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Xenon- and Iodine-Enhanced CT of Diffuse Cerebral Circulatory Arrest

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The role of contrast-enhanced computed tomography (CT) was evaluated in three nonhuman primates with a severe cerebrovascular insult and resulting elevated intracranial pressure and diffuse circulatory arrest. In all three animals the brain vasculature did not opacify after the bolus intravenous injection of iodinated contrast media. In addition, the brain substance did not enhance although the arterial blood enhanced normally after inhalation of a high concentration of xenon. Xenon-enhanced CT scanning, like ^{133}Xe radionuclide scanning, may be used to define the absence of generalized cerebral perfusion.

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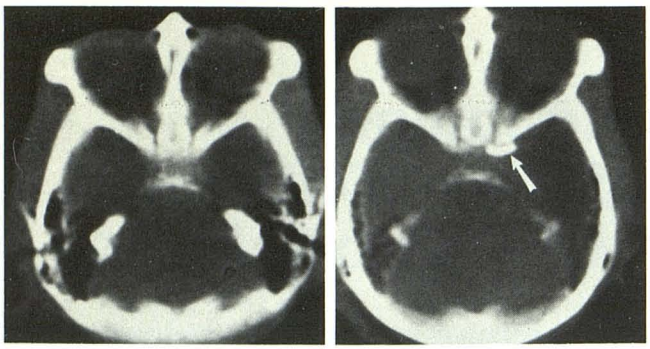
Various clinical, electrical, and radiographic criteria of cerebral circulatory arrest have been described [1]. Clinical criteria alone may not prove sufficient, particularly in the complex legal, social, and medical environment of North America.

Although carotid angiography [2–4] will often provide definitive evidence of an arrest of cerebral circulation, the procedure is complicated and time consuming. Radionuclide brain scanning [5, 6] is fairly simple to perform, accurate, and convenient when a portable scanner is available. However, since cranial computed tomography (CT) [7–9] is often performed to exclude a reversible intracranial process, a technique for using this diagnostic method to define the absence of cerebral perfusion would seem of value. We attempted to define criteria of diffuse circulatory arrest using enhanced (intravenous iodine and inhalation xenon) CT scanning.

Materials and Methods

A 205 PE silastic tantulum embolus [10] (fig. 1) was injected into the left internal carotid artery of three adolescent baboons (*Papio anubis/cynocephalus*) under Halothane (1%) anesthesia. Angiography was then performed to confirm the position of the embolus. In all three animals, the embolus lodged in the most superior part of the internal carotid artery occluding direct flow to both the middle and anterior cerebral arteries rather than the usual horizontal middle cerebral artery segment [10].

Clinical evaluation included neurologic examination (including brainstem reflexes), as well as cardiac, respiratory, and blood pressure monitoring. Arterial blood gases were sequentially measured using a femoral arterial catheter. Intracranial pressure was measured by inserting an 18-gauge Teflon catheter (Deseret Intracath, Sandy, Utah) into the subarachnoid space at the C1–C2 level which was connected to a Statham transducer (Statham Instruments, Oxnard, Cal.). Intracranial pressure and bitemporal electroencephalographic activity were continuously recorded. A Teflon catheter was inserted in the



A B

Fig. 1.—Proximal silastic tantulum embolus. **A**, Preembolus. **B**, Lodgement of embolus (*arrow*) in extremely proximal position occludes both middle and anterior cerebral arteries.

