema is present, more or less, over the whole of the body - It differs however from true dropsy, 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 oedema may occur concomitantly - but accidentally in the lower extremities, and does often present itself towards the end, secondary to vascular changes.

The swelling of myxoedema varies from time to time being most marked in cold weather. This I have noted particularly in Case IV.

Nervous System:-

Sensory functions.

Many of the patients complain of feeling cold. They say they never feel comfortably warm, and sit nursing themselves near the fire, or lie huddled 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 - giddiness.

Exceptional symptoms recorded by Kraepelin [Sajous 1891. Vol IV H] are anxiety, need of warmth and tremors (only one observed before). These symptoms he says occur also in Cachexia strumipriva and exophthalmic goitre.

In a case recently recorded by Mr. Anderson shivering of the sinciput seemed a prominent and troublesome symptom. [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 patients responds to external stimuli of any description.

Notwithstanding the feeling of cold which many patients complain of, there seems to be a deficiency in the perception of external variation in temperature - many of them lie exposed to draughts without taking any notice.

The Special Senses, on the whole may be said to be less acute than normal. There 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 perverted. One case had a "peculiar sour taste in the mouth and foul smell in the nostrils" Ord. [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 tendency for the knees to give way unexpectedly.
Mental functions:- There is marked slowness in perception, thought and action, but as Ord states - 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 patients appear 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).

The 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 described is characteristic.

I remember hearing one of the Edinburgh Professors says that

he could diagnose a case of Myxoedema by hearing the voice and seeing the hands.

Ord [Med: Chir: Trans 1878] describes the mode of speech thus - "When about to speak she closed her lips, throwing 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 leaden with little or no intonation.

It seems nasal and gruff and has been compared to that of quinsey. The alteration in the voice is often noticed by the friends of the patients.

The temperament varies, some are irritable and fretful, others placid.

Alimentary System:-

The lips are thickened and pendulous - the gums swollen

The teeth tend to fall out or decay. The tongue is often broad thick and swollen. It is protruded slowly. The tongue is too large for the mouth, so that false teeth cannot be worn. (Gull).
The fauces and uvula are swollen, and sometimes difficulty in deglutition is experienced.
The appetite impaired. Nausea is frequent. The bowels usually constipated, in one case the act of defecation was attended with difficulty on account of the oedematous condition of the part.
Not infrequently there is a tendency to dyspeptic troubles.

Haemopoietic System:-

The thyroid has almost universally been found atrophied or absent, and as Curling observed [Med. Chir. Trans 1850] that whilst goitre was more or less associated with endemic cretinism, the thyroid was actually absent or

atrophied in **poradic cretinism** occurring in this country, and says assumes the presence of goitre to be a safeguard against cretinism.

A case is recorded in Brit. Med. Journal 1893 of the occurrence of Myxoedema with goitre

The lymphatics have been noted in some cases to be enlarged.

The Blood in Dr's first case was examined microscopically and found normal.

The Report of the Committee on Myxoedema [Med Chir Trans. 1888] states in the blood of 24 cases no characteristic changes were observed. It was normal in 16 cases; in six, 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 anaemia present.
The heart is usually normal, except towards the end, when kidney mischief has started and hypertrophy 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 atheroma.
The capillaries of the face are dilated. There is a tendency to hæmorrhage.

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

appear towards the late stage.
The amount of urea is almost always diminished.

Reproductive System:-

The catamenia may be excessive. The vulva and os have been noted as swollen.

Little alteration is found in the Respiratory system, but a tendency to the development of phthisis is remarked by many.

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 lunatic 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. Ord. [Ueber das Myxoedem V. Berlin Med. Congress 1890].

Pathology:-

The general belief now expressed is that Myxoedema 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 celled 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 sudoriparous and sebacious glands, and the hair follicles are infiltrated with, and surrounded by, a number of small cells.

Ord explains [Med Chir Trans. 78.] the

No. 2984

COUNTY HOSPITAL
YORK

Sep. 27th 1893.

Dear Sir.

Enclosed please find cheque for £6.5.0 for my thesis (on "Myxoedema") for the M.D.

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

I have forwarded the thesis by this post.

April 27th 93

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

I further state that I have passed the subjects of Greek and Logic in the Preliminary Examination at the University - and that

I am 26½ years of age.

Alfred Charles Coles.

M.B. Cy. 1889.

B.Sc Public Health 1890.

"Rivoli"

Grosvenor Pl.

Bournemouth.

Jam D. Sir
Yours tru
J. C.

The Chief Clerk
University Co

University of Edinburgh

Thesis: Coles.

Commend.

W. L. G

inaction of the skin by the atrophy of the sweat glands and by the padding of the nerve termination in the skin with the jelly like substance, so that there is a loss of tonic influence.

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

Harley [Med Chir Trans 1874] 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 fibrous invasion producing a chronic cold debility."

He thinks the myxoedemic and sclerodermic conditions in these patients were the result of some old inflammatory mischief, affecting, amongst others, the pleura, peritoneum and sympathetic.

