most liable to occur between the ages of ten and thirty, when food is consumed in the largest quantity; and we may therefore assume that both affections depend upon a similar condition, and that the retention of indigestible materials in the cæcum and the catarrh so produced is the most usual cause. But as typhlitis and ulceration of the appendix are both common between the ages of twenty and thirty, although concretions are less common at that period than in the ten years before it, we are justified in supposing that a catarrhal condition of the cæcum, either by producing closure of the valve or by propagation of the inflammation to the appendix, often gives rise to ulceration, although no foreign body be present.

Most of the cases of ulcerated appendix in phthisical subjects occur at a later period of life than when it is due to the presence of concretions or catarrh, for out of those I have collected only one was below twenty years of age, seven were between twenty and forty, and three were above forty. All those connected with hernia were above forty years of age.

I have already mentioned the prevalent idea that the concretions so often found in the appendix are always the result of hardened feces, or of indigestible materials of the food, and if such were the case we should expect to find that most of the sufferers had been liable to constipation. Now, I have collected forty-three cases in which the previous state of health is recorded, and of these only three had been subject to a constipated state of the bowels. It is therefore evident that this theory derives but little support from facts. I should be more inclined to believe that the concretions are in most instances the result of an excessive secretion of the mucous membrane of the appendix arising from the stimulus afforded by an undue use of solid and indigestible food. This view derives support from the fact that of twenty-five cases in which a concretion was discovered twenty are described as having enjoyed robust health, and three had been delicate; whereas of eight in whom no concretion was discovered, only five had been robust and three delicate. The presence of a concretion produces no pain until catarrh or ulceration is excited, for out of twenty-five cases of concretion only two had previously complained of abdominal pain; whilst of eighteen in whom no concretion was recorded five, or 30 per cent., had suffered in this way. I have before mentioned that injuries to the abdomen are supposed by some authors to give rise to ulceration of the appendix, and this derives some support from the fact that three cases out of eighteen in which no concretion was discovered referred their complaint to blows or strains. In four instances out of forty-three there was a history of a previous attack of typhlitis from which the patient had perfectly recovered; in two of these the patients died from peritonitis only, and in the remaining two both abscess and peritonitis were discovered after death.

(To be concluded.)

ON THE USE OF COCAINE FOR PRODUCING ANÆSTHESIA ON THE EYE.¹

BY DR. CARL KOLLER.

TRANSLATED AND REVISED BY J. N. BLOOM, B.A., M.D.

GENTLEMEN,—I take the liberty of addressing you in order to inform you about some experiments which I have undertaken in order to produce anæsthesia on the eye. It is not the first communication which I have made on this subject. I have already addressed such a one, in order to preserve my priority in this discovery, to the Convention of German Oculists, which, as it annually does, met on the 15th and 16th of September in Heidelberg. Dr. Brettauer of Trieste was kind enough to bring my communication into notice and to repeat my experiments before the Convention, and since then the same have been repeated and confirmed in various other places.

It is a well known fact that cocaine, an alkaloid produced in 1859 by Nieman from the leaves of the erythroxylon coca, possesses the peculiar property, by its local application,

of anæsthetising the mucous membrane of the tongue. Prof. Schroff mentioned this fact for the first time in 1862 in a lecture on its nervous effect read before this assembly. It is also well known that cocaine narrows the peripheral arteries when taken internally; further, we know that cocaine dilates the pupil by means of its local application as well as by its internal use. We therefore see that cocaine has already been applied to the eye, but until now those phenomena have not been observed which I make the object of my discourse to-day. After repeated experiments with its internal use cocaine fell into discredit and disappeared from the scene. Dr. von Anrep in 1880 produced a comprehensive research into cocaine, at the end of which it was hinted that the local anæsthetising action of cocaine might in the future become of considerable importance. In Vienna, especially, cocaine has been brought to the front through the interesting therapeutical work of my colleague in the general hospital, Dr. Sigmund Freud.

