## Radionuclide Shuntogram: Adjunct to Manage Hydrocephalic Patients

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We reviewed our experience with shuntograms to establish technical criteria that would optimize the reliability of this test in managing patients with shunt malfunction. Methods: Fifty-six shuntograms were performed in 47 children presenting with symptoms of shunt malfunction not elucidated by conventional radiological examination. Shuntograms were performed by injecting 0.5 ml 99mTc-DTPA in the reservoir of the shunt. Results: There were 22 shuntograms in which ventricular reflux occurred and the entire shunt system was visualized. At surgery, three patients in this group presented partial obstruction of the ventricular and/or peritoneal catheter. A second group of patients had 15 shuntograms that showed normal proximal reflux but abnormal distal drainage. Ten patients in this group presented distal obstruction or fracture, valve dysfunction or peritoneal adhesions at surgery. A third group of patients with 19 shuntograms exhibited no proximal reflux. At surgery, twelve had an obstructed ventricular catheter and the last case showed overdrainage. Symptoms of nonsurgical patients abated spontaneously. Conclusion: The shuntogram is a useful procedure in the management of patients presenting with shunt-related problems. For consideration as a normal result, a shuntogram must exhibit ventricular reflux, the shunt system must be entirely visualized and the isotope must diffuse uniformly in the peritoneal cavity. Whereas rapid radionuclide clearance is a useful parameter in eliminating a distal obstruction, it is a misleading sign for proximal blockage. Absence of ventricular reflux is highly suggestive of proximal reflux. Implicit to this conclusion is the fact that the presence of a reservoir proximal to the valve greatly facilitates the performance and interpretation of a shuntogram.

Key Words: shuntogram; cerebrospinal fluid shunt; shunt malfunction; hydrocephalus

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The management of patients with surgically treated hydrocephalus may be challenging, the clinical presentation of a malfunctioning shunt being often nonspecific, especially in young children. Moreover, conventional radiologic examinations, such as shunt series, cerebral ultrasound or CT scans, are not rarely equivocal in cases of shunt malfunction. In these situations, the assessment of shunt patency is extremely difficult.

In recent years, numerous procedures have been proposed to ascertain shunt function. These techniques include: response to digital compression of the flushing device (1), injection of contrast media (2,3) and radionuclide directly into the shunt device (4-15) into the lateral ventricle (6,12) or indirectly into the lumbar subarachnoid space (12,16,17), ultrasound flowmetries (18,19) and thermosensitive procedures (20,21).

This article reviews our experience with radionuclide shuntograms. We correlated the results of this procedure with clinical outcome and surgical findings to establish technical criteria that could optimize the reliability of this test in managing patients with shunt malfunction.

#### MATERIALS AND METHODS

From May 1991 to December 1993, 56 radionuclide shuntograms were consecutively performed in a series of 47 hydrocephalic children (26 boys, 21 girls; aged 1 mo to 17 yr; mean age  $7 \pm 5.5$  yr). These patients had the same type of ventriculoperitoneal shunting system, which consists of a Holter-Hauser ventricular catheter-reservoir typically placed transoccipitally into the frontal horn and secured proximally to a Pudenz-Schulte valve. The latter is, in turn, attached to a peritoneal catheter of which approximately 30 cm are eased into the abdomen. The patients selected for this radionuclide shunt study presented with clinical features compatible with shunt malfunction. Their US or CT scan, however, demonstrated no significant change from baseline.

For the radionuclide shunt examination, all patients were initially placed in a supine position for a minimal period of 15 min. The scalp over the reservoir was shaved, prepared with iodine and draped. The shunt reservoir was punctured with a 25-gauge needle and 1 mCi <sup>99m</sup>Tc-DTPA was gently injected in a volume of 0.1 to 0.5 ml, while manually compressing the valve transcutaneously to demonstrate ventricular reflux. Subsequently, sequential pictures were obtained with a gamma scintillation camera. Data acquisition was performed in two phases: The first phase was a dynamic acquisition of one frame every other second for 500 sec centered over the skull. This was followed by serial static views of 60 sec every 5 min over the skull, neck and thoraco-abdominal regions for up to 20 min or later if necessary. If no migration was observed after 30 min in the supine position, the patient was positioned sitting and rescanned. If no migration occurred in this position, the valve was pumped and shunt patency reassessed under the camera. In half of these procedures, data were acquired to draw a clearance curve and calculate the clearance half-time of the reservoir.

