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OCULAR THERAPEUTICS.

BY

SYDNEY STEPHENSON, M.B., C.M.

Lectures delivered June, 1905, at the Polyclinic, London.

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1905.

THE HISTORY OF THE

REIGN OF KING CHARLES THE FIRST

BY SAMUEL JOHNSON

LONDON: Printed by A. MILLAR, in Pall-mall, 1764.

THE HISTORY OF THE

REIGN OF KING CHARLES THE FIRST

OCULAR THERAPEUTICS.

LECTURE I.

THE general advance in therapeutics that has marked the last few years has been shared in by ophthalmology. It may, indeed, be claimed that in some respects the latter science has led the way, more especially with regard to the principles underlying the local application of remedies. Thanks to the strides of synthetic chemistry, a host of new remedies has been introduced, and although some of these products have not withstood the fire of destructive criticism, yet others have taken a permanent place in the arsenal of therapeutic remedies. There is no organ in the human body better adapted for experimenting with remedies than the eye, since the superficial parts, as the conjunctiva and the cornea, the iris and the crystalline lens, can be kept under close and constant supervision. Not only have new remedies been discovered, but novel methods of applying the older agents have been introduced, as witness the intravenous injection of the soluble salts of mercury.

In the course of the following remarks I shall deal mainly with such things and methods as I have myself used. I have no sympathy with those who look askance at the newer pharmacology. On the contrary, I am convinced that it is the bounden duty of all in a position to do so to try new agents, to endeavour to separate the wheat from the chaff, and to complete their work by publishing with candour results, be they good, bad, or indifferent. "Surely every medicine," said Francis Bacon, "is an innovation; and he that will not apply new remedies must expect great evils." "A froward retention of custome," he continues, "is as turbulent a thing as an innovation; and they that reverence too much old times, are but a scorn to the new."

My subsequent remarks may be considered under two heads:—first, local remedies—that is to say, such as are applied directly to the eye; and, secondly, general remedies, including general anæsthesia, X-rays, radium, serum- and organo-therapy, and the treatment

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of certain diseased states, as syphilis and rheumatism, that are not infrequently associated with affections of the eye.

I.—LOCAL REMEDIES.

It is a matter of familiar knowledge that remedies are applied to the eye in several different ways—as, for example, in liquid, ointment, or powder form. Moreover, as will be explained later, they are nowadays often injected beneath the conjunctiva.

When a drug, as atropine, is dropped into the eye, dilatation of the pupil is soon observed. By what mechanism does this come about? That the remedy does not act through the circulation is shown by the fact that if it did so it would, when placed in the conjunctival sac of the eye, dilate both pupils. The drug, as a matter of fact, acts by the atropine finding its way by diffusion into the aqueous humour, and thereby acting directly upon the tissues, vessels, and nerves of the iris. The truth of this observation is attested by a famous old experiment. If atropine be employed to dilate the pupil of a dog's eye, and some of the aqueous be withdrawn by means of a syringe, this liquid when placed in the eye of a second dog will dilate the pupil. Remedies which act upon the internal parts of the eye, therefore, when dropped into the conjunctival sac, do so by a process of imbibition, and, as we shall see directly, this process may be hastened by certain remedies, particularly by adrenaline and by cocaine. Of the conditions which interfere with the imbibition of fluids from the conjunctiva two stand prominently forward, namely (1) increased vascularity of the surface blood-vessels, and (2) increased intra-ocular pressure, or "tension," as it is usually called. A good example is acute glaucoma, where in addition to being congested, the tension of the eyeball is materially raised. To endeavour to render such an eye anæsthetic by dropping cocaine into the conjunctival sac as a preliminary to the performance of an iridectomy would be a sheer waste of time, a fact recognised by every practical surgeon. Hence, the operation in question is seldom attempted under such circumstances without the administration of a general anæsthetic, as chloroform.

Some remedies, as antiseptics and astringents, act directly upon the superficial structures of the eye, and this is equally true whether they are applied as liquids, powders, or ointments. Ointments compounded with vaseline and lanoline present certain advantages, especially when the eye is reddened or waters freely, since they keep the remedy of which they are the vehicle longer in contact, as it were, with the parts on which it is desired to act.

Of late years, more especially in France, attention has been paid to the advantages of employing oily collyria—that is to say, the solution of alkaloids, not in water, as is usual in this country, but in oil of various kinds. The medium recommended by Dr. Scrini, of Paris, is olive oil, although I have found that most patients upon whom comparative trials are made express their preference for sesame oil. Castor oil may also be used. In this connection it must be borne in mind that the alkaloids themselves, whether atropine, cocaine, or others, must be employed, since the salts of the alkaloids, although freely soluble in water, are but little soluble in oily menstrua. Before the oil is used to dissolve the alkaloid it must be carefully cleansed and sterilised. There are various ways of doing this, but the plan recommended by Delacour is perhaps the best and simplest that can be adopted. It is as follows:—the oil is first well washed with half its volume of strong alcohol, for the purpose of freeing it from fatty acids, and it is then decanted, and, if necessary, filtered. Lastly, it is sterilised by being heated to a temperature of 120° in a sand bath for half an hour. The outstanding advantages of oily collyria are three in number:—(1) they may be kept for many months without undergoing change; (2) they furnish a most unfavourable medium for the development of micro-organisms or moulds; and (3) they produce no irritation when dropped into the eye. It has also been claimed (4) that they fail to set up dermatitis in cases where the same alkaloid dissolved in water has done so (*Ophthalmoscope*, 1905). At all events, oily solutions of atropine and of cocaine offer considerable advantages to country practitioners who in the ordinary course of things must be provided with the several agents, even although they may seldom be called upon to employ them.

There is, as I have said, an important way of applying liquids so as to reach the interior of the eyeball, and that is by injecting them beneath the conjunctiva—the so-called subconjunctival injection, for the popularisation of which we are mainly indebted to Dr. A. Darier, of Paris, the therapeutic leader of our speciality. The principle upon which they are based is a sound one, *viz.*, always to apply the remedy as near the focus of disease as possible. This important principle is now becoming widely recognised in general medicine, as witness the injection into the tuberculous lung of guaiacol, and of the salicyl compounds into the blood-stream of those suffering from acute articular rheumatism.

Subconjunctival injection has received more attention abroad than in this country. Many striking cures have been reported. Its actual position, however

in the treatment of disease has not yet been clearly defined, although it has been on trial for upwards of ten years. The most varied substances have been employed for the injections, but the chief are corrosive sublimate, cyanide or biniodide of mercury, potassium iodide, sodium chloride, hetol, iodipin, methylene blue, and Poehl's physiological salt, which represents the osmotically active constituents of human blood. It seems probable that the precise agent employed is not so important as the liquid menstruum, for it is difficult on any other assumption to explain the cure of a given disease by using several different remedies. It is not quite clear yet how subconjunctival injections act, although it is likely that the irritation they produce causes an exudation from the vessels of the eyeball rich in albuminoids and protective substances from the blood, with the consequence that the aqueous humour becomes strongly hæmolytic.

Indications.—The injections may be employed in many different affections of the eyeball, particularly in those that are scarcely touched by the more usual methods of medication. At the same time it is necessary to insist upon the fact that the method is not one to be adopted without definite indications or in cases that are likely to yield to simpler measures. After all, the injections entail considerable trouble and time on the part of the surgeon, and call for some little fortitude on that of the patient. They are, therefore, not to be adopted without care, thought, and consideration. The indications for subconjunctival injections may be briefly put as follows:—to produce asepsis in infective ulcers of the cornea, notably when accompanied by pus in the anterior chamber of the eye (hypopyon); to exert a specific action upon the lesions in syphilitic choroiditis, retinitis, and, more rarely, irido-cyclitis; to promote absorption in the choroidal lesions of high myopia; to influence desperate cases of sympathetic ophthalmitis; and, lastly, to help in the absorption of the subretinal exudation of detached retinae. There is still another indication, and that is in the corneal opacities left by an attack of keratitis, interstitial or otherwise, where subconjunctival injections render considerable help.

The injections have recently been employed with a view to clearing up the opacities of cataract, incipient or advanced. As yet it would be premature to say anything very definite about the method, although no harm can be done by glancing briefly at what has been accomplished in this direction. A Madrid surgeon, Dr. Verdereau (*Archivos de Oftalmologia Hispano-Americanos*, October and November, 1904) produced cataract experimentally in rabbits, and then endeavoured to clarify the opaque crystalline lens by the

direct injection of a solution of potassium iodide into its substance. The opacity was found to diminish, but, unfortunately, the experiment could not be followed to a conclusion, because severe inflammation came on in the eyes thus treated. In a second series of experiments, he employed subconjunctival injections of the same solution, and found that a distinct effect was produced. Verdereau next applied his experimental results to patients affected with senile cataract. One patient alone had the courage to submit herself to a full course of injections, but the results obtained in that case were truly remarkable, since her sight improved from one-sixth to two-thirds, while the lenticular opacities disappeared step by step with the improvement in sight. Verdereau found a definite improvement in several other patients, even although many of them underwent a single injection only. My own personal experience in this matter may be stated in a few words. During the last three years I have treated by subconjunctival injections several patients who were suffering from choroidal lesions and lenticular opacities. *Pari passu* with the improvement in the choroiditis I have observed lenticular opacities become smaller and in two cases disappear altogether. These experiences encourage me to hope that we may some day be in possession of a remedy that injected beneath the conjunctiva will cause the absorption of lenticular opacities. What is at present merely a scientist's dream may one day become converted into a sound, a substantial, and a salutary reality.

The technique of subconjunctival Injections.—The only instrument needed is a small syringe, Pravaz or otherwise, capable of ready sterilisation. Some surgeons introduce a speculum between the eyelids and keep the eyeball in place by means of fixation forceps. This can be necessary only in intractable patients. In young children, the injection is best made after the administration of ethyl chloride, since local anæsthetics, of course, are useless in such young subjects. In older persons the conjunctiva is rendered insensitive by means of a drop or two of cocaine (2 per cent.), holocaine (1 per cent.), or stovaine (4 per cent.), the upper lid is raised, and the patient desired to look well down and in. The needle (which should be very sharp) is introduced obliquely beneath the conjunctiva which covers the upper and outer part of the eyeball, between the insertions of the superior and the external rectus muscles, as near the equator as possible. The fluid is then slowly injected beneath the conjunctiva, which rises like a bleb. The needle is withdrawn, and the little operation is then complete. In sensitive people or in those not accustomed to the injection, a pad and

bandage should be applied and kept in place over night. Pain, chemosis, hæmorrhage beneath the conjunctiva, and swelling of the eyelid may follow the injection, results that depend upon several factors, of which the most obvious are the individual reaction of the patient, the position where the injection is made, and the nature and amount of the liquid employed. The pain produced is perhaps the most serious drawback to these injections, more especially in private practice. But, as pointed out by Darier, it may be minimised or altogether done away with by adding to the solution for injection a few drops of 1 per cent. or 2 per cent. acoine—that is, di-para-anisyl-mono-phenethyl-guanidine-hydrochloride, to give the substance its full chemical title. Recent investigation by Scrini (*Arch. d'ophtalmologie*, June, 1905) indicate that the new local anæsthetic, stovaine, may be applicable under similar conditions.

