Councilman (W. T.)

A CONTRIBUTION

TO THE

STUDY OF INFLAMMATION

AS ILLUSTRATED BY

Induced Keratitis.

By W. T. COUNCILMAN, M. D.

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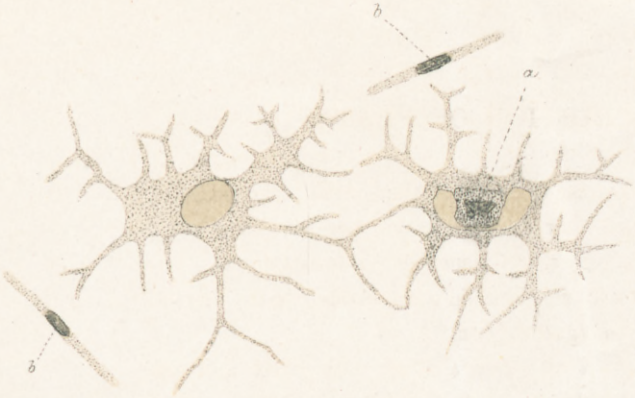
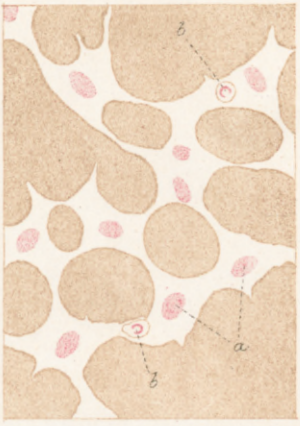


Fig. 1.



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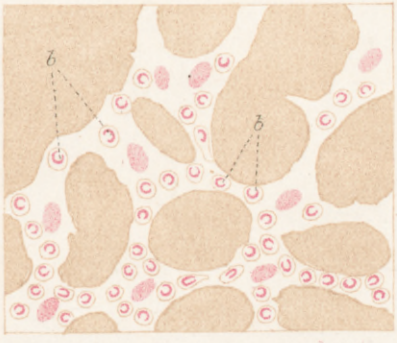

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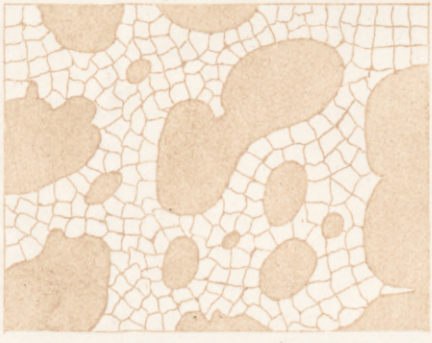

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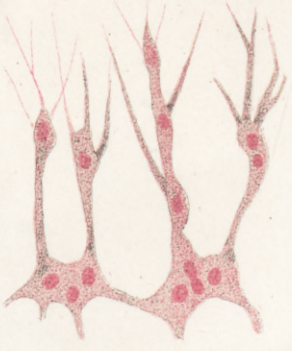

Fig. 6.

E. Huth, Lith. Anst. Berlin.

DESCRIPTION OF PLATE.

Fig. 1. Normal cornea of frog, stained with haematoxylin. Two of the branched corneal corpuscles are shown with a wandering cell, *a*, lying in the cell space with one of them. *b*, *b*, represent two of the wandering cells in the substance of the cornea; these have taken the elongated form.

Fig. 2. Normal cornea of a cat, stained with silver and carmine. The ground substance is stained brown with the silver, leaving the cell spaces unstained. In these are seen the nuclei of the branched cells stained with carmine. *b*, *b*, two wandering cells in the cell spaces.

Fig. 3. Scleral edge of cat's cornea 14 hours after central inflammation. The wandering cells, *b*, *b*, are increased in number, and the communications between the spaces are larger than in *Fig. 2.* Silver and carmine.

Fig. 4. Area of general infiltration, 40 hours after central inflammation. The cell spaces are greatly enlarged and broken up into small areas by the brown silver lines. The ground substance is reduced in amount, in some places represented only as small islands.

Fig. 5. Innermost limit of area of general infiltration. Here, as in No. 4, the cell spaces are greatly enlarged and divided into small areas, in each of which the brightly stained horseshoe nucleus is seen. From this point to the centre no cellular elements are found. Silver and carmine.

