

THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

FEBRUARY, 1933

COMMUNICATIONS

SUPERFICIAL PUNCTATE KERATITIS

BY

J. H. DOGGART

MOORFIELDS RESEARCH SCHOLAR

"SUPERFICIAL punctate keratitis is a morphological conception."* That is to say, the title is applicable to any corneal affection in which the lesion consists of opaque dots involving the epithelium, Bowman's membrane, or the superficial layers of the substantia propria. It has been repeatedly shown that such a clinical picture can be created by a variety of pathological processes, and that it may also arise without any obvious cause. The more numerous the dots, the more densely will they be aggregated, and there is a tendency for adjacent dots to coalesce with each other, with the result that any case coming for the first time under observation at a late stage of the disease may present appearances to which the adjective punctate may seem inapplicable. Nevertheless, it is unusual for the whole extent of the cornea to be uniformly involved. Therefore a close scrutiny of the less opaque portions will nearly always disclose the punctate character of the original lesions.

Koby's conception of the meaning of superficial punctate keratitis has been criticised on the ground that the term was originally applied by Fuchs to a definite clinical condition with which most ophthalmologists are familiar. I am opposed to this criticism, because clinical and pathological descriptions published by many observers in various countries differ from each other not only in

* Koby's *Slit-Lamp Microscopy of the Living Eye*. Translated by Goulden and Harris, 2nd Edition, p. 161, London, 1930.

minute details but in important features. For example, the characteristic position of the punctate opacities was in Fuchs' experience central. Nuel, on the other hand, found them more often at the periphery. A majority of Fuchs' cases were unilateral. Nearly all those of Nuel were bilateral. Yet in most other respects the clinical notes of Nuel closely accord with those of Fuchs. Moreover, many instances of border-line or transitional cases have been seen, especially during periods of epidemic superficial punctate keratitis in Austria, India, and elsewhere. Personal observations and study of the literature alike induce me to believe that only confusion can arise from an attempt to limit the term to one definite disease. It should be applied without prejudice to a group of conditions which may differ widely from each other concerning their aetiology, duration, and clinical signs.

Review of the Literature

The classical paper on superficial punctate keratitis published by Fuchs in 1889 was based on his experience with 38 cases, whose ages ranged from 7 to 52 years. The second decade was the most commonly affected. Neither sex predominated. Two-thirds of the cases were unilateral. The onset of the disease resembled that of an acute catarrhal conjunctivitis in many particulars, but pain, lachrymation, and photophobia were prominent features. Ciliary injection was also mentioned as a point of differentiation from ordinary conjunctivitis. Corneal lesions manifested themselves about four days after the first symptoms. In the meantime the conjunctival affection had often seemed completely to subside. At this stage a number of gray dots appeared on the cornea, and showed a preference for the central rather than the peripheral portion of that structure. The dots were small, rounded, sharply-defined and gray, the intensity of the gray being accentuated at the centre of each dot. Increase in the size and number of the dots might be observed in the course of the next few days, but a single dot rarely exceeded 0.5 mm. in diameter, although the coalescence of several adjacent ones might subsequently appear to break this rule. In many cases the dots were arranged in rows, or else agglomerated like staphylococci. Careful employment of a magnifying lens showed Fuchs that each dot consisted of a number of fine points of opacity, more closely aggregated at the centre. He judged their situation to be immediately beneath Bowman's membrane. Knob-like elevations were noted of the epithelium overlying the dots. Faint striae sometimes occurred as a transient phenomenon in the substantia propria. Other important clinical features were diminution in corneal sensibility, and hyperaemia of the iris. As a result of this engorgement of the iris vessels

miosis occurred, and the pupil's response to the action of atropine was delayed, but in no case did posterior synechiae supervene. The tension of the affected eye was usually normal; only a few cases showed hypotonia. Acute symptoms rarely lasted more than a few weeks, but a minor degree of irritability often persisted until the disappearance of the gray dots—a process that went on gradually until 1-2 years after their original development. True recurrence was never seen, although there might be repeated slight relapses. Fuchs did not profess to know the cause of superficial punctate keratitis, but he was inclined to ascribe it to some form of chill for two reasons: first, the incidence increased in time of winter; secondly, the onset was often associated with acute catarrhal affections of the respiratory tract.

Adler, on the other hand, was unable to detect any association with respiratory disease in his series of 29 cases. His first glimpse of superficial punctate keratitis is interesting because the manner thereof must be paralleled in the reminiscences of many ophthalmologists. In 1888 Adler was confronted by a girl, aged 14 years, who appeared to be suffering from ordinary acute conjunctivitis—a malady which at that time happened to be prevalent in his practice. The customary simple remedies were prescribed, and she was told that her eyes would recover within a few days. On the eighth day, however, she complained that the left eye "saw through a veil," whereas the other eye had completely recovered. This disability of the left eye was due to multiple opacities involving the superficial layers of the corneal substance in its axial portion. Adler proceeded to give a most illuminating description of superficial punctate keratitis. He kept the patient under periodical observation, and a whole year elapsed before the dots had entirely faded. Having been taken off his guard by the mode of onset in this case, Adler kept a sharp lookout for others, and was able to collect 28 more within a year.

