COMPLICATIONS OF ANGIOGRAPHY

REMBRANDT DUNSMORE, M.D., WILLIAM BEECHER SCOVILLE, M.D., AND BENJAMIN BRADFORD WHITCOMB, M.D.
Department of Neurosurgery, Hartford Hospital, Hartford, Connecticut

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The short history of cerebral angiography reveals a constant search for an inert, more miscible contrast medium that is devoid of untoward side reactions. None of the substances thus far used have been free of adverse reaction. The first practical radiopaque material used was 25 per cent sodium iodide. Egas Moniz carried out all angiography with this until 1931. Many complications were seen with this material and his mortality rate was between 2 and 3 per cent. Thorotrust was introduced at about this time and became a very popular substance, although its use was mainly confined to the continent. Complications with this substance were reported by Ekström and Lindgren and Northfield and Russell. The potential danger of radioactivity served to limit its use in this country. Gross introduced diodrast in 1939 and, in the 35 per cent solution, it is now perhaps the most widely used of the contrast media. Relatively few complications with this substance have been reported in the literature. Engeset reported 2 fatalities in a series of 100 patients and in neither case did he feel that death was due primarily to angiography. Bull reported 3 deaths in a series of 1,000 cases, all of which were complicated by large intracranial tumors. Chusid, Robinson and Margules-Lavergne reported 2 cases of transient hemiplegia. Dyke reported a case of thrombosis of the carotid artery. Urticarial reactions have been seen. In the main, however, the literature emphasizes the relative safety of the procedure. Indeed, in Torkildsen’s recent monograph on 2,000 cases of angiography, no major complications nor death have been listed.

The authors have seen a rather wide variety of adverse reactions to diodrast angiography and would like to emphasize its potential hazards. The present study is based on a series of 147 carotid angiograms performed with 35 per cent diodrast on 108 patients in the years 1946 to 1950. The series constitutes 30 cases of brain tumor, 17 of aneurysm, 19 of subarachnoid hemorrhage, 12 of cerebral thrombosis, 7 of degenerative disease, 4 of subdural hematoma and 19 undiagnosed cases. Complications occurred in 14 of the 108 cases.

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1. FATAL (3 cases)

Death occurred in 3 cases in which cerebral angiography contributed, at least in part, to the cause of death.

Case 1. M. J., a 35-year-old female with renal hypertension, was admitted to the
neurosurgical service with diplopia, blurred vision and focal seizures associated with loss of consciousness. Examination was essentially negative except for cardiac enlargement and B.P. of 244/160. Percutaneous angiography under local anesthesia with premedication of 0.4 mg. nembutal and 40 mg. atropine revealed inadvertent filling of the left vertebral artery after an injection of 10 cc. of 35 per cent diodrast. A 2nd injection into the carotid artery gave satisfactory films. The patient was subdued and uncommunicative following this procedure. Twelve hours after angiography, she rather suddenly expired from respiratory failure. At autopsy approximately 250 cc. of blood were found in the neck, deviating the trachea to the opposite side but not obstructing it (Fig. 1). In addition to marked kidney pathology, con-

![Fig. 1. Case 1. Postmortem neck dissection, showing deviation of trachea to the right and hemorrhage into the neck. Patency of airway tube seen through midline incision in the trachea.](image)

siderable cerebral edema was present. It was the feeling that the extravasation of blood into the neck had caused bilateral jugular compression and secondary venous stasis in the brain and that this, in turn, led to edema and respiratory failure of central origin.

