thirds of the mean lethal dose in the mouse). On the other hand, the monkey, dog and cat were highly susceptible. In the cat, the species chiefly studied, single doses of 100–400 mgm./kgm. by mouth or by subcutaneous injection, or 25–50 mgm./kgm. given intravenously, caused loss of the blink reflex and marked dilatation of the pupils with almost complete loss of the pupillary, light and near reflexes. Visual perception, as judged by the animals' behaviour, was also impaired within twenty-four hours. If the compound was acting centrally, all the optic centres would be affected, but this seemed improbable in the absence of other central nervous symptoms.

The instillation of eserine into an affected eye within a few days of treatment, or peripheral stimulation of the oculomotor nerve in decerebrate preparations, caused pupillary constriction, indicating that paralysis of the nerves and muscles responsible for constricting the pupil had not occurred. The mydriasis was not due to an atropine-like or ganglion-blocking type of action. It was therefore inferred that the compound was probably acting directly on the retina or optic nerve.

Ophthalmoscopic changes were first observed after about seven days and consisted in marked constriction of the retinal vessels with pallor of the optic disk; in two weeks there was some pigmentary disturbance which after eight weeks became the predominant feature, producing a fundus picture resembling retinitis pigmentosa. Though this effect on the eye was by far the most characteristic and important toxic aspect of the compound, it also caused vomiting in cats and dogs, when given orally, but no other serious toxic effects were observed.

The significant histological changes in the eye, described in detail elsewhere⁴, were almost entirely confined to the retina, there being widespread injury to the outer layers of the retina with total or patchy destruction of the visual cells, and localized displacement of the outer nuclear layer of the retina with arcade and rosette formation. There was marked degeneration and proliferation of the pigment epithelium. Bipolar cells and ganglion cells were preserved. Histologically these changes most closely simulate those which follow the administration of sodium iodate⁵⁻⁷, rather than those resulting from iodoacetate^{7,8}.

N. D. EDGE
D. F. J. MASON
R. WIEN

May and Baker, Ltd.,
Dagenham, Essex.

N. ASHTON

Institute of Ophthalmology,
London. June 4.

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Test for Cross-linking of Linear Polymers

CERTAIN linear polymers which have been used as picture varnishes are known to become cross-linked by the action of light. It is important to us to find out whether this is likely to happen for any particular

case, since the insolubility resulting from cross-linkage makes it impossible to remove the varnish by solvent action alone.

The method which has been developed requires only a small rectangle of the varnish film (4–9 mm.², 20 μ thick), and can be completed within an hour. The fragment of film is attached near the bottom of a filter-paper strip with one or two drops of a suitable solvent from a micrometer syringe. The fragment is then leached by developing the strip as in paper chromatography, although in this case there is only one solvent phase, and lengthy equilibration is unnecessary. This solvent should be chosen from among the best for the polymer. A dye, absorbed preferentially by either polymer or paper, may be dissolved in it.

Fig. 1. Cross-linkage tests on 1-in. chromatography paper (Whatman No. 1). Origins are marked by horizontal pencil lines: the varnish fragments were placed just above these lines in (a) and (c). Solvent flowed upwards.
(a) A methacrylate polymer after being heated for 4 hr. at 155° C. Solvent and stain: benzene with 0.015 per cent sudan IV.
(b) Blank strip for comparison. (c) Polyvinyl acetate after the same treatment as (a). Solvent: methanol. Light green was used as a paper stain so that leaching could be followed, but the resin was positively indicated by spraying with equal volumes of 5 per cent cerium nitrate and 0.1 N iodine.

A long streak of soluble polymer moves along the paper so long as leaching continues, and ends fairly abruptly, to form a rounded tail, when all soluble polymer has been removed from the varnish fragment. The process is stopped as soon as the tail is clearly separated from the origin. Any polymer rendered insoluble by cross-linkage remains unmoved at the origin, so that the outline of the original fragment is sharply visible. This can be seen in Fig. 1(a), where a proportion of the polymethacrylate is cross-linked. The soluble portion forms a tail just behind the solvent front. Measurements by an interference method of the contraction in thickness suggest that about a third of the film has been rendered insoluble. Absence of resin at the origin in Fig. 1(c) indicates that none of the polyvinyl acetate has become cross-linked.

GARRY THOMSON

Scientific Department,
National Gallery,
Trafalgar Square,
London, W.C.2.
Sept. 8.