Fig. 6. Two corneal corpuscles which have taken on regenerative changes. The nuclei have increased in number, and long processes, which are much branched, have grown out from the parent cell.

INTRODUCTION.

IT would be useless to attempt to give anything but the most limited sketch of the views which have been held concerning the origin of pus and the cellular changes in inflammation, since the time of the establishment of the cell theory. A mere enumeration of the articles written on this subject in the decade of '60–'70 would fill pages. We will however briefly glance over some of the more important ideas which have been or are held on this subject.

Rokitansky was one of the first authors to appear in the field of this literature. He, in accordance with the cell theory of Schwann (that is the free cell formation,) assumed that the pus cells were formed in the exudation, this playing the part of the blastema. These ideas generally prevailed until 1855, when Virchow was led from his knowledge of the connective tissue corpuscle, and its almost universal distribution over all tissues of the body, to dispute this view of the free cell formation and to apply the law "Omnis cellula e cellula," even to pathological new formations. Virchow held that the pus cell was the direct derivative of the connective tissue corpuscle, because wherever he found pus he also found connective tissue in

some of its forms; and since he was obliged from his views of cell formation to have some cell as the parent of the pus cell he took the connective tissue corpuscle.

Stricker now appears as the latest and certainly the ablest defender of these views, though they have undergone essential modifications at his hands. He says that the cells of a tissue under the influence of inflammation, return to their former undifferentiated embryonic condition, become amoeboid and in common with all young cells possess the power of unlimited division. This property holds good for all tissues equally; no matter whether muscle, gland or ganglion cell, they all can undergo this change and become converted into pus cells. He holds also that when the cells return to the embryonic condition they again become capable of differentiation, and that in consequence of this capacity blood-vessels and even blood corpuscles are formed in an inflamed part in the same manner as in the embryo.

Against these views we have what is known as the "wander cell" theory which holds that the pus cells are white blood corpuscles which have escaped from the vessels and then appear in the tissues as pus. Waller, an English physician had as early as 1848, (Philo. Mag., Tom. 29, page 271), observed the passage of the colorless corpuscles through the vessels' walls; at that time his ob-

servations attracted but little attention and were generally distrusted. Cohnheim in 1868, by direct observation (Virchow's Archives, Bd. 40, Seit. 1–86), firmly established this fact that the white corpuscles do pass through the vessels' walls, and as a result of his study of the inflammatory processes in the frog's cornea, tongue and mesentery, asserted that the pus cells are white blood corpuscles. From his study of Keratitis, principally induced by cauterizing the centre of the frog's cornea with silver nitrate, he found that however great the number of pus cells in the inflamed tissue might be, the fixed corneal corpuscles with their processes were unchanged; that the nuclei of the corneal corpuscles did not increase; that the clouding of the cornea always began at the periphery, and from this advances to the centre; that after the injection of pigment granules into the blood some of the pus cells in the cornea were found with similar granules in their bodies.

From these four circumstances, protected furthermore by a direct knowledge that the white corpuscles in inflammation did escape through the vessels in large numbers, he concluded that the pus corpuscles here were not derived from the fixed cells of the cornea, but had wandered in from without. Stricker, as the result of observations made on the frog's cornea and on the cornea of the cat, asserts that the three first arguments of Cohnheim result

from imperfect (mangelhaften) observations and that the conclusion formed from the fourth is illegitimate. According to Stricker the fixed corpuscles do undergo change, their nuclei increase, and the clouding always begins where the injury was inflicted. With regard to the presence of pigment-bearing pus cells in the inflamed cornea, after the previous injection of pigment into the blood, he thinks that the pigment granules could have passed through the vessels' walls as easily as the blood corpuscles and been carried by the lymph streams into the cornea. There they could easily have been taken up by the pus cells which were already produced by multiplication of the corneal corpuscles. Just here I would remark that the passage of solid particles through the vessels' walls without being *carried through* by the white blood corpuscles, easy as Stricker thinks this could take place, has up to this time been seen and described by no one.

That Cohnheim's description does not hold for all cases of induced Keratitis, even in the frog is certain; but the differences can be easily reconciled. Stricker bases all his views of inflammation and of inflammatory new formations on his description of Keratitis. I think I will show in this paper that these views, certainly as far as Keratitis is concerned, are erroneous and may possibly be due even in his case to imperfect (mangelhaften)? observations.

