THESIS

ON

A CASE

OF

CHLOROMA,

With a Study of 13 other Cases

BY

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April 1905.
My apology for choosing such a rare condition as chloroma as the subject of my thesis, is that I have had the opportunity of examining two cases suffering from that disease.

In November 1901, I visited the Edinburgh Royal Hospital for Sick Children, and was shown a case which was then causing wide-spread interest among the members of the medical profession and which had been diagnosed by Dr. Melville Dunlop as one of Chloroma. In 1903 I had under my charge as House Physician to the Northampton General Hospital, a similar case which unfortunately was not diagnosed till after death.

I am indebted to Dr. Hichens, the Honorary Physician to the case, for permission to make use of the notes on the "case sheet" and the notes on the post mortem examination for the purposes of this thesis.
DR. HICHIN'S CASE OF CHLOROMA which was under my charge at The Northampton General Hospital...

The patient was a boy, aged 4 years. He was brought to the out-patient department of this Hospital, on July 4th, 1903, suffering from Paralysis of the left side of the face.

The Family History was good. He was one of a family of seven, one of whom died aged 1½ years, the cause of death being unknown. The mother had one miscarriage before the birth of this boy. Brought on, she said, by fright.

Previous Health. He was a bright intelligent child, and enjoyed good health until January, when he had Mumps. He made a complete recovery from that, and was quite well again until the present illness commenced. The mother said that he had been hit on the left temple two months before, and the patient himself said he had had some sort of injury in the right iliac region. There were no marks on the skin. Inquiries made later disclosed no history of nose-bleed etc.

A fortnight before coming to the hospital he woke up one morning with left facial paralysis. During the fortnight he cried with pain in the head, and in both Mastoid regions.
On examination (July 4th) the skin of the face and body was extremely pale, and of a waxy appearance and of a slight yellow tint. There was a complete paralysis of the left side of the face. The paralysis included the muscles of the forehead. The ocular muscles escaped; there was no squint. The fundi were normal. There was some deafness; pain on pressure over both mastoid regions, especially over the right. There was no history of discharge from the ear. The drums were not seen as there was an accumulation of wax in each meatus. A slight puffy swelling was present over the right temporal bone near the external angle of the eye. The Thoracic and the Abdominal organs showed no abnormality on examination. The case was diagnosed as one of peripheral Facial Paralysis probably of Rheumatic origin, so the child was sent home with a mixture containing 2 grains of Potassium Iodide to be taken three times a day.

On July 15, he was brought back evidently much worse. He was sick and vomited frequently, and could not take his food during the interval. The pain over both mastoids increased, but especially on the right side. He was constantly crying with pain in the right ear. There was constipation. There had been several rises of temperature, on one occasion as high as 104 degrees.
The patient was at once sent up to the wards.

On examination, the temperature was 99.2°. Pulse—rapid 126, but regular. The patient looked dull and ill. On examining the fundi, no definite signs of Optic Neuritis were found. The left disc was a little blurred. The right ear showed a perforation of the membrane and some inflammation of the external auditory meatus but no pus. The left ear appeared to be normal.

The swelling over the right temporal bone was more marked and a similar swelling had appeared in the same position on the left side. The facial paralysis was as before, involving the left side of the face and forehead. There was proptosis of the left eyeball—it was thought at the time to be only apparent proptosis due to inability to close the eyeball properly. No normal physical signs were discovered in the chest or abdomen. The urine was acid, specific gravity 1.025, containing neither albumen nor sugar.

PROGRESS OF THE CASE.

Two leeches were applied to the right mastoid region followed by hot fomentations. The bleeding was rather profuse, and the pain to a great extent diminished.
Potassium Iodide and Mercury were given in the chance of the case being Syphilitic.

**JULY 20.**—Vomiting occurred about once a day since admission. The temperature ranged from 98 to 100 degrees and the pulse was always over 120 per minute, reaching at one time 150. The patient became more and more drowsy and the pain was diminished. The temporal swellings were increasing.

**JULY 25.**—The temperature began to rise on the 24th, and on the 25th was 101.8. He had little or no pain, but had very restless nights, crying in his sleep. He seemed much brighter. There was some dyspnoea. At this time, Sarcoma, with metastasis was diagnosed.

**JULY 26th.**—The temperature rose to 102, and the pulse to MPM 146. —Respirations were 46. The patient seemed much weaker. Some petechial spots appeared for the first time on the skin of the abdomen and flanks, and a small subcaneous haemorrhage was observed close to the inner canthus of the right eye. There was a hard ridge felt between the roof of the orbit and the eyeball on each side.

The patient was extremely drowsy, and could be roused with difficulty. Pressure over the right mastoid caused great pain, and on the left to a less degree.
<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Address</th>
<th>Age</th>
<th>Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joe Smith</td>
<td>123 Main St</td>
<td>45</td>
<td>Worker</td>
</tr>
<tr>
<td>Jane Doe</td>
<td>456 Elm St</td>
<td>30</td>
<td>Student</td>
</tr>
</tbody>
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**Chart Details:**

- **Pulse:**
  - 90 beats per minute
  - Fluctuating between 70 and 100
- **Temperature:**
  - Ranging from 37.5°C to 38°C
  - Showing a trend of increasing and then stabilizing

**Notes:**

- Patient feels generally fatigued.
- Recommendation: Increase fluids and rest as necessary.
JULY 27th.- Temperature 101.8 pulse very rapid and weak. About 6 a.m. the patient began to bleed at the nose. At 7.30 a.m. he vomited blood which appeared to have been previously swallowed, and the epistaxis was still profuse. About 8 a.m. he passed a quantity of bright red blood per rectum. He was then unconscious.

He died at 9 a.m. without regaining consciousness.

The following are the Notes on the Post Mortem which was Examination made three hours later by Dr. Hichins and myself:

Necropsy 3 hours.

The body is warm. Rigor mortis not set in.

The body is that of a well nourished child though extremely anaemic. There are a few small petechial spots scattered about the thorax and abdomen, and there is a small subcutaneous haemorrhage just above the inner canthus of the right eye.

In the temporal regions just above and outside either orbital cavity, are two symmetrical swellings. They are very hard to the touch.

On reflecting the sternum no green color was observed in the substance or periostium of the sternum or ribs.

Abdomen.—Liver, weight 24 oz. somewhat congested. Scattered about in the liver are small masses of whitish green new growth which in many instances grow in a ramifying manner along the portal spaces. In some spaces the growths are conglomerated into roundish masses. They are very numerous under the capsule. Most of the latter are of the size of a split pea. There is no appearance of a capsule round the growth.

Kidneys,—weight 4½ oz. Scattered about both cortices are numerous small masses of whitish green new growths. In the right kidney there are some haemorrhages into the cortex under the capsule.

Spleen,—weight 3 oz. congested, otherwise apparently healthy. Stomach and intestines, contained no naked eye evidences of the new growth.

Just above the pancreas at the back of the small omentum, is a mass of new growth quite green, of the color of turtle fat. The mesenteric glands are enlarged and there are haemorrhages into them but they do not present the same green appearances.
Head.— On removing the skin from the calvarium, the swellings external to the orbits are found to be produced by the same green new growth, which here apparently starts from the perioranum, and is pushing forward and infiltrating the deeper surface of the temporal muscles. There is no appearance of the growth invading or eroding the underlying bone.

The orbital cavities contained small masses of the green growth above the eyes in the orbital fat. It seemed to be connected with the periosteum. It did not project under the conjunctiva.

On removing the calvarium, the dura mater presented a striking appearance. The green growth was scattered diffusely over its outer surface all along and for some distance on both sides of the superior longitudinal sinus. The masses of growth were in no cases dense. They did not invade the underlying brain, but they pitted and eroded the overlying calvarium. On removing the brain, there were found to be much larger growths of the same character in the dura mater in the basal fossae. These were scattered numerously here and there and were noticeable about the petrous portion of the right and temporal bone. They did not invade the bone or the brain anywhere.

There was a large excess of spinal fluid in the leptomeninges. The brain contained no masses of new growth.
The long bones were not examined because of a promise to the mother not to mutilate the body.

It is unfortunate that no examination of the blood was made before death.

Some of the specimens were preserved by Jones' method as modified by Kanthack. Others were hardened in alcohol for microscopic examination. Those immersed in alcohol lost their green color rapidly while the specimens treated by the other method are still almost as green as ever.

A curious fact is that when the latter were kept in a room with whitewashed walls, the color faded, the deposits in the liver and kidneys especially becoming quite colorless, but after they had been for some time in a room with green walls, the coloring reappeared and became as distinct as ever, even when examined in the open or in the old laboratory.

