-:C Y C L I T I S:-

A STUDY OF THE INFLAMMATORY EXUDATE INTO THE VITREOUS BODY IN CASES OF CYCLITIS

by

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-:I N T R O D U C T I O N:-

Several considerations have induced the writer to spend much time upon the investigation of the inflammatory exudates into the eye, and into the vitreous body of it in particular.

Although the cornea has been for many years now a favourite ground whereupon histologists have experimented and investigated the phenomena of inflammation, comparatively little work has been done in regard to the changes to be seen in the vitreous body in the process of Cyclitis.

OBJECTS OF THIS RESEARCH.

Looking at this subject, however, primarily from a histological standpoint, it appeared that, in the vitreous body, an opportunity is obtained of observing the inflammatory exudate in an unaltered state and of seeing what its powers and objects are.

In particular, the writer has been anxious to ascertain whether or not the process of cell proliferation termed "Karyokinesis" occurs with any degree of frequency in acute inflammatory processes, and, also, whether or not the proliferation of the fixed cells of a part is necessary for the successful cicatrisation of an exudate.

Looking at the subject, in the second place, from a clinical point of view it appeared that a study of the process, in various stages, should enable a more accurate diagnosis and prognosis to be made, as giving a clearer understanding of the true nature of the changes which are going on in the interior of an eye.

These subjects appeared to be susceptible of more accurate investigation in the case of the exudate into the vitreous body than elsewhere, for several reasons.

(I) The tissue into which the exudate is poured is perfectly transparent, so that any exudate formed may be readily examined.
(2) The adult vitreous body contains no fixed cells in the normal state, or, at all events, so few that they may be discounted, so that if any cell matter is seen, it may be accepted that it has migrated into its present position.
(3) The tissues are easily prepared, and, what is of greater importance, may be obtained perfectly fresh.
(4) The tissues may be obtained at various stages of the process, and from cases in which the eyes have been removed on account of changes the result of closely similar causes.

Setting out, then, with these objects in view the writer has, during the past four years, investigated many cases of Cyclitis obtained in the course of his work at the Eye Infirmary.

Having, then, stated the object of this enquiry, before going more deeply into the subject, it has been considered advisable to sketch, briefly, the clinical history of an imaginary typical case of Cyclitis, and to follow out its pathological and histological characters in a similar manner, in order that the nature of the process may be more clearly comprehended by all.

CLINICAL HISTORY OF CYCLITIS.

Let it be supposed that a chip of metal enters an eye, close to the margin of the cornea, and passes backwards through the base of the iris into the vitreous body, in which it becomes lodged.

The eye, if not too seriously damaged by shock, speedily shows signs of the presence of an irritant, by its reaction. The conjunctiva

becomes injected and the scleral vessels become tortuous. Irritability to light, photophobia and lachrymation soon become evident. Pain is early present, due, probably, to various causes such as the movements of the eye and eyelids, irritating the fresh wound, or to the actual presence of a sharp substance in the eyeball. Deep ciliary injection soon appears, even as early as the twenty fourth hour.

The wound has probably closed by this time, but is not firmly healed for many days.

The tension of the globe becomes increased, and pain is more marked, especially at night, and is accompanied by great tenderness of the eye. The pain is markedly circumorbital in character, and is difficult to alleviate. The aqueous humour is turbid.

At a variable time, from the fourth to the eighth day, if the media are clear enough to allow it, a yellowish reflex is seen behind the lens. The anterior chamber, which is at first shallow, soon becomes deep and ultimately deeper than is normal. The tension of the globe is now stationary or tending to fall and will soon become subnormal. The pain, at this stage, is almost entirely gone. Pressure on the eyeball, however, brings out the fact that the ciliary region is very tender at some spot, and this, with the presence of engorged vessels in the scleral group, indicates that the eye is in great danger of becoming atrophic.

The tension of the eye continues to diminish slowly, and, owing to the pressure of the four rectus muscles, the eyeball comes to assume a somewhat square aspect. This, in turn, is followed by diminution in the bulk of the eye, and depression of the cicatrix of the original

wound.

The eye is now in the condition which is termed Phthisis Bulbi, and the whole process has occupied perhaps three months.

PATHOLOGICAL REVIEW OF CYCLITIS.

The course of events, then, in this eye which has led to such complete destruction is somewhat as follows.

Owing to the presence of an irritant in the eye great increase of vascularity has taken place, with formation of an exudate consisting of cell elements in a coagulable fluid.

The parts directly injured are united by this exudate. Thus the iris is adherent to the corneal wound, owing to the presence at both the posterior surface of the cornea and the anterior surface of the iris, of an organic substance which, it may be assumed with fair accuracy, is adhesive. The whole uveal tract, iris, ciliary body and chorioid, becomes congested and gives rise to an exudate of similar characters to that in the anterior chambers. This exudate soon begins to undergo changes, termed for convenience "formative," and what was a semi-fluid substance becomes a solid, which is, for a period continually becoming less in bulk, (cicatricial contraction) so that the parts to which the exudate is adherent are drawn together. (Fig. (1).

Thus the exudate which has been formed behind the lens, is adherent all round its periphery to the ciliary body, and, by its contraction, first draws the lens backwards and then pushes it forwards; but at the same time, being adherent to the ciliary body, it draws this centrally and separates its posterior part from the sclera, drawing forwards, in doing so, both retina and chorioid.

Again, the vitreous body having been permeated by this self-contracting fluid, shrinks towards its points of most firm attachment, namely, the lens and ciliary body, and ultimately disappears more or less completely. The contraction of the vitreous body is, most frequently, soon followed by separation of the retina, its support being withdrawn, and it is frequently the case that the retina is firmly adherent to, and involved in, the mass of cicatricial tissue which has been slowly accumulating behind the ciliary body and lens.

During this period, haemorrhages from the displaced bloodvessels in the retina and elsewhere may take place, and may more or less completely mask the appearances.

Lastly, whilst the above mentioned changes have been going on, instertitial formation of exudate, results, by contraction, in the destruction of the delicate structures and diminution of vascularity, and thus the stage of diminished intraocular tension is arrived at, and is closely followed by shrinkage of the globe.

As would naturally be expected, it becomes very evident, at an early stage in the investigation of this subject, that there is a very wide degree of difference in various cases, as regards the date of the different stages of the process, after receipt of injury. It may be explained, here, that it was, in the majority of cases Cyclitis of traumatic origin which came under observation, as Cyclitis of other origin does not often give cause for removal of an eye until a late stage has been attained.

The diversity above mentioned has been attributed to variations of the intensity of the irritant on the one hand, and of the resistive

power of the tissues on the other.

To these same causes was attributed a certain variation in the histological characteristics of the process which was also noticed early in the investigation.

So well marked, indeed, was this difference that the writer was at first inclined to divide the inflammatory processes seen into classes which depended for their distinctions on histological characteristics. Subsequent investigation of the subject, however, has led to the conclusion that, as many cases partake of the characters of different types, such a differentiation would be likely to lead to confusion rather than elucidation of the subject. Each case seems to have its own characteristics as regards cell elements, fibrous tissue, etc., almost entirely independent of the date of onset of symptoms, but few being met with which were quite typical of one particular class.

Hence the subject has been dealt with as a whole, as an average of cases seen, and where deemed necessary, special changes have been treated as such, and indication of the stage of the process at which they are likely to occur, has been given.

HISTOLOGICAL CHANGES.

Turning now to the investigation of the histological changes seen in such an eye as that under consideration, it is to be noticed that it is extremely rarely that an eye is removed at an earlier date than the eighth day after the receipt of injury, as the loss of such an eye cannot well be certain before this time. Hence, the earliest changes can only rarely be seen in the human subject. Of course many

eyes are removed within two or three days of the date of injury, but, as a rule, such eyes are so seriously damaged that the reparative process is delayed.

During the course of some work, however, for a different purpose, opportunity of examining the eyes of animals in an early stage of Cyclitis presented itself, and in this way it has been possible to make comparatively satisfactory observations on this subject.

CHANGES IN AN EARLY STAGE OF CYCLITIS.

The earliest recognisable change, then, is, as would be expected, dilation of the vessels of the uveal tract within the sphere of influence of the irritant, whatever it may be. This may be seen to take place within twelve hours of the injury. A few hours later, multinuclear cells may be seen on the surface of the ciliary body and the iris, and lying in the angle of the anterior chamber.

The origin of these cells is, doubtless, vascular, their appearance on the surface being the result of opening up of natural channels in the epithelial covering.

The exudation being liberated at all points from what may be considered a free surface into a fluid or semifluid medium, much of it is at first carried away by the natural circulation of fluids in the eye, and passing through the pupil goes to form a more or less fluid mass which accumulates in the anterior chamber as hypopyon.

HYPOPYON.

This is found to consist of multinuclear cells, finely granular leucocytes, in a medium which is fluid but coagulable.

The coagulum formed is composed of a dense network of delicate

fibrillae, which join at varying angles, and very frequently have small globules at the points of junction. In this fibrinous network the cells are caught and detained. The degree of fluidity of the hypopyon seems to depend largely upon the proportion of cells to fibrin, the more cellular exudates being more fluid.

From its situation in the angle of the anterior chamber the hypopyon is quickly removed, so far as can be seen, by breaking down of the fibrinous network, and by either breaking up of the cells or by their escape by passage through the spaces of Fontana into the canal of Schlemm, and thence into the circulation.

In the posterior chamber, however, the exudate which remains there is not so readily disposed of, and much of it may remain and generally does so, to become organised.

