AN EXPERIMENTAL EVALUATION OF CERTAIN
CONTRAST MEDIA USED FOR
CEREBRAL ANGIOGRAPHY
ELECTROENCEPHALOGRAPHIC AND HISTOPATHOLOGICAL
CORRELATIONS
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Since the introduction of percutaneous techniques, cerebral angiography
has become a commonplace diagnostic procedure. That the procedure
is not without untoward sequelae is indicated by scattered reports
in the literature.6,7,9,18 It is probable that these reactions are even
more common than reports indicate.

Several studies have attempted to evaluate the effects of substances
used as contrast media. Thus, peripheral pharmacological effects on the
cardiovascular system have been investigated.8,12,14,17 Histopathological
studies of the effect of these substances on the cerebral vessels were carried
out by Kristiansen and Cammermeyer15 with essentially negative findings.
Broman, using the dye indicator technique, has extensively investigated
alterations in permeability of the cerebral vessels caused by many substances
including the Diodrast group of compounds.2,3,4,5 In a previous report we
have described a method of study combining the dye indicator technique
with concomitant electroencephalography.1

This report presents results of the application of this technique to the
evaluation of some common contrast media and three non-iodinated
homologues of these compounds. In addition, correlative histopathological
data are presented.

METHOD

The technique employed was briefly as follows: Experiments were carried out
on adult rabbits weighing between 2000 and 3000 gm. Under light nembutal and
local procaine anesthesia a common carotid artery was isolated and catheterized
with small polyethylene tubing, and branches of the external carotid were ligated.
Tracheotomy was performed, and all animals were curarized and placed on mechanical
respiration. Test substances were generally administered via the catheter over a
30 sec. period, excepting those instances where divided doses were used. All test
injections were controlled with equivalent amounts of Ringer’s solution.

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One hundred to 200 mg. of the tetra-sulfonic acid of copper phthalocyanine were injected intravenously. As with other anionic, organic substances, the cerebral vessels are normally impermeable to this dye. EEGs were obtained continuously during the course of the experiment.

At the conclusion of each experiment the animal was sacrificed by stopping the respirator. All brains were immediately removed and appropriately fixed so that hematoxylin and phloxin, unstained frozen, Pickworth's benzidine, and Eros' fuchsin preparations could be obtained. Brains were selected from each group for cellloidin Nissl preparations.

The substances tested fell into several chemical groups. Pyridine derivatives were represented by Diodrast® (diethanol amine salt of 3.5 diiodo-4-pyridine-N acetic acid) in 35 per cent, 50 per cent and 70 per cent solutions (w/v). The 35 per cent solution contains 0.17 gm. of iodine per cc. Neoiopax® (3.5 diiodo-4-pyrodoxyl-N-methyl-2-carboxylic acid) was used in 37.5 per cent (w/v) concentration in Ringer's solution. The iodine content is approximately 0.18 gm. per cc. We were unable to obtain the non-iodinated homologues of these two compounds. N-methyl nicotinamide hydrochloride, a pyridine derivative and a normal body metabolite, was used as an approach to these structures. This was administered in a 20 per cent solution (w/v).

The benzene derivatives used were: Urokon® (3-acetyl-amino-2-4-6-triiodo sodium benzoate) in 30 per cent solution (w/v) at both pH 5.4 and 7; its non-iodinated homologue,* prepared in 20 per cent solution (w/v) and adjusted to pH 7.4; and para-amino-hippurate (para-amino-benzoyl glycerine) in 20 per cent solution (w/v). Urokon contains 0.19 gm. of iodine per cc.

In order to tabulate these data, the following classifications have been set up:

Electroencephalogram

0 = No change.
1+ = Amplitude decrease or transient delta activity lasting less than 5 min.
2+ = Focal delta activity or generalized slow activity lasting 5 to 10 min.
3+ = Slow activity or abolition of activity persisting up to 1 hr.

Seizure discharges are not included in this classification and are tabulated separately. In general, when these occurred they were associated with severe EEG abnormalities.

Gross Staining with Copper Phthalocyanine (Increased Vascular Permeability)

1+ = Slight staining of a portion of one hemisphere.
2+ = Moderate staining usually involving most of one hemisphere.
3+ = Intense staining usually involving more than one hemisphere, i.e., staining of the opposite hemisphere and/or posterior fossa contents.

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