Studies of the third circulation
Amipaque CT cisternography and ventriculography

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The techniques of Amipaque (metrizamide) computerized tomography (CT) cisternography and Amipaque CT ventriculography are described. Normal, intermediate, delayed, and obstructive cerebrospinal fluid circulation patterns are readily demonstrated by evaluation of ventricular stasis of Amipaque on serial CT scans. Both the morphological and physiological characteristics of intracranial cysts are accurately defined and a diagnostic classification is presented. The functional integrity of ventricular shunts can be appraised using the ventricular persistence of Amipaque as a primary criterion. Other applications of these modalities are described and their place in the neurodiagnostic armamentarium is discussed.

KEY WORDS □9 computerized tomography □9 cisternography □9 ventriculography □9 Amipaque (metrizamide) □9 CSF circulation □9 cysts, central nervous system □9 ventricular shunt

SINCE its early clinical applications in 1964,6 radionuclide cisternography has become the primary radiodiagnostic modality for the evaluation of cerebrospinal fluid (CSF) disorders. This technique has provided important and often diagnostic information in various clinical situations including communicating hydrocephalus,15 ventricular shunt malfunction,12 cysts,4 and CSF fistulas.3 However, radionuclide cisternographic studies have certain limitations16 which include poor morphological detail, a significant incidence of test failures, and the complicated handling of radioisotopic materials.

Cranial computerized tomography (CT),2,14 although an anatomic technique, has proven useful in the evaluation of hydrocephalus11 and extra-axial cysts.18 Direct physiological information concerning the CSF circulation in hydrocephalus has been monitored using small doses of Amipaque (metrizamide) administered via either the lateral ventricles or the lumbar subarachnoid spaces and serially imaged using CT.7,13 This radiodiagnostic modality, Amipaque CT cisternography (CTC), can be used for the diagnosis of the various CSF circulation abnormalities,7,8,13 which was previously restricted to the domain of radionuclide cisternography. For the first time Amipaque CTC provides the capacity for a single radiological examination to accurately and simultaneously assess both morphological and physiological information.

Materials and Methods
Amipaque CTC studies were performed on 63 patients aged 8 months to 69 years. Individuals receiving neuroleptic drugs or with a
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**TABLE 1**

| Circulation Pattern | Primary: Ventricular Stasis† | Secondary: Slow SAS Ascent‡ | Periventricular Absorption§ | Parasagittal Blush||
|---------------------|----------------------------|-----------------------------|--------------------------|----------------|
| Type I: normal      | 0                          | 0                           | 0                        | +              |
| Type II: intermediate| +                         | 0                           | 0                        | +              |
| Type III: intermediate| +                       | +                           | 0                        | +              |
| Type IV: delayed    | ++                        | 0/+                         | 0/+                      | 0/+           |
| Type V: obstructive**| X X X                    | 0/+                         | 0                        | 0              |

*CSF = cerebrospinal fluid; CTC = computerized tomography (CT) cisternography; CTV = CT ventriculography.
†Ventricular stasis of Amipaque: 0 = none at 24 hours; + = mild at 24 hours; ++ = moderate to severe at 24 hours; X X X = site of ventricular obstruction ascertained.
‡Persistence of well defined Amipaque in basal subarachnoid cisterns at 12 hours: 0 = normal, poor definition; + = sharp definition; − = none or minimal amount present. SAS = subarachnoid spaces.
§Periventricular decreased absorption on 0.2 or 6 hour CT: 0 = none; + = present.
∥Parasagittal blush: + = best seen at 6 and 12 hours (normal); ++ = best seen at 24 or 36 hours (delayed); 0 = never well seen.
**Criteria using Amipaque CTV.

Results

Cerebrospinal Fluid Circulation Patterns

Table 1 summarizes the CSF circulation patterns with Amipaque CTC and CTV. The types are more fully described below.

**Type I: Normal.** Thirty-eight patients were categorized as normal (Figs. 1 and 2). On the immediate (0.2 hour) CT, there was rapid filling of the basal subarachnoid cisterns and the Sylvian fissure. Even some cortical sulci were sharply delineated by the contrast material. The circulation of Amipaque toward the outflow arachnoid granulation system occurred via both the anterior and posterior subarachnoid spaces. The fourth ventricle can
Fig. 1. Normal Amipaque computerized tomography cisternograms. Left: Pre-Amipaque, with enlarged lateral ventricles and subarachnoid spaces. Center: Six hours after Amipaque. Amipaque fills the lateral ventricles and cortical sulci. Right: Twenty-four hours after Amipaque. Amipaque has been totally cleared from the lateral ventricles. A very mild blushing of the cerebral regions adjacent to the subarachnoid spaces persists.

usually be completely filled with Amipaque using the described supine filling technique. The third and lateral ventricles contained Amipaque seen by CT in more than half of the cases studied. The brain regions immediately subjacent to the opacified subarachnoid spaces appeared free of Amipaque.