One objection urged against subconjunctival medication is that a cicatrix may be produced between the conjunctiva, on the one hand, and the subjacent sclera, on the other. This is doubtless true if the liquid be injected close to the cornea, but not if practised, as it should be, as far away from the cornea as possible. It is not a little curious that Dr. Deschamps has recently (*Rev. Gén. d'Ophtalmologie*, May 31st, 1905, p. 222), proposed to avail himself of the production of scar tissue with the idea of so modifying the curvature of the cornea as to correct any regular astigmatism that may exist. For this purpose he proposes subconjunctival injections of sodium chloride at the extremities of the most convex diameter of the cornea, and he claims that by these means it is possible to correct as much as 2 D. of astigmatism.

The following rough classification of the local remedies to be now described will render the subject simpler to follow:—(1) Antiseptics. (2) Mydriatics. (3) Myotics. (4) Anæsthetics and analgesics. (5) Miscellaneous remedies.

I.—ANTISEPTICS.

One of the oldest and most efficient antiseptics in eye-work is silver nitrate. Its virtues in that direction were found out by ophthalmic surgeons long before the genito-urinary specialists familiarised themselves with its qualities. "I have sometimes alarmed other practitioners," wrote William Mackenzie, in his famous "Practical Treatise on the Diseases of the Eye," published in 1854 (fourth edition), "by proposing to drop upon the surface of an eye highly vascular, affected with a feeling as if broken pieces of glass were rolling under the eyelids, and evidently secreting puriform matter, a solution of lunar caustic; and I have been

not a little pleased and amused at their surprise when, next day, they have found all the symptoms much abated by the use of this application."

In superficial inflammations, which are nearly invariably due to the action of micro-organisms, silver nitrate has yielded the best results. In bacterial invasions of the conjunctiva, above all, it was until recently simply indispensable.

The agent, however, presents several drawbacks of a somewhat unpleasant nature. These are mainly, if not entirely, due to the nitrate salt with which the silver is combined. I have unfortunately witnessed several accidents, some of a most serious nature, from silver nitrate. For example, a nurse at one of the large Poor-law infirmaries was instructed to apply solid copper sulphate to the eyelids of a child suffering from trachoma. Instead, she rubbed the lining of the lids with pure lunar caustic, with results that may be better imagined than described. When I saw the patient a few hours after the injury, one cornea was converted into a greyish slough, and the sight of that eye was practically abrogated. It is gratifying, however, to note that sight eventually rose to $\frac{2}{3}$ normal. Another case fell under my notice a few years ago in the person of a little boy, æt. 9. According to the history, about six weeks before, a somewhat heroic operation for trachoma had been performed upon the lad's eyes. Chloroform had been administered, the trachoma-growths removed with silver nitrate, and the eyes then irrigated with a solution of common salt. The palpebral conjunctiva, when I examined the child, was traversed with cicatricial bands, the lower lids were more or less adherent to the eyeball, and about two-thirds of one cornea was occupied by a curious, greyish-yellow deposit, much like the one spoken of in the case above. V. = $\frac{1}{30}$ normal. Eventually sight rose to $\frac{1}{2}$ normal. Here are brief details of another case where I myself actually produced a silver opacity of one cornea! A little girl, æt. 4, was under my care on account of ulceration of one cornea, which refused to yield to the ordinary remedies. The intense photophobia induced me to apply, under ethyl chloride, lunar caustic to the ulcer. The consequence was that, although the ulceration was cured, yet its former site was occupied by a dense, slightly-raised, greyish-white deposit, lying beneath the corneal epithelium. Otherwise the eye was free from redness or irritation. An attempt to scrape away the deposit resulted in opening the anterior chamber and the formation of an adhesion between the iris and the cornea, which had to be liberated later by incision. I could quote other instances of more or less severe injuries to cornea or conjunctiva, but enough has been said to show that

silver nitrate is an agent which should be employed carefully, if at all, in the treatment of distempered eyes.

The other drawbacks of silver nitrate include discomfort, irritation, and actual pain, want of penetration, liability to produce local staining, so-called "argyrosis," and in many cases eschars of the mucous membrane. To be quite candid, the fact is that silver nitrate, although invaluable in the hands of those who have learned how to use the remedy, is apt to become a somewhat dangerous weapon if employed without due experience, skill, and discrimination. The knowledge of this fact has led chemists to endeavour to find an agent that shall possess the antiseptic powers of silver nitrate without its undesirable qualities. It has become widely recognised that the clinical value of a silver compound depends upon the amount of contained silver, and that this is modified, often in an undesirable direction, by the other chemical constituents of the salt. The ideal agent, according to Fraenkel, must fulfil the several requirements of not coagulating albumen or of precipitating sodium chloride, of solubility in water, and of not producing pain or of setting up any irritation of the eyes (*Ophthalmoscope*, March, 1904). The list of agents that fall more or less into line with these requirements is a long one, but I shall discuss only protargol, largin, and argyrol, since I have employed the agents named upon a very extensive scale in the treatment of diseases of the eye. A few words of description may be devoted to each product.

Protargol.—This laboratory product contains 8.3 per cent. of metallic silver. Its watery solutions are stable. It is, however, necessary that they should be freshly prepared with cold water, since heat causes an irritating by-product to appear, and this may give rise to pain when the protargol is applied to an inflamed eye. The solution is to be kept, like all silver preparations, in amber-coloured bottles.

Protargol is now widely employed in external inflammatory affections of the eye, such as blepharitis, acute and chronic ophthalmia, and lacrymal disease. As a lotion for acute catarrhal ophthalmia, a 5 per cent. solution may be used as an eye wash three or four times a day, and the same solution, or a weaker one, in cases where the lacrymal sac is suppurating. In ophthalmia neonatorum, particularly when the gonococcus is the cause (about one-half the cases) something stronger is called for. The conjunctiva may be brushed one or twice a day with a 50 per cent. solution, the eyes being kept clean in the meantime by the frequent use of a 2 per cent. to 5 per cent. solution. Upon the whole, this is one of the best treatments for ophthalmia neonatorum with which I am acquainted.

Has protargol, then, no drawbacks as regards the eye? It now and then causes some little pain, but never anything like that following the application of even a weak solution of silver nitrate. It is possible, as already hinted, that these discomforts may be connected with an incorrect way of preparing the solution. The great disadvantage of protargol, to my mind, is the undoubted fact that it tends to an even greater extent than silver nitrate to cause indelible staining of the parts to which it is applied. It is this most undesirable quality that has induced me to look in another direction for the ideal silver substitute. At the same time, there can be no doubt that, clinically, protargol is an active and efficient agent, and one that can never harm the cornea in whatever strength it is employed.

Largin.—This product contains 11.10 per cent. of silver combined with protalbin. It is soluble in water, and may be used as a 10 per cent. solution in the same class of cases as protargol. In gonorrhœal ophthalmia, however, it is, in my experience, nothing like so efficacious, whereas in acute catarrhal ophthalmia—the “blight” of the London poor—it is a veritable specific. It seldom causes pain or other discomfort. Like protargol, it may discolour the conjunctiva if applied for longer than a few weeks, about a couple of months representing the limit beyond which one cannot safely go.

Argyrol.—This, the latest and unquestionably the best of the organic silver compounds, is also known as “silver vitellin.” It does not coagulate albumen, neither is it decomposed by the sodium chloride of the tears. It contains a high percentage of silver (30 per cent.); it is not in the least irritating to the eye; and its powers of penetration are very pronounced. It is extremely soluble in water. It is claimed that argyrol never stains the conjunctiva, no matter in what concentration nor for how long it may be applied. In the light of two patients whose conjunctiva became lightly discoloured after the prolonged use of a 15 per cent. solution, this statement must be modified. It would be more correct to say that argyrol has, as compared with the other products of silver, very little tendency to stain the conjunctiva. This simple fact at once gives argyrol a superiority over the other salts of silver, organic or inorganic, although it is very difficult to explain, more especially when one recalls the ease with which argyrol is able to penetrate animal tissues. The fact nevertheless remains, and forms an additional argument, if one be needed, for the employment of argyrol upon a wider scale.

My observations with argyrol now extend over a period of about two years, and embrace the treatment

of practically every kind of superficial inflammation of the eye. For example, I have used it in all kinds of conjunctivitis, in blepharitis, in phlyctenular conditions of the cornea and conjunctiva, and in diseases of the lacrymal passages. Despite its high ratio of silver-content, I have never yet known it occasion the least pain, irritation, or reaction. No caustic or escharotic action ever follows its use. My experiments have been made with a 15 per cent. solution, except in cases of gonorrhœal ophthalmia, where a saturated solution had been applied. The weaker liquid has been dropped into the eyes by the patient himself two to eight times a day, according to the kind and severity of the inflammation. The stronger liquid has been painted over the exposed conjunctiva, first carefully freed from discharge, once or twice in the twenty-four hours. Almost the first thing that struck me about argyrol was the fact that many patients volunteered the statement that even after the initial application, relief to symptoms was obtained. Indeed, it appeared to act as a direct sedative to the inflamed mucous membrane. Argyrol is most useful in septic ulcerations of the cornea, alone or in combination with other measures.

Argyrol, like all silver preparations, tends to stain linen on which it may be dropped, but a solution of potassium iodide speedily removes the marks thus produced.

There are two special ways of applying the new medicament to the eye that deserve to be mentioned definitely, so useful have I found them, especially in hospital work, where cases of the kind abound. There are few more disheartening tasks than to attempt to cure a case of severe ulcerative blepharitis. It is comparatively a simple matter to obtain improvement, but actual cure is quite another thing. In this disease, as in many others, argyrol has rendered me yeoman service. My plan is to rub the inflamed lids vigorously with a pledget of wool soaked in a 25 per cent. solution of argyrol, and to repeat the process, at first daily, and later at longer intervals. This, combined in the more severe cases with occasional cauterisation of the little ulcers lying at the roots of the lashes with the *acidum carbolicum liquefactum* of the British Pharmacopœia, is the best treatment that I have ever adopted in rebellious cases. The second condition with which everybody must be more or less familiar is eczematous (phlyctenular) conjunctivitis or keratitis complicated with marked photophobia, blepharospasm, and watering of the eyes. Such patients under ordinary methods are often "blind" for months together. An ointment containing 10 grains of argyrol to the ounce of vaseline is simply invaluable in this condition, and when the photophobia is very intense,

two to four grains of alkaloidal atropine and a similar amount of alkaloidal cocaine may with advantage be added to the prescription. The ointment, whether simple or combined, should be applied two or three times a day. There are few cases, even of the most intense and rebellious photophobia, that will not yield to this treatment, especially if at the same time the patient's forehead be painted daily with liniment of iodine until the skin becomes sore and slightly cracked. I need say nothing of constitutional remedies and dietetic measures, which are called for practically in every case of phlyctenular disease. (a)

General Conclusions as to the Use of Silver.—Nitrate of silver owing to its irritating, nay, dangerous qualities, and its small powers of penetration, should be used little, if at all, in the treatment of the superficial inflammations of the eye. In severe ophthalmia, such as that associated with the gonococcus, it should be replaced by protargol, 50 per cent., or argyrol, 50 per cent., while in the slighter forms of acute conjunctivitis, such as those caused by the Koch-Weeks' bacillus or the pneumococcus, argyrol, 15 per cent., may well be used in its place. Weak solutions (5 per cent.) of either protargol, largin, or argyrol may be employed in the secretory purulent affections of the lacrymal sac and passages, and may in those cases with advantage be syringed through the diseased parts, after the duct has been surgically treated, so as to restore its patency. The staining propensities of largin and especially of protargol make me give the preference to argyrol as an agent for general employment. Its recent introduction into practical ophthalmology marks, in my opinion, a forward step.

