Experimental Studies on Electrically Induced Arterial Thrombosis in Dogs, with Special Reference to the Treatment of Intracranial Aneurysms and Arteriovenous Malformations

by

KOREAKI MORI

From the Department of Neurosurgery, Kyoto University Medical School
(Director: Prof. Dr. HAJIME HANDA)

Received for Publication Sept. 10, 1966

INTRODUCTION

The successful surgical treatment of an intracranial aneurysm consists in the occlusion of the lumen by clipping or ligation of its neck or the strengthening of the wall by wrapping it with muscle, gelatine sponge, etc., and coating with various plastic adhesives.

Difficulty in clipping is often encountered in the treatment of intracranial aneurysms which are firmly adherent to the surrounding tissues. In such cases, clipping of the neck is not possible, nor is over all reinforcement of the aneurysm with EDH-Adhesive (Biobond®)[2)14)25)45)], because of the danger involved in exposing the lesion.

Another method that has been tried for the treatment of such aneurysms is obliteraion of the lumen by introducing agents both foreign and natural that stimulate thrombus formation, such as,

1) Hanging of double silk threads in the aneurysm cavity - DANDY[4)].

2) Artificial embolization (catheterization included) - BROOKS (1931)[3)], SPEAKMAN (1964)[44)], LUESSENHOP (1960)[19)20)], SANO (1965)[27)].

3) Pilojection - GALLAGHER (1963)[9)10)11)], FUKAI et al. (1964)[8)].

4) Metal needle implantation - MULLAN et al. (1964)[21)22)].

5) Stereotaxic copper electric thrombosis - MULLAN et al. (1965)[23)24)].

6) Stereotaxic magnetically controlled metallic thrombosis - ALKSNE et al.[1)].

7) Intraluminal plastics - GENEST (1965)[12)].

8) Injection of hypercoagulable serum, thrombin, and other chemical substances (under investigation).

Each one of above described methods has problems and limitations in its clinical application, which have led us to seek other ways of attacking the problem.

We often notice at the time of operation that aneurysms are actually larger than cerebral angiograms indicate. This is due to spontaneous thrombus formation in the lumen, which is considered to be fortunate and protects them against rupture rheologically, since the deposition of blood clots decreases the lateral pressure on the wall (Fig. 1).

During the past five years we have studied artificially induced thrombosis, especially that induced by electric current. Our studies were based on the widely accepted assump-

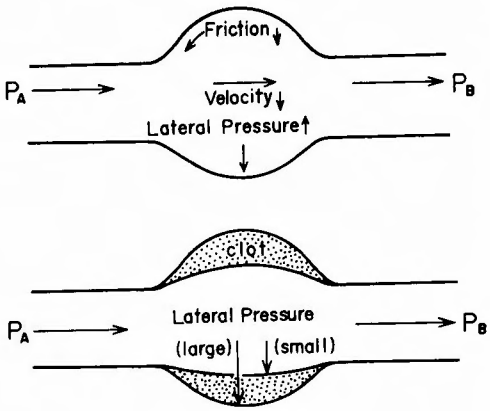

Fig. 1 Diagram of Aneurysm.

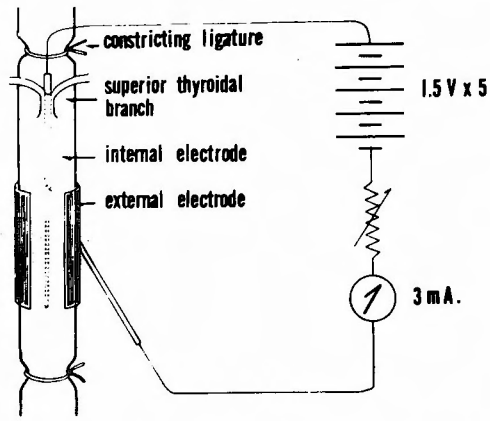

Fig. 2 Electric induction of thrombus in dog carotid artery by applicatipn of bipolar electrodes.

tion that the inner surface of the intact vessel wall has a constant negative charge in respect to the adventitia, and that most blood constituents also have a negative surface charge, so that the blood cell elements are constantly repelled from the inner wall; thrombi are thus prevented from forming on the intact vessel wall[28)29)]. Furthermore, in vessels with injured walls, it has been demonstrated that thrombi frequently develop when the normal polarity of the vessel is altered by intimal damage[29)33)]. It has also been demonstrated that the imposition of a charge on the vessel wall to reverse the normal polarity causes the creation of a thrombus near the positive electrode[28)41)46)]. A standard thrombus can be induced by the application of bipolar electrodes, a positive internal needle type and a negative external plate electrode, and the imposition of a controlled current, 3 ma for 1 hour (Fig. 2)[48)]. On the basis of these experimental studies, a new method was designed to obliterate the lumen of an intracranial aneurysm by electrically induced thrombosis in combination with reinforcement by EDH-Adhesive[15)]. Obliteration by thrombosis is desirable, since plugging up of the lumen is accomplished by physiological blood cell elements, and not by foreign bodies, with their attendant propensity to cause reaction.

For clinical application, we must solve several technical problems:

1) How to apply the electrode in such a narrow operative field.

2) Limitation of the time for inducing a thrombus to less than 20 min. even under hypothermic anesthesia, since the aneurysm must be clipped distally and proximally temporarily in order to interrupt blood flow.

3) Methods of control or confirmation of an induced thrombus in the lumen as to its quality and quantity during or immediately after the passage of the current.

EXPERIMENTAL PRODUCTION OF A THROMBUS FOR A LIMITED TIME BY CONTROLLED ELECTRIC CURRENT

Instead of the production of a thrombus by the application of bipolar electrodes, a unipolar anodal electrode, of the fine platinum needle type (0.2 mm in diameter), was inserted into the vessel lumen without causing rupture either by manual manipulation or by the so-called "Acupuncture" technique (Figs. 3 and 4).

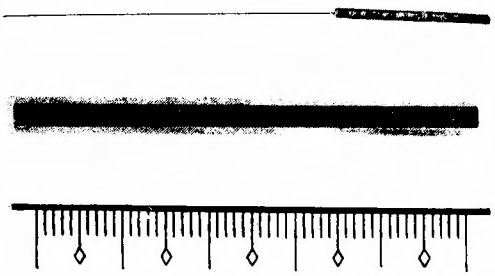

Fig. 3 Acupuncture needle and guide.

