Observations

On the Normal and Pathological Development of Stone.

David Lindsay M.B.
1884.

Permanen Address
Eastfield
Petersham
Berkhamsted
Hemel Hempstead.
I have this day left at the Secretary's Office, Univ. of Edinburgh, the Thesis which I submit for the degree of M.D. —

It consists of:

1. Dissertation
2. Drawings illustrating that
3. Microscopic sections to that statement may be verified.
4. Naked eye preparation (cup of leaves from the cedar)

Thereby certify that the
P.S. I shall call for the tickets after my statement have been fully verified. Shandray.

above is the result of personal investigation, and has been compiled entirely by myself.

(David Lindsay 1883)

Secretary's Office
Univ. of Edinburgh

30th April 1884

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Contents

I. Introduction

II. Description of Sections
   A. Physiological
      1. Series of transverse sections of vertebral bodies, showing stages in the ossification process.
      2. Centre of cartilaginous vertebral body peaking w/calcium matrix & no cells.
      3. Zones of cells
      4. Zones of osseous deposit
         a. Double staining by preserving in Müller fluid retaining in Fox Carnoix
         b. Calcifies cartilaginous matrix pink
         c. True osseous material greenish
      5. Position in which calcification first appears.

II. Section of fetal hands & feet (Human)

   To show:
   1. Stages in ossification
   2. Line of artificial cleavage in articular extremity
   3. Effects of different staining reagents.
(3) Series of longitudinal and transverse sections of the bones of young rabbits from 12 days after birth till 5 % at intervals of a week.

(1) Progressive remineralisation.

(2) Department of the cartilage cells of the rabbit near centre of ossification.

(4) Two sections of the bone of a kitten.

To show.

Peculiar appearance in the osseous matrix. Apparently a whole layer of osteoblasts degenerated in the matrix.

(5) Two sections of ground unsoftened bone.

To show.

The lacunae of an aleurite.

(6) (1) Short consideration of the literature of physiological ossification.

(2) Conclusions from previous observations, more especially with regard to the primary changes in the cartilage. Theory of these changes.
B. Pathological.

1. Formation of Bone in the Choroid

2. Consideration of an Osteosarcoma

3. Destructive Changes in Bone (Molecular)

4. Series of Sections of Osteosarcoma, illustrating the types in the osteous development.

Types: several.
Late in the year 1882, the month of November, after having had two years in a general out
by practice as locum tenens. Subsequently
to graduating M.B. Ed. (Ed Univ) 1880, I
was desirous of undertaking some original
investigations which might ultimately
afford a basis for a thesis to be sub-
mitted for the degree of M.D.
Accordingly, I commenced a course of study
in the Pathological Laboratory (Ed Univ)
under Prof. Greenfield.
Here I was engaged to a certain extent
in general pathological work, but lately
decided to devote more particular at
bention to the study of bone from a de-
velopmental point of view.
It seemed a particularly interesting field
for research, and thus the more readily
induced to undertake it from a consideration
of the fact, that at least some of the joint
both in the normal and abnormal de-
velopment of bone, had not been fully
factorily settled hitherto.
During the course of examining about fifty
Accouphes in the collection of the late Professor Senn, now in the possession of Professor Senn, for the purpose of ascertaining the exact differences of facial structure, I obtained much valuable material. From these I have a tolerably complete series of the types of the abnormal development of bone as observed in the class of accouphes, Ixodes Tarsomatus.

I decided to make this the basis of my thesis, and to combine a study of the normal with the abnormal development in order to have a more accurate understanding of the processes concerned.

Besides these accouphes, I have had opportunity of investigating other diseased conditions of bone, bearing more or less directly on the subject, and in so far as they do to I shall embody them in the work.

For studying the normal development, I endeavored to procure as many foetal bones as possible of different ages.

During the winter months this was done. What difficult but gradually a pretty liberal supply was obtained.

Many of course were without any special
Some instances adopted.

I have collected nearly cases, learning on the work, some of which I have had the opportunity of observing during life, while others are in the form of reports and preserved specimens.

All these have been examined laboriously, they shall not be included in the body of the work, however, to avoid the risk of overburdening it, but shall reserve them as an appendix should this be considered necessary.

The methods employed have been much the same throughout as the results appeared satisfactory.

The specimens were first kept for a few days in dilute methylated spirit. (1 part of water to 2 parts spirit.) In some cases the vessels were injected with Mullers fluid or a mixture of Mullers fluid and spirit.

Small pieces of eggs and portion required were then taken from the specimens and placed in the softening fluid.

For softening adult eggs, or true vesicle tumours, I find the following two fluids answer.
Secrecy in as good condition as possible. The superfluous sections were kept loose in weak spirits and others in a mixture of glycerine and water (equal quantities) with 40% of carbolic acid in 20 B. The spirit answers well enough for some time, but undoubtedly has a tendency sooner or later to produce a granular condition of the tissue and especially of the cells.

Without further introductory remarks I shall also describe a series of most typical sections. The slides will be numbered and the drawings made from these also indexed so that reference may be facilitated as much as possible.

Section 1. Tail of foetal lamb. Transverse.
Stain. Ficarmin (Martindale's).
Mounted in Tarrant's Solution. (12. 3. 84).
L. F. (x50). Hartnagel's lenses. Drawing A.
Necrosification apparent.
For purposes of description this section may be divided into four zones.
Beginning at the centre and passing outwards.
Zone 1. The central apparently composed only of a matrix with very few cells, in fact hardly any.
Diagrammatic

To show relative positions, not exact sizes or proportions.

1. Central Zone.
2. Proliferating Zone.
3. Zone with Cells irregularly arranged.
4. Outermost Zone.
Zone 2. Immediately outside the central, and may be termed the "proliferating zone." The cells here are very numerous, and evidently in process of multiplying even even by the low power. The cells are distinctly arranged in rows, radiating from zone 1 as represented in drawing A.

Zone 3. Here the cells relatively to the matrix are fewer than in zone 2, are more or less rounded and the arrangement is irregular.

Zone 4. This is the most external. The cells are very numerous, appear flattened, their long axis lying more or less parallel to the periosteum of the vertebra.

At this stage we have no signs of ossification, or at all events of the deposit of osseous matter. The section presenting the structure of hyaline cartilage, viz., cells placed in a hyaline matrix surrounding the cartilage, the perichondrium can be distinctly seen.

No blood vessels are seen passing into the cartilage.

The several zones may be represented diagrammatically as in diagram (A).
Section: Hartnack's No. 1 Objective.

Drawing 13.

Central zone is especially noteworthy. It is seen to be composed chiefly of hyaline matrix with very few cells.

Proliferating zone. Cells seen in active state of division and arrangement in zone can be made out.

Zone 3. Here the more or less rounded form of the cells is evident, and also the amount of matrix relatively to the cells.

Zone 4. Cells seen to be elongated and long axis as described under 2. P.

Passing outwards we come upon the perichondrium, where the most internal cells are also elongated and long axis arranged more or less parallel to the circumference of the section.

Throughout the preparation all the cellular elements are more or less granular, and division can be seen in all the zones but very marked in what has been termed the Proliferating zone.

No appearance of blood vessels in the car. lage?
Section 2. Body of Vertebra. Fetal Rabbit. (Transverse)
Stain. Microcarmines.
Mount. Farrant. 18/3/84.

H. Hartnack No. 4 Objective.

1) Central Zone. Apparently no real cartilage here at all, only a dim appearance in some parts. By very careful focussing, however a few cells can be seen, especially towards the external part. Much of the zone is quite unoccupied, and arrangement of ligaments is irregular.

2) Outside Central Zone, we notice an area in which the cells are arranged in rows, some of which radiate from the centre whilst others do not.

3) Then comes an area in which the cells are arranged irregularly, and rounded.

4) The most external area or zone, has the cells elongate their long axis being parallel to the air cell furnace of cecine.

Outside this we have the thin chondrins.
No bloodvessels can be seen in the cartilage.

H. P. Hartnack's No. 7 Objective.

1) Central Area. The dim appearance referred to under H. P. Cell now be distinctly seen. It is arranged irregularly, but chiefly just resemble Zone 2.
is directly continuous with the matrix between the cells in that zone, which indeed it very much resembles, if not exactly alike. It seems almost as if the matrix was becoming deposited just within Zone 2. A few cells exist in it. The part exactly in the center is almost entirely free from any matter.

Zone 2. Cells numerous and arranged in rows which are more evident at some parts than others. Many of the cells are somewhat elongated.

Zone 3. Irregular arrangement of cells more or less rounded.

Zone 4. The cells are elongated and apparently more numerous than in Zone 3. The arrangement is as described under 2.

Then comes the peri-cartilage, the internal part of which is more cellular than the external, long axis of cells parallel to circumference of section.

No appearance of blood vessels throughout the cartilage, as likewise no apparent deposit of osseous matter.
Section 3. Tail of fetal lamb. (Transverse.)

Stain: Picro-Carmine.
Mount: Farrant. 18/3/84.

L. P. Hartnack's No. 10 Objective. Drawing D

Ossific deposit is quite evident in this section.
For descriptive purposes we may also divide it into a number of zones.

1) **Zone I**. Central, where there is no ossific deposit, but is filled with what is apparently a collection of small cells.

2) **Zone II**. Outside the Central. Here there is a beautiful ossific deposit in a circular form, but united to Zone IV at two places by ossific matter.

3) **Zone III**. A cellular zone through which the bands from the Connect. Zone II with Zone IV.

4) **Zone IV**. A more or less circular deposit of ossific matter, arranged rather irregularly and divided into two in some places. Cells are seen passing into the spaces between the Ossous Tubercles. Within the substance of the Tubercles, faint colored faint structures, whilst the rest is of a delicate greenish-brown. Number of cells can be seen in the green part, evidently the Lameae with the loose cor. fuscules. This description holds good for all the ossific deposit in the section.
side just under the peritoneum we notice cartilage
becoming invaded by the basophil deposit.
C. **Peritoneum**
Internal part—composed of several layers
of cells, and these can be seen passing into the
spaces between the fasciculi trabecularis.

External part—is evidently much fibrous.
At one side are that on which cartilage still
exists. We notice what is apparently the trans.
verse section of vein & artery.

H. P. Hartnack's W.O.7. Objective.
The structure can be better seen out with the power.
The cells of the central area around No. 3 are distinctly
seen. Many, almost exactly the size of white blood
corpuscles stained pink, others larger, whilst a few
are very large, and multinucleated evidently the
Morbus plaques. A delicate connective tissue seen
passing amongst the cells. Loops of Capillaries
filled with corpuscles are also shewn.
The true basophil deposit in Zone 2 and 3 is most
beautifully shewn. There is a double staining
The matrix of the basophil deposit contains deli-
cately green, the cells in the lacunae pink.
A faint stained material with margined features
and with double outline occupies more or less
the central part of the green lamellae bone. This is
the remains of the cartilaginous matrix, which
becomes calcified at the commencement of the
ossific process, and around which the true
ossicles deposit takes place. It has been termed
"osseous tissue" by Comte & Hauville, and ulti-
mately disappears. The calcareous matter
has of course been removed during the
process of preparation as no softening reagent
were used in this case. As rule as cells
are to be seen in its substance, still after
eliminating possible causes of error no cells
lying at a different level, and the invasion
of the first matrix by the true osseous forma-
tion, some inclined to believe that in some
places cells do exist in it, these however
being almost invariably degenerated.
in appearance.
The layer of cells (osteoblasts) lining the tube-
place to well chew on some points, can be also
the formation of a Stanniusian Canal.
Highly refractive granules are seen amongst the
osteoblasts, especially on that side next the
bone.
At one end of the section the osseous process was not quite so far advanced. There we see calcification of the cartilage matrix with liberation of the cells in spaces. Some of the cells after liberation seem in tolerably good condition but many appear much degenerated.