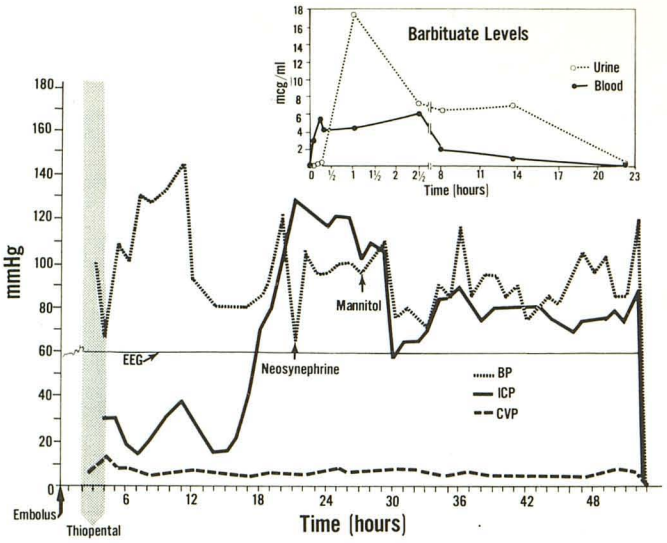


Fig. 2.—Baboon 533. Typical physiologic changes over time. All baboons exhibited prominent elevation of intracranial pressure secondary to massive cerebral infarction. Barbiturate levels returned to normal by 24 hr in all three animals.

femoral vein and advanced to the inferior vena cava to measure the central venous pressure.

The animals were treated with a large dose of thiopental (Abbott Labs., Chicago, Ill.) in an attempt to protect them from massive cerebral infarction. Treatment was initiated 2 hr after embolization with a 30 mg/kg bolus injection of thiopental followed by two separate 50–60 min infusions of 30 mg/kg (total 90 mg/kg) using a Harvard infusion pump. Barbiturate levels were monitored in both blood and urine throughout the experiments. CT scanning was performed using an EMI 5005 dual purpose scanner with 10 mm collimation and a 320 × 320 matrix. Exposure factors included a pulsed 40 sec scan time, 120 kVp, and 33 mA.

Iodine contrast enhancement was carried out using a rapid bolus infusion technique. A volume of 2 mg/kg body weight of diatrizoate meglumine (Hypaque-60, Winthrop Labs., N.Y.) was rapidly injected (5 sec) into the femoral vein using a pressure injector. After obtaining a preinfusion CT scan, serial CT scans were performed immediately after the contrast media infusion and at 45 and 90 sec.

After oxygen inhalation for about 30 min to denitrogenate, commercial, nonradioactive xenon (Airco Inc., Pittsburgh, Pa.) was inhaled by the intubated animals for 16 min. After preinhalation (baseline) CT, serial scans were obtained during the buildup (xenon inhalation) and clearance (abrupt discontinuation of xenon inhalation) phases of the study. Arterial blood samples were placed in a water bath within the scan field to monitor the xenon concentration in the blood.

In one baboon, cerebral angiography was performed 36 hr after embolization of the left common carotid artery. Radiographs were obtained in both the frontal and lateral projections. Angiography was done immediately after iodine and xenon-enhanced CT scans and the animal was sacrificed within 2 hr after these studies. Both gross and microscopic correlation were obtained. The detailed anatomy of the anterior and middle cerebral arteries was studied in the postmortem specimens using the operative microscope (OPMI, Zeiss, West Berlin). The segments of the artery were dissected from the arachnoid covering and photographed at different magnifications (×6–×25).

Results

Clinical and Physiologic Parameters

In figure 2 the changes over time in mean blood pressure, intracranial pressure, central venous pressure, and barbiturate level are defined for one baboon (no. 533). These alterations were similar in all three animals. The electroencephalogram became isoelectric in all baboons within 12 min after initial barbiturate infusion. Even after the blood and urine barbiturate levels returned to zero, the electroencephalogram remained isoelectric. The intracranial pressure was prominently elevated in all three animals. The clinical findings included a generalized absence of movement, an inability to sustain respiration without artificial ventilatory assistance, absent corneal reflexes, absent oculocephalic (doll's eye) response, and fixed, dilated pupils.

Cerebral Angiography

In the one animal with cerebral angiography there was no visualization of contrast media in the intracranial vasculature with selective injection of either the right or left common carotid artery, even on delayed sequential films. The iodinated contrast material slowly filled the extracranial internal carotid artery and external carotid artery branches as it does in man.

Cranial Computed Tomography

Subtle, linear increased density in the straight sinus–tentorium cerebellum region, perhaps representing venous stasis, was noted on the nonenhanced scans (figs. 3A–3E).