Case 2. C.O., a 65-year-old female, was admitted because of a fracture of her right femur. B.P. 128/86. She was seen in consultation because of a rather marked exophthalmos and mental confusion. History revealed that 12 years previously she had noted the onset of exophthalmos and left 3rd nerve paralysis. Surgery had been refused. On examination an additional left 4th and 7th nerve paralysis and a left Foster Kennedy syndrome were found. Skull x-rays confirmed the impression of a sphenoid wing meningioma. Bilateral percutaneous angiography under local anesthesia with 0.4 mg. atropine and 250 mg. sodium luminal was carried out with a total of five 10 cc. injections on the right and two 10 cc. injections on the left. It was noted that the patient was less responsive after this procedure but it was not felt to be related directly to the angiography. Because of previous poor filling on the left side, an open angiogram was performed 2 days later with 50 mg. of demerol and 4 mg. of atropine as premedication, and a total of 50 cc. of 35 per cent diodrast was injected on the left. The patient deteriorated rapidly within the next 24 hours and expired.
the following day. Autopsy revealed a large sphenoid wing meningioma engulfing the internal carotid and part of the middle cerebral artery and, in addition, a large, fresh hemorrhagic and necrotic area in the cortex along the distribution of the middle cerebral artery (Fig. 2).

Fig. 2. Case 2. Section of the left posterior frontal lobe cortex, showing an area of acute infarction with congestion of blood vessels and perivascular infiltration. Cellular architecture is still intact but individual cells are shrunken.

Case 3. L.S., a 54-year-old male, had a 7-year history of alternating hemiplegia, previous ligation of left common carotid artery at another hospital and progressive bilateral pyramidal tract signs, generalized tremor, mental deterioration and emotional lability, culminating in another total left hemiplegia on the day of admission. B. P. was 150/90 and his heart was slightly enlarged to the left. In spite of previous ligation of the left common carotid artery, a percutaneous angiography was carried out on the right with 100 mg. of nembutal and 60 mg. of codein as premedication. Immediately following the 1st injection of 10 cc. of 35 per cent diodrast, the patient became unconscious; respirations became labored and assumed a Cheyne-Stokes character. Stellate block was done immediately with improvement in respirations. The pre-existing left hemiparesis remained unchanged; the patient never regained consciousness and died on the 12th day with terminal hyperpyrexia and respiratory failure. Autopsy revealed multiple recent and old infarcts of the brain. The left vertebral artery was enlarged and thrombosed and there was some generalized atrophy of the brain.

Cases 2 and 3 represent rather massive cerebral infarction in individuals whose cerebral circulation was already impaired. It is of some interest to
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note that death was delayed from 2 to 12 days following angiography. Case 1 represents an error in surgical technique and judgment inasmuch as a cervical hematoma was suspected but not drained prior to her death.

II. NON-FATAL, PERMANENT (4 cases)

Case 4. E.T., a 55-year-old female, was admitted because of 3 grand mal seizures over the previous 3 months. Neurologic and cardiac status were negative. B.P. 130/98. Left percutaneous angiography failed to fill the carotid system. Five days later left open angiography was done under local anesthesia with 0.4 mg. atropine, 50 mg. demerol and 200 mg. nembutal as premedication. A generalized convulsion followed the 1st injection of 10 cc. of 35 per cent diodrast into the left internal carotid artery, with residual aphasia and left hemiparesis. Transitory right facial focal seizures occurred the following day and the stupor and aphasia continued. Two days later an exploratory craniotomy revealed a rather massive infarct of the posterior frontal and temporal lobes with softening and swelling but no tumor or hemorrhage. The patient gradually improved and at the end of 1 month was able to walk with approximately 75 per cent function, but aphasia and mental aberration persisted to a diminishing degree over the ensuing 2 years.

Case 5. E.V., a 35-year-old female, had a spontaneous subarachnoid hemorrhage with sudden collapse on the morning of admission. There had been 2 previous episodes of severe transient headaches. Lumbar puncture yielded a pressure of 580 and grossly bloody CSF. The patient improved under conservative treatment until 1 week later when she had a 2nd episode, this time associated with left facial and hand weakness and a left ptosis. An open right carotid arteriography was performed 3 days later under local anesthesia with 0.4 mg. atropine, 200 mg. nembutal and 80 mg. demerol as premedication. Four 15 cc. injections of the right internal carotid artery were made with 35 per cent diodrast. The next morning, hemiplegia and left homonymous hemianopsia were apparent. Her eyes were deviated to the right and she became drowsy with progressive deterioration, disorientation and incontinence as well as left-sided hypertonicity and right-sided weakness. This state continued for 2 days when a ventriculogram revealed no evidence of a space-occupying lesion but symmetrical dilatation of the ventricles. At the time of discharge 1 month later she was not sufficiently oriented to be able to care for herself. Since then, she has continued to improve slowly in motor function and less so in mental status.