Herbert investigated over 200 cases of epidemic superficial punctate keratitis in Bombay during the winter of 1900-01. On examining fragments of epithelium scraped from the affected cornea for diagnostic purposes he found, in a high proportion of the sufferers, a feebly-staining, capsulated bacillus. This organism he regarded as being responsible for the disease. On the other hand, several ophthalmologists failed to discover it in similar material obtained during subsequent epidemics. But Herbert's cases were manifestly different in many ways from the characteristic condition described by Fuchs. For example, the corneal opacities had usually dispersed within a month; follicles along the upper border of the upper tarsus were a common finding; some of the peripheral spots stained with fluorescein; the limbus was in most cases thickened.

Thickening of the limbal portion of the ocular conjunctiva is mentioned as a prominent feature in Stellwag's paper, and it is significant that in his experience the periphery of the cornea suffered more than the centre. Nuel also found limbal oedema. Wright and his co-workers came to speak of a "limbal type," in which oedema at the limbus was associated with the presence of dots near the edge of the cornea.

Wright's knowledge was gathered from an Indian epidemic during which over 3,500 cases came under the notice of himself and his colleagues. He can therefore speak with authority on the subject of epidemic superficial punctate keratitis. Many of his negative observations are as important as his positive ones. Thus, for instance, he failed to detect the method by which the disease became disseminated. Most of his numerous inoculation experiments were inconclusive. He remarked the *absence* of antecedent catarrhal or febrile illnesses, of associated herpetic affections of the skin, and of neuralgic pains in the area governed by the Gasserian ganglion. The great majority of Wright's cases were unilateral. Symmetrical pupils were the rule—a striking point of distinction from the Fuchs type, in which we expect to see some degree of miosis in the affected eye. Wright's two papers are particularly valuable in that they stress the enormous variety of clinical appearances, and the existence of transitional cases. Dots of opacity were found singly or in hundreds. Their disposition might be central, peripheral, or quadrant. All degrees of severity were recorded; there was the mild, straightforward case of only a few weeks' duration at one end of the scale; at the other end were people suffering from disciform keratitis.

A similar gradation in severity had already been reported by Kirkpatrick at the time of the Madras epidemic ten years before these papers of Wright were published. Wright himself had taken the opportunity to examine some of Kirkpatrick's more severe cases with the slit-lamp, and his observations identified them with the clinical condition of keratitis disciformis, as evidenced by involvement of the whole thickness of the cornea, folds in Descemet's membrane, deposits on the endothelium, and bulging of the posterior surface of the cornea into the anterior chamber. In fact, the large masses of simultaneous clinical material placed at the disposal of Wright and Kirkpatrick by these epidemic visitations enabled them to correlate cases which, if they had occurred sporadically, might have appeared to be members of utterly different groups. Additional support is thus given to a suggestion offered by Fuchs in 1901—namely, that superficial punctate keratitis and keratitis disciformis are essentially the same. Among recent writers who have adopted this view, Verhoeff is conspicuous. Verhoeff, indeed, goes further. He has produced a formidable array of

arguments in favour of his belief that not only these two maladies, but acne rosacea keratitis, recurrent abrasion of the cornea, and various other conditions possess one common pathology. All of them, according to Verhoeff, are types of neuropathic keratitis caused by some shock to the ciliary or to the Gasserian ganglion. In the diversity of the clinical signs he can see no obstacle to this thesis. On the contrary, he argues, uniformity would surely be more surprising, when one considers the immense range of toxic substances to which these delicate ganglia may from time to time be exposed.

Operative interference with the Gasserian ganglion has been known to cause a variety of corneal phenomena, whose consideration is outside the scope of this paper. In most cases any corneal damage that may follow the operation bears no close resemblance to superficial punctate keratitis. Paton has, however, seen such a clinical picture become evident after alcohol injection of the Gasserian ganglion. He regarded it as the expression of a very mild form of neuropathic keratitis.

It will be remembered that Grüter produced superficial punctate keratitis in three subjects by inoculation with the contents of herpes Zoster vesicles. This observer has also seen keratitis profunda appear in a case that began with superficial vesicles. He attributes many of these mysterious corneal affections to the action of the herpes virus, which, he says, exists in two forms. The more virulent variety will produce dendritic keratitis. The milder one will result in vesicular keratitis, superficial punctate keratitis, recurrent erosion of the cornea, keratitis disciformis or profunda. Incongruous experimental lesions may, however, be obtained from the same specimen of virus as a consequence of modifications in virulence brought about by the passage of time or by variations in the medium employed. (Grüter's work has however, been severely criticised by Ridley. See *Trans. Ophthalm. Soc. U. K.*, Vol. LI, pp. 14 and 15, 1931.)

