

THE MYDRIATICS IN OPHTHALMOLOGY.¹

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I CALL your attention to-day to the mydriatics and their employment in ophthalmic practice.

The use of this interesting group of drugs furnishes probably the most important chapter in the local therapeutics of ophthalmology. The promptness and uniformity with which they display the physiological property from whence they derive their name, never cease to command the attention and excite the interest of the careful observer. It should be anticipated however, that any family of drugs possessing such decided potency, would not only be of great value as therapeutic agents, but must possess also great power for harm if unwisely administered. Indeed, I might very properly entitle these remarks "the use and abuse of the dilators of the pupil."

The five members of the group to which your attention is called are those only which experience has proved to be of greatest value in ophthalmological practice, viz.: The salts of atropine, hyoscyamine, duboisine, homatropine and cocaine. These do not comprise all the alkaloids extracted from the solanaceæ but are those which are habitually in use, and are therefore sufficient for the purposes of this lecture.

The mydriatic alkaloids extracted from this curiously interesting family of plants—the solanaceæ—are, chemically considered, very complex. Although much time has been devoted to their study in the laboratory, there remains much confusion, and on the whole they furnish a promising field for skilful and patient chemical work. When subjected to the methods of manipulation now in vogue, they yield a group of alkaloids differing more or less widely in their physiological properties, although obtained from a common source. It seems, moreover, that the methods employed for extraction determine in large measure the nature of the product. For example, the alkaloid derived from the atropa belladonna will be atropine if extracted in the presence of an alkali, as soda or potassa, whereas without these the product will be hyoscyamine. The only means by which the chemist is able to differentiate the product is by the fact that hyoscyamine has the property of rotating a beam of light to the left, while atropine possesses no polarizing power, and chemically they are isomeric, having the common for-

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mula $C_{17}H_{23}NO_3$. This has led to the impression that atropine and hyoscyamine are identical.

As found in the market the alkaloids may be placed in two classes,¹ the first of which would properly include those with a simple homogenous base and having the above formula. To this class belong atropine, crystalline hyoscyamine and hyosine. In the second class are included those having mixed bases, comprising the simple alkaloids of the first class, as they are found mixed in the plants of the natural order of the *salanaceæ*, viz.:—the *atropa belladonna*, *duboisia myopoides*, *datura stramonium*, *scopolio japonica*, etc. To this class belong the commercial daturine, duboisine, amorphous hyoscyamine and scopolin. I shall endeavor to show you to-day that at least three members of this class possess, in some respects, essentially different physiological properties when used as mydriatics, notwithstanding their common parentage, chemical similarity and possible identity; therefore that in their employment as therapeutic agents we should be careful to secure a carefully isolated product as represented in the crystalline salts as against the mixed bases as represented in the amorphous commercial product. Very much of the confusion regarding their physiological properties and relative therapeutic value, doubtless, has grown out of the employment of these mixed bases. The immediate harm resulting from the use of an impure product displays itself first of all in the irritation of the conjunctiva and cornea, and second, by the variable duration of the resulting dilatation of the pupil and paralysis of the accommodation. It is, first of all, important that the solutions of the salts of these alkaloids should be bland, since any irritation of the tissues is especially harmful and directly opposed to the purposes for which the drug is usually employed.

The mydriatics are employed by the ophthalmic surgeon—

- (1) As simple dilators of the pupil for the purpose of better examination of the structures lying behind the iris.
- (2) In the treatment of a large group of inflammations of the ocular tunics.
- (3) For the paralysis of the accommodation.

In each of these it is obvious that any irritation of the external tunics should be avoided, since the excessive lachrymation washes the solution away in the tears, and probably the resulting congestion prevents absorption. To this end, only neutral solutions of the crystalline salts in distilled water should be employed. It is probable that much of the atropine conjunctivitis, of which we formerly heard so much, was due to the neglect by the pharmacist of this precaution. In dispens-

¹ Vide. *Trans. Am. Oph. Soc.*, December 1891, page 203. A Note on Hyoscyamine by S. D. Risley, M.D.

ing them the pharmacist should use mortars or other implements used only for this purpose, since it is very difficult to cleanse thoroughly an ordinary mortar in which some acid mixture has been previously compounded. Such precaution will avoid, in many cases, the irritating properties of many eye-washes from which our patients so often suffer.