Case 6. B.T., a 44-year-old male, was admitted because of a sudden onset of generalized headache, vomiting and dizziness, not associated with loss of consciousness. There had been a similar episode approximately 2 years previously. Lumbar puncture yielded grossly bloody CSF with an initial pressure of 250. Neurological and cardiac findings were essentially negative. B.P. 124/60. The CSF began to clear after 10 days, at which time percutaneous angiography was attempted under local anesthesia and poor filling obtained on 2 occasions. One week later right open internal carotid angiography was done under local anesthesia with 100 mg. demerol and 300 mg. seconal for premedication. A total of 45 cc. of 35 per cent diodrast was injected with good filling but no evidence of aneurysm nor ill effects. One week later left open arteriography was performed under local anesthesia with 200 mg. nembutal as premedication, using 75 cc. of 35 per cent diodrast in a series of 5 injections. Three hours later the patient became confused and aphasic and a right hemiparesis de-
veloped. His condition progressed to a moribund state and for 12 hours it was critical. He received stellate blocks and the carotid artery was stripped of its sympathetic fibers. There was no immediate improvement from either procedure but the following day the patient gradually began to improve. At the time of discharge 1 month later he had gross clumsiness of right leg with increased deep tendon reflexes and a mild expressive aphasia. After 2 years he has returned to full-time work as a telephone executive with a residual minimal slurring of speech and clumsiness of extremities.

Case 7. L.S., a 30-year-old male, was admitted with a 16-year history of episodic headache and visual disturbance. B.P. was 115/60. Cardiac limits were normal. Right percutaneous carotid angiography was done under local anesthesia without premedication, using a total of 24 cc. of 35 per cent diodrast in 3 injections. A complete left hemiplegia, lasting approximately $\frac{1}{2}$ hour, followed the 3rd injection, with gradual return to normalcy in 14 days although a persistent paresthesia of the left leg has continued to date.

Three of these 4 patients exhibited serious neurological deficits following angiography. Although the onset of symptoms was delayed in all but 1 case, the nature of the complications, with pathological confirmation in 1 case, suggests that their occurrence was more than coincidental.

III. NON-FATAL, TRANSIENT (7 cases)

(A) Transient Hemiplegia.

Case 8. C.B., a 43-year-old female, was admitted because of mild headaches during the previous 8 months. Examination revealed a right exophthalmos with a normal cardiac status. B.P. 124/70. Right percutaneous angiography was performed under local anesthesia with 200 mg. nembutal and 0.4 mg. atropine as premedication with satisfactory demonstration of the carotid circulation. Two days later a similar procedure was carried out on the left side, again under local anesthesia, with 200 mg. nembutal and 100 mg. demerol as premedication. Following a 2nd 10 cc. injection of 35 per cent diodrast, hemiplegia and aphasia developed. Within 3 hours the patient was able to move her arm and leg but her aphasia persisted until the following day.

Case 9. H.G., a 57-year-old male, had had previous hospital admissions for multiple cranial nerve palsies of undetermined etiology. On this admission, he exhibited a complete left 3rd and 4th cranial nerve palsy and a partial right 3rd and 4th palsy. B.P. was 145/90. Cardiac status was normal. Left open carotid angiography was done under cervical block anesthesia, with 10 mg. morphine and 0.5 mg. atropine for premedication, with demonstration of a normal cerebral carotid circulation and no sequelae. The neurological status remained unchanged and 5 months later right carotid arteriography was done by percutaneous injection under local anesthesia with 200 mg. nembutal for premedication. Following the 1st 10 cc. injection of 35 per cent diodrast, the patient suffered a left hemiparesis and aphasia, which subsided within 1 hour.

