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# Preembolization Functional Evaluation in Brain Arteriovenous Malformations: The Ability of Superselective Amytal Test to Predict Neurologic Dysfunction before Embolization

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**Purpose:** To describe the incidence of neurologic dysfunction following embolization of supratentorial AVMs, and to correlate findings with results of preembolization Amytal tests. **Materials and Methods:** Data from 147 embolizations of supratentorial AVMs following Amytal tests in 30 awake patients were analyzed retrospectively. **Results:** Of five embolizations done after a positive Amytal test, two were followed by neurologic complications. Eighty-two embolizations done as single embolizations immediately after a negative Amytal test were associated with no neurologic complications. The remaining embolizations were parts of multiple series of embolizations, each beginning with an Amytal test and followed by a number of embolizations without catheter movement or repeat Amytal testing. Since any prior embolization in the series might reduce the sump effect of the AVM, embolic agent delivered later in the series could potentially reach functional brain tissue not fully tested by the Amytal test. Therefore, repeat embolizations (not immediately preceded by an Amytal test) were considered separately. In 60 repeat embolizations, six (10%) were associated with some neurologic complication. **Conclusions:** Repeat Amytal testing might detect the loss of sump effect as the AVM is embolized. We conclude that use of data from superselective Amytal tests adds to the safety of AVM embolizations and that repeat Amytal testing potentially could be valuable when serial embolization of a vessel is planned.

**Index terms:** Arteriovenous malformations, cerebral; Embolism, therapeutic blockade; Interventional neuroradiology, provocative testing

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Intracranial arteriovenous malformations (AVMs) may hemorrhage, producing potentially devastating neurologic symptoms (1). Therapy of these lesions requires total ablation of the nidus of these lesions if the risk of hemorrhage is to be elimi-

nated (2). While small AVMs may be totally obliterated by embolization alone, larger lesions with multiple feeding vessels not infrequently require surgical ablation. To make surgical resection easier, some of these AVM patients are referred to interventional neuroradiologists for presurgical embolization. In these cases, the goal of the interventional neuroradiologist is to block as much of the AVM nidus as possible and to reduce blood flow to the AVM without reducing blood flow to the nearby functional cerebral tissue. This is done by meticulous evaluation of the preembolization superselective angiogram to rule out the presence of arterial branches to normal brain tissue. In addition, careful patient monitoring during embolization will help detect any neurologic complication during embolization that could be due to decreased blood flow to functional areas of the brain. A modification of the Wada test (3) has been used at our institution over the past 36 months to identify functional

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brain tissue within an arterial distribution prior to embolization. The results of our experience with the superselective Amytal (amobarbital, a short acting barbiturate) test was described in an earlier paper (4). In this paper, we describe the incidence of neurologic dysfunction following embolization correlated with the preembolization Amytal test.

## Materials and Methods

The data from patients with AVMs of the brain who underwent embolization were analyzed retrospectively to evaluate the efficacy of preembolization injection of Amytal into the feeding vessel of the AVM as a predictor of safety for embolization. As was discussed in our earlier paper (4) on the Amytal test, all patients had cerebral AVMs and all patients were awake during the entire embolization. A neurologist was present throughout the procedure, to monitor both the clinical examination as well as the electroencephalogram (EEG). The neurointerventional embolization procedure was carried out through a coaxial catheter system that was placed through a sheath in the femoral artery, with a microcatheter (either a Tracker catheter, Target Therapeutics Inc., San Jose, CA, or a Balt catheter, Balt, Montmorency, France) positioned in the brain AVM feeding vessel. A digital superselective angiogram was done to show that the microcatheter was properly positioned near the AVM and to confirm that there was no filling of normal-appearing cerebral vessels. Intraarterial injection of 30 mg of Amytal was then performed through the microcatheter. Positive Amytal tests consisted of focal slowing of the EEG (decrease in alpha activity or an increase in delta activity) or development of new focal neurologic deficits. If no change in the baseline clinical neurologic examination or EEG was seen, the Amytal test was considered negative and embolization of the AVM was done.

Over the last 36 months, 33 patients with supratentorial brain AVMs were evaluated with Amytal tests for possible embolization. Thirty of these patients were judged to be suitable candidates for embolization. The embolization was performed through microcatheters using either particles (polyvinyl alcohol particles suspended in a water-soluble iodine contrast agent) or a liquid embolic mixture (isobutyl-2-cyano acrylate mixed with pantopaque and tantalum powder), using techniques previously described (5, 6).

