THE NONFILLING PHENOMENON DURING ANGIOGRAPHY IN ACUTE INTRACRANIAL HYPERTENSION

REPORT OF 5 CASES AND EXPERIMENTAL STUDY*

OLIVER CHARLES MITCHELL, M.D., ERNESTO DE LA TORRE, M.D.,†
EBEN ALEXANDER, JR., M.D., AND COURTLAND H. DAVIS, JR., M.D.

Department of Surgery, Section on Neurosurgery, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, North Carolina

(Received for publication April 23, 1962)

Nonfilling of the cerebral vessels during carotid angiography in cases of acute intracranial hypertension is a recognized but poorly understood clinical fact. These patients usually are moribund and often require artificial respiration throughout arteriography.4,6,8,9 The angiographic picture of acute intracranial hypertension resembles that of thrombosis of the internal carotid artery. Collateral circulation through the external carotid artery sometimes is demonstrated in cases of thrombosis,6-8 but never in acute intracranial hypertension. In the presence of great intracranial pressure the internal carotid artery usually does not fill with contrast medium beyond the carotid siphon intracranially; while the external carotid artery and its branches are well demonstrated. Because patent internal carotid arteries have been found at necropsy, the mechanism of this nonfilling phenomenon has been unknown.

Riishede and Ethelberg5 reported 5 patients with intracranial space-occupying lesions in whom this angiographic picture was observed. They concluded that the nonfilling phenomenon was the result of decreased cerebral blood flow secondary to herniation of the brain by the severely increased intracranial pressure.

Horwitz and Dunsmore4 reported 4 similar cases. They also related the angiographic findings to acutely increased intracranial pressure and postulated that reflexes mediated by the diencephalon had altered the intracranial circulation.

Newton and Couch6 presented 1 case of pseudo-occlusion of the internal carotid artery as demonstrated by angiography. Massive intracerebral and intraventricular hemorrhages and patent internal carotid arteries were found at necropsy.

Pribram8 reported 11 well documented cases of acute intracranial hypertension. He postulated that in some of his cases the abrupt rise in intracranial pressure could have been caused by a blood clot or tentorial herniation blocking the aqueduct of Sylvius. After tapping the ventricles in 1 patient, he was able to demonstrate the intracranial vessels by arteriography. He surmised that an acute rise in intracranial pressure was responsible for the nonfilling phenomenon, and he suggested that in similar patients lowering of the intracranial pressure would permit visualization of the cerebral vessels.

In the past 12 months, 5 patients have been seen at the North Carolina Baptist Hospital with acute intracranial hypertension in whom the cerebral vessels failed to fill during carotid arteriography. In each instance the needle was placed correctly within the lumen of the vessel, but only the common and external carotid arteries filled well with contrast medium.

CASE REPORTS

Case 1. A 19-year-old man was in an automobile accident a few hours before admission. He was in
deep coma when brought to the hospital and tracheostomy was performed in the Emergency Room.

Bilateral carotid angiograms showed apparent obstruction of both internal carotid arteries at the level of the siphon (Fig. 1A). The patient ceased spontaneous respiration during the procedure and died soon afterwards.

Postmortem examination was not obtained.

Case 2. The day before admission a 33-year-old white woman complained of intense headache and nausea, accompanied by weakness of her right arm and dysphasia. On the day of admission she had a generalized seizure, extensor rigidity developed, and she was admitted in coma. Both pupils were dilated and paralyzed and she stopped breathing in the Emergency Room. Intubation was performed and artificial respiration was initiated.

A right ventricular tap revealed the pressure to be greater than 600 mm. of water. Air was injected and roentgenograms showed deviation of the right lateral ventricle to the right. A left ventricular tap and injection of air revealed poor filling of the left lateral ventricle.

Bilateral carotid arteriograms then were done and showed nonfilling of the intracranial portion of both internal carotid arteries (Fig. 1B). The patient died the day following angiography and postmortem study revealed a left frontotemporal abscess and herniation of the cerebellar tonsils. The internal carotid arteries were patent.

Case 3. An 11-year-old white boy was admitted to the hospital because of coma. Six years previously the patient underwent a Blalock procedure for tetralogy of Fallot and he had done well until 5 days prior to the present admission. At that time he complained of a left frontal headache with nausea and vomiting, and he was treated symptomatically with improvement. The night before admission he complained of a severe headache. He went to bed but the next morning he could not be aroused and was brought to the hospital.

On physical examination the patient was comatose, areflexic, and flaccid, with positive Babinski's sign bilaterally. Pupils were dilated and paralyzed and bilateral papilledema was present. Respiration was irregular and he was mildly cyanotic.

