Experimental Study of the Intraventricular Instillation of Radioactive Gold*

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Continued interest in the surgical management of hydrocephalus has resulted in the development of many techniques designed to divert the cerebrospinal fluid into other receptive areas. The successful use of these techniques may enhance survival and intellectual function. Certain complications may occur with disturbing frequency, however, when foreign materials are introduced into the cerebrospinal fluid and vascular systems. These complications include obstruction, thrombosis, and infection. Thus, although the ventriculo-atrial shunt has attained a certain success, the numerous complications, as well as the required revisions, tempt one to consider other means of controlling progressive hydrocephalus. The popular concept of cerebrospinal fluid production solely by the choroid plexus and its absorption via the arachnoidal villi is no longer tenable. Current concepts indicate that the fluid is in a constant exchanging equilibrium involving water, electrolytes, and protein occurring throughout the ventricular and subarachnoid spaces.

Brain and ependyma may perform a significant role in cerebrospinal fluid production; however, it is the choroid plexus that plays an important and unique part in the dynamics of cerebrospinal fluid physiology. The choroid plexus actively secretes fluid containing a high sodium content, the significance of which is not understood, and acts as a pump pulsating synchronously with the arterial pulse wave. This pulsatile force produces the unidirectional flow of the cerebrospinal fluid from the ventricular compartments to the subarachnoid spaces and is thought to be the factor responsible for ventricular dilatation when obstruction is present.

Consideration of these features has for years invited therapeutic attacks on the choroid plexus for controlling progressive hydrocephalus. Morbidity, mortality, and uncertainty of success have encumbered the surgical removal of the choroid plexus and prevented widespread adoption of the procedure.

We undertook a study of the ablation of the choroid plexus by an agent instilled into the ventricular cavity. Such an agent, we felt, should possess the following qualities:

1. It should be contained in a liquid vehicle that would be maintained and tolerated in the cerebrospinal fluid.
2. It should be evenly dispersable throughout the ventricular system.
3. It should be selectively effective in destroying the choroid plexus.
4. It should be free of harmful effects on brain parenchyma.

For evaluation we selected radioactive gold (Au198), a superficially penetrating radioisotope capable of local destruction by virtue of beta particle emissions (Table 1). A colloidal solution of this material is known to remain in the subarachnoid space following intrathecal injection and to emit its maximum radiation dosage while confined to this space. Besides offering the desired beta activity source, Au198 provides soft, lightly ionizing, gamma energy which enables identification and localization of the material by standard counting techniques (Table 2).

Previous reports of the intracerebral injection of Au198 suggested a possible concentration in the areas of the choroid plexus. This study was therefore designed to investigate the distribution, selectivity, and safety of Au198, as well as the patho-

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logical changes produced by its use, in the hydrocephalic animal.

Experimental Method

Hydrocephalus was produced in dogs by the injection of aluminum silicate (Kaolin) suspension into the cisterna magna. This provided a dilated ventricular system for accurate cannulation. After an appropriate delay for hydrocephalus to develop, ventricular cannulation was performed stereotaxically, via a parietal craniectomy, with the use of an overhead microcraniomaniipulator. Then, 10 to 20 millicuries (mc) of Au198 were instilled into the atrial area of a lateral ventricle. The animals were sacrificed in accordance with a schedule from the third to the tenth postoperative day; the brain was fixed in situ by carotid perfusion to permit gross, radiological, and histological investigation. Ten animals were satisfactorily analyzed in this manner.

Results

Gross Data. Gross pathological study of the brains revealed that a hydrocephalus of moderate degree was present in each instance. The dura and arachnoid were not remarkable. The cortical gyri appeared flattened. The basilar cisterns were obliterated by Kaolin and inflammatory reactions. Within the moderately dilated ventricles, the ependyma was smooth and intact. Each choroid plexus presented as a swollen, smooth, whitish-gray, peppered black, coagulum cast, with total loss of the normal fibrillary vascular character. This was true for the plexuses of the lateral, third, and fourth ventricles, regardless of their anatomical relation to the injection site. This structure could be easily extracted intact from its locus with a minimum of manipulation and no recognizable remnants left (Figs. 1 and 2).

Radiation Data. Twenty matched-weight samples were taken from each brain (Fig. 3). Each 200-mg sample composed of 2 mm cubes of diced tissue was then counted in a sodium iodide well crystal using a gamma-ray spectrometer with a pulse height analyser. A radiological activity index was determined as counts per minute for each sample. These numbers were then converted