## Results

### *Patient Population*

Thirty-three patients between ages 16 and 73 years were evaluated by Amytal test. Of these, 30 patients' AVMs were embolized. The remaining three patients had positive Amytal tests on all vessels injected and were never embolized.

### *Vessels Studied*

The vascular distributions of the vessels studied by Amytal tests were as follows: anterior cerebral artery, 13 patients; middle cerebral artery, 32 patients; posterior cerebral artery, 18 patients. Note that the number of vessels exceeded the number of patients because many patients had AVMs fed by more than one artery.

### *Amytal Tests*

Each of the vessels embolized was first injected with Amytal. If multiple embolizations were performed on a single vessel (without movement of the catheter), the Amytal injection was not repeated between embolizations in many cases. Because of this, the total number of Amytal tests, 109, was less than the number of embolizations completed. The Amytal test was considered positive if either the EEG or clinical exam or both were changed following Amytal injection. There were 23 positive Amytal tests. The neurologic changes that were seen were evident within 1 minute of Amytal injection and all changes had resolved within 10 minutes.

In general, embolization was not done if the Amytal test was positive. This was true in 18 of 23 positive Amytal tests. However, in five cases, embolization was performed despite a positive Amytal test. This was done only when the location of the AVM suggested that any neurologic deficit that might be produced would not be of great clinical significance. Of the 86 negative Amytal tests, 82 were followed by embolization. The remaining four were not embolized for technical reasons. Generally this was due to partial occlusion of the microcatheter.

### *Embolizations Performed*

There were 147 embolizations performed. This number exceeded the number of major trunks embolized. There were often two or more small vessels of a main trunk that were embolized (for instance, two different anterior temporal arteries feeding the AVM). In addition, a single vessel often required more than a single embolization to achieve satisfactory occlusion, and each of these fractionated embolizations was counted as a separate embolization. (A single embolization will be considered to consist of an injection of sufficient particulate embolic material to achieve a change in flow of the embolic material or a single bolus

of liquid embolic agent. This is described in the discussion section below.)

If the five embolizations done following a positive Amytal test are excluded, there were a total of 142 embolizations performed after a negative Amytal test. Of these, 82 were done immediately following a negative Amytal test. The remaining 60 embolizations had one or more embolizations done in the interval between the last Amytal test and the embolizations. These 60 embolizations will be designated "repeat" embolizations to differentiate them from embolizations done immediately after a negative Amytal test. We feel these embolizations deserve separate consideration because the intervening embolizations had the potential to alter the blood flow to the AVM. With progressive embolization, the sump effect of the AVM could be diminished and a larger fraction of blood in the feeding vessel might reach functional brain tissue not previously detected. This change in blood flow could direct embolic agent to functional brain tissue. This same change in blood flow might also have had the potential to direct more Amytal to the functional brain tissue, if the Amytal test had been repeated.

### Complications of Embolization

Eighty-two embolizations were done immediately following a negative Amytal test. There were no neurologic sequelae of these embolizations identifiable by clinical exam or EEG. Of the 60 repeat embolizations done without an immediately preceding Amytal test, five embolizations were followed by changes in the neurologic examination, plus one additional embolization was followed by development of focal slowing on EEG, without change in the clinical examination.

Of the five patients embolized after a positive Amytal test, two patients had changes on neurologic exam following embolization. Both of these occurred in patients whose Amytal test showed only slowing on EEG, with no change in the clinical neurologic exam.

This data is summarized in Table 1.

### Discussion

There were no technical difficulties or permanent neurologic deficits associated with the Amytal test. This is more completely described in our previous paper on the superselective Amytal test technique (4). The preembolization angiogram and Amytal test were done to help determine

TABLE 1: Summary of data of results following embolizations

A. Results following embolizations performed immediately after a negative Amytal tests	
No change in clinical exam	82
New focal clinical abnormality	0
B. Results of embolizations following a positive Amytal test	
No change in clinical exam <sup>a</sup>	3
New focal clinical abnormality	2
C. Results following repeat embolizations performed without intervening Amytal test	
No change in clinical exam	55 <sup>b</sup>
New focal clinical abnormality	5

<sup>a</sup> One of these three patients had the catheter moved prior to embolization and a second patient was (correctly) believed to be protected by this flow pattern even though the Amytal test was positive (see Discussion), giving a total of only one patient who had a simple positive Amytal test in whom embolization was done and there were no postembolization findings on neurologic exam.