A few other antiseptics should be mentioned, *viz.*, chinosol, chloretone, sublammin, sodium hyposulphite, cuprocitrol, collargol, cuprol, mercuriol, formalin, and trikresol. Time, however, precludes me from attempting to describe their individual powers, properties, and uses in ophthalmic work.

LECTURE II.

2.—MYDRIATICS.

WE may first usefully distinguish between "mydriatics"—that is, agents capable of causing dilatation of the pupil—and "cycloplegics"—that is, agents

(a) Mr. Charles Wray (*Lancet*, April 29th, 1905) has recently described a most effectual way of employing argyrol in that obstinate condition, follicular conjunctivitis. He first empties the follicles by means of pressure between the two thumb-nails, and touches the parts with argyrol, 20 per cent. The argyrol is fixed in the tissues by applying a little adrenaline, 1:1,000.

capable of paralysing the ciliary muscle and consequently the function of accommodation. Every cycloplegic with which I am acquainted is also a mydriatic, but the converse proposition, as we shall see immediately, is not true, or is true in a restricted sense only.

The two groups, cycloplegics and mydriatics, serve different purposes. Broadly speaking, the first-named are employed before estimating refraction, whereas the last-named are used to dilate the pupil in disease or to facilitate full ophthalmoscopic examination of the media or the fundus of the eye.

The agents that act mainly upon the musculature of the iris and affect the ciliary muscle scarcely at all are three in number—cocaine, euphthalmine, and mydrine. On the other hand, those that paralyse the ciliary muscle, together with the sphincter of the iris, are four in number—atropine, homatropine, eumydrine, and the methylbromate of atropine. I leave out of account several other agents that act in the one way or the other, such as scopolamine, duboisine, daturine, hyoscine, atroscine, picramine, and hygrine, because there is still some doubt with regard to their chemical composition, and few of them, except perhaps scopolamine, seem likely to render any great practical help in eye work.

Let us suppose that we desire to dilate the pupil, for the purpose of obtaining a satisfactory view of the fundus oculi with the ophthalmoscope. Atropine is about the last drug that a progressive ophthalmic surgeon would employ, because his experience tells him that the resulting disturbance in sight would be considerable, and would persist for several days. On the contrary, he would use a mydriatic pure and simple. Until the last few years cocaine was practically the only agent at our command which would dilate the pupil moderately and yet produce no considerable or lasting effect upon the function of accommodation. Even that agent now and then played us false, and caused an uncomfortable dimness of sight. Modern pharmacy, however, has again stepped in, and supplied us with *Euphthalmine*, a mandelic acid derivative, the hydrochloride salt of which appears in the form of a white crystalline powder, soluble in cold water. It may be used to dilate the pupil simply as a 3 per cent. to 5 per cent. aqueous solution, although its action in that direction is heightened and hastened by the addition of cocaine hydrochloride, 2 per cent. The mixture, moreover, is somewhat cheaper, since it allows the lower percentage of euphthalmine (a very costly drug) to be employed. A few drops of this combination placed in the conjunctival sac will cause the pupil to dilate in about thirty minutes, with a

minimal effect upon the function of accommodation. The dilatation passes away in a variable time, which averages about four hours, a process that may be quickened by applying a drop of physostigmine, 0.5 per cent., to the eye after the examination is completed. It will be gathered from what has been said that euphthalmine, alone or mixed with cocaine, is the agent to employ when it is desired to dilate the pupil for purposes of ophthalmoscopic examination without causing anything beyond the most trifling discomfort to the patient.

Mydrin is a compound of ephedrine and homatropine hydrochlorides, and when used as a 10 per cent. solution acts in the same way as euphthalmine. It is, however, a mixture, and, so far as I know, presents no single advantage over the last-named agent. The pupil, moreover, retains its action after mydrine has been used, and the amount of dilatation is less than after euphthalmine.

The important point to bear in mind is that after the employment of either euphthalmine or mydrine patients may be assured that they will be able to transact their business as usual, which is certainly not the case after atropine has been dropped into the eye. Mydrine solutions, it may be added, are very stable.

With regard to atropine, I have no new facts to bring under your notice, except perhaps the claim lately made by Dr. T. K. Hamilton (*Ophthalmoscope*, May, 1905) that the annoying conjunctivitis and dermatitis sometimes produced by it may be obviated by employing a solution of chloretone as the vehicle instead of ordinary distilled water, and of Dr. W. G. Sym (*Ibid.*, April, 1905) that the same end may be attained by using the alkaloid dissolved not in water at all but in pure olive oil.

Eumydrine.—This new mydriatic, which occurs as a white powder, readily soluble in water, has been investigated by Goldberg (*Heilkunde*, 1903) and by Lindenmeyer (*Berl. Klin. Woch.*, November 23rd, 1903). According to the former observer, a 1 per cent. solution acts more promptly than atropine (1 : 1,000), and its effects pass away more rapidly. No injurious results have been noted. Eumydrine, indeed, is stated to be fifty times less poisonous as regards the central nervous system than atropine, from which, by the way, it is obtained. Eumydrine acts as a trustworthy cycloplegic. Lindenmeyer found the new agent to be of service in such inflammations of the eye as would ordinarily be treated with atropine.

Speaking for myself, I have employed eumydrine in a solution containing two grains to the ounce of distilled water, and have satisfied myself that it is a

speedy, painless, and trustworthy mydriatic. Complete cycloplegia follows its use. It differs in two important points from atropine. First, the paralysis of accommodation induced by eumydrine, instead of lasting for upwards of a week as with atropine, usually passes away in the course of two or three days. Secondly, its action both upon the pupil and the ciliary muscle may be neutralised in half an hour or so by means of a weak solution of physostigmine (0.5 per cent.), which is not possible after atropine has been employed.

In the course of my experiments with eumydrine I have been impressed by one point, namely, that it is usually an excellent substitute for atropine when appearances of local intolerance to that remedy are present. In order to bear out this somewhat important practical observation, I may briefly quote one or two illustrative cases. (1) Jessie H—, æt. 12, was ordered atropine (grs. 2) on July 4th, 1904, as a preliminary to estimating a considerable error of refraction. After four applications of the atropine drops, the child's face became red. When seen on July 8th, the eyelids were puffy, and, like the neighbouring parts, red and angry-looking. The skin of the eyelids, when grasped between the fingers, conveyed a parchmentous feeling. There was dried muco-purulent discharge about the eyelids. A solution of eumydrine, grs. 2 to the ounce, was substituted for the atropine. The new drops were used twice a day until July 25th, without setting up the least irritation. (2) Maria M—, æt. 60, was ordered atropine drops (gr. 1 to the ounce) on August 8th, 1904, on account of choroiditis accompanying high myopia. A fortnight later (August 22nd) she presented herself suffering from extensive atropine irritation of the eyelids and neighbouring skin. The affected skin was parchmentous, dry, shiny, and red. The patient complained bitterly about the drops that had been given to her. Eumydrine (grs. 2) was substituted for the atropine. A week later the patient was free from all symptoms of irritation, and the eumydrine has produced no discomfort at all. (3) Emily G—, æt. 18, ordered to both eyes atropine drops, grs. 4 to the ounce, on December 12th, 1904. After one application, the skin on the left side of the face, as far as the level of the nostril, became red, swollen, and tender, and "seemed tight." Furthermore, she was only just able to open the eye. Eumydrine, grs. 4 to the ounce, acted well upon the pupils, and produced no irritation, though used three times a day for three days. (4) The effect was not so happy in the fourth case, that of a young woman, who was affected with bilateral interstitial keratitis, the result of inherited syphilis. In that case the usual type of irritation was induced by atropine, duboisine, hyoscy-

amine, and by eumydrine. It is, however, the only instance of the kind I have met with.

The slight poisonous qualities of eumydrine lead me to think that it may prove useful in children for paralyzing the accommodation before estimating the static refraction of the eye, and that in certain cases where the long-continued employment of a mydriatic is desirable—for example, in squint, interstitial keratitis, and so forth—it will be found to offer some advantages over atropine.

Methylbromate of Atropine.—This product occurs as white crystals freely soluble in water. It is, like eumydrine, a good substitute for atropine. Its action depends upon its strength. A 1 per cent. solution produces rapid dilatation of the pupil accompanied by cycloplegia. But combined with 1 per cent. cocaine it dilates the pupil without having much effect upon accommodation.

General Conclusions with regard to Mydriatics.—In certain inflammations of the eye, as iritis and iridocyclitis, no mydriatic, except perhaps eumydrine, can, according to our present knowledge, equal atropine, employed either as the sulphate, grs. 2 to grs. 4 to the ounce of distilled water, or as a solution of the alkaloid of the same strength in olive or castor or sesame oil. To dilate the pupil in suspected iritis for the purpose of ascertaining whether adhesions exist, it is better to select some agent, as the methylbromate of atropine, the effects of which pass off rather quickly. For estimating refraction in children, atropine sulphate (grs. 2 to grs. 4) is at present in almost universal use, although it may well be replaced by eumydrine, on account of the slight toxic properties of the latter. A similar remark is equally applicable to cases where the long-continued employment of a mydriatic is called for. For estimating refraction in adults, atropine, in general, should be avoided, and recourse be had to homatropine and cocaine, each 2 per cent., to eumydrine, 1 per cent., or to atropine methylbromate and cocaine, each 2 per cent. To enlarge the pupil for ophthalmoscopic examination, mydrine, 10 per cent., or, better, a mixture of euphthalmine and cocaine, of each 2 per cent., should be adopted. Atropine is absolutely contra-indicated under the circumstances. Remember, finally, that atropine is not the panacea it is sometimes believed to be for almost every inflammatory affection of the eye. When in doubt do *not* prescribe that drug. No mydriatic agent whatever, no matter how quickly its effects pass away, should ever be used in grown-up persons until tension has been estimated with the finger and glaucomatous cupping of the optic disc has been excluded by a glance with the ophthalmoscope.

3.—MYOTICS.