By the 6-hour CT, the subarachnoid spaces were sharply defined. Mild persistence of Amipaque in the lateral ventricles was not unusual. A prominent staining now occurred in areas adjacent to the cerebral and cerebellar subarachnoid spaces. The deeper cerebral regions and the brain stem did not stain.

On the 12-hour CT, visualization of the basal subarachnoid cisterns became less distinct. Minimal or no Amipaque could be detected in the lateral ventricles. The parasagittal, lateral convexity, and cerebellar blushing remained prominent.

The 24-hour CT showed almost total clearing of Amipaque from the subarachnoid spaces. The ventricles were free of contrast media. The symmetrical brain blushing was far less evident.

Types II and III: Intermediate. Nine patients fell into the intermediate group (Fig. 3). The general circulation of Amipaque through the various subarachnoid spaces in its ascent to the arachnoid granulations was sometimes delayed, especially when the basal cisterns were capacious. This was evidenced by persistence of well defined contrast media in the basal subarachnoid cisterns for 12 hours or longer and by a delayed appearance of the maximal parasagittal blush. A mild amount of ventricular stasis of Amipaque at 24 hours was the cardinal feature of the intermediate patterns. No periventricular rim of decreased absorption was visualized in these cases.

Type IV: Delayed Pattern. Ten patients showed a delayed pattern (Fig. 4). The most prominent feature of this circulation pattern was the moderate-to-severe ventricular stasis of Amipaque seen on the serial CT at 24 hours. Associated findings that were diagnostically useful, although inconstant, included a periventricular rim of decreased absorption and a diminished parasagittal blush. Radionuclide (163T) cisternographic findings
correlated with the Amipaque CTC results in the four patients who were examined by both techniques.

**Type V: Obstructive Pattern.** Four patients exhibited obstruction (Fig. 5). When Amipaque was introduced via the ventricular diversionary shunt (Amipaque CTV), the presence of an obstructive phenomenon in the ventricular system or outflow tract was readily demonstrated by non-filling of the ventricular system or subarachnoid spaces distal to the obstruction. Sites of obstruction studied have included the foramina of Monro (two cases) and Magendie and Luschka (two cases). Amipaque CTC, when done, confirmed the location of blockage. In one patient who was studied following surgical removal of an obstructing mass, free flow to Amipaque was restored.

**Intracranial Cysts**

A morphological-physiological classification of central nervous system (CNS) cysts as defined by Amipaque CTC and/or CTV emerged from this study (Table 2). A total of
<table>
<thead>
<tr>
<th>Cyst Classification</th>
<th>Filling Following Subarachnoid Amipaque Administration (CTC)</th>
<th>Filling Following Ventricular Amipaque Administration (CTV)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Immediate</td>
</tr>
<tr>
<td>Subarachnoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>capacious normal cistern†</td>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>communicating EAC (immediate)†</td>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>communicating EAC (delayed)</td>
<td>3</td>
<td>+</td>
</tr>
<tr>
<td>noncommunicating EAC (such as epidermoid, neuroepithelial, arachnoid, poorly differentiated)</td>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>Outlet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dandy-Walker cyst</td>
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<td>+</td>
</tr>
<tr>
<td>Ventricular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>porencephaly (comm)</td>
<td>1</td>
<td>+</td>
</tr>
<tr>
<td>intra-axial cyst (noncommunicating)</td>
<td>3</td>
<td>+</td>
</tr>
</tbody>
</table>

*CTC = computerized tomography (CT) cisternography; CTV = CT ventriculography; EAC = extra-axial cyst.
†Even with a combination of Amipaque CTC, pneumoencephalography, and angiography, it is often extremely difficult to separate the normal enlarged cistern (such as in cisterna magna) from the freely communicating extra-axial cyst.

15 patients were studied, with a diagnosis of CNS cyst or enlarged cisterna magna. Pneumoencephalography and/or angiography were performed in all 15 individuals and eight of these had surgical intervention.