As Dilators of the Pupil.—In the thorough examination of the eye it often becomes necessary to enlarge the pupil. This is especially necessary for the careful inspection of the crystalline lens and vitreous body. It not infrequently happens that opacities of the lens, commencing in the extreme periphery, may be overlooked if the examination is made through the narrow pupil, since the iris then lies in front of that part of the lens involved in the pathological process.

In disease of the choroid and ciliary body, web-like or fine granular opacities frequently occur in the vitreous, and veil or obscure more or less any image of the eye ground, giving a foggy appearance to the tissues under inspection, and are therefore liable to lead to erroneous opinions as to the cause of the obscuration, the condition of the vitreous being difficult to detect through a narrow pupil. With the dilated pupil, however, and a magnifying glass, the cause of the blurred image, if due to want of transparency in the vitreous, can readily be detected. For this purpose cocaine or homatropine should be selected, or the two may be used in combination. The latter course is ordinarily preferable, since a wider dilatation is secured than where either is used alone. They are desirable, furthermore, because of the shorter duration of the mydriasis than when atropine is employed. In many cases the cocaine, in two per cent. solution, is quite sufficient, and to be preferred, since the accommodation is very slightly disturbed, and in from one and a half to three hours the pupil is quite restored. The patient is thus saved the great annoyance arising from the blurred vision due to paralysis of the accommodation, and also the prolonged mydriasis produced by the other mydriatics. The annoyance will last about twenty-four hours if homatropine is used, between three and four days from solutions of duboisine, while hyoscyamine will last one week and atropine from ten to fifteen days. The great saving of time and annoyance to the patient, therefore, most forcibly commends the employment of cocaine or homatropine where the purpose designed is simply the advantage gained by a temporary dilatation of the pupil.

If there are adhesions between the iris and lens capsule the use of the mydriatic will reveal their presence for diagnostic purposes, as in cases of iritis, but where used to detach these adhesions, one of the stronger mydriatics should be selected.

The Treatment of Inflammations.—The mydriatics are used as therapeutic agents in the treatment of a large number of inflammations

of the eye, both for their local anesthetic properties, and their mechanical effects as dilators of the pupil.

In abrasions of the cornea, in severe traumatism, both by accidents or after many operations, in keratitis, phlyctenular disease, iritis, etc., they are of great value, and for this purpose the salts of atropine are usually employed. The drug is first of all cheaper than the others of the group, and I have a suspicion that it possesses local anesthetic properties in greater degree than hyoscyamine or duboisine. In the milder forms of inflammation, or in minor injuries, as superficial abrasions of the cornea, which usually make a speedy recovery, homatropine either alone or combined with cocaine is to be preferred.

The method of employment is often of much importance. In the treatment of inflammations you will find solutions of sulphate of atropine, gr. iv—f̄i a useful standard strength to employ. In the case of children with phlyctenular disease of the cornea, so many examples of which you have seen under treatment at the clinic, it has long been my habit to detain them, making frequent instillations of the standard atropine solution until full dilatation of the pupil is secured. When this is reached you will often have the satisfaction of seeing the photophobia and lachrymation disappear, and the little sufferer open the eyes and look about, possibly the first time for many days or weeks. Not infrequently the cure will date from such a treatment, but oftener it may have to be repeated day after day, each succeeding day the child returning with contracted pupils. The parents should have a solution at home, and be instructed in the method and frequency of its use. In young children the head should be firmly held between the knees of the surgeon and the parents instructed to use the same method. The excessive flow of tears in such cases not only dilutes the solution, but makes it difficult to have the drug retained sufficiently long for absorption. In these cases you need have little fear of poisoning the child, partly because of the overflow of tears, but also for the reason that the nose and lachrymal passages are involved in the pathological process, and the latter partially or entirely closed by the turgid mucus membrane. While a single drop of the standard atropia solution dropped into the healthy conjunctival sac of a child may cause constitutional symptoms, by entering the stomach, through the tear ducts it may in these cases of phlyctenular disease be used with the most lavish freedom without general disturbance.

