Eye damage caused by crystal violet

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Crystal violet (hexamethylpararosaniline hydrochloride; medicinal gentian violet) is still widely used by topical application in the treatment of a variety of bacterial and fungal infections of skin and mucosae (Esplin, 1966). Although crystal violet is known to produce local ulceration of oral and vaginal mucosa (John, 1968; Meyler & Herxheimer, 1968; Slotkowski & Redondo, 1966), its ability to damage the eye is less well appreciated. The effects of crystal violet on the rabbit eye have been investigated.

Using a standard rabbit eye irritation test (Ballantyne & Swanston, 1972) it was found that 20 mg/ml of crystal violet in water rapidly produced severe and persistent blepharitis with hyperaemia, oedema and necrosis of the conjunctivae and nictitating membrane. Mild keratitis was apparent within 24 h, and over the ensuing 21 days became progressively more severe. At 3 weeks there was gross opacification, deformity and vascularization of the cornea. Keratitis often obscured a severe iritis. Studies with more dilute solutions demonstrated the damaging effects to be concentration-dependant; the no-effects concentration was around 0·25 mg/ml. With concentrations below 20 mg/ml there was characteristically a latent phase of several days before corneal damage became apparent.

Applanation tonometry (Callaway, Glazzard, Price Thomas & Swanston, 1973) demonstrated that crystal violet caused a concentration-dependent elevation of intra-ocular tension. Using groups of 6 rabbits and applying 0·1 ml of solution to the eye, the mean rises in intra-ocular tension 1 h after application were 22·2%, 5·4% and 3·2% respectively for 5, 2 and 1 mg/ml of crystal violet in water. Changes in tension were prolonged. For example, using 1 mg/ml tensions progressively rose to a peak at 9 days after a single instillation, and thereafter gradually returned to control values by 1 month after contamination of the eye (Fig. 1).

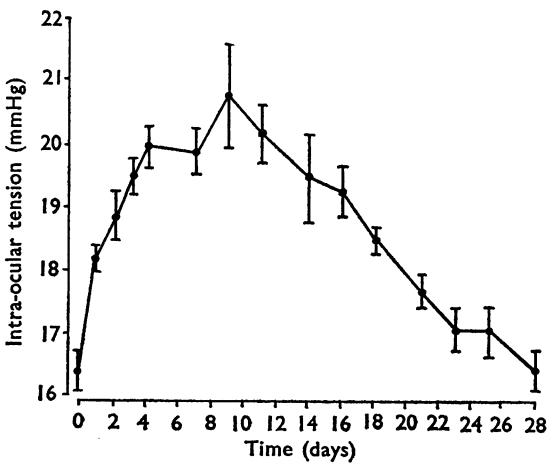

FIG. 1. Changes in intra-ocular tension in the rabbit eye following a single application of 0·1 ml of crystal violet in water (1 mg/ml). The control tension is shown at zero time. Each point is the mean of measurements on 6 rabbits ± S.E.M.

These findings demonstrate the potential of crystal violet to cause severe structural damage to the eye, to induce prolonged increases of intra-ocular tension, and emphasize the necessity to avoid splash contamination of the eye with solutions of this substance.

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Chemical sympathectomy of the rabbit with 6-hydroxydopamine

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Despite the now considerable literature on 6-hydroxydopamine (Thoenen, 1972), we could find no recommended dose régime for producing chemical sympathectomy in the rabbit. The present study describes a schedule of pretreatment in this species which produces a marked reduction in sympathetic nervous function in tissues of the cardiovascular system and gut.

6-Hydroxydopamine was dissolved in 0·7 ml ice-cold, nitrogen-saturated, 1% ascorbic acid and injected immediately into a marginal ear vein. Rabbits were given 30 mg/kg at 17.00 h on day 1, followed by 20 mg/kg at 13.00 h and again at 17.00 h on day 2. The animals were killed for removal of tissues about 10.00 h on day 3. The preparations used were the perfused heart (Langendorff, 1895), spirally-cut aorta (Furchgott & Bhadrakom, 1953), spirally-cut renal artery (Kelly, 1971), perfused ear artery (de la Lande & Rand, 1965), spirally-cut portal vein (Kelly, 1971) and duodenum (Finkleman, 1930). Whenever practical, the sympathetic nerves were stimulated electrically. Those of the heart were stimulated chemically with dimethylphenylpiperazinium. The responses of each tissue to noradrenaline and tyramine were also routinely tested. In most cases, full log concentration/frequency-response curves were established in order that accurate comparisons of potency could be made. Tissue noradrenaline levels were assayed by the method of Welch & Welch (1969), and demonstrated histochemically by the method of Spriggs, Lever, Rees & Graham (1966). The results are summarised in Table 1.

TABLE 1. *Changes in a number of parameters recorded from tissues taken from rabbits pretreated with 6-hydroxydopamine.* (*20 mg/kg, day 1; 2 × 20 mg/kg, day 2; killed, day 3*).

Tissue parameter	Heart	Aorta	Renal artery	Ear artery	Portal vein	Duodenum
Sympathetic nerve stimulation	—		—	——	——	—
Noradrenaline sensitivity	O	+	+	+	+	O
% Reduction in noradrenaline content	97	74	65		86	86
Fluorescence characteristics	——		—	——	——	——
Tyramine sensitivity	——	—	——	——	——	

——=Absent
—=Much reduced
O=No apparent change
+=Increased
A gap indicates, where, for practical reasons, the test proved inconclusive.

If the effects produced by stimulation of the sympathetic nerves are taken as the most reliable indication of their functional integrity, then, in all the tissues investigated (except aorta), a very considerable degree of sympathectomy is apparent. This inter-