PATHOLOGY

OF

INDUCED KERATITIS.

THERE is no tissue in the body which has been so much used for the study of inflammation with the special view of ascertaining the origin of the pus corpuscle as the cornea. It offers special advantages for this purpose from the comparative ease with which it can be investigated microscopically both in the fresh and prepared condition, from the facility with which inflammation varying in extent and intensity can be produced here, and from the unity of its cellular elements. I can only excuse my temerity in entering upon a field of research in which so many and distinguished investigators have labored, by the fact that when endeavoring to satisfy myself of the correctness of Stricker's views on this subject, I obtained results which lead to conclusions utterly at variance with his, and which I think go far towards clearing up some of those points in the pathology of Keratitis over which there has been most contention.

The corneas of the frog and of the cat have been principally used in my investigations; the latter animal being chosen for studying the processes in the mammal, from the advantages its cornea offers over many others for investigation, and in addition to this, cats can always be readily and cheaply obtained. It will perhaps be well before entering upon the pathology of this tissue to go briefly over its normal histology.

The cornea can be considered to belong to the connective tissue group from the fact that it is made up of branched cells lying in a fibrillated ground substance, and is developed in the mesodermic layer of the blastoderm. These cells, usually spoken of as corpuscles, are large irregular branched bodies arranged in the cornea in layers and flattened antero-posteriorly. If we make a section parallel to the surface we see them represented as large branched cells, appearing then as the hand with fingers extended when we look at the palm, (See Fig. 1). On a section perpendicular to the surface, being seen then in their least diameter, they seem to be little more than mere lines, or following out the former comparison of the hand, as this appears when the side is looked at. These cells communicate by their long processes with the cells next them on the same plane and also by means of short processes with the cells above and below them on different planes.

The balance of the tissue is mainly composed of fibres, which run in various directions, arranged in planes; all those of the same plane having the same direction. These fibres are joined together by a cement substance (Kittsubstanz), which is characterized by its property of always staining brown with silver nitrate. The tissue is richly supplied with nerves arranged in plexuses; the larger of these lying below and giving off branches which go to form finer and finer ones as they ascend towards the epithelium. On the outside over all there is the epidermic layer of conjunctiva and on the posterior surface the layer of flattened cells which forms the outer lining of the anterior chamber. This lamellar arrangement is of especial advantage to us in studying the pathology of the cornea; for although owing to its thinness and curvature it is almost impossible to obtain sections exactly parallel to the surface, we can split it up by means of forceps into leaves as thin as the finest sections could be made.

If we stain the cornea of any animal, preferably that of the frog, with silver nitrate, we find a number of large colorless branched spaces lying in a brown field, and on comparing this with a haematoxylin or gold preparation we see that the two are very similar. In the latter we have the colored cells, communicating with neighboring cells lying in an unstained field; in the other, we have the

colorless spaces in a colored ground communicating with similar spaces. If we now make sections perpendicular to the surface the relation of the two is not altered. Again where in the haematoxylin preparation we had the nerves as dark lines running across the field, in the silver we have corresponding colorless channels. The silver preparation is the negative, and bears much the same relation to the other as the negative of the photograph bears to the positive picture. In the haematoxylin preparation we had the corpuscles and nerves stained; in the silver we have the spaces and channels in which they lie, unstained. This relation of the cell to the cell space must not be supposed to be that of a pea in a bottle; it is much nearer that of the hand in a glove, the cells filling tolerably completely the spaces in which they lie. The channels between these spaces are filled with lymph and form the "Saftcanälchen" of Recklinghausen; lymph channels also surround the nerves. But now we also find even in the normal cornea another sort of cells which do not deserve to be considered along with its fixed histological elements. Their numbers are variable; in some corneas of the same animals being abundant, in others few; sometimes in greater numbers at one portion of the tissue, sometimes at another. In fresh preparations they can be seen to pass by active amoeboid movements from one portion of