Savage thinks [Journal Mental Science Jan 80] that the delusions etc 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, fat etc 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 Myxoedema - finally state that

there is strong evidence that myxoedema sporadic cretinism, endemic cretinism cachexia strumipriva - (is the term applied by Kocher to the condition which develops after total extirpation of the thyroid) - and the operative myxoedema 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 annihilation of the thyroid body. [Clin Soc Trans. Supplement. XXI.]

What the cause of the destruction of the thyroid is - seems as yet undetermined.

Bircher reports ~~four~~ cases which support the theory that the function of the thyroid is to prevent the accumulation of mucin in the tissues. [Centralblatt fur Chirurgie Leipzig June 28/90]

He considers 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 cysts in the gland structure.

They however remark that Dr Hadden

never found the pituitary body enlarged in myxoedema.

Treatment:-

Till recently the treatment of myxoedema has been very unsatisfactory, and the condition regarded as practically incurable.

Tonics, especially iron, strychnine, quinine etc, have been used, but with little success.

On 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: Granger 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 etc were impossible - the improved

the skin and relieved her other symptoms by rubbing the skin with a rough flesher. This in conjunction with a good diet - the administration of arsenic and tonics, was followed by marked improvement.

Lately the treatment of myxoedema has taken new lines, and very remarkable results have been obtained with the "Thyroid treatment."

As Ord pointed out, the primary and constant constant-condition present in myxoedema 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 thyroidectomy could be diminished by transplanting a thyroid gland previous to the operation. Prof Horsley suggested the transplanting of thyroid in

myxoedema, and the benificial results which followed were evidently due to the absorption of some substance in the gland.
Vassale and Gley showed that the injection of an extract made from the thyroid, removed the acute symptoms which followed thyroid-ectomy in dogs.
Brown-Séquard and D'Arsonval suggested in 1891. that such an injection - subcutaneously - would prove successful in Myxoedema.
Previous to this, and quite independently of these observers Dr. G. Murray of Newcastle had tried this method with good results, and afterwards Dr. Napier and others, published successful cases.
Murray's Method of preparing the Extract was as follows [Braithwaite Retrosp. 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 mxxxv. of this extract are injected (with antiseptic precaution) 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 occurrence of induration or abscess at the point of injection, the occasional appearance of alarming symptoms & the difficulty of preparing an aseptic aqueous extract.

Drs Fox and Mackenzie independently and about the same time suggested the administration of fresh thyroid gland by the mouth.

The freshly minced gland is given with brandy or beef tea.

Mackenzie minces the gland - adds a few teaspoonfuls of water and allows it to stand for ½ 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 troublesome 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, diminishes — the hands and feet desquamate and the harsh rough skin is replaced by soft fresh 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 tabloids 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 myxoedema, 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 everted especially the lower. The eyelids swollen

but did not pit on pressure
The hands were thick, swollen and awkward.
The tongue was large and thick, it was protruded slowly, its size seemed to interfere with her speech.
She spoke imperfect English very slowly, the 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 the legs after her, with the head bent forward.
The skin was everywhere dry and harsh - the subcutaneous 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 altered 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
with 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. till I was struck
by her peculiar physiognomy.
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 enjoyed good health till the last child was born some 6 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 extremity - 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, so much so, that her brother after three years absence could not recognise 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.
It is expressionless - the features blunted and coarse, the naso-labial furrow etc are completely obscured by the general swelling.
The face looks pale and anaemic,

but there is at times a well mark-
-ed localized malar flush.
The skin of the face is smooth and
dry, puffy and transparent looking.
The Eyelids, especially the lower, are
swollen and look oedematous.
The lips are thickened, ill
coloured 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 denuded
of hair, beyond a few short
stumps. It is not as clear or
shiny as in alopecia areata, but
the skin has an atrophic dry
scaly appearance.
The hair over the fore-part of the

head is thin and scraggy, 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 enlarged and this was commented upon by the patient.

Her speech is slow, monotonous and drawling - The voice is thick guttural and somewhat indistinct. Her thought seemed slow. When asked a question, it takes her sometime to realize what is said and is a long time in answering. Her movements are clumsy 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 felt as though the knees would give way.
The urine which was examined frequently showed no trace of albumen.
There ~~was~~ no oedema 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 Hyd. 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 been lost sight of.

Photograph of E. S. Case III.
Taken some time after
treatment had commenced

Case. III.

E. S. widow aged 53 living at Clifton near York. Admitted into County Hospital Nov. 21st 1892. Was sent into hospital as probable commencing uraemia.

Complains chiefly of weakness, giddiness, occasional headache and nausea.

History.

Hereditary Tendencies:-

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 her father's second marriage, the other three died in childhood but does not know the cause of death.

Father died at the age of 90 from old age.

Patient married at age of 27 and had six children, the second died in infancy, the other members of the family are in good health

The eldest living 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 Illnesses.
Patient had measles when a child and - says - scarlet fever at the age of 30, having to keep to 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 gained from the patient as to the time and mode of origin of the present illness. She complains of dizziness which has lasted for a year, of blindness 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 inpatient at the hospital and regarded then as a case of Myxoedema.