I have started with the premise that a substance which paralyses the terminal sensory nerves of the mucous membrane of the tongue would not act very differently on those of the cornea and conjunctiva; so I undertook a series of experiments on animals, which I carried out in the laboratory of Prof. Stricker. My results, in brief, are as follows:—If a few drops of an aqueous solution of muriate of cocaine² are dropped upon the cornea of a guinea-pig, a rabbit or a dog, or if the solution is instilled in the usual way into the conjunctival sac, the animal blinks for a while, clearly as the result of a weak irritation. After a period of from thirty seconds to one minute the animal opens its eye, which gradually assumes a peculiar expression of rigidity. If one now touches the cornea of the animal with the head of a pin, being careful not to come in contact with the eyelashes, no reflex closure of the lids occurs, the bulb does not deviate, and the head is not thrown back, as would otherwise happen. On the contrary, the animal remains quiet, and by the employment of a stronger irritation we can convince ourselves that the cornea and conjunctiva are completely anæsthetised. For instance, I have scratched the cornea of the animals upon which I experimented with a needle, pricked the same, irritated the cornea with an induction current which was so strong that it produced a painful sensation in the fingers and was unbearable on the tongue, and cauterised their cornea with a pencil of nitrate of silver until it became as white as milk; all without a single movement on the part of the animals. The last two experiments convinced me that the anæsthesia included the whole substance of the cornea, and not only its surface. However, after I had cut into the cornea, the animals showed decided signs of pain at the moment, when the aqueous humour gushed out and the iris prolapsed. Even in my later experiments on animals I was unable to determine whether the iris also could not be anæsthetised by the instillation of the solution into the corneal wound, or by a continued instillation into the conjunctival sac, begun and kept up for some time before the operation; for experiments testing sensibility of animals which are not narcotised are very difficult, and, especially if they are in the slightest degree complicated, are apt to give equivocal results. I had yet to find out experimentally whether cocaine could produce anæsthesia of the inflamed cornea, and this question was answered in the affirmative, when the animals upon which I produced an artificial keratitis, by means of a foreign body, showed the same anæsthesia of the cornea as the healthy ones. Complete anæsthesia lasts on the average ten minutes, when a 2 per cent. solution is used.

After such successful experiments I did not hesitate to apply cocaine to the human eye. At first I experimented upon myself and a few colleagues; later, on a large number of other individuals; the results of which without exception proved that the cornea and the conjunctiva were thoroughly anæsthetised by its use. The sequence of the symptoms is as follows:—When a few drops of a 2 per cent. solution are introduced into the conjunctival sac, or, better still, if they are allowed to run over the cornea, together with an increased secretion of tears, a slight burning sensation is felt, which disappears after an interval of from thirty seconds to a minute, to give way to an obscure feeling of dryness. To the observer an eye thus treated has a peculiar rigid expres-

² A solution of cocaine in water, up to 5 per cent., can be made without the addition of an acid. The solution is always cloudy. The addition of an acid is to be avoided, as even a very small quantity of an acid causes a very strong burning sensation. When filtered the solution becomes as clear as distilled water.

¹ A paper read at the meeting of the Vienna Royal Imperial Society of Physicians on Oct. 17th, 1884.

sion, very like that which I noticed as remarkable on the animals upon which I experimented. This expression arises from a decided widening of the palpebral fissure, the explanation of which I shall give later. If now the head of a pin is brought in contact with the cornea we note the absence not only of the pain usually associated, but we absolutely do not feel the contact, and all reflexes are absent. The same holds good for the conjunctiva, which loses its sensibility to heat and cold. Without any inconvenient sensation, or the slightest reflex movement on the part of the patient thus treated, we can grasp the conjunctiva of the bulb with a toothed forceps, or we can pit the cornea by pressure. In this connexion the only thing to be observed is that the appearance of objects becomes indistinct, which naturally is caused by the changed curvature of the cornea. This complete anæsthesia lasts from seven to ten minutes, to give way to the normal condition after a considerable period of subnormal sensibility. From fifteen to twenty minutes after the instillation the pupil begins to dilate; the dilatation reaches its maximum during the first hour, decreases decidedly in the second hour, and disappears completely in a few hours more. The dilatation is never a maximal one, and during the whole time the pupil reacts promptly to light and on convergence; therefore the feeling of dazzlement which is connected with atropia-mydriasis is either entirely wanting or is present to a slight degree only. With mydriasis there appears and disappears a very slight paresis of accommodation; the near point of myself and one other person whom I examined for this purpose was lengthened half an inch. I have observed in the normal conjunctiva, especially in the conjunctiva palpebrarum, a decided ischæmia, about the duration of which I can say nothing certain. I shall for the present pass over certain other observations not yet completely confirmed, as, for instance, those concerning the appearances shown by the ophthalmoscope, only stating that I have never seen any symptoms of irritation arise from the use of cocaine. As for the previously mentioned widening of the palpebral fissure, the symptom precedes in point of time, at any rate, its action on the iris and ciliary muscles, and as it appears almost simultaneously with the anæsthesia of the cornea and conjunctiva, I have referred it to the anæsthesia as a cause, and explained it by the disappearance of the irritations which normally affect the cornea and conjunctiva and cause the usual width of the palpebral fissure. As regards the anæsthesia, I have still some practical and important points to bring forward.

