THE BACTERIOLOGICAL ASPECTS OF THE PROBLEM OF NEUROPATHIC KERATITIS.

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I.

THE intimate relationship of neuropathic keratitis to disturbance of the fifth nerve and Gasserian ganglion has resulted in the pathology of this lesion being regarded in a very different light from that of other corneal affections, the eye changes in all cases being considered as secondary to the morbid condition or disturbance of the Gasserian ganglion. That the cause of the disease is difficult to elucidate is seen by the many hypotheses which have from time to time been propounded as the solution to the question, from the number of opponents who have taken the field on one or the other of the sides, and also from the manner in which these have at various times altered or modified their views. Before, then, we can bring forward the result of our investigations it is necessary that the several hypotheses should be mentioned. But as Wilbrand and Saenger¹ have set out the details of the work and controversies on this subject so fully we need only briefly enunciate these hypotheses and give in outline the arguments for and against.

1. THE PURELY TROPHIC HYPOTHESIS.

Magendie² showed that neuropathic keratitis occurred in animals after section of the Gasserian ganglion, and asserted that trophic fibres for the cornea travelling in the fifth reached their destination by the ciliary nerves. Further, by experiments conducted by Magendie and Claude Bernard³ and later still by Gaule,^{4,5} it was shown that when the Gasserian ganglion was cut across, especially in its anterior part, neuropathic keratitis developed rapidly, but that when the fifth root was divided, although corneal anaesthesia was produced, keratitis either did not supervene, or else was late in onset and mild in character. This fact is supported by the clinical observations of Bernhardt⁶ and Erb,⁷ also by v. Graefe,⁸ who regards the lessened secretion of tears, a necessary result in his opinion of extirpation of the Gasserian ganglion, as only accelerating the condition. These trophic fibres were thought by Gaule to be connected with the numerous cells which he found in the intracranial portion of the ramus ophthalmicus in rabbits.

2. THE TROPHIC TRAUMATIC HYPOTHESIS.

(a) *Trophic with Central Irritation.*

Wilbrand and Saenger¹ consider that trophic nerves play a considerable rôle in the preservation of the eye, but do not believe that the preservation or destruction of these fibres alone determines the presence or absence of keratitis. They support the view that whilst the loss of trophic fibres is the predisposing cause, the exciting cause depends on central irritation of the roots of the nerves or of the ganglion cells. In those cases of trigeminal neurectomy of Krause's⁹ which developed neuropathic keratitis the extreme severity of the operation entailing rupture or irritation of the trigeminal branches and the loss of the trophic fibres were in their opinion the etiological factors, else, had it depended only on the severance of the cornea from its trophic nerves, all the cases would have developed keratitis. By this means also they explain those cases of trophic keratitis, as they term the affection, associated with impaired or increased sensitiveness of the cornea.

Parsons,¹⁰ referring to the work carried out by Head in conjunction with Sherren,¹¹ Rivers,¹² and Thompson,¹³ dealing with the paths of efferent impulses in the peripheral nerves and cord, and to the work of Bayliss,¹⁴ in relation to antidromic impulses in afferent nerves, shows that the absence of protopathic sensation favours bed-sores; that on the recovery of these fibres decubitus tends to heal rapidly; and also that antidromic fibres can be experimentally excited in a nerve of a cat after that nerve has been divided and reunited. "Hence," he continues, "it may be considered proved that the power of producing

changes in the skin of the periphery is a function of fibres which run in the protopathic system." These fibres may conduct impulses antidromal in character the stimulation of which by some central irritation produces "a deleterious effect upon the nutrition of the peripheral organs." That the neuropathic condition of the eye is due to similar factors appears to Parsons as probable, and for these reasons he considers that the trophic-and-central-traumatic hypothesis "explains better than any other all the diverse clinical facts which have accumulated."

Flemming,¹⁵ another supporter of this hypothesis, states in favour of the trophic element that other trophic changes may be observed in fifth nerve lesions, and in support of the necessity of the added factor—central irritation—gives cases to show that when neuropathic keratitis develops the fifth nerve has been only partially divided. In conclusion he says "that the nutrition of the eyeball is directly dependent on the integrity and nutrition of certain nerve fibres contained in the Gasserian ganglion and ophthalmic nerve, and that irritation of these fibres leads to those changes in the nutrition of the cornea which are regarded as neuropathic keratitis."

(b) *Trophic with Peripheral Irritation (other than Organisms).*

Samuel,¹⁶ from observations on other parts of the body, imagines a system of centripetal and centrifugal trophic nerve fibres, whose centre he places in the Gasserian ganglion, the disturbance of which renders the eye less capable of resistance, so that slight irritations of the cornea which a normal eye would withstand without injury are capable of setting up this condition. Büttner¹⁷ found that a glass shield or a wire net strapped in front of the eye was a preservative measure against traumata which a normal eye could withstand without injury. He considers the loss of sensation an unimportant factor.

3. THE VASOMOTOR HYPOTHESIS.

Spalitta¹⁸ is the chief supporter of this hypothesis. He bases his conclusions on certain experiments in which, after removing the Gasserian ganglion, he noticed very marked vaso-constriction of the vessels of the eye, especially in the pericorneal area, and also necrosis of the cornea. This necrosis he attributed to the vaso-constriction. When, however, he removed the cervical sympathetic ganglion and subsequently the Gasserian ganglion, the vaso-constriction of the uncomplicated Gasserian ganglion paralysis could not be effected and keratitis did not develop.