Trantas made observations on the cornea of some 40 patients suffering from measles. In the great majority he found a condition of superficial punctate keratitis emerging within a few days of the outbreak of the skin rash. Bilateral cases predominated. Age and sex did not appear to modify the incidence. There was no impairment of corneal sensation. At the centre of each affected cornea he discovered an area of epithelial haze, behind which were situated gray spots resembling grains of sand in the anterior layers of the substantia propria. These corneal manifestations were for the most part effaced within a week, and without the need for any treatment. Trantas maintained that similar lesions occur in small-pox, chicken-pox, syphilis, pemphigus, eczema and erythema polymorpha.

Valude identified a streptococcus in the conjunctival sac of the

case reported by him in detail. The staphylococcus was held to be responsible in Watkins' case. Rosenzweig described two examples of superficial punctate keratitis arising in the period of convalescence from influenza. To this question of influenza as a possible factor in the aetiology I propose to return later.

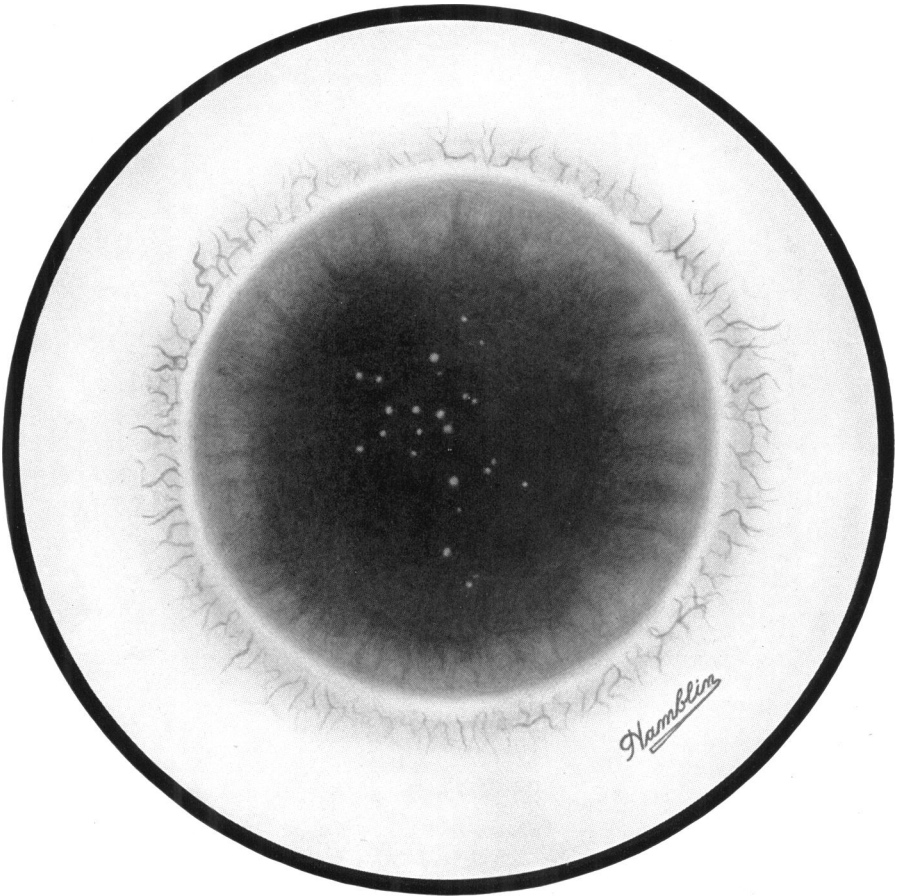
The pathological researches of various observers serve to strengthen the impression that superficial punctate keratitis is not a single disease. Nuel examined slices of cornea shaved from its peripheral region, and the essential condition appeared to him to be a lymph-stasis of the superficial portion of the cornea. He found that the anterior interlamellar spaces were dilated, and that the overlying epithelial cells were oedematous. The actual dots consisted of filamental networks arising in connection with the corneal corpuscles. No adventitious cells were discovered by Nuel. Wehrli, on the other hand, encountered a dense accumulation of lymphocytes in the deeper layers of the epithelium at the affected areas. Stellwag found not only cells, but cocci in the dots. In Verhoeff's case the opacities were disc-shaped necrotic foci immediately beneath Bowman's membrane, and the cellular infiltrates which had invaded adjacent portions of the substantia propria consisted of polymorphonuclear leucocytes. Wright specifically mentions the absence of leucocytic invasion in his specimens.

In the treatment of superficial punctate keratitis a large number of different remedies have been tried, but so far no method appears to have been discovered by means of which the absorption of the corneal opacities can certainly be hastened. So far as the commoner varieties are concerned, nature seldom fails to complete the dispersal of the dots in her own time; but whether that time will be one month or two years is not ascertainable in advance. Nuel's experiences taught him to avoid strong, irritant preparations in cases of superficial punctate keratitis. Chambers' recent paper advocates the same moderation, and he suggests that normal saline solution is as good as any lotion for this purpose. X-ray applications to the cornea have been recommended by several writers.