Further back along the ciliary body, where the exudate formed passes into the space in which the fibres of the lens ligament lie, the tendency to organisation is even greater, and it is here that the first formed fibrous tissue is usually found even as early as the eighth day of the process.

The cells liberated from the pars ciliaris retinae pass with the natural current into the vitreous body, along its anterior part to-wards the posterior pole of the lens, in a backward direction deeper into the substance of the vitreous itself or in a backward and outward direction along the anterior part of the retina.

In this way, a more or less dense white cloud is formed in the anterior part of the vitreous body, which increases both in size and in density as the process of cell migration advances.

Attention has been called above to the fact that as early as the eighth day, it is seen that fibrous tissue is developed in close approximation to the ciliary body and from the exudation itself. This process of fibrous transformation continues to advance throughout the whole course of the affection and extends in all directions in which the exudate is being formed. The process of fibrous transformation is regarded as of high importance and will be considered further at a later stage.

CELL MIGRATION FROM THE CILIARY BODY.

It has been seen that cellular exudate is found in the vitreous body, then, and it must be shown that these cells do really migrate into the positions in which they are found, that is, to show that they are not produced by proliferation of fixed cells in the vitreous body.

THE VITREOUS BODY.

The writer's experience of the examination of the histological structure of the vitreous body has been fairly extensive, including as it has the vitreous of man at various ages from three months upwards, that of the ox, sheep, pig, dog, cat, frog and some varieties of birds and fishes. Further, several different means of fixation of tissues have been used, such as formaline in fluid and vapour which is the quickest, osmic and chromic acids, perchloride of mercury, Müller's fluid, alcohol and freezing (in ice and salt.)

The only means which has been found reliable as demonstrating the existence of any structure in the vitreous body are alcohol (70%) and freezing.

The only structure shown by even these last methods was only distinguishable as a microscopic object, and consisted of the existence of indefinite septa which seemed to pass in a radial direction from the centre towards the anterior, and, to a less distinct degree, towards the posterior part of the jelly-like substance.

A distinct central canal was never seen, nor has the existence of fixed cells been demonstrated, although staining, by different stains in varying strengths and exposures to them, has been resorted to.

The statements regarding the passage of exudate from the ciliary body into the central canal made by MacGillivray (No. 15) have not been verified, although the subject has been carefully investigated. According to the writer's experience, when the exudate seems to take the form of a cone whose apex is at the optic nerve entrance, this fact is due to shrinkage of the whole vitreous body to this shape, which considering the connections of this latter, is a natural one.

Taking it for granted then that, if there are any fixed cells in the vitreous body, they are extremely difficult to demonstrate, it may be assumed that if cells are found in any considerable quantity in this situation, they have gained entrance to it from the exterior.

As will be seen later, however, there are not only large numbers of cells found in the vitreous body, but also several varieties of cells. Hence, this assumed migration of cells must be accepted as an element in the inflammatory process.

THE ORIGIN OF THE CELLS.

The next subject for investigation, then, must be the origin of the cells which are found in the vitreous body in cases of Cyclitis.

It has been shown above that in the very early stage of Cyclitis multinuclear cells were found lying, in considerable numbers often, upon the surface of the ciliary body. Similar cells are found in the sulci between the ciliary processes, on the posterior and anterior surfaces of the iris, and in the anterior chamber.

It may with fair reason be assumed that all the cells thus found, have a common origin so far as the nature of the origin is concerned. By this is to be understood that, being the result of a single cause, these cells are either the result of migration from from bloodvessels, of proliferation of fixed cells or of both these processes combined, and not, each according to its situation when first seen, the result of some special method of production.

It may here be mentioned that the endothelial cells on Descemets' membrane show no signs of proliferation in, at all events, the early stages of Cyclitis. (Note) This subject will be alluded to more fully later on.

LOCAL OR HAEMIC ORIGIN.

Two views only require to be considered in regard to the origin of the migrating cells.

(I) That which supposes that they are of local origin, derived from the proliferation of fixed cells in any situation near the site of appearance, and,

(2) That which supposes that they are derived from the blood vessels, by migration.

At the beginning of the investigation the writer was inclined to the opinion that a large proportion of the leucocytes found were

the direct result of the proliferation of the endothelium covering the ciliary body, and more especially of the non-pigmented internal layer of the pars ciliaris retinae..

Further investigation of the subject, however, induced him to abandon this view in favor of the haemic origin of the cells.

The reasons which seemed to point to the local origin of the cells were as follows.

(I) Whilst, as is seen in the photographs of bleached sections of the ciliary region, large numbers of cells were accumulated on the surface of the endothelium and many were seen lying between, and often apparently, in the endothelial cells, but few were to be found outside this layer of non-pigmented cells or in the interstices of the pigmented layer..

(2) Whilst the non-pigmented layer was frequently found to be much broken up, it was very rarely found that, except in advanced cases, the pigmented layer was much disturbed.

(3) There was rarely seen any distinct accumulation of cells round or near the blood vessels in the ciliary body, such as is seen in other situations as the conjunctiva, the retina,etc., when cells of haemic origin are migrating from the vessels.

The reasons which, on the other hand, point to the haemic origin of the cells, and which weighed more heavily than the preceding, were as follows.

(I) The nuclei of the cells composing the non-pigmented layer were only very rarely seen in a state of active proliferation, although, as above seen, leucocytes were found in abundance in the interstices

of the layer and close to the nuclei of the endothelial cells.

(2) Large number of leucocytes were found in the interior of the vitreous, which contained pigment granules, and, also, pigment granules were found free internal to the pigmented layer, indicating apparently that the leucocytes had to some extent broken up the pigmented layer in forcing a passage through it..

(3) The accumulation of leucocytes on the surface of the ciliary body and between the cells of the epithelium, might be the result of delay in transference of the cells through the layer of fibrous tissue, which is early formed on the surface of the ciliary body.

(4) It is seen that, in other situations, where there is a discharge of leucocytes from an epithelial surface, the cells composing the epithelial layer are rarely found in a state of proliferation, even though large numbers of leucocytes may be escaping through its interstices to the surface, so that it is quite invalid to assume that those escaping leucocytes are of local origin.

(5) Lastly, whilst it is admitted that endothelial and epithelial cells do frequently proliferate and give rise to cells which are multinuclear leucocytes, when such proliferation is going on it is a very manifest change and can easily be recognised.

In the case, for instance, of the proliferation of the endothelium on Descemet's membrane, as has been so ably demonstrated in recent years by Dr. Reid, the change in the cells is a very manifest one.

Now, as we have seen, this is not so in the case of the ciliary body, in the early stages. Hence it may be concluded that the large majority of the leucocytes found on the surface of the ciliary body are of haemic origin and have escaped from the vessels in the ciliary

body, which, in point of fact, are usually found to contain such leucocytes in large numbers, and have migrated into their new position.

This migration is probably accelerated or facilitated by the existence of perforations in the membrane of Bruch in this situation, as can be demonstrated microscopically.

VARIOUS KINDS OF CELLS.

It has been seen above that there are in the early stages of the Cyclitic exudate, multinuclear cells of various origin, but there are also cells which present different appearances. These first appear about the seventh day and are large mononuclear leucocytes of oval or irregular shape. They are much less numerous than the multinuclear variety. They may be found lying in the spaces, which are usually distended (by oedema) between the layers of the pars ciliaris retinae, and even outside the pigmented layer close to the hyaline membrane of Bruch.

No single origin can be definitely assigned to these cells, as they may be seen in the blood vessels in the ciliary body and, also, in close relationship with fixed cells in the stroma of the ciliary body which are manifestly in a state of active proliferation.

It is probably the case that they are of dual origin, as the fixed cells of the ciliary body do proliferate, even at a comparatively early stage in the inflammatory process.

Whatever may be their origin, however, they have been closely associated with the change from the fibrinous state to the fibrous condition of the exudate, as will be seen when discussing the individual cell elements.

FIBROSIS OF THE EXUDATE AND ITS CONSEQUENCES.

As above noted fibrous transformation or fibrosis of the exudate begins on the surface of the ciliary body at a comparatively early stage, but it does not interfere, to any great extent at least, with the continuance of the accumulation of cells in the vitreous body.

This fact is due to several considerations, the most important of which are as follows.

(1) The area of exudation surface tends to increase at a greater pace than does the advance of fibrosis.

(2) The fibrous membrane becomes vascular and in this way participates in the formation of the exudate.

(3) The cells composing the exudate themselves proliferate and thus assist in the formation of new exudate.

As these facts are of considerable importance in connection with the histological process which is going on, they may be looked into more fully here.

RAPIDITY OF EXTENSION OF AREA OF EXUDATION.

As there is a free surface, as it may be considered, all round the ciliary body, and as there are currents in the vitreous body which convey in various directions the fluids which enter it, if an irritant capable of diffusion enters and causes inflammatory disturbance in the vitreous body, its action will not long remain local.

The extension of the area of irritation and exudation, then, depends upon the currents from the ciliary body and in the vitreous body. If, in the early stages, the ciliary body is only in part in-

fluenced, the distribution of the irritant will soon set up irritation in other parts, until not only the whole of the ciliary body and iris, but even the anterior part of the retina will participate in the inflammatory process. The endothelial lining on the membrane of Jacob is seen to proliferate, sending off large epithelial cells into the vitreous body or into the space which frequently exists between them.