4. THE VASOMOTOR TRAUMATIC HYPOTHESIS.

Schiff¹⁹ holds that, following the excision of the Gasserian ganglion, there is a hyperaemia which lasts for about twelve days. After this time it begins to subside, appearing only at increasingly long intervals till it finally disappears. Occasionally, however, the hyperaemia persists, and only when this occurs can external injurious mechanisms come into operation. Seydel,²⁰ another upholder of the hypothesis, reports his observations in 6 cases. In 3 of these there was an uncomplicated trigeminal paralysis, and no evidence of neuropathic keratitis was found. In the other 3, in addition to the trigeminal paralysis, there was disease of the sympathetic, as was evidenced by the enophthalmos, narrowing of the palpebral fissure, and myosis. All these cases developed keratitis. Seydel's view is that vasomotor disturbance, anaesthesia, and sympathetic paralysis are all necessary as predisposing causes, and that slight traumata of the cornea in the centre where the nutrition is least good are the exciting cause, a necrosis associated with inflammatory symptoms being the first change produced.

5. THE PURELY TRAUMATIC HYPOTHESIS.

Snellen, Senfleben,²¹ and Gudden²² attempted, by experimental investigation, to prove that when the eye was kept carefully protected, as by a shield or by sewing the lids together, neuropathic keratitis never occurred. They held that animals, owing to the anaesthesia of the part, were not so careful in avoiding obstacles; and that foreign bodies gaining admittance were not so promptly expelled as their presence was not recognized. Cases of lagophthalmos associated with paralysis of the fifth are given, and cases also cited of paralysis of the fifth and ptosis without neuropathic changes.

6. THE DESICCATION HYPOTHESIS.

This is supported by Feuer,²³ Hippel,^{24, 25} and Ollendorff,²⁶ who consider that after trigeminal neurectomy there is a marked diminution in the secretion of tears, and that there is also a great lessening in the frequency of blinking on the affected side—a diminution more evident in animals than in man. As a result of these the part of the cornea exposed in the palpebral fissure becomes dried, and necrosis results. The necrosed part then acts as an irritant, inflammation sets in, and the slough is expelled. Protection of the eye by a shield or by stitching the lids together necessarily diminishes the evaporation and prevents the onset of neuropathic keratitis.

CRITICISM OF THE ABOVE HYPOTHESES.

Before proceeding to the last hypothesis—the mycotic—some of the chief arguments against the views above mentioned must be brought forward.

It is a recognized fact that, especially in human beings, after trigeminal neurectomy only a certain proportion of the patients develop neuropathic changes of the cornea. Wilbrand and Saenger give the proportion as a third, and our own statistics, as will be seen later, are almost the same. Now if the loss of the trophic fibres were the cause of the neuropathic condition, the eye should always be affected after removal of the ganglion. Wilbrand and Saenger attempt to overcome this argument by assuming either a greater power of resistance of these fibres or that those passing to the eye have escaped injury. In practically all our cases, however, the Gasserian ganglion was completely removed, together with the intracranial branches of the avulsed sensory root. Ranvier denies the existence of trophic fibres in that as a result of a series of experiments in which the nerves to the cornea were cut he has never noticed any alteration in the nutrition of the part. Certainly aseptic wounds heal as readily in an anæsthetic as in a normal cornea. Again, if the keratitis is dependent on the loss of trophic nerves, how is it that when properly treated the condition clears up?

The existence of trophic changes other than in the eye as a result of lesions of the fifth nerve is frequently brought forward. In 50 cases in which the Gasserian ganglion had been removed we have only once noted any change other than the corneal. This was in a woman who four years previously had had an extremely severe attack of herpes on the right side, after which in the area of distribution of the right ophthalmic division there was intense pain, anaesthesia bounded by a zone of hyperaesthesia, loss of hair, loss of the eyebrow and eyelashes, and patches of leucoderma over the upper part of the forehead.

The part played by trauma in the production of this pathological condition of the cornea is only supported by one out of 50 cases of trigeminal neurectomy which we have observed. This patient (A. H.), a man aged 26, remained free from all eye trouble for twenty months after his operation. During this interval he worked in brick fields. At the end of twenty months his eye showed a mild degree of keratitis, but after a few weeks of treatment cleared up. Six months later he again attended for keratitis. On both occasions he thought that the trouble had originated from some brick dust which had irritated his eye. The second attack cleared up after seven weeks, and for the last two and a half years, although he has continued his work without other precaution than occasionally bathing the eye, the cornea is quite healthy and shows only some old opacities.

We have observed that in nearly every case where neuropathic keratitis is going to appear it will be seen first during the stage of convalescence. If the patient remains free during this period only very exceptionally does the condition manifest itself at a later time. Further, in some of the cases we have seen, during the first few days, islands of loss of epithelium on the cornea without any indication of neuropathic keratitis developing either then or later.

The following case affords arguments against both the trophic-and-peripheral-traumatic and the trophic-and-central-irritation hypotheses:

The patient had an endothelioma of the left Gasserian ganglion; the tumour and ganglion were removed. The resulting anaesthesia of the area supplied by the ophthalmic division was not complete. The outer and lower portion of the cornea was anaesthetic, but over the upper and inner surface

there still remained slight sensibility for touch. Within a very short time the patient had a recurrence of the growth, which eventually involved not only the cornea and the cut ends of the peripheral branches of the fifth but also the sensory root, causing great pain in the trigeminal area. Infected glands appeared at the angle of the jaw and over the parotid on the same side, and there was complete peripheral paralysis of the left facial nerve. Despite the lagophthalmos, and on two occasions a superficial loss of epithelium of the cornea; despite the irritation round the peripheral branches (and the sensory root) of the divided fifth, there was never at any time any indication of neuropathic keratitis.