Personal Observations

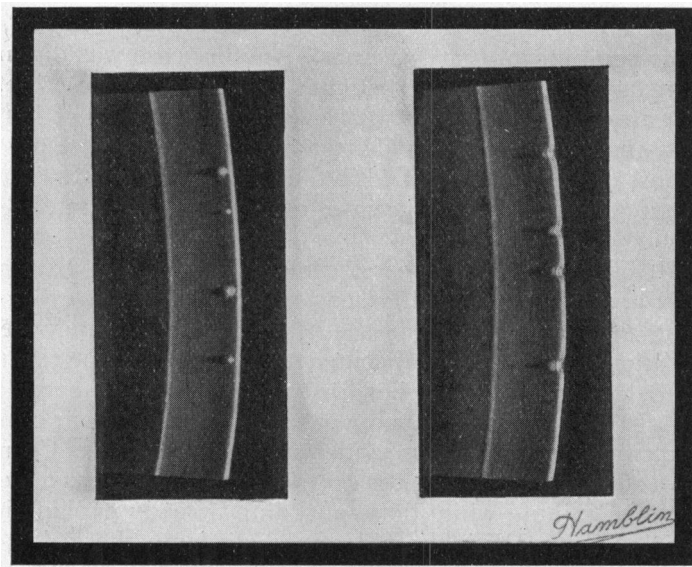
The cases presently to be discussed may for descriptive purposes conveniently be described under three main headings:

- A. Non-recurrent superficial punctate keratitis, in which the main lesions are situated in the anterior layers of the substantia propria.
- B. Multiple epithelial erosions, with or without involvement of the substantia propria.
- C. Miscellaneous conditions in which multiple superficial lesions of the cornea are a prominent feature.



TYPE A and/or B.

A. 43 cases of superficial punctate keratitis of the Fuchs type have been observed, including 19 males and 24 females. The average age of the males was 19 years; that of the females, 27 years. With four exceptions the cases were unilateral. No association with any recent illness or general dyscrasia was detected. In none of these cases was there any loss of epithelium. Some degree of epithelial oedema was, however, invariably present, affecting the whole surface of the cornea sooner or later, although in the early



TYPE A.

TYPE B.

stages it was occasionally confined to the immediate neighbourhood of the dots. The rate at which the dots of opacity became absorbed varied from a fortnight to many months. Nearly one-third of these cases showed some impairment of sensation to a light touch on the lids of the affected eye. It is difficult to explain this sensory disturbance without assuming a lesion of some part of the Gasserian ganglion. In all cases there was complete recovery of sensation as soon as the active stage of keratitis had ended.

The onset of this condition is in my experience commoner in winter than in summer. During the winter 1930-31 such cases appeared at different hospitals in London so frequently as to constitute an epidemic visitation. On the other hand, it is possible to do hospital work for months at a time without encountering a single case, and it is during those periods that the physical signs are most likely to be misinterpreted or overlooked.

It is perhaps inevitable that cases seen before the emergence of the corneal dots should often be diagnosed as ordinary conjunctivitis. In a busy out-patient department it is not difficult for the same mistake to occur even when corneal signs have manifested themselves, because these signs may consist merely of two or three small, inconspicuous maculae. The patient's eye is not endangered by this error, although the reputation of the surgeon may be lowered when the patient comes to the height of his discomfort at a time when, according to the original prognosis, he might have expected to have become free from symptoms. I have more than once seen a case diagnosed as foreign body of the cornea, and treated by scraping of that structure. Another case was diagnosed elsewhere as glaucoma. This patient was treated with eserine, and told that an operation would be necessary. In neither of his eyes was there the slightest real evidence of glaucoma. These mistakes can almost always be avoided by attention to careful routine examination. Three illustrative cases of superficial punctate keratitis will now be described.

CASE I, a girl, aged 15 years, came to hospital in November, 1931, giving a history of gritty sensations in the right eye for the preceding two days. I did not see her at her first attendance, but her condition was noted as subacute conjunctivitis of the right eye. One week later, when I saw her for the first time, she complained that the right eye now felt much worse. On examination, conjunctival and ciliary injection were evident in the affected eye. Corrected vision was 6/24. Occupying the centre of the cornea was a closely-set cluster of minute white dots, affording a ready explanation of the visual defect. With the aid of the slit-lamp these dots were located in the anterior layers of the substantia propria. Epithelial oedema and the presence of floating particles in the anterior chamber were noticed. There was total anaesthesia of the right cornea. The skin of the right upper and lower lids was insensitive to light touch, whereas no such abnormality was found on the lids of the unaffected left eye. For the next few weeks this patient was examined at weekly intervals, and remained under treatment with normal saline solution, 0.5 per cent. atropine drops, and dark glasses. The opacities rapidly faded until no trace of them remained at the end of six weeks, by which time the sensation in the cornea and the skin of the lids had become restored, and corrected vision had recovered to 6/5.