In physostigmine and pilocarpine respectively we have two agents capable of contracting the pupil, the former energetically and the latter in a milder way. The salicylate of physostigmine has been recommended by Dr. T. K. Hamilton (*Ophthalmoscope*, May, 1905) as a particularly suitable salt for prolonged use in chronic glaucoma. A substance named isophysostigmine, another alkaloid of the Calabar bean, has recently been investigated by Ogiu, a Japanese oculist (*Die Therapie der Gegenwart*, November, 1904). That surgeon found that the drug acted more quickly upon the pupil, and with greater energy, and for a longer period than physostigmine. These claims, if substantiated, are likely to lead to the general employment of isophysostigmine. Another comparatively new myotic, Arecoline, has fallen under my personal notice. It is one of the several alkaloids of the betel nut, and used as the 1 per cent. solution of the hydrobromide salt, has rendered service in glaucoma. By several observers, Mr. Richardson Cross, of Bristol, among the number, it is considered to be the best myotic for general use. But according to the younger Galezowski (*Recueil d'ophtal.* XXV., 1903, p. 112) even a half per cent. solution now and then gives rise to irritation of the conjunctiva.

4.—ANÆSTHETICS AND ANALGESICS.

Anæsthetics may be defined as agents capable of rendering the eye insensitive to the pain of surgical operations, while analgesics are agents capable of obtunding any pain that may exist. The distinction between the two classes comes out very clearly in eye work when we compare the action of two such medicaments as cocaine and dionine. The former, when dropped into the eye, renders the superficial parts insensitive, but has no definite influence upon the deep-seated pains of, say, iritis and glaucoma, whereas the latter deadens such pains without at the same time rendering the parts insensitive.

The anæsthetic for choice is still cocaine hydrochloride, as a 2 per cent. watery solution. In actual practice, however, it still leaves something to be desired, and to some extent, especially in America, it has been replaced by a 1 per cent. solution of the hydrochloride of holocaine. Holocaine, it is true, has advantages over cocaine. For example, it is a pure local anæsthetic, without action of any kind, sort, or description upon the pupil, accommodation, tension, or corneal epithelium. For the relief of deep-seated ocular pain, as Hinshelwood has pointed out (*British Medical Association*, 1898) it is greatly superior to cocaine. My personal experience has convinced me

that it has bactericidal powers, and, further, that it is better absorbed by a reddened eye than is cocaine. Its only drawback is that owing to its toxic properties it cannot safely be injected into the lacrymal passages or beneath the conjunctiva or the skin.

Dr. Carl Koller, who brought cocaine under the notice of the profession twenty-one years ago, has lately made a practical suggestion with regard to its use in cataract and other operations upon the eye (*Ophthalmoscope*, September, 1904). One or two minutes after placing a few drops of cocaine in the conjunctival sac, he injects 2-3 drops of a 5 per cent. solution beneath the ocular conjunctiva at the spot where he intends later to apply the fixation forceps. Five minutes afterwards, operations upon the eyeball, even such as involve the iris, can be performed without pain. I cannot help thinking Dr. Koller's suggestion has not yet had the attention paid to it that it deserves.

Eucaine lactate is a white powder, readily soluble in water. Its sole action is to induce local anæsthesia. For use in eye work, Langaard (*Therapeutische Monatshefte*, August, 1904), who regards the new agent as a substitute for cocaine, recommends a 2 per cent. or 3 per cent. solution, combined, if necessary, with adrenaline.

After a tolerably extensive trial of a 2 per cent. watery solution of eucaine lactate, I have reached conclusions regarding its action upon the eye that may be summarised as follows: the agent has no action whatever upon the pupil, ciliary muscle, or epithelium of the cornea. It produces neither redness nor anæmia of the superficial parts of the eyeball, nor does it give rise, as cocaine often does, to retraction of the upper eyelids. Its effect upon tension is *nil*. It sets up about the same amount of smarting when placed in the eye as cocaine—certainly not more, as Ellis (*California State Journal of Medicine*, Vol. III., No. 5) has stated. Thus, twelve adult patients æt. 27 to 77, had a drop of 2 per cent. cocaine placed in one eye and of 2 per cent. eucaine lactate in the other, and the discomfort was greater in the first eye in two instances, in the second eye in five instances, and was equal in the two eyes in five instances. Finally, local anæsthesia of a satisfactory nature is quickly induced, three minutes sufficing for the purpose, according to the mean of twenty experiments. In some cases of pain from irido-cyclitis and other causes, the discomfort was lulled for an hour or more by a few drops of eucaine lactate. In short, my personal experience confirms Langaard's claim that in eucaine lactate we have an agent whose sole action is to produce local anæsthesia. Additional good points about the new remedy are its

ready solubility in water, its comparative cheapness, its relative non-toxicity, and the fact that it undergoes no appreciable change when boiled, so that it may be kept sterile for an indefinite period. Further trials should be made with this interesting product, which possesses, as we have seen, some decided advantages over cocaine.

A good deal of attention, especially in France, has lately been paid to another local anæsthetic, the discovery of Fourneau, called Stovaine, the hydrochloride of amylein- α - β . It occurs in small white flakes, is extremely soluble in water, and its chemical reactions are almost identical with those of cocaine. Its solutions are not altered by boiling until a temperature of 120° C. has been reached, clearly an advantage from a practical point of view. Coakley (*Medical News*, April 15th, 1905) finds that the aqueous solution can be boiled for an hour without undergoing the least change, and that the stovaine can then be recovered intact by simple evaporation. The toxicity of stovaine is equal to one-half or one-third, that of cocaine being represented by one.

My experiments were made with a 4 per cent. watery solution of stovaine hydrochloride. I have found that it is a good local anæsthetic, and I have now performed a fair number of operations under its influence. Its action is that of an almost pure local anæsthetic, although retraction of the upper eyelid and slight dilatation of the pupil may follow its application, as pointed out by Fromaget and Dion and myself (*Ophthalmoscope*, November, 1904). Accommodation, however, is not affected. In a 1 per cent. or 2 per cent. solution it is very suitable for injection beneath the conjunctiva before operating for squint, removal of a piece of iris, or cataract. In brief, I conclude that in stovaine we have a trustworthy and relatively non-toxic local anæsthetic, and one capable of ready sterilisation by boiling, and as such I commend this latest product of synthetic chemistry to your notice. It may be combined with cocaine or adrenaline, and there are some reasons for thinking that the admixture acts better than the individual drug. In the treatment of disease, stovaine may be combined with other remedies, as ammoniated mercury or yellow oxide of mercury, in an ointment. But in that event the general rule applies, namely, that the alkaloid itself must be used and not a salt. A similar remark applies to oily menstrua.

Yohimbine, an alkaloid from Yamabehea bark, has enjoyed a reputation for a few years as an aphrodisiac. Magnani, Salomonsohn, Loewy, and Muller have employed a 1 per cent. solution as an ocular anæsthetic. Claiborne and Coburn (*Medical News*, July 9th, 1904), who used a 2 per cent. solution, concluded as the

result of their experiments that yohimbine, in addition to being a local anæsthetic, caused smarting and suffusion of the eye, moderate dilatation of the pupil, and slight blurring of sight, due not to paresis of accommodation but to spherical aberration. The high price of yohimbine, together with the fact that it is not a local anæsthetic, pure and simple, will militate against anything like its general employment.

An analgesic of practical importance has lately been introduced in the shape of Dionine, the hydrochloride of ethyl-morphine, a white powder, soluble in water, and employed in eye work as a 1 per cent. to 10 per cent. solution. It has little if any action on superficial structures, as conjunctiva and cornea, thus differing markedly from cocaine. When dropped into the eye, especially of children and unhealthy adults, it not infrequently gives rise to pain, chemosis, and swelling of the eyelids, and, by finding its way into the nasal passages, to sneezing—"ophthalmologic fireworks," is the expression applied by Dr. A. B. Hale (*Ophthalmic Record*, December, 1903) to describe these untoward effects of dionine. After use for some days (two or three usually) reaction of the kind described either fails to appear altogether or manifests itself in a trivial way.

The changes alluded to (which are more striking than dangerous) are ascribed to an inundation by lymph of the tissues of the eye, and this lymphagogue property of dionine has been utilised for the removal of inflammatory products, such as opacities of the cornea and the lenticular remains after cataract operations. Bulson (*Ophthalmic Record*, August, 1904) writing on this subject, says: "In fact, the remarkable results secured by dionine in clearing the pupillary space following cataract extraction has led to the belief that, with the more or less general employment of dionine after cataract extractions secondary operations will be greatly lessened in number." Time alone can show whether this claim can stand! Dionine is useful in interstitial keratitis in hastening the absorption of corneal deposits late in the history of the disease. In this condition I have myself obtained excellent results. In such cases there is, as usual, a right and a wrong way of using dionine. The right way is to drop a 5 per cent. solution into the eye three or four times a day for a couple of days, and to repeat the process after waiting some three days. In children I have cured many septic ulcers of the cornea, associated with pus in the anterior chamber, by simply dropping dionine into the affected eye.

Darier has pointed to another and even more practical use of the new product—namely, the induction of analgesia lasting for several hours in some of the more painful affections of the eyeball, as episcleritis,

hypopyon-keratitis, irido-cyclitis, and glaucoma. This action is most useful, since agonising pain may often be calmed by the simple expedient of applying to the eye a few drops of a 5 per cent. solution of dionine. In acute iritis, especially when of "rheumatic" origin, I often prescribe: Atropine sulphate, grs. 2; dionine, grs. 5; water $\frac{1}{2}$ oz.; the liquid to be used two to six times a day, according to circumstances. Dionine may also be combined with physostigmine or pilocarpine in the medical treatment of glaucoma. A useful combination is—physostigmine sulphatis, gr. $\frac{1}{2}$; dionine, grs. 5; water, drachms 4.

Blanco (*Archivos de Oftalmologia*, August, 1904) has successfully treated two cases of intra-ocular hæmorrhage by means of the subconjunctival injection of dionine.

As a symptomatic rather than as a curative agent, dionine is well worth the earnest attention of practising physicians. In my experience, it is a most efficient analgesic. For the relief of deep ocular pain the 5 per cent. solution should be employed every four to six hours, according to the particular circumstances of the case.

One other analgesic remains to be mentioned, viz., acoine, the employment of which for rendering subconjunctival injections painless or almost painless has been alluded to earlier in these Lectures.

General Conclusions as to Anæsthetics and Analgesics.—To my thinking, the ideal anæsthetic or analgesic should fulfil three requirements: first, it should exert simply an anæsthetic or analgesic action, as the case may be; secondly, it should not irritate the eye; and, thirdly, it should be readily soluble in water, economical in price, and non-toxic in use. Bearing these various points in mind, it will be found that the best agents to employ preliminary to an operation on the eye, named in their order of merit, are holocaine, 1 per cent.; eucaine lactate, 2 per cent.; stovaine, 4 per cent.; and cocaine, 2 per cent. For injection, holocaine must be carefully eschewed, and the preference be given to stovaine, 1 per cent.; eucaine lactate, 1 per cent. or 2 per cent.; or cocaine, 1 per cent. or 2 per cent. To obtund deep-seated pain in the eye, irrespective of its cause, we use dionine, 5 per cent.; combined in iritis with atropine and in glaucoma with physostigmine or pilocarpine. To render subconjunctival medication as little painful as possible, acoine, 1 per cent. or 2 per cent., is the agent *par excellence*.

LECTURE III.

5.—MISCELLANEOUS REMEDIES.