### RESULTS

No mortality or morbidity was encountered with this radioisotopic study. Three patterns of radionuclide flow were observed. The first pattern, present in 22 patients, characterizes what was considered as normal radionuclide shuntograms. Ventricular reflux was demonstrated, the entire shunt system was visualized without any blockage, the isotope passed uniformly into the abdominal cavity and no loculation was observed around the distal end of the peritoneal catheter (Fig. 1). In most of these shuntograms, radioactivity diffused in the abdominal cavity by 10 min. The clearance half-time of the reservoir ranged from 1 to 7.5 min. Three patients in this group had to be operated on because their clinical manifestations persisted. At surgery, a partial obstruction of the ventricular catheter was found in one patient, an incomplete occlusion of the peritoneal catheter was found in another and partial obstruction of both ventricular and distal catheters were found in the

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last patient, leading to a 14% rate of false-negative results (3/22). In all other patients, the clinical manifestations abated spontaneously over a short period of time and no surgery was required.

In 15 radionuclide shuntograms (Fig. 2), the pattern of isotope flow was characterized by a blockage at the valve or in the distal catheter with little or no clearance of the radionuclide through the shunt system and, consequently, a flat clearance curve was recorded. The clearance half-time of the reservoir ranged from 30 min to infinite values. In three patients,

radioactivity never reached the abdominal cavity. Ventricular reflux was present in these 15 shuntograms. Ten patients in this group required surgery. In three patients, the distal catheter was patent; the resistance to isotope outflow in the peritoneal cavity was considered to be due to intra-abdominal pressure exceeding the ventricular pressure. In these three patients, radioactivity did not reach the abdominal cavity more than 10 min after injection of the radioisotope. In two patients, peritoneal adhesions with loculations were encountered with radioactivity remaining localized where it initially appeared in the abdomen and typically



FIGURE 2. Shuntogram with distal obstruction. (A) Static views at 10, 15, 20 min show ventricular reflux but no migration of radioactivity in the distal tubing. (B) Shunt reservoir's time-activity curve is flat with no washout (y = kcps, x = min). (C) After imaging in the sitting position and pumping the valve, there is some radioactivity in a peritoneal loculation.



FIGURE 3. Shuntogram with proximal obstruction. (A) Immediate postinjection sequence. No visible ventricular reflux. (B) Ten- and 15-min static views show slow migration of the radioactivity in the distal tubing. (C) At 20 min, there is no free activity in the peritoneel cavity. Radioactivity is seen after 5 min. (D) Time-activity curve shows good washout half-time (y = kcps, x = sec).

failing to diffuse uniformly in the peritoneal cavity. In four other patients, an obstruction (two patients) or a fracture (two patients) of the peritoneal catheter was found. In the last patient, an obstructed valve was discovered at surgery.

Nineteen shuntograms exhibited a peculiar feature of absent ventricular reflux (Fig. 3). Thirteen of these 19 shuntograms showed normal to accelerated isotope voiding with a half-time clearance of the reservoir ranging from 0.5 to 8 min. In the six other patients, not only was absence of proximal reflux observed but so was retarded clearance of the radionuclide; the radioactivity had not reached the abdominal cavity after 20 min. In only one patient was there a proximal obstruction clearly outlined on shuntogram. Thirteen patients in this group were operated on for persisting symptoms, and an obstruction of the ventricular catheter was observed in 12. The last surgical patient exhibited a patent shunt system with a valve of relatively low resistance with subsequent overdrainage. In this patient, preoperative intracranial pressure monitoring performed to distinguish slit ventricle syndrome from overdrainage, showed negative pressures in the upright position. Among the 12 patients with surgically proven obstruction of the ventricular catheter, 7 exhibited normal isotope voiding with half-time clearances of the reservoir ranging from 0.5 to 8 min and most of radioactivity diffusing in the abdominal cavity 10 min after isotope injection. Five of these 12 patients had slow clearance with an infinite value of half-time clearance of the reservoir. No radioactivity was detected in the abdomen 20 min postinjection.

#### DISCUSSION

Assessment of the patency of a shunting device in hydrocephalic patients is a challenging problem. In young shunted children, it can be extremely difficult to differentiate the prodrome of an acute viral illness which may include nonspecific symptoms such as headache, irritability, nausea and vomiting from a true shunt malfunction, particularly when shunt series, cerebral US or CT scans appear unchanged. Consequently, numerous different techniques have been described to evaluate shunt function, knowing that the simple palpation of the shunt flushing device is far from accurate (1,13). As early as the 1960s, radioisotopic techniques were used to assess shunt patency. These procedures involved injection of the isotope directly into the lateral ventricle or the lumbar subarachnoid space (22-24). Radioactivity clearance from the ventricles was evaluated by multiple blood samples. In 1966, Di Chiro and Grove refined the technique by injecting the isotope directly into the shunt system and imaging the radioactivity all along the shunt pathway (5). Subsequently, this technique was further improved by combining pressure recordings with radionuclide clearance studies (10,11,13). These methods are only qualitative. Quantification is possible, however, if the volume of the valve/reservoir and the clearance of the isotope are known (9). Despite these technical advances. some authors have established the misdiagnosis rate of shunt patency at 40% using nuclear shuntograms (6).