But the retina itself may be affected, leucocytes may be seen leaving the engorged vessels in the fibrous layer and accumulating around them in groups and ultimately passing out into the vitreous or into the fluid behind it, if it be shrivelled.

Thus, there is a greatly extended area of exudation even at a comparatively early stage in the process, and at a period when the process of fibrosis is confined to the surface of the ciliary body and along the fibres of the lens ligament.

FORMATION OF BLOODVESSELS IN THE EXUDATE.

This second consideration is of great importance and interest in so far as it gives an instance of the powers of new formation of bloodvessels, which seem to follow an exudate through an almost unbroken endothelial membrane.

The means by which this new formation of bloodvessels takes place is not clear. That there are normally, minute apertures in the membrane of Bruch at its anterior part, through which, in the first instance, cells of haemic and other origin may pass, and, in the second, through which blood vessel loops may be protruded from the distended

vessels in the vascular layer of the ciliary body, can hardly be denied.

Such solutions of continuity can be seen microscopically, and through them it may be that the glands of the ciliary body protrude outwards as the photograph shows.

Capillary loops may surround the base of these glands or may not (the writer has not been able to demonstrate this) but, at all events, it is probable that, with the demand for an increase of nourishment in the vitreous body, capillary loops developed from the ciliary body pass out at an early stage into the vitreous chamber and take part in the formation of new exudate.

The presence of bloodvessels in the fibrous layer at an early stage, say the tenth day, can easily be demonstrated, but in later stages the vessels are of large size and are present in large numbers, penetrating, often, to a considerable depth into the vitreous exudate. From these new formed bloodvessels cells can be seen to migrate in considerable numbers thus assisting the formation of the exudate in the vitreous body.

In later stages, as will be seen, the vessels play an important part in the removal of the exudate.

CELL PROLIFERATION IN THE EXUDATE.

This, last mentioned consideration, is the activity of the cells which compose the exudate, both fibrinous and fibrous, in dividing, often with what may be considered to be almost violent rapidity, and sending off a progeny which passes forwards and, ultimately, like its parent, will proliferate.

The proliferation of the cells which form the exudate is a very

large and important element in the production of new cell matter, and is by no means confined to one set of cells.

Before going on to describe the means by which this proliferation takes place, however, a few words may be said regarding the condition of the eye when the exudate into the vitreous body is fully developed.

THE FULLY DEVELOPED EXUDATE.

In the fully formed exudate there is usually a certain arrangement of the cell elements into layers, which is of some importance.

In order to understand completely this arrangement, it may be well to enumerate the various structures and layers seen in a section, in radial direction, through the ciliary body, although the photographs may give a fair idea of them.

From outside passing inwards, then, we find the sclerotic and, to the inner side of it, the outer layers of the ciliary body with the ciliary nerves superposed at intervals. The ciliary body is composed of layers of fibrous and muscular tissue, and has on its inner surface a rich vascular layer, which, in turn, lies closely applied to the membrane of Bruch. To the inner side of this latter lies the pigmented layer of the endothelium of the ciliary body and it is often found spaced out, as it were, by oedema. Further in we come to the non-pigmented layer of the endothelial covering.

These two layers, which compose the pars ciliaris retinae, are often broken up and pushed apart, as seen in the various photos which represent these layers in an early and a late stage of Cyclitis, and occasionally a layer of fibrous tissue is developed between them.

Internal to the non-pigmented layer is found a moderately dense layer of fibrous tissue, which, again, passes by fairly abrupt transition into a thick layer of loose fibrinous exudate.

Passing still more deeply into the vitreous body and still well defined from the layer of fibrinous exudate, is a layer of dense cellular exudate, which, as will be seen, consists of cells of various kinds, in a fibrinous network.

Now it may be understood that the thickness and extent of these layers of exudate in the vitreous body will depend largely upon the nature and intensity of the inflammatory process.

In some cases, the masses of deposit, which have somewhat the appearance of clouds, may be of quite limited extent and may be quite close to the ciliary body, though not in contact with it.

In other cases, the whole vitreous body may be occupied by exudate, leaving a translucent layer close to the ciliary body.

The lens may or may not be infiltrated according as it has or has not been injured.

Even at this stage that cicatricial contraction which has taken place has caused separation of the posterior part of the ciliary body, and distortion of the iris and lens.

THE CELL ELEMENTS IN THE EXUDATE.

To return now to the consideration of the arrangement of the cell elements in the exudate, it is found that, in the layer of loose fibrinous exudate which lies in an intermediate position, there are very few multinuclear cells in this advanced stage.

In the early stage they were numerous, as above noted, but have now passed more deeply into the vitreous body, leaving in their place, apparently, a comparatively small number of rounded or oval large cells of (medium) size. These are the mononuclear cells noticed before as being seen first about the seventh day, and which have been associated with the process of fibrosis. (Fibroplasts)

It will be noticed that this fibrinous layer lies close to the fibrous layer, and that it is at its outer margin that fibrosis is advancing.

THE PROCESS OF FIBROSIS.

The conversion of fibrinous into fibrous matter is evidently undertaken, from its beginning, by mononuclear cells which never penetrate into the exudate further than the fibrinous layer.

The changes seen are somewhat as follows.

From being simple rounded mononuclear cells, the fibroplasts, as they have been termed, become cigar shaped or a very much elongated oval. The longer axis of the oval is usually found to be parallel with the advancing edge of the fibrous layer. Now it is seen that in the neighbourhood of this elongated cell the fibrinous strands become condensed, as it were, round the cell itself.

A much elongated double cone is thus produced by the enswathing of the cell in fibrin.

This is at first opaque and granular, but soon becomes translucent and takes on a form which is indistinguishable from that of an ordinary fibre of fibrous tissue.

The action of the nucleus in this matter is evidently all important, but whether it has the power of transforming the fibrin

into protoplasm, which considering the appearances is probable, or converts the fibrin, by feeding on it as it were, into protoplasm, cannot be definitely determined.

In the inner part of the fibrinous layer, it has been seen that there are but few cell elements. Passing inwards towards the centre of the vitreous, however, a layer is come to in which great cellular activity is going on.

This is a mass of cell matter of varying kinds, in a matrix consisting of fibrinous strands which form septa passing in various directions and dividing the exudate into loculi.

The cells are of several varieties, five of which may be mentioned.

CELL FORMS IN THE EXUDATE.

(1) A Multinuclear Cell whose protoplasm is finely granular, and which is seen actively engaged in proliferation.

(2) A Mononuclear Cell of medium size, which is seen to undergo division.

(3) A Large Epithelioid Cell, which is occasionally seen undergoing division.

(4) A Small Round Mass of Nuclear Matter, probably a young cell.

(5) A Large Mass of more or less ill-defined protoplasm without nucleus.

These varieties of cells may be accounted for briefly as follows.

The first is a leucocyte which has migrated from a vessel or is the result of the division (in situ) of the nucleus of a mononuclear

cell.

The second is a lymphocyte, which may be either of vascular origin, derived from the budding of other exudation cells, or from the budding of fixed cells in the ciliary body.

The third is derived from the internal surface of the retina, the membrane of Jacob.

The fourth is a bud from the proliferation of some other cell in the exudate, varies greatly in size and can be followed through various stages.

This variety is found most abundantly in the most advanced portion of the cellular mass.

The fifth, and last, cannot properly be termed a cell at all, as it is merely the protoplasm of a cell, the nucleus of which has passed out, either as a whole or in fragments, more or less numerous.

Such protoplasmic masses are usually found in large numbers in the less advanced and middle regions of the cellular mass, and are manifestly undergoing degeneration, the less advanced masses being always extremely indistinct, only a vague outline remaining, before they finally disappear in the fibrinous layer. They have been termed "Ghost Cells."

CELL PROLIFERATION IN THE EXUDATE.

Allusion has been made several times to the subject of proliferation of the exudation cells, and to this subject we now turn, having delayed giving any detailed description of the process in its varying characters until the nature of the mature exudate was explained.

Four distinct varieties of activity of the nucleus have been observed, and it is to be noted, as especially interesting, that the method termed Karyokinesis is not amongst them.

Gemmation or budding, fission, fragmentation of the nucleus and total emigration of the nucleus, have been frequently seen, but in no instance has Karyokinesis been observed in any stage.

Remark will be made later regarding the non-appearance of Karyokinesis, and in the meantime a few words will be devoted to each of the methods of proliferation which are so well illustrated in this form of inflammatory exudate.

It is of course impossible to observe the actual process of nuclear division, etc., but although the process cannot be followed out in any one cell, the various stages of the change are so frequently seen in any one section, that but little imagination is required to enable an observer to arrange them in order and form a series.

Similarly, it would occupy too much space if a very complete series of photographs of the various stages of the processes were reproduced, hence only a few instances have been shown.

Taking, however, first <u>Gemmation,</u> even the four photographs shown, will, it is imagined, show so much of the process that but little doubt can remain that the complete process is somewhat as follows.

<u>GEMMATION.</u>

The first evidences of change are seen in the nucleus, the protoplasm remaining, so far as can be seen, inactive.

First, without any previous manifest alteration in the cell, a fine notch appears in some position on the edge of the nucleus. This notch gradually spreads more deeply into the substance of the nucleus, and is seen as a curved line of light, which extends,ultimately, across a small portion of the usually spherical mass.

The appearance is as if a small lid were being lifted off the pole of the nucleus, at this stage. Later, however, it is manifest that, by extension of the notch, a small spherical portion of nuclear matter is separated from the parent, leaving a cup-shaped depression in this latter.