Supra-renal Extract.—In 1896, Dr. Bates, of New York, familiarised surgeons with the effects of an ex-

tract of suprarenal capsule upon the eye by showing that a 1 per cent. solution acted simply and solely as a powerful vaso-constrictor. The observation was not taken up widely, mainly because the suprarenal was difficult to procure and not easy to keep in an active state. Still, the experiments that were made confirmed Dr. Bates' main assertions. Since then, as everybody knows, adrenaline chloride has been introduced by Dr. Takamine, and placed upon the market by Messrs. Parke, Davis, and Co., thus giving us a most convenient, cleanly, and active preparation of suprarenal body. More recently still, three substitutes, namely, "renoform," "hemisine," and "paranephrin," have been introduced as cheap and convenient substitutes for adrenaline. "Renoform" is a fluid extract of the active principle of the suprarenal bodies, manufactured by a Berlin firm of chemists. Goldschmidt (*Die Therapie der Gegenwart*, July, 1903) recommends it as an economical, active, and non-irritating substitute for adrenaline, which, truth to tell, is somewhat costly. "Hemisine," one of Messrs. Burroughs Wellcome and Co.'s preparations, is described as "a derivative of the suprarenal gland, and is put up in ophthalmic tabloids, each of which contains approximately 1-100th of a grain." One of these tiny tabloids dissolved in 10 minims of water forms a solution of 1 in 1,000. I can testify to the fact that "hemisine" is an active preparation. "Paranephrin," a new product of the Darmstadt firm of Merck, is a stable 1 : 1,000 solution of paranephrin in 0.6 per cent. solution of common salt. Polte (*Archiv für Augenheilkunde*, November, 1904) has made careful experimental trials of the product, the action of which is that of suprarenal extracts in general.

From what has been said it will be obvious that we are now in possession of several trustworthy suprarenal preparations, British and foreign.

When a physiologically active preparation of suprarenal gland is dropped into the conjunctival sac, the mucous membrane becomes markedly blanched in the course of a few moments. As regards its whiteness, the eye may be said almost to resemble an artificial eye in appearance. There is no action upon the pupil, the accommodation, or, indeed, upon any other structure or function of the eye. The anæmic condition lasts for about an hour, more or less. The knowledge of this property of adrenaline has spread beyond the members of the medical profession. It appears that trachomatous immigrants seeking admission to the United States have endeavoured to turn the vaso-constrictor powers of adrenaline to good purposes in concealing their disease. They have found that all

evidences of mild trachoma can be obliterated for about half an hour if adrenaline be dropped into the eyes. However, the inspectors have been equal to the occasion, and now make not one but several examinations of suspicious cases.

It was at first thought that the intense vaso-constrictor action of adrenaline might be turned to advantage in the treatment of superficial diseases of the eye, and many trials in that direction have been made. But as Dr. J. A. Menzies has well said (*Ophthalmoscope*, Vol. II., 1904, p. 500), "congestion is Nature's attempt to remove the cause of a conjunctivitis by a free flushing with blood and lymph. To use adrenaline in such a case, without at the same time attacking the disease, is to thwart Nature's attempt at cure without introducing an alternative attempt. . . . The use of adrenaline in such a case is, therefore, a confession of helpless ignorance." In short, accumulated experience now shows that the main use of adrenaline must be sought in directions other than the relief of actual disease. The agent, it is true, does exert a beneficial effect upon a conjunctival disease, rare in England, Spring catarrh, but common enough in some other countries. At the same time, in my experience, it is not a specific even in that disorder. In glaucoma, also, adrenaline is certainly not devoid of power. Grandclément (*La Clinique Ophtalmologique*, 1904) has insisted upon the fact that it is capable of curing glaucoma without operation, provided the disease has not lasted long enough to produce organic tissue changes, and, further, that the drug, combined with physostigmine, be used very frequently—say, every half-hour for several days. The same author (*Die Ophtal. Klinik*, August 20th, 1904) has improved sight in a case of buphthalmos—that is, congenital glaucoma—by using the following collyrium: eserine, 0.50; adrenaline, 1:1,000, 3; distilled water to 10.0. At the same time, it must not be forgotten that Mr. A. F. MacCallan (*Trans. Ophthalmological Society*, Vol. XXIII., 1903) has reported five cases of glaucoma in which adrenaline caused an increase in tension, an observation more recently confirmed in two cases of glaucoma by Dr. A. Senn (*Woch. f. Therapie u. Hygiene des Auges*, 1905). The result is, however, very unusual, and it would be unfair, as MacCallan himself admits, to lay undue stress upon the fact.

For my own part, I have never seen anything but benefit result from the addition of adrenaline to physostigmine in the medicamentous treatment of chronic glaucoma. The prescription I usually give combines $\frac{1}{4}$ grain of the sulphate of physostigmine with 4 drachms of a 1:2,000 solution of adrenaline chloride, and, if pain be a prominent feature, as stated

before, five grains or more of dionine are added to the liquid.

The fact should be mentioned that the reckless employment of adrenaline has been known to produce failure of sight and softness of the eyeball, the latter lasting, as in Grandclément's case, for several months (*Die Ophthal. Klinik*, August 20th, 1904).

There are three other uses to which adrenaline or its substitutes may be put—(1) to prevent hæmorrhage during operations upon the eye; (2) to assist in the absorption of other remedies; and (3) to aid in the diagnosis of certain diseased conditions of the eye.

(1) With respect to the first of these uses, the prescription may stand: cocaine hydrochloride, 2 per cent. dissolved in adrenaline hydrochloride, 1 : 2,000; a drop into the eye every two minutes for six or eight minutes before operation. Cohn (*Woch. f. Therapie u. Hygiene des Auges*, November 24th, 1904) has experimented with a new combination of cocaine and adrenaline, which goes under the name of "eusemin." It contains, in addition to the two alkaloids mentioned, chloretone and physiological salt solution. It is most useful as a local anæsthetic in eye operations, and may be injected beneath the skin or the conjunctiva. There can be no doubt that when operating for squint, adrenaline does render the parts more or less bloodless, and in that way simplifies the operation, an important point, more especially if my plan of lengthening instead of dividing the tendon be adopted. For iridectomy and cataract, however, the preliminary vaso-constriction may be followed by reactionary bleeding into the anterior chamber, as happened to me in four successive iridectomies. Since that experience I have used adrenaline less frequently as a hæmostatic than I did formerly.

(2) With respect to the second use of adrenaline, namely, of helping the absorption of other remedies, it is a fact that when the eyeball is markedly reddened, as in acute iritis, atropine will act better upon the pupil if combined with adrenaline than if employed alone. But, according to Dr. R. Mengelburg (*Woch. f. Therapie u. Hygiene des Auges*, No. 32, 1903) there is a danger in that very fact, since symptoms of atropine poisoning are apt to be set up. It is thought that the lumen of the lacrymal passages is widened by constriction of the vessels, so that the passage of atropine from the conjunctival sac into the nose and throat is thereby facilitated. Again, in using fluorescein for the staining of raw spots on the cornea, the preliminary drop of cocaine or of adrenaline will render the process of colouration quicker and more complete. In the passage of a lacrymal probe, too, adrenaline by acting

as an astringent to the mucous membrane, is often of service.

(3) As to the third point, by applying adrenaline to an inflamed eye, the distinction between conjunctival and ciliary redness may often be established in a very conclusive and pretty way, since the conjunctival system is alone affected by a single drop of the medicament.

Jequiritol.—This agent, introduced by Römer, of Würzburg, represents, as Dr. Albert B. Hale (*lococitato*) has well said "the application of the modern laboratory idea to botanic as well as to therapeutic science." *Jequiritol* is a standardised abrin preparation obtained from the seeds of the *Abrus precatorius*, and intended to be a scientific and exact substitute for the older jequirity solutions, which in their turn replaced the ancient inoculation of an eye with gonorrhœal pus. It is supplied in four different strengths, with a curative serum and printed instructions for use in a wooden box by Merck, of Darmstadt. No. 1 concentration is the mildest, and No. 4 is the strongest. No. 1 kills a white mouse weighing 20 grm. within four days if $\frac{1}{6}$ grain be injected subcutaneously. Dropped into the eye in slowly increasing amounts and strengths, these liquids give rise to intense reaction, marked by redness, and swelling of the eyelids, chemosis, enlargement of the neighbouring glands, and so forth. When the symptoms appear likely to exceed the desired end, they may be mitigated by using the *jequiritol*-serum—that is to say, an antitoxin prepared upon the principle of Behring's serum.

Jequiritol is employed mainly for the clearing of corneal opacities, especially such as result from trachoma, eczema of the cornea, and interstitial keratitis. The agent does not appear to have been much used in this country or in America, although from other parts of the world conflicting reports as to its value continue to appear periodically. One school is represented by Dr. Henri Coppez (*La Clinique Ophtalmologique*, January 25th, 1903) who treated about 100 cases, and succeeded in healing ulcers, clearing pannus, and rendering the conjunctiva smooth. The other school is represented by Dr. Wecker (who introduced jequirity), who dwells upon the dangers and disadvantages of the new agent.

The preparation is expensive, and during its use patients must be confined to bed, or, at least, be made to keep the house. The pain and other discomfort caused by jequirity are serious drawbacks to anything like its general use. These and other considerations have led me to employ *jequiritol* in a sparing way and in selected cases only. I have careful notes of twelve such cases, and I will endeavour to summarise the results in ten of the cases as follows:—

The series included seven males and three females, whose ages ranged from six to fifteen years. In three both eyes were treated, and in seven one eye alone. The underlying condition which had caused the corneal opacities was trachoma in six instances and eczema in four. Reaction, as a rule, was insignificant until the strongest concentration of jequiritol was applied. Pain, membrane on the conjunctiva, chemosis, vascularity of the cornea, mastoid redness, swelling of the side of the face, enlargement and tenderness of the preauricular and cervical glands, and a rise in temperature to 100° F. or 101° F., were constant accompaniments of the cases in which jequiritol set up marked reaction. The complications of the treatment included abscess of the lacrymal sac—acute in one case, a child suffering from hereditary syphilis, and chronic in two others. In one patient, a girl, æt. 8, affected with active and vascular trachomatous pannus, seven applications of jequiritol led to severe reaction, associated with exfoliation of the anterior layers of the central region of the cornea. It became necessary in this case, the only one in the series, to make two applications of the "heilserum." With regard to the effects upon vision, there was no change for the better in four cases, and slight improvement in the remaining six cases. I am bound to say, however, that in no instance was the improvement in this respect greater than could be accounted for by the mere efflux of time, and was certainly not so pronounced as could have been obtained under simpler, more economical, and less painful methods of treatment.

In my hands, therefore, the results obtained from jequiritol treatment, although of some little scientific interest, are scarcely such as to justify me in undertaking further experiments.

X-RAYS.

