MYDRIATIC SYNERGY**A note on the use of mydriatics by
sub-conjunctival injection**

BY

FRANK FLYNN

HOUSE SURGEON, MOORFIELDS EYE HOSPITAL

THE usual method of producing mydriasis by the instillation into the conjunctival sac of atropine sulphate in the form of drops does not cause maximal dilatation of the pupil even in normal eyes; and it is well known that in cases of iritis, when the iris is congested and becoming bound to the anterior lens capsule by plastic synechiae, atropine drops often produce only a very slight effect.

This has led to a search for a more powerful mydriatic. Laevoglaucon (Laevo-rotatory deltanephren two per cent. and methylaminoacetopyrocatechol two per cent.) is certainly a very potent one. It is used in the form of drops—two drops being instilled at intervals of 15 minutes until five applications have been given. Besides requiring an hour for its administration it is often accompanied by much pain which the previous use of cocaine may or may not relieve, and further it is a very expensive drug. Its routine use, therefore, is hardly practicable.

But why does atropine fail? It is, I think, because the rate of absorption when given in the usual manner is slow, and the actual concentration in the aqueous at any particular time during treatment is very low. Moreover, this line of action aims merely at paralysing the sphincter muscle so that any dilatation that occurs depends on the normal tone of the dilator muscle and the elasticity of a congested oedematous iris, which factors necessarily are not great.

The solution used here is essentially a synergic mixture of atropine, cocaine and suprenin, given sub-conjunctivally. Sub-conjunctival injection has the obvious advantage of causing the drugs to enter the aqueous in a very much higher concentration than occurs when they are placed in the conjunctival sac. At the same time it increases greatly the rapidity with which their effects are produced.

As regards the action of the drugs, atropine, by its inhibitory effect on parasympathetic nerves, paralyses the sphincter muscle. Suprenin, by its action on the sympathetic, stimulates the dilator muscle, and by vasoconstriction of the conjunctival and ciliary vessels prevents the solution passing rapidly into the general

blood stream, thus tending to localize the effects of the drugs to the site of injection. Further, it lessens the vascular engorgement of the iris and so diminishes its volume. Cocaine aids the suprenin in the production of the above three actions through the sympathetic, besides rendering the injection and the resulting mydriasis painless.

At first small doses were used; (atropine 1/120 gr., cocaine 1/30 gr., suprenin 1/1,500 gr.) later these quantities were gradually increased and untoward effects carefully watched for—fortunately none was noted—until the dosage that is now recommended was reached.

Preparation of the Solution

The solution, which for convenience has been termed mydricain, contains, in each five minim dose, atropine sulphate gr. 1/60, cocaine hydrochloride gr. 1/10 and laevo-rotatory suprenin gr. 1/600, in the form of the hydrochloride, together with sodium chloride gr. 1/80 and chlorbutol gr. 1/120, in sterilized water.

The method of preparation is that usually employed for hypodermic injections. Atropine sulphate, cocaine hydrochloride, and sodium chloride are dissolved in sterile water and the solution sterilized for 30 minutes at a temperature of 115° C. to 116° C. Chlorbutol is then dissolved in this solution; finally, when it is cool, the suprenin hydrochloride is added. Six minims of this solution are introduced into brown ampoules, which have previously been sterilized in an autoclave at a temperature of 150° C. for one hour. The ampoules should conform to the test for alkalinity of glass. By this method of preparation the danger of decomposition, owing to oxidation, is eliminated; the solution is sterile and its activity persists.

Therapeutic Value

The indications for the use of mydricain are similar to those for laevo-glaucon, that is, when a powerful mydriatic is desired. It is not, however, suggested that the iris of a patient with acute iritis should be subjected repeatedly to the rather drastic stimulation of this preparation. The essential object which should be aimed at in the treatment of such a case is, of course, prolonged rest for the iris, and this can be achieved by means of atropine alone. But in the initial stages of an attack, when posterior synechiae are in process of formation, in my opinion an energetic attempt should be made to get the pupil well dilated and the iris free from the anterior lens capsule before being content with a

less vigorous mode of treatment. The injection may, however, have to be repeated if a sufficient effect is not obtained the first time—this may be the case when treatment is not begun until late in the course of the disease. If another injection is considered necessary it should not be administered until the following day, so that not more than five minims are given in each 24 hours.