In this cup-shaped depression the daughter cell lies completely enclosed within the protoplasm of the parent.

From this position the new formed nucleus ultimately departs, passing straight out through the protoplasm, and taking with it, it may be, a small portion of protoplasm to act as a protective envelope. It at once comes within the sphere of influence of he irritant and passes outwards and onwards, building up for itself, as it goes, from the nutrient fluid surrounding it, a thicker protoplasmic layer.

This new formed cell at first has the appearance of a small lymphocyte, but soon gains bulk and,ultimately, like its predecessor, if necessary gives off a progeny which shall repeat the process above described.

The mother cell can,apparently,give off a large number of buds, indeed a nucleus can give off, as has been seen, more than one bud at a time.

FISSION.

The parent or primary cell may divide by simple division of the nucleus into equal parts, each portion taking a share of the protoplasm with it.

FRAGMENTATION OF THE NUCLEUS.

In this process the whole of the nucleus is divided into small masses, of spherical shape, with great rapidity. Each of the small portions passes out from the protoplasm leaving what is virtually an empty husk. Their departure is probably almost simultaneous, as many of these little nuclear masses may be seen lying outside a parent protoplasm husk in the fibrinous network.

MIGRATION OF THE NUCLEUS.

Lastly, as seen in the photographs, the nucleus of a cell may take a worm like shape and project itself into a new space entirely, or may, apparently, project itself partially out of its protoplasm, and in this new position a small portion may be cut off and remain as a separate nucleus, the parent retracting into its protoplasm.

In the former instance an empty husk is left as in the last described method.

It is hardly necessary to remark that the empty protoplasmic husks left, are the Ghost Cells above described.

The appearances presented by these masses of empty cell protoplasm, being many and differing somewhat widely, gave rise to considerable conjecture when at first they were seen, but subsequent study of the subject has established the correctness of the views taken of it.

Considering the vast numbers of these bodies seen, as the photographs show, they must remain visible for a considerable time after being left by the nucleus and before being disintegrated, as they eventually are. Further, they are always more fresh or natural looking near the advancing edge of the proliferating zone, and more faded or ghost-like near the border of the fibrinous layer of exudate.

This subject forms matter for much interesting speculation, indicating as it does that the protoplasm of a cell is a purely passive agent, and, also, that the position of maximum activity in an exudation is constantly changing.

This latter statement is supported by the fact that, in the most advanced edge of the exudation zone, it is, almost entirely, new formed cell matter which is found.

From the foregoing it will be evident, then, that cell proliferation in the exudate is very active, and that it is a highly important part of the function of an inflammatory process.

It provides, that, in the front rank of what may be compared, not inaptly, to an army advancing into a hostile country, young and active units are constantly present, and, further, it assures that rapidity and probably endurance will be present when it is urgently required.

But, as the urgency of the case in point, in many instances, if not all, depends upon the proximity and virulence of micro-organisms in the tissues, it may be well to turn aside to the investigation of the presence of organisms in the exudate.

MICRO-ORGANISMS IN THE EXUDATE.

It is not difficult to demonstrate the presence of organsims in the exudate, and, by comparison of sections, to ascertain the position which they occupy.

Thus, they have usually been found in the more advanced portions of the exudate.

It is usually micrococci, staphylo- or streptococci, which are found, but occasionally a somewhat doubtful bacillus has been seen. The bacteriological investigation of the subject has not, however, been closely followed out, as the information to be derived from the knowledge of their presence is solely connected with their influence on the exudate.

From the facts, then, that organisms found in the exudate are usually found in the advanced edge only, and that they are usually found, in considerable numbers, in the interior of cells, it may be concluded that the cell activity is intimately connected with the removal of the organisms.

Further, it is only rarely that the presence of organisms can be shown in the ciliary body or Choroid, and then, also, it is in the interior of cells, and often of cells in bloodvessels, that they are found.

FUNCTION OF THE EXUDATE.

These various appearances, then, have led to the adoption of certain views regarding the function of the exudate, in this inflammatory process, as being those which best satisfy the requirements of the case.

First: The migration of cells from one position to another is not a passive but an active response to a definite demand which is chemiotaxis.

Second: This chemiotaxis is a very well defined call for a purpose which is probably dual. In the first instance active proliferation is required, and in the second, active phagocytosis.

Third: It is highly probable that the mature cell is not able to move with the same rapidity as young cells are, and, also the mature cell has not the same power of resistance as young cells.

Fourth: As living protoplasm is to be pushed forward into the neighbourhood of, and, indeed, into close proximity and contact with noxious matters, be they animal, vegetable or chemical, it is necessary that this protoplasm should possess the maximum activity and resistive power when first brought into such contact.

Fifth: The cells of the exudate having these functions, the fluid and semi-solid (nature) act as a support and a nourishing medium. structures

Before going any further, the absence of evidences of Karyokinesis may be inquired into.

KARYOKINESIS NOT SEEN IN THE EXUDATE.

The absence of this type of cell proliferation may be readily explained if it be accepted, that it is a less rapid method of division than the others, and, also, that it may be a sexual process, the other types being asexual.

The writer has had abundant opportunities of examining inflammatory exudates as in pneumonia, pleuritis and corneitis, and, although he has investigated, in the case of the cornea especially, many sections

in regard to this subject during the past four years, no instance of undoubted or even doubtful Karyokinesis has come under notice in an acute inflammatory process. Only once, indeed, has the process been seen in the true corneal tissue, and that in a case of very slow form of inflammatory change.

All the various modes of division may be seen in the cornea (acutely inflamed), and several varieties in other situations in which a similar change is advancing.

Again, in the epithelium on the anterior surface of the cornea, in the ordinary state, Karyokinesis is frequently seen. In the case, however, of rapidly growing epithelium, which is extending over a cut surface as a protective agent, as was beautifully shown at a demonstration in the early part of 1900, by Dr. Reid, to occur within a very few minutes, no instance of Karyokinesis was seen.

Here, then, is an instance in which cells which under ordinary circumstances do show, but when required to reproduce with great rapidity do not show Karyokinesis.

May it not then, with these various facts in support, be contended that the process of Karyokinesis is not sufficiently rapid for the exigencies of the case?

Leaving this part of the inquiry now, we will turn to the investigation of the means by which the exudate is removed and a further supply stopped.

THE CESSATION OF EXUDATION.

As would be expected, the formation of exudation will not stop suddenly but more or less gradually, and the cessation will de-

pend upon the removal of the cause.

In this way, when all the irritant(and its source)has been removed (or enclosed in a protective envelope) the demand for new cells will cease. Then the vessels will begin to contract; diapedesis will be lessened and ultimately will be checked.

But the proliferation of the exudate itself will not be stopped so abruptly, and many new formed cells endowed with the power of rapid proliferation will be formed. The chemiotactic attraction will be wanting, however, and,consequently,activity will be no longer required and no longer shown.

There will still, however, be a considerable bulk of cell matter lying unoccupied, as it were, and the process of removal of this must now be investigated.

THE ABSORPTION OF THE EXUDATE.

It has been seen that the areasover which the exudate is formed and over which it is spread are both large,and also that, even at an early stage in the inflammatory process, change is going on in the exudate, which results in its assuming a more stable form.

Now as it is largely with this same change, or fibrosis of the exudate,that we are now concerned,it is important that the positions in which the exudate is found should be again enumerated.

SITES IN WHICH THE EXUDATE IS DEPOSITED.

First, then, the posterior surface of the ciliary body,from the iris to the retina, is covered with a dense mass of more or less completely cicatrized fibrous tissue.

Backwards from the ciliary body, a mass of exudate, likewise undergoing fibrosis, is found to pass round the posterior surface of the lens.

Extending further backwards still, the exudate in the vitreous body is found to reach a greater or less distance, according to the intensity of the irritant, presumably.

From the ciliary body again, backwards and outwards along the surface of the retina, a considerable bulk of the fibroplastic mass may extend even to the equator of the eye.

The position in which the largest mass of the tissue is accumulated is just behind the ciliary body, where, owing to cicatricial contraction, the ora serrata has been drawn forward, and the mass of exudate lying over it is brought up to increase the bulk..

In close proximity to the fixed tissues, however, fibrosis has been going on, but in the central parts of the vitreous body the exudate is entirely fibrino-cellular.

It is with increasing difficulty, as can be understood, that nourishment is conveyed to this central area, at this stage. Much of the vitreous body has been destroyed and the remainder is useless as a circulating medium.

Moreover it is from the ciliary body that nourishment is to come, and, as is seen, this region is cut off, to a large extent by fibrous tissue, which is now contracting on itself and occluding the vessels which formerly acted as a source of supply.

Hence, it is seen that many of the cells of the vitreous exudate undergo fatty degeneration, as seen in one of the photographs.

The protoplasmic matter degenerates and the nuclei, which have probably undergone proliferation, are left to assist in the process of cicatrization by fibrosis.

Fibrosis advances rapidly all round the mass of exudate and large distended bloodvessels may be seen, but the circulation is sluggish in them.

Fatty degeneration of the tissue goes on, as seen in the photos, and it is many weeks, even months, before the mass comes to a state of rest.

All fatty debris must be removed; all superfluous cells taken away, until ultimately the fibrous tissue is hard and firm like cartilage, possessing little or no vascular supply.

Much variety is seen, however, by one who sees many cases of Cyclitis in later stages.

Thus, if the amount of cellular matter in the vitreous body is large, cicatrization goes on all round it and ultimately a solid mass, of spherical shape, white color and great firmness, remains in the centre of the much contracted vitreous body.