Bilateral twist-drill holes were placed in the frontal region and needling on the left yielded clear fluid under increased pressure. Twenty cc. of ventricular fluid were withdrawn; air injected into this region was not shown on roentgenograms. Bilateral carotid arteriograms demonstrated no intracranial filling, although there was good filling of the common and external carotid arteries.

Bilaterial occipital burr holes then were made and tapping on the left side yielded cloudy fluid

Fig. 1 A and B. Cases 1 and 2. Common carotid arteriograms demonstrating nonfilling of intracranial portion of internal carotid artery and its branches.
under increased pressure. Air was injected into the left side and roentgenograms revealed good filling of the left lateral ventricle with a shift to the left. The right side was tapped and an abscess cavity was entered from which 5 cc. of thick, foul-smelling, bloody, purulent material were aspirated and the cavity was irrigated. At this point the patient stopped breathing and was intubated and carried on artificial respiration for 36 hours, after which he died.

Postmortem examination of the body was not obtained but postmortem carotid angiograms demonstrated patency of both internal carotid arteries and their intracranial branches.

Case 4. A 44-year-old white woman was admitted to the hospital because of progressive stupor during the previous 48 hours. There was a history of headaches and an inflammation of the ear 3 weeks before.

Physical examination revealed weakness of the right arm and face and a positive Babinski's sign on the right. Electroencephalogram showed evidence of an expanding lesion in the left hemisphere. The day following admission she had a right-sided convulsion, dilated paralyzed pupils, and extensor rigidity developed. Bilateral carotid arteriograms showed incomplete filling of the internal carotid and cerebral vessels. Attempted pneumoencephalography was unsuccessful. Because of extreme respiratory distress, a tracheostomy was done and artificial respiration was instituted, but the patient died the following morning.

Postmortem examination revealed generalized miliary tuberculosis and a left temporal-lobe abscess with acute suppurrative and exudative reaction, diagnosed as tuberculosis. The internal carotid arteries were patent.

Case 5. A 44-year-old white woman fell downstairs on the night of admission and she was brought to the hospital comatose. There was slight bleeding from the nose and left ear. Roentgenograms showed a stellate fracture in the left parieto-occipital area, extending down to the posterior fossa.

Bilateral angiograms showed no filling of the internal carotid artery beyond the carotid siphon on the right. Filling with dye was seen up to the internal carotid bifurcation on the left. At this time, respiratory difficulty occurred and the pupils were dilated and paralyzed.

Bilateral exploratory burr holes revealed a subdural hematoma on the right with obvious cerebral swelling and contusion. Ventricular and lumbar punctures were not done. The patient died at the end of the procedure.

Necropsy revealed severe cerebral swelling, more on the right, with slight right temporal and cerebellar herniations. The internal carotid arteries were patent.

EXPERIMENTAL MATERIAL AND METHODS

The mechanism of the nonfilling phenomenon, to our knowledge, has never been studied in the experimental laboratory. The present investigation was undertaken to determine if an acute increase in intracranial pressure alone would prevent filling of intracranial arteries with contrast medium.

Two Macaca mulatta monkeys and 23 adult dogs (average weight 12 kg.) were used. The animals were anesthetized with intravenous pentobarbital sodium (Nembutal) and endotracheal intubation was performed. A femoral artery was cannulated to record the systemic blood pressure and the cannula was flushed at intervals with 2 to 3 cc. of Ringer's solution containing aqueous heparin.

Short, 18-gauge lumbar puncture needles were placed in the cisterna magna and in the lumbar subarachnoid space through the 4th or 5th lumbar interspaces. Through a left parietal burr hole, a rubber balloon was placed over the surface of the brain in the subdural space in 5 dogs.

Tracings of the subdural, cisternal, or lumbar pressure in mm. of mercury, and of blood pressure and respiration were obtained with a Sanborn recorder (Fig. 2).

In 15 dogs and 2 monkeys, the increased intracranial pressure was produced by a constant drip of Ringer's solution at variable rates into the lumbar subarachnoid space. The increased intracranial pressure in 5 dogs was produced by inflating the subdural balloon with 4 to 10 cc. of Ringer's solution.

The experiments were divided into three groups; arteriography was carried out in the last two.

Group I—controls and basic observations. The intracranial pressure was increased either by the lumbar-drip method or by subdural inflation in 5 dogs. Correlations between subdural, cisternal, and lumbar pressures were studied, as well as cardiovascular and respiratory responses occurring at different levels of increased pressure. In 3 other dogs, 3 to 5 cc. of the dog's own blood were added through the cisternal needle to ascertain the effect of subarachnoid blood on the animals with increased intracranial pressure.