Still near the periphery of the vertebral body at this end we notice the cartilage cells much larger and the matrix more plentiful than it is quite near periphery of the cartilage. Some of these large cells can be seen in process of dividing and others have evidently just recently done so.

Passing further out we come to the periosteum and it is worthy of note that at this part we observe the transverse section of blood vessels. The periosteum may be roughly divided into an internal cellular part from which prolongations pass into the spaces in the bone, and an external more or less fibrous part.
Section No. 4. Tail of foetal lamb. (Transverse).

Stain. Period Carmin.

Mount. Farnsoil. 21/3/54.

L.P. (X 50) Hartnack's No. 4 Objective Drawing C.

The primary deposit in the ossification process has evidently just commenced, and so far as the body of the vertebral is concerned it is first evidenced in the centre. The central area filled only with cells is not evident in this section. There is certainly a tolerably large space just about the centre of the deposit but not sufficiently large to be designated an area.

The calcified trabeculae are seen stretching out into the cartilage. They are more deeply stained than the surrounding cartilage.

Outside the deposit there is a zone in which the cartilage cells seem comparatively small. Outside this again we have a zone where the cells are very much larger or several lie very close together.

More external still, the cells are again smaller, somewhat elongated, their long axis lying parallel with the surface of the vertebral body.
Above one end of the section of the vertebral body, we notice a transverse section of a blood-vessel in the peristeam (or perichondrium). Just under this the cartilage cells are arranged irregularly for the most part, except where it projects into the peristeam in the form of two horns one on each side, and in these a distinct coned arrangement of the cells is visible. The most external cells have their usual arrangement, as far as is concerned. The peristeam has the usual characteristics. No sections of blood-vessels in the vertebral body.

H. P. (x 350) Hartnack's No. 7 Objective. The central deposit is seen to be the primary calcareous one. The appearance may be described as trabecular irregular in form and thickness, deeply stained by the Carmine, and showing numerous granules of a highly refractive nature. The peripheral parts have a more granular appearance, and the outline is double. These trabeculae bound spaces irregular and varying in size, containing granular cells apparently liberated cartilage cells. At the periphery of the
deposit, cartilage cells can be seen becoming liberated. Immediately outside this, the cells relatively to the matrix are coarsely granular. The nuclei are brightly stained while the external part of the cell is very granular. Nevertheless, there is evidence of division which process begins at the nucleus and then spreads to the rest of the cell. We see two nuclei in one cell at some places. Outside this area the condition of the cells is distinctly. At first sight they seem very large but an closer inspection we see that active division has been going on. And cells lie in the same capsule as evidenced especially by the nuclei which are brightly stained. Granular matter however prevents it obscures the cells in this area. This possibly has resulted from change during or after preparation. They lie more or less in groups. Matrix almost constant.

As we proceed outward, we find that at each end of the section of body, the cells are smaller but numerous. It is to be noted however that at one end the cells are larger than those at the other, and these we find from observing
several sections that ossification is completed before the end where the cells are smaller. At least there are signs of divisions. As usual those cells immediately under the peristeam are elongated with long axis parallel to circumference and around them the matrix is delicately pink.

The peristeam has the usual characteristics. Several bloodvessels can be seen in it. None however are seen in the vertebral body.

Section No. 5. Tail of fetal lamb. (Transverse)
Hæm. Picro cæm.ine.

Mount. Faranck. 24/3/84.
L. P. (x 50) Hartnack's No. 4. Objective.

Ossifying process well advanced. The cartilage has all disappeared except a small portion at one end of the long diameter of section where a transverse section of an artery is seen in the peristeam. Four areas or zones can be indistinctly made out. There are more complete at one end than the other, and we notice that it
is where the occupying process is most complete.

Area I. Central filled chiefly with cellular matter, rather irregular.

Tissue II. Occupied chiefly by the osteous deposit. This having the same appearance as before described viz. true bone deposit greased upon joined cartilaginous matrix.

Tissue III. Cellular interrupted in some places by bands of osteous deposit passing between II and IV.

Tissue IV. Pretty complete, occupied by the osteous deposit. Above and off the field it has only reached the stage of calcaneous deposit as evidenced by its separation. Some cartilage still exists here which has not yet calcified.

Periosteum seen surrounding body and passing upon it are prolongations, lining the spaces in the trabeculae. Sections of blood vessels seen in it.

H.P. (x 350) Hartnack's No. 7 Objective.

This shows beautifully the structure of the bone trabeculae and also the other appearances. The corpuscles in the laminae are at times pink. Their long axis is always parallel with the long axis of the trabeculae. These are lined.
by osteo-blasts which can be seen passing upon
the under layers of the periosteum.
Multinucleated cells were lying against the
bone in some places (osteoblasts).
The other appearances are similar to what have
been already described.

Section No. 6. Tail of foetal lamb. (Transverse)
Stain. Dyes, Carmine
Mount. Farrant. 24/3/84.
L.P. (x50) Hartnack's No. 4 Objective
Shows ossific process pretty well advanced, the deposit
being tolerably general throughout except at one or
two places.

Near the centre there is an area filled chiefly with
cells. A little to the one side of this there are true
spaces with nothing in them, the content, having
probably got displaced during the process of
preparation. At one side of the field the
ossific process has evidently advanced rather
further than at the other. There is at that place
an almost continuous layer of green-coloured
ossicular deposit just under the periosteum. It
Theideaexactlyoppositeinthesuppuratingprocessseems chieflytohavethesuppuratingstageswithlittle
granulomapedest,andyetitisnotedthatall
thecartilagesunderthesynostosehasnotyet
beendestroyed.

Attheendofthesectioncomescartilage.B
taneous,但不限于theendwhereablood
vesselisnotedinthesynostose.Inthis
pieceofcartilageweplanthecellsapparent
muchenlargedatoneplaceassseentothis
power. Thescellsimmediatelybordering
thecalcereousdepositareenlargedandthe
matrixplentiful.
Thecharacterofthedepositissimilaritowhat
hasbeenalreadydescribed.

AP(350)HartroodlesNo.7.Objection.
Theendifferentstagesinthesuppuratingprocessisnow
distinctlyshown.

1. Cartilageundergoingalterationasregardsthe
cells,viz:proliferation,severaloccupyingthe
samecapsule,seenatthetendofsectionwhere
(d)thecelltendedtobedescribedasapparently
enlargemuchenlarged.

2. Calcificationofcartilagesmatrix.Noverydeposit
(3) The posterior deficit of a green tint around the cartilaginous matrix stained pink.
Occupants of these spaces in this deficient; chondroclasts, otopo-clasts, or chondro-clasts.

It shows liberation of cartilage cells where calcification process seems, which then occupy the spaces (primary).
Also the continuous line of osseous deposit drawn one side of section (vertebral body) whilst on the other cartilage still remains.

Diagram to aid above description

- Protogonemic cells
- Calcification of cartilaginous matrix
- Continuous line of ossification deposit
- Cartilage not yet calcified
- Calcification of cartilage matrix

Drawings E.F & G

I shall now describe a number of sections of foetal hands and feet (human) variously stained.
The process of ossification is essentially the same, but there are some points of in...
Diagram illustratingacey cleanses. It represents a long transverse section of a long bone such as a phalanx.
tact to be observed. More especially would I direct attention to a series in which I have induced artificial cleavage of the cartilaginous extremities of some of the long bones, e.g. Meta tarsus. This can be brought about by pressing on the cover glass, but also sometimes happens very conveniently during the process of preparation before the cover glass has been applied. The number of sections showing this cleavage is, I think, sufficiently great to go a certain way in proving that the direction assumed is almost invariably the same, transversely to the long axis of the shaft. There are some exceptions to this rule, but these seem to be readily explainable, and rather strengthen above statement than otherwise. This when viewed in connection with the development of the cartilage cells when proliferating in rows is exceedingly interesting and well be considered further on.
Section No. 7. fascial strand. (Plut. from mid to tip of bone)
Decalcified in nitric acid.
Stain: Carmine.
Mount. Ferrum. 12/12/83. Lines of Cleavage.
The section has not folded on itself in some places.
stuff of shows appearance very well.
How the section has been made will readily be seen by looking at it with the naked eye. The other sections have all been done the same way. (hands & feet).

Taking the shaft of a single-spool bone we find ossification has proceeded to some extent. There is a deposit of bone under the periosteum. This is stained deeply Carmine as is also the outer layers of the periosteum.
The bone has the usual structure in exhibits at this stage trabeculae of cancellous matrix in which lie the lacunae, surrounding in regular spaces sit which we notice prolongations passing from the internal layers of the periosteum.
The central part of shaft in some of the bones is quite unoccupied, the contents evidently having became displaced. Towards each extremity of this however we observe the osseous
process going on briskly. Here the cartilage cells have been proliferating very freely, and are now arranged in rows, the long axis of which is parallel to the long axis of the shaft. While the long axis of each individual cell lies transversely. With this power we can only see the deeper parts i.e. those nearest the newly deposited bone have taken up more of the carmine than the rest of the cartilaginous matrix. It has evidently reached the stage of calcification at least. The calcaceous matter has of course all gone in this section. We can notice that the calcific deposit extends some little distance between the cartilage and the periosteum.

**Enucleation**

The separate centre of calcification has not yet appeared in the cartilaginous extremity. The appearance of the cells there will be better seen in H.P.

**Cleavage**

In looking over the section several slits can be seen in the cartilaginous ends. Direction of slits transverse to long axis shaft. About half there is the appearance of a slit bene
The deposit of bone under the periosteum covering the shaft is plainly seen. The long axis of the lamellae lies parallel with the long axis of the trabeculae. The cells are seen passing into the spaces from the outer layer of the periosteum. The appearance is more granular than when examined before the time the tissue has undergone some slight change.
Towards each end true bone is prolonged for some distance between the cartilage and periosteum. After examining numerous specimens besides the ours, I am inclined to believe that there is evidence of cartilage cells becoming bone corpuscles at this place. I arrive at this conclusion by looking more particularly at the appearance of the bone corpuscles and their axes. and contrasting them with the appearance and direction of axes of the cartilage cells immediately adjoining. The evidence I think is strongly in favour of the transition occurring.

If we trace the cartilage cells from this place around the articular extremity we find that those next the periosteum and articular surface are more or less elongated and with long axis parallel with the surface. I have noted this appearance in many preparations. The cells appear to be more numerous around the articular surface & to absorb more of the Carmine. Beginning at the articular surface (center) and passing deeper the cells are arranged somewhat irregularly, are more or less rounded, granular in appearance, clearing rings of proliferation.
deeper still the appearance is very characteristic. Great proliferation of cells. These are seen to divide transversely to long axis of sheet and as a result we have beautiful rows of cells each being elongated transversely. That each cell lies in a separate capsule is shown clearly where any happen to have dropped out.