It is rather difficult to produce experimental aneurysms in animals which simulate intracranial aneurysms in human beings, and thrombus formation frequently occurs in the process. Normal dog common carotid arteries were used, since thrombosis rarely occurs in them.

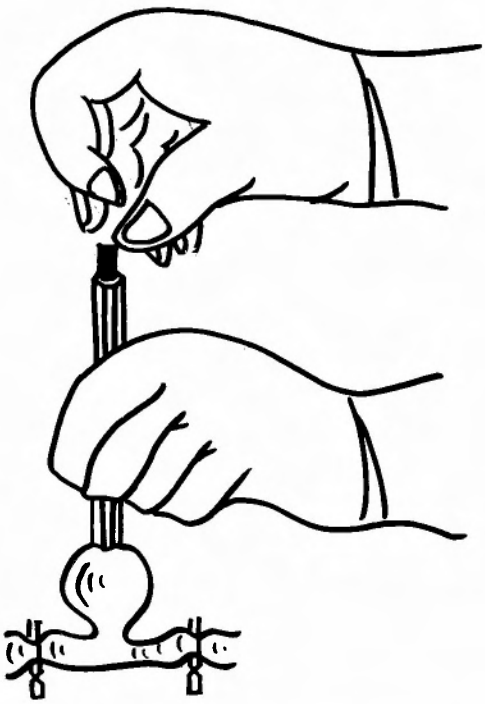

Fig. 4 "Acupuncture" technique.

METHODS AND MATERIALS

Method I (15 dogs) : Relationship between the kinds of electric current and thrombus formation.

Adult mongrel dogs, weighting 7 to 13 kg, were used. Under intravenous anesthesia with 5% nembutal (0.6 cc/kg), a skin incision about 5 cm long was made in the midline of the neck anteriorly. The common carotid arteries, measuring approximately 2.5 to 4.5 mm in diameter, were exposed and carefully dissected free from the surrounding tissues.

The lumen of a 2 cm long segment of the common carotid artery was completely occluded by two silk sutures, and a fine platinum needle electrode was inserted for 1 cm into the lumen at the midportion of the segment either by manual manipulation or by "Acupuncture" technique. The segments, one experimental and the other control, were carefully insulated from the surrounding tissues by rubber sheets to prevent electric leakage. A stainless-steel hypodermic needle was then inserted for about 1 cm into the tissues near the platinum needle and was used as a counter-electrode. 3 mA and 5 mA D. C., positive and negative, and A. C. were imposed for 15 to 20 minutes. Immediately after the cessation of the electric current, the electrodes and the two silk sutures were removed. Two or three days later, the segments were exposed and excised to determine, both macroscopically and microscopically, whether or not a thrombus had formed.

Method II (60 dogs) : Influence of the blood flow and postoperative CAG on thrombus formation.

Procedure similar to Method I were carried out both with and without ligations and/or immediate CAG. CAG was performed by injection of 1 cc of 60% Urografin from the proximal portion of the common carotid artery exposed by sharp and blunt dissections. The segments were examined again by CAG on the second or third day.

Method III (25 dogs) : Relationship between strength of positive electric current and rate of thrombus formation.

Varying amounts of anodal imposition upon the segment were tried, and the segments were excised 2 or 3 days later for histological studies.

Method IV (10 dogs) : Follow-up studies of electrically induced thrombosis.

The 2 cm long segments subjected to a positive electric current of 5 mA for 20 min. were examined by manual palpation for 3 days and again after 5 weeks. All segments were excised after 5 weeks and examined histologically.

Method V (3 dogs) : Measurement of the local temperature of the electrode inserted into the segment during the passage of a direct current.

Local temperature around the platinum electrode, and of the vessel wall at a distance from the electrode during the passage of an electric current was measured, by thermocouple (Copper-Constantan), with a precise potentiometer connected to a recorder.

RESULTS

Method I : As shown in Table 1, 2 out of 3 vessels were occluded by thrombus formation when treated with D. C. +3 mA for 20 min.; all 3 vessels were occluded with D. C. +5 mA for 20 min.; and 1 out of 3 vessels was occluded with D. C. −5 mA for 20 min. D. C. −3 mA for 20 min. and A. C. 5 mA for 20 min. caused no thrombosis.

Table 1 Results of angiographic observation on the rate of thrombus formation in various conditions.

Applied currents for 20 min.		Ligatures	Immediate CAG	No. of vessels	Results of late CAG: Occluded	Results of late CAG: Patent
D. C. (+)	3 mA	⊕	⊕	3	0	3
			⊖	3	2	1
		⊖	⊕	3	0	3
			⊖	3	1	2
	5 mA	⊕	⊕	3	2	1
			⊖	3	3	0
		⊖	⊕	3	0	3
			⊖	3	1	2
D. C. (−)	3 mA	⊕	⊕	3	0	6
			⊖	3		
		⊖	⊕	3	0	6
			⊖	3		
	5 mA	⊕	⊕	3	0	3
			⊖	3	1	2
		⊖	⊕	3	0	6
			⊖	3		
A. C.	5 mA	⊕	⊕	3	0	12
			⊖	3		
		⊖	⊕	3		
			⊖	3		

Table 2 Relationship between the amount of electric current and the rate of thrombus formation.

	No. of Vessels	Totally occluding thrombosis	Partially occluding thrombosis	No Thrombosis
D. C. + 5 mA 20 min.	10	8	2	0
5 mA 15 min.	5	3	2	0
3 mA 15 min.	5	1	3	1
3 mA 10 min.	5	0	2	3

Method II : The results are summarized in Table 1. Even when treated with D. C. +3 or +5 mA for 20 min., the incidence of occlusion of the lumen was lower when there were no ligatures, and much lower with immediate CAG.

Method III : The strength of positive electric current was almost proportional to the rate of thrombus formation (Table 2). A positive electric current of 5 mA for 15 to 20 min. was found to be enough for the production of a thrombus in all cases (Fig. 5).

Method IV : All of 10 vessels were occluded up to the fifth week after the procedure (Fig. 6).

