DIBENZYLİN† IN GLAUCOMA*

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The Dibenamine group of drugs acts at the sympathetic nerve endings, blocking their pressor and other actions, and reversing the pressor effect of circulating adrenaline. It is said to penetrate the cells and prevent the action of nor-adrenaline at its site of liberation. The group is effective only when given systemically, and it produces widespread actions. The particular drug called Dibenzyline† is said to be free from the irritative side-effects (gastric and cerebral) of Dibenamine and to be more powerful in its sympatholytic action. Certainly no serious side-effects were encountered in the series of cases reported in this paper, although one or two subjects felt rather drowsy, and some who were already vomiting on account of their glaucoma or an excess of eserine continued to do so occasionally.

This drug is effective orally, though in this survey, to be more certain of a rapid action, it has usually been given intravenously.

As there is some degree of urgency in cases of acute glaucoma, the Dibenzyline was given diluted in 5 ml. saline over a period of about 3 min., and not by continuous drip which might affect the osmotic balance. This is contrary to previous practice with Dibenamine, but no serious side-effects ensued. The most suitable dose was found to be 15-25 mg. (intravenously) but a dose of 40 mg. was given to a woman aged 48 years in the hope of obtaining a dramatic clinical response.

The systemic action of Dibenzyline in a normal person is illustrated in the Figure.

![Figure](http://bjo.bmj.com/)

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†Supplied for this trial by Smith Kline and French.
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There is an almost immediate fall of blood pressure which reaches its lowest in about 1-1½ hrs, and gradually rises to normal in 3-6 hrs. There is a proportional tachycardia (Marey's law). There is some vasodilatation, especially of the splanchnic bed. Postural hypotension may occur, the subject feeling light-headed or even fainting on rising suddenly. It might be thought that younger persons with a more labile vascular system might show greater changes of blood pressure than older persons, but the reverse is rather the case, the younger persons probably having greater compensatory reserves. In older subjects there may be some risk of precipitating a cerebral or other thrombosis from the lowered blood pressure or of heart failure from the tachycardia, but no such events occurred in this series.

The pupil shows a paralytic miosis, small in amount as a rule unless it has previously been of the wide, hyperactive type. The dilated pupil of the acute glaucomatous state shows no change unless the ocular tension responds well, and even when pupillary contraction occurs it seems to be too slight to account for any fall in tension—a view shared by Christensen and Swan (1949). In normal subjects there is little change in ocular tension; in two cases the tension fell from 15 to 13 mm. Hg Schiötz in one hour. No change in accommodation is detected, the near point and far point of clear vision being unaltered. The eyelids usually feel heavy and droop appreciably. The tone of skeletal muscle is not noticeably affected, and the lids can be widened again by raising the eyebrows, as occurs in tabes. There is then a small degree of bilateral Horner's syndrome.

It has been suggested (Posner, 1950; Weinstein, 1953) that acute glaucoma is part of a general sympathetic upset, possibly from the activity of a hypothalamic centre associated with a rise of blood pressure, sudden dilatation of the pupil and other vegetative disturbances. Though this may not apply to all closed-angle cases, many, especially those precipitated by emotional stress, do show a systemic upset. At any rate it seemed likely that such acute cases in which a vascular crisis probably occurs in the eye would be more likely to respond to a drug, the main effects of which are vascular, than would cases of simple glaucoma.

Results

Simple Glaucoma.—Two cases showed, if anything, a slight rise of tension (from 30 to 35 mm. Hg Schiötz) in the glaucomatous eye about two hours after the administration of Dibenzyline. A third case, in which the glaucoma was under better control, showed no change of tension. It was decided that cases of simple glaucoma were not benefited, but on the contrary might be provoked.

Absolute Glaucoma.—Two cases, probably thrombotic, were treated out of interest. Here the tension fell slowly (e.g., from 50 to 40 mm.) as the blood pressure dropped considerably; the tension rose again as the blood pressure returned to normal.


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*Acute Glaucoma.*—In this group there were some surprises and some disappointments. All the patients had undergone the usual intensive therapy with miotics and had been admitted to hospital as being unlikely to respond. This treatment was, in most cases, continued in bed, and the patient was comfortably settled with sedation in an attempt to reach some sort of baseline, however crude, before starting the Dibenzyline.

The cases detailed in the Table all show some response of the tension. In Cases 1, 5, and 6 this was small in amount. Perhaps if Case 1 had been observed for a longer time a better response would have been noted. In Case 6, which was of only 2 days’ duration, a better response might have been expected, but the lowest Hg Schiötz reading taken was at 35 min. after the injection; thereafter, the tension rose again. In Cases 2, 3, and 4 there was a good response. Case 3 may be discounted as it is probable that a response to eserine started before the Dibenzyline was given. Where circumstances permitted, the period of observation was extended and the tension was seen to rise again. Although the tension had been lowered, if the angle had not