Still deeper there is a brachial appearance of the cells. This is stated to be due to shrinking of the protoplasm, here the cell does not occupy all its capsule. Here being in most cases a clear space around the cell.

Then we come upon another change. The cell wall breaks down and two or more beginning to grow together enclosing two or more cells. Here begins the process of calcification of the cartilage matrix upon which ultimately true bone is deposited.

Other preparations will show the specific deposit more plainly. The fringe is referred to under L.P. Caro now is now be studied more minutely. The direction has been plainly enough been. Some fringes cells.
are lying and occupy the entire breadth of the fringes just coming to the edge. In others no cells can be seen, whilst in cases where the fissure is of a more gross nature, cells are seen lying in it.

That the parallel solution of continuity is upon destruction of cartilage and not a mere fissure or tear is now clearly shown.

Carpel bone. HP x 350.
The cells around the transverse section of blood vessels exhibit a more or less distinct, rounded appearance, are granular and in process of dividing.

In looking over the field the shape of the cells seem to be somewhat irregular. Many of the cells have a single process projecting from one end.

At the articular surface, the cells are more deeply stained, more crowded, and appear flattened with long axis parallel with surface.
Section No. 8. Total hand.
Decalcified by Pierce Acid.
Stain: Carmine.
Mount: Farrand. 14/12/82.

Cleavage. Sides of.
This section shows several good examples.
In one or two instances the two sides of the cartilaginous end are as if it were torn from each other, giving a superficial appearance of a parallel fissure or with reference to long axis of shaft. On closer inspection, however, it will be seen that if the process of pulling one side from the other had been completed, the result would have been each edge, beautifully fringed with transverse fringes.

The stages in process process also show.

Section No. 9. Total foot.
Decalcified as before.
Stain: Carmine.
Mount: Farrand. 12/13/84.
Cleavage. Several examples with a direction
as before described. Also transverse section of bloodvessel seen in one of the cartilaginous extremities.

In this lateral bone transverse sections of blood vessels, also some longitudinal sections of bloodvessel passing through the periosteum seen.
Stages mosaiic process shown.

Section M 10. Foetal foot
Decalcified as before.
Stain Carmin.
Mount Sarraut 14/12/84.
Gleusa 49 lines
One passes right through a cartilaginous terminal phalanx transversely.
Transverse section of bloodvessel in one of the cartilaginous cart.
Sections of bloodvessel passing into the dorsal bones from the periosteum.
Stages in osaific process.
No. 11. Fetal hand
Stain: Gentian Violet
Mount: Farrand 23/12/32
Lines of Cleavage very well shown both in the Cartilaginous ends of the long bones and also in the Carpal bones.
The cells are stained violet but the cartilaginous matrix is also pretty deeply stained violet.
Stages of ossification.

No. 12. Fetal foot
Stain: Anilin Brown
Mount: Farrand 24/12/32
Lines of Cleavage. In some Places there are slightly oblique.
The centre of ossification or rather where the calcification of the Cartilaginous Matrix is occurring is more deeply stained than the rest.

No. 13. Fetal foot
Stain: (1) Methylene Blue
(2) Picro-Carmine
Mount: Farrand 6/2/33
Lines of Cleavage. Some what oblique in some places, but still in the main transverse.
The Methylene blue got the first chance and it left.
Stained many of the cellular elements in the bone and cartilage.

The calcifying cartilage matrix is blue whilst at others it is green evidently due in some measure to fading and also to the double action of the two stains.

The carmine of the stroma carmine has stained the matrix of the bone markedly. The other cellular elements, those in the space amongst the bone trabeculae are stained greenish.

No. 14. Tectal foot
1) Methyl blue 25 ml.
2) Carmin 4g.


Lines of Cleavage Transverse.

The calcifying cartilage matrix has taken up the blue stain whilst the cells included in the spaces have taken up the carmine hence a double staining at this part.

The vascular matrix is deeply stained carmine. It is rather interesting to note that the central part of one end of the long bone is the car
dilatation and here distinctly taken up the blue stain. This is the proximal end of a phalanx.
Diagram showing the position in which oblique or parallel lines of cleavage occur as seen in the section with the matrix having been weakened by the proliferating cells.
which has a separate centre of ossification at a later stage of development.

No. 15: Fetal foot
Stains: Methylene Blue
Carmine

Mount Fermor 6/2/83.
Tissues of Cleavage. Parallel with long axis of shaft pass up through calcifying matrix into the cartilaginous head. It must be noted however that these lines pass through an area where the proliferation of cells is exceedingly marked, and as a consequence the cartilaginous matrix is by so much weakened, thus no doubt explaining why the fissure is parallel and not transverse.

In the cartilaginous head we notice numerous sections of blood vessels. Between the largest blood vessels and the ossifying cartilage further down the proliferation of cells is enormous.

In the tarsal bones many sections of blood vessels exist.
Under HP we can get a beautiful demonstration.
of cells proliferating in rows, and each individual cell becoming elongated transversely to long axis of shaft.

No. 16. Foetal hand.
Stain (1) Methyl blue 24 hrs.
(2) Neutral Carmin.

Mount Ferranti 18/11/83. Line of Cleavage oblique.
The calcifying Cartilage’s matrix is stained deeply blue.
The cells in the spaces at that part yellowish brown.
The formed bone is stained decidedly Carmin.
Cartilage matrix as a whole tinged blue but more deeply towards central extremity (surface).
The line of cleavage is oblique but it passes a certain part of its course, through the area where the Cartilage’s cells have proliferated to form rows.

No. 17. Foetal foot.
Stain. Same as 16.
Mount Ferranti 14/11/83. Line of Cleavage transverse.
The methyl blue blue staining is deeper.
Some parts of the central bones are stained more deeply than others.
Lines of Cleavage in the Cartilage are transverse.
No. 18. Foetal foot.

Stain slow Methylamine
Mount Ferrum 24/12/32

Line of cleavage parallel.

The cleavage has only taken place to a certain extent and that through the proliferating area (rows of cells). Had it gone further it is easily seen that its edges would not have been smooth but ragged.

We observe the appearance of bloodvessels passing through the calcifying area into the cartilage where it ends in a wider space containing a number of small cells.

Seen with the high power the cells immediately surrounding the vessel in its course are elongated and lie parallel with the vessel. Whilst those further out lie more or less transversely.

The cells appear more numerous just where the vessel ends. They are all beautifully stained blue.

In the small bones there is no evidence of ossifie deposit but several sections of blood vessels can be seen around the transverse sections, a more or less distinct arrangement of cells in rows can be made out.
No. 19. Fetal foot.
Stain (1) Osmic Acid
(2) Picro-Carmine.

In one of the long bones ossification is much further advanced at one side than the other.
At the terminal part of one of the ungual phalanges, a beautiful deposit of bone is seen. (distal extremity).
One of the tarsal bones? has got broken up into pieces of cleavage are seen.

No. 20. Fetal foot.
Stain (1) Osmic Acid
(2) Picro-Carmine.

Illustrates various stages of ossification.
The shrinking of the cartilage cells near centre of ossification is very well shown.
Sections of bloodvessels in tarsal bones and arrangement of cells around them. (Somewhat crowded).

No. 21. Fetal hand.

No. 22. Fetal foot.
Stain Picro-Carmine

Mount. Ferrnct. 12/12/83.
Various stages of ossification. Numerous sections of bloodvessels in small bones and arrangement of cells around
No. 23. Fetal Hand. Very young.
No. decalcification
Stain. Picro-Carmine
Mount. Farrand. 7.2.83.
Shows very well the calcification of the cartilage matrix. No appearances of bloodvessels in the carpal bones.

No. 24. Fetal Hand.
W. Methylene blue.
Stain (2) Picro-Carmine
Mount. Farrand. 11/12.83.
Shows the staining of the cartilage cells very well. We observe in the case of one of the long bones that the osseous process is further advanced at one side than another.
Sections of bloodvessels in carpal bones.

No. 25. Fetal Hand.

Stain. Auriculic Brown
Mount. Farrand. 15/12/83.
Flavine of the cartilage cells near occupying areas well marked in both.
Ossous formation in shaft of some of the bones pretty entire. Sections of bloodvessels in carpal.
No. 27. Fetal foot

28

29

Stain in every case Iodine Green.

Mount: Farrand. 6/21/83. This series shows the effect of the Iodine green staining. The cellular elements both in the bone and cartilage are stained beautifully blue, whilst the calcifying cartilaginous matrix is stained delicately green.

The shrinking of the Cartilage cells before referred to is also well marked.

No. 30. Fetal foot

Stain: Picro-Carmine

Mount. Farrand. 12/12/83.

Shows transverse lines of cleavage.

The sections of bones from the series of Rabbits (of different ages) will now be considered and first shall describe them in longitudinal section.

The stain is Picro-Carnine.

Some sections are mounted in Farrand's, Others in glycerin.
N° 31 L. S. (Knee joint) Tibia & Femur  

Rabbit 12 days old. 22/5/88.

In the articular extremity of the Femur ossification is tolerably well advanced, whilst in that of the Tibia there are but premonitory symptoms as if were, sections of blood vessels and an appearance as if the matrix had become somewhat calcified near the centre. The calcaneous matter has of course been removed by decalcification.

Femur. L. P.

Between the ossific deposit in the Cartilage mous extremity and that of the shaft there is a layer of Cartilage & the epiphysial cartilage. In this the cells are beautifully arranged in rows. There is a layer of matrix and then a row of cells. These cells are very numerous and arranged just like so many coins (pouleaux). The long axis of the rows are parallel with the long axis of the shaft. Whilst the cells, as seen by this power are of anything transverse.

The rows extend through the whole thickness of the layer but the cells appear to be most closely packed along each to each side of the central transverse axis.

Above and below this layer the process of ossie.
Description is in active progress.

All around the articular surfaces there is a dense arrangement of cells, deeply stained. The bone formed under the periosteum of the shaft is plainly seen.

H.P. Hartnack's No. 7 objective.

The ossific areas with the layer of cartilage lie between them are plainly seen, as is also the formed bone of the shaft.

Epiphyseal Cartilage. In some places the rows can be seen extending through the whole breadth of this layer of cartilage. In others there is a somewhat irregular arrangement of the cells between the rows and the ossific centre in the end. Still an obscure rowing may even be made out there.

Rows of Cells. The individual cells are seen to be elongated transversely. Between each of the cells there is a layer of matrix. This is rendered evident where the cells have dropped out of their capsules. The nuclei are bright by stained. All the cells are granular.

As we pass deeper down the trabecular base come plainer. The cells, having evidently
Diagrammatic showing the different forms assumed
by Human + Rabbit Cartilage Cells in Thrombosis:  
A. Human Fetal Cartilage Cells  
1. Rabbit...

Diagrammatic showing the apparent changes in the degenerative
process of the cartilage cells in rabbit near specific lesion.  
Agranular condition starting at the periphery and
progressing gradually to the centre until the whole
cells is degenerative. Progressive changes from (1 to 6).
shrunk and left a clear space in the capsule around. There is sometimes the appearance of more than one cell, but on careful focusing this is seen to be due to cells at a deeper level.

The shrinking of the cells here does not take place in the same way as in the human testis. Here they assume a branched appearance. 

* Human Cartilage Cell.