CASE II was a boy, aged 10 years, who first came to Moorfields in July, 1930. The right eye was said to have been red and irritable for two months, without any history of trauma or of antecedent illness. Conjunctivitis was present in the right eye. The right cornea showed a multitude of round, gray opacities, situated chiefly in the centre, and involving the superficial layers

of the substantia propria. The whole of the corneal epithelium was oedematous, and numerous particles were floating in the anterior chamber. A moderate degree of engorgement of the iris vessels was observed, but full mydriasis was attained by the use of homatropine, although the response of the right eye to this drug was delayed as compared with that of the unaffected left eye. The right cornea was anaesthetic. Corrected vision in the right eye was 6/36 only. During the next few months further examinations were made at intervals, and the same treatment employed as in Case I. By November, 1930, the dots had definitely begun to retrogress, having become less distinct and less rounded, but at least 30 of them were still visible. A slight feeling of irritability, similar to that which is occasioned by the presence of a foreign body in the conjunctival sac, was still occasionally noticed by the patient in his right eye. By the beginning of 1931, the only remaining symptom was a sensation of faint haziness in front of the right eye, the corrected vision of which had now recovered to 6/12. Only three small, faint, irregular-shaped opacities could now be detected. In May, 1931, all symptoms and physical signs had disappeared. Corrected vision was 6/6 easily. This last state of affairs was also found on re-examination during September, 1931, and there had been no further trouble in the intervening months.

CASE III, a girl, aged 22 years, came complaining of an irritable left eye for the previous three months. Her left corneal opacities were obvious even to naked-eye examination. They were confined to the centre, and were so large and distinct that they recalled to mind the condition of nodular keratitis. The slit-lamp proved that they were situated in the anterior layers of the substantia propria. Corrected vision was reduced to 6/18. When I saw her again three weeks later, I was astonished to find that no trace of the opacities remained. Corrected vision had recovered to 6/9, and would no doubt have been better than this, but for the presence of a considerable astigmatic refractive error.

In the three cases described above, there had been no known disturbance in general health. The fundi were normal. Treatment was limited to simple remedies, which are, in my opinion, at least as valuable as more heroic measures. I have seen cases where strong lotions and repeated applications of silver nitrate have been employed, and my impression is that these strong chemicals merely enhance and prolong the symptoms of irritability.

B. Multiple epithelial erosions of the cornea occur under many different conditions, and are usually accompanied by some disturbance of the adjacent anterior layers of the corneal substance. The vulnerability of corneal epithelium to gonococcal pus is well-known, but it is not uncommon for epithelial loss to be associated with acute conjunctivitis caused by far less virulent organisms.

For example, during the Autumn of 1931 I saw several cases of multiple epithelial erosions with acute conjunctivitis, in which bacteriological examinations revealed only the Koch-Weeks bacillus.

During the convalescent period after an attack of acute infectious disease, people commonly suffer from a conjunctivitis in which lacrymation and blepharospasm are outstanding symptoms. Influenza is particularly prone to be the forerunner of this complaint. Measles and scarlet fever are frequently to blame. In such cases the epithelium of the cornea is seldom intact. On examination there will probably be found multiple staining-points, as well as grey dots representing areas of incompletely healed earlier erosions. If none of the dots takes the fluorescein stain at the time of examination, then the case may closely resemble those of the Fuchs type which have been considered in the previous section. Differentiation is sometimes impossible without recourse to the slit-lamp. This instrument will at once reveal the depth of the opacities, which, if they involve the epithelium as well as the anterior layers of the substance, probably represent healed erosions. The opacities in Fuchs' superficial punctate keratitis are limited to the substantia propria: there will, of course, be some degree of haziness of the overlying epithelium from oedematous changes, but such haziness is easily distinguishable from an opacity that is the result of actual scarring. Some writers have ascribed to influenza the preponderant aetiological rôle in cases of superficial punctate keratitis, and it is certainly true to say that influenza is an important causative factor, provided we accept Koby's definition quoted at the beginning of this paper. It is manifest, however, that some confusion has formerly arisen between the Fuchs variety and the type with multiple erosions. So far as the Fuchs type is concerned, I have never been able to find any relationship with influenza, and I suspect that the connection alleged by some authors is due to their not distinguishing the Fuchs cases from those in which loss of epithelium occurs.

The differentiation of these two groups by means of the slit-lamp is not a matter of mere academic interest or hair-splitting. It has some practical importance in building up a prognosis, because there is great diversity of behaviour between the two groups. In Fuchs' superficial punctate keratitis no true recurrences have been recorded. Although the dots of opacity may endure for as long as two years, and although some degree of irritability may persist until their complete disappearance, yet they do not come back when once they have gone. Thus it is reasonable to tell a patient suffering from this malady that he will in all likelihood steadily improve. Multiple erosions, on the other hand, are apt to behave very differently, especially when they are the sequel of such a

debilitating disease as influenza. Even with comparatively mild attacks, recovery is seldom uninterrupted. A fresh collection of staining-points may appear immediately after the original erosions have healed over. Some of these cases are difficult to distinguish from dendritic ulcer. In this connection I am not referring to the classical type of dendritic ulcer with its well-marked buds and branches, but to a border-line, less well-defined type of case, which begins insidiously, and conceals its dendritic nature for some time. However, it may be that there is no real distinction.