Again, if the vitreous body has been almost entirely replaced by exudate, it is frequently the case that this, containing as it probably does, much noxious matter which is being removed, cannot be got rid of in such a simple manner, but sets up a secondary irritation, which causes erosion of the coats of the eye, and in this way, by perforation of the globe, finds an exit as pus.

In extreme cases, where the irritation has from the first been of very high intensity, the inflammatory process spreads to all the tissues of the eyeball, and the exudate, by degeneration, forms pus,

which can only be removed by perforation of the sclerotic or opening up of the original wound. Such a case is termed panophthalmitis.

In all cases of cyclitis, then, it is seen that a certain amount of fibrous tissue may be left to contract to a quiescent state, after the inflammatory synptoms have passed away, and in this remaining fibrous tissue another and most interesting change may take place.

OSSIFICATION OF THE EXUDATE.

This change has been recognized for nearly a century now, and consists in the formation of true bone in the exudate.

This is ossification as distinct from calcification. In both cases there is a deposition of lime salts in the tissues, but whereas, in the former, such salts are acted upon by living cells, in the latter, they remain inert and passive in an amorphous or crystalline mass.

Both the forms of deposition are found more or less commonly in the eye after inflammatory changes, but the one is common in situations where the other is rare.

In the cornea, for instance, lime salts are frequently deposited and may assume the crystalline or the amorphous form, but bone, the result of organic influence on the salts, does not form.

In the situations where bone is most frequently developed, simple calcification is not found. In the lens, however, we have a common meeting ground where calcification is very common and bone is occasionally developed.

Calcification is a mere mechanical deposition of lime salts, but bone is a transformation of the tissue which is formed after inflammatory changes have subsided.

The formation of bone in the eye is to be regarded as entirely separate from the formation of bone plates in the sclerotic, as it occurs in certain fishes and reptiles, and is not an ossification of a cartilaginous plate such as is found in the sclera of some birds.

Nor is to be compared with the formation of plates of bone in tendons, etc., which are in direct continuity with the periosteum.

Finally, it is to be distinguished from the ossification of secondary growths of tumors which are growing in connection with bones.

The process here dealt with is practically an ossification of a cicatrix, and so far as can be ascertained, the formation of true bone in a cicatrix elsewhere, and which is certainly unconnected with periosteum, is unknown.

Two cases are known in which bone has been developed in a cicatrix which has replaced blood clots, after an extensive bruise to a limb, one of which may be quoted here.

During the evening of January 13th, 1899, Mr. Eve showed to the Clinical Society of London a case in which a large plate of bone was developed in the substance, apparently, of the Vastus Externus muscle, and was separated from the femur by a distinct interval. This was the sequel to the formation of an extensive blood clot in the thigh, following a kick from a horse. Mr. Eve expressed the opinion that this was an instance of ossification of fibrous tissue derived from the organization of a blood clot.

The second case has not been published, so far as can be found, but was in many respects similar to that quoted.

Now, in this interesting case, there is a possible source of osteoblasts, in that the periosteum might have been ruptured, so that a single or multiple centre of ossification might have been the starting point of the osseous change.

In the case of ossification of the fibrous tissue deposit in the eye, however, there is no question of direct connection with bone or periosteum, yet some definite cause must exist to explain the comparative frequency of the occurrence.

A possible source of explanation is suggested in the facts that a direct prolongation of the brain is exposed to danger of injury, both by contraction of the fibrous tissue in the eye, and by external agency. Further, so far as is possible, all the great nerve centres are preserved from such injury in bony cavities. Hence, it may be the case that, in the instance under consideration, the means of protection being within easy reach, and still, until converted, a source of danger, this fibrous tissue is converted into bone for a similar reason.

Again, the fact that the fibrous tissue developed in the eye is lying in close proximity to a highly vascular membrane, may have some influence in bringing about the change of condition.

However, no matter what may be the actual cause of the transformation, it is exceedingly difficult to explain the determining cause, or in other words, in what way osteoblasts are conveyed to the eye. For, even admitting that calcification of cicatrices is not uncommon, the conversion of this mineral matter into bone is only accomplished by the intermediation of specialized cells which are uniformly present

in such cases.

In the case under discussion, then, it must be admitted that the process of formation of bone is undertaken in answer to a definite demand, and that the necessary osteoblasts are either brought to the eye from some other situation, by the circulation, or are formed locally.

As regards the actual formation of bone, the writer has come to the conclusion that the process is somewhat as follows.

THE FORMATION OF THE BONE.

In close proximity to a bloodvessel, and probably from it, minute granules, of spherical shape, appear at some point in the mass of fibrous tissue. These granules gradually increase in both size and number. Those which were first formed coalesce, whilst new ones remain for a time separate. These globules show by their reaction to acids that they are composed of lime carbonate, and by their coalescence form a mass of what seems at first to be inorganic lime salt.

The mass,thus formed, is homogenous in appearance, of considerable density and stains with great readiness. Its edges are ragged and terminate in globules which diminish in size as they are further from the mass.

At an early stage, long delicate fibres and occasionally stellate corpuscles, may be seen lying between the globules and radiating from the mass into the surrounding tissue. These are evidently comparable to the osteogenetic fibres and osteoblasts.

The more advanced portion of the mass thus formed, early encloses the bloodvessel from which it may be said to have originated,

and soon shows a marked change in structure. Formerly dense and homogenous, it soon exhibits a fine striation, as if indicating an arrangement in layers round the somewhat irregular cavity in which the bloodvessel lies. This cavity becomes more open and its limits are well defined.

At a somewhat later stage it is seen that the spaces are lined with osteoblasts which are regularly arranged, and in the lumen of the tube, as such spaces really are, besides the bloodvessels, fat and often fatty crystals in sheaves are found.

In the completely formed bone the cavities tend to open up even more, and the striation which was before seen becomes better marked. At this stage it can be clearly seen that there is a definite arrangement of the bone corpuscles along the margins of the layers, and of the whole structure around the bloodvessels.

The growing end of the bone continues to be ill defined, and consists usually of a series of fibres which pass outwards into the surrounding fibrous tissue.

Round the fibres, it is apparent that the cells which are about to enter into the formation of the bone, arrange themselves in columns; and, as the process advances, it seems as if the fibres and cells are both surrounded by the calcareous deposit.

It is of interest to notice this fact regarding the cells of the fibrous tissue, as such a conversion into bone corpuscles surely indicates a certain power of adaptation as regards functional activity.

We have thus seen that there is formed in connection with, and probably, by conversion of, the fibrous tissue of the cicatrix in the

eye, true bone, and it only remains to be mentioned that this ossification is by no means rare.

Indeed, the comparative frequency of occurrence of ossification in the eye in a certain class of cases, is remarkable; during six years' work as pathologist in the Eye Infirmary the writer has examined over six hundred eyes and has found that bone was developed in over fifty of them.

Now a large proportion of these eyes examined (600) were removed in early stages of Cyclitis or on account of other diseases in which no fibrous tissue is developed in the eye, so that, if one takes only these eyes which have been rendered liable to the conversion of fibrous tissue into bone, the percentage will be found to be not far from fifty-five or sixty.

As regards the age of the patients in whose eyes bone has been developed, it is interesting to note that, although for various reasons, the average is over forty, many quite young persons of either sex are so affected.

The youngest patient whose eye,in the writer's experience, has contained bone was aged twelve, whilst the oldest was seventy-seven.

The shortest period which has elapsed between the date of injury and the discovery of bone was eight years, and the piece of bone found was of almost microscopic dimensions-1 M.M. long and .50 M.M. thick only.

It has, thus, been seen that the formation of bone in the cicatrices in the eye is a comparatively common occurrence, that it occurs in both old and young subjects and in both sexes.

Now, as before remarked, the formation of bone in cicatrices in other situations in the body, if it does occur at all, is of extreme rarity, may we not, then, argue, with good reason, that there is a special reason in the case of the eye for its development.

Having, then, followed out in a comparatively brief manner the main features of the process termed Cyclitis, and having dwelt at some little length upon some features which appeared to be of special interest, the writer is willing to acknowledge that the subject is by no means exhausted.

Much could have been added on a number of branches of this wide subject and the whole might have been entered into in fuller detail.

As, however, it was originally intended to let the ophthalmological side of the subject remain, to some degree, in the background, and to bring forward the histological details, it was considered that enough has been said regarding the experiences and findings which are the result of these investigations.

-:SUMMARY AND LITERATURE:-

It is to be regretted that, so far as can be found, there is no literature dealing with the whole subject chosen for investigation here.

It is true that a moderate amount of work has been done upon the subject from an ophthalmological point of view, including clinical observations upon Cyclitis with a few notes upon the principal features of the exudate, and a considerable bulk of literature upon the subject of "Ossification of the Eye," as it has been termed.

The subject of this investigation, however, has hardly been dealt with in detail in any work, and thus it has been more than usually difficult for the writer to obtain assistance from the comparison of his results with those of others.

The best recent text books in Ophthalmology give but a cursory glance at the histological processes involved.

Thus Fuchs (1), says that The exudate consists of fibrinous strands with cells in varying proportions, whilst the subject is similarly briefly dealt with by the writers of the article on the subject in Norris and Oliver's (2) work on Ophthalmology. Weichselbaum (3) refers to the subject briefly and gives an illustration in many respects similar to one of the writer's photographs.

Indeed the various works, Histological, Pathological and Ophthalmological, to which an observer would turn for assistance, show that no detailed research has been made in this subject.