**Subarachnoid Cysts.** Amipaque fills either a communicating extra-axial cyst or a capacious, normal cistern (for instance, an enlarged cisterna magna) immediately. The distinction of these two entities (Fig. 6) was

![Fig. 5. Undifferentiated cyst and obstructive hydrocephalus. Left: Pre-Amipaque, markedly dilated lateral ventricles can be seen with a large cystic structure either adjacent to or communicating with the ventricle. Center: At 0.2 hours post-Amipaque, Amipaque fills the lateral ventricles but not the cystic structure, that is, the low-absorption area is not in communication with the lateral ventricles. The third and fourth ventricles and basal subarachnoid cisterns did not opacify with Amipaque, denoting an obstructive hydrocephalus. Right: Six hours post-Amipaque. No filling of the cyst occurred on delayed scans. At surgery, an undifferentiated cyst was removed which was not in communication with the lateral ventricles, and compressed but did not infiltrate the brain substance.](image-url)
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**Fig. 6.** Retrocerebellar (communicating) extra-axial cyst versus enlarged cisterna magna.  
_Upper:_ Routine computerized tomography (CT) scan. Large area of diminished attenuation coefficient posterior to a small cerebellum. The fourth ventricle (arrow) and brain stem (B) are compressed from behind.  
_Center:_ Amipaque CT cisternograms at 0.2 hours. Amipaque immediately fills the large retrocerebellar cystic region.  
_Lower Right:_ Pneumoencephalogram, anteroposterior, brow down view. Oxygen fills the large retrocerebellar area noted on computerized tomography. On lateral views the fourth ventricle was displaced anteriorly. Vertebral angiography displayed the anteriorly displaced vermian and hemispheric branches of the posterior inferior cerebellar artery as well as the small cerebellum. Therefore, a definitive distinction between cisterna magna and cyst cannot be made, although a communicating cyst is most likely.
difficult with Amipaque CT techniques as with pneumoencephalography and angiography. The differentiation was often dependent on associated findings (such as, hydrocephalus and abnormal CSF circulation favoring cyst) which were best delineated with Amipaque CTC.

When no communication was present between the Amipaque in the subarachnoid space and the cyst on the immediate (0.2 to 1.0 hour) CT scan, diffusion-penetrance of Amipaque into the cyst (Fig. 7) sometimes occurred over several hours (delayed communicating extra-axial cyst). In some individuals, no Amipaque entered the cystic area (Fig. 5) on either the immediate or delayed CT scans (noncommunicating extra-axial cyst). A cleavage plane of subarachnoid Amipaque often separates an intracranial cyst from adjacent brain, thus definitively establishing its extra-axial nature.

Outlet Foraminal (Fourth Ventricle) Cysts. Amipaque CTV showed ready filling of the large region of diminished absorption in the posterior fossa (Fig. 8). Moreover, definitive proof of outlet foramina obstruction (Dandy-Walker cyst) was obtained by the absence of Amipaque in the basal subarachnoid cisterns.

Ventricular Cysts. The diagnosis of porencephaly was established by the ready opacification of a lateral ventricular outpouching with water-soluble contrast media. With both extra-axial and intra-axial brain cysts, no filling of the cystic region occurred even with adequate Amipaque in the ventricles and positional manipulations.

Ventricular Shunt Function

Eight individuals were studied by serial CT following the administration of Amipaque into a ventricular shunt system (Amipaque CT ventriculography). With “normal” shunt function (four patients), the immediate CT showed Amipaque filling the lateral ventricles. When ventricular obstruction was not present, Amipaque also opacified the basal subarachnoid cisterns. If a body scanner was used, the contrast media could also be promptly visualized at the peritoneal end of the shunt tubing. Within 12 hours, the lateral ventricles were fully cleared of Amipaque. Shunt “malfunction” (four patients) was readily distinguished by the persistence of Amipaque in the lateral ventricles at 24 hours (Fig. 9).

Cerebrospinal Fluid Fistulas

Cerebrospinal fluid rhinorrhea (two patients) was readily defined following lumbar injection of Amipaque by the layering of contrast in the appropriate nasal passage with the patient prone. The site of the fistula was also delineated using an EMI 5000 body scanner (Fig. 10).

Adverse Reactions

Among the 39 adults and 24 children, headache (20 adults and four children), and nausea with vomiting (18 adults and six children) were the most common side effects. Subtle perceptual alterations (four adults and one child) were noted only if the patient and
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Fig. 8. Dandy-Walker cyst demonstrated on Amipaque computerized tomography cistograms. A: A large cystic region in the posterior fossa immediately fills with Amipaque (1.5 ml of 190 mg I/ml) injected through the ventriculoperitoneal shunt reservoir. The anterior pointing of this abnormality excludes an enlarged cisterna magna. B: The cystically dilated fourth ventricle is now clearly seen. On this scan and on serial scans over 24 hours, the basal subarachnoid cisterns never opacified, affirming fourth ventricular outlet obstruction. C, D, and E: The superior extension of the cyst has a maximum height of 32 mm (overlapping slice determination, confirmed radiographically). The straightened medial margins of the lateral ventricles suggest concomitant agenesis of the corpus callosum. F: Specific attenuation coefficient (+35 Hounsfield units) of B better defines the cyst and its relationships to the inner table posteriorly.

family were questioned in detail. Adverse reactions were usually delayed in onset and in most instances persisted for less than 24 hours. No side effects were observed in 15 adults and 15 children.