From the eldest daughter I ascertained that her mother came to the hospital on account of swelling - particularly of the eyelids 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, the 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 recognises 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 sent 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 uraemia and advised

her removal to the hospital.
On looking at the case, I thought it to be either one of Bright's disease or myxoedema, 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 I 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. Her position was exactly that which would be taken to keep the body warm.

She is rather a small women weighing on admission only about 7 stones 2 lbs. slightly built, not very muscular about 5ft 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 thrown into folds on the forehead. It feels thickened.

There is at times a slight delicate rose coloured malar flush, and what is rather noticable 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 bag 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 attenuated 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 eye, she has to thrown back the head to counteract the drooping of the lids.

There is a tendency to catarrhal condition of the conjunctivae.

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 orifice 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 cretinoid - 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 universally thin and scanty, but at the occipital and posterior 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 boggy.

The neck is thickened, especially at the posterior part.

The Hands are dry, smooth, with an atrophic look of the skin which is shiny more particularly at the finger tips. The hand is somewhat thickened, the fingers taper off at the extremity with the 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 tissues over the trunk seem to be increased: over the whole of the chest and upper part of the abdomen the skin can be grasped in handfuls.

There is no true oedema of the lower extremities. Over the lumbar region it was noticed that the tissues seemed very thick, and on prolonged deep pressure one could fit a peculiar pitting which I have never seen before: the pit persisting longer than a quarter of any hour, and had a hard ridge round it, very like the pitting one can obtain

in a fat cadaver, as if the sub-cutaneous tissue were setting.

The patient complains of the difficulty she experiences in keeping warm, and says when up she is always sitting over the fire. The pigmentation of the skin of the legs attesting to the truth of this statement.

The temperature is subnormal, the averages of the first three weeks being 96.5° Fah. The lowest was 96° Fah. The highest 97.4° F. 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.re

Nervous System.

Sensory Functions:—

Patient complains chiefly of giddiness. 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 pricking with pin - somewhat slower response than usual.
She distinguishes easily between hot and cold test-tubes.
Vision somewhat impaired.
The 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, epigastric & skin reflexes normal - as 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 fore-finger - 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 still sleeps much during the day.

She often complains greatly of headache - 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 peevish.

Alimentary System:-

The lips are dry, not anaemic. There is a tendency to eversion 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 weary languid feeling after a meal.
She has, for the past few months, felt sick particularly before breakfast. 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 was 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 dulness on percussion, of the liver in the nipple 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 ankle she cannot hurry as it gives her headache all the day. She feels dizzy and has occasional attacks of giddiness 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 (aortic) 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 fluttering - rather than an impulse - at a point 1½ inch below the left nipple, in the nipple line.


C S: Case II. Press. 2½ oz

The outline of cardiac area, by percussion, seems fairly normal.
Auscultation :- Over the whole of the cardiac area, little beyond the 2nd sound is audible - which, 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 as 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 rythym and force.
The vessel is somewhat small.
The tension of the pulse, as tested by

rolling it transversely under the fingers - is normal.
The strength, as measured by the compressibility, is somewhat diminished. No atheroma or tortuosity of vessel wall.

Respiratory System :-
The breathing is slow and deliberate rapping about 14-15 per min. very 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 & 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.
Auscultation :- The normal vesicular 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 apex 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 apices, 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 1/15.
No blood was found by the guaiacum test.
On microscopical examination it

was seen that the sediment consisted of pus, and several varieties of epithelial cells from the genito-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 flocculent yellowish-white deposit.

Its odour was peculiar.

The specific gravity was on an average 1022.

The reaction was constantly faintly acid.

There was no albumen present.

The quantity of urea was greatly diminished - only 99 grains being excreted in the 24 hours.

No sugar or bile was detected.

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

Reproductive System:-

Menstruation began when 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.

Haemopoietic 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 Thoma-Zeiss 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.]

Locomotive System:-

At first the patient was quite unable to stand alone, and only lately has she been able to walk without support. To-day she walked down the ward, touching the beds when she

felt herself falling.
The walks is irregular, the legs are drawn after her in a bailing manner, and she tends to fall forward.
The joints are normal, except those of the knee, in both of which the patella is rotated inwards, and the whole of the knee inverted. The tibiae having, so to speak, a compensatory curve on them.

Treatment and Progress.

On admission - Nov. 22, the case was put on digitalis and iron, and milk diet, simple aperients being given almost every day.
From November 22nd to Dec. 12th the temperature remained subnormal at an average of 96.5° F. the pulse 61. and respiration 15 per minute.
Then the temperature rose a little and remained at about 97.4° F. for a month.
A mixture of soda, gentian and

arsenic was then given and quinine sulphas for the headache. Strychnine 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.

On 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.

On Feb. 14th a whole thyroid gland was given, minced, as a sandwich. The temperature rose from 96.7 on the 14th to 99.6° on the 15th and to 100.5 on the 16th inst, the pulse being 82 and the respiration 16 per minute. Patient immediately complained of headache and nausea.