1. The anæsthetic effect of cocaine can be increased to a certain limit—that is, if cocaine is dropped into the eye after the partial cessation of the anæsthesia, a second complete anæsthesia results which lasts longer than the first. In this way I have produced complete anæsthesia lasting from fifteen to twenty minutes from the last application by a continuous repetition of the application at intervals of five minutes. 2. The anæsthetic effect is pre-eminently a local one—i.e., it is stronger on those places to which the solution has been directly applied and where it has been for some time in contact. 3. Since, as may be proved, cocaine is absorbed, and after every instillation a quantity, even though small, reaches the anterior chamber, one would *a priori* expect that the deeper portions of the eye could be rendered anæsthetic were it possible to introduce larger quantities of cocaine into it. But as, on the one hand, a certain time is necessary for its absorption, and on the other the anæsthetic effect in point of time is limited, the anæsthesia of the cornea would be over when the iris and ciliary body began to be affected; it would therefore be necessary to anæsthetise the cornea again. I believe I can meet both of these conditions, as the following will show. By means of a continuous application repeated every five minutes with a 5 per cent. solution kept up for some time (about half an hour) I succeeded in producing such an effect upon the deeper parts of the bulb that its sensibility to strong pressure was very decidedly diminished.

Through the kindness of Professor von Reuss, who placed at my disposal for experimental purposes the material of his (formerly Jaeger's) clinic, I was able for two or three weeks to test the effect of cocaine upon the pathological eye. From the very beginning I held cocaine to be valuable therapeutically for two purposes: one for its use as a narcotic in painful diseases of the eye; the other as an anæsthetic in operations on the eye. As for its use in the first instance, I expected much good from its action, especially in diseases of the cornea and conjunctiva, where there is much pain and

intolerance of light. Indeed, I used cocaine in a 2 per cent. solution on a large number of patients with conjunctivitis pustulosa (herpes corneæ). Several minutes after the instillation all the patients thus treated expressed an improvement as regards their subjective condition. The pain was diminished and the intolerance of light was decidedly lessened. With the same unanimity the patients complained that the pain and intolerance of light returned two or three hours after the instillation. We would expect that the pain and intolerance of light could be done away with, or at least diminished, by a frequent application. This method of application could not be carried out up to the present time because of the expense of the drug. I have not observed any influence, beneficial or otherwise, on the course of the disease in the experiments I have made as given above.

Similar results were obtained by me with the use of cocaine in the case of a man with painful erosions on the limbus. I hope also to control the pain in iritis by the use of cocaine, since I believe I have previously shown that its anæsthetic action includes to a certain extent the iris and the ciliary body. The mydriatic effect would not be of so much importance; still one might expect an influence upon the course of the disease from the vaso-constricting power of the drug; perhaps combined with atropine it might be successful. Up to the present time I have had no opportunity of using it in this disease.

The pain connected with cauterisation of the conjunctiva with nitrate of silver is entirely done away with, or, at least, decidedly lessened, by the previous instillation of cocaine. Most of the patients thus treated experimentally expressed themselves as having experienced no pain. In some cases, after a period of latency, the pain appeared, but after a fresh instillation it disappeared. One patient asserted that the pain, although much less than usual, lasted longer. I have little, and, in part, contradictory experience in the use of cocaine with the sulphate of copper treatment; at any rate, in this latter use it must be applied much stronger than in cauterisation with nitrate of silver.