We have already referred to the suggestion made by Parsons that neuropathic keratitis develops because the "afferent tract is still open, but an irritative lesion has set up abnormal antidromic impulses in the protopathic system." In the case just mentioned there was evidence of a partial division only of the sensory fibres of the cornea and of an irritative lesion in the form of a malignant tumour surrounding the afferent tract. Here all the factors necessary on such a hypothesis for the production of neuropathic keratitis were present, yet neither in this nor in the following somewhat similar case did the cornea show any pathological change.

W. P. suffered from neuralgia of the first and second divisions of the right trigeminal for five years. His Gasserian ganglion was removed, but, owing to the strength of the adhesions, the anterior and inner part of the ganglion had to be left attached to the ophthalmic branch. The patient made an uneventful recovery. Two years later he was readmitted suffering from a recurrence of pain in the first division. A note made at that time says that his eye was perfectly normal, and the cornea quite clear. There was no absolute loss of sensation of the cornea or conjunctiva, but the corneal reflex was sluggish. At the second operation the *cavum Meckellii* was found to be empty, but "a little blunt dissection further on through some tissue which appeared to be of inflammatory origin revealed a nerve trunk distinctly larger than the normal sixth nerve, and running outwards over the edge of the petrous just in front of the apparent anterior limit of the *cavum*." This was removed. No weakness of the external rectus resulted, and the patient was free from his pain. The cornea also became completely anaesthetic. At no period before or subsequent to the second operation, which was nearly five years ago, has there been the slightest trace of keratitis.

After section of a nerve, degeneration begins to appear in the peripheral part within the first twenty-four hours, and is complete in twenty days. Since the publication of Halliburton's Oliver-Sharpey lectures²⁷ we may now take it as certain that regeneration of a cut nerve originates from the central end, and that towards ultimate reunion and complete regeneration the peripheral segment contributes practically no help. If, then, after excision of the Gasserian ganglion, keratitis is due to an irritative stimulus producing antidromic impulses, when not seen within the first twenty days it should not appear at all. How, then, did it occur in the case of A. H., already mentioned, in whom there was no indication of keratitis till twenty months after the removal of the ganglion?

Certain authorities maintain that the anaesthetic condition of the eye prevents it from reacting to the stimulus of foreign bodies, which are thus allowed to remain and to cause trauma. But it must be remembered that in over 60 per cent. of the patients who for years are exposed to this risk no such deleterious consequences appear. On the other hand, cases have been reported of keratitis in eyes which are sensitive or even hypersensitive, and which should therefore have been able to recognize immediately the presence of foreign particles.*

Angelucci²⁸ was unable to corroborate Spalitta's experiments in connexion with the vaso constriction hypothesis. On the contrary, by ligaturing the common carotid and at the same time excising the cervical sympathetic ganglion he produced a most marked degree of vaso-constriction without neuropathic keratitis supervening. The occurrence of vasomotor fibres in the fifth nerve has not indeed been proved. Krause states that the eye after excision of the Gasserian ganglion shows no deviation from the normal; nor have we been able to find any dilatation or constriction of the vessels either directly after or at periods extending up to eight years after the neurectomy. Turning now to the desiccation or xerotic hypothesis, one of us,²⁹ as the result of repeated observations of 30 cases of trigeminal neurectomy, has found that

* Wilbrand and Saenger have collected four cases of neuropathic keratitis in patients who had some lesion of the trigeminus but whose cornea was sensitive, and three such in which the cornea was hypersensitive.

there is no difference in the secretion of tears or in the rate of blinking of the eyelids on the affected side. Krause,⁹ however, states that the secretions of the lacrimal gland are delayed. In the case of endothelioma of the Gasserian ganglion with associated homolateral paralysis of the facial nerve mentioned above, the rate of onset of the flow of tears was distinctly delayed, and in addition only very slight and infrequent winking movements occurred on that side. Yet, despite this, keratitis did not develop.

Seftleben found that if an animal in which a trigeminal neurectomy had been performed was tied down on its side with the anaesthetic eye uppermost so as not to hinder evaporation, the cornea remained perfectly healthy, and keratitis did not develop until the animal was allowed to run about. Farther, keratitis has been seen in patients who have had the eye protected from evaporation both by ptosis* and by careful bandaging.

7. THE MYCOTIC HYPOTHESIS.

Turner,³⁰ in conjunction with Ferrier, performed a series of experiments on animals. Two out of the eighteen cases showed destruction of the cornea and panophthalmitis from septic infection; two also exhibited progressive corneal opacities. As a result of experimental irritation of the cornea, a transitory inflammation followed by healing was produced. From this Turner considered that irritation of the first branch of the fifth exercised no neuropathic effect upon the cornea, and attributed the disturbances of this part to an inflammatory irritant, the result of a septic infection. This view Krause, from his clinical observations, tends to support, and he believes that after removal of the Gasserian ganglion there exists a reduced power of resistance to inflammatory influences. Baylock, in his experiments, produced traumatic loss of the epithelium of the anaesthetic eye, thus rendering it possible for micro-organisms to enter and to form the exciting cause of the keratitis. Whilst Hippel, who at first did not regard micro-organisms as an etiological factor, later thought it very probable that bacteria play an important rôle in the establishment of the disease.† Parsons believes that organisms are important only in the more advanced stages.