... (Human Cartilage Cell), but here the cell becomes surrounded by delicate fringes. 

* Rabbit Cartilage Cell. 

The external part becomes more granular, and on period a number of cells, we find that this granular appearance begins at the circumference and gradually spreads towards the centre until the whole cell seems entirely broken up. 

... Fertility degeneration probably occurs.

Deeper down we observe how the blood vessels make their way amongst the cartilage rows; they pass up opposite the layers of cells where the passage seems easiest. 

* Table E of Cartilage lie on each side of the capillaries of cells. These trabeculae become calcified and ultimately have deposited on them the true osseous deposit.

The spaces between the calcified trabeculae are seen to be filled with cellular elements.
Where true bone is deposited the matrix contains lacunae with bone corpuscles. This calcified matrix (ossiform tissue) as a rule contains no cells.

Further down in the shaft the osteogenic process is seen plainly going on from the periosseum. The protrusions from the internal cellular layer of the periosteum passing into the spaces among the bony trabeculae, lining the spaces. The cells, lying on the bone evidently search a matrix just next the bone and ultimately all around so that they become quite enclosed and from the bone corpuscles in the lacunae.

That a layer must necessarily already lie next the bone is apparent from the consideration of any space filled with comparatively round objects e.g. a box of oranges.

There followed out the several stages from different sections.

(Found these sections have become somewhat more granular from the time of last examining and describing them).

Ossific Centre in Cuttagonia extremity.

Evidently there has been a great influx of cells here. We may describe appearances as trabecular
Involving irregular spaces which in many instances are literally traversed with cells brightly stained. These trabeculae are lined with cells (starch granules) and consist evidently of cartilage which has been calcified, and also true connective tissue upon them. The process involves destruction of the cartilage matrix at some parts of first (although ultimately entirely) with liberation of the cells. Some of these appear altogether degenerated, but others apparently would be quite fit for further duty.

It must be admitted however that the cells became chiefly degenerated. This latter point is brought out by Prof. Huxley (Text-Book, part I, page 155.) All around the centre of ossification the cells are actively proliferating, but the rows are not so well marked on the side next the articular surface. Indeed the arrangement here is rather irregular. In the epiphyseal cartilage near this center there is certainly the appearance of the cells having multiplied so quickly that several occupy the same capsule. This may be deceiving however and is not the rule.
Just under the articular surface the cells are very numerous and have freely taken up the colouring matter.

Those cells next the articular surface and indeed all around the extremity are elongated and lie more or less parallel with the surface.

No. 32. Line of Cleavage parallel.
Similar section to No. 31. (12 days old)

It illustrates a line of Cleavage parallel with shaft. This however occurs where the cells have proliferated formed rows consequently weakening the cartilage matrix.

No. 33. L.S. Lower End Femur.

Rabbit. 19 days old.

Osteo process further advanced.

Section is slightly broken up but shows appenances very well.

The rows of cells in the epiphysial layer of cartilage are very beautifully seen.

The rest of the series can be briefly referred to.
No 34. 19 days old.

35  26  very good.
36  38
37  40
38  47  Epiphysial layer especially good.
39  54

All these indicate the progressive development of bone is the development at different stages and show that the deposit occurs by layer after layer on the surface of already formed trabeculae of bone. The first deposit occurring on the surface of calcified cartilaginous trabeculae, which act as directing rods.

Brief reference must now be made to transverse sections of above series.

No 40. T. S. Femur of Rabbit. 12 days old.

Picos. Carmine. Farrant. X50

The section appears to be somewhat oblique but cause there is a piece of cartilage at one side.

Periosteum surrounds the newly formed bone. This composed roughly of an outer and inner part.
The inner part consists of several layers of cells deeply stained brown.
The osteous matrix consists of trabeculae enclosing irregular spaces in which cells are lodged. The lacunae are plainly seen as dark spots in the matrix.
Cartilaginous part. The cells are deeply stained and each seems bent incompletely to fill its capsule. The cartilage's matrix is delicately pink and seem blended insensibly with the periosteum.
There are fibrous bands passing off from the arc. time and the periosteum fuses gradually into these.
The center of the section is empty. The contents having evidently got displaced.
× 350
Periosteum. External part composed of young fibrous tissue with many spindle cells. It is not as deeply stained as the internal cellular layers which are deeply brown. These dark cells pass into the spaces in the bone trabecular there is a slightly fibrillated appearance among the cells and that is prolonged in along with these shape of cells varies. Some are elongated, others rounded. All are deeply stained and content are granules. Generally a tolerably complete layer.
lace each space. The cells are seen becoming excluded in the loose matrix. The stages can be traced the bone. Beautifully pink almost homogeneous matrix but with signs of delicacy striation, chiefly somewhat circularly around the large spaces the lacunae are well seen containing granular bone corpuscles.

The following sections are similarly stained and show the stages in development at intervals of a week:

No. 41. 14 days old. T.S. ossification in cartilage.
arterial extremity.

No. 42. 26 days old. Same position as preceding.

42 (a)

No. 43. 33 days old.

No. 44. 40 days old. T.S. shaft. Femur.

No. 45. 47

45 (a).

No. 46. 54

This then completes the description of the series of sections long due clinical and brace of rabbits killed at intervals of a week beginning at 12 days after birth.
Sect. 17. Longitudinal. Head of Femur. Young Rabbit
There are of cartilage cell at specific area. Thinking of the cartilage cell much the same as in human foot bone.

Sects. 48. + 49. Longitudinal. Base of Young Rabbit
Decalcified in nitric & Chrome fluid
Stained with Methylene blue.

Mounted in Jarrant. 17th. 5. 83.

Examined under lens X 600. 18th. 6. 83. Drawing H

The epiphyseal layer of cartilage with its covering cell is very beautifully visible. This also the formed bone.

With regard to the osseous trabeculae. Here is a specially interesting appearance. For example when just out of the field notice a layer of osteoblasts lining an trabecula. Four of these osteoblasts seem to have united to form one huge cell which however has still some slight indication of its original constitution (254 cells). Looking at the trabecula we see a layer of osseous material, and in this just one or two cells at one end. Then here is a granular layer in which 304 cells lie. This granular layer lies in the osseous matrix and has just the appearance any a whole layer of osteoblast had degenerated. The drawing will make this clear.
The same appearance of a granular layer in the osseous matrix in pretty general throughout the sections and offers an interesting point.

Sect. 50. Plane of fossa lateralis. Slightly oblique.

Stained with Alcian Carmin.

Mounted in glycerin.

Shows newly formed bone. Haemorrhagic Canal, etc.

Commencement of osseous process in cartilage near end.

Where evidently great proliferation of cells.

N°. 51. 52. Sections of Adult Unossified bone.

51. T.S. Radius.

Shows beautifully Haemorrhagic Canals (5). Traeanae and Canaliculi.

52. Flat Section of Fractured bone.

Haemorrhagic Canaliculi beautifully shown.

(Except plate however that these two last were made for us.)

This concludes the description of Sections illustrating of the intra-osseous haemorrhagic Development of bone.

I shall describe but shortly the intra-osseous haemorrhagic as evidenced in section from the foot-fracture.

Flourish a great part of the long bones is al.
performed from membrane, i.e. without the cartilage preceding the process. Sect. XII. 52. 54. 55. Where cartilage is taking place in the facial or cranium. The stages are pretty well advanced. The lacunae in the bone matrix being plainly seen. The bone is observed to shoot out from a centre in the process of increasing. The absence of pre-existing cartilage was first pointed out by Herbst. The long trabeculae are lined by cells, which ultimately become the bone corpuscles and Haversian spaces are formed in the same way as under the peristeme, or long bone.

The literature of the subject of ossification will now be considered and observations made from personal observation more especially with regard to the primary change in intra cranial, sigmoïdous ossification.
Literature. Conclusions with regard to the osseous
changes in the intra-cartilaginous epiphysis.
The subject of ossification has long attracted the
attention of numerous observers.
There are two varieties of it described, (a) the intra-
membranous, of which the Periosteal bone may be
taken as the type. (b) the intra-cartilaginous, with
its type in the Femur. In the latter however we
have also intra-membranous from the Periosteum
for which the thickening of the bone is chiefly due.
The intra-cartilaginous variety especially has
been long celebrated. This is due to the fact
that the bone of Femur is preceded by a cord
of hyaline Cartilage growing down as the future
bone, covered by the Perichondrium which ult-
mately becomes the Periosteum. In process of
time the Cartilage all disappears except at
the articular surface where a layer persists.
The sealing of the Cartilage and particularly
of the cells was long obscure.
This variety which I have had especially in
view in describing the series of sections,
it may be well to state some of the opinions which
have been held with regard to ossification gen-
erally. Attention was early directed to ch
Nicolaus, Eppesonus, Coiterus, Kerckringus, and
Engliandt all wrote on the subject.
Nesbitt (Memoirs of the Royal Society, 1780) quotes
Eggiardius' words as follows: "Superficies otis
florum humidum sustineat membranam et
plures sibi centum superficilae, quam
prae depleatur corporibus haeret e secreto ductilibus
derivatis; illae secretae per arterias adveniunt
(vel.
flucentibus per veins, partibus fluidoribus ex-
tellacet in foros membranasque quae crescent
ulug or Constituant."
Nesbitt agrees with this in as far as it relates to
agree impregnated corporibus haeret aut materiis
superficial, being brought to the ossifying part by the
arteries, the more fluid part returning by
the veins.
In his two lectures he endeavours to show that
the general notion at that time of all bones
being formed from cartilages, was a mistake.
Not only that he went further and tried to prove
that no part of any bone is formed from carti-
lages.
He says, the quantity of cartilages is much greater
at the first part of life because nature uses it
to supply and fill up the place of those bones.

(1) Phil. Trans. 1780.
or parts which require not so hard a substance as bone to perform its natural function, until a considerable time in some cases after eve-
ning and in others after birth, which carti-
lage serves as beds for the ossification to shoot
securely in.

(Leet. 1 page 9. 10. Line 9 from bottom of page)

She also says the bony particles in fractures
begun to be deposited, or to shoot either between
membrane or within cartilage.

(Leet. 1 page 10. 10. Line 1 from both)

It is recognized separate centres which afterward
 unite. She could not perceive or feel a bony
particle in the cartilage until there was a
visible influx into it "the appearance of an
inflammation."

She denotes that in ossification cartilage must
first be formed of states that neither the fluid
nor the hard parts of cartilage are in the least
concerned with bony production.

Dry cartilage & precedes bone in some instances.

She says it is due to the fact that nature never uses
hard substance where a softer will do to
make cartilage more nearly resembles bone
than any other tissue.
In connection with above views Eskull studes
another at a much later period
Recherches sur le developpement. Aes 8 et
les dent. Locarn. 1842.

He sums up his results and introduces them
thus: "J'ose croire pourtant qu'il sera diffi-
cile aux physiologistes de se pas accepter

come autant de points definitivement
fixes par mes experiencs les points qui
actue savoir
(buriting pour).

Et que l'ossification (ce phénomene par le
quel on a tant ecrit et jusqu'a present
et inutillement ecrit, n'est que la transfor-
nation regulation et successive, de perite
du cartilage et du cartilage en os.