I come now to the second use of cocaine—namely, as an anæsthetic in operations on the eye. Cocaine is used with excellent results in the removal of foreign bodies from the surface and substance of the cornea, an operation which is often rendered so difficult by the restlessness of the patient. I anæsthetised a considerable number, almost thirty, of such patients, making each, either seated or standing, look downwards, and allowing two drops of a 2 per cent. solution to flow down the cornea. After a period varying from three to five minutes the instillation was repeated. All the patients thereupon asserted that they had lost the sensation of a foreign body in the eye, and believing it was removed, prepared to go home. They held their bulb quiet during the extraction of the splinter by means of needles, and when asked what they had felt answered that they had felt nothing at all. Cocaine was used with the same good results in a case of tattooing of cicatrices on the cornea, and in the operation of pterygium. Good results might be obtained with cocaine in cauterisation of corneal ulcers with the actual cautery in the puncture of the cornea and discissio cataractæ.

Dr. Reuss performed the operation for staphyloma upon two children—one a boy, aged ten years, the other a girl of seven—without narcosis, using only cocaine in the manner to be described later on. The children remained perfectly quiet, and, according to their own confession, experienced no pain. Dr. von Reuss kindly allowed me to employ cocaine in several cases of iridectomy and cataract operations after Graefe, which he performed. In general, I only wish to state that these cases, one and all, ran their course without any irritation, and this, to say the least, calls for further trials of the drug. The experimental use of cocaine gave results which were more or less favourable according to the strength of the solution and the manner in which it was employed. The most favourable and almost completely satisfactory results as regards painlessness in operations were given by the cases in which the following method was carefully observed. For at least half an hour before the operation two drops of a 5 per cent. solution are instilled every five minutes. The patient is placed horizontally (without a pillow under the head), the upper lid is elevated, and, while the patient is told to look towards his feet, the solution is dropped upon the sclera just above the cornea.

Among those so treated was a woman, upon whom a linear extraction was made and who was questioned during each

stage of the operation; she answered that she felt absolutely no pain from the corneo-scleral incision, the seizure and cutting off of the iris caused her but little pain. During the whole operation there were no reflex movements. A like result was obtained in the case of an idiotic woman upon whom the same operation was performed, and upon whom Dr. von Reuss hesitated to operate because she was in other respects very sensitive.

The following case appears to me to be worthy of notice on account of its peculiar circumstances. Iridectomy was performed upon the left eye of a man with a bilateral *seclusio pupillæ*. Cocaine was employed. The man did not move in the slightest degree during the operation, and asserted he did not feel the corneo-scleral incision at all; that he felt the seizure and cutting off of the iris, but it did not pain him. Eight days later the other eye was operated upon, but this time without the use of cocaine; he writhed and "bore down," so that the operation was rendered decidedly more difficult. Although a large majority of people who have to undergo such operations are torpid individuals and bear their pain with patience, nevertheless, the last case appears to me to prove that even in such cases an anæsthetic might be of excellent service.

The translator of the above paper on the anæsthetic use of cocaine has been requested by the author to add the following short notice, the results of later experience in the use of the drug. Lack of time and space prevent details. Operations for cataract are almost painless when performed with cocaine. Hence in those cases of prominence of the bulbs, where there is great danger of escape of the vitreous humour during the operation, the elevator has been dispensed with. The importance of this will be appreciated by oculists. As predicted by Dr. Koller when he wrote his article, the operations of puncture of the cornea, *discissio cataractæ* and cauterisation of corneal ulcers have since been frequently performed under the cocaine anæsthesia, and absolutely painlessly.

That cocaine is of great value in relieving pain in iritis, the following case, given in brief, will show:—

A woman, M. F—, forty-five years old, in Dr. von Reuss's wards, suffered so much pain from iritis as to be unable to sleep. The insomnia was complete, and had lasted seven days and nights. Atropine had been employed continuously. Cocaine in 5 per cent. solution was instilled six times in half an hour in the manner already detailed. The pain disappeared completely but reappeared three hours later. Cocaine was again instilled; this time three times in fifteen minutes. The pain vanished and the patient slept comfortably for the rest of the night. The next day on the reappearance of the pain a third instillation was used, and the pain disappeared and did not return.

In the clinic of Dr. von Reuss nearly all the operations are now performed under the cocaine anæsthesia according to the method already given in detail.

NOTE ON THE VALUE OF HYDROCHLORATE OF COCAINE IN OPHTHALMIC SURGERY.