The results of the microscopic examination will be given later.
ANALYSIS OF CASES.

I have been able to collect the descriptions of fourteen cases, viz: my own case, those published by Allan Burns, Dr. Balfour, Dr. Cave, S.C. Ayres, Adolf Alt, Rosenblath & Risel, two cases—Dr. Lindsay Steven, L. R. Sutherland, Dr. Melville-Dunlop, Dr. Trevithick, Dr. Dock—two cases—Dr. Bramwell, and Drs. Harris and Moore. The references are to be found at the end.

Of the fourteen cases, 13 are males, and only one is a female. Dock's analysis gives males 10, females 6.

THE AGE INCIDENCE.—The average age of the fourteen cases works out at 14.9 years. There were 5 in the first decade, 7 in the second decade, one in the 3rd, none in the 4th, and one in the 5th.

THE DURATION OF ILLNESS.—I have been unable to find the duration of illness in two of the fourteen cases i.e. in Burns and Dr. Trevithick's cases.

The average duration of the remaining 12 cases, is 4½ months. Nine were three months and under, one was eight months and two extended over a year. The shortest course occurred in my own case, 5 to 6 weeks. The commonest period was 2 to 3 months. Dr. Dunlop's case had had been ill for over a year. The Family History was good in all cases except two. In Balfour's case
there was a distinctly tubercular family history.
In Sutherland's case the father was delicate, and
the mother died of "decline". The information
regarding health is not very instructive. Mumps,
Measles, and Whooping cough had occurred some time before
the illness each in three cases. Ral"our's patient
suffered from pulmonary complications a year before his
illness. Exciting causes occur fairly frequently
in my group of cases. There is a history of injury
preceding the illness in two cases. Dr. Hichins' case had received a blow on the head, and Rosenblath's
boyfall on the ice and hurt his head,- prominence of
the eyeball appearing eight days later. Dr. Dunlop's
case had been dipped into a horse-trough two months
before admission, but there had been a previous his-
tory of icthyosis. Ayre's case had suffered from
repeated attacks of parotitis after one of which the
illness developed. In Lindsay Steven's case,
the illness followed close upon a month's exposure
to the weather, and a carbuncle on his leg. Suther-
land's case had suppuratory ears all his life, and
an attack of diarrhoea two months before the commen-
cement of his illness.
ANALYSIS OF SYMPTOMS.

The pulse rate is high in nearly every case. Some of the cases had a pulse rate of over 120 from the date of examination. Two ranged between 110 & 120 and one only, Dr Docks 2nd case, kept below 100. Others not recorded. The temperature seems to range from about 99 degs. at the outset to 102 immediately before death. The temperature was recorded in 6 cases only. The urine was examined and the results recorded in 7 cases. It was normal in 4, and in 3 cases there was albumen. No sugar was found. Headache in some form was generally present. The pain was referred to the back of the head, the mastoid regions, and the orbits. It was an early symptom in every case. Deafness was described in 11 cases, occurring early in seven, and late in four. Sickness and vomiting were only reported in four cases, in two it occurred early. Constipation occurred in four cases, in three of which it was extremely obstinate. (In Balfour's case, Trevithicks, and Docks second case) Marked drowsiness occurred late in four cases. Sleeplessness and disturbed rest were present early in three cases late in two. Symptoms of Anaemia occurred in most cases and seem to be almost pathognomic of the disease. Striking pallor appeared early in 11 cases, in four of which it was one of the first symptoms noticed. It was not evident in Dr. Bramwells case.
until near the end. Burns and Harris & Moore do not mention the symptom. Petechial spots appeared in two cases. They generally appeared late— in 8 cases. In Dunlop's case patches of oedema were present for a year. Haemorrhages were described in all the cases except three. (Bramwell's, Burns' and Harris & Moore's.) There was epistaxis in 4 cases.

Bleeding from the mouth and gums in two, and coffee ground vomiting in three. Haemorrhage into conjunctive in one, and haemorrhage from the conjunctive which resulted in death in one (Ayre's) All these occurred late. Fatigue and languor are usually present early. In Balfour's case it was extreme.

Ocular Symptoms.—Fundus. There was haemorrhage into the retinae in 4 cases, in one of which there was optic neuritis. In my own case the left disc was blurred. Vision defects were present in six cases occurring late. There was impaired vision in three. Two were blind in one eye, one in both eyes. Proptosis was present in the great majority of cases. In 11 cases both eyes were prominent. Usually one eye became affected, then the other a short time later. In my own case there was prominence of the left eye. This was the first indication of disease in seven of the cases. It occurred about the middle of the illness in four cases. It was associated with broadening of
the face in six cases. The symptom was absent in three
\textit{viz.}-- Stevens, Bramwell's and Dock's 2nd case.

A hard ridge was felt during life between the roof of
the orbit, and the eyeball, in ten of the cases.

Swelling over the Parietal bones and consequent broad-
ening of the face, was seen in seven cases. The tum-
cours were always symmetrical. This symptom occurred
in later the disease. In one case only, was it early.
\textit{(Ayres case)} It usually developed some weeks after
\textit{proptosis} appeared. In one case it was present with-
cut \textit{exophthalmos}, coming in late in the disease.
\textit{(Bramwell's)}

\textbf{Glandular enlargement} There was general enlargement
of the superficial glands of the body in 5 cases.
The cervical glands alone were enlarged in 3 cases.
This was a fairly early symptom.

\textbf{Tumours in other parts of the body} Several tumours
appeared over the head in Balfour's case one of which
discharged a greenish fluid. In Ayre's case both
parotids were enlarged. The palate and eyelids were
infiltrated in Rosenblath's, Sutherland's and Dunlop's cases.
The pre-auricular region and right cheek showed tumours
in Sutherland's case. In Trevithick's case there were
tumours in both breasts and hard irregular
nodules over the sternum and ribs. In Bramwell's case
the parotids, tonsils, epiglottis, gums, and larynx
were infiltrated with green matter. In Harris and Moors case, the tonsil was also infiltrated.

**Skin eruptions** were present in three cases. In Bramwells case this was the first symptom to appear. It was present over the thorax, abdomen, back, arms, face and scalp, consisting of flat-topped nodules varying in size from a pins head to a sixpence. In many places the nodules were confluent and produced a uniform raised infiltration of the skin. They were painless, not adherent to the deeper parts, and of a slatey grey or purplish grey colour. Rosenblath's second patient developed halfway through the illness, an eruption of numerous small papules over the buttocks and lower limbs resembling Cutes Anserina. In Stevens case there were a number of small rounded steel coloured nodules about 12 in all varying from the size of a millet seed, to a threepenny bit, and irregularly distributed in the upper arm, and small of the back. They were situated in the skin, and had the appearance of multiple melanotic sarcomata.

The Spleen was enlarged in three cases.

The Liver in one. (Bramwells)

Pains In Rosenblaths case and in that of Harris and Moore, there was present a pain resembling the pain of sciatica. In Dock's two cases, pressure on the sternum elicited pain. In Rosenblaths second case there was tenderness
Nervous Symptoms Paralysis was found in four cases of which two had facial paralysis, one from the beginning and the other at the end of the illness. The lower extremities were paralysed in Burns' case. The upper and lower limbs were partially paralysed in Harris and Mocres' case, late in the illness. There were tumours and numbness of the legs in Salfours' case. The early nervous symptoms were as follows:— Paralysis (1) Headache, Deafness (7) Sickness and vomiting (2) Constipation (3) Sleeplessness and disturbed rest (3) Pallor (11) Sciatic pain (1) petechial spots (1) Fatigue and languor, proptosis (7), tumour of the mammary gland (1) tumour of parotid 1, skin eruption (2) Emaciation Symptoms occurring later are: Frequent pulse, rise of temperature, deafness, proptosis, broadening of the temples, nephritis, haemorrhages into retinae, skin conjunctivae, nose bleed, obstruction of the nose, glandular enlargement, skin eruption tumours of the head, parotid pre-auricular region, infiltration over sternum of tonsils, epiglottis, gums and larynx, Paralysis tremors, difficulty of micturition and retention of urine. Vision defects coffee ground vomits, sleeplessness, pallor, enlarged spleen, enlarged liver, pain in thigh and legs.
Distribution of the tumours found after death

In all the cases where the head was examined with the exception of one, (Stevens) the periosteum of the bones of the skull was affected. In Docks 2nd case, and Bramwells case, the head was not examined. Scattered tumours external to the calvarium were found in 7 of the 12 cases. They were found grouped along the sutures, or symmetrically arranged on each side of the head and temple. Green matter was present over the sutures, in 5 cases, growing from the lower aspect of the pericranium, but not adherent to the bone.