<sup>b</sup> In one of these 55 embolizations there was focal slowing seen on the EEG without any change on neurologic examination.

whether it was safe to embolize the AVM. The embolizations were performed using a fractionated embolization technique.

Table 1 summarizes our data for a single embolization of an AVM feeding vessel immediately following a negative superselective Amytal test. None of these 82 embolizations produced any change in neurologic exam or the EEG. Thus, a negative Amytal test appeared to predict that it was safe to embolize an AVM using a single embolization.

Since none of the patients were embolized without a preceding Amytal test, no true control group exists for comparison. The Amytal tests done with the microcatheter in place for a possible embolization did show a 20% positive rate (23 of 109 Amytal tests). How many of these cases would have had neurologic sequelae if the vessels had been embolized is difficult to determine. Most of these positive Amytal tests were not followed by embolization. However, the five cases that were embolized despite a positive Amytal test showed a 40% rate of neurologic sequelae (Table 1). This is significantly greater than the 0% rate of neurologic sequela of embolization immediately following a negative Amytal test ( $P < .001$  using a  $\chi^2$  test with continuity correction). Furthermore, of the five embolizations performed after a positive Amytal test, two were performed using the data of the angiogram and the Amytal test to improve the safety of the embolization (see below), and these two had no neurologic complications. Of the remaining three patients who were embolized following a positive

Amytal test without some change in technique, two patients developed neurologic deficits. This equaled a complication rate of 67% for embolization after a positive Amytal test and a false positive rate of 33% for the Amytal test. This suggests that doing embolization after a positive Amytal test is associated with a high rate of neurologic complication.

Embolization after a positive Amytal test was performed in only a few cases. These were cases where the likely neurologic sequela of damage to nearby neuronal tissue was judged to be relatively minor. This was based on the known functional organization of the brain (7, 8) (ie, production of a quadrantanopia, if the region of the optic radiations in Meyer's loop was embolized). The possibility of such a deficit was discussed with the patient prior to the time of embolization. As noted above, the positive Amytal test led to minor changes in the embolization technique in two cases (moving a catheter beyond the take-off of a small normal vessel or selection of particulate embolic material to avoid a small normal vessel arising at a right angle from the main vessel) making the embolization potentially safer. Of the two cases developing neurologic symptoms following embolization, one is particularly interesting. The embolization involved a left temporal-parietal AVM following an Amytal test in which there were very subtle changes on the EEG but no changes on the patients clinical examination. The subtle changes were not detected on the computer-analyzed EEG but were evident on the standard paper EEG record, both of which were available in the angiographic suite. The EEG changes were so subtle that they were felt to be insignificant during the procedure. However, these changes were recognized at one of the weekly EEG review sessions. Even if these EEG changes had been appreciated at the time of embolization, the significance of such minor changes had not been previously shown and the embolization likely would have been performed. Unfortunately, following a single embolization, this patient developed a fairly dense receptive aphasia. Luckily, this deficit largely resolved over a period of 1 month, but the case does illustrate the potential significance of even minor EEG changes during the Amytal test. Based on this case, we now feel that even subtle EEG changes should be searched for following the Amytal test injection. If these EEG changes are seen, one should consider avoiding embolization of this ves-

sel, especially if an eloquent region of the brain might be involved.

In many instances, the AVM was not optimally occluded by embolic material after a single embolization. If the microcatheter was moved after initial embolization, the entire procedure was repeated with angiography, Amytal testing, and embolization, if the Amytal test was negative. However, in many cases the microcatheter did not move during the initial embolization. In these cases, if angiography confirms that the AVM needed additional embolization, a decision was made to either embolize the AVM again (called repeat embolization and listed in Table 1C) or the Amytal test was repeated prior to embolization (such an embolization would then be called a single embolization post-Amytal test and listed in Table 1A). In general, a repeat Amytal test was done when the feeding vessel to the AVM was likely also to supply an eloquent region of brain (an area involved with speech such as Broca's or Wernicke's area or the motor-sensory strip near the Rolandic fissure). The reasons for limiting the repeat Amytal testing to only eloquent regions were 1) Amytal has a cumulative effect, producing drowsiness in the patient that could potentially interfere with both the clinical examination and EEG, and 2) a complication involving a noneloquent region of the brain was less likely to be of clinical significance.