The face on the 16th inst was flushed.
The skin hot. She says she feels
ill, the temperature in evening
reaching 101.2°F the pulse 99.
She vomited twice.
Feb 17 18th Still feels ill. Complains
very much of frontal headache, and
at times, is very cold. Generally, she
feels, to use her own expression funny.
Tongue is not altered. She feels
very sick and frequently giddy.
The eyeballs seem sunken.
In the morning she wandered a little,
and seemed very excited for about
an hour. In the evening cheeks
and forhead flushed - temperature 100°
vomited once, the ejecta being bile
stained.
Feb. 19th To day the speech is very
slow and plaintive - she is pirish
and groans continually. Vomited
once. She asks vacantly and
repeatedly for a drink. Says her
feet 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 remaining normal till March 7th when it again became subnormal - the pulse however kept at about 84, but now it is normal again. (12 for her - 60 per minute) the temperature being sub-normal.

Some days after she had recovered from the effects of the first gland, we tried to give her half a sandwich thyroid minced, in a sandwich, in beef tea, and in brandy but much as she herself tried 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

up. 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°7 at 6p.m. The urine increased from 12 to 56 ounces in the 24 hours.

April 1st Slept all night and day and complained - when roused - very much of her 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 The urine decreased to 14 ounces The legs normal in size.

Temperature was 102°7 at 6p.m.

April 2nd Vomited bile stained - green - liquid. She has been quiet and sleepy all day. Took her milk better. Temperature 100°7 at 10a.m. and

99.7 at 6pm.
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 attacks but said it was due to her head being so painful.
She vomited three times to-day. The vomited matter being green. Hardly took any milk - said her throat was very painful.
Gargle of Potass. Chlorate was given on April 2nd and hot fomentations applied to the neck.
Face flushed. Respirations 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. Urine decreased to six ounces.

April 5th 6th & 7th Patient greatly improved - quite sensible.
Bowels very constipated and urine decreased.

Finding it impossible to give her fresh thyroids, we have commenced the administration of tabloids of thyroid, each said to contain gr½ of thyroid gland.

Photograph of M. A. Case IV.

Case IV.

M. A. spinster aged 52 - a servant. Born at Pocklington near York; residing in York.

The patient came as an out-patient 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 I expected, no albumen.

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

This was in Nov. 92. and although much interested in her case I

lost sight of her till January of this year.

History.

(α) Family History:-

The patient states that her grandmother, on maternal side, enjoyed good health and lived to be 86. The grand-father was always thin; he suffered much from cough and shortness of breath and died at the age of 85, "choked with blood."

There was no history of the grand-parents 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. So weak was she

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 - with the exception of the last - were normal, and there is no history of flooding.
She died at the age of 49.

Patients father died of consumption aged 60.

There were eleven 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 this 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. A brother 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 36 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 good 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 Pocklington.

Whilst a child she had quinsy. She then remained in good health till 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 states 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 characterised by head symptoms and delirium. This fever lasted some time, and when she got up, found that she could not get 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 1886. There is no history of syphilis.
Patient says she has never sustained any accidents.

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 1886. 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 thickness 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. The limbs 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 giddy, 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 breasts. She never suffers from headache.

State on Admission :-

Patient is 5/t 5 ins 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 bulky. The face is swollen and broadened, 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 everted. 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 occasionally and there is profuse lachrymation, 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 cretinoid.

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 spade like, the skin being rough and harsh. 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 brings

about a feeling of stiffness and numbness. When the hands are at their worst, she can sew 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 scaliness 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 bulky, the upper arms are 10½, and the forearms 8½ inches in circumference.

The chest, at the level of the 3rd

costo-sternal articulation, measures 33/2 inch in circumference, at the level of the ensiform cartilage 28/2 inches: the abdomen at the level of the umbilicus 33/2 inches.

The tissues of the back are thickened, but there is not pitting 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 time to time, 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 sebaceous secretion.

The patient has always a feeling of coldness.
Her temperature is subnormal and averages 97° Fah.

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, sew, 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 shivering.
The sensibility to touch, heat etc is normal. The muscular sense, as tested by lifting bodies 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's types, showed R = $\frac{15}{40}$ and L = $\frac{15}{200}$.
Retinoscopy revealed hypermetropy to the extent of Right = + 4 D. Left + 3 D. With glasses + 4 D oph. for the right and + 5 D oph. 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 so well with the right ear. The hearing is easily affected

by cold. Her 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. She notices that when walking down stairs, the left leg appears sometimes to catch, and she easily trips over a slight obstacle.