It is of interest that in both of these cases the opposite side had been injected first without complications.
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(B) Seizures.

Case 10. G.S., a 62-year-old female, was admitted because of a sudden episode of unconsciousness associated with a left Jacksonian seizure followed by right-sided headaches. Lumbar puncture yielded grossly bloody CSF. Neurologic and cardiac findings were negative but her B.P. was 260/110 and renal damage was evident. Percutaneous angiography was attempted under local anesthesia, with 200 mg. nembutal and 0.4 mg. atropine for premedication, with inadequate filling. One week later right open arteriography was done under cervical block anesthesia, with 10 mg. morphine, 0.4 mg. atropine and 100 mg. seconal as premedication. Two 10 cc. injections of 35 per cent diodrast were performed. Following the 2nd injection, a transient, left-sided Jacksonian seizure occurred, associated with loss of consciousness. X-rays revealed an aneurysm in the right posterior communicating artery. Ligation of the right common carotid artery was undertaken. During trial occlusion, an immediate and complete left hemiparesis developed. Upon release, the hemiparesis cleared completely. This was repeated 3 times over several hours until finally ligation was accomplished by tantalum clip. No neurological deficit ensued and her convalescence was uneventful.

Case 11. W.B., a 33-year-old male, was admitted after a spontaneous subarachnoid hemorrhage which had been treated for 4 days in another hospital. Neurologic and cardiac findings were negative with the exception of nuchal rigidity. B.P. was 110/65. Left percutaneous carotid angiography was attempted under local anesthesia with 240 mg. sodium luminal as premedication. The vertebral artery was inadvertently entered, with satisfactory visualization of the vertebral circulation. The operator was unable to obtain carotid arterial filling. Three days later right percutaneous angiography was carried out under local anesthesia with 120 mg. of sodium luminal as premedication. During the 1st 10 cc. injection of 35 per cent diodrast the patient had a grand mal convolution without other sequelae. Three days later right open carotid angiography was done, using 120 mg. of sodium luminal, 75 mg. of demerol and 0.4 mg. atropine as premedication, with 40 cc. of 33 per cent diodrast in a series of 4 injections. A right anterior cerebral aneurysm was demonstrated. There were no sequelae.

(C) Thrombosis of Internal Carotid Artery.

Case 12. C.T., a 56-year-old diabetic male, was admitted with pain in the left eye of 5 days' duration. Neurological and cardiac findings were negative except for dilatation and fixation of his left pupil. Percutaneous angiography was attempted in the left common carotid artery under local anesthesia, with 100 mg. of demerol as premedication. The internal carotid artery did not fill but external circulation was normal. Four days later open arteriography was performed and the entire internal carotid vessel was visibly and palpably thrombotic. After ligation, it was found to be filled with recent clot (Fig. 3). Paralysis of the right arm and leg gradually developed during the ensuing month.

(D) Injury to Cervical Sympathetic Chain.

Case 13. C.D., a 23-year-old female, was admitted with a spontaneous subarachnoid hemorrhage. Right percutaneous angiography was performed under sodium pentothal anesthesia with 240 mg. sodium luminal and 0.4 mg. atropine as
premedication. Five 10 cc. injections of diodrast were made and satisfactory angiograms obtained. During the course of the examination a right ptosis and myosis developed. Subsequently, a left-sided injection was done by the open technique and no complications were seen. It is thought that the ptosis and myosis were due to damage of the cervical sympathetics during the attempts to pierce the carotid artery.

Fig. 3. Case 12. Photomicrograph of left internal carotid showing organizing thrombus within its lumen.

(E) Diodrast Sensitivity.