Multiple erosions may also arise in certain factory workers as a result of contact with irritating chemical vapours or fragments of dust. Mustard-gas is one of the substances that affect the cornea in this way. There are men to-day who still suffer from severe relapsing ulceration, the result of burns from mustard-gas 15 years ago. In some cases I have seen multiple erosions appear in healthy adults who could give no history of antecedent illness, nor of trauma, nor of exposure to any noxious substances. It is at least possible that some of these people may have sustained injury from dust or vapour without their having been aware of it at the time.

Multiple erosions of the cornea, however they are caused, may be the prelude to an invasion of the cornea by large superficial blood-vessels developing in continuity with those that supply the conjunctiva. It is well-known that vascularisation is one of the devices employed by Nature to assist in the healing of corneal ulcers, and that these adventitious vessels in a favourable case undergo considerable shrinkage after the completion of their useful purpose, although they seldom or never become entirely obliterated. In many cases of multiple erosion, however, the beneficent purpose of the new-formed vessels is more than counteracted by their obstinate progress toward the centre of the cornea. These superficial vessels may become so large that the whole surface of the cornea is rendered opaque and irregular, so that not only is there serious impairment of vision, but the patient is subjected to recurrent attacks of irritability over a period of many years.

Nobody has yet explained why a lesion that originally seemed to be localized and insignificant may in some patients excite the formation of large, intertwining vessels all over the cornea; whereas, in other patients, a lesion presenting almost identical signs may heal up without any vascular encroachment. I was interested to learn from Mr. F. T. Ridley last year that vascularisation is the normal response of the rabbit's cornea to almost any infection. He found experimentally that various organisms selected at random and deposited on to a small corneal abrasion in one of these animals will nearly always lead to the creation of adventitious vessels.

The distinction between the corneal opacities described in Section A, and those that have been dealt with in Section B, is emphasised in the accompanying slit-lamp diagrams.

CASE IV, a man, aged 49 years, was confined to bed for several days with a sharp attack of influenza. During the first week of convalescence he began to suffer pain in his right eye. The left eye also became painful a few days later, and he therefore attended hospital. He said that both eyes had been similarly affected during convalescence from influenza several times during the previous ten years. On both corneae there were a few small areas which were stained with fluorescein. Multiple small, irregular-shaped nebulae were seen scattered over all portions of the corneae, but chiefly in the lower peripheral regions. On slit-lamp examination the corneal surface in each eye exhibited numerous irregularities in the situation of these nebulae, which were seen to involve the epithelium as well as the anterior layers of the substantia propria. Numerous particles were seen floating in the anterior chamber. The irides appeared normal.

CASE V, a healthy-looking man, aged 20 years, came recently to hospital, complaining that both eyes had suffered from intermittent attacks, often lasting for weeks at a time, of redness and watering during the past year. Until a year ago he had never noticed anything wrong with his eyes. The left one had been the first to suffer. There was no history of trauma. On examination the right eye was white and quiet. A few superficial opacities were observed on the right cornea, situated in the anterior layers of the substantia, and in the epithelium. In the left eye the conjunctiva was much inflamed. Ciliary injection was obvious. Superficial vessels were seen encroaching on the periphery of the cornea for a distance of 2-4 mm. The whole of the surface epithelium was oedematous. At least 50 corneal opacities were present, involving the same layers as those that were seen in the right eye, and showing a preference for the nasal half of the cornea. In neither eye was there any evidence of trachoma.

CASE VI is a girl, aged 17 years, whose right eye has been intermittently irritable for over six years. She has been under my observation at intervals for the last two years. In the right cornea there is well-marked peripheral vascularisation, together with numerous superficial opacities similar to those described in Case V. Whenever she has a recurrence, it is possible to demonstrate a few staining-points on the right cornea. The left eye is normal. General health is excellent.

CASE VII, a man, aged 35 years, came recently to hospital, having suddenly noticed that his left eye could not see so well as his right. He gave a history of both eyes having been bandaged for three weeks after exposure to mustard-gas in 1918. He was more

fortunate than most victims of this injury, in that he had escaped recurrent inflammatory attacks. The corneal appearances in both eyes may best be likened to a combination of nodular and reticular keratitis. The opacities, which involved the epithelium and the anterior layers of the substantia propria, were situated for the most part centrally and below. The fact that they were more abundant in the left than in the right eye amply accounted for the difference in visual acuity noticed by the patient. There were also a few superficial, irregular-shaped hyaline deposits near the limbus. The conjunctival vessels exhibited the "beading" phenomenon—a sign highly characteristic of injury by mustard-gas, and produced by alteration in calibre at frequent intervals along the course of the individual vessels.

C. The following section is intended to deal with a variety of conditions in which multiple superficial lesions of the cornea are a prominent feature.