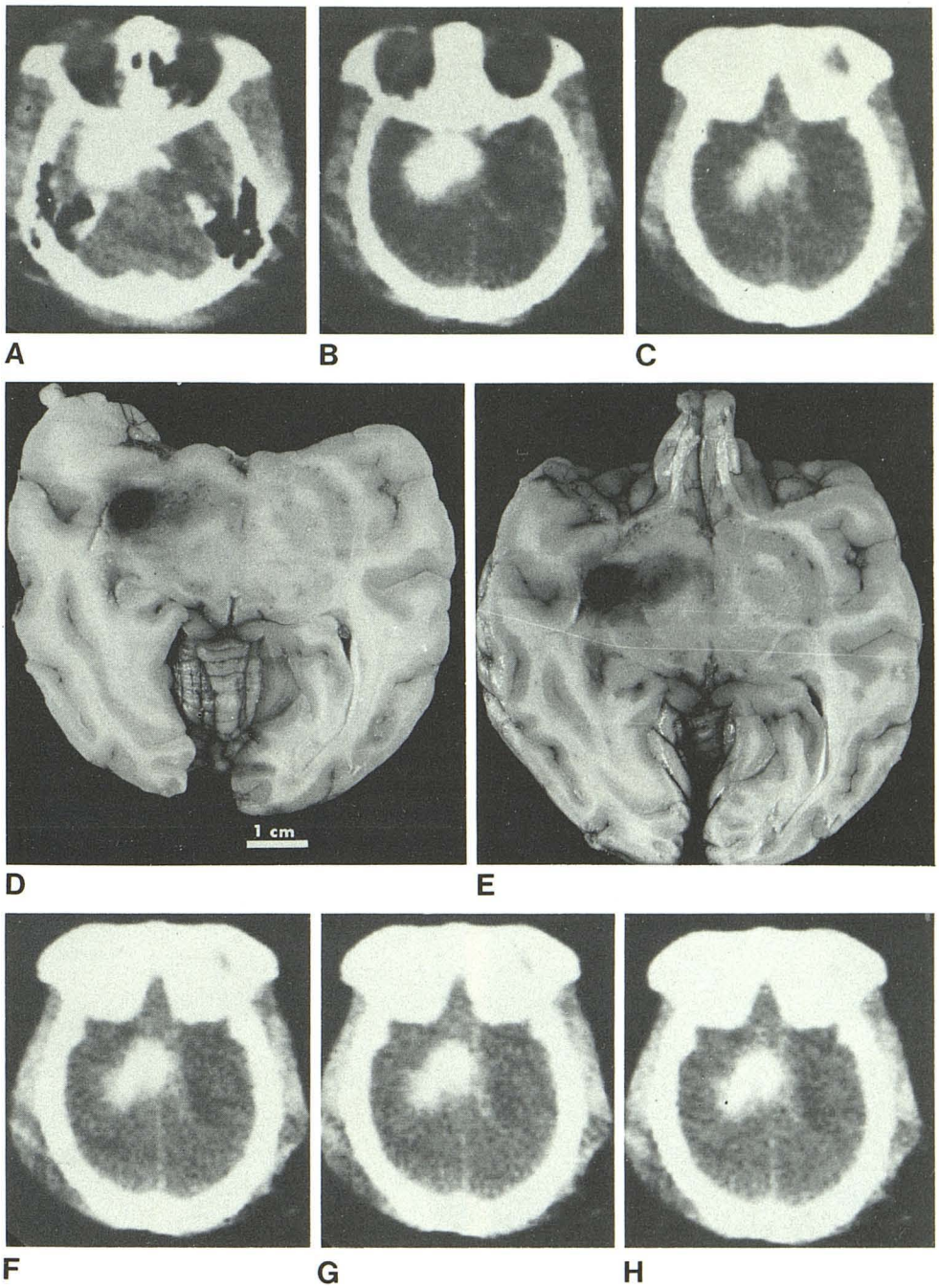


Fig. 3.—Baboon 534. Hemorrhagic infarction, 2 days after embolization. **A–C**, Nonenhanced scans at progressively higher brain levels define extensive nature of hemorrhagic infarction. **D** and **E**, Hemorrhagic infarction involves basal ganglia region in distribution of lenticulostriate arteries. Absent cerebral perfusion, rapid bolus intravenous enhancement: Baseline scan (**F**) compares with scans immediately (**G**) and 90 sec (**H**) after rapid bolus intravenous injection of iodinated contrast media. Lack of significant enhancement in brain substance or vasculature affirms cerebral circulatory arrest. Local palpation of injection site, scan at level of renal pelvis, or blood iodine level drawn from contralateral limb confirms successful intravenous injection.

The normal visualization of larger surface vessels and blushing of the gray matter capillary bed was not seen after rapid intravenous infusion of iodinated contrast media (figs. 3F–3I). After prolonged inhalation of a high concentration of the inert gas, xenon (freely diffusible indicator), normal enhancement occurred in the peripheral arterial blood while no enhancement was detected in the gray or white matter (fig. 4). An absence of enhancement with prolonged xenon inhalation indicated either a lack of blood flow or a dramatic, diffuse decrease in the blood/brain partition coefficient. However, the latter is not likely to occur uniformly throughout the brain tissue.

Pathology

Extensive hemorrhagic (figs. 3A–3E) and ischemic (fig. 4) infarction was found in the distribution of the lenticulostriate arteries. The extent of brain parenchymal involvement is summarized in table 1. Compression, collapse, and displacement of the adjacent lateral ventricle, cerebral edema, and transfalcial and transtentorial herniation were present.

Microscopic Vascular Anatomy

In all baboons, the silastic tantalum embolus occluded the internal carotid artery bifurcation and the anterior choroidal