As the arguments against all these hypotheses other than the mycotic appeared to us to outweigh those in their favour, and recognizing, moreover, the great part played by micro-organisms in most progressive and relapsing inflammations, we decided to attempt a further investigation of neuropathic keratitis from the bacteriological aspect in the hopes of finding some organism which was constantly present only in those eyes which developed keratitis after trigeminal neurectomy, and which by experimental inoculation into monkeys would produce the condition.

The results of our researches we shall now record. From the clinico-pathological aspect they appeared to us to be very encouraging, but our experimental work carried out with the desire to corroborate the former, whilst in some respects it supports our earlier investigations cannot be regarded as conclusive.

The whole of the experimental work has been performed for us by Sir Victor Horsley, and we cannot sufficiently express our gratitude to him for his kindness in doing it and for the time he has devoted to this piece of work.

II.

BACTERIOLOGICAL INVESTIGATIONS.

Our investigations have been based on the examinations of 21 clinical cases. All these cases had the Hartley-Krause operation performed for trigeminal neuralgia; 11 of them developed neuropathic keratitis, whilst the other 9 up to the time when they were last seen, showed no affection of the cornea. These patients have been under observation for periods ranging between five days and five years.

In one case the keratitis, which had been neglected by the patient, had progressed to a condition of hypopyon and phthisis bulbi and the eye was excised. Mr. Parsons,

* In fifty-four cases of ptosis associated with paralysis of the fifth nerve collected by Wilbrand and Saenger, twenty-two had neuropathic keratitis.

† Hippel describing, however, the results of the pathological examination of an eye affected by neuropathic keratitis, says: "Mikroorganismen irgend welcher Art konnten in der Cornea bei eingehendster Untersuchung nicht nachgewiesen werden."²⁵

who performed the operation, most generously gave us the pathological specimen, our findings on which and on four eyes taken from monkeys who had developed neuropathic keratitis will be recorded in due course. In addition we have made a bacteriological examination of twenty-two normal eyes.

Finally, Sir Victor Horsley undertook by a series of operations on animals—8 monkeys, 1 cat, and 2 guinea-pigs—the investigation of the pathogenic properties of that organism which we found to be constantly present only in the eyes of patients affected with keratitis.

We wish to express our thanks to the following gentlemen, who have very kindly allowed us to examine the cases under their care: Sir Victor Horsley, Mr. Flemming and Mr. Parsons, Sir William Gowers, Dr. Ormerod, Dr. Risien Russell, and Mr. Armour. Also to Dr. Thiele for inoculating and making *post-mortem* examinations on two guinea-pigs.

Bacteriological Examination of Twenty-one Clinical Cases.

In the earlier cases we were able to obtain cultures from the eyes only after removal of the Gasserian ganglion, but in most of the others we made bacteriological examinations both before and after the operation.

The cultures were taken from the conjunctival sac of the eye on the side of the trigeminal neuralgia or neurectomy, from the interior of the nostril on the same side, and in most cases from the conjunctival sac of the opposite eye. They were grown on agar-agar. After twenty-four to thirty-six hours' incubation, the colonies were examined

Fig. 1.—*Bacillus x.* × 1,000.

macroscopically and microscopically. When a colony was not pure it was plated out and separated into its various constituents, each of which was again subcultured on to agar agar.

In a few cases blood serum was used. The pure cultures were then individually investigated. In practically all the cases *Staphylococcus aureus* was found; less frequently *Staphylococcus albus*, streptococcus, pneumococcus, xerosis and proteus. But there was also one other bacillus which we found only in those eyes which showed neuropathic keratitis. This organism, of which the following is an account, we shall refer to as *Bacillus x*.

Description of the Organism.

The organism is a short thick bacillus (about 2.0 μ long by 0.6 μ thick) with rounded ends, frequently arranged in pairs, short chains and parallel groups (Fig. 1). In structure it is homogeneous and shows no evidence of spore formation. It is non-motile and has no flagella. It stains with all the ordinary dyes and gives a positive reaction with the Gram method. It grows readily on all the ordinary media.

On agar-agar it forms a thick yellowish-white succulent growth with irregular rounded margins.

On serum the growth is similar but not so profuse.

Gelatin stab cultures show liquefaction only after some weeks without gas formation.

On potato the organism forms a profuse opaque growth of a dirty cream colour.

In ordinary peptone broth a uniform turbidity is produced, but no indol reaction can be obtained.

In litmus milk a fine coagulum appears, and in the early days an acid reaction which subsequently becomes strongly alkaline.

In neutral litmus broth (glucose) there is no gas formation.

We have repeated the examination of the cultural properties of this bacillus many times, and our results,

which have been constant, have also been corroborated by independent investigations. On this account, although further investigation is undoubtedly necessary, we feel justified in looking on these characteristics as fairly definite.

It would appear, then, that this organism belongs to the group of pseudo-diphtheria bacilli, and its characteristics agree very closely with those of that form known as the pseudo-diphtheria bacillus of Loeffler.

The *x* bacillus is very difficult to distinguish from the pseudo-diphtheria organism, but the following three factors help in the differentiation: The *x* bacillus shows occasional granule formation, gives no naked-eye growth on potato, and does not render bouillon turbid.

Clinical Cases.