In the treatment of acute iritis we witness, however, in the highest degree the value of this important medicine. The permanent damage resulting from this serious disease is in a large measure due to adhesions of the iris to the anterior capsule of the lens. The soft and elastic iris, in health, lies in contact with the lens and moves

to and fro over its surface with every change of light and shade, but when the plastic forms of iritis occur, the small beads of lymph poured out from its surface glue it, very speedily to the lens capsule, and very firmly too, if the attachment is not disturbed at an early stage of the disease. It is not my purpose here to detail the unfortunate sequelæ of these attachments, or posterior synechia, as they are called. They are however, often the *fons et origo* of some of the most destructive pathological processes, which we are called upon to treat. This is particularly true in cases of recurrent iritis. It is therefore of the greatest importance to recognize the disease at the beginning and prevent the formation of these attachments by securing a wide dilatation of the pupil. By this means you draw the iris back from its contact with the anterior capsule of the lens and prevent the plastic adhesions. This disease is usually a painful affection so that the anesthetic properties of the mydriatics are important in securing your patient's comfort. If seen early, in the stage of hyperemia, it is usually not difficult to dilate the pupil, but later when synechia have formed, or the tissues of the iris are not only turgid with blood but infiltrated with the products of inflammation, the task is more difficult and often impossible until other measures for its relief have been adopted, *e. g.*, local, blood-letting, the use of mercurials, etc. Here also as in phlyctenular disease it is often necessary at the first sitting to make frequent instillations of atropine solutions gr. iv, or even gr. viii— \bar{f} i, at intervals of fifteen minutes. If after an hour or more there is no result, I have often seen the pupil rapidly dilate, and the pains relieved by the abstraction of blood from the temple. Caution should be observed, lest the unpleasant constitutional effects of the drug are produced by its entrance into the stomach by the way of the tear ducts. This can be avoided by placing the finger, armed with a napkin or absorbing cotton, between the lids at the inner canthus, allowing it to absorb the tears for a moment after the instillation. The use of 2 per cent. or 4 per cent. solutions of cocaine with the atropine adds greatly to the anesthetic effect of the drug, but must be used with caution, lest it disturb the nutrition of the cornea. It is probable that the anesthetic properties of the cocaine depend upon its power to deprive the tissues of their blood supply. If this is true, it is not prudent to keep the tissues too continuously under its influence.

I cannot pass the use of the mydriatics in inflammatory diseases of the eye without a caution. There is one form of disease in which they certainly do harm. A form of disease moreover which possesses many symptoms in common with iritis in which as we have seen it is so important that these drugs should be used early and vigorously. I allude to glaucoma. A brief analysis of the symptoms of each will serve to set forth the danger of mistake.

<i>Iritis, acute.</i>		<i>Glaucoma, acute.</i>
Redness.		Redness.
Pain.		Pain.
Dim vision.		Dim vision.
Photophobia.		Photophobia.
Lack lustre to iris from infiltration.		Lack lustre in iris from steamy cornea.
	<i>Differ</i>	
Small pupil.		Pupil moderately dilated.
Cornea transparent.		Cornea steamy.
Cornea sensitive.		Cornea insensitive.
Tension normal.		Tension increased.
Field normal.		Field abnormal.
Anterior chamber normal depth.		Anterior chamber shallow.
Bright zone of ciliary redness.		Dark or purplish dilatation of blood vessels.

Thus it will be seen that while these severe forms of eye disease possess many features in common, there is also a large group of symptoms which in typical forms of the disease definitely separate them. It leads me beyond the purpose of this lecture to discuss fully why this family of drugs do harm in glaucoma, since it involves the theories regarding the cause and nature of this disease.