The underlying bone in most cases was thinned. Green masses were found under the temporal muscle in 7 cases. These were attached to the periosteum and to a greater or less extent, infiltrated the deeper surface of that muscle. The underlying bone was thinned in some cases but never eroded. In 4 cases it was stained green.

In Docks 1st case the pericranium was thick and green. In Sutherlands case, there was infiltration in front of both ears. Sometimes these nodules corresponded with similar growths underneath the skull cap.

The Orbital Cavities contained similar masses in 11 of the cases. In Stevens' case the orbits were unaffected. They were not exposed in Framwells case, but superficial examination failed to determine their presence.

The growth occurs between the periosteum, and the
bone. In Rosenblath's two cases, the tumours were not attached to the periostium, but seemed to proceed from the lids. The cranial bones and the periostium were free from chloroma. The tumours were only slightly attached to the orbital walls. In Trevithick's case the tumour was easily separated from the periostium and the bone. In Burns' case the tumour was thought to have originated in the lacrimal sacs; at any rate both sacs were diseased. The tumour originated from the periostium in Dunlop's case. In the other cases the tumours were attached to the bone and periostium at different points.

The orbital structures in every case escaped infiltration. The nerve was compressed and elongated in nearly all the cases.

Internal tumours of the skull.

The skull cap was removed in 12 cases. In three (Rosenblath's 2, Stevens, 1) there was no infiltration found in the cranial cavity. In 3 cases the infiltration was extensive. In the remaining 4, the affection was first much more marked. In Dock's case, the dura mater above was affected, the infiltration being chiefly disposed in and around the walls of the sinuses.

In Trevithick's case, the dura mater showed masses of green color. The only other seat of the growth being the left choroid plexus. Infiltrations were found on the dura in 7 cases. These showed a marked
partiality to the neighbourhood of the sinuses.

The growths were present on the internal and external aspects of the membrane, both in the vault and in the basal fossae. The dura could always be stripped off the brain and bone. Infiltration of the substance of the brain was never found except in the case of the choroid plexus. Both plexuses were affected in Sutherland's case and the left only in Trevithick's case.

The neighbouring bone shewed signs of erosion, pitting and thinning in three cases. In two of these, it was of a greenish hue. There were intercranial haemorrhages in Balfour's and Dunlop's cases. Around these green nodules were grouped. The petrous portion of the temporal bone was covered with a green layer in 5 cases, in two of which the middle ear contained masses of green growth. In Ayre's case the cancellated part of the petrous portion was softened and infiltrated with a dirty green fluid that looked like pus.

Other sites. In Burn's case there were green tumours of the frontal bones, frontal and ethmoidal sinuses.

In Balfour's case the orbital plate and the crista galli were thinned. In Dunlop's case all the bones on the anterior aspect of the base of the skull, especially their spongy tissues, were infiltrated with a dull green material. There was a small nodule in the sella turcica, another behind the left posterior
Another behind process. The posterior surface of the lesser wing of the sphenoid: the whole of the frontal bones and the upper surface of the orbital plate. There was apparent erosion of the left cribiform plate with green colour showing through it. The lining membrane of the Ethmoidal Sinuses was thickened and of a dull green colour.

Ears. — Middle ear, mastoid process and periostium on under surface of temporal bone with the adjacent soft structure were affected.

Vertebral Column: The anterior aspect of the vertebral column, showed green deposits in 7 cases.

In Docks two cases and in those of Stevens and Dunlop there is a continuous layer of green tissue, extending from the neck to the pelvis. This layer, lying under the serous membrane, generally branches out for a short distance over the ribs. It is pierced by the nerves and blood vessels whose sheaths it replaces. In Dock's second case it is thinner over the inter-vertebral discs, so that the body of each vertebrae is clearly outlined. In Sutherland's case, green nodules are dotted over this band. — prevertebral glands.

This layer is thickest at the insertion of the muscles. In the other three cases the exudation occupies only a portion of the vertebral column. Dorsal and lumbar vertebrae.

In Harris and Morses' case, there are numerous
nodular growths, dotted over the anterior aspect of the spine. This green band seems to be composed of periostium and surrounding connective tissue, which has been infiltrated. In Dock's second case, the vertebrae showed enlarged narrow spaces filled with green material. The bone was softened, easily cut, the trabeculae rarified. In Dunlop's case the vertebral bodies were infiltrated with green material and were of a dirty green color, in the spongy parts.

The vertebrae of Sutherland's case, were incised, but disclosed no green color. In Rosenblath's 1st case, the vertebral column was exposed from behind. A tough green growth was found along the deep muscles of the back, extending along the vertebral foramina.

towards the spinal cord. A similar mass lay between the dura, and the upper lumbar vertebrae.

In Dock's 1st case green material covered the spine and laminae of the vertebrae, passing for some distance into the fibrous tissue, running into the dorsal muscles.

On opening the spinal cord, the dura was unaltered, but the periostium was thick and grey. The loose fat in the spinal canal, was totally converted into soft greenish masses having only a loose connection with the dura.

Of the 14 cases examined, 12 showed a lesion of some tissue intimately connected with the skull and vertebrae. One case only, Stevens', showed no such lesion.
Bones.—In Docks' 1st case, the conciliated portion of the sternum, and ribs, was pale, but healthy.

In my own case no green color was seen in any of the bones examined (Skull, sternum and ribs).

In Sutherland's case the sternum was infiltrated with green material. The spongy bone of the sternum was of a dull greenish color in Dulopo's case. In Trevithick's case, the cancellous tissue of the sternum contained minute collections of green material. In Dock's 2nd case, the sternum was soft, friable, easily cut.

The marrow was hyperplastic, pyoid, of a greenish tinge. The sternum pericostium was infiltrated in 6 cases, all showing growths on the inner surface. In Dock's 1st case, the external pericostium was thickened and green.

In Trevithick's case and Dock's second case, small nodules were found growing between the external pericostium and the bone. In Rosenblath's 1st case, the marrow of the humerus was greenish and purulent. In his 2nd case, the lower part of the shaft of the right femur, was surrounded by a new growth. The marrow was red and rather soft. In Dunlop's case, the pericostium of the femur, was of a bright green color. The fatty marrow had disappeared and its place was taken by a greenish pus-like material. In Dock's 2nd case the bodies of the vertebrae were as already described.

The red marrow was replaced by greyish green pyoid
marrow of green tinge. An instructive fact is that there was direct constantation between the marrow and the green growths between the peristium.

In 6 of the cases examined, there was infiltration of the bone and marrow. The ribs, sternum, skull cap, and bodies of the vertebrae being most frequently involved. The humerus once, and the femur twice, was found to be implicated. As the long bones had been rarely examined, it is possible that infiltration might have been present in them in other cases without having been discovered.

Enlargement of the Lymphatic glands.

Glandular enlargement was reported in 12 cases.

The MeSenteric glands seemed to be the most commonly affected. The MeSenteric were the only glands affected in Rosenblath's 1st case. In Dunlop's case where there were one or two enlarged green glands in the mesentery in Hichens case, in Docks 1st case and in Harris and Moores' case. They were associated with enlarged glands in other parts of the body in 6 cases. In one case (Bramwells) they were not involved.

Other glands described as enlarged and infiltrated:

- Cervical (5)
- Trachial (1)
- Axillary (2)
-inguinal (2)
- bronchial (3)
- posterior mediastinal (1)

and prevertebral. In Trevithicks case, there was a thick firm layer to the left side of the lumbar spine.
spine which was thought to have originated from the thoracic duct. The parotid and the submaxillary glands were infiltrated with green matter in Sutherland's case. The skin lesions in Bramwell's and Stevens' cases showed greenish color in section.

The Thoracic and Abdominal Organs

THORAX. — The heart was enlarged in Dock's 2nd case. Punctate haemorrhages were found in the pericardium and under the endocardium in 6 cases.

In Dunlop's case small green patches occurred near the base of the ventricles to the right and left of the septum. There was fatty degeneration of the endocardium. In Trevithick's case and Dock's 1st case, greenish clots were found in the heart chambers. In the latter, pale green nodules also occurred over the left auricle. The lungs were affected in 5 cases. In Sutherland's case there was subpleural infiltration of both lungs. The surface of both lungs was of a pale yellowish green color. In Dunlop's case there were small irregular patches of congestion in the lungs and occasional haemorrhages. The large bronchi contained green mucus. In Dock's 1st case green matter was present under the pleura. In the posterior part of the lower lobe of the left lung, there was a deposit of greenish material under the pleura, stripping off with it; the right lung had
a similar deposit. Rosenblath's 1st case had a small
green growth on the under surface of the right lung.