Discussion

Amipaque is an investigational, non-ionic, intrathecal contrast agent of lowered toxicity due to its decreased osmolality. The relative safety of this water-soluble glucosamide of metrizoic acid has been evidenced in laboratory and human experience with radiculomyelography, cisternography, and ventriculography. Since large volumes and high concentrations of this contrast medium seem to correlate with an increased incidence of adverse reactions, reduced dosages are obviously preferred and are permitted by the high resolution of CT imaging. However, even using this method with lowered doses, adverse reactions (usually mild to moderate in intensity and lasting less than 24 hours) occurred in 53% of the individuals studied. These side effects were delayed in onset and correlated closely with the maximal Amipaque blush.
FIG. 9. Ventricular shunt malfunction. Left: Pre-Amipaque, showing dilated lateral ventricles and shunt artifact. Center: Twelve hours after Amipaque, prominent opacification of the lateral ventricles with Amipaque can be seen. Right: Twenty-four hours post-Amipaque, ventricular stasis of Amipaque continues, thus confirming the malfunction of the ventriculoperitoneal shunt.

FIG. 10. Cerebrospinal fluid (CSF) leak, visualized by supine computerized tomography. Left: Amipaque, introduced by lumbar puncture, is seen in the basal subarachnoid spaces defining the midbrain (M). Air was incidentally introduced and fills the temporal horn of the lateral ventricle (T). Note the Amipaque (arrowhead) layered in the posterior portion of the ethmoid sinus denoting a CSF fistula (confirmed at surgery). Right: Amipaque (arrowhead) is visualized in the pharynx (P) confirming CSF leakage. The patient described tasting iodine.
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Following either the intraventricular or lumbar intrathecal introduction of Amipaque, the contrast medium progresses in a unidirectional fashion toward the intracranial arachnoid granulations in a manner paralleling that described for subarachnoid injected radionuclides.\(^5,6\) Amipaque therefore appears to accurately reflect the circulation characteristics of CSF. Amipaque CT suggests that the CSF follows both an anterior and posterior route (rather than predominantly anterior\(^6\)) in its ascent to the convexity and parasagittal regions.

The most important criterion of "abnormal" CSF circulation is ventricular stasis, whether using Amipaque CTC/CTV or radionuclide cisternography/ventriculography. Ancillary signs are often helpful using either technique, that is, parasagittal activity with radionuclide or parasagittal blushing with Amipaque. Computerized tomography enhanced with water-soluble contrast material affords the advantage of improved morphological detail which enables the distinction of subtleties such as periventricular edema. Elaborate precautions must be taken in the handling of radioactive substances as opposed to the simple mixing of lyophilized Amipaque with its diluent. The only disadvantage of the Amipaque CT studies was the incidence of adverse reactions, which are not severe enough to limit the usefulness of the technique. With differing premedication regimens before the use of Amipaque and with the development of even lower toxicity water-soluble contrast agents, this disadvantage should be readily overcome.

Amipaque CTV seems a simple and reliable method to evaluate the functioning of a ventricular shunt system. In the clinical situation in which a shunt malfunction is suspected and previous CT scans are not available or the comparison CT findings are not definitive, ventricular persistence of Amipaque and the absence of abdominal contrast media (if the shunt is totally obstructed distally) confirm the presence of malfunction.

A combination of Amipaque CTC\(^6\) and/or Amipaque CTV\(^6\) has proven the most useful diagnostic approach to intracranial cysts. Angiography provides mainly anatomical information. Pneumoencephalography is of limited physiological usefulness and carries a high morbidity. Routine CT again provides basically morphological data, although the visualization of hydrocephalus allows mechanistic suppositions. Amipaque CTC or CTV present both precise morphological (such as extra-axial location of cyst) and functional (such as Dandy-Walker versus posterior fossa extra-axial cyst; delayed communication of cyst) information in a single, rapidly performed study. In addition, the circulation of the CSF, the mechanism of the hydrocephalus, and the functioning of a therapeutic shunt may also be defined by this single test. It appears that the use of pneumoencephalography, angiography, and radionuclide studies may be obviated in the diagnostic evaluation of most brain cysts.

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