During the last two years, X-rays, as well as currents of high intensity, have been widely employed in the treatment of diseases of the eye, sometimes with the best results. A timely note of warning, however, has been sounded by Dr. A. Birch-Hirschfeld (*V. Graefe's Archiv für Ophthalmologie*, II., October, 1904), with regard to the use of these powerful therapeutic agents in ophthalmic work. They may, indeed, unless used with proper precautions, cause most untoward complications, as, for example, loss of the eyebrows and eyelashes, inflammation of the conjunctiva, cornea, and iris, and in the deeper structures of the eye such changes as degeneration of the macular region and ganglionic layer of the retina and of the medullary fibres of the optic nerve. Birch-Hirschfeld, therefore, urges that the eyeball should be efficiently protected, and that

exposure should neither be unduly strong nor repeated too frequently.

The list of diseases that have been treated with X-rays is already quite a long one, and includes (1) rodent ulcer and epithelioma of the eyelids, and sarcomata and other orbital growths; (2) trachoma; (3) tuberculosis of the conjunctiva; (4) spring catarrh; (5) blastomycetes; and (6) scleritis, superficial and deep.

(1) *Rodent Ulcer, &c.*—The cure of rodent ulcer and epithelioma of the skin or the eyelids has now gone far beyond the experimental stage. In this connection, I will merely quote Dr. Sweet (*Medicine*, April, 1904) who has treated upwards of twenty such cases, with success in every instance except two. Sweet is of opinion that in our present state of knowledge it is no longer justifiable to resort to the excision of rodent ulcers and epitheliomata of the eyelids. With regard to sarcomata the position of X-rays is not so clear. However, an inoperable case of orbital sarcoma has been reported by Webster Fox (*Archives of Ophthalmology*, January, 1904) where restoration to the normal followed forty-six exposures to the focus-tube. Kienbock (*Woch. f. Therapie u. Hygiene des Auges*, February 25th, 1904) cured a sarcoma, which had produced bilateral exophthalmos and optic atrophy, by thirteen exposures spread over the course of three months. Béclère (*Gazette des Hôpitaux*, June 14th, 1904) has also reported a successful case.

(2) *Trachoma.*—Trachoma has been treated with X-rays by Mayou, Walsh, Cassidy and Rayne, Bettremieux, Goldzieher, Pardo, and myself, with results that, upon the whole, compare most favourably with those obtained by the ordinary methods. Walsh and myself were the first to employ the high frequency current in this intractable disorder. The results were excellent, and cure was obtained, always without pain, and often in a surprisingly short time. It seemed to make little difference whether the current was applied directly to the diseased parts or merely transmitted to them through the closed eyelids. The tedium inseparable from holding the lids everted, as well as the exposure of the nurse's hands, may be avoided by employing the ingenious clip devised by Reid and Edmunds (*Lancet*, August 15th, 1903).

(3) *Tuberculosis of the Conjunctiva.*—I was the first to endeavour to cure this disease by means of X-rays. My patient, a girl, æt. 4, was cured in a month, without visible cicatrization of the conjunctiva, by thirteen exposures applied for ten minutes at a time, the tube being held six to ten inches away from the eye. In these somewhat rare cases I believe that X-rays will usually suffice without excision or scraping or cauterisation of the affected parts. Moreover, there is always

a risk of exciting a generalised tuberculosis when we interfere surgically with these lesions, which as regards the conjunctiva are, in my experience, usually primary.

(4) *Spring Catarrh*.—Recovery of this curious affection by exposure to the emanations of the focus-tube have been reported by Starr, Bennett, and Allport. Allport (*Ophthalmic Record*, October, 1903) first removed the palpebral outgrowths, and then exposed the conjunctiva, everted by means of a lid-clamp, to the action of the X-rays. Cure followed eighty exposures.

(5) *Blastomycetes*.—The best cure for that singular disease, blastomycosis of the skin of the eyelids (instances of which have so far been met with almost exclusively in Chicago, U.S.A.), appears to be by the local application of X-rays, together with the administration internally of large doses of potassium iodide.

(6) *Scleritis, superficial and deep*.—Pardo (*Arch. di Ottalmologia*, January and February, 1905) has treated scleritis by the X-rays, and he claims that "these rays represent a real discovery, inasmuch as up to the present day there is no other direct therapeutic agent, but only means amounting to a purely symptomatic treatment."

RADIUM.

It would indeed be singular if that mysterious element radium had not been pressed into service in the treatment of eye disease. As a matter of fact, it has been employed in (1) epithelioma, rodent ulcer, and nævi of the eyelids; (2) trachoma; (3) relapsing inflammation of the uveal tract; and (4) various painful diseases of the eye and surrounding parts.

The method adopted has been simply to place a few mg. of radium bromide of varying degrees of uranium activity (U) in a sealed glass tube, and to apply the little apparatus close to or over the eyelids for a given time. Two points seem to stand out clearly—first, that radium is simpler to apply than the X-rays, and, secondly, that it may be used with comparative impunity about the eye. At the same time our knowledge of the therapeutic values of the α , β , and γ rays respectively may be said to be almost non-existent. The gamma-rays seem to be identical with the X-rays, and it is possible that the therapeutic results obtained from radium are more closely connected with them than with the other emanations, known and unknown, notwithstanding the fact that radium is estimated to give off a very small proportion only of these exceedingly penetrating rays.

(1) *Epithelioma, &c.*—With regard to rodent ulcer as it affects the skin of the eyelids, there can be no doubt whatever that radium is directly curative and that without pain, as witness successful cases reported

in this country by J. Mackenzie Davidson (*British Medical Journal*, January 23, 1904), Sichel (*ibid.*), and A. S. Green (*Lancet*, March 19th, 1904). This method of treatment, although by no means always rapid in its results (as in a case of my own) has obvious advantages as compared with surgical measures. Nævi have been treated successfully with radium in several instances by Justus (*Woch. f. Therapie u. Hygiene des Auges*, June 22nd, 1905, p. 302).

(2) *Trachoma*.—Hermann Cohn (*Berliner Klin. Woch.*, No. 1, 1905) cured three cases of trachoma by means of a crystal of radium bromide, enclosed in a thin glass tube, the end of which was employed to touch each trachoma-body from ten to fifteen minutes daily. The observation has to some extent been confirmed, and, indeed, even antedated, in this country, although it may be noted that Mr. N. B. Harman (*The Conjunctiva in Health and Disease*, 1905, p. 196) obtained no improvement in two patients upon whom he experimented.

(3) *Inflammation of the Uveal Tract*.—Dr. Charles H. Williams (*Trans. American Ophthalmological Society*, vol. X., pt. ii., 1904, p. 269) obtained considerable improvement in a case of inflammation of the uveal tract by one minute applications of radium (1,500,000 U.), carried out for about four months two or three times a week with occasional intermissions. Williams also saw benefit follow the employment of radium in two other cases—ulcer of the cornea, and acute iritis with turbidity of the aqueous humour.

(4) *Painful Affections of the Eye*.—Dr. Darier (*Ophthalmoscope*, June and July, 1905) has made the important observation that the metalloid is capable of relieving pain when applied to the eyelids in such affections as rheumatic iritis, specific choroiditis, orbital neuralgia, and so forth. This result, in Darier's hands, now and then came about from a single application of radium of 240 U. for one or two hours. Besson, in his book upon "Radium and Radioactivity," (reviewed in *Centralbl. f. praktische Augenheilkunde*, June, 1905, p. 177) confirms Darier's observations so far as regards the pain of rheumatic iritis, traumatic irido-cyclitis, and epibulbar carcinoma.

LECTURE IV.

6.—GENERAL REMEDIES.

General Anæsthesia.—Since the introduction of cocaine by Koller in 1884 there has been a growing disinclination among ophthalmic surgeons to operate under general narcosis if it can be avoided. This tendency is reflected in a recent paper by Dr. Otto Meyer, of Breslau, upon removal of the eyeball under

combined local anæsthesia, which appeared in the *Klinische Monatsblätter f. Augenheilkunde* for February last. He had undertaken eighty enucleations of the eyeball under the local anæsthesia produced by instillations of cocaine and the injection deeply into the orbit of Schleich's No. 2 solution. The reaction, however, has assuredly gone too far when we find so eminent an author as Professor Haab, of Zurich, practically advocating the abandonment of general anæsthesia in operative eye work. In his recently published *Augen-Operationslehre* (a work that should be in the hands of every ophthalmic student) Professor Haab takes what strikes me as an altogether exaggerated view of the dangers attendant on almost every form of general narcosis. Everyone will of course admit that if an operation on the eye can be done painlessly under local anæsthesia so much the better, on account of the preparation needed, the time consumed, the risks incurred, and the possibility of vomiting. Professor Haab, however, goes much farther, and advises against the induction of general anæsthesia on account of its danger to life. If his views were accepted generally, the present generation would be denied one of the greatest blessings bestowed upon mankind, namely, the possibility of performing the most severe operations without inflicting the least pain upon the patient. It is obvious that a certain percentage mortality is bound to attend the administration of any general anæsthetic, be it chloroform, ether, ethyl chloride, nitrous oxide, or any other. The relatively greater risk attending the first-named agent has rendered its administration by trained anæsthetists rarer than was once the case. The common practice now is to give gas or ethyl chloride at the start, and then ether or chloroform. Accidents will become less numerous as training in the giving of anæsthetics becomes more general. After all, the danger in skilled hands of giving ethyl chloride or gas and ether is a small one, and I seriously question whether the infinitesimal risks thereby incurred justify us in withholding from our patients the boons of general anæsthesia.

In point of fact, a general anæsthetic is almost indispensable in certain operations upon the eye—as, for example, in acute glaucoma and some other conditions where the parts are so deeply engorged with blood as to be incapable of absorbing the amount of cocaine or holocaine necessary to produce local anæsthesia. In children, again, there are few operations that can be done with comfort to the surgeon or with safety to the patient under cocaine, for in them it is not pain so much as fright that has to be contended against. Until recently chloroform was the favourite

anæsthetic, probably because it was generally available and called for no complicated apparatus, like ether, liable, perhaps at a critical moment, to get into the operator's way. Doubtless, chloroform or ether will remain the anæsthetic for such operations as require a period of prolonged unconsciousness. For brief periods of anæsthesia, however, such as suffice for most operations upon the eye, ethyl chloride is the best agent. It is speedy, relatively safe, easy to give, and produces an anæsthesia free from muscular twitchings, so embarrassing to the eye surgeon. Vomiting, in my experience, is generally due to an overdose.

Much of my personal experience, which now extends to upwards of three hundred administrations, has been gained with "kélène," merely an extraordinarily pure form of ethyl chloride. But Duncan and Flockhart's "chloryl anæsthetic" and Hedley's "ethyl chloride" also represent pure products at a cheaper rate. With regard to the apparatus, there are now several good inhalers available, among which may be mentioned the modified Ormsby ether inhaler made by Messrs. Krohne and Sesemann, and the "Simplex" inhaler of Messrs. Duncan and Flockhart. The point to be aimed at in a good apparatus is the complete or almost complete exclusion of atmospheric air. The mask is fitted to the patient's face, 2 c.c. to 6 c.c. of ethyl chloride sprayed into the face-piece, and the apparatus held over the mouth and nose until general anæsthesia is produced, a thing that, as a rule, does not take more than thirty seconds. The unconsciousness from a single dose lasts from one to three minutes—that is, long enough to perform many of the operations of ophthalmic surgery. If necessary, a longer period of anæsthesia may be obtained by giving a second dose of ethyl chloride or by continuing the inhalation with ether or chloroform. Insensibility is shown by snoring respirations, insensitive corneæ, flaccid limbs, and in the case of children by absence of muscular response to a sharp nip in some tender portion of the body. With ethyl chloride a patient may be anæsthetised, operated on, and recover within five minutes, an economy of time that will be appreciated by all who have to work in a crowded and busy out-patient department.