In Dock's second case there were many small whiteish
areas in both lungs. The thymus gland was affected
in 3 cases (Sutherland's, Dock's (2) )

Abdomen:— The liver was affected in 5 cases.

It was generally slightly enlarged. The green growths
showed a tendency to follow the Portal Vein. Small
green growths of varying intensity of color. were
found in the substance pressing apart and replacing
groups of lobules. The tissue under the capsule was
infiltrated in all cases. In 2 cases the liver was
enlarged without infiltration.

The Kidneys showed deposits of the new growth in 9

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subcapsular area is the part most affected. The infiltration varies in extent from a
subcapsular band of green tissue, replacing the original tissue (Trevithick's case) to sparsely scattered
collections of nodules throughout the cortex.

The medullary portion and pelvis show infiltration
to a less extent.

The Spleen contains green deposits in two cases only.

In Dock's 1st case there was a greenish shimmer.
the vessels had greenish walls, and the
bodies were indistinct. In Sutherland's case there
was an irregular layer of green-yellow material
under the capsule. In Dunlop's the Malpighian bodies were enlarged and prominent. In Dock's second case the follicles were scanty. The organ was enlarged in Ayres's case and Bramwell's.

The Intestinal tract showed green infiltration in 4 cases. In Dock's 1st case there was ecchymosis and pale green patches in the intestine. In Sutherland's case the the Peyer's patches and solitary glands were enlarged and green and the appendix had a layer of green matter applied to the mucous membrane in its distal extremity. In Dunlop's case there were numerous minute haemorrhages and the follicles of the larger intestine were green and prominent. Dock's 2nd case showed prominence of the lymphoid follicles of the stomach.

In the submucosa of the fundus, was a small round green tumour with the mucosa intact over it. In Stevens case the Peyer's patches were prominent and the stomach showed a purpuric eruption so marked as to be almost papular.

The Pancreas was infiltrated in two cases (Dunlop's and Trevithick's) In Hichin's case, there was a mass of green growth between it and the small omentum.

The results of our examination of the distribution of the growth, shows that the growth has a marked predilection for periosteum and that the
periosteum involved in every case is that of the skull, vertebrae, sternum, or ribs (the last in Bram-wells and Stevens' cases) only three of the long bones are described as having periosteal infiltration and in each case there was accompanying replacement of the normal marrow, by a structure similar to that of red marrow. It is significant, I think, that the periosteum of red marrow bones is always attacked, and that in the few cases where the periosteum of the long bones shows infiltration, there are always red marrow deposits in the marrow spaces beneath.

Ayres reports that the cancellous part of the petrous portion of the temporal bone was infiltrated with a dirt green fluid resembling pus. Dunlop found apparent erosion of the left cribriform plate with green matter showing through. I observed that the bone over the tumours on the dura showed pitting.

These phenomena can easily be explained if we assume that in the marrow there is active formation and proliferation of new cells which find their way to the surface of the bone by the lymphatics or by a combined process of compression and absorption of the bony elements. This view is supported by the microscopical examination of the bone and the surrounding deposits.

The theory then suggests itself that the...
bone marrow is the primary seat of the growths and that the deposits in the heart, lungs, liver, kidneys, spleen, skin, medullary spaces of the long bones are secondary metastatic infiltrations.

The enlargement of the lymphatic glands which to a certain extent occurs in all the cases, raises the question whether these are also primary seats or whether the enlargement is due to metastasis and proliferation of the secondary deposits.
EXAMINATION OF THE BLOOD.

DOCK'S SECOND CASE.—

On Dec 3rd, the red blood cells were 509,600. The leucocytes were 35,669. On Dec. 8th the red blood cells were 820,000.

The blood shows very few nucleated red cells; almost all normoblasts. The only megaloblasts found have degenerated nuclei. In all the preparations of one day, Dec 4th, there were many "free nuclei" (1.8 %). At other times there were too few to count.

The small lymphocytes are usually typical, but some of them show slight fragmentation of the nucleus. There is a small proportion of typical large lymphocytes, some of which also show fragmentation of the nucleus. These two groups together are only slightly increased above normal.

From 79.6 to 82.6 % of all the leucocytes differ from typical lymphocytes, but resemble these cells in certain respects, and differ still more from other normal leucocytes. They resemble closely the undifferentiated lymphocytes of the bone marrow, and for convenience they are classed "marrow lymphocytes." They range from the diameter of a red blood corpuscle to two or more times that size. They are often oval or even broadly spindle shaped. Many of them have no visible protoplasm. Others show a narrow
crescentic or annular rim, and still others, a wider protoplasm up to an amount usual in large mononuclear cells of normal blood. In most cells of this class the nucleus is round or oval, almost or quite filling the cell. In some, the nuclei are uniform, or more or less inclined on one side, or sometimes bilobed. The nuclei stain moderately well. marked failure to take the stain and other evidences of degeneration so often seen in leukaemic blood are unusual. The protoplasm is without granulation, but often with a spongy or reticulated appearance, sometimes ragged at the edges.

The distinction between these and the ordinary large mononuclear cells is based on the different appearance of the protoplasm and the relatively smaller and more distinct nuclei of the latter.

A few cells having the general shape and proportion of the large mononuclears show a few eosinophile granulations. The polynuclear cells (5 -7 $\mu$) vary much in size. The nuclear structure and protoplasm resembling in their polymorphism the polynuclears of mixed celled leukaemia. In size they vary from one to four times the diameter of a red blood cell. The polynuclear eosinophiles relatively rather low, but absolutely within normal limits, show no marked abnormalities in size or structure.
Mononuclear eosinophiles were present only two days out of four in small proportion. The myelocytes vary in the usual manner from small to large. Basophiles appeared only on the last day. They all have round or elliptic eccentric nuclei. The red blood corpuscles show slight changes apart from their very scanty number. The cells vary sometimes in size, but marked departures in size and shape are not present. The cells usually stain well. They show very little polychromatophilia.

Normoblasts are few: no typical megoblasts are found.

In Dunlop's case the blood on the day of admission (Sept 30/01) shows haemoglobin 32 %, red blood corpuscles 1,800,000 leucocytes 24,500. On Oct. 25th, the leucocytes were 54,000. On Nov 2nd the blood shows red blood corpuscles 850,000 leucocytes 68,000 Haemoglobin 20 % On Nov. 12th reds were 815,000 whites 107,000. Haemoglobin 12 %.

On the day before the patient's death, the leucocytes had increased to 123,000. The gradual increase in the number of leucocytes from 24,500 to 123,000 is remarkable, as is the reduction in the number of the red cells.

A differential count made on Sept 30, showed a large number of lymphocytes great and small, the former predominating.
The result was,—

Lymphocytes, 73%
polymorphonuclear 17%
Myelocytes, 5%
Transitional forms resembling
Myelocytes, 5%
Few nucleated reds.

Dr. J. S. Fowler described the blood in this case

He records on Oct. 5th.—

Leucocytes. 25,000
Large lymphocytes 48.5
Small ditto. 15
Polynuclear leucocytes 31.5
Myelocytes 5
Eosinophiles, few.

On Nov. 11,—

Leucocytes. 64,000
Large lymphocytes, 53.5
Small, ditto. 15.5
Polymuclear cells 16
Myelocytes 15
No Eosinophiles.

Fowler's figures do not quite agree with those of Dunlop, but we can see that there is an enormous increase of the white cells going on during the
progress of the disease, and that this increase is chiefly due to the preponderance of cells of the large lymphocyte variety. The tendency is for the eosinophiles to diminish and disappear. The polymuclear cells also tend to diminish in number.

Lindsey Stevens' case shows the same characteristics. The blood count was:

Red blood cells, 766,000
White, " 491,000
Haemoglobin 15 %

The differential count was:

Large Lymphocytes. 94.6 %
Small ditto. 1.4 %
Polynuclear cells 2.7 %
Eosinophiles. 1.3 %
One "mast cell" was seen.

The eosinophiles were unlike normal eosinophiles of the blood, and those found in the marrow. The granules were too small for the former, and too large for the latter.

In Stevens' case the noticeable features are the enormous number of white cells, the great deficiency of reds, and the large proportion of the cells of the large lymphocyte type.