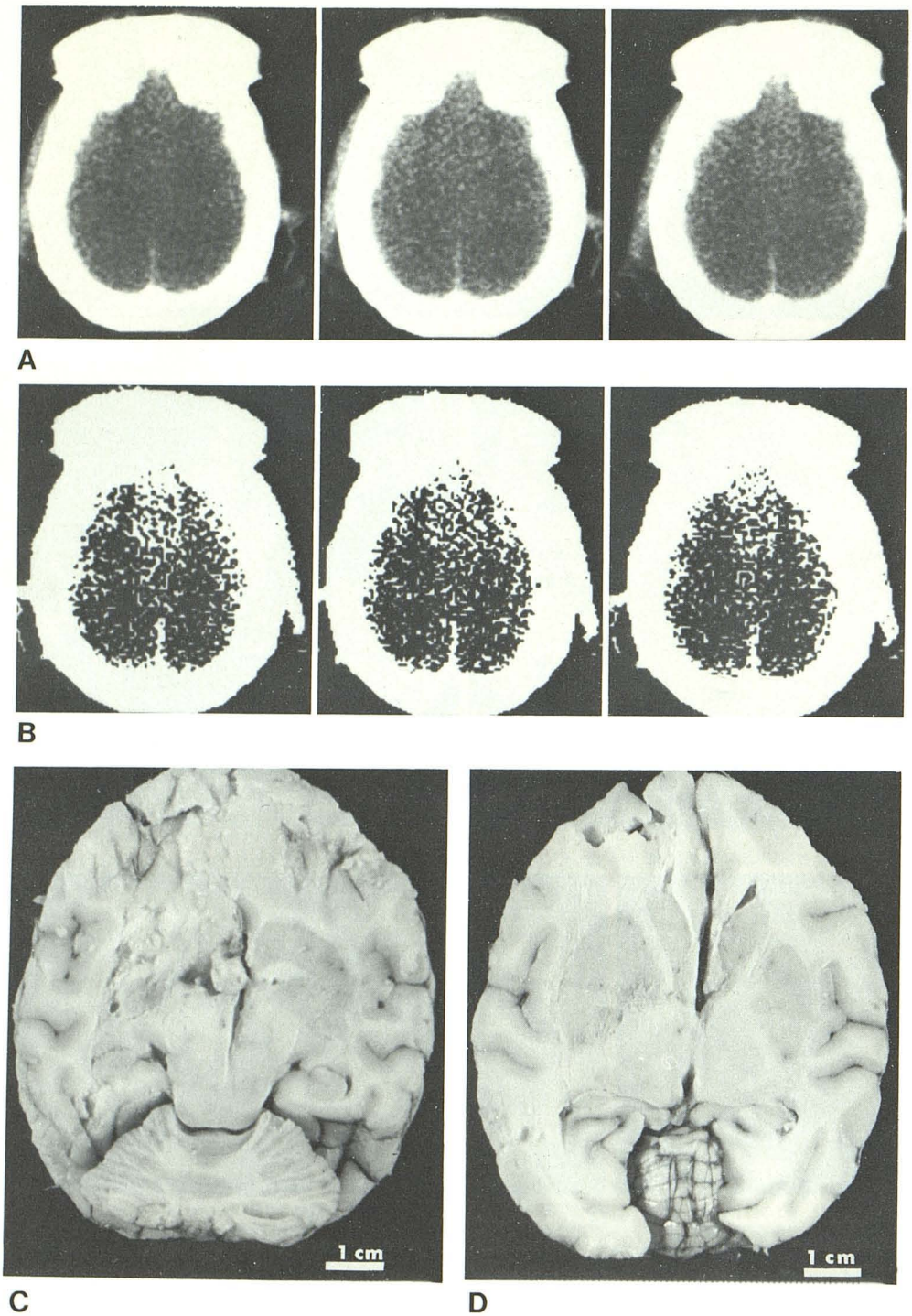


Fig. 4.—Baboon 533. Absent cerebral perfusion, xenon-enhanced CT: **A**, Baseline, 3 min, and 6 min scans at 36 hr after embolization (see table 1 and fig. 2). Concentration of 80% xenon inhaled for 6 min with arterial blood increasing 10 CT (EMI 5005) units. No concomitant increase in brain density either visually or numerically after 3 or even 6 min of continuous inhalation. **B**, Same as **A** using measure mode (window width 2) to better illustrate absence of brain enhancement denoting cerebral circulatory arrest. **C** and **D**, Gross pathology. Massive ischemic infarction involves left putamen, globus pallidum, and temporal lobe. Associated compression and collapse of adjacent lateral ventricle and transfalcial herniation of left frontal lobe and transtentorial herniation of left temporal lobe.

artery origin (fig. 5). In baboon 533, the origin of the posterior communicating artery was obstructed and the origin of the orbitofrontal artery was obstructed in baboons 531 and 533. In baboon 534, although the distal tip of the embolus was just proximal to the orifice of origin of the orbitofrontal artery, the artery itself was found to be occluded by an organized thrombus. In the same animal, the proximal tip of the plug was lodged in the proximal anterior cerebral artery occluding the origin of the thrombosed recurrent artery (homologous to the Heubner artery in man). In all three baboons, the embolus occluded the perforating vessels originating from the dorsal aspect of the middle cerebral artery proximal to the orbitofrontal artery trunk.

Discussion

A characterization of absent or severely impaired cerebral perfusion as seen with cerebral circulatory arrest is possible

