An Experimental Approach to the Problem of Cerebral Aneurysm*

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The somewhat unsatisfactory results obtained by extravascular occlusion and exclusion of cerebral aneurysms, together with occasional evidence of satisfactory spontaneous intravascular thrombosis, have led us to consider the possibility of controlled intravascular thrombosis. Such controlled thrombosis should be carried out early if we aim to avoid the mortality of recurrent hemorrhage. The method should be a simple one, for the brain will not tolerate extensive surgery in this early period after hemorrhage. We therefore visualized access to the aneurysm by means of a cannula or needle introduced through a burr hole. Having experimented unsuccessfully with local injury to the arterial wall (beta necrosis) which was supplemented by intravascular injection of sticky platelets (with excess of thrombin),4 and hypercoagulable serum (serum obtained from freshly clotted blood)9 in an attempt to induce thrombosis in the canine femoral artery, we turned to an investigation of alterations that might be produced by an electric current.

It has long been known that red cells, white cells, and fibrinogen are negatively charged at the normal pH of blood, and about 40 years ago Abramson1 demonstrated migration of white cells to the positive pole in an electrophoretic cell. Bigelow and DeFoyes2 in 1952 have shown that washed platelets behaved similarly. Soon after this Sawyer et al.5,7 commenced an extensive investigation of the bioelectric phenomenon of intravascular thrombosis. They demonstrated that there is a potential difference between the adventitia and the intima of the normal aorta of the canine. This has a magnitude of 1-5 mV., the intima being negative. Injury can alter this potential and the intima may become positive. They further demonstrated that thrombosis could be induced by passing a small D.C. electric current, comparable to the current of injury so as to reverse the normal polarity. They succeeded in thrombosing the aorta, the carotid and the femoral arteries. They also produced thrombosis in vitro in heparinized blood and aggregation of cells in citrated blood and later they examined formation of thrombus in the mesentery of the rat under the microscope. The electrodes which they employed in many instances were rather large, having a surface area of about 45 sq. mm. Our first task, therefore, was to investigate the possibility of formation of thrombus by means of very small electrodes that could be applied to an aneurysm through a burr hole.

Another approach to the problem is based upon the clinical observation that the blood clot which seals the initial aneurysmal hemorrhage seems to have a very short life span. Hence, any method which could preserve it for a longer period might help tide the patient over the mortality of the early weeks after hemorrhage. Definitive surgical treatment could then be carried out with the lower mortality figure indicated a decade ago by Norlén and Olivecrona.5 Since blood clots (at least partially) disappear under the influence of a lytic enzyme, an antithrombolytin might have some therapeutic merit. Epsilon aminocaproic acid8 which competes with the activator of plasminogen offers some possibilities worthy of clinical trial. In addi-
tion, it might be expected to prolong the life span of any thrombi that might be induced electrically in an experimental animal.

**Material and Methods**

Owing to the unpredictable behavior of artificially induced aneurysms in the dog, we choose to use the intact femoral artery for most experiments. Insulated electrodes were placed in relation to these arteries by open exposure (more commonly) or by percutaneous puncture. Nembutal anesthesia was used in all instances.

The electrical apparatus consisted of a system of dry batteries in which the current was controlled by a tapped potentiometer and a series resistance of a value exceeding the average tissue resistance by at least several hundredfold. This resulted in an essentially constant source of current. The current was monitored by a shunted microammeter with an accuracy of ± per cent of full scale. Variations in resistance of tissue and delivered voltage were not monitored. It is estimated that the average potential difference of electrodes was in the range of 0.75 to 1.0 V. D.C. Experiments were designed for the investigation of the role of strength of current, duration of current, and the position and type of electrode in formation of thrombus.

At the end of the earlier experiments, the patency of the artery was determined by transecting the vessel distal to the experimental area. Blood flow, if any, from the stump was estimated and the extent of the thrombus was determined by histological examination of the excised segment of artery. In later experiments the progress of thrombosis was determined by serial angiography. The angiographic catheter was, in most instances, introduced into the right obturator artery and threaded up to the aortic bifurcation. Injection of contrast material* allowed visualization of both femoral arteries. Late follow-up angiography usually was accomplished by percutaneous aortic puncture, but on some occasions catheterization of the obturator artery was again employed.

The experiments were divided into 5 groups in order to study:

1. **Electrodes Applied Externally to the Femoral Artery.** Two types of electrodes were used, silver and platinum. After the first 2 experiments it was found that the electrical current caused deposition of silver around the positive electrode and so platinum was used thereafter. The electrodes consisted of wire, 1.0 mm. in diameter, insulated up to 3 mm. from the tip. These uninsulated portions were placed against either side of the artery. It was shown that:

   1. Current of 100 μA. induced a slight formation of thrombus on the arterial intima underlying the positive electrode after 30 min. This increased but did not become complete even when maintained for 10 hours. Silver was deposited on the adventitia in contact with the positive electrode, but not on that in contact with the negative electrode.

   2. If the polarity of the current was reversed every 80 min., thrombus did not accumulate, though silver was deposited on the adventitia underlying each electrode (100 μA. for 10 min.).

   3. If electrodes were placed on either side of the main artery just below a branch (pudendal or profunda femoris), the main vessel remained patent. If the positive electrode was in the axilla between the main vessel and the branch, then a thrombus developed in the small vessel (100 μA., 40 min.) but it would remain free from thrombus when the negative electrode was in the axilla (100 μA., 260 min.), as shown in Fig. 1.

   4. The extent of thrombosis in the femoral arteries could not be increased by intermittent digital compression of the proximal artery. In this experiment digital pressure was used 20 sec. on and 20 sec. off for a total of 5 hours, the current being 200 μA.

2. Increasing the current to 1,000 μA. resulted in subtotal occlusion of the femoral artery in 210 min.

3. Complete thrombosis could not be produced by (a) tripling the surface area of the positive electrode, (b) removing the negative electrode up to 2 cm. from the wall of the artery, and (c) increasing the duration of the current up to 240 min.

* Hypaque supplied through the courtesy of Winthrop Laboratories.