The first point which has been found to be dealt with, in looking over the literature of the subject, is the origin of the

leucocytes which are found on the surface of the ciliary body.

Thus, Haensell (4) says that proliferation of the cylinder cells of the pars ciliaris retinae takes place by indirect division.

Again, Alt (5) says "More frequently we see that these layers (the uveal and retinal layers of the ciliary body) take an active part in the formation of the ciliary membrane, especially the retinal part of the ciliary body." And "The cylinder cells of this layer proliferate and begin to grow out into long spindle cells, and finally into long connective tissue fibres."

This, then, is apparently in line with the opinion at first inclined to but subsequently rejected in favour of the haemic origin of the cells.

The latter part of Alt's view above quoted, could not, however, be accepted at all.

Regarding the occurrence in the exudate of tubules, sometimes pigmented and at other times not so, considerable prominence has been given to it by various writers.

The writer has only seen such tubules (non-pigmented) once (see photo), and was satisfied that they were, in this case at all events, the result, as Collins (6) has suggested, of proliferations and " hyperplasia" of the glands associated with his name and situated in the pars ciliaris retinae.

At all events such structures are by no means essential, but are rather accidental in the formation of the ciliary exudate.

Structures resembling tubules, but the result of oblique sections being made of the ciliary processes, are often seen.

Hamilton (7) remarks upon the occurrence of proliferation of the endothelium of the peritoneum in inflammatory conditions of that membrane.

The subject of the early transformation of fibrinous into fibrous tissue is of interest as indicating, possibly, an attempt to protect the ciliary body, as well as the fact that all necessary conditions are present at an early stage.

Turning now to the subject which is regarded as of most interest and importance, namely, the proliferation of the leucocytes which compose the exudate, it is seen that it has not been very fully investigated.

For many years it has been contended for and against, and the balance has been gradually turning in favour of the view that the cells which compose inflammatory exudates do proliferate.

Hamilton (Ibid) thinks that it is probable that many of the cells, which compose the exudate in croupous pneumonia, may be of such origin.

Hohnfeldt (8) remarks, in his work on abscess formation, that fragmentation of the nuclei was seen in the central area, but that karyokinesis was not seen in either the leucocytes or the connective tissue corpuscles.

Several writers regard this process of fragmentation of nuclei as an evidence of degeneration, but it might as well be taken to be a sign of great stimulation of a living cell.

The protoplasm may, and does degenerate, when left by the nucleus, but the process of fragmentation is seen, in the class of case under consideration, so frequently associated closely with evidences of great vital activity, that the weight of evidence is

rather against the assumption that the nuclei are degenerating.

Regarding other evidences of proliferation of cells in the exudate, evidence of such great activity in inflammatory conditions of the cornea is so abundant, that, here as there, there is no doubt but that the process is one of high importance in the production of the exudate and the maintenance of the state of activity required of it.

The absence of Karyokinesis has been commented upon at some length before, and it is only to be noted here, that it has been contended that many cases of supposed direct division have proved really to be indirect. The precautions which have been taken, however, in the preparation of tissues and staining of sections, render it somewhat improbable that the true nature of the process has been overlooked.

The presence in the exudate of large numbers of rounded masses of protoplasm without nuclei (Ghost Cells) is of interest. No reference to the occurrence of similar structures in the exudate in other situations has been found. This may be attributed to various facts. The condition of transparency, as found in the vitreous, is absent elsewhere; degeneration of such bodies and subsequent removal may be more rapid elsewhere, owing to differences of vascularity of parts.

The staining affinities of the bodies are indifferent, which fact renders them in either new or old condition, liable to oversight, as also,it may be mentioned, difficult to photograph.

It is imagined that even indistinctly as they are shown in the photographs, the various considerations of size, relations, position and appearance in various states being taken into account, it will be difficult to account for the presence of such bodies in any

more satisfactory manner than that given.

The evidences of motility of the nucleus, as shown in the photographs, are also of interest, and are of frequent occurrence in the exudate, especially in the advanced portions.

Generally speaking it may be concluded from the appearances seen, that the activity of the leucocyte is by no means restricted after the passage into a new sphere, but rather increased, possibly by the intervention of new conditions and by the presence of an irritant.

Further it is clear that the role of the leucocyte in the exudate is a many sided one, including phagocytosis, production or proliferation and repair, so far as it is possible, of the tissues.

Adami (9) concludes from various appearances that "The new growth to replace the tissue destroyed by the irritant proceeds in the main from the fixed cells of the tissue."

Regarding the process of ossification of the fibrous exudate, the opinion has been before expressed, that the osteoblasts may be derived from specialization of the connective tissue corpuscles.

Twelve years ago, unknown to the writer, this view had been taken by Dr. Reid (12), who says "The connective tissue corpuscle seems to be transformed into the bone corpuscle."

Although much has been written on the subject of ossification, and many cases have been recorded of its occurrence, the early stages, or what seem to be such, of the process have been but little investigated.

This may be accounted for by the fact that centres of ossifica-

tion are naturally difficult to find, and that, although bone may be present in the eye in masses varying in size from a microscopic point to complete conversion of the contents of the sclerotic, as in one case which the writer has seen, unless it is formed by accident, when it occurs in small particles its presence is not sought.

The first writer who seems to have seen the true relationship of the process in its pathological aspect, was MacKenzie (11), who pointed out that bone was usually found in the eye only after the occurrence of long continued inflammation.

Hoene (12) remarks upon the subject that an embryonal tissue is laid down and undergoes fibrous changes, after which bone is deposited.

Had this subject been more fully grasped when the occurrence or non-occurrence of ossification of the lens, iris, retina and vitreous, was being discussed by Knapp (13), Alt and others, the possibility of such changes would have been seen at once.

Alt (Ibid) records a case of bony deposit in the lens cavity within the crumpled lens capsule, De Wecker (14), ossification in the retina, and the writer has seen bone formed within the limits of the iris, lens and retina.

Regarding the actual process of bone formation, it is admitted that the method described above may not be the only one possible.

Alt thinks that ossification of the chorioid or, as he says, near the inner surface of the chorioid, very frequently has for its origin the vitreous bodies (verrucose excrescence) on the lamina vitrea.

In conclusion, as regards the whole subject dealt with here, it may be the case that, although there is an apparent diversity of appearance between the changes seen in the exudate into the vitreous body in Cyclitis, and those seen in inflammatory exudates elsewhere, the diversity is more apparent than real. The nature of the tissue into which the exudate is thrown, must have a very powerful influence upon the amount of detail seen.

Thus, in the case of pleuritic exudate the resemblance is strong, whilst in pneumonia it is not so strong.

In corneitis, on the other hand, there is, in many of the varieties seen, no apparent resemblance at all, only close investigation of the process revealing the fact that the fibrinous matrix is the chief element of difference, the cells behaving in much the same manner in the various processes.

So, indeed, it may be, and probably is, the case that different forms of the inflammatory process, catarrhal, fibrinous and purulent, are only different in degree, the changes involved being much alike.

-:HISTOLOGICAL METHODS EMPLOYED:-

Hardening and fixing of the tissues has been carried out by the use of chromic and acetic acids, as in Flemming's Solution, without osmic acid, and by Formaline, in 5% Sol.

The Formaline gives the best results in the preservation of the vitreous body and its exudate.

Bleaching has been accomplished by the use of Euchlorine Solution, made by adding to one dram of Chlorate of Potassium three drams of strong Hydrochloric acid, shaking in a stout stoppered bottle, and then adding three ounces of water.

Sections, after fixing in any medium, are steeped in the fluid for twenty-four hours and then washed for six hours in running water.

Decalcifying has been carried out in the Chromic acid solution with 10% of Hydrochloric acid added.

Various stains and mountants have been used according to the requirements of the case.

Sections have been cut in gum, except when bone was being examined, when celloidin was preferred, on account of the liability of the bone to fall out, if gum be used.

A Cathcart's microtome was used in the first and a Jung's in the second instance.

Photography has been carried out by the use of Zeiss' apochromatic lenses and projection eyepieces.

Most of the sections photographed have been stained with Ehrlich's Haematoxylin Solution.

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14 De Wecker, Traite Complet d'Ophthalm. De Wecker et Landolt, t. 2nd., page 591.

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DESCRIPTION OF PHOTOGRAPHS

Of Sections

From Cases of CYCLITIS

Photographs by
Jessie Buchanan

No. I.

Cyclitis: 14 days duration. Section radial through anterior segment of the eye.

To show, the cornea and sclerotic above, the iris and ciliary body with thickening of the pars ciliaris retinae in middle distance, and the empty lens capsule and a large mass of exudation into the vitreous at the lower part.

The fibrous layer of exudate is clearly visible as is also the variation in density of the fibrinous and cellular layers.

X 9 diams.

1

NOS. 2 & 3.

(No. 2) Cyclitis: Several years' duration. To show the corneo-scleral junction and sclerotic to the right, the ciliary body much contracted and drawn from the sclerotic. To the left is seen above part of the distorted lens, pushed forwards by a mass of dense exudate, to the posterior surface of which the retina much folded and tightly compressed is adherent. X 14 diams.

(No. 3) Cyclitis: 1 month's duration. To show the ciliary body slightly separated from the sclerotic, with a mass of moderately dense exudation adherent to its posterior surface.
The exudation is fibrous and is freely vascular.
X 40 diams.

2

3

Nos. 4, 5, & 6.