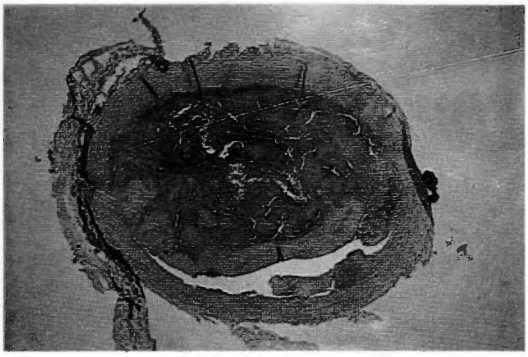

Fig. 5 Three day old specimen. Dog common carotid artery containing thrombus. (H. E. ×20)

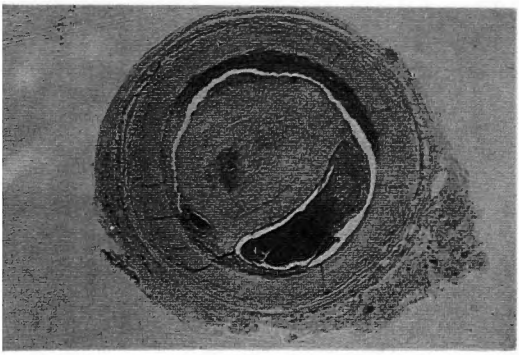

Fig. 6 Five week old specimen. (H. E. ×10)

Fig. 9 Electrolized specimen of arteriovenous malformation. (H. E. ×10)

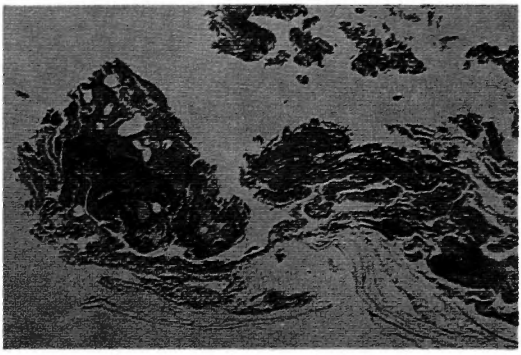

Fig. 17 Electrolized specimen of varix of the superior ophthalmic vein. (H. E. ×10)

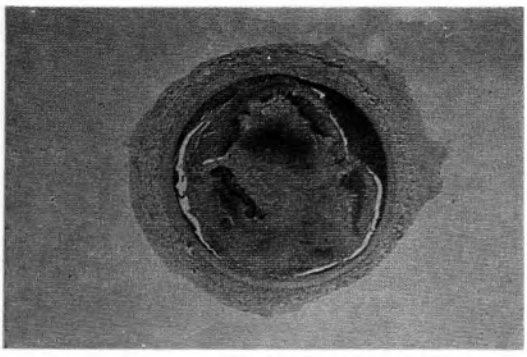

Fig. 36 One week old specimen of dog common carotid artery containing a thrombus (H. E. ×10)

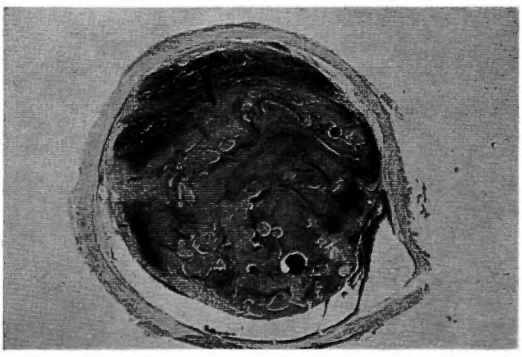

Fig. 38 Dog femoral vein containing thrombus three days after the procedure. (H. E. ×20)

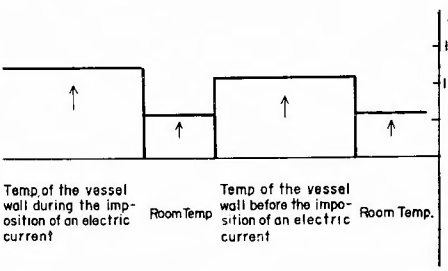

Fig. 7 Potentiogram evolved by thermocouple (C-C).

Method V: No significant difference was noted between the temperature at the electrode inserted into the segment during the passage of D. C., and that of the vessel wall far from the electrode (Fig. 7).

There were fewer bubbles of gas formed with A. C. than with D. C.

DISCUSSION

In Method I, thrombosis was induced only with anodal insertion, except with cathodal insertion and a current of 5 mA for 20 min. (1/3 dogs). These results are in keeping with those of earlier studies[5)28)31)32)]. SCHWARTZ[41~43)], and RICHARDSON[26)] reported the prevention of thrombosis with the use of a negative electric current. SAWYER et al.[34)35)38)39)47)], on the other hand, demonstrated the use of electrical hemostasis for uncontrollable bleeding during major surgery or in severe hemophilia.

Fundametally, thrombus formation is based on one or more of the following disturbances: 1) slowing of the blood stream, 2) damage to the vessel wall, 3) hypercoagulability of the blood. In Method II, the great influence of the blood flow on thrombus formation was observed. It is also evident from the data that immediate CAG is unfavourable for thrombus formation, presumably because of its flushing effect on the induced coagulum around the electrode.

In Method III, a positive electric current of 5 mA for 15 to 20 min. was found to be enough to produce a thrombus in all cases. It is reasonable to presume that this amount of current is satisfactory for occluding the lumen of an intracranial aneurysm. In the obliterating method of treatment of intracranial aneurysms and/or arteriovenous malformations, two main problems must be solved: spontaneous dissolution of an induced thrombus, and its embolic nature. In Method IV, electrically induced thrombi were examined for more than a month, and no tendency towards spontaneous dissolution or absorbability was observed. Further, no neurological dificits were observed during these follow-up periods. No extension of thrombosis from the aneurysm into the parent vessel occurs, since the rapid flow of blood across the mouth of the aneurysm prevents the clotting process from going beyond that point.

In Method V, the etiology of the bubbles of gas appearing around the electrode during D. C. was investigated. Measurements of local temperature indicated that these bubbles are evolved by electrolysis, not by coagulation of protein due to Joule's heat.

CLINICAL TRIALS

Case 1. A 20-year-old male had an episode of loss of consciousness for a few minutes five months prior to admission. In the morning of the day of admission, he had another episode of headache and vomiting followed by loss of consciousness immediately after exercise. A lumbar puncture revealed bloody fluid under an initial pressure equivalent to 185 mm of water. Right carotid angiography showed an arteriovenous malforma-

tion in the right occipital region (Fig. 8). A segmental and fractional positive direct current of 5 mA was applied to the tangled vessels, along with clips. Total extirpation of the angioma was then accomplished with ease and minimal bleeding (Fig. 9). The postoperative course was uneventful (Fig. 10), and the patient has been doing well for a year and eight months.

