Cerebral Arterial Spasm*
Part 2: Experimental Evaluation of Mechanical and Humoral Factors in Pathogenesis

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Constriction of arteries has been considered one of the physiological mechanisms for the control of hemorrhage since the time of John Hunter. The occurrence of this phenomenon, termed spasm, in association with ruptured intracranial aneurysms has, however, been recognized for only 18 years. During this time surgeons have come to agree that ischemia of the brain, secondary to arterial spasm, is one of the principal causes of the morbidity and mortality in patients with subarachnoid hemorrhage, and some have stated that spasm is the greatest single problem in aneurysm surgery today.

Arterial spasm, in addition to being an important clinical problem, remains one of the least understood of the physiological mechanisms for hemostasis. The arteries at the base of the brain are especially suited for study of the phenomenon, for it is only here that arteries are found bathed by clear fluid and covered by an avascular membrane which can be incised without exposing the outside of the artery to blood. These vessels also present a column of bright red blood outlined against the white tissue of the brain, a situation ideal for photography.

From the work of others we know that cerebral arteries constrict in response to mechanical and electrical stimulation, and the topical application of autogenous blood or a variety of chemical compounds including serotonin, angiotensin, and barium chloride. We have also observed these vessels to constrict when exposed to such nonspecific substances as room air and distilled water.

This discussion is confined to one specific question: What stimuli are responsible for initiating and maintaining constriction of a cerebral artery when the artery itself, or another cerebral vessel, ruptures into the subarachnoid space? By considering the possible changes that could occur in the environment of a vessel during and after subarachnoid hemorrhage, one can subdivide the problem into three parts.

First, a cerebral vessel is certainly subjected to mechanical stimulation when it ruptures (intrinsic distortion of its wall, displacement by hematoma, or traction by arachnoid bands). Is this sort of mechanical stimulation alone sufficient to initiate and maintain spasm?

Second, when blood is released into the subarachnoid space, a number of changes in the chemical environment of the vessel occur. Certain ions and inorganic materials, especially calcium, magnesium, and iron, are released into the cerebrospinal fluid in concentrations much higher than those normally found in cerebrospinal fluid. Could inorganic substances of this sort be responsible for initiation and maintenance of spasm?

Third, when blood enters the subarachnoid space, certain normal vasoactive constituents of blood which have been observed to cause constriction when applied topically to cerebral vessels, come into contact with the outside of the vessel wall. Can the degree of spasm seen with subarachnoid bleeding be explained by the presence of such substances in physiological concentrations?

**Materials and Methods**

Adult cats were anesthetized with intravenous barbiturate and maintained with oxygen and carbon dioxide. The cerebral arteries were isolated for direct observation and photographed. The effects of various agents were studied in vitro and in vivo.

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peritoneal pentobarbital. A tracheostomy was performed, and respirations were controlled by a Harvard respirator. The basilar artery was exposed transorally, as previously described,\footnote{1} and continuously irrigated with Ringer's solution at 37\(^\circ\)C to 39\(^\circ\)C. Body temperature of the experimental animal was maintained at 37\(^\circ\)C to 39\(^\circ\)C, and arterial pressure was continuously monitored via a catheter in the femoral artery. Techniques for manipulation of the vessel, and preparation of fractions to be assayed for spasmogenic activity, will be described. For assay of solutions for spasmogenic activity, the solutions warmed to 37\(^\circ\)C were substituted for control Ringer's solution in the gravity irrigation system. Vessel diameter was determined by measuring the column of blood within the lumen of the vessel on color photographs taken through the operative microscope. Results after manipulation or irrigation of the vessel with various solutions were expressed as per cent change in vessel diameter relative to the control diameter during the immediately preceding irrigation with Ringer's solution.

Results

Mechanical Stimulation of the Arterial Wall. The mechanical stimulation to which a vessel that ruptures would be subjected is difficult to produce experimentally without inducing bleeding from the vessel. In the vessels of the subarachnoid space, a significant mechanical stimulus would be that caused by the blood escaping under pressure from the lumen of the vessel, since this separates the vessel from the adjacent arachnoid, and thus puts traction on the vessel via the fibrous bands that connect the arachnoid to the vessel wall. A second stimulus, which does not occur during the process of spontaneous bleeding but might be important in cases where the vessel is manipulated, is blunt trauma to the vessel wall. A third stimulus, laceration of smooth muscle fibers and vascular nerves as the vessel ruptures, cannot be studied without inducing bleeding from the vessel, and thus introducing the additional variable of blood in contact with the outside wall of the vessel.

The first of the stimuli to which a vessel that ruptures would be subjected, traction on the vessel by fibrous bands, was adequately reproduced during arachnoid removal, for the traction placed on the vessel as the arachnoid was incised was usually sufficient to elevate the basilar artery from the surface of the medulla. The response to this stimulus was varied, with vessel constriction ranging from 0 to 61\%. The important observation, however, was that this spasm is transient and, in all animals studied, the vessel had relaxed within 15 minutes after the stimulus was applied. The results of these studies have already been discussed in detail.\footnote{1,1}

A second series of experiments was done to evaluate the effect of direct mechanical stimulation of the vessel wall. In 12 cats, the dura was opened to expose the vessel. Before opening the arachnoid, the basilar artery was stroked five times with a pledget of cotton held in forceps. Photographs were made 1 min after application of stimulus, and, in four cats, serial photographs were made at intervals until spasm was no longer present. Constriction produced by this maneuver ranged from 0 to 48\%, and averaged 25\% at 1 min.

In the animals in which spasm was observed by serial photography, spasm had completely relaxed within 5 min (Fig. 1).

The Role of Autogenous Blood. The rupture of an artery involves more than mechanical stimulation of the vessel wall, for the blood normally contained within the lumen of the vessel is now in contact with the outside of the vessel wall where it may stimulate receptors to which it normally does not have access. Also, the blood changes in composition when it escapes from the lumen of the vessel. Clotting occurs, and cells and platelets may lyse, releasing chemical substances into the surrounding medium normally bound within them.