the tissue to another, and they never, as far as we can see, stand in any fixed histological relation to the balance of the tissue. I allude to the "wander cells." Their position is not at all constant, sometimes we find them lying in the cell space along with the branched corpuscles, (See *a*, Fig. 1), sometimes in the narrow communication between two spaces, sometimes as long-drawn-out rods in the tissue between the fibres, (*b. b.* Fig. 1), sometimes in the nerve lymph channels, and in one preparation I have been so fortunate as to get one seemingly in the act of passing from the nerve channel into a cell space communicating with this, half of its body lying in the channel, and half in the space.* They can be clearly distinguished from the branched corpuscles both in the fresh condition and when stained; they are much smaller and with most reagents they stain more brilliantly than the others. In fresh preparations in aqueous, they are easily distinguished by their amoeboid movements, their greater index of refraction and their granular contents. So much for the normal cornea. We will now take up the pathological changes which occur after an acute Keratitis has been induced; taking up first the changes which go on in the frog's cornea.

Various means have been used for exciting inflammation here. The passing of a thread through

* The preparation was shown.

the centre of the cornea and bringing it out through the sclera, the various caustics such as croton oil, silver nitrate, caustic potassa, the hot iron (actual cautery), have all been used. With few exceptions they produce results relative to the severity of the stimulus used. Agents such as the hot iron, which at once kill the tissues with which they come in contact, will of course produce less inflammation in surrounding parts, than those like the thread whose working is always more or less continued. A method which I have used on the frog's cornea with excellent results has been to pass a thread through the membrana nictitans and then make several pricks in the cornea with a needle. The inflammation produced by this method will be discussed separately, since results can in this way be obtained which at first seem perplexing. As one of the most typical we will take a cornea which has been inflamed by touching it at the centre with a crystal of silver nitrate. This may be examined after various intervals of time have elapsed, both in the fresh condition and after staining. After about twenty hours from the application of the caustic the most important changes can be seen. To examine fresh, it is necessary to puncture the sound eye and collect the aqueous on a slide; the inflamed cornea is then carefully excised and spread out in this with the posterior surface uppermost. To avoid folds in

the tissue it is better to make three or four incisions at the edge extending for some distance toward the centre; it is then carefully covered with the cover-slip. The powers I have found most satisfactory to use have been the No. 2 immersion of Zeiss ($\frac{1}{17}$), and the E of his dry system ($\frac{1}{8}$).

The first thing to notice here is that the large branched cells are visible; in the normal they cannot be seen at all directly after the cornea is cut out; and only appear after an interval of one-half to one hour. They are more granular than in the uninflamed and present no changes from the normal an hour after the excision of the latter. Why they become at once visible I do not know; it may be due to some change in the refraction of the ground substance caused by the greater amount of fluid now in the tissue, or to some change having taken place in the corpuscle only revealing itself in this way, or to both. The wander cells are now present in vast quantities, exhibiting the most active and varied movements. Sometimes they may be seen to send out a long process, at the end of which a knob presently appears which, growing larger and larger, finally becomes the main body of the cell: as though in this way it had passed from one space to another through a narrow communication. Sometimes we see them as more or less irregular bodies undergoing changes of form and not of position and again as the long staffs

(*b*, *b*, Fig. 1), spoken of in the normal. They are present in the greatest number at the scleral edge, becoming fewer as we proceed to the centre.

Since in the fresh specimens our observations must be made with the cornea in its whole thickness, all these changes become much more clear and can much better be studied after it is stained and split up. For staining I always use the double staining in silver and haematoxylin or carmine; the former being much preferable for the frog. The cornea is exposed by pushing the eye upward from the roof of the mouth, and rubbed smartly with the solid crystal of silver, cut out at the expiration of ten minutes and exposed in glycerine to the action of diffuse daylight. After becoming of a light brown color it is split up and stained in one of the two reagents mentioned, in the usual manner. With care the frog's cornea can easily be split into eight or nine layers. I vastly prefer this method of staining to the gold chloride method which has hitherto been almost exclusively used in these investigations. It has the great advantage of being always certain in its results; while gold, although sometimes giving us beautiful preparations, is the most uncertain of all reagents and its success depends for the most part on unknown circumstances. Another great advantage is that we have both the negative and the positive picture at once, the cell space shown with