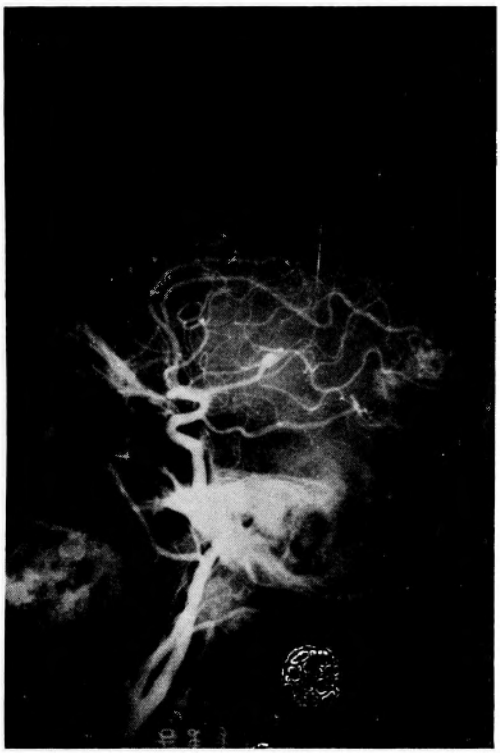

Fig. 8 Preoperative CAG.

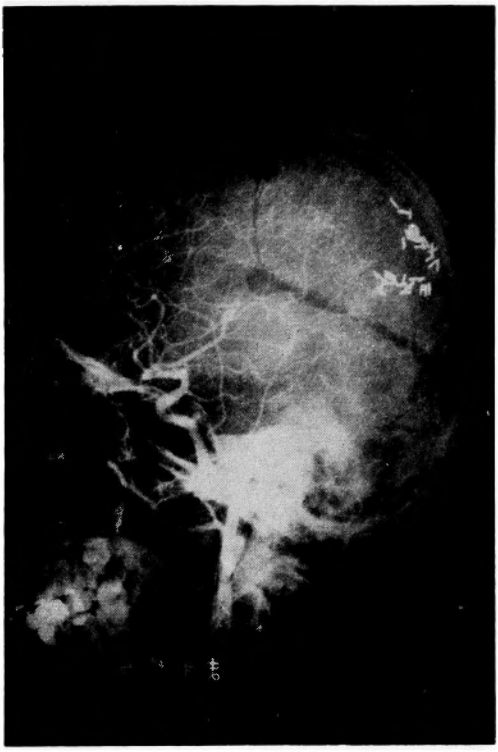

Fig. 10 Postoperative CAG.

Case 2. 26-year-old female was found by bilateral carotid angiography to have an aneurysm arising from the anterior communicating artery (Figs. 11 and 12). At the time of operation, the aneurysm was firmly adherent to the adjacent brain, and the neck of the aneurysm was rather broad. Since clips could not easily be applied, and even our method of coating with "EDH-Adhesive" was imperfect, obliteration of the lumen with electrically induced thrombosis was tried. A temporary clip was placed on the right anterior cerebral artery, and a platinum needle was inserted manually through which a positive direct current of 3 mA was applied for one minute. This procedure was repeated nine times at at different angles to the aneurysmal sac, so that a blackish-brown discoloration of the aneurysm was obtained. Each time just before removal of the needle, "EDH-Adhesive" was applied to control the bleeding and also to coat the aneurysmal sac completely. The patient tolerated these procedures and is perfectly well postoperatively. Postoperative angiograms showed partial obliteration of the aneurysmal lumen to about two-fifths of its preoperative size (Figs. 13 and 14). She has since been asymptomatic for a year and four mohths.

Case 3. A 60-year-old male was admitted to our clinic with complaints of inter-

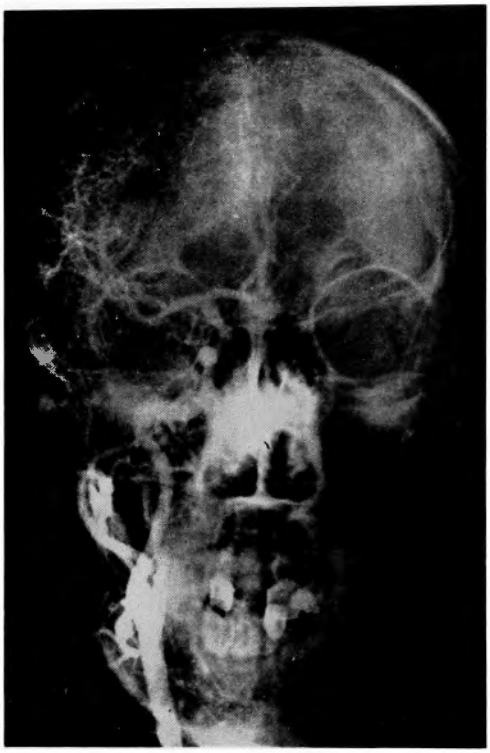

Fig. 11 Preoperative CAG.

Fig. 12

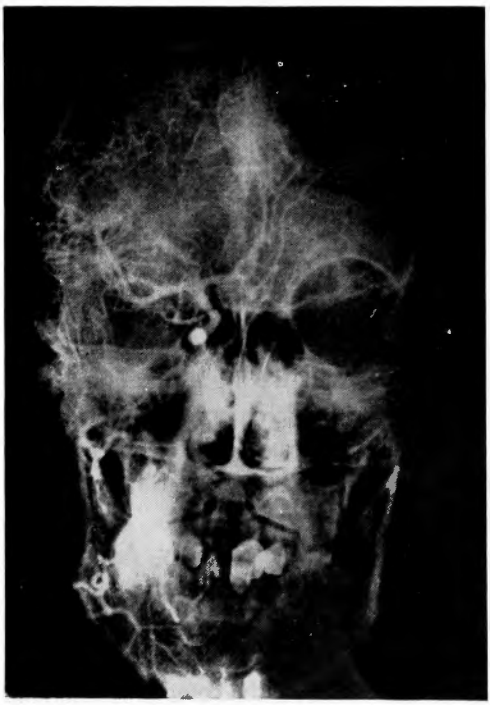

Fig. 13 Postoperative CAG.