Group II—internal carotid artery injections. The right internal carotid artery was cannulated with a PE-50 polyethylene catheter in 10 dogs and arteriography was performed by injecting 1 cc. of diatrizoate methylglucamine (Renograin 60) in 4 sec.; the intracranial pressure was increased by the lumbar-drip method.

Group III—common carotid artery injections. Four cc. of Renograin 60 were injected in 4 sec.
into the right common carotid artery after cannulation with a PE-100 catheter in 5 dogs and 2 monkeys. The intracranial pressure was elevated by both methods in these animals.

Four arteriograms were taken on each animal: 1. Control—at normal cisternal or balloon pressure. 2. Cisternal or balloon pressure equal to or exceeding the diastolic blood pressure. 3. Cisternal or balloon pressure equal to or exceeding the systolic blood pressure. 4. Final control—after cisternal or balloon pressure had been restored to normal.

The arteriograms were spaced at least 15 min. apart. A slow drip of Ringer's solution through the common or internal carotid catheters prevented clotting between injections of contrast medium.

RESULTS

Group 1. An increase in the drip-rate of Ringer's solution into the lumbar subarachnoid space made it possible to achieve cisternal pressures from 5 to 400 mm. Hg. It was also possible to maintain a desired pressure for any length of time and to observe the cardiovascular, respiratory, and neurologic responses occurring at any particular intracranial pressure.

When the subdural balloon was inflated with 6 to 10 cc. of Ringer's solution, the intracranial subdural pressure reached levels up to 300 mm. Hg, but simultaneous recordings of cisternal and lumbar subarachnoid pressures revealed an elevation of only 5 to 10 mm. Hg in pressure. After the subdural balloon had been inflated sufficiently to record an intracranial pressure of about 100 mm. Hg, dripping of Ringer's solution into the lumbar region increased the cisternal pressure to a level approximating that recorded from the subdural balloon. After this equalization of pressure, further increases of subarachnoid pressure by lumbar dripping produced increases that were equal in both the subdural and the cisternal recordings.

It was concluded: first, that readings of the cisternal and lumbar pressures did not represent the true levels when the increased pressure was produced by a rapidly expanding intracranial mass (subdural balloon); second, that the subdural balloon reflected the true value of increased pressure within the cranium only. When the intracranial pressure was increased by the lumbar-drip method alone, either the cisternal or the subdural recordings reflected the true value of the increased intracranial pressure and were equal.
All dogs had respiratory arrest at intracranial-pressure levels of 100 to 150 mm. Hg (1,360 to 2,040 mm. H$_2$O); see also Fig. 2. No difference was noted between the two methods of achieving this level of pressure. In most animals, this cessation of respiration occurred when the intracranial pressure approached or equaled that of the recorded diastolic blood pressure. So long as this critical level of intracranial pressure was maintained, spontaneous respiration was not observed; however, the animal started breathing if the intracranial pressure was lowered within 3 min. after the onset of apnea. Otherwise, resuscitation of the animal was not successful, even with the aid of a respirator for more than 1 hour.

Systemic hypertension and bradycardia were noted only after the intracranial pressure was elevated to 100 mm. Hg or more; these levels agree with those observed by Browder and Meyers\textsuperscript{1} and by Evans \textit{et al.}\textsuperscript{2} These animals, therefore, were able to withstand a great intracranial pressure before a change in systemic blood pressure or pulse rate occurred.

When the intracranial pressure was elevated and maintained at a level even below that of the diastolic blood pressure (60 to 100 mm. Hg), a continuous drip of fluid was observed coming from the nostrils of all the dogs, except for one boxer-type animal. This also occurred in the monkeys but at a much slower rate. A communication through the cribiform plate, as described by Strain \textit{et al.}\textsuperscript{11} was substantiated by adding methylene blue through the lumbar subarachnoid space and observing it drip from the nostrils in less than 1 min. At necropsy the cribiform plate was stained blue.

The 3 dogs in which blood was added to the subarachnoid space became more sensitive to an acute increase in intracranial pressure; systemic hypertension occurred at a cisternal pressure 10 to 20 mm. Hg lower than the original level in these animals. Also the absorption of Ringer's solution injected into the subarachnoid space was 50 per cent slower, which permitted a decreased drip-rate to maintain the desired intracranial pressure.