In Dock's 1st case, the same peculiarities present themselves. Fresh drops showed an enormous increase of the white cells which were apparently
as numerous as the reds. An actual count showed
3,150,000 reds, and 743,000 whites. Haemoglobin
was 60%. Films stained with eosin and methylene
blue showed great increase of lymphocytes few normal
large mononuclear cells with faintly staining nuclei.
relatively diminished polymuclear cells no eosinophiles
no myelocytes, and a few normoblasts.
The actual count was.

Large lymphocytes. 65%
Small ditto. 7%
normal mononuclears 1½%
transition forms. 6½%
No mononuclears with neutrophile
granules.
Polynuclear cells. 20%
(granules not so distinct as normal)
Normoblasts. 2 in 5,000
One eosinophile.

In Rosenblath's 1st case, the blood was normal
at the beginning, but after the haemorrhages marked
leukaemia set in. Five days before death, the leu-
cocytes numbered 300,000 and the red cells 1,000,000.
The most numerous of the former were small mononuclear
leucocytes of varying size and shape. Lymphocytes
were scanty. Marked poikilocytosis was present.
The 2nd case of Rosenblath showed at the beginning.
Reds, – 3,700,000 Whites, – 40,000. Later the reds were 2,300,000. Whites, 37,000.
The blood corresponds in general with the first case, except that there were not nearly so many mononuclear leucocytes. There was distinct polycytosis, a nucleated red cell—usually a normoblast—in every preparation.

In Trevithick's case, no actual blood count was made. The blood was first examined three weeks before death, and there was then a great increase of white cells.

On comparing these films with films prepared shortly before death, it was evident that the number of white cells in the blood increased very rapidly. The change in fact resolved itself into a enormously great and rapid increase of mononuclear cells. These cells approximated in number to the red cells and amongst them was a considerable number of bodies which Trevithick thought to be degenerating nuclei derived from defunct cells. These varied in size and shape, some of them being six times the diameter of a red cell. Similar bodies had been noticed by Professor Lorrain Smith in a case of Lymphatic Leukaemia (These bodies, which were also observed in the blood of Dock's 2nd case, seem to occur frequently in
some of the mononuclear cells were very large. They showed great variety in size and were distributed in groups.

In Sutherland's case the white cells were not counted, but from examination of films he concluded that there was great increase of white blood corpuscles as many as 180 occurring in a field. The increase was due to lymphocytes of varying size. There were numerous small farms, with scanty protoplasm equal in size to a red cell. Cells twice as large with abundant protoplasm and more faintly staining nuclei were also numerous. The majority were intermediate in size. Polynuclear cells were not increased. Eosinophiles were not found. A single nucleated red cell was present in each field.

In Ayre's case, the blood does not exhibit the same characteristics as the others. Three days before death, the multinucleated cells were markedly increased. White cells characteristic of Leukaemia were not increased. Eosinophile cells were were sparingly present; the condition of the blood indicating only leucocytosis.

The blood in Bramwell's case also differs in one respect from the others. The blood count showed the red corpuscles 4,480,000 Whites 8,000

The white corpuscles were almost entirely (95% or more)
lymphocytes, chiefly large lymphocytes, with large nuclei and clear non-granular protoplasm.

During the month the patient remained in hospital, the blood condition remained practically the same.

Framwell remarks that the condition of the blood corresponds with that of acute lymphatic leukaemia, and that it is very important to note that the leucocytes (95% or more of which were lymphocytes) did not increase in number. The mere fact that leucocytes did not increase in number, did not exclude leukaemia.

In our case, those of Burns, Balfour, Hichens and Harris & Moores, the blood was not examined. Unfortunately also, the blood was examined at the early period, only in three cases—Dunlop's Rosenblath's two.

In Dunlop's case, the white cells increased from 24,500 to 123,000 in six weeks. In Rosenblath's first case the blood was normal at the beginning but five days before death the leucocytes numbered 300,000.

In Rosenblath's 2nd case, the blood examined eleven days after the first symptoms, contained 40,000 whites which slightly increased in number for a time, then diminished to 37,000 at the end of two months.

The data are insufficient to give us an accurate idea of the changes which occur in the blood in the early
stages of the disease.

After considering the conditions of the blood found in the 10 cases, we see that the following phenomena occur in all:

1. There is a marked decrease in the number of red cells, and a diminution of the haemoglobin percentage.

2. The white cells undergo quantitative and qualitative changes.

   (a) The total number of white cells is increased, and there is an absolute increase in the number of cells of the lymphocyte type. A relative diminution of polymuclear cells.

   (b) These lymphocytes are identical with the normal lymphocytes of the blood but are similar in every way to the cells which predominate in lymphatic leukaemia.
THE COLOUR OF THE CHLOROMATOUS GROWTHS.

Tumours of various shades of green were present in various parts of the body in all the cases cited. The intensity varied from a light green to a dark green. The tint has been described as greenish yellow, bright olive green, greenish grey, pale green, bright green, green resembling turtle fat. In most cases the intensity faded on exposure to air, the disappearance of color, taking place from the periphery to the centre. The color also tended to disappear on immersion in one or other of the preserving agents. The fluid itself ad a rule does not appear to be tinged. Trevithick stated (Lancet 1903 Vol2 p.530) that specimens had lost their color, regained it on being treated with peroxide of hydrogen. I tried the effect of that reagent on portions of the growths on the dura, liver and kidneys with negative results. I have noticed that specimens of the kidneys and liver which were mounted in glycerine and formalin and had become colorless, when kept in a poorly-lit laboratory with white-washed walls and windows facing the north, entirely regained their original color when removed to a room with green walls and a south west aspect. I have not as yet been able to determine whether this increase of color is due to absorption from the surrounding green, or to the effect
of sunlight. The deposits on the dura mater were mounted in Kanthacks modification of the glycerine and formalin method. These retain their original grass green color, and the preserving fluid is not tinged. Specimens which were frequently washed in chloroform and ether, and alcohol are quite colorless nor are they affected by treatment with hydrogen peroxide. Alt states that the tissues retained their dark green color in formol solution, and that the fluid itself was of a dirty green color, and contained fat globules. The whole of the green fluid was pervaded by octohedric crystals like calcium oxalate.

On evaporating the fluid, darker droplets of dark green oily substance were found and these crystals filled the field.

Balfour suggested bile pigment as the cause of the green color, but investigations made by later observers have failed to confirm the suggestion.

In Rosenblath's case, haemosiderin crystals were present in the liver. Risel thought that their presence was due to the breaking down of the red cells, and that the green color was due to some other substance of haematogenous origin. He thought it similar to the "green granular pigment" found in the dogs' placentae.

Bramwell thought that the marked increase in the green color which was noticeable at the necropsy, was suggest-
ive, -in part at least, of post mortem change.

He raised the question whether in all cases of chloroma, the green color was due to the same cause. It was possible that it might be due to different causes in different cases. It was possible that the green tumours were not invariably due to the one and same pathological condition. Further, though this at first sight seem to be a contradiction in terms, it seemed to him probable that cases of chloroma occurred in which there were no green tumours, and no green lesions. He was strongly disposed to think that the green discolorations though they had hitherto been considered to be essential and characteristic of the disease, might in some undoubted cases of chloroma, be absent.

Heck pointed out that in Koerner's case, some of the tumours were not green, though they had the same structure as the green ones. This was also true in Weinberger's case, and in a case of leukaemia Framwell found a few lymph glands.

It appears then, that in chloroma some of the deposits show the color characteristics of leukaemia, and that in rare cases of leukaemia, infiltrations occur, which to the naked eye, are pathognostic of chloroma.

It is also evident that the changes in the blood are due to a morbid condition of the haematogenic tissue of the body - red marrow, the primary
MICROSCOPIC EXAMINATION OF THE AFFECTED TISSUES
IN DOCK'S FIRST CASE.

Sections were stained for bacteria with negative results.

The growth shows the same characteristics in all parts modified according to the structures in which it occurs. It is made up of round cells larger than a lymph nodule, lying in a vascularised reticulum. The latter is sometimes fine, sometimes coarse, the coarser fibres being the fibres of the original connective tissue of the part. Connective tissue in all parts shows a predilection for the new growth.

The nerve sheathes and the adventitia of veins passing through the growths, are entirely replaced by lymphoid tissue, the arterial coats are not so completely involved.

There are vessels of old and new formation in the deposits. Lymphatics are numerous, and are in many places dilated or open out of cystic cavities filled with white cells. The cells are rounded, sometimes elongated, but never spindle shaped, with a small amount of protoplasm, sometimes none.

The nucleus is about two thirds of the cell diameter with finely granular protoplasm. The cells in the growth resemble those in the blood. There is no
evidences of degeneration. Mast cells are numerous in various organs in or near the new growth.