(Dedication at beg immag to M. Marshall Hall)

At page 61 I fill of space work near middle
of page the states the following:-

"Le perioste passe done par deux etat condi-
crits, il devient d'abord cartilage, et puis
il devient os. Le perioste se transpose en os
et cartilage, se transpose en os, et c'est
je le repete ce qui est elementat par toutes
mes experiences."
Huxley investigated the action of radicles upon growing bone, and gives beautiful results. It
stimulates the growing bone and that only from
an affinity to the jodphosphate of lime.
Experiments have been repeated and corroborated by Hunter, Baller, Bethelty ete. so far as
the action of radicles is concerned.

Hunter proved that bones increase in length at
the epiphysial cartilage from his well known
peg experiment.

Again in Müller's Elements of Physiology, by
J. Müller, M.D. Translated by W. Bubey M.D.
Quoted at stated. (1843)
The idea that bones are formed from the peri-
atome appears to me to be a barbarous
unworthy the present state of physiology.

Oliver demonstrated the power of the peri-
atome to form bone.

Lobin believed that all the osteoblasts were
descendants of the connective tissue corpuscles.
H. Müller believed that the osteoblasts were pro-
liferated cartilage cells.

That the cartilage matrix does not become bone
matrix is a fact pointed out by Sharpey.
That the cartilage cells as a rule do
not become bone corpuscles is pretty gen-
erally accepted now, but whether a cartilage
cell may not sometimes become a bone corpus-
cle is a point not altogether made apparent.

Prof. Rutherford suggests the possibility
of a cartilage cell ceasing to secrete a cartil-
age matrix and producing the periosteum
of bone from observation of the department of
cartilage cells near the bone.

(From book of Physiology, 1871, page 107)

From above statements it is evident that intra-
cartilaginous ossification has long been
debatable territory.

Several stages are now recognized and the
appearances beautifully described but quite
as discovered in the literature of the subject, a
recognition of a fixed and definite law which
will be universally applicable, and tends to
explain many points which are proved to exist, but of which the explanation is still a complete

statement.

This is the law that seems chiefly to confuse my attention, and with reference more particularly to the primary changes in intra-cartilaginous ossification.

At a certain period in the development of the embryo, the representatives of the future bones are like all the rest of it composed of a number of cells. They are then in a state of cellular cartilage. By and bye the cells begin to secrete a matrix, and this becoming deposited around and between them, the stage is reached of hyaline cartilage. These then are the representatives of the future bones, and are like them, in form and position, composed of the usual structure of hyaline cartilage, cells placed in a hyaline matrix. They are surrounded by the perichondrium.

In this stage they are practically non-vascular structures, containing no capillary network, but dependent for their nutrition on the surrounding tissues.

The vertebral bodies. These afford a very good oppor
Cartilaginous Vertebræ. Notch chord still present

Transverse section:

Diagram illustrating relation of Chorda Dorsalis to vent of vertebral body.

Longitudinal Section

Vertebral body

Diagrammatic

A. Transverse. A longitudinal section of a vertebral body (Diagrammatic). The arrows indicate the ways in which the intraspinal current flows.

C. Chorda Dorsalis in the centre.
Attention for studying not only the Chondrification of the cellular cartilage, but also the different stages in the successive process. Nevertheless it is well to remember that up to a certain point their development is somewhat peculiar. They are deposited around a fetal structure the Chorda dorsalis which persists for a certain time after the rest of the body has become Chondrified in making a transverse section of a vertebra at that stage we would find that the external part consisted of hyaline cartilage but the centre not. Gradually the notochord disappears, string become disintegrated and get carried away, or it may afford nourishment to the cartilage cells leaving directly surrounding it.

In either case the central part of the cartilage would be very favourably situated as regards nourishment. If the notochord disintegrates and get carried away it would leave a very convenient channel for nourishment getting down the centre of the body, and if its substance affords food to the cells then the nourishment is close at hand. It does disappear and something takes its place.
Vertebral Bodies

[Diagram of vertebral bodies]

A Haemovas: Longitudinal section of vertebra fully chondrified. Although centre may have fewer cells than rest. The arrows indicate the direction nutrient must pass. Supposing each section to be exactly through the centre of a vertebral body then the dark spot will indicate where nutrition is likely to be most easily interfered with.
Section No. 1. reveals what that something is. It is cartilage but that somewhat peculiar in kind. It contains practically no cells but simply matrix. That is to say there is great deposition of matrix where the nutrition, so far as could be judged was best.

In section No. 2 the matrix is apparently just beginning to be deposited and this deposit originating from the cells around.

At this stage (Section 1) the centebrae are practically analogous to the carpal or tarsal bones in composition i.e. hyaline cartilage throughout. Bearing in mind the existence of matrix without cell in the centre of the centebrae.

Let us revert for a moment to the nutrition of cartilage. This practically a nonvascular structure receiving all its nourishment from adjoining tissues. Its capillary meshes in it. The nutrient must thus all pass through the periphery before it can get to the centre. This central part is farthest removed from the fountain of nutrient, it will thus be the least vital part, or at all events that part most likely to suffer from any interference.
with the normal nutrition of the cartilage. Granting a condition in which there was barely sufficient nutrient for the exterior part of the cartilage, then there would be none left for the centre which must inevitably suffer.

We may regard the cartilaginous body of a vertebræ as placed in a nutrient medium the surrounding tissues; we may regard the centre of a vertebral body as placed in a nutrient medium the outermost part of the body.

Here what was apparently the least nourished party the body before it was fully chondrified becomes after chondrification the part least favourably placed as regards nutrition.

But the vertebræ are not destined to remain cartilaginous at least in the higher vertebrates. They tend upwards to develop bone and in this upward process certain changes are observed.

The first most evident changes are concerned with the cells, and that in a steadied and uniform manner. Processes in a fixed and uniform position. The changes is evident, but it will not
Diagrammatic transverse section of body with perichondrium

External Raphirial part of Perichondrium
Internal Cellular Part
Cartilage

The cellular part is evidently where a primary change must occur in the formation of bloodvessels adding with which cells are prolonged in.
plain that for its production there must have been a preceding cause. The cells enlarge some what and then proliferate vigorously as near the centre as possible because in the centre there are no cells. There is then proliferation of cells at that part which we have seen is most liable to be affected by interference with the nutrition. But how can there be this interference here? A little consideration will make it apparent. The cartilaginous body is surrounded by the perichondrium, which consists of an internal cellular part and an external more or less fibrous tougher part.

At a stage further advanced than at present under consideration, there is more perfect formation of blood vessels which invade the cartilage and carry with them cells and delicate connective tissue from the internal layers of the perichondrium which is then becoming the periosseous tissue. Now, at the very beginning of this formation there must inevitably be some change occurring between the external part of the perichondrium and the cartilage.
There is thus a change in that part where the cartilage derives its nourishment. This must necessarily lead to affect the nutrition of the cartilage, and it seems to us the proliferation of the cells at the centre is the natural response to the changed nutrition. That pressure is exercised by the invading bloodvessels, at a later stage is undoubted, but there must also be a certain amount in the earlier stage between the external part of the perichondrium and the cartilage, and this leads to interference with the normal nutrition, and brings about a certain degree of innutrition, although apparently at this stage there is an abnormal abundance of nutrition; it is the very fact which, to a certain extent, turns the nutrition of the cartilage upside down, the effect being first evidenced in the central vital part over the centre.

But if the central cells are badly supplied with nourishment why should they divide?

This leads me to refer to the relation between nutrition and reproduction.

Dr. James brought this subject prominently
before the Edinburgh Medical Chirurgical Society (Meeting 4th July 1883). After speaking generally about the case of a cell to show how insufficiency could lead to reproduction. He supposed a cell placed in a nutrient fluid. It grows by absorption and assimilation of the nutritive fluid in which it floats. Therefore its size increases in size but as it does so what happens? It is a well known fact that if we compare two bodies of similar shape but different sizes, their respective volumes vary as the cube of their diameters, whilst the proportion of their surfaces is as the square of their diameters, that is, if we take our cell its volume increases more rapidly than its surface. Now, of course it is through its surface that it gets its nourishment, it is therefore getting less and less nourishment because its surface is becoming less and less in proportion to its mass. Finally a time comes when it cannot get a sufficient supply. What happens then? It simply breaks down into two or more small pieces, but these small pieces having a larger surface in proportion to their masses, ...
at once begin to grow and form cells like the original ones.

I think this theory besides tending to explain the proliferation of the cartilage cells in the centre of the vertebral body receives support from the proliferation and considerations regarding it in this case. If one of the nutrient was quite cut off the cells would inevitably die.

With regard to the individual cells, we may consider the nucleus as placed in a nutrient medium namely the cell. All the nourishment for the cell and consequently for the nucleus must pass through the cell wall. The nucleus however remains furthest removed from the point of nourishment because it is inside the cell. This is astoundingly that when a cell wants to divide it is the nucleus which first divides and then the rest of the cell.

Classification of the long bones

The femur be taken as the type. This of course is preceded by a rod of hyaline cartilage shaped like the future bone. This rod however quite as regular.
on the body of a vertebra. There is the shaft and two extremities, the lower of which is the largest,
and in fact it is the largest mass in the cartilaginous
bar. If what has been stated with regard to
the nutrition of cartilage be correct, the
centre of this mass will be the level where
part of the cartilage is more fleshy, other
of course being equal. It will then be the
part most likely to suffer first from any
interference with the nutrition. Now be
ving in mind what occurs in the vertebral
body, one would expect to see the primary
changes in the annular process manifested
here. But they are not. They begin first
in the centre of the shaft and are practically
the same as in the vertebra as far as
the cells are concerned. Is this then
an exception to the general rule?
Besides the vitality of the cartilage we
must take into consideration another
factor, namely that which produces
interference with the nutrition, and
this seems to be the explanation.
The centre of the shaft is quite surrounded
by perichondrium. Moreover it is seen
this place that the nutrient artery forms. Hence the force tending to disturb the normal nutrition of the cartilage is here greatest. And with the natural result, a manifestation of this interference is seen in the shape of the cartilage's cells proliferating at the centre of the cartilaginous shaft.

Although the centre of the lower articular extremity may be the part possessed of least vitality, still it has not in the first instance received force brought to bear upon it. The periosteum stops short near the articular surfaces and although bloodvessels can be seen invading the articular extremity at a later period (which means pressure interfering with nutrition) we never see any bloodvessels invading the articular extremity from the articular surface which is the source from which the cartilage derives nourishment.

Anticipating for the moment what is going to be said with regard to the other stages in the vertebral body, we find
Diagram of Great Cacholoom, femur indicating where osseous change are first evidenced.
First at +1. Secondly at +2 as separate centre.
The arrows seem to indicate the direction of the pressure therein concerned.
It begins in the centre of the shaft and then progresses towards each end.
in the shaft of the femur, the cells proliferate, matrix calcifies, bloodvessels invade the extracellular matrix. The calcified matrix is broken down in part, the cells are liberated and on some of the calcified matrix which remains as directing trabecular. The ossific deposit occurs. The bloodvessels progress towards each extremity of the shaft, and then the ossific process goes on. When the matrix becomes broken down it seems to act as a cap to allow for the pressure and allows the ossific deposit to take place quickly.

A time comes however when ossification begins in the articular extremity. But in which one first? In the centre of the lower articular extremity which we have seen is probably the least vital part of the whole cartilaginous femur. Looking at the tibia, ossification begins in the upper articular extremity before the lower, the former being the larger.