Oedema of the corneal epithelium occurs with severe conjunctivitis, especially in that variety which is due to the gonococcus. It accompanies raised intra-ocular pressure, and inflammation in any portion of the uveal tract. It can, moreover, be detected in nearly all affections of the cornea. When this oedema has been provoked by some inflammatory trouble deep in the globe, the resulting vacuoles tend to be regularly disposed over the whole surface of the cornea. Individual vacuoles may in these circumstances be small enough to escape detection as such, on being examined through a loupe. They will, however, collectively produce some diminution in the natural polish of the cornea, thereby suggesting the use of the slit-lamp, whose superior magnification will display them.

In epithelial oedema due to corneal affections, on the other hand, we seldom see this fine, uniform "bedewing." There is usually some considerable range of variety in the size of the vacuoles, whose larger examples are visible under such magnification as can be obtained by using the loupe. In many cases the oedema is confined to a fraction of the surface of the cornea, or may be far more advanced in some regions than in others.

Epithelial oedema can be seen localized in the neighbourhood of recent corneal abrasions, old corneal scars, superficial new vessels, and dots of infiltration, although the oedema will, in the last-mentioned condition, probably be more widespread after the initial stages. In Fuchs' epithelial dystrophy the centre of the cornea is the first region to be affected by oedema. A typical case will show numerous large vacuoles at the centre; smaller ones in the paracentral region; and perhaps at the periphery there will be none at all, with the exception of those exceedingly small ones which constitute a normal feature of the zone immediately

within the limbus. Widespread oedema of the corneal epithelium is a characteristic feature of neuropathic keratitis, which, in mild cases, engenders small vacuoles. In severe cases adjacent vacuoles may coalesce with such rapidity that the whole of the epithelium may be floated off within a few hours. Oedematous changes also occur in the corneal cells when they are unduly exposed to the atmosphere, *e.g.*, in severe cases of exophthalmic goitre. In this connection it will be remembered that epithelial oedema represents the earliest stage in band-shaped opacity of the cornea. It is necessary to regard oedema of these cells as the earliest evidence of their degeneration. When the oedema is moderate in amount, and especially when it is due to some removable cause, it does not preclude recovery on the part of the cells concerned. On the other hand, oedema is often merely the forerunner of further degenerative changes.

The walls of the vacuoles that are formed by swollen epithelial cells not uncommonly fail to withstand the pressure of their fluid contents. When they have ruptured, there is a tendency for the surface loss to be made good by the surviving epithelium, but the attempt at repair may be frustrated by the continuance or intensification of those conditions which originally gave rise to oedema. In these circumstances epithelial proliferation may proceed in wasteful and irregular fashion to form the clinical picture of filiform keratitis. The cornea will be dotted with white flakes comprising coils of abortive epithelium. Calcification is another possible sequel of oedema, especially after the oedema has been prolonged. In advanced cases of Fuchs' epithelial dystrophy it is not uncommon for calcareous changes to manifest themselves on the surface of the cornea. Further examples of swollen epithelium becoming calcified will presently be given among the illustrative cases.

During the last two years I have seen at least six instances of a bilateral condition which, for want of a better name, I shall designate "granular substantia propria." On examining this type of cornea with a loupe, one is at first puzzled. In the corneal substance there are irregular-shaped grey areas with indistinct margins. Surface polish is unimpaired. With the slit-lamp these grey irregularities appear to consist of broken and distorted corneal lamellae, reminiscent of that broken vitreous framework which is so constantly to be seen in severe uveitis. In the first case of "granular substantia propria" that came to my notice, the grey areas were most abundant in the centre of the cornea; under the magnification of a loupe they were sufficiently obvious to be described as opacities; but I was surprised to find that the patient's vision was normal. I noticed the same absence of visual impairment in cases seen subsequently. It occurred to me that a parallel,

or at least an analogous non-interference with vision was associated with relief of the adult nucleus—a phenomenon which, even in its most exaggerated form, does not indicate defective vision.

Recurrent corneal abrasion is a term that covers a multitude of diverse clinical appearances. It was originally intended to express the conception that, after partial denudation of the corneal epithelium by a scratch, the resulting defect may be repaired by cells whose abnormally loose attachment exposes them to the risk of being plucked off by sudden movements of the upper eyelid, even after many months have elapsed since the original lesion. That this theory may account for some of the cases it is impossible to deny. It is equally impossible to accept the same explanation for all of them. I have on several occasions been able to observe, in patients whose clinical behaviour in all other respects imitated the classical recurrent abrasion, that the lesion at the second attack was in fact remote from the original abrasion. In other cases the corneal trouble, having first presented the appearances of a recurrent abrasion, may finally display the signs of superficial punctate keratitis. Opacities of all shapes and sizes may develop. Relapses and recurrences may be numerous, until the vision of the affected eye is much reduced.

It would be superfluous in this paper to comment in detail on nodular keratitis and leprosy of the cornea, although the possibility of these conditions must sometimes be considered in the diagnosis of a difficult case. Acne rosacea, on the other hand, is sufficiently common to deserve consideration. It is well-known that, in a minority of cases of this disease, the ocular manifestations may precede those of the face, thereby leading to confusion in diagnosis. Furthermore, the cornea may be dotted with small opacities before it has undergone the characteristic vascularisation. The conclusion to be drawn is obvious. A patient in the early stages of acne rosacea may at first appear to be suffering from those varieties of superficial punctate keratitis which were considered in Sections A and B.