Of the 21 cases under observation, in all of which the Gasserian ganglion had been removed by the Hartley-Krause method, 11 were suffering or had suffered at some previous time from neuropathic keratitis.* In 9 of these patients we were able to take cultures from the eye and nose on various occasions when the eye trouble was in an active condition. The growths all showed, in addition to staphylococci and occasionally streptococci, pneumococci, *xerosis*, and *proteus*, *Bacillus x*. From 6 of the patients cultures were obtained at various periods after the cornea had healed (J. G., 2 years; A. H., 7 months; M. H., 3 months; C. W., 2 months; V. E., 2 months; E. G., 5 weeks). None of the colonies except those grown from the nose of A. H. and from the eye of M. H. showed the presence of *Bacillus x*. The latter patient, from whose conjunctival sac the bacillus could still be recovered, had another outbreak of neuropathic keratitis nine months later.† The absence of *Bacillus x* after the complete subsidence of keratitis was moreover shown by our observations on the patient J. J. This woman had the Gasserian ganglion removed in December, 1902. A very severe attack of keratitis followed in January, 1903; her eyelids were then sewn together, and kept united until April, 1904. Three days after they were undone there was a fresh outburst of keratitis. The lids were reunited until March, 1905, but the separation of them then was again immediately followed by a recurrence. This was less severe than the previous ones, was treated without closure of the lids, and cleared up within two months. In March, 1905, cultures showed staphylococci and *Bacillus x*. In November of that year, although the eye was still clear, the same organism was found. During June, 1906, there was a fresh though very slight outburst of keratitis, which soon subsided. Cultures still gave the same results. In January, 1907, however, only staphylococci and *proteus* were obtained. There has been no return of keratitis since this time.

Ten patients on whom bacteriological examinations

* This must not be regarded as in any way representing the true proportion of cases which develop keratitis after trigeminal neurectomy. We have the notes on 50 patients on whom this operation was performed. Of these, 18 (that is, 36 per cent) showed keratitis at one time or another after the neurectomy.

† This patient was then unfortunately too ill to come and see us.

were made (in seven both before and after the operation) have never suffered from any corneal affection consequent on the excision of the ganglion. The cultures from these cases contained staphylococci, streptococci, pneumococci, and *xerosis*, but no evidence of *Bacillus x* was found except in those growths taken from the eye and nose of S. F. before the removal of the ganglion. This patient, however, died of meningitis five days after the operation; his lids had been stitched together all the time, and no keratitis had developed. These facts may be put in tabular form thus:

	No. of Cases Examined	Presence of Staphylococcus.	Presence of <i>Bacillus x</i> .
Cases with neuro- { Acute stage ...	9	9	9
pathic keratitis { Quiescent stage	6	6	1*
Cases without neuropathic keratitis	9†	9	0

* This case developed another attack of keratitis later.

† The case of the patient who showed the presence of the *x* bacillus before the operation, but who died five days after (before the stitches were taken out of the eyelids) without developing keratitis, is purposely omitted.

We have had the opportunity of making a pathological

Fig. 2.—Showing triangular ulcer and punctiform keratitis of left eye.

examination of one human eye which was excised by Mr. Parsons owing to the advanced state of the neuropathic keratitis and associated phthisis bulbi. There was an extensive ulcer occupying a large part of the surface of the cornea. As soon as the eye was excised a culture was made from the surface of the ulcer, but no growth was obtained.‡ Cultures were also taken from the anterior and posterior chambers, the vitreous and the cut end of the optic nerve, but in every case the result was negative. A strip of the coats of the eye, including part of the cornea and the ulcer, was hardened, embedded in paraffin, and sections were cut and stained by several of the most common methods. Among the epithelial cells at the edge

of the ulcer numerous masses of staphylococci can be seen. The largest clumps are to be seen along the edge itself, and they diminish rapidly in size as the healthier parts of the cornea are approached. Scattered among the staphylococci, and lying in between the epithelial cells, a few *x* bacilli can be detected. We have not, however, been able to corroborate the presence of the *x* bacillus among the cells of the cornea in the eyes of the four monkeys which developed keratitis.

It would seem, then, that whatever part the *Bacillus x* plays in the initial stages of neuropathic ulceration, once the process is established the staphylococci carry on the work of destruction. Nor is there any evidence to show that at this stage the tissues of the neuropathic eye react to the destructive processes of sepsis in any way different from that in which reacts an eye the nerve supply of which is intact.

Wilbrand and Saenger consider that a third of the patients who have had a lesion of the trigeminal or extirpation of the Gasserian ganglion suffer from neuro-

‡ A culture taken from the conjunctival sac on the previous day showed the *Bacillus x*. After this the eye had been thoroughly irrigated to ensure the asepsis of the operation.

pathic keratitis. Our own statistics, based on the notes on 50 patients, work out at a proportion of 38 per cent. It seemed to us that if the keratitis was produced by an organism which had a special pathogenic power on eyes the sensibility of which had been in some way impaired, and that 38 per cent. of such people developed the corneal lesion, we might succeed in discovering the organism in about the same proportion of normal eyes. For this reason, therefore, we made an examination of the cultures obtained from twenty-two normal eyes. All the cultures showed staphylococci, and in seven out of the twenty-two the *Bacillus x* was also found. A curious point was noticed: 15 of the cases chosen were hospital patients; the remaining 7 were resident officers in the same institution. The seven cultures which showed the presence of the *Bacillus x* were all obtained from the hospital patients.

EXPERIMENTAL INVESTIGATION.