We may suppose that the disturbing influence brought to bear upon the
lower extremity of the femur and upper extremity of the tibia contain the same size force. The former is the larger and thus nearer regard the centre of the upper extremity of the cartilaginous tibia as having somewhat more vitality than that of the lower end of femur.

What do we find? We find that the primary osseous changes occur first, what earlier in the femur than in the tibia in the parts above referred to. That is to say they occur first in that part probably possessed of less vitality and more easily influenced by nutritional changes.

This is well shown in section No. 31. (Knee joint of a rabbit 12 days old).

Reverting to the case of the vertebral bodies. We left off at the stage of cell proliferation which I have endeavoured to show is dependent on imperfect nutrition.

The next stage is that of calcification of the cartilaginous matrix, another stage, as it is, and of altered nutrition. This quite differ
cut from the true osseous deposit. This bone, by Comil and Ravinier, osteon tissue, and is stated to contain two cells. But as I tried to show in a section of the tissue, it occasionally does but there are of a disintegrated nature. It ultimately disappears but during its existence, besides being a natural consequence of the disordered nutrition it performs a useful function. Some of it acts as directing trabeculae for the osseous deposit. Bloodvessels penetrate and break down the calcified cartilaginous matrix in part, liberating the cartilage cells and forming the primary medullary spaces, in which the true osseous formation is about to take place. When these spaces are formed they seem to act as safety valves for the pressure. Although these spaces with a certain amount of obscurity it seems to me that these spaces allow in the most beautiful manner, the osseous deposit to take place quietly. They are filled with cells and among these are capillarics and delicate connective tissues. What
better arrangement could not have been for nutri-
tion? As a matter of fact the cells begin to secrete around them in a
definite way, a matrix, and form
the true osseous tissue with lamellae
and canaliculi, quite different from
cartilage, which is a much more
dependent structure, the bone being
highly organised.

The matrix of the cartilage certainly
disappears but whether a cartilage cell
may at all times become a bone corpuscle
is a point not so easily settled.
The difficulty arises chiefly from the num-
bers of cells which fill the primary medullary
spaces and make it difficult to de-
tect a cartilage cell from the others.
I have devoted some attention to the
appearance of cartilage cells at the
trice of their liberation from the matrix.
Some are undoubtedly quite definite,
gated and this is especially the case
in the Rabbit. Other again appear
in good condition and quite fit for
further duty. It would seem to be a case
of vitality whether the cells could survive under the conditions in which they are placed during the primary changes.

I have noticed a cartilage cell apparently becoming absorbed as a process where the bone developing in the shaft is prolonged into the cartilage at the end. (Vide drawing.)

Prof. Rutherford suggests the possibility of this transition (Text Book, p. 107.)

The arrangement of the cartilage cells in
dow.

rows of cells.

Numerous examples of this are plainly seen in the sections submitted. This well marked in the articular extremity where ossification is proceeding and especially in that cartilage between the ossific centre in the extremity and that of the shaft, the epiphyseal layer in fact. The long axis of the bone is parallel with the long axis of the shaft, whereas the individual cells are elongated transversely. Between the
From these exist, cartilaginous matrix, as also between the individual cells unless the proliferation be very marked when several cells lie in a single cavity.

Now, the weaving is a very striking feature, and it takes place so uniformly and exhibits so peculiar a constant that there must be some fixed and definite law regulating the secretion, not only of the rows but also of the department of the individual cells.

That the proliferation is purposeful occurs evident. The purpose served is certainly the way made easier for the invading blood vessels which are passing onwards in the sacifice for luration. These appear as a rule to press up opposite the proliferating cells where the matrix is weakened, and thus besides the way being easier, the calcified matrix between the rows acts as directing trabeculae upon which the sacifice deport primarily take place.

That the formation of the rows must be influenced by the surroundings in plain, causes the department of the cells.

Let us consider what takes place with regard.
to cleavage. Numerous examples of this have been submitted and in these the line of cleavage is practically constant, transversely to being axial. There are some exceptions to this but these seem rather to strengthen the above statement than otherwise because the parallel or oblique clefts invariably occurred where the matrix had been weakened by the proliferation of the cells.

What does this mean? Evidently means that in the cartilaginous extremity there are planes along which it cleaves more readily than another direction. Now this being the case we may look upon it as composed somewhat like leaves of a book. The flat surface of the leaf looking towards the articulating surface. That is to say these are layers of planes in which the cartilage cleaves more readily.

That this must have its effect is obvious. The cells in the rows always assume the plane direction because elongated transversely. It is simply any intention to correct the coming of the cells with the cleaving of the cartilage, and suggest explanations.
Is it not possible that the cells elongate in the way of least resistance, or according to the effect of surrounding circumstances? Could the individual layers of the cartilage be easily separated from each other? Possibly the way of least resistance would be in the opposite direction. But we know that these layers do not separate in this proliferation.

As the formation of the cross the case is somewhat altered. Here we know there is evident absorptive of the matrix. Rutherford remarks: "It cannot be said that the absorptive of the cartilage matrix is entirely owing to the bloodvessels. It is in large measure due to the proliferation of the cartilage cells."

(Footnote, p. 104)

Hence there is destruction of matrix and this evidently occurs on the flat surface of what we have regarded as leaves of a book. Perhaps this surface may admit of being more readily absorbed than the other, or perhaps it may be on the side where the cells must require nourishment.

Where the proliferation of cells is not excessive
There is evidently formation of matrix, as well as de-
struction of the older matrix, well seen when some of the cartilage cells have dropped out of their capsules.

Around or rather just under the articular sur-
face, and indeed all around the articular ex-
trmity there is a dense arrangement of
cells with their long axis arranged parallel
with the long axis of the surface. This is prob-
able the result of pressure, which might ex-
plain both the number of cells and also the line of their axes.

So far the argument has dealt chiefly with
the primary changes in the ossific process.
These seem to be preparatory for the true
ossific deposit. This rest any intention
to enter more fully into the processes
than has been done in describing the
sections. They illustrate fairly well the
different stages not only in the formation
of the matrix but also of the Haversian
Canals and so forth. More especially
interesting is the series of bone growth
rabbits of different ages. The formation of bone in the vertebrae show very beautiful double staining. The preparations had been kept in Müller's fluid and to this the green colour of the bone is due.

The picro-Carmine has stained the cartilage a


As a source of the skeleton we may state those of the tail of foetal lamb. Vertebra of foetal rabbit shown.

Wheat at a certain stage the centres is not fully chondrified.

(c) That by and by it becomes so but that in a certain way and all matrix and no cells.

(d) That the primary change in concretion (so far as the cartilages is concerned) remained fixed in...
The centre, cell proliferation.
(1) That zones are to be distinguished in the section, with relation to cells.
(2) That calcification first occurs in the centre.
(3) That after ossification zones can generally be made out.

(4) Beautiful double staining of the organic deposit on cartilage: tetrachrome from the Mollenhoff and Von Kossa.
Stained hands and feet.

(5) Slow stages in ossification but especially lines of cleavage, and effects of staining reagents.

Groups of Rabbit Bones.

(6) Progressive stages in ossification: development of the cartilage cells.

Feet Bones.

(7) Apparently degeneration of whole layers of osteoblasts in the osteous matrix.

Ureteral Sections.

(8) Shows beautiful lacunae and canaliculi.
It is not within the scope of the present work to discuss fully the various pathological conditions of bone. It is the intention rather to deal with the pathological development of its and to refer briefly to the opposite condition viz. molecular destruction, because this if it does not give us an entire hypothesis to the building process, nevertheless aids in strengthening and confirming observations made with regard to the normal development, and when viewed along with the latter is an exceedingly interesting and instructive process.

It is always essential in the consideration of any subject to first study the normal appearances and trace the developmental Changes before proceeding with the pathological conditions, but if possible it is even more so in the case of bone. One is not long in perceiving that different appearances are assumed by bone in pathological development.

We may commence with the study of beautifully formed bone as for example in true osteo-tumours, but as we enter more deeply into the sub.ject, our ideas with regard to bone are almost necessarily modified and our perception stimulated.
We observe gradual stages in the development, until at last we come upon a tissue to which the term bone is applied and the conclusion justified by the possibility of having the transitional stages between it and well-formed bone.

Again, there is a structure which has long been noticed and described, a tissue resembling bone but to which the term bones could not be properly applied. We therefore call it osteoid. It frequently occurs in sarcomatosous tumours which are then designated osteoid sarcoma.

The normal development of bone is very peculiar, in many respects. It is very generally preceded by cartilage, the destiny of which has been explained to show in the former part of this thesis. Where it is not preceded by cartilage, it bursts out in membranes, well seen in the case of the seminal bone, and here several stages occur also in the bone, culturally ending in the formation of cartilage, canalis Ultra, etc. with all the characters of adult bone. The first appearance of the deposit is slightly different from the fully formed bone.

In the pathological development the building process may tend towards and be destroyed ultimately
to form, what can only at the best be designated as very imperfectly formed bone. Nevertheless, it is
true. As in nature, with regard to annuals, for example, we often come across imperfectly formed indi-
vidual specimens, while the fact of their being so does not preclude them from assuming the title of
the genus or species by which they are. But
imperfect representatives, so to the minute
study of osseous development, we cannot jus-
tifiably preclude imperfectly formed specimens
from the title of bone or osteo-
the characters of this imperfect formation may dif-
fer in different specimens, but if in a certain num-
ber they remain tolerably constant then
the term "types of osseous development" may
with all due propriety be adopted.
And of these we may have several.

The Formation of Bone in the Choroid

This seems to offer a very suitable introduction to
the study of this pathological development of bone.
The formation is often most complete in character,
both as regards the extent to which the Choroid
is ossified, and also as regards the quality of
the bone deposited. Even in cases where the
bone is well formed, we can often detect patches of tissue
Where the structure is not so complete and several degrees of the defect, so to speak, may be noticed in the same patch.

I have examined over a dozen preparations of this condition from a naked eye point of view, one clinically before removal, and of which sections were made as representing the microscopical characters of the series. There observed some cases in which the condition was one of complete calcification. The twelve preparations however showed beyond the shadow of a doubt their true non-caseous nature, prone in the form of beautiful cups. To be presently described, whilst others existed as plates at the posterior part of the eye near the entrance of the Optic nerve.

The cup formation will admit of a condensed description applicable to all

Naked eye description

The formation of bone is cup-like, one diameter known or being longer than the other (Wide photographs and dried preparation that is). There is a rounded aperture posteriorly for the Optic nerve. The bone occupies the position of the Choroid Iossa—rule more developed at internal part, and generally with the remains of
The choroid covering it in the shape of a dark reddish-brown layer with straight lines running in it evidently the bloodvessels or remains of them. The external surface is more or less indented but on the whole tolerably regular. Internal surface regular and comparatively smooth in most. Anteriorly it stops short at the ciliary processes and around the anterior border as well as some little distance behind this an external surface is a layer of dark coloured pigment.

Contents in every case examined appeared to be partly red material into which the optic nerve or its representative (wasted) could be traced. In the preparations preserved except the consistence of the contents was tough and greasy.

There was at deposit of bone in the position of the iris.

As above mentioned there were some cases in which the bone existed simply as a plate posteriorly. Minute perforations could be seen on the surface of the bone.