It is sufficient for my present purpose to state, that our present knowledge of glaucoma seems to teach that at least one important element in its etiology is the closure of the angle of the anterior chamber, so that the exit of the intra-ocular fluids by the way of Schlemm's canal is retarded or entirely prevented. It is obvious that crowding the iris into the angle by dilating the pupil would render its closure more complete, and thus in cases of *glaucoma imminens*, be liable to precipitate an acute glaucoma. The obvious lesson taught both by experience and these theoretical considerations is to avoid the use of these drugs in doubtful cases. The wise surgeon will avoid their use except with the greatest caution in all cases where there is increased tension of the eyeball, with diminished range of accommodation not accounted for by other recognized conditions, or with characteristic abnormalities in the field of vision.

Before entering upon the use of mydriatics for the purpose of paralyzing the accommodation, in the correction of errors of refraction, I call your attention to their employment during and after middle life. There is a wide-spread opposition to their employment after the age of forty, since it is during the middle period of life that glaucoma usually occurs. I am sure that the fears upon which the opposition is based are not well founded if due caution is exercised on the lines I have already pointed out. It is quite as important between forty and fifty years of age to use these drugs for the satisfactory correction of many eyes as before this period of life. The cases of retino-choroidal irri-

tation, and accommodation cramp with tonic contraction of the iris and ciliary muscle, are quite as frequent as before the age of forty, and the therapeutic value of the mydriatics is just as marked. A wide experience fully justifies this statement. I have used these drugs with impunity, both in private and public practice in many thousands of eyes, after the time of life specified. If harm comes from them it is because a sufficiently careful study of the case has not preceded their use. I have yet to meet the first instance of an acute glaucoma, precipitated by the employment of a mydriatic, but I have always exercised the caution which I have pointed out and again emphasize as the duty of every person essaying their use.

In Philadelphia, probably more universally than elsewhere, the use of these drugs has been insisted upon as necessary to the accurate correction of errors of refraction. This has largely grown out of the claim that the emmetropic eye is not only the model, but the normal eye, and that all departures from this simple standard of refraction are defects, and in the presence of asthenopia apparently due to their existence, should be carefully, accurately and fully corrected by glasses. I accepted this view very early in my practice, and a steadily widening experience has served only to strengthen the conviction then formed. In the endeavor to correct the manifest error of refraction we are dealing with an unknown, because an ever changing quantity, which constantly vitiates results, and the work done is unsatisfactory because it does not secure perfect relief.

There is a wide-spread notion among the laity that the avoidance of reading glasses as long as possible is to save their eyes; that the necessity for a glass to read or work with is a sign of failing vision. They should be taught that the diminishing range of accommodation is physiological not pathological, and it is not only useless but harmful to resist it. This working without a glass to correct the presbyopia is a source of much harm to the eyes, and the cause of much suffering. I have, in a very large number of persons, seen violent headache and other reflex symptoms disappear as soon as a proper reading glass was secured. I recall the case of a celebrated clergyman, in charge of a large parish, and doing a large amount of literary work besides, who suffered from occipital pain, which had been ascribed to cerebral hyperemia. He was advised to relinquish his work and travel abroad to secure relaxation and thus avoid a nervous breakdown. He was fifty years of age and prided himself upon his excellent eyes, since he had not required a glass to aid him at his work. His pupils were the size of a pin's head; the conjunctiva was hyperemic; the caruncles swollen; $V = \frac{6}{vi}$ and he read easily $D = 0.50$, at $30^{\text{ctm.}}$, but had no range of accommodation.

A few days' use of a solution of homatropine, gr. viii- $\bar{3}$ i, dilated the pupils to large medium. The headache promptly disappeared and H = 1. D was revealed. He received + 2.75 for reading, increased in six months to + 3.25. He was no longer able to read even large type without his glasses, but he had no return of his trouble and abandoned all idea of relinquishing his work.