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Duration of Attack</th>
<th>Eye</th>
<th>Time</th>
<th>Ocular Tension (mm.Hg)</th>
<th>B.P. (mm.Hg)</th>
<th>Dose Intravenously (mg.)</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>About 8 days</td>
<td>R</td>
<td>0</td>
<td>50</td>
<td>200/120</td>
<td>25</td>
<td>Insufficient time</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30 min.</td>
<td>42</td>
<td>175/90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>69</td>
<td>24 hours</td>
<td>R</td>
<td>0</td>
<td>76</td>
<td>190/95</td>
<td>25</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 hrs</td>
<td>36</td>
<td>160/85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>Some days (occasional haloes for months)</td>
<td>L</td>
<td>2 hrs</td>
<td>48</td>
<td></td>
<td></td>
<td>Good, then relapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>32</td>
<td>160/80</td>
<td>15</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45 min.</td>
<td>20</td>
<td>140/70</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 days</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>24 hours</td>
<td>R</td>
<td>0</td>
<td>62</td>
<td>174/90</td>
<td>25</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 hrs</td>
<td>35</td>
<td>90/55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4 hrs</td>
<td>45</td>
<td>100/60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>5 days</td>
<td>L</td>
<td>0</td>
<td>74</td>
<td>200/95</td>
<td>20</td>
<td>Poor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1½ hrs</td>
<td>65</td>
<td>175/75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>48</td>
<td>2 days</td>
<td>R</td>
<td>0</td>
<td>55</td>
<td>140/75</td>
<td>40</td>
<td>Poor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>35 min.</td>
<td>36</td>
<td>105/55</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>65 min.</td>
<td>41</td>
<td>100/55</td>
<td></td>
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</tbody>
</table>
meantime re-opened and the vicious circle broken, the tension rose again as the general circulation recovered from the effects of the drug.

Case Report

Some clinical notes on Case 6 will serve as an example. A woman aged 48 years with acute glaucoma had been fretting over the loss of a pet dog. The right eye had been sore and the vision very blurred all the previous day and she had been seeing haloes the evening before (48 hrs in all). She had occasionally seen haloes 4 years previously.

Visual acuity in the right eye was hand movements; the eye was injected, with steamy cornea, shallow anterior chamber, and fixed semi-dilated pupil; the ocular tension was 58 mm. Hg Schiotz.

Visual acuity in the left eye was 6/9; the eye was white, with shallow anterior chamber, small reactive pupil, and normal disc; the ocular tension was 18 mm. Hg.

Therapy.—Intensive eserine administered to the right eye in the out-patient department was without effect. Further eserine drops 1 per cent. and pilocarpine drops 2 per cent. were given half-hourly in bed with a Maddox heater.

Morphine gr. ¼ (2.35 p.m.) was also given. The patient vomited.

Dibenzyline 40 mg. intravenously was given at 4.40 p.m. At 5.55 p.m. the ocular tension was 41 mm. Hg, the cornea was still steamy, and the pupil unchanged. At 6.15 p.m. a right broad iridectomy was performed. There was no bleeding.

Results.—The post-operative course was uneventful apart from slight striate keratitis. When the patient was last seen on January 21, 1955, the discs were normal, fields full, tension normal (left fully controlled on guttae pilo. 1 per cent. o.d.), and visual acuity 6/9 in the right eye with +2 D, and 6/5 in the left eye with +2 D.

These six acute cases all underwent iridectomy either at the time or within a few days, with good end-results except Case 1 and Case 3. When the iridectomy had to be done at the time, the eye was in better condition for the operation as a result of the Dibenzyline, and certainly the general excitability of the patient and his raised blood pressure were much reduced. Incidentally, the operations were rendered practically bloodless, so the drug is of value for producing controlled hypotension; in this respect it is probably better than hexamethonium, which tends to dilate the pupil. But these drugs have their dangers, and the general condition of the patient has to be carefully assessed and watched.

It is clear even from these few observations that the shorter the duration of the attack before initiating treatment, the more chance there is of a good response—a result which would be expected. The results described in enthusiastic early reports (e.g., Clark and Duggan, 1951) have not been substantiated. This may perhaps be because the acute cases reported by these workers all started treatment within 48 hrs of the onset of the illness whereas we have not usually obtained our cases so early. Dibenzyline has been used only after the usual miotic therapy has been tried; it is therefore difficult to assess its independent effect, but its action is short-lived, and probably the best use of the drug is to improve the condition of the eye so that operation may be more safely undertaken.

It is apparent that the ocular tension in any type of case shows no direct
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relationship to the fall in blood pressure produced by the Dibenzyline. The depression of the general circulation, which is a measure of the effectiveness of the drug, tends to lower the intra-ocular pressure. In early closed-angle and simple glaucoma probably the local vascular action of the drug is of more effect on the ocular tension than the general lowering of blood pressure. The results here may be compared to some extent with those effected by stellate ganglion block (Miller, 1953). In this technique the sympathetic was blocked without any change in the general circulation; early closed-angle cases responded and simple glaucoma was aggravated. In our closed-angle cases which were not so early and in absolute glaucoma the ocular tension was only slightly lowered—probably a passive effect—and soon returned to its previous level, much sooner than the blood pressure took to recover.

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REFERENCES

Dibenzyline in Glaucoma

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