Clinically in looking over the history of these cases one finds
Seemed worthy of note, that the existence of the degeneration in the Choroid was a fertile source of sympathetic irritation. This was also the case with the one I observed clinically such is the naked eye description, and the appearances in the different preparations were so much alike that I think we may well take one case as representing the microscopic characters of the series. For this purpose I have selected the most recent one and the nature of the deposit is as follows:

I. Short History

A. M. female age 14. Eye had been atrophied from birth. Feel from even hand. Head periodic, Punetates for 2 months before admission. No history.

Never had any pain in atrophied eye.

II. Naked eye Appearance of deposit.

Beautiful cup of bone as above described.

III. Microscopic Character. Drawing I and II.

Decalcified in nitric and chromic fluid. Also photographs stained in Picro Cinnamic.

Mounted in Tannin. Sealed with Canada Balsam.

Send six sections for examination. All exhibit the character of beautifully developed bone.

L. P. (x 50) Bone matrix with secondary changes.
and canals filled with what are apparently cells, or chiefly so. Concentric arrangement of canals in Laeuncas somewhat numerous.

 Białe matki. The canals are in part arranged concentrically around the spaces and in part irregularly just as in normal lung.

The Laeuncas. These are plainly seen and within the loose corporules. The latter are distinctly spherical. The form of the laeuncas varies: some are more or less rounded, others spindle-shaped whilst others again are as mere lines. The corporules have the same shape as the laeuncas in which they lie. Minute branches stretch from the laeuncas, one from each end of the elongated one, but from the round they seem to pass off all around. In some places the elongated laeuncas predominate, whilst in others the rounded are more numerous. These latter are probably just transverse sections of the elongated.

The Spaces present a beautiful appearance. They contain numerous cells somewhat rounded and granular, resembling the cells of granulation tissue, lying between the cells. We observe a delicately fibrillated tissue. The whole appearance is fact...
very much like granulation tissue. Some cells are rather larger and of irregular shape. There are also sectors of what are probably bloodvessels. At another part filling up one of the spaces there is a much more dense tissue or fully formed fibrous tissue, and numerous large spindle cells, probably about to be transformed into fibres judging from the transitional stages to be seen. The cells are also granular.

In looking around the pieces of bony tissue it is very evident that the cells in the spaces become the bone corpuscles in the laminae because the different stages can be traced. The process appears essentially the same as in the normal development of bone, but I should like to point out one thing: the osteons another aspect seems to be deposited around the cells and in the tissue around them. The result being that the cells are rendered more or less in communication with one another, granting that the Capillaries in the tissue also become very crowded, as inevitably they must. Then there would be established a free anastomosis in the osteous matrix, which anastomosis in normal bone is represented by the Canaliculi stretching from the laminae.
Pagenethcher refers to a member of cases, described as formation of bone in the Choroid, along with a condition of the eye: Phtisis Oculi.

Some of the cases had distinctly the microscopic characters of true bone, in some instances lamellas in others the structure was somewhat indefinite.

Atlas Pathologische Anatomic der Augapfel.

Hir Ausgegeben von Dr. Herm. Pagenethcher. Ued. H. E. S.c.c.

Seite 81-916. lat. text.

All refers to the subject as follows:

"Besides acute parasitic matus Choroiditis which goes over to the chronic form, we sometimes observe a paracellular Chorioiditis which is from the beginning of a chronic character. This frequently leads to the deposition of lime in the paraeeye men of the choroid and to the formation of ossuous tissue. The formation of bone in the Choroid in the beginning usually takes place in its inner layers (Knopps).

Lectures on the Human Eye.

By Adolf Alt. 1880.

Pap. 122. 123.

I shall conclude the subject of Development of Bone in the Choroid by giving a review of the work.
From what has been stated we may gather:

1) That true bone is developed in the Chorioid.
2) That when far advanced it assumes the form of a caps perforated posteriorly for the Optic Nerve.
3) That stages may be seen in the development and that apparently the process is leading in some parts to the formation of but imperfect bone, whilst in the same eye, beautifully formed bone is seen, side by side with the former.
4) That the inner layers of the Chorioid are just involved.
5) That the formation stops short at the hair processes.
6) That clinically, although the presence of bone may not cause pain in the eye in which it exists, nevertheless, it is a fertile source of sympathetic irritation associated by inflammatory changes often occurring in the other eye.

7) That in some cases there is a condition of Calcification which may be mistaken for ossification but is quite different both in nature and microscopic characters.
From the consideration of bone developed as a normal structure, the Choroid, we pass to the study of bone developed in the form of a tumour.

A short history will be a fitting way of introducing this.

A man, 29 years old, a miner, admitted into the Edinburgh Royal Infirmary under Dr. Chirn, 28th June 1873.

Complaining of a tumour on front of left thigh.

About 2 months before admission he noticed about the size of the end of his thumb, on front of left thigh.

Cause. Eight months before admission, while he was at work he was struck on that part by a piece of coal falling down. As a result he had a swelling there. Had to leave work on account of pain. After rest, blisters, and so forth he went to work again but had to leave of 2 months before admission on account of pain from a second swelling, that of which he now complains. This increased slowly for 2 months but during the last month it had increased more rapidly.

Examination guided by sight and touch.

There is a swelling on the front of left thigh of a rounded shape longer than broad. The mark of a blister coincident on the skin. The swelling is glossy, hard, not moveable with a rough feeling. On extending and flexing the thigh a feeling of
Junction referred to opposite.

Represent relation of muscle, projecting lower end, and lower juxta. These are all coloured blue. The red represents the muscles.
Crepitus is elicited when the tumour is held firmly. The swelling is 3 inches long and 3 inches wide.

General state of health is good. Different x-rays examined systematically.

Treatment: Amputation was advised, but on July 14, Mr. Thiers operated as follows:

A longitudinal incision was made along the outer and anterior aspect of the thigh and 3 or 4 pieces of apparently non-tumorous tissue were removed.

The lower end of the femur was quite free and normal, but extending from the middle of the bone to within an inch or two of the superior extremity was a tumourous with its lower end projecting over the surface of the bone. This tumour was excised. Over the projection was a piece of casesous tissue once probably connected with it and now movable. This was the explanation of the crepitus. The projection, the loose piece over it, and two or three of the nodules were removed.

The wound was then dressed. It healed satisfactorily and patient was discharged on Aug. 7, 1883, with the wound healed, but a large hard swelling still on anterior aspect of left thigh. That then, in the history.
Microscope Examination of Tumour.

Re-examined as before.

Stained Pepsin Carmin. Mounted in Eucain.

m. P. x 350. Drawing II.

Exhibit. Characteristics of well formed bone. Lamellar of bone with lacunae, bearing apparently granular contents, beautifully red. The lacunae however appear very numerous. At one part an interlacing appearance of the bone tissue is seen. And in this the lacunae are in multitudes. The articulations are apparently due to lines crossing each other obliquely. (See opposite.)

Haversian Spaces well marked some filled others empty. The contents having probably been displaced during preparation.

m. P. x 350. Drawing II.

In the spaces there are two kinds of cells (a) spindle shaped the ends of the spindle being very sharp.

(b) somewhat rounded cells which evidently lie close the bone corpuscles. The spaces are large. In some places the tissue adjoining the perfectly formed bone, has a peculiar refraction, apparently indicating a stage in the bone formation. Fibrous tissue
is observed attached to the base and in some of
this numerous bloodvessels are seen filled
with Corporcles.
The laceras appear somewhat numerous.

I have referred to the history of this case somewhat
more fully than the others because it seems to
show the following points:

1. That the starting point of the man's complaint
was an injury which was an irritant to the
point of the thay at the penetration, or per
aza perforation and bone suffering.
2. That as a result of the irritation a tumour
formed.
3. That in consequence of the connection with
bone the tumour assumed the characteristics
of bone.
4. That after a period of rest with some local
applications the man went back to his work
comparatively free from pain.
5. That evidently a part of the tumour got
detached and as a result more pain was experienced.
6. That the detached piece of the tumour set
up more irritation, which was inevitably
Insufficient in kind from the eyeballs during walking. Consequently the tumour increased more rapidly than it had ever done before. (7) Microscopically it has been observed that the lacunae are apparently somewhat more numerous than in normal bone, and also those in some parts an apparently trabecular tissue in the bone formation can be seen.

**Destruction of Bone**

**Drawings M.W. Q.V.P**

Molecular destructive process

Having considered the formation of bone in the Choroid, and the tumour just described, as types of the pathological formation of true and well developed bone, references will now be made, and that but briefly, to the molecular destruction of bone.

In the normal development we have seen that the cells (osteoblasts) lining the Haversian spaces are at first not surrounded by osteous matrix but gradually because to the matrix being formed secondly. Now in the destruction of it, it appears to use from observations made that exactly the opposite process occurs. The
matrix is first destroyed and thus the cells are liberated, but these on liberation may be either disintegrated, or in fairly good condition. These latter again may be cleared to become disintegrated in the discharge, or they may be seeded in the discharge in a fairly well sustained condition. I speak more especially with regard to Caries but it appears manifest that the matrix must generally in all cases of disintegration processes be acted upon first (1) because it surrounds the Cartilages (2) because the Cartilages are the usual constituents of the bone.

There observed a case where there was evident destruction of bone and its place apparently taken to a great extent by fat. This was on the leg of the Stark Delineic of which I spoke along with the other. Another point appears worthy of noting in these sections and it is this. There is evidently "excessive proliferation" of the cartilage cells in the epiphyseal layer of Cartilage.
case of "proliferation of cells" with a destructive process going on in the remaining tissue, not only destruction of the bone but destruction of the articular cartilage as evidenced in naked eye examination.

It might be well here to bear in mind in this connection the "proliferation" of the cartilage cells in normal ossification taking place where destruction of the cartilage matrix was occurring, from the invading blood vessels which play such an important part in the actual ossific deposit.

No. 66. Caries of Os Cuneis. Drawing IV
Piero Carminio. 23. 3. 83. Ferrant
Illustrated beautifully destruction of bone, the cells becoming liberated as the matrix is destroyed.

No. 67. (Piero Carminio). 68. 69. (John Green)
Sections from leg of a child in which there was evident destruction of cartilage (naked eye). Moreover, especially it shows destruction of bone and ad. joining this, proliferation (excessive) of cells in chondro- and cartilage. (Proliferation & Nutrition side by side)

Drawings 50. P.
Series of Osteo-Sarcomatous tumours.

These are an example of bone developed neither in a normal structure, nor in the shape of an osteous tumour, but developed in a tumour and that of a sarcomatous nature.

The sections illustrate in a tolerably complete series the various types assumed by the specific growth in sarcomatous tumours. Here and there throughout the sections there are patches of well formed bone with saecue as before.

As a rule, however, there is not quite so perfectly formed bone as we have hitherto been considering. Never the less there is an approximation hereto, and in some of the best worked examples, one is almost inclined to say, that the structure of it does not exactly correspond to that of normal bone, exhibits a difference as slight as to be almost imperceptible.

In all, there is the upward tendency to form bone, upward because bone is undoubtedly a highly developed structure.

It is the intention to treat of these tumours some what briefly, because the appearances are so beautifully marked, a glance at the whole will make the import apparent, treating the evil.
yet in this way it is of the highest importance that any meaning should be plain and unequivocal. The points to be noted may be summarised as follows:—

It appears to me (1) that these tumours belong to the Class Sarcomata.