The headache of old people is very frequently due to the eye strain brought about by the use of too weak glasses, or from the neglect of astigmatic corrections. It is true, they have lost the power of adjustment through the hardening of the lenses, but they have not lost the ciliary muscle, and the fruitless strain to see with an improper glass is quite as painful and often as harmful to the eyes as earlier in life. It is in these cases you will find the solutions of homatropine of signal service. It should be used in from iv to viii gr. solution three times daily until the ocular irritation subsides and then the proper glasses chosen.

It is in young eyes, however, that the use of these drugs is most frequently needful. I wish to impress upon you, however, that they are not to be employed for the sole purpose of paralyzing the power of accommodation. This is of great importance, and in most cases a necessity if you are not to be satisfied with more or less close approximations in ordering the correcting glasses. My purpose has always been to determine with the greatest possible accuracy the static refraction of each eye. Having ascertained this it may be used in any way the judgment of the surgeon may dictate, but until this knowledge has been gained all subsequent action must be based upon unknown factors, and this knowledge cannot be had except through measurements made after thorough paralysis of the accommodation.

You will not use these drugs for this alone, however. A very large percentage of refraction cases suffer from irritation and pathological changes in the intraocular tunics, the result of neglected eye-strain. The wooly choiroid, hyperemic retina and optic disc you will find to rapidly disappear under the sedative and restful influence of the mydriatics. I am sure you will soon learn to prize them for their therapeutic value as well as for the paralysis of the ciliary muscle.

How shall you employ them?

The method of their employment and the member of the group you select will depend in large measure upon the condition of the eyes in any individual case. In eyes which are nearly or quite free from retino-choroidal irritation, homatropine hydrobromate will prove sufficient and the most desirable agent to employ. The property which most commends it, in comparison with the other members of the group, viz., its evanescent control over the power of accommodation,

makes it necessary to keep your patient at hand so that the determination of the refraction can be made before the subsidence of its effect. I employ an viii gr. solution of the drug, instilling one or two drops in each eye every fifteen minutes for an hour or more, and often associate its use with a four per cent. solution of cocaine. They are not used at the same moment, however, since the cocaine solutions cause much temporary irritation. After the smarting has subsided the homatropine is instilled. In many cases you will be able to save your patients much time and annoyance by this method, since in from twenty-four to thirty-six hours its influence over the pupil and accommodation will have disappeared. It may also be selected in cases where retino-choroidal irritation is present, but must then be used for many days, or long enough to secure the needed rest and therapeutic effects already noticed. When employed for this purpose, it should be used at home, one or two drops being instilled in each eye four times daily. When used in this way, however, it proves of but little if any advantage in point of time over duboisine or hyoscyamine, since what is lost by the longer time required to recover from these drugs is gained by the shorter period required to accomplish the result wished for. All things considered, I prefer the hyoscyamine to either of the other mydriatics in the average case of asthenopia, and employ habitually a ii gr. fʒi solution. One drop in each eye three times daily. It has the advantage of being less liable to cause constitutional symptoms than a iv gr. solution of atropine or a ii gr. solution of duboisine. Furthermore, the accommodation is recovered several days sooner than when atropine is employed—the average duration of the paralysis with hyoscyamine being seven or eight days while that of atropine is from ten to fifteen days. In order to secure this result, however, you must be sure that the preparation used is hyoscyamine. Some recent investigations, still in progress at the Wills Hospital, seem to show that the atropine of commerce is in fact hyoscyamine, while, on the other hand, much of the hyoscyamine is really atropine. This grows out of the fact that the product secured in the laboratory depends upon the manipulation used in its extraction. If too great heat and alkalies are avoided the product is hyoscyamine, which, by either heat or alkalies, is converted into atropine. Therefore, the manufacturer may furnish your druggist unwittingly with bottles labeled, the one atropine the other hyoscyamine, when they may be the same drug. I have recently been impressed by the very wide variations in the returning range of accommodation when compared with the most carefully conducted observations made twelve years ago with the same drugs. Later studies show that some of the specimens of atropine give the same results as hyoscyamine, while certain samples of hyoscyamine have the same effect as those observed from atropine in my earlier investigations.