the cell within, and the relation of the one to the other always is kept in view. The preparations are mounted in slightly acidulated glycerine. In preparations of the twenty hour cornea examined after this treatment we can easily make out three distinct parts. A central one on which the caustic was applied and which is now represented by a black scar in which the cell spaces are imperfectly seen. Around this is a zone of variable width, in which absolutely no change from the normal can be made out. Here we see the sharply defined cell space with the nucleus, or in deeper staining the body of the cell within. The width of this zone is dependent on the extent of the injury, the length of time which has elapsed since its infliction, and on the general irritability of the tissues of the animal used. Without doubt, from the same amount of irritation, the extent of the pathological changes will, in some animals of the same species, be different. This zone then passes separated by no well defined line into the outermost one. In this outside zone along with the corneal corpuscles other elements can be seen, in numbers far in excess of the branched cells and always in the greatest quantity at the outer edge. These other elements stain in all respects similarly to, and are always of the same size as the wander cells previously described in the normal cornea. They can always be distinguished from the branched

cell even when lying in the same cell space with this. In one place we see the nerve channels filled with them, in another we see them lying in the tissue between the fibres elongated until they have the appearance of rods. Again we see them in the cell spaces or in the narrow inter-space between two cells, their form always influenced by the shape of the cavity in which they lie. Often where they are most numerous in the tissue, the branched corpuscles cannot be made out at all. It may be that these are simply concealed by the vast numbers of the others, or it is surely not unreasonable to assume here that the fixed corpuscles have been absorbed, directly devoured by the young and vigorous strangers. In no case do we see in the cornea corpuscles any indications which would lead us to suppose that multiplication had or was taking place. They stain with any reagent as did the normal and the nucleus always has the same shape as this, except in instances where it may be indented by the presence of the wander cell in the narrow space, (Fig. 1, *a.*) If the cornea be examined at an early period, say twelve hours after the injury, these wander cells will be confined to a small area at the outer edge; if later than twenty, forty for example, they will be found to fill almost the whole cornea, obliterating the intermediate zone in some cases entirely. If we examine the surrounding portions of the sclera and conjunctiva

we will find the blood vessels full of cells just like these and the whole tissue here also infiltrated with them.

A still further proof is furnished by the result of the injection of finely divided coloring matters into the blood. The white blood corpuscles have, as is well known, the power of taking up small foreign bodies with which they come in contact. Now if we inject finely divided cinnabar particles into the anterior abdominal vein or into one of the lymph sacks of the frog, and examine the blood after an interval of a few hours we will find these same particles in many of the white corpuscles. If the cornea is cauterized shortly after the injection and examined after the usual time, we find among the wander cells a great many in which pigment granules are plainly visible, though they differ in no other respect from the others. Sometimes a few granules can be seen in the tissue, not enclosed in the cells. These may be accounted for by supposing that they were here dropped by the wander cell which brought them from the vessel. Stricker himself says that he and Norris have seen one wander cell transfer to another cell of the same nature, some of the vermilion granules contained in its substance. Since the vermilion granule can in no wise contribute to the nutrition of the cell and forms rather a heavy load to be carried around, we can see excellent reasons for this generosity,

and even believe that in the case of not meeting a destitute stranger, the cell would even be willing to throw one away, so to speak. The number of cells containing these granules is far too large to suppose they could have gotten them in any other way than by taking them up in the blood vessels.

The inflammation produced by methods involving a laceration of the corneal tissue gives some results differing from the last described. Here, as in the last case, we see the peripheral portion of the tissue infiltrated with wander cells; *but we see them also elsewhere.* Around the spot where the injury was inflicted, we see cells of the same appearance and offering the same variety of form and position as those at the outside, and here narrowing the zone which in the cauterized corneas we have described as free from them, very materially. How came these cells here? From the outer edge they could not come, for we have lying between this and the centre a zone which in the earlier stages of the process certainly is free from them. If now we combine both methods of producing the inflammation and having cauterized two corneas we make a prick at the outer edge of the cauterized spot of one, and examine the two after the usual interval of time, we will find plenty of wander cells around the laceration in the cornea whose tissue was lacerated, and none in the same spot in the other. Only one conclusion is possible;

that is that they have entered the cornea where its tissue was broken. This is easily comprehensible, since a Keratitis can scarcely be produced in this way without involving at the same time an extended conjunctivitis; and, as a consequence of this, having quantities of white blood corpuscles in the conjunctival secretion. From this source they could easily enter the tissue where broken. The results obtained after passing the ligature through the membrana nictitans point clearly to this. Here a violent conjunctivitis is necessarily set up; many blood vessels in this membrane ruptured and plenty of white corpuscles poured out. As a consequence, in these preparations we have large numbers of wander cells at the point where the prick was made; in some cases they are so plentiful here that every thing else is obscured. After the injection of pigment granules these wander cells also contain them. *No change is seen in the branched corpuscle at either place.*