No.(4.) Cyclitis: 16 days duration.
Section of the posterior part of the ciliary body. To show slight infiltration of the ciliary body, great disturbance of the epithelial layers.
The pigmented layer is thickened and irregular; the non-pigmented layer is very much thickened and infiltrated, the outlines of the cells being entirely lost. On the surface of this layer lies a layer of fibrous tissue and behind this a layer of fibrinous exudate. Pigment granules are seen in the non-pigmented layer and also in the fibrous layer. X 100 diams.

No.(5.) Cyclitis: 20 days duration.
The pars ciliaris retinae in cyclitis to show the breaking up of the layers of epithelium; the pigmented to a less, the non-pigmented to a greater degree. The two layers are separated by a thin layer of exudate.
There is a layer of moderately dense fibro-cellular exudation in the vitreous body.
X 100 diams.

No.(6.) Cyclitis: 16 days duration.
Section bleached by Euchlorine to show accumulation of leucocytes on the surface of the pars ciliaris retinae.
There is comparatively little alteration of the pigment layer.
The ciliary body (below) is somewhat infiltrated and there is a layer of fibrous tissue in the vitreous body.
X 100 diams.

4

5

6

Nos. 7, 8, 9 & 10.

No. (7) Cyclitis: Same specimen as No. 6.
To show that there is little alteration in the nuclei of the non-pigmented layer of the pars ciliaris retinae, although there are abundant leucocytes passing up to the surface between the cells.
This section shows also a few fibroplasts in the free exudate.
To the left below is seen a gland dipping down through the basement membrane. The whole tissue is evidently opened up as it were by oedema.
X 300 diams.

No. (8) Cyclitis: 18 days duration.
Section through the exudate in the vitreous body, to show the junction of the fibrinous and fibrous layers.
The condensation of the former as it approaches the latter is well marked. X 150 diams.

No. (9) Cyclitis: Same section as No. 8
To show the stratification of the fibrinous layer with fibroplasts becoming elongated and lying parallel to the direction in which the fibres are to be placed.
The vascularity of the exudate is manifest.
X 200 diams.

No. (10) Cyclitis: 4 month's duration.
Cicatricial changes are going on in the exudate. The pars ciliaris retinae is broken up and its layers driven apart.
The pigmented as well as the non-pigmented layer is disturbed.
The exudate seen is fibro-cellular.
X 150 diams.

7

8

9

10

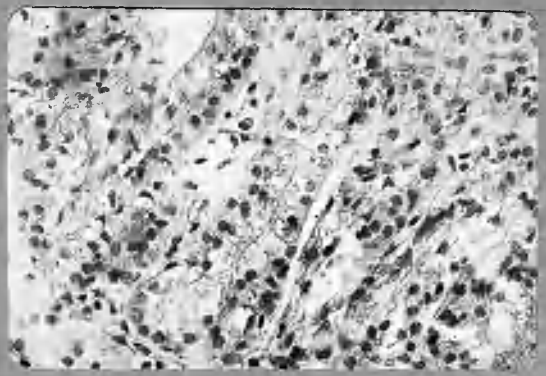
Nos.11,12, 13 & 14.

No. (11) Cyclitis: 18 days duration.
To show proliferation of the cells near the ciliary processes, with hyperplasia of the glandular structures resulting in the formation of tubules. X 350 diams.

No. (12) Cyclitis: 20 days duration.
To show the inner surface of the retina near the ora serrata, with the vitreous body separated from it and infiltrated.
Numerous large Epithelioid cells are seen lying on the retina and adherent to the vitreous body. X 120 diams.

No. (13) Cyclitis: Same case as No. 12.
Showing the inner surface of the retina and the adjacent vitreous body.
Both structures are infiltrated, to a considerable degree, by cells of various kinds, and leucocytes can be seen passing out of the vessels apparently, in the retina.
X 150 diams.

No. (14) Cyclitis: 18 days duration.
The exudate in the vitreous body, to show the existence of fine fibrinous septa, and cells of various kinds, large epithelioid, small round cells, etc.
Taken from the junction of the fibrinous with the cellular part of the exudate.
X 100 diams.



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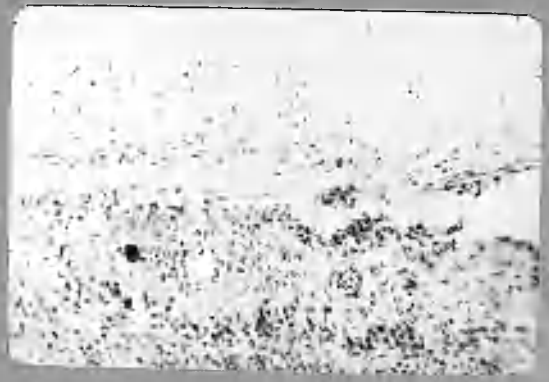

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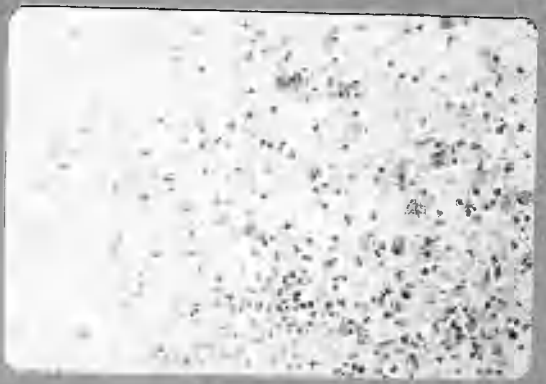


14

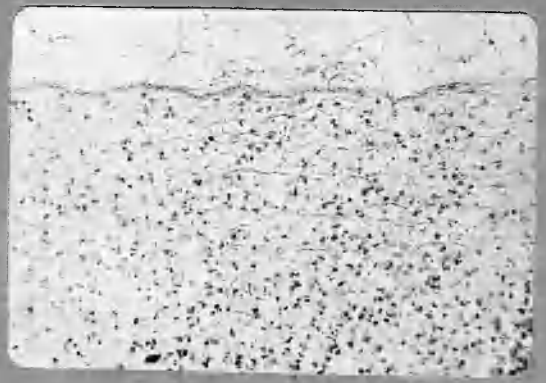
NOS. 15, 16, 17 & 18.

No. (15) Cyclitis: Same case as No. 14.
The exudate in the vitreous body, to show a strongly marked fibrinous septum with many fine septa and a portion of the more cellular part of the exudate. Various kinds of cells can be seen, and many "Ghost Cells" are dimly distinguishable.
X 100 diams.

No. (16) Cyclitis: Part of No. 14.
To show a variety of cell forms, the dimness of outline of the Ghost Cells being well marked on account of the position from which the section is taken. X 300 diams.

No. (17) Cyclitis: 20 days duration.
To show the more highly cellular part of the exudate. Large numbers of "Ghost Cells" are seen much more distinctly than in the last photo. Comparatively few nucleated cells are seen.
X 300 diams.

No. (18) Cyclitis: Part of No. 16.
High power view of the exudate near the junction of the fibrinous and the cellular parts. The "Ghost Cells" are more distinctly seen, whilst the nuclear activity is evidenced by the number of free nuclei seen, and the varieties of shapes which they take.
X 650 diams.



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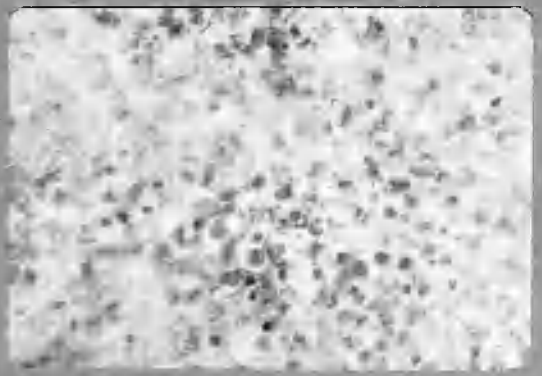
16



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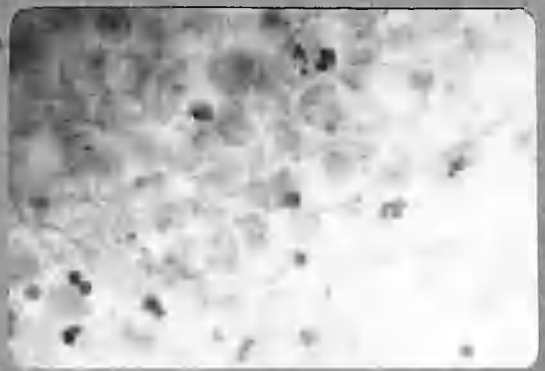
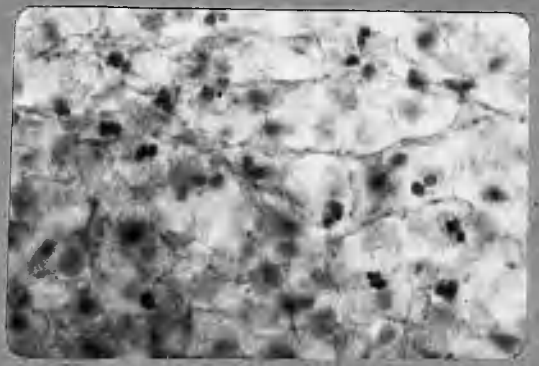


18

Nos. 19 & 20.

No. (19) Cyclitis: Part of No. 15.
To show a high power view of the fibrinous network with its enclosed Ghost Cells, etc.
Instances of nuclear activity are seen.
X 600.