By J. CRAWFORD RENTON, M.D. EDIN.,
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FOLLOWING the recommendation of Dr. Koller of Vienna, which was brought under my notice by Mr. Marcus Gunn of London, I have recently been using the hydrochlorate of cocaine in all operations on the cornea. Two per cent. and four per cent. solutions, some made with distilled water alone, others with boracic acid and glycerine to prevent putrefaction, have been used, as also the discs of the strength of $\frac{1}{20}$ gr., made by Savory and Moore on the suggestion of Mr. Nettleship, and I have no hesitation in saying that my best corneal anæsthetic results have been obtained with the discs, two being quite sufficient to produce complete anæsthesia in six minutes, and being maintained from fifteen to twenty minutes. The 2 per cent. solution in distilled water acted well, but that made with glycerine was not satisfactory. One patient, who had both solutions used in a double iridectomy he required for lamellar cataract, stated that he felt no pain whatever with the plain solution, but slight pain with the glycerine preparation. In cataract extractions and

needle operations the anæsthesia of the cornea is most satisfactory, and patients state that they feel no pain. For the removal of foreign bodies from the cornea the cocaine promises to be most serviceable. As a mydriatic, in some patients it is very decidedly so, our present house-surgeon, Dr. McIntosh, who kindly allowed me to use it in his eye, found that his pupil remained fully dilated for a week. As a controller of ciliary pain I have not yet found the cocaine of much value, nor have I been able to satisfy myself that the conjunctiva or skin is much affected by it; but its value in preventing pain during an operation and keeping the eye soothed for some time after cannot fail to conduce to good results in ophthalmic surgery.

Glasgow.

CHOLERA.

By MAX VON PETTENKOFER, M.D.,
OF MUNICH.

(Continued from page 905.)

THE same considerations hold good in India. The famous places of pilgrimage, whose sanctuaries are annually visited by many millions of individuals, always have some cases of cholera amongst them, but it is only occasionally that an epidemic breaks out, and then it is only at those times when the predisposition to cholera exists—periods, be it noted, which do not for the most part coincide with the time when the number of pilgrims is at its greatest, nor when the principal feasts are in progress. For instance, Bryden has drawn up tables showing the number of admissions into the hospital at Puri in the neighbourhood of the sanctuary called Dschagganath for the years 1842 to 1866, and these statistics show the number of receptions of cases of cholera for each month of the year. This journal, extending over so many years, must give a good idea of the frequency of cholera in pilgrimage even though the numbers be but small. The principal feasts, when the chariot of the deity is drawn over the breasts of the faithful, occur in the middle of March, but the period at which cholera is at its height is in June, when there are many fewer pilgrims assembled. Altogether there were 313 cases in March during twenty-five years, whilst the number was 1155 for June, or nearly four times as many admissions for cholera into the hospitals. Puri lies on the south-west border of the territory where cholera is endemic, and has the same rhythm so far as cholera is concerned as Madras. Hardwar lies in the north-west of India, where the chief feast occurs in April, the principal day being the 12th, and often hundreds of thousands of pilgrims, if not millions, stream together here; yet cholera only breaks out in an epidemic form when the regions are predisposed to it. It will be interesting to go further into detail on this question. Hardwar is situated about 1000 feet above the level of the sea where the Ganges quits the Himalayas, and belongs to the holiest of places which the Hindoos worship. Cholera only occurs occasionally in an epidemic form. In the last century (1783) a severe epidemic was known to have occurred amongst the pilgrims at Hardwar. From 1858 to 1867 the feasts passed on without the occurrence of any epidemic of cholera, and this immunity was believed to be due to the soundness of the arrangements which were enforced by the Government. In 1867 the whole prophylactic armour was thrown aside. But already in November, 1866, an epidemic of cholera was approaching the neighbourhood of Hardwar from Agra. The pilgrims began to arrive at Hardwar on April 1st. On April 3rd the majority had assembled, although the stream of pilgrims continued to increase till the 12th. The whole number of pilgrims reached about three millions. On April 9th the first case of cholera was detected by Dr. Kindall and taken into hospital. Other cases soon followed. On April 12th, on holy day, the pilgrims bathed from sunrise to sunset in the Ganges, in a holy fort which is separated from the torrent of the river by a rail, so that the people could not be drowned. Through this fort there was an incessant movement of men all day long. The water became thick and muddy, partly from the ashes of the dead which the pilgrims had brought with them to strew in the stream, and partly from the washing of the clothes and persons of the bathers. Every time a pilgrim entered the holy fort he dipped himself three times under, drinking the