FAILURE TO DEMONSTRATE GLIOMAS
WITH EVANS BLUE

PRECAUTIONS IN USE OF INTRAVITAL DYES IN MAN

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About 8 years ago I injected intravenously the azo dye Evans blue, T 1824, into 2 patients with intracranial tumours in the hope that it might concentrate differentially in the neoplastic tissue and enable the surgeon to make a sharper distinction between normal white matter and white matter invaded by tumour. Evans blue was chosen since Duran-Reynals2 had found in normal and tumour-bearing animals that healthy sarcomas and carcinomas localized the dye, whereas necrotic tumour and the normal central nervous system were the only tissues impervious to it. A large experience had already accumulated in man demonstrating its harmlessness and Brunschwig, Schmitz and Clarke1 had found visible discolourations in and about malignant neoplasms in 20 of 30 human patients after 30–100 mg. of this dye were injected intravenously.

The dye proved to be unsatisfactory not only because it was not apparent to the naked eye in gliomatous tissues, but also because it stained the patient’s skin undesirably and for a protracted interval in the amounts used. The results were reported at a meeting of the Society of British Neurological Surgeons in 1942; in view of the renewed interest in the differentiation of cerebral tumours by dyes it seems desirable to place these fruitless results on record to discourage repetition of the same tactic.

CASE REPORTS

Case 1. In D.P., a 33-year-old female, 100 mg. of the dye were injected intravenously in sterile normal saline on Mar. 12, 1942. Over the course of several hours a pronounced blue colour appeared in the skin everywhere and persisted. On March 15, another 50 mg. of the same dye were injected intravenously; a pimple on the skin was noted to be a much deeper blue than the remainder of the skin. On Mar. 16, 1942 osteoplastic craniotomy disclosed a left frontal meningioma which was intensely blue, whereas the colour of the brain, including that part adjoining the tumour, was normal. The encapsulated meningioma was, of course, readily distinguishable from normal brain without the aid of the dye. On microscopic examination a highly fibroblastic type of neoplasm was seen, the collagen of which was stained blue. This led to the suspicion that the patient’s subcutaneous collagen had also taken up the dye, a disturbing thought which was confirmed by the fact that the blue colour to the skin faded only gradually; several months elapsed before it was no longer noticeable. For her first postoperative month she was a striking pastel shade of blue. Happily she did so well on other scores that neither she nor her husband minded the colour change.

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Case 2. In T.B., a male aged 40 years, 100 mg. of Evans blue were injected intravenously on Mar. 17, 1942. In a few hours his skin became about as blue as that of the previous patient. On March 18 a glioblastoma multiforme in the posterior inferior part of the right frontal lobe was partially removed. This tumour was unusually well supplied with blood vessels. Despite this fact it was not possible to be certain on inspection that the grayish-red neoplasm or the adjoining cerebral white matter had taken up any of the Evans blue injected the previous day. On his 14th postoperative day meningitis developed in which \( \beta \) hemolytic streptococcus was the organism, and he died on April 3, 1942, 2 days later. At postmortem study his skin retained the unattractive blue colour that had developed on the day of the injection, but careful inspection of the freshly cut brain showed no more evidence of the Evans blue in tumour or adjoining brain than was seen at operation 16 days previously.

A further review of the literature at that point disclosed that Hamperl\(^5\) had noted persistence of a marked blue-gray colour in the skin of a woman 9 years after treatment of her presumed carcinoma with another azo dye, isamine blue. The total dose of the dye was not stated but it was given both orally and parenterally. At postmortem examination granules of dye were present in the connective tissue of the papillae of the skin as well as in collagen elsewhere. Incidentally there was after this long interval no dye in the reticulum cells of the spleen or in the Kupffer cells, sites of predilection as described by most authors in the early period after injection. Proponents of the administration of the dye had alleged that it left the body in 2 to 3 months (Bernhardt, Roosen).

This report and our own experience suggest that elimination of dye from the skin is an additional desideratum to be noted with care in further searches in this field. The initial trials of any new dye staining the skin should certainly on this account involve small doses, no matter how low the toxicity of the agent.

REFERENCES