The *Bacillus x* obtained from a patient who was suffering from neuropathic keratitis was placed in the right conjunctival sac of three monkeys, a cat, and two guinea-pigs, to see if any pathological changes could be produced on the normal eye. At the end of a month all the eyes were perfectly healthy. The subsequent experiments on these monkeys will now be given in fuller detail:

Rhesus 1.—A culture taken from the right eye on April 3rd, 1906, showed staphylococcus and the presence of the xerosis bacillus. On the same day the right conjunctival sac was inoculated with the *Bacillus x*, obtained pure by sub-culturing from colonies grown from the eye of J. J. The next day this organism, together with staphylococci, was found in the conjunctival sac. The right eye remained healthy during the rest of the animal's existence. On April 6th the left eye was closed by suturing the eyelids, and Sir Victor Horsley extirpated the left Gasserian ganglion. Three days later the stitches cutting out, the eye opened, and the cornea was seen to be quite healthy, but the next morning keratitis was already present and making rapid progress. A culture taken on this day showed staphylococci and an abundance of the *x* bacillus. By the 15th an anterior staphyloma had formed with prolapse of the iris; and on the 30th, when the animal was killed, there was only the shrunken collapsed eyeball to be seen between the closing lids. Cultures were taken on April 10th, 17th, and 30th. On each occasion numerous growths of the *Bacillus x* and of *Staphylococcus aureus* and *albus* were obtained.

Rhesus 2.—The right conjunctival sac was inoculated on April 3rd from the same tube as that used for Rhesus 1. Cultures taken from the eye on this day (before inoculation) and on the 4th showed only staphylococci. Sir Victor Horsley removed the left Gasserian ganglion on April 7th, having previously stitched together the lids of the left eye. Two days later the stitches had cut out of the lids, and the cornea was seen to be healthy. There was no conjunctival reflex. On the 18th the left conjunctival sac was inoculated from the same tube as previously. No change had taken place by the 28th, and the conjunctival sac was therefore inoculated from the discharge from the left eye of Rhesus 1. This was again repeated in two days' time. On May 2nd there was some dried discharge round the inner canthus which had increased by the 5th, but the cornea remained clear. Cultures taken from the conjunctiva grew only staphylococcus.

Rhesus 3.—The right conjunctival sac, which contained only staphylococci, was inoculated on April 3rd, 1906, with the *Bacillus x*. On April 7th, the left eye was closed by stitching together the lids and the left Gasserian ganglion removed by Sir Victor Horsley. Four days later the eyelids were undone, and the cornea appeared dry but otherwise healthy. From a culture then taken staphylococcus and the xerosis bacillus were obtained. The following day there was a slight loss of epithelium in the centre of the cornea. This condition was only transient. On the 18th slight pin-point ulceration was observed. The conjunctival sac was inoculated on that day from an old growth of the *Bacillus x*. The next day the ulceration showed some progression, but by the 23rd the eye had recovered. On the 28th the conjunctival sac was inoculated with the discharge from the eye of Rhesus 1. Two days later distinct cloudiness of the cornea was evident; the cloudiness increased, punctiform keratitis and a triangular ulcer appeared. On May 5th the monkey was killed, and the condition of the eye at that time is shown in the accompanying photograph (Fig. 2). Cultures taken before death produced a copious growth of the *Bacillus x*.

Rhesus 4 and 5, and Bonnet 3.—In Rhesus 4 the *Bacillus x* was found on the conjunctival sac before the operation. In Rhesus 5, growths of *Staphylococcus albus* only could be obtained; whilst in Bonnet 3, *Staphylococcus aureus* existed. After the operation for the extirpation of the ganglion in these three cases the cornea was found to be still sensitive. No keratitis appeared either immediately after the operation or after inoculation with pure cultures of the *x* bacillus.

Bonnet 1.—No culture was made before the neurectomy. On May 19th the left Gasserian ganglion was removed, but the eye was not closed. Keratitis was already present on the following day, and cultures taken on the 22nd and 28th, by which time the eye was almost destroyed, showed the presence of staphylococci and of the *x* bacillus.

Bonnet 2.—The monkey had the *x* bacillus in its eye before the operation on May 28th. Keratitis appeared four days after the excision of the left Gasserian ganglion on the day after the stitches cut out of the eye. By June 6th the keratitis was far advanced, and cultures showed staphylococci and the *x* bacillus. These were separated by plating. A pure culture of staphylococci was obtained and injected into the thigh of one guinea-pig and into the peritoneal cavity of another. Local tenderness was produced in the thigh, but this had passed off in four days. Dr. Thiele, who injected these animals for us, made, twenty-one days after inoculating the peritoneal cavity, a *post-mortem* examination of the guinea-pig. The peritoneum was slightly pinker than normal, but was otherwise perfectly healthy. There was no effusion, no lymph, and no adhesions.

CONCLUSIONS.

1. The *Bacillus x* we have found to be present in about 30 per cent. of normal people.

2. The *Bacillus x* was present in the conjunctival sac of all those patients who had neuropathic keratitis, and the organism could be demonstrated, together with staphylococci, among the epithelial cells at the margin of the ulcer of the excised eye.

3. In those cases which did not develop keratitis after excision of the Gasserian ganglion no *x* bacillus was found.

4. We therefore conclude that we are justified in suspecting that the presence of the bacillus in the sac is necessary for the production of neuropathic keratitis.

5. The presence of the *x* bacillus, however, without an associated lesion of the Gasserian ganglion, does not lead to keratitis.

