EXPERIMENTAL EVALUATION OF CEREBRAL ANGIOGRAPHY*

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Cerebral angiography was introduced in 1927 by Moniz.\textsuperscript{13} With accumulating experience it has become essential in the diagnosis of surgical intracranial vascular lesions and is also assuming great importance in the diagnosis of expanding, intracranial lesions.

One deterrent to its more universal use is the occurrence of complications attributed to the toxic effects of the contrast media.\textsuperscript{5,7,9,17}

In this laboratory, an extensive search has been undertaken for compounds that will so alter cerebral permeability as to allow staining of the cerebral tissues by such dye substances as trypan blue, disulphine blue, and sodium fluorescein. One such substance proved to be Diodrast. In view of clinical implications, detailed studies of this effect were done and are the subject of this report.

METHOD AND MATERIALS

Stock rabbits under 1 per cent pentobarbital anesthesia were the test animals.

(A) A control group of animals (1–18) were subjected to the basic procedure as described below (B) except that normal saline at the same injection rates was substituted for Diodrast injection.

(B) Animals 19–46. The right carotid artery was isolated and a cannula was inserted. Continuous saline was injected to prevent clot formation. A water manometer was placed in the system of tubing through which injection is made so that the arterial pressure could be observed at any time. A measured amount of 70 per cent Diodrast\textsuperscript{†} was injected into the artery; the duration of injection was recorded. The force of injection was so controlled that normal arterial pressure was not exceeded. Three minutes after the completed injection, the indicator dye (trypan blue, disulphine blue, or sodium fluorescein) was given intravenously and the animals were then sacrificed by cardiac section at varying time intervals. The brain was removed, examined, often photographed, and sections were taken for microscopic study. When the test agent was sodium fluorescein, the brain was examined and photographed under ultraviolet light, as described by Moore.\textsuperscript{16}

(C) Animals 47–57 were subjected to the same procedure except:

(1) Only Diodrast from a single batch\textsuperscript{‡} which had consistently been injurious to animals in group A was used.

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† Iodopyracet (Diodrast) is also known as Perabrodil, Umbradil, Pyelosin, Diodone, and Pyelumbrin.

‡ All Diodrast is identified by a batch number.
(2) Injection of the indicator dye was delayed until just before sacrifice of animals at 1, 3 or 6 hours.

(D) In animals 58-62 the effect of 35 per cent instead of 75 per cent Diodrast was studied as in group B.

(E) The cortices of animals 53-74 were first exposed by removal of the calvarium and bilateral portions of dura; the cortices were placed under continuous observation under the dissecting microscope; then injections of 70 per cent Diodrast and indicator dye were carried out as described above. Animals 69-74 received Diodrast from a batch not used on any other animals in these studies.

(F) Three rabbits (75-77) were sacrificed after the usual procedure, but in addition, radioactive diiodofluorescein was injected with the test dye. These brains were examined grossly for staining and were then sectioned sagittally. The radioactivity of each separate half was measured with a Geiger-Mueller tube.

(G) Four patients (brain tumor suspects) were injected with measured amounts (in terms of radioactivity) of radioactive diiodofluorescein and were examined with a shielded Geiger-Mueller counter in the routine manner for localization of brain tumors as described by Moore.14,15 Twenty-four hours or longer after this examination, unilateral percutaneous carotid angiography was performed with 35 per cent Diodrast. Previous studies have shown that after 24 hours the blood level of diiodofluorescein is negligible, but that some of the radioactive dye is still retained in the liver and gastrointestinal tract.15 Therefore, following the angiogram, a second counting was done utilizing the same positions and sequence of counting as in the initial counting. In this manner the contribution of the residual radioactivity to each counting position was measured. Then the same dosage in milligrams of radioactive diiodofluorescein was again injected and another counting made in identical manner. The second counting was considered as background for the third and was subtracted from it. The resulting differences were then compared directly with the counts obtained at the first counting.

RESULTS

(A) The control animals (1-18) revealed no gross staining, but animals that received a very high dosage of fluorescein did show a very faint degree of fluorescence under ultraviolet light. Such high dosages were avoided in the experimental animals. The control animals are summarized in Table 1.

The experimental results for the animals receiving the contrast media are tabulated in Table 2.

(B) The first 10 animals (19-28) studied after the injection of 70 per cent Diodrast revealed no systemic or localized cerebral reaction grossly or pathologically. Unfortunately the batch number of this Diodrast was not recorded. Because Broman and Olsson3,4 had reported such consistent breakdown of the blood-brain-barrier with 70 per cent Perabrodil (Iodopyracet), a new supply of Diodrast was obtained and the series extended with no other change in the experimental method. Three separate batches of 70 per cent Diodrast were used in these animals. A complete reversal of the previous results was obtained. In every one of these animals (29-46) examination showed a deep staining on the ipsilateral side, and occasionally the homolateral cerebellar hemisphere was also involved. In animal 46, the arterial pressure was exceeded, and in this animal the cerebral and cerebellar hemispheres were bilaterally deeply colored.