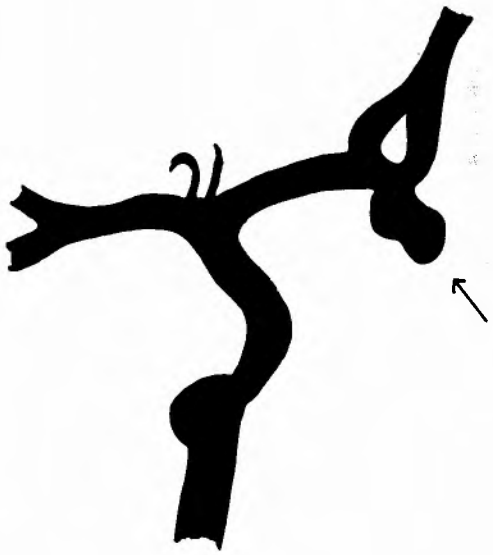

Fig. 14

mittent right exophthalmos and diplopia of four years duration. A right angular phlebogram showed a large varix of the right superior ophthalmic vein (Fig. 15). After removal of the right orbital roof, a varix, approximately 2.0×1.5 cm, came into view (Fig. 16). Because of indistinctness of the main trunk of the varix, treatment by positive direct current was decided upon. A platinum needle was inserted manually into the varix and a positive direct current of 5 mA was applied for 15 to 20 minutes four times from different angles. Shrinkage of the varix was observed, and total extirpation was accomplished without much difficulty or gross bleeding (Fig. 17). He was discharged very much improved and has been perfectly well for eleven months.

Comments: Complete obliteration of the lumen of an intracranial aneurysm is not always necessary from the rheological standpoint. In order to stop the increasing strain leading to its rupture, even partial obliteration of the lumen by the deposition of blood clots is enough to decrease the lateral pressure on the vessel wall.

An anodal current works better in shrinking arteriovenous malformations before complete extirpation and in controlling bleeding by electrical hemostasis than in causing complete obliteration of the lumen.

Dr. MULLAN's Copper Electric Thrombosis of human intracranial aneurysms[24] is very similar to our new method, and was performed coincidentally paralleling our studies. However, his method is technically distinct from ours. In his method, the anode is inserted into the aneurysms stereotaxically through a burr hole, and a current of up to 2 mA is applied for 24 to 48 hours.

It should be stressed that our new method is intended for the treatment of selected craniotomized cases not treatable directly by any known procedures after the nature of the aneurysm and its relation to the surrounding tissues have been determined, in the hope of decreasing the lateral pressure on the aneurysmal wall and thereby preventing the increasing strain leading to its rupture.

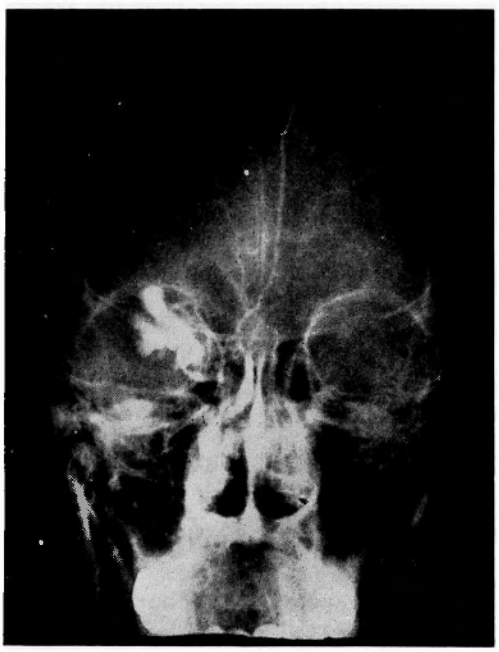

Fig. 15 Preoperative angular phlebogram.

Fig. 16

RELATIONSHIP BETWEEN POTENTIAL DIFFERENCE CHANGES AND ELECTRICALLY INDUCED THROMBOSIS

Although a thrombus can be produced by controlled current electrolysis with 5 mA for 15 to 20 min., we cannot determine whether or not a thrombus will be produced, or estimate its quality and gross quantity, if induced, during the passage of the current or immediately after the cessation of the current. In an attempt to find this information, a correlation between the currents and changes in potential difference (P. D.) was sought.

METHODS AND MATERIALS

Method I (10 dogs) : Measurement of the potential difference across the wall of the normal dog carotid artery.

A 1 cm long platinum needle type electrode, 0 3 mm in diameter, connected to an insulated wire by enamel was inserted into the lumen of the common carotid artery via the superior thyroid artery, and the inserted portion of the superior thyroid artery was tightly ligated together with the insulated wire. A 10 × 5 mm platinum plate type electrode, 0.15 mm in thickness, connected to the vinyl-coated wire was placed on the wall of the common carotid artery corresponding to the internal electrode, which was carefully insulated from the surrounding tissues with rubber sheets. Using a precise potentiometer connected to a high impedance recorder in series with a pair of measuring electrodes, measurement of the potential difference was carried out without any current. Care was taken not to form a short circuit (Fig. 18). The P. D. across the vessel with no interfering blood flow was measured first, and then the portion proximal to the electrodes was ligated followed by ligation approximately 2 cm distal to the electrodes to observe the changes in P. D. caused by stasis of the blood flow were thus determined.

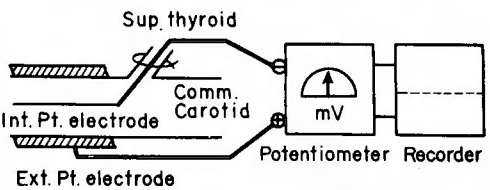

Fig. 18 Measurement of the P. D. across the wall of dog common carotid artery.

Method II : Changes of the P. D. in various situations.

1) A crushing injury was inflicted with Kocher clamp applied for one minute close to the electrodes (3 dogs).

2) Intravenous injection of 5 ml of heparin sodium (5000 U) at a rate of 0.5 ml per second, and intraarterial injection of 1 ml of heparin sodium proximal to the electrodes at a rate of 0.1 ml per second were given (3 dogs).

3) Protamine sulfate, 5 ml (50 mg) intravenously, and 1 ml intraarterially was injected in a similar fashion (3 dogs).