Vasomotor functions:-

There is pallor of the face, with a variable malar flush.
Perspiration 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 ages etc of the members of the family with great readiness but forgets what happened yesterday 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, the voice is hoarse and thickened and somewhat monotonous.
Her walk is slow, as if engaged 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 motions natural in appearance.
The abdomen:- The abdomen is tumid, the walls flaccid and thickened - The umbilicus not depressed. There were linea albicantiae at the lower part. Palpation and percussion showed no alteration in the size of the liver or spleen.
Haemopoietic 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-Zeiss apparatus gave as an average 4.880,000 per cubic millimetre of blood - with Gowers Haemocytometer the red cells numbered on an average 4.900.000 per cubic millimetre.
The leucocytes showed no marked increase. [for further description of the leucocytes see below.]


Case IV. Press 3½ oz

Circulatory System:-

There is occasional palpitation on exertion.

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

On palpation, the apex beat is felt as a diffused somewhat weakened impulse, displaced downwards and outwards.

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

Auscultation - The 2nd sound of the heart is short and sharp in all the areas. The 1st sound is heard distinctly but somewhat distantly.

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 fremitus and resonance are normal. There is no alteration in percussion note - and the breath sounds are natural.

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.
The urea measured about 350

grains in the 24 hours.
For microscopic examination, the deposit was seen to consist of mucus. No tube casts 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 iron - 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:-
1st In the fresh condition.
2nd With the aid of some preservative.
3rd By dried film preparations.

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

If a ring of Canada balsam be run round the edges, 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
2nd Preservative fluid may be used.
Of these, Hayem's solution, which
consists of Sodi Chloride 1. Sodi Sulph.
5. Hydrarg: perchloride ½ and distilled
water 200 parts is extremely useful.
Bizzozero's methyl violet salt solution
i.e. .6% Sodi chloride tinted with
~~methyl~~ violet may be used. or
a solution of Sodii sulphate of spec:
gravity 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 Fluid film Method.

The method of making dry
films on coverglasses, suggested by
Ehrlich, for the examination of
bacteria in liquids, has also been
applied to the examination of the
blood.

The usual description [Muir. Journal of

Anat & Phys. Jan 1891] is that a drop of blood of suitable size is allowed to spread itself out into a thin film between two coverglasses, which must be scrupulously clean. The two coverglasses 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 120° C. This seems necessary to fix the elements in position and to allow the corpuscles to retain the haemoglobin.

Knowing the difficulty of manipulating the coverglasses, 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 sputum for tubercle bacilli. Making films on slides is much easier than on

coverglasses. It is not easy to clean very thin coverglasses without breaking them, and when clean it is extremely difficult to spread a film of blood uniformly on them, without getting the outside greasy, and besides, the process has to be performed rapidly or the blood begins to coagulate, or the corpuscles to crenate.

The lobe of the ear, or the tip of the finger, which-ever 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, pricks the largest drop of blood with the least pain.

It facilitates matters, if the lobe 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 grasped at their extremities - On one, the lower, the drop of blood is allowed to touch near the grasped end, and the other is used in one of two ways - either both slides laid flatly and then gently slid apart, or, as I latterly found better, the bottom slide held horizontally, and the top 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 top slide would scrape all the blood off, but if carefully done, and if the slides are perfectly flat, it leaves

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 waved to and fro 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 films 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 &c, and in manipulating the slide with the film, on the stage of a microscope, it is important that the fingers 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 this film.

If to one of the slides so prepared a drop of stain be 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 osmic acid - 1% solution, or of making the puncture through a drop of osmic ac: solution, the blood being allowed to mix with it, and the film spread and dried.

Muir [Journal Anat & Phys. 1892] quite recently suggested placing the films downwards - before any drying can occur, on the surface of a saturated solution of corrosive sublimate - 3/4% with 3/4% solution of sodic chloride added, preferably heated to a temperature of about 50°C and allowing them to remain for about half an hour.

They are then washed thoroughly in a 3/4% 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 uppermost- over the flame of a spirit lamp, heating gradually and getting 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, I 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 gives good results is Methyl blue in a saturated alcoholic solution. It is only necessary to stain for about ½ - 1 minute. The nuclei of the leucocytes 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. Fuchsin 5% alcoholic solutions is recommended as a good contrast stain.

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

As the leucocytes with eosinophile granules are of most importance in pathological conditions, we have in this Haematoxylin & Eosin a very useful stain for clinical diagnosis.

The double staining is better performed in two stages than using the stains in combination.

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

The Method of Staining:-

As I was using slide instead of coverglass films, the stain 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 takes very little stain, which can occasionally be filtered to prevent any deposit.

The time necessary for staining with the acid haematoxylin solution 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. I here 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, cleared with xylol and mounted in Canada balsam.

Examination of the Blood of Myxoedema.

Although it is now acknowledged that the thyroid gland has not the blood-forming properties once attributed to it, yet I 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. Megalocytes - others not more than 4 or 5 μ - Microcytes.

Eichorst's duply stained red cells were not seen at any time.

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

fragmentary.

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 plates 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 Leucocytes.

These have been divided by several observers, into different classes, either according to the number and condition of their nuclei, the size of their cell, or the appearance of their protoplasm.