Ayres thought that the growth in his case was sarcomatous. There were collections of small round cells, with very few spindle cells, and little intercellular substance. There were no large blood vessels but numerous lymph spaces.

Later examination by Alt, of unstained sections, showed small and large round elements containing fat globules. The round elements lie loosely together, held by an intercellular tissue so delicate as to be hardly visible. The shape of the cell is not similar to any cell found in the blood. The section takes the stain badly, the nuclei showing badly. Alt thinks this is due to the fat globules present.

Risell in the 1st case found that the tumours consisted of small meshed network of connective tissue filled with round cells, the nuclei of which were as large as red blood corpuscles showing a distinct framework of granular chromatin threads surrounded by a small quantity of protoplasm.

In the 2nd case the appearances were similar but there were more giant cells. The marrow was softened, and contained a preponderance of mononuclear marrow cells of medium size and a few giant cells.

From the symptoms, results of his blood examinations
and from the microscopical data, he thought that the disease resembled leukaemia.

Lindsay Steven examined the green clot he found in the heart chamber. It consisted of a collection of mononuclear non granular cells lying in a delicate fibrinocous network, the red cells being almost absent except at the periphery. The cells are mostly of the lymphocyte class, but a considerable portion are of a larger size than lymphocytes, rounded in form and some granular. A small amount of cells with neutrophilic granulation were found. These, which he considered must have entered the blood from the bone marrow shortly before death are present through the various organs. Their proportion is insignificant, and they are seldom found outside the blood. Nucleated reds of normoblast type are occasionally met with.

He found rare evidences of nuclear division, but frequent signs of fragmentation and degeneration.

Lymphatic Glands.— The entire adenoid reticulum is overrun with lymphocytes which are also present in large numbers in the cortical and deep sinuses of the gland. For this reason, the germinal centres are almost indistinguishable. He found evidences of cellular activity in these places. The capsule and periglandular connective tissue are deeply infiltrated with lymphocytes. There is evident proliferation of the endothelium.
of the sinuses.
The spleen showed a fair number of the above mentioned neutrophile granular cells.
Bone marrow of the ribs and femur.
There was replacement of the normal bone marrow by mononuclear cells. The neutrophile and eosinophile cells were greatly diminished. There was not much blood nucleated reds were rare and giant cells were reduced in numbers. Large cells with single contorted nuclei containing cellular fragments or blood pigment were fairly numerous.
The liver and kidneys were infiltrated with the same cells.
The skin nodules were composed of dense collections of mononuclear cells, while elsewhere the connective tissue fibres of the subcutaneous tissue were separated by the diffuse lymphatic infiltration.
In the case of the smaller nodules, Steven thinks that they might be thrombi of lymphocytes in a small vessel with subsequent emigration.
In the stomach and intestines there was increase of the lymphoid tissue normally present and the mucus membrane in other parts was infiltrated with this cell.
Steven draws attention to the cellular activity found in the germinal centres of the lymph glands and, in association with this phenomenon, the other
abnormal sites of active lymphoid tissue.
Sutherland found similar conditions in his case, i.e., masses of lymphocytes scattered through the tissues. He detected numerous refracting granules scattered between the cells and sometimes in the protoplasm of a cell. Trevithick found that cells making up the deposit in all the tissues he examined were identical. It seemed to him as if the blood had become charged with multitudes of mononuclear colorless corpuscles and that great crowds of them had migrated thence and taken up positions in various organs and tissues. He rejects the theory of Sarcoma because of the symmetry of attack, the relative positions of the organs attacked, the irregular disorderly disposition of the individual invading cells and the marked absence of vascularisation. He conjectures that the key is to be found in the lymphatic glands where, near the hilum, the vascular and lymphatic endothelium is undergoing immense hyperplasia so that large vessels have their lumen blocked with cells similar in character to those found in the tissues.

Dunlop found that the deposits were due to large lymphocytes and that tissues unaltered to the naked eye contained the same cells in abundance. He also found scattered among the cells...
refractile granules which stain faintly with osmic acid. They disappear when treated with solvents.

The sections seem to indicate that the color is due to the peculiar clusters of fatty nature and possibly, in addition, to the presence of an oxidisable pigment.

In Bramwell's case, the nodules in the skin were found to consist of lymphoid deposits made up of small uninucleated round cells. The gums, tonsils, epiglottis and larynx were swollen, the swelling being due to lymphoid infiltration.

The bone marrow of the ribs contained some, but not very numerous lymphoid cells similar to those in the skin gums, and blood. The kidneys were infiltrated in places.

An exhaustive microscopical examination of the infiltrated tissues of Dock's case was made by Dr. Walthin. I propose to give a short account of his examination because they throw considerable light on the nature and the possible origin of the disease.
The prevertebral green tissue shows an upper adipose layer and a lower and denser layer composed of connective tissue and pericistleum, both layers infiltrated by cells corresponding to the cells in the blood already described.

In the lower layer the cells are arranged in rows in lymph spaces and blood vessels circumscribed by and running parallel to, dense fibres of the reticulum.

In the upper layer the cells run in irregular columns between the fat cells.

The General Characteristics of the Cells:

The nuclei are rounded in the loose tissue, oval or even spindle shaped when cells are packed in the dense tissues. They stain moderately deeply or are pale with a fine network of chromatin. Sometimes a cell contains two nuclei, in which case they stain more deeply and the chromatin filaments are coarser. This suggests to Dr Warthin a recent mitotic division.

The protoplasm in most cells appears in a small rim. In some it is more abundant, in others it is absent. The most striking feature is that those cells with well marked rims contain eosinophile granules. These granules resemble in every way the granules in ordinary eosinophile cells. A small number have neutrophile and a smaller number have Basophile...
granules. There are transition forms between these two. There are also transition forms between the non-granular cells and the eosinophile cells.

The eosinophile cells are the most abundant, the proportion being from 50 to 75%. Walthin is of the opinion that the eosinophiles are derived from the large lymphocytes, it being impossible to distinguish them from the eosinophile myelocytes. There are few polymorphonuclear cells and few basophile cells. Small lymphocytes were also rare. No giant lymphocytes were found. No pigment was found by any of the tests applied. Degeneration of individual cells was not found, but of groups of cells.

The blood vessels showed signs of proliferation. The tumour was poorly vascularised, the vessels being filled with cells of the same type as the deposits.

There were evidences of red cell destruction with granules of pigment containing iron.

The reticulum was that of the deeper tissue with some increase in the deeper layer. The nerve trunks and the ganglia as they passed through were compressed.

The ganglion cells were atrophic and degenerating and the nerve trunks showed infiltration by the blood vessels.

The deposits resemble a tumour in spreading by the blood vessels and pushing apart the original structures for compressing and causing them to atrophy.
The infiltrating cells are of the type of large lymphocytes or myelocytes, the majority showing eosinophile granulation. The green tissue from the sternum shows the same microscopic characteristics.

The Bone Marrow of the Sternum.

Sections show that the normal red marrow is almost completely replaced by cells of a similar character to those already described, i.e. large lymphocytes, the majority having eosinophile granulation. There are no bone marrow giant cells, very few red blood corpuscles, only two nucleated red cells, few neutrophile myelocytes, few small lymphocytes, and few polynuclear cells. There are numerous transitional forms between the large lymphocytes with small rims and those with more abundant protoplasm containing eosinophile granules. Inasmuch as the eosinophile large lymphocyte passes by transition forms into cells morphologically identical with eosinophile myelocytes this fact may be taken as evidence of the derivation of the latter, type from the former.

Polymorphonuclear eosinophiles are very few. The nuclei of the majority of eosinophile cells resemble those of the non-eosinophile large lymphocytes. All possible transition forms exist between such eosinophiles and normal eosinophile myelocytes.
VERTEBRAL MARROW.-

Sections made by Warthin through the vertebral seem to shed light on the origin of chloroma.

The narrow spaces were enlarged with rarification of the bony trabeculae. These enlarged spaces were closely crowded with cells of the large lymphocyte variety, a number of them having a larger amount of protoplasm than elsewhere. These cells showing eosinophile granulation were not so numerous as before but form a high proportion of all the cells. In sections fixed in Muller's fluid the protoplasm of many of the cells is distinctly chromaffinic, having brownish or greenish yellow color.

There were few red cells, no nucleated reds, no mast cells, no bone marrow cells, and rarely polymorphonuclear and small lymphocytes.