6. Mere presence of the organism in a patient whose Gasserian ganglion has been removed is not sufficient to produce neuropathic keratitis, because, if the eyelids are sewn together, the disease does not develop, or, if the condition is already present, it will tend to heal rapidly after suture of the lids. We are, therefore, driven to conclude that there is a third necessary factor, and that this factor is in some way prevented from acting by closure of the lids. This result of closing of the lids may be due either to the effect on the organism or to the effect on the eye. The organism continues, however, to live in the conjunctival sac, in spite of the closure of the lids.* It is, of course, possible that the closure of the lids may act by diminishing the virulence of the organism and separating the lids by increasing it again to its normal level, but the facts that the effect on the keratitis of closing the eye is so prompt, and that keratitis may follow so immediately on again separating the lids (see case of M. H.), seem to be contrary to such an explanation.

Now, closure of the lids must act on the eye in one of two ways: Either by affording protection to the cornea or by abolishing the recurrent friction of the lids. We are not in a position to indicate which of these modes of action is the efficient one, but it is at least suggestive to note that in one case in which the Gasserian ganglion had been removed the patient had also facial paralysis, and, although he repeatedly had slight abrasions of the cornea, he never developed neuropathic keratitis. It is, however, important to add that no bacteriological examination was made, so that the case provides not more than a hint which inclines us to suspect that closure of the eyelids may act through cessation of the friction. It would be interesting to try experimentally whether mere suspension of movement of the eyelids would prevent the lesion or hasten the cure.†

Our investigations, then, lead us to suspect that for the production of neuropathic keratitis three factors must be present: (1) Removal of the Gasserian ganglion; (2) the presence of the bacillus; (3) a factor of undefined nature dependent on the eyelids and removed by closing them. (1) and (2) are not adequate alone, as suture of the lids prevents or cures neuropathic keratitis; (1) and (3) are not adequate alone, because, as we have shown, keratitis only occurs after destructive lesions of the Gasserian ganglion

* The bacillus was found to be still present in one case after the lids had been united for three months.

† Wilbrand and Saenger have collected 30 cases of lagophthalmos in conjunction with anaesthesia of the cornea from paralysis of the fifth nerve; 14 of these had neuropathic keratitis.

when the organism is present and in the same proportion of patients as that in which the organism occurs in normal persons.

The mode of action of the first factor is, of course, in no way elucidated by our investigations.

REFERENCES.

1. Wilbrand and Saenger: *Die Neurologie des Auges*. Bd. ii. Wiesbaden, 1901.
2. Magendie: Suite de l'expérience sur les fonctions de la cinquième paire de nerfs. *Journal de Physiol. Expér. et Pathol.* 1824. T. iv, p. 302.
3. Bernard, Claude: *Lec. sur la Physiol. et Pathol. du Syst. Nerv.* T. ii. 1893.
4. Gaulé: Der Einfluss des Trigeminus auf die Hornhaut. *Centralbl. f. Phys.* 1891. Bd. v, Nr. 15.
5. Gaulé: Wie beherrscht der Trigeminus die Ernährung der Hornhaut. *Centralbl. f. Phys.* 1891. Bd. v, Nr. 16.
6. Bernhardt: *Die Erkrankungen der peripherischen Nerven*, Th. 1. Wein, 1895, s. 142.
7. Erb: *Krankheiten der peripher. Cerebro-spin. Nerven*. Leipzig, 1876.
8. Graefe: Neuroparalytische Hornhautaffection. *Arch. f. Ophthalm.* Bd. i, 1854, S. 306.
9. Krause: *Die Neuralgie des Trigeminus*. Leipzig, 1898.
10. Parsons: Lesions of the Trigeminal Nerve. *Lancet*, May 25th, 1907.
11. Head and Sherrin: The Consequences of Injury of the Peripheral Nerves in Man. *Brain*, pt. cx, Summer, 1905.
12. Head and Rivers: The Afferent Nervous System from a New Aspect. *Brain*, pt. cx, Summer, 1905.
13. Head and Thompson: The Grouping of Afferent Impulses within the Spinal Cord. *Brain*, pt. cxvi, vol. xxix.
14. Bayliss: On the Origin from the Spinal Cord of the Vasodilator Fibres of the Hind Limb. *Journal of Physiology*, vol. xxvi, 1901, p. 173. Further Researches on Antidromic Nerve Impulses. *Journal of Physiology*, vol. xxviii, 1903, p. 276.
15. Flemming: The Pathology of Neuropathic Keratitis. *Lancet*, July 2nd, 1898.
16. Samuel: *Die tropischen Nerven*. Leipzig, 1860.
17. Büttner: Ueber die nach der Durchschneidung des Trigeminus auftretenden Ernährungsstörungen, am Auge und anderen Organen. *Zeitsch. f. Rationelle Medizin*, R. 3, Bd. xv, 1862, S. 254.
18. Spallitta: *Arch. de Otol. et Ocul.* ii, 1894.
19. Schiff: Ueber die nach Durchschneidung des Trigeminus am Auge eintretende Ernährungsstörung. *Zeitsch. f. Rationelle Medizin*, R. 3, Bd. xxix, 1867, S. 217.
20. Seydel: Ein Beitrag zur Lehre der Keratitis neuroparalytica. *Arch. f. Ophthalm.*, xlviii, Abth. 1, S. 142.
21. Sanfleben: Ueber die Ursachen und das Wesen der nach der Durchschneidung des Trigeminus auftretenden Hornhautaffection. *Virchow's Archiv*, Bd. lxxv, 1875, S. 69.
22. Gudden: (Aus den Gesellschaften.) *Neurolog. Centralbl.*, iii, 477.
23. Feuer: Untersuchungen über die Ursache der Keratitis nach Trigeminus Durchschneidung. *Mediz. Jahrbücher von der Ges. der Ärzte*, 1877, Bd. 7, 1877, S. 197.
24. Hippel: Zur Aetiologie der Keratitis neuroparalytica. *Arch. f. Ophthalm.*, Bd. xxv, R. iii, S. 217.
25. Hippel: Anatomische Befunde bei eitriger Keratitis des Menschen. *Arch. f. Ophthalm.*, Bd. xlvii, 1899, S. 157.
26. Olleendorf: Ueber die Rolle der Mikro-organismen bei der Entstehung der neuroparalytischen Keratitis. *Arch. f. Ophthalm.*, Bd. 49, 1900, S. 455.
27. Halliburton: New Facts in Relation to the Processes of Nervous Degeneration and Regeneration. *Lancet*, 1907, pp. 1201 and 1273.
28. Angelucci: *Arch. die Otol. et Ocul.*, xli, Palermo.
29. Davies: The Functions of the Trigeminal Nerve. *Brain*, Part cxviii, vol. xxx, 1907.
30. Turner: The Results of Section of the Trigeminal Nerve. *BRITISH MEDICAL JOURNAL*, 1895, p. 1279.