I have, for the purpose of enumeration and description of the white blood cells, classified them into the easily recognisable and distinctive groups of:-

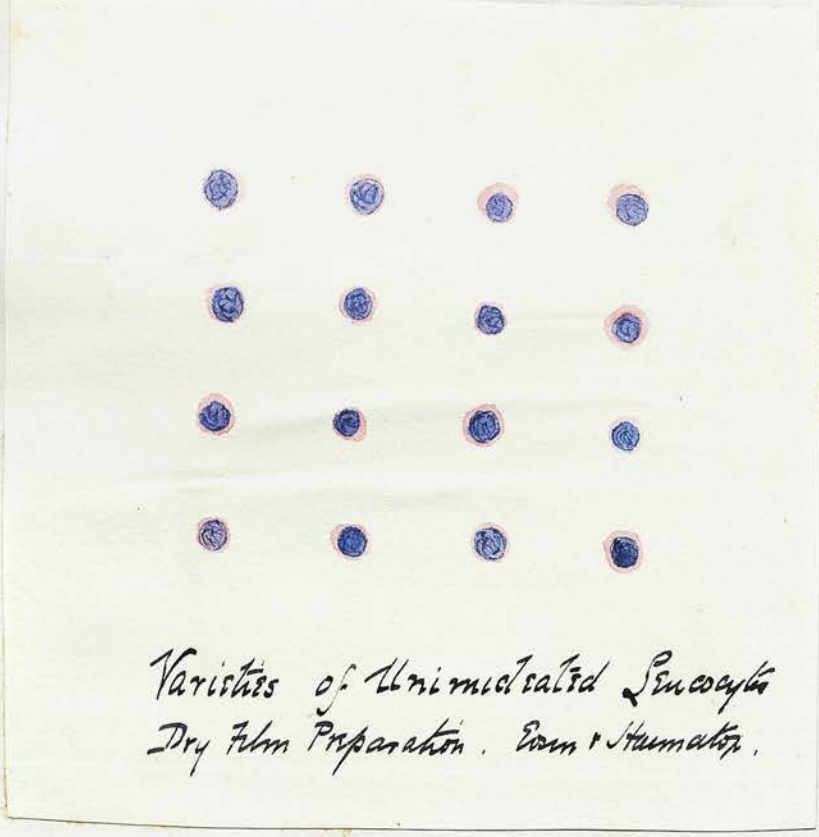
1st Uninucleated Leucocytes - those possessing a single nucleus, and of which a large and a small variety is to be seen.

2nd Multinucleated Leucocytes - 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 joined more or less together, might be correctly termed 'leucocytes with multipartite nucleus.

3rd Eosinophile Cells - i.e. leucocytes, the protoplasm of which contains granules which stain deeply with acid aniline dyes e.g. eosin & aurantia. Not an aniline dye —

4th 'Large Uninucleated Cells' termed by Ehrlich - 'Marrow Cells' and by Hayem - 'Leucocytes hypertrophies'

The following water-coloured drawings by R. Cattley Esq. illustrate exactly the microscopic appearances of the various elements.



Varieties of Unimucleated Leucocyte
Dry Film Preparation. Leon & Staumaton.

Uninucleated Leucocytes:-

The most common form of this variety seen, 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 intra-nuclear 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 deeply. Sometimes however none is to be seen.

The small uninucleated cells vary somewhat in size - some are but

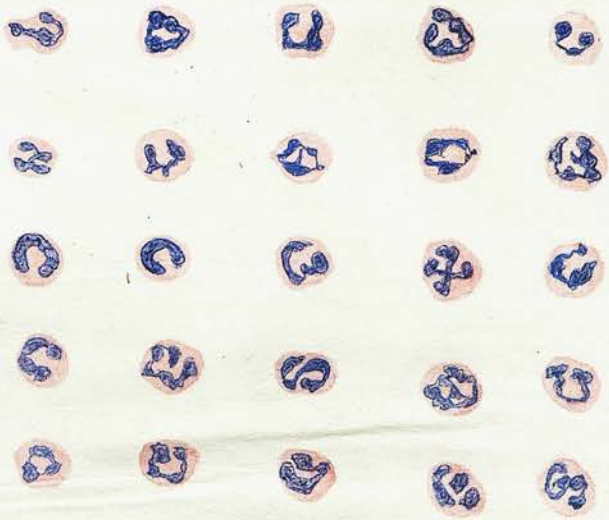
slightly larger than the red blood corpuscles - others not so large.

The large uninucleated 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. Found that the small uninucleated leucocyte measured about 6-7½ μ in diameter and the large about 9 μ. in diameter.

Case III.



Varieties of Multinuclealed Leucocytes.

Dry Film Preparation. stained with Eosin & Haematox.

Multinucleated Leucocytes:-

These vary in size, they are larger than the uninucleated but not as large as either the eosinophile 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 Methyl 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 five or six being in some cases counted - and there is usually some attempt at arrangement, thus if there are two nuclei, they are often at opposite ends, if three, in the form of a triangle, four taking 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 horse-shoe, surrounded by, and enclosing, more or less protoplasm. Figures like 2. 5. S or Z are often seen.