(2) That they arise in connexion with the periosteum or perimetrium of bone.

(3) That in them there is osseous development and are hence termed Osteo Sarcomata.

(4) That type of the Osseous development may be formulated.

(5) That stages in the formation of the types can be traced.

(6) That in all these is the upward tendency to form bone but that while some go on to form tolerably perfect bone, others abort at that and form but imperfect bone.

(7) That some parts appear to be cartilaginous and to exhibit Change tending to the formation of bone.

(8) That in some places, particles of calcification (croupy) are seen apart altogether from the formation of bone.

I have used the term type, and by that I mean
"The relative arrangement of matrix & cells."—

The matrix seems to exhibit two chief characteristics, as regards kind.

1. It may be primarily homogeneous. This homogeneous appearance becoming altered as development goes on.

2. It may be fibrillar in a primary sense. This appearance also becoming altered as development proceeds.

Again it may be arranged in at least two ways, both the homogeneous and the fibrillar form.

1. The homogeneous may be arranged more densely, or rather in greater amount, relatively to the cells, and from this, as a center, radiate outwards among the cells.

2. It may be arranged pretty equally among the cells.

The same holds good with regard to the fibrillar substituting fibrillar for homogeneous.

We have thus at once four well marked types in the osseous formation.

The patches of well formed Bone seen in some of the sections should I think be regarded
as a well developed stage of one or other of the different types.

Some of the types are better marked in some parts than others. These afford examples of stages in the development of the types.

I feel unwilling to enter into a more minute division as regards types. That such is possible I doubt not. It seems preparable however to point out the more evident and well marked ones which are a subject of easy demonstration. Such are the four types tabulated as under.

1. Matrix homogeneus, radiating from a centre. (Graduating from a centri.)
   - But may be slightly attacked, e.g. from calcification.
   - Generally diffused, maybealked.

2. Matrix fibrocellar, (Graduating from a centri.)
   - Generally diffused

In every from the homogeneous or fibrocellar nature is primary and aparents became altered during the upward developing process.
The individual sections will now be briefly considered.

In describing these the following points require to be studied:

(1) Condition of Matrix
(2) Condition of Cells
(3) Relative arrangement of cells and matrix

Drawings 2 4 5 9 7

It is worthy of note that all these tumours had been preserved for a long time in spirit for a long time before the sections were made, in some cases as long as 20 or 30 yrs. They were in fact museum preparations (inked eye). Still the microscopical appearance is very well brought out. Of 40 other tumours which I examined at the same time, all had been kept an equally long time in spirit and all exhibited well marked characteristic appearances. This is a useful fact where the nature of any museum preparation may from any cause be obscure. The cells are certainly some what granular but the characteristic structure in all the cases have been were well preserved.
Section (262. Museum Number) No. 70 Series Number
Osseous Sarcoma

Stained with Pico Carmin.

Mount: Farrant. 23/2/83.

Matrix homogeneous becoming calcareous. Cells granular of a yellowish colour, some small rounded, others larger. There is a tendency to the formation of fibres (fibroblasts) Calcareous patches seen here and there.

It seems part of the periosteal development.

Types: At least one type is well marked in this portion. Most or less homogeneous matrix as a centre and radiating thence among the cells.

(W. 255) No. 71
Osseous Sarcoma. From Femur.

Stained with Pico Carmin.

Matrix: (1) Arranged more at one part and radiating among the cells.
(2) Arranged pretty generally among all.
(a) Homogeneous. (b) Slightly altered and radiating from a dense centre among the cells. (c) In some parts the matrix is pretty generally arranged among the cells without much appearance of radiating from a centre.

Pretty well-formed bone at one place.

Cells: These vary somewhat in form and size. Many are comparatively small and rounded, others are larger and spindle-shaped. They are granular, and most are yellowish with the nucleous indistinct. In some the nucleous is stained deeply purple with dark pigment observed over the field here and there.

Types: From above description several are evident.

(N° 134) No. 12

Osce. Sarcoma.

Stained with Eosin-Pernic acid. 16/2/83.

Here again more than one type can be made
Matrix. Homogeneous, at some places, and at
other parts and occurs pretty generally diffused.

Cells
Yellowish, granular, mostly small rounded.

Other sections further illustrate the various
types and will be very briefly referred to.

(N° 88)
Desz. Sarcina.

Picro. Carmine.

Larrant. 2/3/83.

Matrix. (a) Homogeneous
(b) Fibillary
Calcification at some parts.
There is also the appearance of cartilage,
becoming altered in the upward process.
Cells. Nuclei of many stained hem.
Tupilly Carmine.

(N° 253)  (N° 74)
22/1/83. Matrix. (a) Homogeneous.
(2) Fibres, which shoot out very prettily much after the manner of the Panetal bone in the child. Cells: yellowish altered.

(N° 257)  
Osteoid Sarcoma. From Leg.  
This case so well marked as the others and may be termed osteoid.

(N° 271)  
Osteo Sarcoma. From Femur.  
Exceedingly well marked specimen. In some parts simple calcification so obliterated but in others the stage and type or at least some of them are very well shown.

(N° 44)  
In this there is a change in the surrounding nodules.
to the osseific formation, in some places freely marks, but in others well.

No. 78.
Section of left isch of Os sacrum from which it's
proecing tumour arose.
Per. Cormine. Terrault 16.1.84.
The bone appears widened as to its spaces
the surface of the trabeculae however
remaining tolerably smooth.
The sacrum are well shown.

No. 258.
Osteosarcoma from leg.
Further illustration of appearances already
described.

I have had ample opportunity of studying the various
diseased conditions of bone during the last winter
session when I had charge of Prof. Cheesie's private
surgical museum. I have thought it well however
Not to enter particularly into these conditions, except very briefly molecular destructive schemes. It is thus that I have adhered closely to the development and considered that both in its physiological and pathological aspects.

David Lindsey
1887
Drawings
1826
[Signature]
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Drawing A.
T.S. Tail of foetal lamb (Section No.1.)
L.P. x 50.
To show especially
1) Central area composed almost entirely of hyaline matrix, no cells.
Corresponding to position occupied by the Chorda dorsalis.

2) The space immediately outside the central in which the cells are proliferating rapidly.
13

Represents the preceding section 1) under HP. x 350

1) Central Area.
   Hyaline matrix

2) Proliferating zone immediately outside the central.
C. Section No. 4.

T.S. Tail of foetal lamb. × 50. Picrocarmine

To show the calcareous deposit occurring first near the centre.

(a) Calcareous deposit (Cartilage & Matrix)
(b) Enlarged cells in process of dividing
(c) Perichondrium
T.S. Tail of fetal lamb. (Section 3). X50.

True osteous deposit (green) on the calcified cartilaginous trabeculae (pink). Certain zones can be made out respectively from centre 1, 2, 3, 4.

(a) Cartilage not yet calcified (as is matrix)
(b) Cartilage matrix calcified
(c) True osteous deposit in which are seen the lacunae
(d) Calcified cartilage trabeculae on which the osteous deposit has occurred.

E. E. Bands of osteous tissue connecting Zone 2 with Zone 4.

5. Periosteum

Zone 1. Central Cellular
2. Osteous deposit on trabeculae (calcified)
3. Cellular
4. Somewhat irregular osteous deposit on calcified trabeculae.
Section of foetal foot (tarsal and inter-tarsal bones) flat from heel to toes. Carmine. x 50.

(a) Periosteum

(b) Tarsal bone (Calcaneus)

(c) Longitudinal section of blood vessels issuing from the periosteum

(d) Transverse section of blood vessels

(e) Metatarsal bone?

(f) Tarsus, inter-tarsal articulation

(g) Articulation between two tarsal bones?
Section of foetal long bone, L.P. x

(a) Periosteum

(b) Bone deposited under the periosteum and extending towards either extremity

C. a. Cartilage cells proliferating in rows about ossific point

d. Transverse section of ossified belt
C

T. S. of Articular Extremitv. affected long bone
where ossification is proceeding, and where the
bone forming in the shaft is prolonged for some little
way into the Cartilages. X 350

a. Cartilage cells mostly branched axis transversely
b. Cartilage cells axis changing direction

c. Cartilage cells along and parallel with surface.

d. Cartilage cells apparently becoming bone

Capsules.

e. Cells derived from the periosteum

f. Cellular layer of periosteum

9. Outer layer of periosteum

d. Cells prolonged up from the periosteum

H. T. S. Mithrid's bone. Periosteum. X 600

Vide Section (48 & 49)

a. Layer of osteoblasts

b. Large cell apparently formed of several cells

c. Osteon Matrix

d. Apparently whole layer of osteoblasts wanted.

f. Lamina with bone corpuscle.
Formation of bone in the Choroid.

I. x 50.

Shows the structure of true bone.

Osteo-sarcoma with lacunae containing bone corpuscles.

Cartilaginous plates

Canals filled with cells, etc.

Formation of bone in the Choroid.

x 350.

Shows structure of true bone.

Vide sections in eye.
Formation of bone in the Choroid.
Photographs showing two views of an osseous cup which developed in the Choroid.
The aperture for the Optic Nerve is plainly seen.
Section of Osseous tumor which developed in part of thigh.
Curie referred to in thesis.

50. Stained with Feiss Carminic
(a) Haversian Canal, filled with Cells etc.
(b) Cells etc. filling Space in the bone trabeculae.
(c) Osseous matrix with Carminic.
7

Section of same as preceding

× 350.

(a) Lamina with bone marrow contained in it
(b) Ossuous matrix
(c) Cells etc filling space
(d) Layer of osteoblasts.
Mr.

Relatious Degeneration

Piero Carmine

siving small fragments of several times

lying amongst cellular matters.
N

Caries of Os. Calcis Lr. (Sept. 66)

@ Piece of bone lying amongst cellular material
the bone is friable becoming liberated
Section (Longitudinal) was where there was destruction of bone (its place apparently taken by fat) also of the articular cartilage. In the epiphysyal layer of cartilage there was evidently excessive proliferation of cells.

(a) Fatty material
(b) Excessive proliferation of cells in (c) the epiphysyal cartilage.
P.

2. Section from preceding case. × 350.

Showing a piece of osseous tissue lying among cellular matter in which fat cells with crystals can be seen.

(a) Osseous matrix containing the bone corpuscles stained deeply carmine.

(b) Fat crystals.

(c) Small deeply stained cells probably chiefly the liberated bone corpuscles.
2.

Fibro Sarcoma. Piero Carminio. £350.

Examining the osseous material after doing away with the cells.

Matrix tolerably homogeneous, stained pink and arranged pretty regularly among the cells, (b) the nuclei of which are deeply stained Carminio.

Vite Pietro, B.D. (Museum London)
R.

Data: Specimen

Protein: Pero Carmine

Methods: H. & E. Objective

The matrix stained pink slightly homogeneous and seems to radiate from a centre among the cells which are stained yellow.
Petro-Sarcoa. Picro-Carmine x 350
Matrix pink, arranged pretty regularly among the cells, most part of which is yellowish but central deeply stained Carmine.
Tadpole sarcina from Sepulva.
Stained with Paro Carmine + 350
A pinkish material resembling a
ossuous deposit is seen stretching
among the cells which are stained
yellow.