This method is also convenient for producing rapid maximal mydriasis preparatory to the extraction of an intra-ocular foreign body. The injection is best given immediately before the operation, when the patient is already on the table. The same remarks apply to cases with a perforating corneal wound with prolapse of iris tissue.

Other types of cases where this treatment is helpful will suggest themselves; for example, a child with congenital cataract appearing for the second or third needling, whose pupils have not responded to the prolonged use of atropine drops. If such a patient is to have a general anaesthetic the usual pre-operative hypodermic injection of atropine must be omitted.

It is important also that the limitations of this method be recognized; obviously it will be ineffective in separating long-standing organized synechiae. It seems, from experience so far gained, that a result can be expected if the synechiae have not existed for longer than a month. In one case, where a small synechia had definitely been present for three weeks, dilatation was finally produced and the pupil became regular in outline, but only after injections had been made at a point corresponding to the position of the synechia, for three successive days. It is essential, therefore, to apply the treatment early if success in this respect is to be assured.

Other beneficial results, beyond the mere breaking down of synechiae, are often produced. Thus cases of iritis with plastic exudate in the anterior chamber and corneal ulcers with generalized haze of the corneal stroma show a more rapid improvement than with the usual method of treatment. The cornea becomes brighter more rapidly, and absorption of the exudate and clearing of the anterior chamber are aided considerably. These, which may be termed remote effects, must surely be secondary to the changes produced in the iris, at any rate, no other explanation is offered here.

Again, in cases of recurrent iritis with numerous old synechiae, it is sometimes impossible to decide by the usual clinical methods how much of the pupil is permanently bound down, and the onset if iris bombé may be feared. An injection of mydracain will show exactly how far the process of pupillary seclusion has advanced.

Another interesting point is that patients who have had atropine

Right and left fundus oculi. Insets from periphery of fundi.

irritation tolerate this treatment quite well and without a repetition of the dermatitis. In one such case where there was some doubt as to whether the patient had really been irritable to atropine this fact was subsequently proved by the instillation of drops.

Technique

A few drops of cocaine (four per cent.) are instilled beforehand, first, to eliminate the possibility of a cocaine idiosyncrasy, and secondly, to prevent the patient feeling the initial prick of the hypodermic needle—the subsequent action is, in any case, quite painless. I have observed a synechia in process of breaking down while examining a patient with the slit-lamp immediately after an injection, and on repeated questioning he would not admit that he felt pain. Atropine drops or ointment usually are instilled after the injection with the object of providing a steady absorption of this drug.

As regards the site of injection, it is a good plan to decide what will be the most resistant part of the pupil, for example, where there is an obvious synechia. The injection should then be made subconjunctivally, raising a bleb, a few millimetres from the limbus at a point corresponding to this part, because the first and maximum effect will be produced here and become proportionately less marked at points on the corneal circumference more remote. On the other hand, if the iris is a comparatively normal one and general maximum dilatation is required, it is not a difficult matter, by gentle pressure with a swab over the site of injection, to make the fluid spread around at least three-quarters of the globe. Should a sub-conjunctival haemorrhage occur it is of no consequence.

A word about the rapidity of action should be added as this is rather startling when seen for the first time. Accurate records of the time factors have been made. It will be sufficient to say that the pupil first begins to dilate 30 to 60 seconds after the completion of the injection and the effect is at its maximum in three to four minutes, though further dilatation may occur for some hours.

I am indebted to the honorary staff of Moorfields for the opportunity of treating, by this method, patients under their care. I would also like to thank Sister Hartshorne for her much appreciated assistance, and Mr. Clarke, hospital pharmacist, for the preparation of the various solutions and for his helpful suggestions.