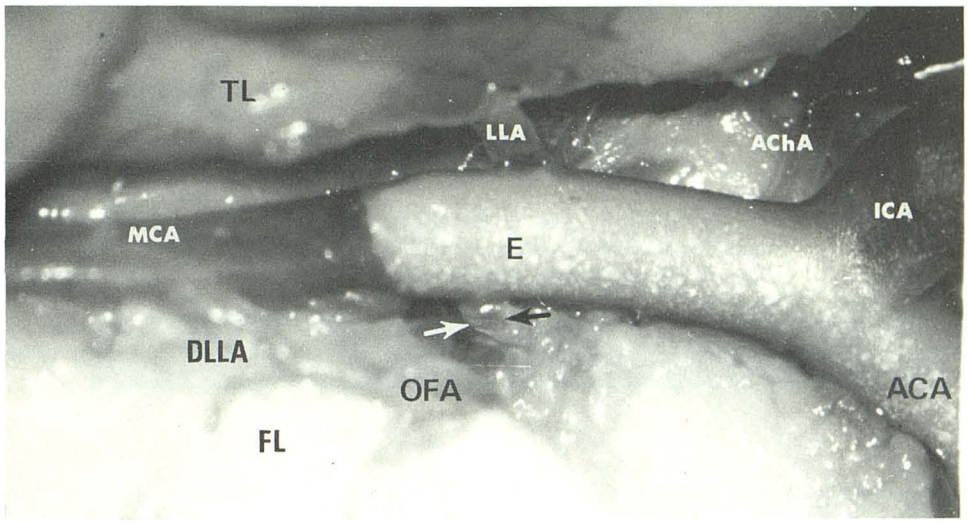


Fig. 5.—Baboon 531. Horizontal segment of left middle cerebral artery (OPMI microscope ×25). Silastic tantalum embolus (E) in both proximal anterior (ACA) and middle (MCA) cerebral arteries. OFA = orbitofrontal artery; LLA = lateral lenticulostriate arteries; DLLA = distal lenticulostriate arteries; AChA = anterior choroidal artery; ICA = internal carotid artery; FL = frontal lobe; TL = temporal lobe.

TABLE 1: **Pathologic Summary of Involvement by Cerebral Infarction**

Location	Baboon No., Infarct Type		
	534, Hemorrhagic	531, Ischemic	533, Ischemic
Caudate	−	−	+
Globus pallidum	+	−	+
Putamen	+	+	+
Thalamus	+	−	−
Internal capsule	+	+	−
Insula	−	+	+
Centrum semiovale	+	+	+
Frontal Lobe	−	+	−
Temporal Lobe	−	+	+

Note.—+ = infarction; − = no infarction.

using CT scanning. Enhancement with either infused iodine or inhaled xenon is essential to the diagnosis. Concomitant samples of arterial blood must be obtained to affirm the adequate entry of the indicator into the arterial blood in association with no entry into the brain parenchyma. The blood concentration of iodine or xenon may be measured by chemical methods or by placing a plastic, blood-filled syringe in the CT scan field.

Xenon, an inert gas with an atomic number and k-edge similar to that of iodine, freely diffuses across the blood-brain barrier and enhances the opacity of the brain [11]. By analyzing either the buildup (washin) or clearance (washout) of xenon using serial CT scans, both the brain/blood partition coefficient and cerebral blood flow may be derived [12–15]. While focal areas of markedly diminished blood flow and decreased partition coefficient are noted with cerebral infarction, the total absence of enhancement with xenon in all areas of the brain in our experimental subjects reflects instead the negligible flow condition of generalized cerebral circulatory arrest associated with markedly elevated intracranial pressure. The greater spatial resolution of CT eliminates the problem of extracerebral contamination that may limit radionuclide (e.g., ^{133}Xe) flow studies in this situation.

Iodinated contrast media do not normally cross the blood-brain barrier (nondiffusible indicators) and are thus seen in the brain vascular channels rather than within the brain substance. Therefore, the absence of contrast media within intracranial vessels on CT correlates with absent perfusion as defined by radionuclide [4–6] (e.g., ^{99}Tc) or angiographic [2, 3] techniques. As CT scanning is now widely used to exclude potentially treatable abnormalities in the individual with suspected "brain death," it seems worthwhile to perform an iodine-enhanced (bolus infusion) as well as a non-enhanced scan. If for various reasons the clinical and electroencephalographic criteria are not completely met, the absence of cerebral perfusion as defined by enhanced CT scanning provides an important additional piece of prognostic information. Many better designed CT scanning suites have been planned to accommodate respiratory apparatus and to be located near the intensive care unit.

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