4) An injection of 20 cc of 1/10N HCL solution was given intravenously at a rate of 1 ml per second (2 dogs).

5) An injection of 20 cc of 1/10N NaOH solution was also given intravenously at a rate of 1 ml per second (2 dogs).

6) Twenty cc of normal saline solution was injected proximal to the electrodes at a rate of approximately 0 26 ml per second (2 dogs).

Method III : Changes in P. D. caused by electric current.

1) D. C. and A. C. currents of 3 mA were applied for 15 seconds, through both internal and external electrodes, and the P. D. changes were measured immediately after the current was turned off (6 dogs).

2) D. C. and A. C. of 5 mA were applied for about 15 seconds, through a fine unipolar platinum needle type electrode, 0.2 mm in diameter, inserted into the vessel lumen almost parallel to the internal electrode. Care was taken to avoid contact between the electrodes in the lumen. The counter-electrode, a stainless-steel hypodermic injection needle, was inserted 1 cm into the surrounding tissues. Immediately after the application of the currents, the changes in P. D. were measured (6 dogs).

3) Five mA of a positive electric current was applied for about 15 min. upon a 2 cm long segment between two silk ligatures, During the passage of the current, the P. D. between the needle electrode and the counter-electrodes was measured at intervals of 2 min. (3 dogs).

RESULTS

Method I: The measured P. D. across the intact wall of the dog common carotid artery varied between −10 mV and +480 mV (average 174.4 mV). The P. D. at the ligature proximal to the electrodes tended increase slightly (up to 40 mV), but at the distal ligature there was almost no changes in the P. D.

Method II:

1) Potentiograms of injured vessel walls showed a tendency for the P. D. to decrease slightly (up to 80 mV), but not enough for the P. D. to be reversed.

2) and 3) No definite changes were observed in the potentiograms after the administration of heparin sodium or protamine sulfate.

4) The intravenous injection of 20 cc of 1/10N HCL solution decreased the P. D. by approximately 20 mV (Fig. 19).

5) In contrast, the i. v. injection of 1/10N NaOH solution slightly increased the P. D. by approximately 20 mV (Fig. 19).

6) Potentiograms following the rapid injection of 20 cc normal saline solution into

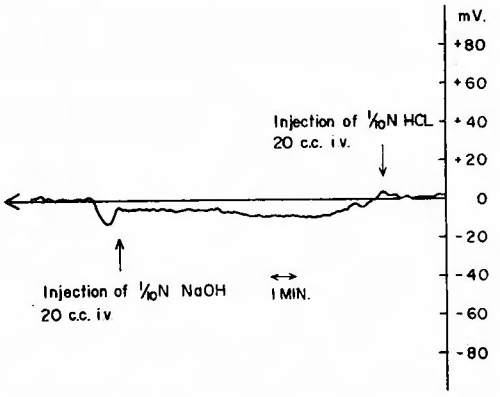

Fig. 19 P. D. changes following injection of strongly alkaline and acid materials.

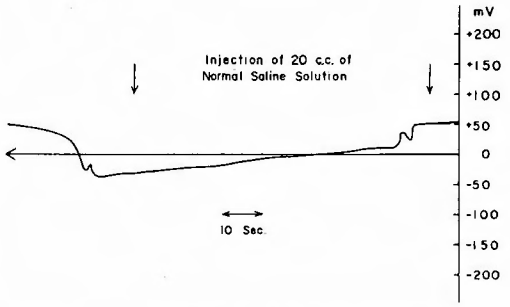

Fig. 20 P. D. change following rapid injection of normal saline solution.

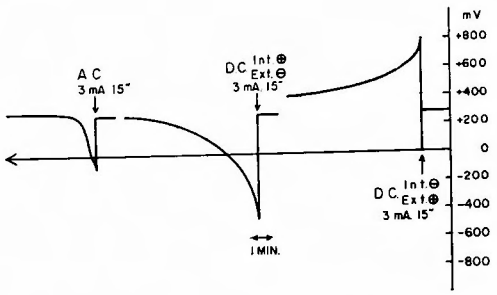

Fig. 21 P. D. changes caused by electric current through bipolar electrodes.

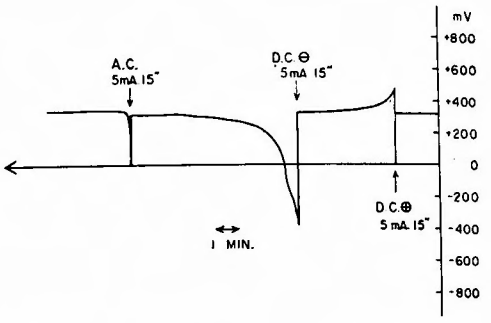

Fig. 22 P. D. changes caused by electric current throhgh unipolar electrode.

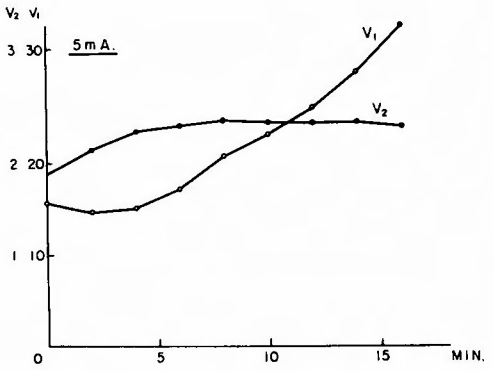

Fig. 23 Changes of voltage (V_1) and P. D. (V_2) between acting and counter-electrodes during contrrolled current electrolysis.

the lumen proximal to the ligature showed moderate changes of the P. D. of up to 100 mV (Fig. 20).

Method III:

1) When the internal electrode was connected to the negative terminal of the potentiometer and the external to the positive terminal, potentiograms showed a moderate increase of the P. D. of up to 330 mV, but when the electrodes were reversed, the potentiograms showed a marked decrease, of up to 760 mV. A. C. also decreased the P. D. moderately, of up to 400 mV (Fig. 21).

2) A positive current of 5 mA caused a slight increase of the P. D., of up to 160 mV, and a negative current caused a marked decrease of up to 760 mV. The passage of A. C. also showed a moderate decrease of the P. D. of up to 450 mV (Fig. 22).