The nuclei are all darkly stained by Methyl blue or haematoxylin, and show extremely well their intra-nuclear 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 faintly granular with a distinct cell wall.

Eosinophile Cells:-

Ehrlich has shown-[Von Jaksch Clin: Diagnosis 1893. page 31.] that the leucocytes can be variously classified according to the staining reaction of the granules within their protoplasm.

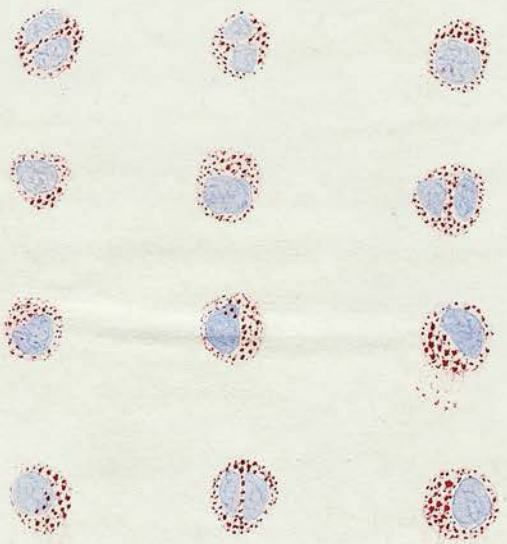
Those cells containing granules which stain with acid aniline dies- E.g.

aurantia, eosin etc are termed Eosinophilous or Oxyphilous.
Basophilous granules are those which stain with basic aniline dies eg.- dahlia, fuchsin etc.
Neutrophilous granules, those staining with neutral dies eg. methyl blue and acid fuchsin.

The eosinophilous cells have assumed great importance of late, in the differential diagnosis of leucocytosis and early leucocythaemia, and in the part 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 11μ or 12μ.
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 eg ⅙ inch objective - these cells are

Case III.



Varieties of Eosinophile Cells.
Dry Film Preparation. stained Eos. Haematox.

easily recognised 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, thus giving 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 leucocyte being 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 fainter, and therefore probably nuclear in structure. Most frequently they are separate and unconnected. Sometimes the nuclei are horse-shoe shaped, and, unlike the nuclei of the multinucleated leucocytes, occupy a peripheral and not a central position.

The nucleus stains of a lighter colour with haematoxylin than that of the uninucleated or multinucleated cell, but frequently one sees dark granules in the nucleus, stained very deeply.

Between the eosinophile granules 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 is 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.
I have seen and attempted to draw various other modifications.
In specimens stained with Methyl blue alone without eosin, I was able to identify one or two eosinophile cells by their peculiar shape, the arrangement of their nuclei, the granular highly refractile appearance of their protoplasm, and the peculiar tint with which they are stained.

Large Uni-nucleated Leucocytes - "Narrow Cells" of Ehrlich or termed by Hayem "Leucocyte Hypertrophie"

Case III.

Varieties of Marrow Cells.
Dried Film preparation. Stained with Eosin & Hæmatoxylin

In my examination of several films of blood stained with haematoxylin and eosin from Myxoedema 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 multinucleated and uninucleated cells stain with haematoxylin, in these, both the nuclei and protoplasm are stained, and I therefore, at first, in my enumeration, for want 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 as regular as the eosinophile 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 16μ 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 colour, 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 deeper in colour than the general nuclear substance.

The nucleus often shows indentations and is very like that of the intermediate variety of leucocyte.

The surrounding protoplasm is of

a still paler blue, of the same tint, often almost colourless and glassy.

In one I 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.

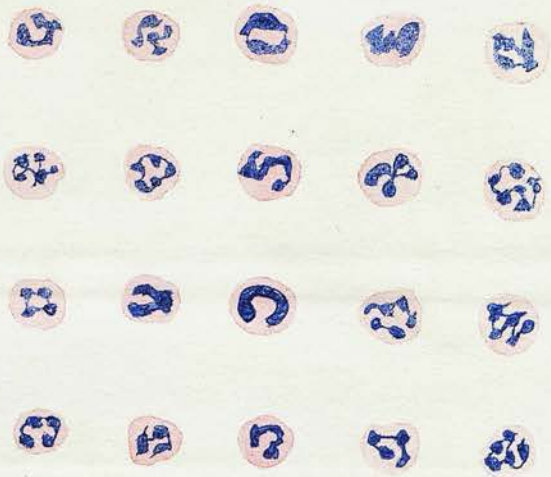
Examination of the Blood of Myxoedema-

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 Leucocytes.
Dry Film Preparation stain with Eosin Haematox.

The Uninucleated Leucocytes:-

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

The nuclei of both the large and small variety showed particularly well the granular 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 multinucleated 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.

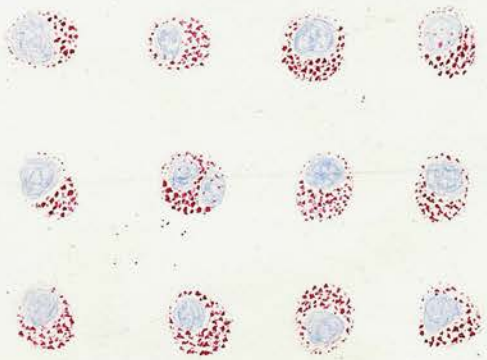
The Nuclei are more fragmentary and often show complete division. They are more granular and show the intra nuclear network better.