Proceeding now to the cat's cornea we meet here even in the normal, some difference from that of the frog. The corpuscles are smaller, are more numerous and the cell spaces communicate by larger passages than in the frog. The brightly staining wander cells in the normal cornea here are fewer in number than in the frog's cornea and only found in the cell space, (Fig. 2.) Their special characteristics will be described when we come to speak of the pathological changes.

As a means of exciting inflammation I have, following Stricker, used the solid stick of caustic potassa and found it vastly superior to any other agent. A young cat is preferable to an old one from the fact, that the cornea of the former is much more easily split up into its lamellae than that of the latter. The animal is first aetherized and the cornea touched with the caustic; particular care must be exercised in doing this, as the potassa melts so rapidly on contact with the moist surface that there is great danger of its involving too great an extent of tissue. To avoid this the caustic stick must be pointed (which is easily effected by holding it in a stream of water), and the cornea dried carefully with filter paper. By varying the period of contact an eschar extending a few lamellæ in depth or one involving the whole thickness of the tissue can be produced. The animal is then left in quiet and the cornea cut out and examined after periods of from fourteen to sixty hours.

The silver staining *in vivo* and the after staining with carmine are used. If we examine a cornea now, say forty hours after cauterization and as yet unstained by carmine, the changes found can be divided under two heads. Of these, the first will comprise the changes around the corneal edge, and the second those in the immediate neighborhood of the eschar. In the first we find the cell spaces

somewhat larger and the communications between them wider than in the normal. Scattered about through the tissue we find the strongly refracting rod-like cells, appearing very similar to those we have seen in the frog. If the silver staining has been very deep we find the silver precipitated in the substance of the cell as well as in the ground substance, leaving a clear unstained nucleus in every space. In the immediate neighborhood of the eschar the change is more pronounced and different from anything we have hitherto seen. These changes are all the more important to us, since it is here that Stricker says the corneal corpuscles are undergoing the most rapid proliferation. In the silver preparations we see, lying in the colored ground, groups of small white spaces with dark brown lines separating them from one another; these groups correspond in shape to the enlarged cell spaces, (Fig. 4.) Stricker seems to have confined his observations to this spot and explains the picture by supposing the corneal cell has here broken up into a number of smaller cells and the brown lines mark off the cell limits.

Let us now see what the carmine staining shows in the two parts. In the outer ring we have in each of the slightly enlarged cell spaces the large oval nucleus of the branched cell totally unchanged and staining in all respects exactly like the normal. In rare cases we find, as is also the

case with the normal, (Fig. 2), two of the nuclei in a space. In addition to these, there are other cells which from their characteristic appearance merit a more detailed description. These have a difference in shape according to whether they are found in the cell spaces and nerve canals, or in the proper corneal substance, in which they lie between the fibres. In the former they are round with a brightly staining granular nucleus of the shape of a horse shoe, (Fig. 3, *b*, *b*.) Here they correspond with the wander cells in the normal cornea, (Fig. 2, *b*.) Under higher powers, (eight hundred to one thousand,) the apparently single nucleus is usually found to be composed of three or four small bodies lying in juxtaposition: the mass being always arranged in the shape of a horseshoe. When lying in the tissue between the fibres, they are always elongated and then appear as jointed rods, each joint having the highly stained granular nucleus. At first sight these rod-like bodies would seem to be entirely different from the round cells in the spaces; but, on close inspection at different places, every variation can here be seen, from the slightly elongated cell with an elongated horseshoe nucleus to the long rod. If we now stain some of the blood of the cat, we find that the white blood cells have a nucleus of this horseshoe shape and stain in all respects like these wander cells. Proceeding now from the corneal edge