In this study, the presumptive diagnosis reached after shuntogram was confirmed at surgery in 22 of 23 surgical patients suspected to have proximal or distal shunt malfunction. One patient, exhibiting rapid clearance and no ventricular reflux, required preoperative intracranial pressure monitoring in combination with the shuntogram to clarify the diagnosis. We encountered only a 14% rate of false-negative results. Three of the 22 patients exhibiting "normal" shuntograms ultimately demonstrated an obstruction of the proximal and/or the distal catheter of their shunt system at surgery. Of note, in all three patients, the obstruction was found to be partial rather than complete. One cannot, however, ignore that 11 of 34 patients in this study showing abnormal shuntograms, compatible with either proximal or distal obstructions, did not require surgery because their symptoms abated during the observation period. These false-positive studies do not necessarily represent failure of the technique. Among patients with shunt failure symptomatology not explained by conventional radiological examination is a group believed by Epstein et al. (25) to have transient shunt obstruction. We did not believe it ethically justified to repeat the shuntogram once the patients became asymptomatic. Overall, 14 of the 56 shuntograms were misleading. This 25% misdiagnosis rate is lower than that quoted in the literature (6). The results of the present report therefore seem to indicate that the radionuclide shuntogram is a useful tool in the management of patients presenting with shunt-related problems not elucidated by conventional radiological examination.

In this study, special attention was paid to radionuclide clearance. This parameter proves to be useful in patients with partial or complete distal obstruction or in patients with peritoneal loculation (6-8, 13, 15). In instances of distal malfunction of the shunt system, the clearance curve is flat and the half-time clearance of the reservoir indicates infinite values. For complete distal obstruction or rupture of the abdominal catheter, the isotope fails to migrate through the tubing, whereas in partial distal obstruction due to relatively high abdominal pressure or obstruction of the valve, extremely low radionuclide clearance is encountered. Peritoneal loculations are typically characterized by stagnation of the radioactivity at the initial site of appearance within the abdominal cavity and absence of uniform diffusion in the peritoneum.

Whereas delayed clearance of the radionuclide seems to be a useful feature in distal obstruction, we found it to be a misleading sign in proximal obstruction. Of the 12 patients with surgically proven obstruction of the ventricular catheter, 7 exhibited a normal isotope voiding curve. Only 5 of these 12 patients would have been diagnosed with shunt malfunction solely on the basis of slow radionuclide clearance. Consequently, we do not think that clearance studies of the isotope are of much help in proximal obstruction as previously reported (6-8,11). This high rate of misdiagnosis based on the interpretation of radionuclide clearance is predictable. The time required for the isotope to reach the distal site of the shunt depends on a multitude of factors, including the patient's CSF production, the proportion of CSF circulating through normal pathways, the resting intraventricular pressure, the patient's position prior to the test, the opening pressure of the shunt system, the length of the tubing (the so-called siphoning effect), the force with which the radionuclide is injected and the variations of intraventricular pressure due to coughing, straining or crying (6).

Conversely, the absence of ventricular reflux seems to be a highly reliable scintigraphic feature in proximal obstruction. In this study, 12 of the 13 surgical patients with absence of proximal reflux on the shuntogram had an obstruction of the ventricular catheter confirmed at surgery. When reviewing the literature, different shuntographic parameters, other than the

clearance curve, have been mentioned as suggestive of proximal obstruction. Inability to measure intraventricular pressure, to aspirate CSF freely or to inject isotope into the ventricle were considered of some help in assessing proximal shunt obstruction (6-8,15). Hayden, using a method combining pressure recordings and a radionuclide clearance study, stated that a proximally obstructed shunt will not transmit pressure to the reservoir to give a low, flat tracing. The injected radionuclide reportedly did not clear spontaneously in this situation. Voiding of the isotope was obtained, if the distal catheter was patent, by pumping the flushing device (11). It must be stressed, however, that a dry tap of the reservoir or flat waves, if occasionally suggestive of proximal obstruction, can also occur with a patent shunt and slit ventricles. In this latter situation, ventricular reflux would still be observed. Previous articles insisted on the slow or absent migration of the radioactivity down the distal catheter in proximal obstruction (6-8). In these studies, not much attention was paid to the occurrence of ventricular reflux. Some authors have even reported that absence of ventricular reflux, if occasionally suggestive of proximal obstruction, could also occur in normal shunts (8). Our study would suggest that one cannot assume that if the radionuclide flows down the shunt, it is being pushed by CSF emanating from the ventricles. Siphoning and gravity, for instance, may contribute to the migration. In our hands, a shuntogram exhibiting good opacification of the distal shunt system and normal clearance of the isotope, but no ventricular reflux, cannot be considered as normal but rather as inconclusive.