3) As shown in Fig. 23, the voltage (V_1) required to provide a constant flow of 5 mA increased with time, but the P. D. between two electrodes (V_2) did not show a corresponding increase with time. V_2 was relatively constant, and the P. D. was maximum around 8 min. after application of the current. During the passage of the current, V_2 varied between 1.4 and 2.5 V. At the level of the maximum P. D., the segments were all almost totally discolored. In some cases, the maximum level of the P. D. could not be determined readily because of a plateau-shaped flat curve.

DISCUSSION

In the present experiments, the measured P. D. is not the transmural P. D. Variability in the measured P. D. across the normal intact wall of the dog carotid artery, in Method I, suggests that the blood present between the two electrodes exerts a great influence upon the P. D. Demonstrable P. D. is presumably brought about mainly by the blood and its diffusion across the vessel wall. Stasis of the blood flow did not bring about P. D. changes of an easily measurable magnitude. The initial hypothesis that the intima is negatively

charged in respect to the adventitia, presented by SAWYER et al.[29], has been modified by several investigations done to determine the possible existence, magnitude and polarity of the normal P. D. across the vessel wall, both in vivo and in vitro. EISNER et al.[7] reported that a potential difference was not detectable across the aortic walls of dogs when the electrodes were directly opposite each other, and if potentials normally exist across blood vessel walls, these are less than 1 mV. In vitro experiments by HARSHAW et al.[16] on isolated canine aorta and vena cava showed that the P. D. across the canine blood vessel wall was roughly $0 \pm 50\ \mu V$, and that vessels did not possess any significant intrinsic transmural P. D. in vitro.

In Method II, measurements of the P. D. changes were attempted in various situations. SAWYER et al.[28] indicated that the polarity of the normal vessel wall is reversed after injury to the vessel and noted a correlation between the development of a positive charge on the intima and an increased incidence of thrombosis. However, investigations of thrombosis using a new experimental model devised by GILSDORF et al.[13] have provided interesting results: the P. D. across the wall of an intact vessel and the wall of the reanastomosed control vessel was 20 to 25 mV negative in relation to the outside, and the same polarity existed in a segment turned inside out although the P. D. was 30 mV. Vessel segments of carotid and femoral arteries turned inside out were found to develop thrombotic occlusions in all cases.

The first experiment in Method II, in which the carotid artery was crushed with a Kocher clamp, failed to produce any remarkable P. D. changes. The administration of an electronegative agent, heparin sodium and an electeopositive material, protamine sulfate, had almost no influence on the P. D. The administration of a strongly basic material, 1/10N HCL, slightly decreased the P. D. In contrast, a strongly alkaline material, 1/10N NaOH, slightly increased the P. D. These results suggest that the measured P. D. is influenced by the changes of blood pH. Rapid intraarterial injection at a high pressure of normal saline solution caused moderate changes of the P. D., probably due to rheological factors, by changing the P. D. between the flowing intraluminal solution and the vessel wall. According to HARSHAW and SAWYER[17], the size of the potential difference and charge could be varied by changing the pH of the solution of the overall ionic movement, which refers to the zeta potential on the mesh work of pores traversing the vessel wall. SAWYER and HIMMELFARB[40] pointed out that the measured flow potential apparently changed linealy with changes in flow rate and disappeared with cessation of cardiac output. They also mentioned that the zeta potential of the blood-intimal interface was negatively charged with reference to the flowing blood and in addition, the zeta potential, though not quantitatively calculable from the flow potential, was probably of the order of magnitude of hundreds of millivolts.

The experiments in Method III were designed to investigate the P. D. changes caused by the passage of the different kinds of electric current. In the first and second experiments, changes of the P. D. were constantly seen in relation to the polarity of the electric currents. The passage of A. C. also tended decrease the P. D. slightly. These results suggest that the vessel wall is a diffusion membrane, and that at the same time active ion fluxes occur across it. The P. D. changes caused by the passage of A. C. are considered to be brought about by the presence of a semipermeable membrane or autoregulation of the ion transport across the vessel wall, which may act like a rectifier for A. C.

Recently, SAWYER et al.[36] have also reported finding active ion transport occurring across the aorta and vena cava in vivo experiments, with a net Na and Cl flux taking place from the intima to the adventitia across the aorta, and from the adventitia to the intima across the vena cava at low P. D. s. They also alluded to the possible relationship of derangement of active ion transport mechanisms produced by electric current and tissue injury P. D. to intravascular thrombosis. It has been postulated by SAWYER and others[37] that the porous graft allows the transport of ions across the prosthesis, preventing the accumulation of a large electrical potential on the inner face between the prosthesis and the blood stream. This concept is supported by the fact that thrombosis almost uniformly occurs if the prosthesis is totally impermeable to the transport of ions, whereas porous grafts develop thrombosis less readily[6]. The solid plastic structure has been considered an electrical condensor which allows the build-up of ions which, at times, may produce a positive charge and lead to thrombosis. P. D. changes in the present experiments were found to be influenced by various operating factors other than the P. D. of the vessel wall itself (Fig. 24).

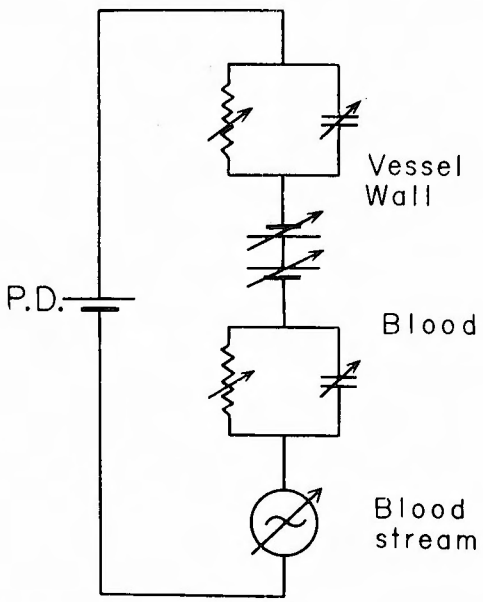

Fig. 24 Diagram of circuit equivalent to blood vessel.

The last experiment was designed in an attempt to find a definite way to obtain information about the quality and gross quantity of electrically induced thrombosis. Changes of the P. D. between the acting electrode and the counter-electrode were not so marked as the changes of the voltage which allows a flow of 5 mA in the circuit in relation to the lapse of time. Therefore, quantitative evaluation is difficult, even if the qualitative changes can be determined to some extent.