towards the eschar we come to a place where the corneal corpuscles are wanting, and those limiting this district have taken on changes which will occupy our attention further on. Beyond this line, which can be seen by even a simple lens, the corneal corpuscles are dead—have been destroyed by the caustic. The cell spaces can be seen, most of them much shrunken, but no nucleus in them or anything which would afford us proof of the existence here of a corneal cell. Lying in these cell spaces, but mostly in the tissue are seen multitudes of cells similar to those aforedescribed. These cells become more numerous as we proceed, until we reach a territory where the cell spaces are filled with them. The cell spaces here are enlarged and the communications between neighboring ones are wider; spaces and communications are all full; and no one comparing these cells with those of the outer edge can doubt for a moment that they are similar, (Fig. 5.) Beyond this line of general infiltration the tissue is totally destroyed; by this I mean that not only its living protoplasm is killed, but its physical properties are also altered. Nothing of the cell spaces can here be seen, and apparently the wander cells can make their way no further. Within this line the tissue sloughs.

In corneas examined ten to fourteen hours after cauterization this district of general infiltration is wanting; no wander cells are here seen. In the

other district however, that around the corneal edge, the wander cells are numerous; sometimes at the edge so many will be seen that the faintly stained nucleus of the branched cell is entirely obscured, the wander cells filling up the space. From this edge they become fewer and fewer as we proceed towards the centre. The line of corneal corpuscles, marking off the portion of the cornea in which the corneal corpuscles were destroyed from that portion of the cornea where the corneal corpuscles were uninjured, is not now so well seen, as these corpuscles have as yet taken on no change by which we can distinguish them. We can readily see however, even here, where the living tissue ends.

Now it was beyond this line that we got from the silver preparations the appearance as though the corneal corpuscles had proliferated. Here were the small colorless areas separated by brown lines, (Fig. 4.) From this place was Stricker's drawing made, and here he, judging merely from silver stainings of forty-eight hour corneas supposed the proliferation to have been most rapid. Further examination by better methods and at different periods after cauterization shows us that there is nothing here to proliferate. The tissue is here as bare of living corneal corpuscles as a sheet of paper. In forty-eight hour preparations the line of demarkation is still more evident, and the

tissue beyond more infiltrated with cells than in the twenty-four hour preparations. In all of the portion first described, that along the edge of the sclera, no change can be seen in the nuclei of the branched cells.

In corneas sixty to eighty hours after cauterization, that portion of the tissue surrounded by the infiltration is converted into a slough which easily comes away, and the peripheral portion around the sclera still contains wander cells. In the corneal corpuscles which form the line separating the dead from the living tissue we find changes as early as twenty hours after cauterization. These changes are at this early period only shown by a brighter staining, the whole substance of the cell here stains and elsewhere only the nucleus. At a later period, thirty to forty hours, the nuclei can be seen in different stages of division, and at the same time, long processes are sent out from the cells into the tissue. These processes become longer, nuclei travel up from the old cells into them and thus they form in the dead tissue *new corneal corpuscles but never pus*, (Fig. 6.) These processes and new cells stain in all respects similar to the parent cell from which they originated, and the nuclei have the same shape as those of the old cells though they are stained more brightly and are more granular.

The appearance of a segment of the cornea taken three or four days after injury, in which the proper

branched cells are undergoing this proliferation is most beautiful. The nuclei of the new corpuscles divide rapidly, and in some as many as four can be seen. Even if the whole cornea is destroyed with the exception of a small strip along the outer edge, the corpuscles limiting this take on this renewed activity. The difference between these two processes, the suppurative on the one hand, in which the wander cells are the agents, and the regenerative on the other, by which *new corneal corpuscles are produced from corneal corpuscles* is so clear that no one seeing them side by side could mistake them. In no tissue in the body can the processes of repair be so clearly studied as in the cornea, and in no other tissue can the wander cell theory as to the origin of the pus corpuscle, be so clearly proven to be correct.* These investigations were carried on in the Biological Laboratory of the Johns Hopkins University. I desire to express my thanks to Prof. Martin for facilities afforded me.

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* NOTE.—At a meeting of the Baltimore Academy of Medicine, it was resolved, "That in awarding the prize to any essay, the Baltimore Academy of Medicine is in no wise responsible for the opinions therein expressed."