The important fact observed was that the contents of the narrow spaces communicated directly with the green prevertebral growths. Sections through both showed that masses of cells in the marrow spaces were in many cases directly continuous with the periosteal infiltration by means of relatively large openings in the bone. Smaller cords of cells extend from the marrow spaces through small openings in the bone. These openings, so numerous that they are visible in every section, were considered by Warthin to be enlarged lymph spaces.
or blood vessels, as they often contained red blood cells as well as large lymphocytes.

Other communications seem to have been the result of the contents of the medullary spaces eating their way outwards through the bone towards the neighbouring green tissue. It seemed likely to Warthin that the was from within outwards, because the growth round the vertebrae was marked where it communicated with the marrow spaces, and because masses of cells coming out through these openings lifted the periosteum from the bone.

The spinal nerves and ganglia are surrounded by the infiltration and are to some extent themselves infiltrated. "The careful study of such sections leads to the conclusion that we have to deal with a primary growth within the marrow spaces which infiltrates or grows directly through the lymphatics and blood vessels, or breaks through the bone and secondarily involves the periosteum and surrounding tissues."

Marrow from Tibia.

The marrow contains small irregular islands of tissue exactly like that in the sternum and vertebrae, consisting of cells of the large lymphocyte type. Irregular cords of cells extend from these islands outward through the distended capillaries, and blood spaces between the fat cells, the cords becoming smaller.
as the distance from the main island increases.

"The general appearance is of a growth extending from these foci, through the blood and lymph spaces."

"Portions of the fatty marrow appear fairly normal, with collections of apparently normal red marrow but even here the prevailing type of cell is the large lymphocyte."

The Spleen.— There was diffuse hyperplasia of the cellular and reticular elements with almost entire absence of the follicles. Cells chiefly of the large lymphocyte type filled the reticulum, a large proportion of these being eosinophile. There are many neutrophile myelocytes present, and other normal cells are present in greater amount than in the bone marrow. The pulp presented as the whole a myeloid character except for the absence of red cells and giant cells. The same follicles were almost entirely made up of small lymphocytes with few or no eosinphiles. The splenic veins were distended with red blood corpuscles, and contained a relatively small proportion of white cells, of the large lymphocyte variety.

Lymph Glands.—

These present cellular hyperplasia with large numbers of cells of the large lymphocyte type infiltrating the lymphoid tissue and replacing to e
some extent its cells. In some deposits the large lymphocytes are chiefly in the sinuses and medullary cords. Germinal centres are rare. Eosinophile cells are found in large numbers in association with the large lymphocytes. They are also present in the connective tissue trabeculae particularly near the hilum. Haemolymph nodes from the retro-peritoneal region.

These are similar to the lymph glands on section.

Phagocytes containing red cells and pigment are fairly numerous in some nodes but diminish on the whole.

Few neutrophile myelocytes are present and some giant cells like those of the bone marrow.

"The general picture is a gradual replacement of the tissues of the lymph node by the new atypical lymphocyte tissue. As a rule such proliferations appear to begin in the sinuses and not in the lymphoid follicles or germinal centres, the latter being latest involved."

The atypical cells in the peripheral sinuses infiltrate the capsule, and the surrounding adipose tissue.

Large numbers of eosinophiles occur in such infiltration. These also form a large proportion of the cells infiltrating the lymphoid tissue. The large lymphocytes are most numerous in the blood sinuses.

"The picture presented is that of a proliferation of these beginning in the sinuses and not in the lymphoid tissue."
The Lungs. On section the larger vessels are distended and filled with cells of the large lymphocyte type. Eosinophiles are not so numerous as elsewhere. The arteries are more distended than the veins and the capillaries of the alveolar walls are also distended and filled with similar cells. The general type is that of a leukaemic lung. Large and small masses of these cells are scattered everywhere throughout the lungs and pleurae. Mononuclear eosinophiles are numerous but not so numerous as elsewhere.

The Liver. The intralobular capillaries and central veins are often distended and crowded with large lymphocytes. Some islands of Glisson's capsule.

In the cells of the central zone of the liver, lobule there is abundant pigment (haemotoxylin). The cells of the peripheral zone contain a moderate amount of haemosiderin. Some islands of Glisson's capsule show marked infiltration with large lymphocytes, others show little of none. In some islands nearly every cell is an eosinophile. In the larger islands the impression is gained of an infiltration in which the cells are proliferating. Small masses of cells, chiefly eosinophiles, scattered throughout the liver lobules.

These apparently consist of similar cells in the dilated capillary with their further proliferation and the resulting compression of the neighbouring...
liver cells. " In some portions the capillaries are so distended that they look like cords of deeply staining cells with degenerating liver cells between.

In these areas there are a great many degenerating lymphocytes in the capillaries, relatively few eosinophiles are seen in the distended capillaries.

In many capillaries occurs well marked endothelial proliferation. It is to be noted also that the number of eosinophiles in the large vessels in the liver, is relatively much less than in the infiltration in Glissons capsule or in the large collection of cells in the lobules.

" In interpretation of the liver changes, the condition may be regarded as due to the presence in the blood vessels of the liver of cells having the power to proliferate both in the vessels and after passing out into the connective tissue. The process is therefore analogous to tumour metastasis and infiltration."

**Stomach and Intestines -**

In the mucous there were numerous small collections of these cells many being eosinophile. These were independent of the lymphoid follicles which were somewhat hyperplastic and contained an increased number of large lymphocyes. A larger mass was found in one instance in the muscular coat of the intestine small cords of cells extending from the main mass
and infiltrating the surrounding muscle.

Kidneys

The blood vessels of the medullary pyramids are frequently filled with large lymphocytes. In these masses eosinophiles are numerous. Throughout the cortex there are numerous deposits of similar cells situated under the capsule which is thickened and infiltrated. From these irregular cords of cells infiltrate the kidney tissue, following the inter-tubular connective tissue. The kidney substance is lost in the deposits and compressed and atrophied between them. Sometimes there is a growth of fibrous tissue resembling chronic interstitial nephritis. Sometimes this is absent.

Many of the cells are eosinophiles.

"The general picture presented is that of a metastatic growth of cells of the large lymphocyte type replacing the kidney substance by means of a slow infiltrative process."

Similar collections were found in the blood vessels of the bladder, prostate, testis, spinal cord. The blood vessels generally throughout the body contained an excess of white cells, the majority being mononuclear cells of the large lymphocyte type.

Summing up the histological changes Warthin states that the primary condition appears to be a tumour-like hyperplasia of the red marrow of the sternum and
vertebrae with secondary infiltration of the periosteum and neighbouring structures, and the occurrence of metastasis-like infiltrations and nodules in the lungs, liver, kidneys, haemolymph nodes tibial marrow, associated with a cellular hyperplasia of spleen and lymph glands and evidence of cell proliferation within the smaller blood vessels in various parts of the body.

The marrow lesion is primarily he thinks, because its normal elements are completely replaced by the new cells, because the spaces are enlarged and because of the direct extension outward of the cell growth into the neighbouring periosteum.

These cells are similar in every way to two of the normal red marrow cells i.e. "large lymphocytes" e.g. large mononuclears, and cells of the myelocyte type both eosinophile and neutrophile. From the character of the transition forms between these, he judges that the cells of the myelocyte type are derived from those of the larger lymphocyte type. The atypical character of the large new lymphocytes and myelocytes produced by this abnormal proliferation may be taken as evidence that the process is neoplastic.

"The neoplastic character of the marrow hyperplasia is further shown by the changes in the walls of the marrow spaces, the infiltration through the blood and lymph
vessels and the direct extension from the bone into the tissues of the periosteum and other neighbouring structures. The infiltrating cells are proliferating in the tissue spaces and are destroying and replacing the tissues infiltrated. Such destruction is nowhere rapid, and it does not appear to be strongly resisted by the marrow tissues probably because the invading vells are normal constituents of the body more or less altered. The kidney is the only tissue in which much antagonism is evident. There, around some of the deposits, conditions suggestive of chronic interstitial nephritis are apparent. The proliferation of the cells is chiefly by amitotic division because of the constrictions and indentations found in the nuclei; the double nuclei "Division and growth of the cells within the blood vessels undoubtedly takes place."

Throughout the body distended blood vessels were found filled with masses of the new cells, in many of these the vessel walls are grown through or infiltrated with them. The nodules in the lungs, liver kidneys haemolymph nodes and tibial marrow appear to be true metastasis arising chiefly through the intravascular proliferation of cells and the secondary invasion of the surrounding tissue. In general the effect on the surrounding tissue is a simple atrophy.
The blood vessels throughout the entire body present a picture of marked leucocytosis or leukaemia. The case therefore presents a picture of a leukaemia of the large lymphocyte type associated with a primary neoplastic hyperplasia of the bone marrow, chromomatos infiltrations of the periosteum and metastasis in various organs. That the leukaemia is secondary to and dependent on the marrow condition, there can be no doubt.