Case 14. A.B., a 32-year-old male, was admitted because of spontaneous subarachnoid hemorrhage. Left percutaneous angiography was carried out under local anesthesia with 100 mg. nembutal, 10 mg. morphine and 0.4 mg. atropine as premedication. Two 15 cc. injections of 35 per cent diodrast had been completed when a rash appeared over the left arm and clavicular region. Patient had shown a slight sensitivity on skin test to the diodrast and further attempt at angiography was discontinued. The rash was transitory and there were no other sequelae. It is of interest that this is the only patient in the entire series exhibiting sensitivity by skin test and no neurological complications followed injection of the radiopaque substance.

DISCUSSION

A far higher proportion of complications have occurred than indicated in the literature when inclusion is made of delayed complications. From 1940 to 1946, 22 angiograms performed by one of the authors (WBS) and limited to cases of suspected aneurysm were not accompanied by any known com-
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complications.* However, since the War, when angiography was extended to include all cerebral diagnostic problems regardless of age or condition, there have been nearly 10 per cent of complications. Out of 108 cases and 147 angiograms, there were 14 complications (nearly 10 per cent), of which 8 were major (5 per cent), including 3 deaths and 4 permanent paralyses, and 6 were minor (4 per cent), including 2 convulsions. The technical procedures were carried out by both the attending and resident neurological staff, totaling 9 surgeons. There does not appear to be any direct relationship between the complications and (a) open vs. closed technique; (b) the surgeon performing the procedure; (c) premedication; (d) rapidity of injection or quantity used, and (e) presence of hypertension. There does appear to be a direct relationship to the selection of cases, complications arising in those older patients having a tendency toward thromboses (Fig. 4) or in patients having impaired cerebral circulation from one cause or another (tumor and aneurysm).

Vasospasm probably plays the major part in the causation of complications, although statistical proof cannot be offered from this series. Diodrast is known to cause vasospasm. Holm⁹ noted the difference in caliber of cerebral vessels when injected with 35 per cent diodrast as compared to thorotrast. The delayed sequelae as reported in diodrast urography by Pendergrass, Chamberlin, Godfrey and Burdick¹² may well be due to impaired cerebral circulation. The delayed nature of many of the complications in this series suggests thrombosis following initial vasospasm or tissue anoxia. The rather extensive infarction in the pathological specimens so far obtainable confirms this impression. Inasmuch as only 1 patient in the entire series showed a skin reaction, it seems unlikely that organ sensitivity to diodrast is a cause of complications. The rationale of both treatment and prophylaxis in the complications of angiography would appear to lie in the relief of vasospasm. Vasodilators, especially papaverine, novocain infiltration of the carotid sheath, unilateral or bilateral block of the stellate ganglion, as well as its removal or isolation have all been recommended.

The following prophylactic measures are recommended by the authors for use in those cases in which there are signs of defective cerebral circulation as indicated by age, history or neurologic deficits:

1. Pre- and postoperative papaverine administration for 1 and 2 days respectively.
2. Preoperative intravenous sodium luminal, gr. iv.
3. A general anesthetic and/or a short delay between injections have been considered on theoretical grounds.
4. In those cases in which a thrombosis develops, repeated stellate novocaín blocks on alternating sides at intervals of 4 to 6 hours.

CONCLUSIONS

1. Fourteen complications of cerebral angiography are reported. These include 3 fatalities, 4 cases of hemiplegia with permanent residual deficits, 2 cases of transitory hemiplegia, 2 cases of convulsions, 1 case of carotid artery thrombosis, 1 case of injury to the cervical sympathetic chain, and 1 case of diodrast skin sensitivity.
2. The technical details of proficiency, quantity, methods and medication used in the performance of arteriography apparently are not important factors in the etiology of complications.
3. The selection of cases is important with the older age group, especially those having thrombotic tendencies or other evidence of impaired cerebral circulation exhibiting the greatest liability.
4. The delayed nature of most of the serious complications of angiography is stressed and the probability of cerebral thrombosis secondary to irritative vasospasm is suggested as the pathologic etiology.

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REFERENCES