References to Ethyl Chloride in Eye Work—

1. Fromaget.—*Annales d'Oculistique*, 1901, p. 196.
2. Stephenson and Chaldecott.—*Ophthalmoscope*, 1904, p. 129.

3. Valude.—*Recueil des Travaux Xe Congrès international d'Ophthalmologie*, Lucerne, September, 1904.
4. Hird, B.—*Ophthalmoscope*, March, 1905, p. 122.

ANIMAL ORGANOTHERAPY

Apart from suprarenal extract, which has already been considered, two animal extracts have been employed in eye work—"didymine" and "optocine." The treatment of exophthalmic goitre by Dr. Moebius's "antithyroidin" (Merck)—i.e., the blood-serum of rams from which the thyroid gland has been removed, with 0.5 per cent. of added carbolic acid—need scarcely be described in this place, although it is clearly of interest to ophthalmic as well as to general surgeons.

Didymine, or testicular substance, has been used internally in locomotor ataxy. Dr. Lloyd Roberts has recently reported several cases of exophthalmic goitre relieved by its administration, one to five 5-grain tabloids (Burroughs Wellcome and Co.) being administered several times a day. Testicular extract has been put to a curious and out-of-the-way use by Dr. L. Dor (*Recueil des Travaux Xe Congrès international d'Ophthalmologie*, September, 1904), who gave the product to five children in whom rapid growth was associated with symptoms of asthenopia. Growth was retarded, and incidentally asthenopia improved.

Optocine is the name given to a potent extract from the retinae of freshly slaughtered animals. It is administered in various forms of retinal exhaustion—as, for example, in tobacco amblyopia, in retinitis pigmentosa, and in myopic choroiditis. The dose is one drachm two or three times a day. Mr. Robert W. Doyne was the first to bring this novel product under the notice of the medical profession, and those interested in the subject are advised to consult his original communications in the *British Medical Journal* of July 25th and September 26th, 1903. In this place I will merely say that it does appear to expedite recovery in tobacco amblyopia, although it is most difficult in that as in other diseases that tend to self-cure to estimate "optocine" at its true value. I have, however, more than once seen sight improve in such cases even when the patient continued to smoke immoderately. As a matter of some slight historical interest it should be pointed out that extracts from various parts of the eye have been employed by Dor in 1897, by Lagrange in 1898, and by Darier in 1900.

SERUMTHERAPY.

Antitoxic sera have been employed in ophthalmology in the treatment of four conditions, viz. :—1. Diphtheria of the conjunctiva ; 2. Hypopyon-ulcer of the

cornea; 3. Ocular tuberculosis; and 4. Streptococcal and staphylococcal invasions.

1. *Diphtheria of the Conjunctiva*.—Diphtheria of the conjunctiva is tolerably common among young children of the lower classes in London. According to my personal experience, it forms 1·26 per cent. of the eye cases presented for treatment in the ophthalmic department of a children's hospital. It usually occurs in a mild form, much resembling acute muco-purulent ophthalmia, and is doubtless often mistaken for the latter disease. There is, however, membrane upon the conjunctiva, a point that should suffice to distinguish the two affections. Even fatal cases are not unknown in this country. Mr. Percy Flemming has described such a case in an infant of four months; Dr. Bullar had a fatal case in a baby of ten days; and I have myself had two fatal cases in children, aged respectively 11 and 16 months. The treatment, which should be commenced as early as possible, is by the injection of diphtheria antitoxin, the dose of which will depend not upon the age of the child but upon the severity of the disease. Indeed, the serum appears to be productive of nothing but good, no matter in what dose it is injected. "Mixed infections," as they are called, are very common. Thus, among forty-two cases of diphtheria of the conjunctiva published by me a year or so ago, they occurred in no less than 86·04 per cent. Hence, in addition to antitoxin, local antiseptics should be applied to the conjunctiva. Many remedies may be used for this purpose, but, upon the whole, I have found a 15 per cent. solution of argyrol to succeed as well as anything else I have tried.

2. *Hypopyon-Ulcer of the Cornea*.—There is no more fatal disease of the eye than the one usually termed in England "hypopyon-ulcer," and elsewhere "ulcus serpens corneæ." An elderly person, usually of the labouring classes, with unsound lacrymal passages, receives, in the course of his work, some trifling injury to his cornea. The little wound or abrasion, instead of healing promptly as it would do in a healthy subject, becomes infected with pneumococci from the diseased lacrymal passages, pus appears in the anterior chamber, the ulcer spreads, and in the absence of prompt and well-directed treatment, the eye is only too likely to be lost. The usual treatment of the condition includes slitting the canaliculus, in order to give exit to the infectious secretions of the lacrymal sac, and, above all, the application of the galvano-cautery to the aggressive edge of the corneal ulceration. Saemisch's method—that is, opening the anterior chamber by means of an incision including the entire thickness of the ulcer—

is practised by many operators, despite the fact that it is often followed by an adhesion between cornea and iris, which later may have disastrous consequences.

Römer, of Wurzburg, has experimented in this condition with a polyvalent serum of high potency, prepared by Merck, of Darmstadt (*von Graefe's Archiv f. Ophthalmologie*, Vol. 54, No. I., and *Bericht der Ophthalmologischen Gesellschaft, Heidelberg*, 1902 and 1903). The hypopyon-keratitis was produced in rabbits and monkeys by inoculating the cornea with pneumococci, and Römer's series also included clinical cases as met with in man. Cases treated early almost invariably healed well, whilst almost 80 per cent. of successes were obtained even when the condition was advanced. In 95 per cent. of cases of hypopyon-keratitis the pneumococcus is present. In the earlier experiments the serum was injected beneath the skin and the conjunctiva and also applied directly to the corneal ulcer, but, later, Römer discarded the subconjunctival injections. Several Continental observers have now experimented with Römer's pneumococcic serum, and, as usual, there is no unanimity of opinion with regard to its true clinical value. It is, however, agreed that *ulcus serpens* produced by experimental inoculation does yield in many instances to the serum. Paul, Augstein, and Zur Nedden, who among them treated 32 ordinary cases of hypopyon-keratitis, obtained a cure with the serum in six only. In the remaining cases, amounting to 81 per cent. of the total number, the cautery had to be applied or the Saemisch section performed before the destructive corneal process could be checked. Paul, one of the most recent writers on the subject, goes so far as to say that the pneumococcic serum should be adopted in exceptional cases only, and that commonly preference should be given to surgical measures (*Klin. Monatsblätter f. Augenheilkunde*, January, 1905). Another writer, Oliveres (*La Clinique Ophtalmologique*, June 25th, 1905), has treated three cases of *ulcus serpens* with Römer's serum, but in every instance had to resort to other measures, especially the subconjunctival injection of mercury cyanide, before he could obtain cure. Finally, from certain observations made by Zeller (*Med. Corresp.—Blatt des Württ. ärztlichen Landesvereins*, September 3rd, 1904), it appears that the use of serum is not always free from danger. For example, in a case mentioned by him the injections are stated to have been followed by myocarditis.

3. *Ocular Tuberculosis*.—The tuberculous diseases of the eye are numerous and important, although not perhaps altogether common. They include tuberculosis of the conjunctiva, iris, choroid, and lacrymal

sac. The superficial manifestations can be attacked with the knife, sharp spoon, cautery, or X-rays, but until recently our means of dealing with the deeper lesions were limited indeed. In fact, the management of such affections was on the lines now generally adopted in treating phthisis pulmonalis—that is to say, by living in open air and bright sunshine, by well-cooked and generous diet, and by careful attention to the state of the skin and other emunctories. Now, thanks to serumtherapy, we appear to be reaching more tangible and solid ground. "Tuberculin T.R." has been employed by von Hippel (*von Graefe's Archiv f. Ophthalmologie*, August 9th, 1904), in the treatment of fourteen cases of ocular tuberculosis, affecting cornea and uveal tract in thirteen cases, conjunctiva in three cases, and sclera in one case. The injections are gradually increased from 1—500 milligramme up to, but never beyond, 1 milligramme of the product, and are made every other day. The temperature is taken at two-hourly intervals, and should it exceed 100.5° F., no increase in the dose of the tuberculin must be made. In serious cases quite six months' treatment is called for. Von Hippel has never met with any bad effect as regards the general health. But a case recently published by Contino (*La Clinica Oculistica*, November-December, 1904), shows that there may be a reverse to the medal. A child of 10 years suffering from a tuberculous ulceration of the conjunctiva was treated by serum, antitoxic and another, with the consequence that the lesion healed in about a month. Five weeks later, however, the child became very ill, and died comatose in a few days from tuberculous meningitis.

I am not disposed to attach undue importance to Contino's observation, because I have seen something of the same kind happen where serum had not been injected. A child, *æt.* 17 months, presented a tuberculous ulceration towards the centre of the free edge of one lower lid. Twenty-one days later, she was found to have double optic papillitis and tubercle of the choroid. She died twenty-five days after the first examination from milary tuberculosis (*British Medical Journal*, May 3rd, 1902.)

4. *Pyogenic Invasions of the Eye.*—In certain streptococcus invasions of the eye, as occurs in infected wounds, operative or accidental, antistreptococcus serum has been tried. Claiborne and Coburn, however, as the results of their experiments upon rabbits, conclude that it exerts no favourable influence upon the course of these invasions (*Medical News*, August 6th, 1904). The same serum has also been successfully employed by Darier in a case of purulent ophthalmia

in a baby associated not with the gonococcus but with streptococci.

7.—GENERAL CONSTITUTIONAL REMEDIES.

Almost every constitutional affection has its correlated eye disease, and he would be indeed a benighted specialist who employed local treatment to the neglect of general remedies. From a purely practical point of view, two affections of general nature stand prominently forward as causes of disease of the eye, viz., syphilis and rheumatism.

1. *Syphilis*.—Syphilis, acquired and inherited, is the commonest constitutional cause of ocular disease. The acquired disorder is responsible for iritis, cyclitis, choroiditis, retinitis, and for some cases of interstitial keratitis, to name a few alone among the so-called "specific" affections of the eye. The inherited disorder is the common and usual course of interstitial keratitis, and also produces choroido-retinitis, and occasionally oculo-motor paralysis.

In the treatment of the several conditions named mercury and potassium iodide are still our sheet-anchors. But during the last few years new and efficacious ways of administering mercury have been widely employed, more especially upon the Continent. These comprise (a) subcutaneous or, rather, intramuscular injection, and (b) intravenous injection, in each case of soluble mercurial salts. The employment of insoluble compounds, as calomel, appears to be attended with considerable danger, and personally I have had no experience of the method.