The idea of a general lymphatic affection was rejected because the metastasis do not necessarily occupy the site of the lymphoid tissue of the organs in which they are found. Their location is determined by proliferating collections of cells in the blood vessels.

The myeloid character of the spleen was thought to be due to some effort at compensation for the lost marrow function. The extreme anaemia is explained as being due to the replacement of the original marrow cells with cells of the large lymphocyte type. This atypical proliferation may be due to an intoxication having a marked myelotoxie action. Of such an intoxication there is no proof, although there are great numbers of individual degenerating lymphocytes in the liver which may give rise to some intoxication.
MICROSCOPICAL EXAMINATION OF THE TISSUES AFFECTED
IN DR. HICHERS'S CASE.

The Growths infiltrating the Temporal Muscle

The deposits seem to grow outwards from the pericranium towards the muscle. Near the bone they include isolated remnants of muscle fibres. As they extend outwards, the fibres become more and more numerous, and evident, until at the periphery of the deposit, the fibres appear to be approximately normal.

The deposits are made up of a large number of cells set in a rather fine reticulum of connective tissue. The cells are all of the lymphocyte type, ranging from ordinary small lymphocytes to cells whose diameter is two or three times the size of the small lymphocytes. The great majority of the cells are the large lymphocytes and there are all sizes of transition forms between the two.

The nuclei are round as a rule but oval when the cells are closely packed together. Sometimes the nuclei of the cells are reniform, sometimes bipartite, and frequently a cell contains two nuclei, a fact that indicates active division. The nucleus stains well showing fine but distinct chromatin filaments.

The protoplasm varies in amount, sometimes it is represented by a narrow rim around the nucleus,
at other times the diameter of the cell is two or three times that of the nucleus. The small lymphocytes have no protoplasm, appearing only as a deeply staining nucleus. The protoplasm of most of the cells is nongranular, or finely granular staining a uniform pale pink with eosine. In some of the cells it contains fairly large granules which take on a deeper stain with eosine (Eosinophiles). There are a few neutrophiles but I have been unable to find any basophiles.

The connective tissue in the deposits is fairly abundant and appears to be the connective tissue of the original nuclei. It is much denser here than in the dura mater.

Blood vessels are relatively few. The veins are distended but in most cases they only contain a few of the cells described above with a small quantity of debris. It is probable that the contents have been washed away during the process of preparing the sides. Their walls very often are infiltrated with the same cells to such an extent that they are sometimes unrecognisable. The cells are often packed thickest around the veins and these collections of cells are sometimes so large that they press the walls inward, leaving only an elongated narrow slit. The smaller arteries have collections of these cells in their lumen. Their walls are infiltrated
to a less extent than the veins.

Lymphatics are numerous. Some of them are packed with cells and often appear as cords of cells running in between the muscle fibres. At the junction between the muscle and the growth we find these cords running in between bundles of muscle fibres, surrounding the bundles and causing atropic changes. From these cords individual cells penetrate between the fibres.

We also find cells advancing into the muscle along the connective tissue independently of the lymphatics. There is no sign of a capsule only the connective tissue around the periphery seems rather more evident.

The neighbouring muscle fibres show condensation and cloudy swelling probable owing to the mechanical effects of pressure. There are numerous new cells scattered about the muscle some distance from the deposit and some of the capillaries are choked with the same cells.

The Growths in the Dura Mater.

These growths are composed of dense masses of cells of a similar type to those which occur in the temporal growths. These cells are set in a very delicate reticulum.

Blood vessels are not numerous, the lumen is distended and filled with large numbers of the new cells. The vessel walls are infiltrated with
the same cells.

There are numerous lymph spaces. Some parts of the section have a honeycomb appearance, the walls being formed of single, double, or treble rows of deeply staining cells of the same large lymphocyte type. The spaces are of the size of rather distended lymphatics and contain blood debris and a few cells which stain more faintly. These areas appear to me to be made up of large numbers of distended lymphatics running in all directions through whose walls the cells have migrated.

The Kidneys.

Scattered throughout the kidneys are large and small masses of these cells. The deposits are set in the cortex just under the capsule. There is infiltration of the capsule when it covers such a deposit.

The Deposits: The masses of cells are densest around the glomeruli and compress them, causing various stages of atrophy. The capillaries of the glomeruli are also distended with the cells.

The large loops show various stages of atrophy from cloudy swellings to complete atrophy, and disappearance according to the density of the surrounding infiltration. Their walls are sometimes infiltrated. The inter-
tubular capillaries contain many such cells. The infiltration merges gradually into the kidney tissue; there is no sign of a line of demarkation, the cells between the tubules becoming fewer and fewer and the kidney substance gradually regaining its normal appearance. Capillaries in the neighbourhood of the deposits are here and there blocked with cells and run like cords for a short distance between the tubules.

The endothelium of the blood vessels and lymphatics are in many places in a state of active proliferation. This is more marked when there are deposits of new cells present around them. The walls are also infiltrated. The larger blood vessels contain granular debris and a few cells of the lymphocyte type. The cells in the deposits and blood vessels appear to be proliferating.

Liver.—Deposits of varying size are seen on section. These are made up of the same cells as before and are distributed chiefly along the portal spaces. The larger infiltrations seem to be more circumscribed than those in the kidney. They are invariably connected with the portal spaces and numerous cords of cells run off with the smaller ones as they branch. The lumen of the portal vein and hepatic artery is choked with the cells and their walls are sometimes infiltrated. The deposits are very thick
around these vessels. In the lobules away from and a deposit both the interlobular and and intralobular capillaries contain these cells, the former more so than the latter. The central vein is sometimes seen choked with the same cells. Liver cells show cloudy swelling. In the smaller deposits the new cells run up between the columns of liver cells causing atrophic changes in them. These smaller deposits also occur in the smaller portal spaces.

On examining the margin of these infiltrations more closely one finds that the boundary between the liver substance and them is not so distinct as it appears to be with the low power. We find cords of cells spreading by the smaller branches of the portal tract and we also find large numbers of individual cells migrating from the main body among the liver cells of the adjacent lobules. The surrounding lobules show signs of compression and rarification. The new cells show numerous double nuclei and appear to be in a state of proliferation both inside and outside the vessels. The endothelium of the walls of the lymphatics and smaller vessels also shows proliferation.

The lower layer of the capsule as it passes over these deposits shows infiltration.

The new cells in the liver are similar to those in the temporal muscle, but rather smaller
There are fairly numerous eosinophiles.

The mass from behind the pancreas shows the same features as the other deposits. The reticulum is much finer, in places hardly visible. There are numerous blood spaces, and the vessels, both arteries and veins, are often blocked with cells.

The microscopical examination of the lesions in chloroma then indicates that we have deposits of a certain type of cells replacing portions of the original tissue of most parts of the body. That these deposits increase by metastasis and by actual proliferation of the component cells of the deposit, and that there is compression and atrophy of the neighbouring tissues but very little intolerance of the new growth. The cells are similar to those which make up the great majority of the abnormal white cells during life, and are identical with those found in the bone marrow.

The growths do not appear to be sarcomatous. They are not lymphomas because the lymph follicles over the body are not all affected. Dock's theory that the original deposits are in the red bone marrow with secondary infiltration of the periosteum seems most likely. He thinks that the origin of the growths is essentially myelogenous and that the existence of primary chloroma in the spleen or lymph nodes may
yet be demonstrated.

The growths throughout the organs have a decidedly leukaemic appearance, and when we take into consideration the history, physical signs, and blood changes and the macroscopical and microscopical appearances of the growths, we are bound to admit that there is some intimate connection between leukaemia and chloroma. Chloroma appears to me to be a form of leukaemia with the distinguishing characteristics of very rapid course and a green calcification of the metastatic growths. The latter characteristic might possibly be absent and we would have a condition which would be unrecognisable from one of rapid acute leukaemia.

Chloroma is characterised by anaemia with increasing weakness, symptoms caused by growths deposited in any of the internal organs, external manifestations of growths if they lie comparatively near the surface and certain blood changes. After death green deposits are found infiltrating the internal organs; and the structure and mode of spread of these deposits have been found to be the same in all the cases examined, i.e. metastasis by the blood vessels and active proliferation of the cells in the blood vessels and in the part of the body in which they have taken up their position.
seat of growth being the red bone marrow.

PHOTOGRAPH OF SECTION OF THE
DURA MATER. ...
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