Multiple foreign bodies embedded in the cornea may be confused with superficial punctate keratitis. Another possible source of fallacy arises when some trivial affection, *e.g.*, conjunctivitis or a small corneal abrasion, happens to attack an eye whose cornea is studded with dots marking the site of former foreign bodies. Unless care is exercised in the examination, these opacities may be confused with active infiltrates, and so lead to an incorrect diagnosis of superficial punctate keratitis. Such mistakes are rendered far less likely by the use of the slit-lamp in all doubtful cases.

CASE VIII, a woman, aged 60 years, came to hospital in September, 1930, complaining of failure in the vision of the left

eye for the previous three years. On examination the right eye showed epithelial bedewing all over the cornea, numerous opacities, vacuoles and crystals in the anterior cortex, early cupuliform cataract, vitreous floaters, old central choroiditis, and attenuated retinal arteries. Corrected vision was 6/24. In the left eye there was an even more pronounced bedewing of the corneal epithelium. Many pigment granules were seen on the back of the cornea, but the endothelium appeared healthy. A hypermature cataract was present. Vision was limited to the appreciation of hand movements. A few months later the left lens was extracted, the anterior chamber irrigated, and the greatly thickened anterior capsule removed. She recovered well from the operation, and six weeks later underwent a left needling operation, after which her corrected vision was 6/12 partly. Fundus examination revealed large patches of old choroiditis. Six months after the cataract extraction the left cornea showed numerous white, apparently calcareous dots confined to the epithelium, scattered more abundantly at the centre than in the upper portion, and still more abundantly down below. Corneal sensation was normal. Corrected vision was maintained at 6/12 partly.

CASE IX is another example of calcareous changes following prolonged epithelial oedema. The patient is a woman, aged 56 years, who has suffered from lack of sensation in the area supplied by the first division of the fifth right cranial nerve ever since an operation 15 years ago. The right cornea was of course completely anaesthetic. Flat vesicles, irregular in shape and in size, were seen over most of the surface of the cornea, but in the central region many white dots were seen to have replaced the vesicles. Corrected vision in this eye was 6/36; in the fellow eye, 6/9. Early diabetic retinitis was present in each eye.

CASE X, a woman, aged 53 years, was first seen at hospital in October, 1931. She was diagnosed as right conjunctivitis, painted with silver nitrate, and given a lotion containing boracic acid and zinc. One month later, when I saw her for the first time, she said that her right eye was still more uncomfortable. In addition to the right conjunctivitis, it was now possible to see that the right cornea was oedematous over its whole surface. On the lower portion of the cornea, where the oedema was most intense, there were a few white dots involving the epithelium and the anterior layers of the substantia propria. One month later the left cornea was dotted with a few similar opacities, and conjunctivitis was present in this eye also. After the lapse of another fortnight there were no opacities to be seen on the left cornea. The right cornea showed some closely-set dots on the lower and inner quadrant, but many of those that were previously seen had disappeared. When I saw this patient again five months later, she had a typical

acne rosacea of the face. She assured me that her face had never before suffered in this way. I have very little doubt that later she will proceed to develop acne rosacea keratitis in its more characteristic form.

CASE XI, a woman, aged 52 years, has had irritable eyes for four and a half years. For the last ten years she has suffered from dryness of the mouth. There has been no appreciable change in her condition since she began to come for periodical examinations nearly three years ago. The tongue is exceedingly dry, large, and wrinkled. There is bilateral enlargement of the parotid and submaxillary salivary glands. Conjunctivitis is present on both sides. She cannot form tears. Both corneae show roughening of their surface, superficial gray opacities, and tags of swollen, irregularly proliferated epithelium. She has undergone a short course of local X-ray applications for the corneal condition within the last six months, but no benefit has accrued. Normal saline lotion and parolein drops afford her more relief than any other of the remedies employed. It is said that deficiency in the lacrymal secretion does not of itself deprive the cornea and conjunctival sac of their proper lubrication. If this statement be true, then one must also assume some derangement of her accessory conjunctival glands.

CASE XII, a man, aged 24 years, recently attended hospital with a history of gritty sensations in the right eye for one month, and in the left eye for two months. There were many small, superficial opacities on each cornea. Both conjunctivae were somewhat inflamed. On examination with the slit-lamp the opacities were seen to involve the epithelium as well as the anterior layers of the substantia propria. A number of golden granules were found embedded near the surface of each cornea. Enquiry revealed that the patient was working in a sulphurous atmosphere, and was often employed in scraping-off paint. This case of multiple foreign bodies had been, on preliminary investigation with a loupe, most suggestive of superficial punctate keratitis.

I desire to thank all the surgeons at Moorfields Eye Hospital for their kindness in allowing me to make these observations on the patients under their care. To Sir John Parsons and to Mr. Charles Goulden I am particularly indebted for the encouragement and the clinical instruction which they have so generously given.

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