(a) Intramuscular injections have yielded me some brilliant results in cases, as interstitial keratitis and choroiditis, that refused to yield to the ordinary modes of administration—that is, by the mouth or by inunction. I once employed a solution of corrosive sublimate (1 grain of the salt to 1 drachm of sterilised water: dose, 10 minims twice or thrice a week), which was deeply injected into the gluteal muscles, after the skin of the buttocks had been carefully cleansed with soft soap, hot water, ether, and a solution of corrosive sublimate in carbolic lotion. There were, however, certain inconveniences. It was sometimes inadvisable to expose the buttocks, especially in the case of an adult member of the opposite sex. Although I never saw suppuration follow injection, yet the formation of a hard and tender lump on a sensitive part of the body, persisting for several days, was not a thing to be particularly desired. Then, the frequent repetition of injections rendered the part hard and indurated. Moreover, gummata may very occasionally appear at the point of injection of the mercurial fluid, either speedily or not until several

months or even years have elapsed. Thus, Juliusberg (*Munch. Med. Woch.*, April 14th, 1903), reported three cases in which such gummata appeared nine months, eighteen months, and several years respectively after the injection. A patient of my own, where injections had been made into the biceps of the upper arm, developed a gumma locally in the course of two or three weeks. The points named have led me to employ not corrosive sublimate but a 1 per cent. solution of mercury cyanide. The results were as good as with the other salt, and no painful lump is ever produced at the site of injection. The exposure of the patient, however, is still a disadvantage. I have no experience of sublammin, a 3 per cent. to 4 per cent. solution of which has been recommended for intra-muscular injection (*Therapist*, January 15th, 1904).

(b) The method I now prefer is the intravenous injection of a solution of mercury cyanide in physiological salt solution. The formula is:—Cyanide, 1; sodium chloride, 0.75; boiled distilled water, 100. Dose, 20 to 40 minims in urgent cases daily, and in others twice or thrice a week. The biniodide salt may also be employed according to the formula:—Mercury biniodide, 1; sodium iodide, 2; boiled distilled water, 100. Dose, 20 to 60 drops (1 c.c. to 3 c.c.).

The injection may, of course, be made into any accessible vein that is large and prominent enough, but usually the veins at the end of the elbow—the median cephalic and the median basilic—are the most convenient. Occasionally, the veins of the forearm or the cephalic or the basilic of the upper arm are suitable vessels for our purpose.

The parts are exposed, the vein selected, and a fillet is tied rather tightly around the upper arm. The skin over the arm is next carefully cleansed and sterilised. The vein is then steadied with the operator's thumb, and the needle pushed obliquely through its anterior wall. Penetration will be at once obvious either by blood falling into the syringe (which should, of course, have a glass barrel) or by rising on slightly withdrawing the piston of the instrument. No injection should ever be made until one of these two things has happened, as otherwise the fluid may be forced into the perivenous connective tissue, where it may cause considerable irritation. The contents of the syringe are then slowly pressed into the vein, the fillet having first been removed. Finally, the needle is withdrawn, and the tiny puncture sealed with collodion, or, if it does not leak, left without dressing of any kind. The injection is painless, provided the needle is passed into the vein without bungling.

Timid patients may become faint when the first injection is made. Sometimes a curious and indescribable taste in the mouth is complained of a few moments after the operation is completed.

It is important to bear in mind that signs of mercurial intolerance tell mainly upon the intestinal canal and not upon the mouth in these methods of administering the drug. They include colic and diarrhœa. For some few years I have been familiar with another sign of the mercurial action, which, so far as I know, has not yet been described. It consists in the formation of a red crescent at the free border of the nails, and its dimensions, in my experience, afford an excellent guide to the action of the mercury. It is better seen on the finger nails, since they are thinner than the nails of the toes, and for obvious reasons it is generally much better marked among the upper than the lower classes.

Before leaving the subject I should like to state clearly that I am in no sense an advocate of injections, except in particular and selected cases. There are many specific affections of the eye that can be treated efficiently by the internal administration of mercury with chalk or other familiar preparation of mercury. It is in diseases, the existence of which threatens to destroy sight or which refuse to yield to ordinary methods that we should, I think, inject the remedy. The disadvantages of intravenous injection are that it consumes time, may alarm timid patients, and that it is not always easy, and indeed sometimes impossible, especially in women and children, to find a vein suitable for our purpose. On the other hand, the process is simple, painless, free from danger, speedy in its effects, and presents the advantage that it is carried out by the medical man himself. I have satisfied myself that it is efficacious in many cases of choroiditis, specific and otherwise, upon which the ordinary preparations of mercury failed to procure any effect.

2. *Rheumatism*.—The precise relationship of rheumatism to many diseases of the eye is still unsettled. The word "rheumatic" is a legacy from old times, and is often even nowadays employed to cloak our ignorance of the essential nature of some ocular disorders. At the same time, certain diseases of the eye are undoubtedly of rheumatic origin. Of these the best-known is perhaps irido-cyclitis. A few years ago a theory was propounded by Dr. David Walsh that certain skin affections could be accounted for by excretion from the body of various irritants, such as drugs, micro-organisms, and toxins. It occurred to me (*Lancet*, February 29th, 1896) that the explanation, if correct, should apply to organs other than

the skin, engaged in the work of excretion. Now almost all the general ailments capable of causing an inflammation of the iris are associated with, if not actually caused by, micro-organisms. That fact will be disputed by none as regards syphilis, gonorrhœa, tubercle, leprosy, influenza, and relapsing fever. If the bacterial origin of rheumatism be admitted, then a common cause of iritis will fall into line with the rarer causes enumerated above, for it must be remembered that the ciliary body secretes the aqueous humour (E. T. Collins). The position might be stated in terms of a syllogism, as follows:—Most inflammations of the iris and ciliary body are dependent upon a constitutional ailment; a majority of these ailments are of bacterial nature; therefore, most forms of irido-cyclitis result from the action of micro-organisms. It was suggested as possible that the immediate cause of these inflammations might be sought in the vicarious glandular excretion of microbes or their products circulating in the blood or other nutrient fluids of the body. Since then Drs. Poynton and Paine have isolated from the lesions of acute rheumatism a minute diplococcus, now very generally accepted as the specific pathogenic agent. Not the least interesting result obtained by those workers has been the experimental production in rabbits of iritis by the injection of a pure culture of their "diplococcus rheumaticus" into the auricular vein of rabbits. The animals died of heart disease, and the causative organisms were found in the cloudy fluid of the anterior chamber of the affected eyes. A culture from that fluid, when injected into another rabbit, gave rise to chronic arthritis (*Ophthalmoscope*, October, 1903). The rheumatic origin of certain cases of irido-cyclitis has therefore been established both theoretically and experimentally.

In my own mind, I entertain no doubt that conjunctivitis is rarely and episcleritis commonly due to chronic articular rheumatism.

As to palsy of the ocular muscles and its "rheumatic" origin I am somewhat sceptical. Such patients, when watched long enough, are not infrequently found to develop serious nervous lesions, more especially insular sclerosis or tabes dorsalis. I may quote briefly the main facts of two such cases, of which the first eventually proved to be an instance of insular sclerosis, and the second was one of tabes dorsalis, presenting some resemblance to a so-called "rheumatic" paresis. *Case No. 1.*—Miss Y———, æt. 24, who gave a history of chronic articular rheumatism, consulted me in February, 1890, on account of a palsy of the left external rectus muscle,

of some weeks' duration. The paralysis was assigned to rheumatism, a diagnosis apparently confirmed by the fact that recovery took place in about three weeks under ordinary anti-rheumatic treatment. In the beginning of 1900—that is, ten years later—Miss Y———again came to me, on this occasion with paralysis of the right external rectus muscle. She also presented nystagmoid movements of the eyes, trembling of the legs, exaggerated knee-jerks, ankle clonus, and paræsthetic areas about the lower extremities. There was a history of occasional incontinence of urine, and of unsteadiness in the street. The diagnosis of insular sclerosis then seemed obvious, and it was reasonable to look upon the first attack of ocular palsy ten years before as a premonitory sign of that disease. *Case No. 2.*—Mr. W———, æt. 33, seen May 26th, 1905, complained that he had seen double for two days, and gave a history of a similar attack ten years ago, which lasted for about five weeks. Rheumatic fever at 7 years and “rheumatism and pleurisy” at 13 years of age. Patient subject in damp weather to pains in the arms and legs, and for three months had suffered from pains over the right eye and at the back of the neck. Upon examination, paresis of the right external rectus. Both optic discs, especially the right one, greyish; retinal vessels of good size. R.V.=6/60 and No. 18 Jaeger; L.V.=6/36—1.25 D. Sph.=6/12. Knee-jerks absent, even on re-inforcement. No pupillary signs. This patient furnished an excellent example of tabetic paresis (and optic atrophy) resembling a so-called “rheumatic” paresis, and easily capable of being confounded with the latter.

In “rheumatic” affections of the eye, in addition to local measures, one generally administers liberal doses of sodium salicylate, a drug that often acts admirably in relieving pain and subduing inflammation. Foucher (*L'Ophtalmologie provinciale*, August, 1904) has gone a step further, and treated three cases of rheumatic iritis by injecting beneath the conjunctiva a few drops of a 1 per cent. solution of sodium salicylate, and in another case he obtained relief to pain by injecting the same solution beneath the skin of the temple. For some little time I have employed in these rheumatic affections of the eye another salicyl compound, the name of which will certainly be familiar to all in this room, namely, aspirin. It is non-depressant, rapid in action, and seldom causes unpleasant symptoms, such as nausea and tinnitus. Administered in doses of 15 to 30 grains three or four times a day, its action upon rheumatic iritis is often surprising, while its power in relieving pain is sometimes as grateful to the

patient as it is unexpected by the practitioner. It is a remedy in rheumatic diseases of the eye that I would commend to your very earnest attention. Galezowski (*Recueil d'Ophtalmologie*, 1903, p. 179) and Frank (*American Journal of Ophthalmology*, June 1904) have testified to the efficiency of aspirin in rheumatic iritis. I would add, in concluding, that the pain of severe rheumatic iritis was relieved by Frank (*loco citato*) by painting the affected parts with diluted mesotan, the methoxy-methylester of salicylic acid. The remedy should be mixed with an equal part of olive or cotton seed oil, and be painted on the affected parts, the skin having first been carefully freed from moisture.

CONCLUSION.

The limited time at my disposal has allowed me to touch only the fringe of an interesting but somewhat extensive subject. Several new agents and methods, of which some give every promise of being of practical importance in the treatment of eye disease, have either been passed over altogether or else merely glanced at. Among these may be mentioned pressure-massage, intra-ocular disinfection by means of iodoform, and the treatment of infected wounds of the eye by intensive doses of mercury. What has been said, however, will, I hope, convince you that ophthalmology has not lagged behind the other branches of medicine and surgery as regards advances in the twin sisters of pharmacology and therapeutics. The results of that activity have made themselves felt in ophthalmic work by the introduction of new and valuable remedies, by accuracy of dosage, by precision of physiological action, and last, but not least, by convenience of application and of storage. It can be claimed, indeed, that the medicinal treatment of diseases of the eye is now, thanks to the labours of modern chemists and pharmacologists, fast approaching the position of an exact science.