These considerations stress the need to optimize the technical conditions to obtain, when possible, some ventricular reflux. The presence of a proximal reservoir, the manual compression of the valve during injection of the isotope and the injection of a sufficient volume of radionuclide (ideally approximately 0.5 ml) are therefore mandatory requirements for adequate interpretation of a shuntogram.

## CONCLUSION

This study shows the radionuclide shuntogram to be a useful adjunct in the management of patients presenting with shuntrelated problems not elucidated by plain roentgenograms, cerebral US or CT scan. To be considered as normal, it must exhibit ventricular reflux, the shunt pathway must be entirely visualized and the isotope must diffuse uniformly in the peritoneal cavity. While the rapidity of drainage of the radionuclide is a useful parameter in distal obstruction, it is a misleading sign in proximal obstruction. On the contrary, absence of ventricular reflux is highly suggestive of proximal obstruction. The surgical implication is that the presence of a proximal reservoir within the shunt system greatly enhances the adequate performance and interpretation of a shuntogram. The eventuality of a shunt malfunction must, however, always be considered, even if the shuntogram fulfills all the above criteria of "normality" in children with persistent symptoms.

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# Hypoperfusion in the Limbic System and Prefrontal Cortex in Depression: SPECT with Anatomic Standardization Technique

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Depression is a common psychiatric illness, and several reports have described cerebral blood flow (CBF) abnormalities on SPECT studies in affected patients. However, because region of interest analyses were used to determine significant CBF changes in these studies, there were methodological limitations. Therefore, we investigated CBF distribution abnormalities in depression on a pixel-bypixel basis using SPECT and an anatomic standardization technique that has been commonly used for PET activation studies. Methods: Eleven patients with unipolar depression, six patients with bipolar depression and nine age-matched normal control subjects underwent HMPAO brain SPECT studies. The radioactivities of SPECT images for each subject were globally normalized to 100 counts/pixel. Then, each SPECT image was transformed for standard brain anatomy using a computerized Human Brain Atlas system. For each group, the mean and variance images were calculated from the standardized anatomic SPECT images, and group comparisons were performed on a pixel-by-pixel basis. Results: Significant decreases in CBF in the prefrontal cortices, limbic systems and paralimbic areas were observed in both depression groups compared with the normal control group. Conclusion: Decreases in CBF in these regions may be related to impaired attention as well as cognitive and emotional responses, which have been recognized as usual symptoms in depression. The anatomic standardization technique promises to be useful for group comparison analysis of brain SPECT on a pixel-bypixel basis for individual neurological and psychiatric diseases.

Key Words: depression; SPECT; anatomic standardization; limbic system; prefrontal cortex

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**D**epression is a common psychiatric illness (1), and many reports have described associated cerebral blood flow (CBF) and metabolism abnormalities on SPECT and PET studies in affected patients (2-12). Several investigators have described CBF decreases in the paralimbic regions (2); left prefrontal and both temporal regions (3); selective frontal, central, superior temporal and anterior parietal regions (4); whole brain (5); and left cerebral hemisphere (6) in patients with different types of depression. However, a lack of any significant changes in CBF in depression has also been reported (7). Decreased glucose metabolism in the left dorsal anterolateral prefrontal cortex may occur in some types of depression ( $\vartheta$ , $\vartheta$ ). The use, however, of region of interest analyses to determine significant CBF changes in these studies introduced limitations in the sensitivity of the imaging approaches (13).

Fox et al. (13) reported that intersubject averaging of PET images, a technique requiring transformation of brain images of individual subjects into a standard brain shape and size in three dimensions (*anatomic standardization*), allows enhanced detection of focal brain responses. The anatomic standardization technique also permits group comparisons between normal control subjects and patients on a pixel-by-pixel basis (14,15). Recent reports describe CBF abnormalities on PET studies with anatomic standardization in patients with depression (11,12). These studies reported the finding of hypoperfusion in the left anterior cingulate and left dorsolateral prefrontal cortex (11). Assessment of brain SPECT abnormalities using the anatomic standardization technique has also been proposed (16).

Recently, Roland et al. (17) developed a new computerized human brain atlas (HBA) system that transforms the brain anatomic structures of subjects into a standard anatomic format using linear and nonlinear parameters. The purpose of the

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