Once the animals were anesthetized initially, no additional Nembutal was required to maintain the desired level of anesthesia, regardless of the length of the procedure. Fixed, dilated pupils, and at times a divergent squint were observed in all animals when the intracranial pressure was elevated to just below the level of respiratory arrest. Pallor of the fundi, followed by blurring of the optic-disc margins and venous engorgement, was observed with rising intracranial pressure.

\textit{Group II.} In the 10 dogs in which arteriography was carried out through an internal carotid catheter tied securely in the artery to prevent reflux of dye and to allow flow only in a forward direction, a progressive increase in resistance to the manual injection of the contrast medium was noted as the intracranial pressure was elevated; a forceful injection then was required to fill the intracranial vessels. In 3 of these dogs, the complete circle of Willis, including the basilar artery, was demonstrated after forceful injection. This suggests total interruption of intracranial arterial flow, since this angiographic picture does not occur with a normal intracranial pressure.

\textit{Group III.} In common carotid arteriography, which we consider analogous to arteriography as performed in the human, it was found that the intracranial pressure must equal or exceed the measured systolic blood pressure to prevent filling of the intracranial vessels with contrast medium (Figs. 3 and 4). The intracranial pressure was increased by the inflated subdural balloon (2 dogs); by the subarachnoid fluid-drip method (2 monkeys); or by a combination of the two methods (3 dogs). The combination method consisted of elevating the pressure in the balloon and then equalizing the spinal subarachnoid pressure by dripping Ringer's solution through the lumbar needle. By any method, regardless of which animal was studied, the intracranial pressure must equal or exceed the systolic blood pressure before nonfilling occurs. Arteriograms made at an intracranial pressure below the recorded systolic blood pressure appeared no different from the control arteriograms. The diameter and position
of the intracranial vessels had not changed in the second when compared with the first control arteriogram.

**DISCUSSION**

In the present investigation, a direct relationship was established between increased intracranial pressure and nonfilling of the intracranial portion of the internal carotid artery during carotid arteriography. Elevating the intracranial pressure to the level of the diastolic blood pressure produced no change in the angiogram. Increasing the intracranial pressure to the level of the systolic blood pressure prevented filling of the intracranial vessels with contrast medium. If the intracranial pressure was lowered to below that of the systolic blood pressure, the cerebral vessels then filled well. Delayed roentgenograms by Pribram and Riishede and by Newton and Couch failed to show intracranial filling, with up to a 12-sec. delay after injection of the contrast medium.

A relationship of the nonfilling phenomenon to the existence of intracranial arterial spasm was not suggested in the present experiments. Vessels appearing normal, similar in diameter to those of the control arteriograms, were demonstrated as soon as the intracranial pressure was reduced. Cerebral vessels visualized during increased intracranial pressure and forceful injection into the internal carotid artery were not altered in diameter. Pribram and Riishede and
Ethelberg⁹ also felt that arterial spasm was not a valid explanation for the nonfilling phenomenon in their cases.

The question of whether the intracranial pressure did equal or exceed the level of the systolic blood pressure in these previously reported patients cannot be answered. One of the patients reported by Riishede and Ethelberg⁹ had a measured ventricular pressure of 1,240 mm. H₂O (91 mm. Hg). Evans et al.⁵ experimentally increased the intracranial pressure in patients up to 2,000 mm. saline; at levels of 800 to 1,000 mm., hypertension, tachycardia, and tachypnea, accompanied by restlessness, confusion, and anxiety, were observed in some of their patients. Stephen et al.¹⁰ reported pressures of subarachnoid fluid up to 1,900 mm. H₂O (140 mm. Hg) during the induction phase of anesthesia.

The lumbar-puncture pressures reported in patients with the nonfilling phenomenon and acute intracranial hypertension ranged from normal to 800 mm. H₂O.⁴,⁶,⁸,⁹ It is most unlikely that the lumbar-pressure readings in these patients reflected the true level of the increased intracranial pressure. At necropsy many of them were noted to have pronounced pressure cones, and it is doubtful that a free communication existed between the intracranial and the lumbar subarachnoid spaces.

When the intracranial pressure was elevated acutely by inflation of the subdural

---

**Fig. 4.** Common carotid arteriogram of dog. (A) Arteriogram with intracranial pressure normal. (B) Arteriogram with intracranial pressure equal to systolic blood pressure. (C) Arteriogram with intracranial pressure again normal.
balloon in the experimental animal, the cisternal and lumbar needles recorded normal or very slightly elevated (5 to 10 mm. Hg) subarachnoid fluid pressures. It is thought that this inequality in pressure was caused by lateral and downward displacement of the cerebral hemispheres and caudal displacement of the brain stem and cerebellar tonsils through the foramen magnum, obliterating the free communication between intracranial and spinal subarachnoid fluid spaces. This may explain why expansion of a subdural balloon to raise the intracranial pressure does not reflect accurately this increase throughout the spinal subarachnoid space. Obstruction of the aqueduct of Sylvius may result in the same inequality in pressure. The pathologic lesion reported in most clinical cases has been massive intracranial hemorrhage, invading brain substance or the ventricular system; in the remainder, an acute inflammatory process was found.