A PLEA FOR THE IMPROVEMENT IN THE TEACHING AND AN ENCOURAGE- MENT IN THE STUDY OF LEGAL MEDICINE.*

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It seems almost superfluous in these days, when so much is said of the necessity of improved technical education, and when such rapid strides and developments are being made in the various branches of medical science, to have to call attention to the backward condition of one very important medical science.

I venture, therefore, to point out some of the defects of our present knowledge of the subject of forensic medicine, together with the causes of the present lack of interest in the subject, and the possible remedies for this state of things.

It is commonly said—nay, it is almost an accepted dictum—that medical men make bad witnesses. So far as the public may think this it does not really concern us for a moment, as they are dissatisfied and critical because the medical witness is often not able to give a definite but only a speculative answer to the questions put. These, the unthinking majority, will never appreciate the

difficult points that have to be considered in order to arrive at an accurate solution of the various problems presented. In fact, it is often rather creditable to the medical witness that he is guarded in his replies than that he should endeavour to give precise answers at the expense of truth and justice. Of course the criticism of medical evidence has become more acute of late, since the amount of litigation produced by recent enactments has brought such a mass of conflicting evidence into the civil courts. But I wish to speak more particularly of the medical witness in relation to criminal cases. In this direction I think we shall have to concede that, after making due allowance for the criticism of the unthinking and uneducated, the value and status of the medical witness will bear a deal of improvement. Whilst making this admission, I think that I can show, in pointing out the causes of the backward condition of the study of the subject of forensic medicine, that no reflection is implied upon the skill or ability of the various members of the profession who testify in the courts. In fact, in some cases our most eminent surgeons and physicians make the weakest witnesses. But rather the medical witness suffers from a lack of opportunity being afforded him in our system of education, and in the failure of the State to do its part in making provision for a number of skilled medico-legal experts.

What, now, are the causes of the condition to which I have just referred? I think they can be divided into two main classes, namely, defective teaching and a lack of material, together with a want of support on the part of the State.

Defective Teaching.

In the first place, our teaching is defective because we have not in our medical schools lecturers who are specially qualified to teach the subject. There are, I admit, several brilliant exceptions, but in most cases the gentleman who is appointed to teach the subject has usually distinguished himself in surgery or medicine, or he is the next one who is entitled to a post on the teaching staff. This calls to my mind the remarks of Mr. Lynn Thomas when delivering his presidential address two years ago. He called attention to the fact that up till quite recently the gentleman who was a surgeon on the staff of the Cardiff Infirmary suddenly blossomed forth into the dignified position of a physician, by reason of seniority, on the resignation, retirement, or death of a colleague who had been a physician. I remember how the allusion drew forth the smiles of the members. Now I maintain that the idea of a surgeon or physician being appointed a lecturer on forensic medicine at a medical school simply because it is his turn to get the next post, is equally a matter of amusement. Would we appoint as lecturer on medicine or surgery, even at the smallest provincial school nowadays, one who is a general practitioner? Would we appoint as lecturer on gynaecology one who has not devoted some considerable time to special study and practice of diseases of women? Yet we find that in a number of schools gentlemen are appointed as lecturers on forensic medicine—eminent physicians or surgeons no doubt—who have little or no experience of a practical character in the subject which they are expected to teach. It may be said that the number of gentlemen so qualified and experienced is very limited. That I readily admit, and will deal with this dearth of specially qualified medical jurists when I come to the second cause, lack of material together with a want of support on the part of the State.

Secondly, the lectures are, generally speaking, not made interesting and attractive, and little inducement is held out to the students to pay more than a cursory attention to the subject. The consequence is that the student attends just sufficiently often to get signed up for his examination, and learns just enough to scrape through.

Thirdly, the course of lectures is defective in not providing for some instruction on legal procedure, and some explanation of certain legal definitions, as well as an elementary course in the law of evidence and criminal law. There are many, I have no doubt, who would join issue with me on this point, but I consider that this is of the greatest importance if the medical witness is to command a greater respect in our courts. In my experience, one of the greatest reasons that the medical witness fails to do himself justice is not that he is unintelligent or unskilful, but that he fails to thoroughly appreciate his

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