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

The protoplasm is, on the whole, more granular.

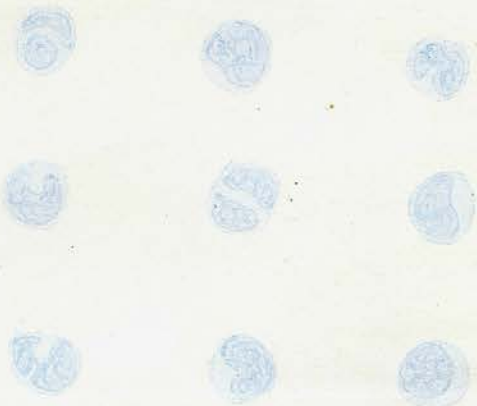
There were a few form of leucocytes intermediate between the ordinary multinuclated and the typical eosinophile cell, in which the protoplasm was granular and stained deeply with eosin, but did not contain

Case IV.



Varieties of Eosinophils Cells.
Dry Film Preparation stain Eosin + Haematox

Case IV.



Varieties of Marrow Cells.
Dried Film Preparation. Stained with Eosin Haematox

definite spherical granules.

Little alteration was noted in the appearance of the Eosinophils Cells. The Uninucleated or "Narrow Cells." or as I have termed them "all blue 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 Myxoedema, and found that haematoxylin and eosin were the most useful double stains for this purpose.

By counting a large number on a mechanical stage of a microscope

using an 1/6" objective, fairly constant results were obtained.
I found it 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.

TOTAL COUNTED.	MULTINUCL^{R}	UNINUCLEATED	MARROW CELL.	EOSINOPHILE.
112.	72.	20.	6.	14.
164.	140.	18.	4.	2.
219.	143.	57.	15.	10.
244.	175.	38.	13.	18.
141.	103.	20.	10.	8.
165.	117.	29.	13.	7.
1045.	750	176	61	59.
Percentage	71%	16%	6%	6%.

CASE IV.

TOTAL COUNTED.	MULTINUCL.	UNINUCLEATED SMALL	UNINUCLEATED LARGE	MARROW C.	EOSINOPH.
456	360	45	20	23	8
342	260	38	22	15	7
566	400	66	53	33	14
532	375	77	31.	36	13.
1896	1395	226	125	107	42.
Percentage	74%	12	6.5	5.6%	2.2%
		18.5%			

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 1st the Eosinophile cells were more numerous in Case III than in Case IV: they numbered about 6% in the former and only 2.2% in the latter.

Ehrlich finds the eosinophile cells to be 2 to 4 % in health and according by the increase in (former) case III is decidedly pathological.

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

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

i. The nuclei of the small uni-nucleated leucocyte showed more

nuclear structure.

ii. The nuclei of the multinucleated leucocytes were more fragmentary and often separate.

iii. The occurrence of cells intermediate between the ordinary multi and the typical eosinophile cells.

iv. A larger number of the large variety of the ordinary uni-nucleated leucocytes

The most noticeable features in both cases were:-

1st 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.

2nd The presence in both cases of distinctly pathological elements

viz "Marrow cells" or very large Uninucleated Leucocytes.
In the former case they numbered 6% in the latter 5.6%.

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

Muir, in an article on Leucocythaemia [Journal of Pathology. Part 2. 1892] describes the appearance of large uninucleated corpuscles in the spleno-medullary variety of that disease, "as corpuscles sometimes reaching 16μ 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 blood, 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 intra nuclear network.
In dried film preparations, the nuclei of these cells are more diffusely 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 multi nucleated leucocytes.

There is a general agreement amongst observers – Ehrlich, Muller, v. Limbeck etc – that leucocythaemia is the only disease in which these large neutrophile uninucleated 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-uninucleated Leucocytes."

I have come to this conclusion after reference to drawings and literature on the subject from:-

Firstly- The peculiar manner in which they react with staining reagents

Ordinary multinucleated or uninucleated 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 Myxoedema, - 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 Leucocythaemia more than any other blood disease.

Competent observers - Ehrlich 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 Myxoedema, and at first one is inclined to attribute their presence in this disease, as having some immediate relation to the atrophy or absence of the Thyroid gland.

In favour of this view is Hoches' statement that after excision of the Thyroid for disease, anaemia followed, and he suggested that this might lend support to the theory of Crede and Lesas, that the Thyroid gland has blood-forming functions, but

on careful examination, he found no enlargement of the spleen.

Lockhart Gibson [Journal of Anat. & Phys. Vol XX. 1886] has however shown that the blood possesses no such power, and is not compensatory to the spleen.

I think, on careful consideration, that in Myxoedema there is, as in leucocythaemia, 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 Myxoedema after death, will prove.