No. (20) Cyclitis: 18 days duration.
From photos chosen from the region of the exudate shown in No. 14, to show stages in the process of Gemmation.
(a.) Cells with one and two nuclei.
(b.) One nucleus shows a lateral groove.
(c.) Groove opened out; daughter cell cut off; cup shaped depression in parent.
(d.) Parent left in protoplasm.
X 750.



19

d.

c.

20

b.

a.

No. (21) Cyclitis: Same position as last.
Four photos to show appearances of nuclei indicating motility and fission.
(a) Nucleus assuming a wormlike form, pushing a head from one space into another, possibly a mode of migration.
(note) The middle of the nucleus is at a lower level than either extremity, and is narrowed.
(b.) More marked instance of the same process. Here the neck is very narrow and the head very sharply defined.
(c.) Instance of a nucleus pushing out a head in a definite direction and the neck being narrowed down until the head is left free. The parent nucleus has a rounded head at the extremity opposite that at which the daughter is being sent off, probably indicating that another bud is going to be cast off here.
(d.) Showing a completely formed and separate nucleus, below and above an older nucleus regarding which there are two points for consideration. It is flask shaped, a long, thin process being pushed out above, whilst below, an oval light spot is seen. The significance of such a light area is doubtful, but it is frequently seen and is probably the cup-shaped depression or scar from which the last daughter cell has been liberated. The free nucleus is very probably the daughter cell last sent off.
X 750 diams.

No. (22) Cyclitis: 2½ months duration.
The exudate into the vitreous body undergoing degeneration shows swelling of the protoplasm and migration of nuclei.
X 220 diams.

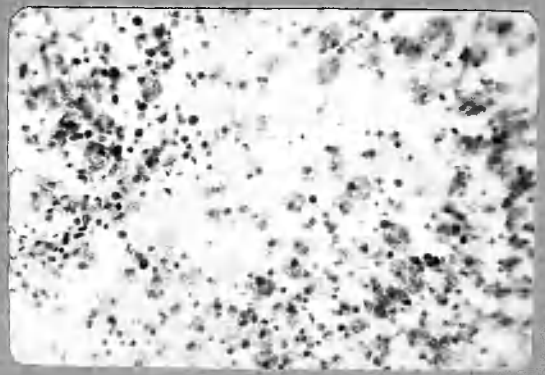
a.

b.

21

c.

d.



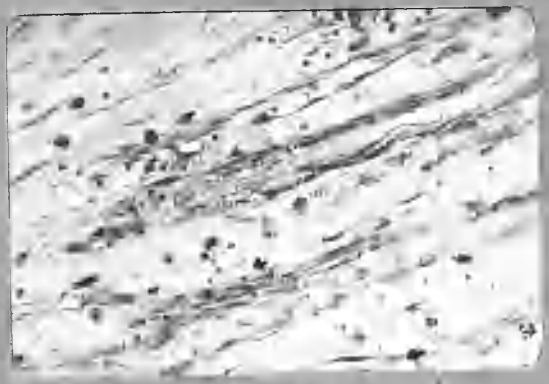
22

No. (23) Cyclitis: Same case as No. 22.
To show fibrous transformation of the exudate in a later stage with fatty degeneration of the included cellular matter.
X 100 diams.

No. (24) Cyclitis: 3½ months duration.
The fibrous tissue formed by fibrosis of the exudate, with longtitudinal sections of large new formed bloodvessels.
There is no fatty degeneration going on now, and the tissue is becoming quiescent.
X 300 diams.

No.(25) Cyclitis: 17 years duration.
To show complete bone formed in the curve of the displaced ciliary body.
X 10 diams.

No. (26) Cyclitis: 11 years duration.
Early stage of ossification taking place in the curve of the displaced ciliary body.
The more advanced portion bears some resemblance to bone, the less advanced portion is opaque, granular and ragged.
X 20 diams.



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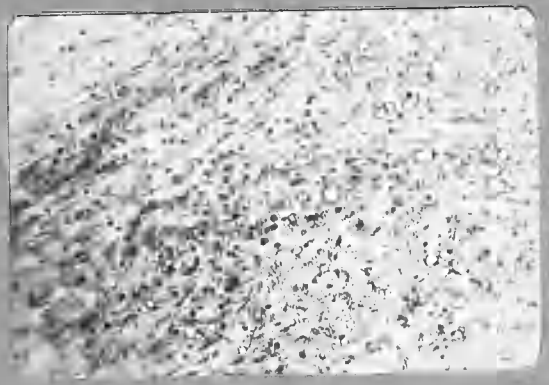

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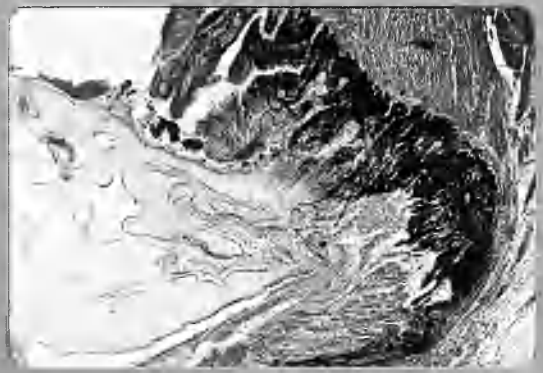

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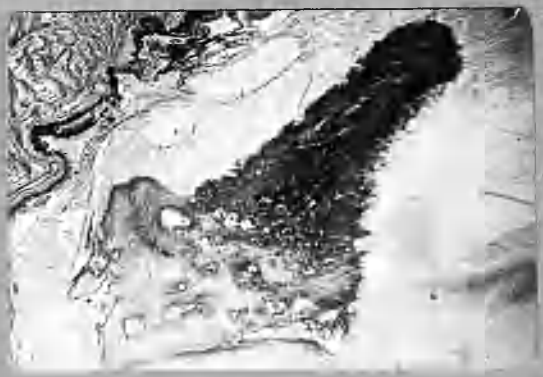


26

Nos. 27, 28 & 29.

No.(27.) Cyclitis: Same section as No. 26.

To show the nature of the growing edge of the bone. Calcareous particles of various sizes are seen in large numbers.

X 150 diams.

No.(28.) Cyclitis: Duration uncertain.

To show the nature of the connections of the growing bone with the surrounding tissues. Fibres are seen spreading out in fan-like form, and fibrous tissue cells are arranged in rows between the fibres. X 150 diams.

No.(29.) Cyclitis: 12 years duration.

To show again, the nature of the connections of the bone with the surrounding tissues. A band of fibrous tissue is seen passing into a cavity at the extremity of a piece of bone. The cavity is partially lined with osteoblasts. The free end of the bone terminates in a strand of fibres between which the cells are becoming arranged in rows.

X 150 diams.

27

28

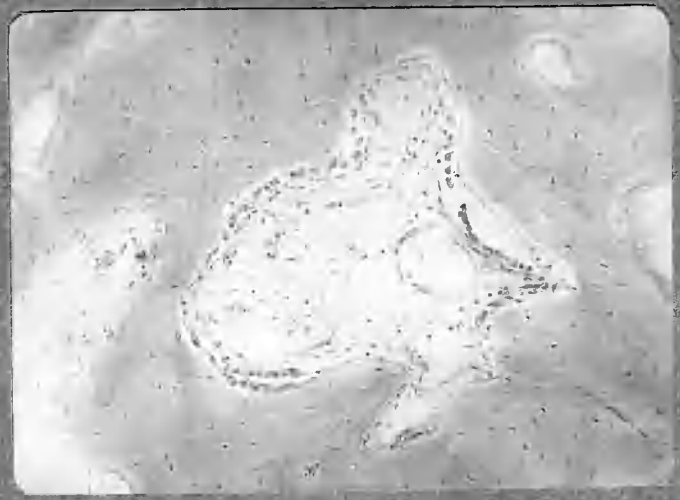
29

No. 30.

Cyclitis: 13 years duration.

To show the structure of the fully formed bone. A large cavity lined with osteoblasts, and containing vascular channels and fine fibrous tissue, is seen surrounded by bony laminæ. The bone corpuscles are seen arranged in rows and indicate the laminae.

X 150 diams.



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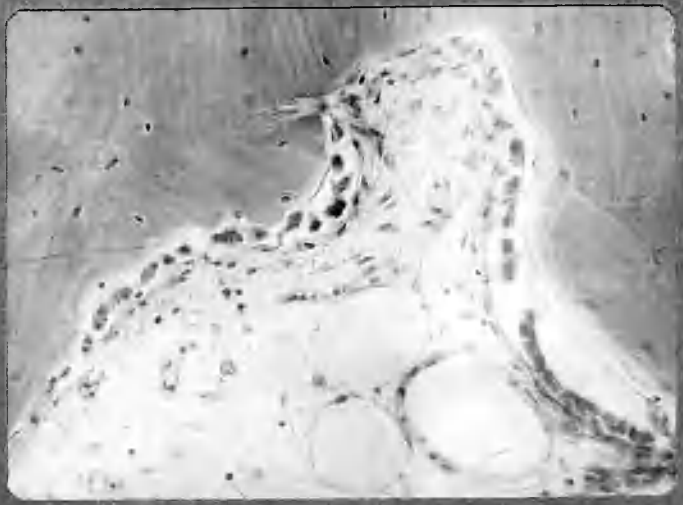
No. 31.

Cyclitis: Part of No. 28.

To show the osteoblasts arranged round the cavity, and the bone corpuscles lying in lacunae.

X 300 diams.



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