Of the 60 repeat embolizations done without an immediately preceding Amytal test, there were five episodes of neurologic dysfunction (8%). This is significantly more than the 0% rate associated with embolization immediately after a negative Amytal test ( $P < .05$  using a  $\chi^2$  test with continuity correction). This difference is even more significant if an additional case is included in which repeat embolization was followed by focal EEG slowing only (without change on the clinical examination). There were no similar cases seen in the group embolized immediately after a negative Amytal test. In total, there were six cases of some type of change in neurologic function (examination or EEG) in the 60 repeat embolizations (10%).

The meaning of this comparison of embolizations performed immediately after a negative Amytal test to repeat embolizations is somewhat unclear. A possible explanation for the increased incidence of neurologic sequelae seen in the repeat embolization group is that vascular branches supplying healthy brain tissue arose from the same feeding vessels supplying the AVMs. The

low pressure and resultant sump effect that existed in the AVM may have made these normal vessels difficult to detect on angiography. These vessels supplying normal brain may have been so small as to be difficult to detect even under optimal angiographic conditions. With embolization of the AVM, the sump effect would gradually disappear and more of the embolic material could then flow to other vessels (9). Thus, the repeat embolization group, which only included AVMs that were embolized multiple times, might be expected to have a higher complication rate than the embolization group with immediately preceding negative Amytal testing (which contained two types of cases: 1) those in which embolization was discontinued after a single embolization, and 2) those in which multiple embolizations were performed, each preceded by its own Amytal test).

Another explanation of this data should be considered. The same sump action of the AVM that initially acted to direct the embolic agents to the AVM and which was later lost with progressive embolization, might also be expected to initially direct a large fraction of the Amytal to the AVM. The small fraction of Amytal that did reach normal brain at the time of the initial Amytal test might not have been sufficient to produce detectable changes in neurologic function. If repeat Amytal testing had been done after partial AVM embolization, it is possible that more of the Amytal would have reached the normally functioning brain that was later adversely affected by the embolization. If this were the case, one might expect the Amytal test to have become positive, although it had been negative prior to embolization. Because Amytal tests were not repeated before all repeat embolizations and because the neurologic complication rate was relatively low, there are few such cases of conversion of Amytal test from negative to positive. However, there was one patient in whom an initially negative Amytal test was followed by an embolization and who subsequently underwent an additional Amytal test (without catheter movement) who then had a positive Amytal test (with transient focal neurologic dysfunction). Because of this, additional embolization was not performed. However, if this patient had had repeat embolization, it is likely that a neurologic complication would have been produced. This case suggests that the Amytal test can indeed change from negative to positive following embolization.

If one accepts the above arguments, one should consider doing repeat Amytal tests following embolizations to determine whether the risk of additional embolization has increased. It must be realized that all these patients had AVMs that were at risk of hemorrhage, or had hemorrhaged in the past, and who were to undergo surgical excision of the AVM. Either hemorrhage or surgery could result in neurologic complication. Furthermore, the embolizations may make the surgery less complicated. The risk of neurologic complication, especially relatively minor ones, must be considered in this context.

## Conclusion

This article reviews our experience with the superselective Amytal test, consisting of the injection of 30 mg of Amytal through a microcatheter prior to embolization of an AVM, which was performed to identify the existence of blood vessels supplying functional brain tissue. Our findings are:

1. A positive Amytal test suggested there was a high likelihood of neurologic complication if the patient was embolized without change in catheter placement. This was true even if the Amytal test produced changes only in the EEG, without a change in the clinical examination.
2. Single embolizations immediately following negative Amytal tests were performed without neurologic complication.
3. Using the fractionated embolization method, the incidence of neurologic complication was significantly higher in cases where a series of embolizations was performed after a single Amytal test as compared to a single embolization performed after an Amytal test. Repeat Amytal tests should be considered during a series of multiple step embolizations (also called fractionated embolizations), especially when an eloquent region of the brain could be involved.

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