Whether herniation of the uncal through the incisura tentorii or of the cerebellar tonsils and brain stem through the foramen magnum is important in the nonfilling phenomenon cannot be determined definitely by the present experiments. The fact that some of these patients did not have pressure cones at necropsy and that respiratory arrest could be produced in the experimental animal without producing pressure cones lends support to the theory that neither uncal nor cerebellar pressure cones are absolutely necessary for the production of the nonfilling phenomenon or respiratory arrest.

As noted, the animals ceased spontaneous respiration at an intracranial-pressure level approximately equal to that of the diastolic blood pressure. Significantly, 5 of the 11 patients reported by Pribram,8 the 1 reported by Newton and Couch,9 3 of the 5 patients of Rüshede and Ethelberg,9 and 3 of our 5 patients were being maintained on artificial respiration at the time of angiography. Respiratory arrest in these patients possibly was caused by the greatly increased intracranial pressure, since angiograms shortly afterwards demonstrated the nonfilling phenomenon. One can suggest that the intracranial pressure had risen to the level necessary to cause cessation of spontaneous respiration and then continued to rise to the level necessary to prevent filling of the intracranial vessels at angiography.

In the present experiments, it was found that the classical blood pressure, pulse and respiratory responses occurred at an intracranial-pressure level below the recorded systolic blood pressure. This agrees with the findings of others, but differs from those recorded by Harvey Cushing10 who thought that the intracranial pressure must equal or exceed the systolic blood pressure before these cardiorespiratory changes occur.

It has been argued that clinically the intracranial pressure does not reach the level of the systolic blood pressure and, therefore, medullary anemia must not be the causative factor for Cushing's triad. Thompson and Malina11 investigated this phenomenon and concluded that these changes occur because of acute dynamic axial distortion of the brain stem and not because of increased intracranial pressure per se. It is easy to conceive that inflation of a subdural balloon will produce the proposed downward axial distortion of the brain stem, but it is difficult to accept that elevation of the intracranial pressure by dripping Ringer's solution into the lumbar subarachnoid space can produce downward axial distortion of the brain stem. It has been suggested also that the perforating branches of the vertebral-basilar arterial system possibly are kinked during the downward distortion of the brain stem, and the blood supply to the brain stem might be impaired as a result. But, because these classical cardiorespiratory responses occurred each time in the present experiments with an intracranial pressure equal to the diastolic blood pressure, it is felt more strongly that these responses are on a basis of hydrodynamic ischemia rather than on a mechanical origin. If the flow of blood during diastole is interrupted by direct compression with increased pressure of the subarachnoid fluid, ischemia of the tissues will result. The increased pressure also will impede the venous return and promote stagnation in
the tissues drained by the affected veins.

In previous experiments performed in this laboratory, air-foam embolization of the brain stem was investigated.\textsuperscript{13} The cardiorespiratory response and death were similar to those seen in the present study, namely systemic hypertension and apnea resulting in death of the animal. In those animals, there was no downward displacement of the brain stem, but the classical cardiorespiratory response attributed to increased intracranial pressure was elicited. This enforces the concept that these responses occur because of vascular embarrassment and ischemia, rather than mechanical shifting of the brain stem.

**SUMMARY**

1. Five patients with acutely increased intracranial pressure and nonfilling phenomenon during carotid angiography are reported.

2. The relationship between cerebral circulation and increased intracranial pressure was studied by angiography in the experimental animal. The method of study is presented.

3. In this investigation, the intracranial pressure had to equal or exceed the measured systolic blood pressure before nonfilling of the intracranial portion of the internal carotid artery occurred. This did not occur at lower levels of intracranial pressure.

4. The cardiovascular and respiratory responses to increased intracranial pressure also were studied. Apnea occurs in the experimental animal when the intracranial pressure equals the diastolic blood pressure. On the basis of findings in the present experiments, it is felt that the cardiorespiratory responses to increased intracranial pressure occur because of vascular embarrassment and ischemia of the brain stem.

5. The results of this experimental investigation are discussed and correlated with associated clinical findings in patients with greatly increased intracranial pressure.

**REFERENCES**