EXPERIMENTAL PRODUCTION OF A THROMBUS FOR A LIMITED TIME BY CONTROLLED POTENTIAL ELECTROLYSIS

Measurements of P. D. changes of the vessel wall were carried out in PART II in order to establish indicators of whether or not a thrombus will be induced, and to estimate the quality and gross quantity, if it can be produced, during or immediately after the procedure. However, no definite correlation between the application of the current and the modes of thrombus formation was observed. At this point, controlled potential electrolysis was used in an attempt to obtain this information.

METHODS AND MATERIALS

Method I (20 dogs) : By a procedure similar to that used in experiments described in PART I, a 2 cm long segment of the common carotid artery was tied off, a fine

platinum needle-type positive electrode was inserted 1 cm into the segment, and a stainless-steel hypodermic injection needle was inserted into the surrounding tissues as a negative electrode. A current of up to 35 volts was supplied by a regulated D. C. power source connected to a precise milliammeter. Under the various controlled voltages (10, 15, 20, 25, 30, 35 V), electrolysis was performed, and the amount of the current was checked and plotted every minute to make the I-t curve. The changes in the segment were observed during the application of the current, and the segment was then removed immediately for histological studies. Ten segments thus electrolized were followed for 2 days to 5 weeks, after removal of the silk sutures immediately after the procedure.

Method II (5 dogs) : A 5 cm long segment between two silk ligaures was studied in the same way.

Method III (5 dogs) : A silk ligature was tied together with an 18 gauge injection needle placed parallel and attached to the common carotid artery, then the injection needle was gently slipped out of the loop. Another ligature was made in a same fashion at a distance of 2 cm, and the current was applied.

Method IV (5 dogs) : Without interruption of the blood flow, controlled potential electrolysis was attempted.

Method V (5 dogs) : Negative controlled potential electrolysis was tried in a 2 cm long segment, with a platinum needle as a negative electrode.

Method VI (5 dogs) : Alternating current was imposed upon the segment.

Method VII (5 dogs) : Before the application of the current, the segment was injured mechanically with a Kocher clamp at the midportion for one mintute.

Method VIII (5 dogs) : At the time of preparation of the segment, the distal portion was ligated first, and 0.5 ml (250 U) of heparin sodium was injected from the peoximal poetion. Then, the peoximal portion wat ligated. The 2 cm long segment was then electrolized under controlled voltages.

Method IX (5 dogs) : Similar to Method VIII except that 0.5 ml (5 mg) of protamine sulfate was injected instead of heparin.

Method X (18 dogs) : Approximately 5 cm long skin incisions were made in the inguinal regions, and the femoral veins were exposed and carefully dissected free from the surrounding tissues. A section of the femoral vein with no branches was tied by two silk ligatures 2 cm apart. Then Methods I to IX were carried out in the femoral veins.

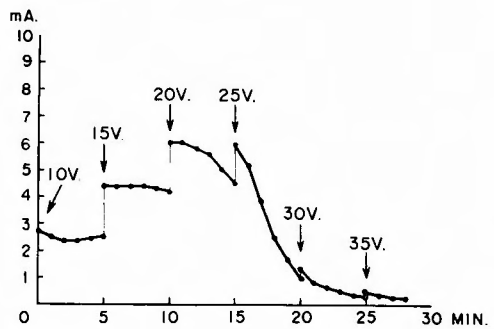

Fig. 25 Controlled potential electrolysis at various voltages.

RESULTS

Method I : As shown in Fig. 25, no changes in the amount of the current were observed with positive controlled potential electolysis at 10 and 15 V. The current began to decrease at over 20 V. Controlled potential electrolysis with 10 V caused bubbles of gas to appear, but no discoloration of the segment. Electrolysis at over 20 V resulted

in blackish-brown discoloration of the segment starting from around the needle electrode, as the current began to decrease. When the current went down to 1 mA, the segment were totally discolored. Ten segments electrolized with current above 5 mA at the start of electrolysis were all totally occluded by thrombus formation on the second day after the procedures. In all of cases, the current fell to less than 1 mA within 10 to 15 min. Even with the same voltage, the I-t curve showed individual variations in respect to the time when the current fell to less than 1 mA, the shape of the curve, etc., but in all cases, the segments were totally discolored when the current fell to less than 1 mA. When the initial current was higher, it took less time for it to fall to 1 mA.

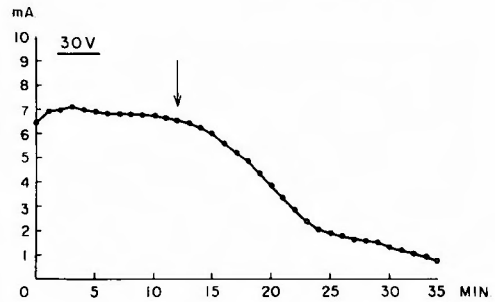

Fig. 26 Controlled potential electrolysis in a 5 cm long segment.

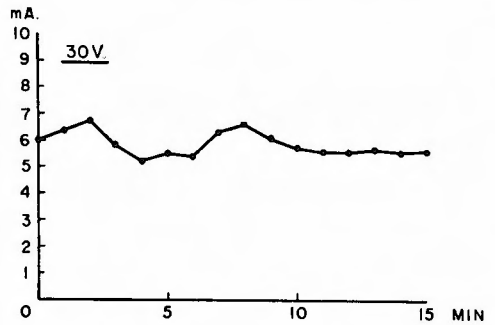

Fig. 27 Controlled potential electrolysis in a segment between two constricting ligatures.

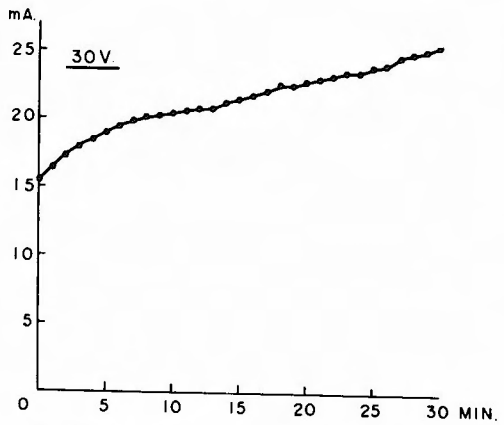

Fig. 28 Controlled potential electrolysis without interfering blood flow.

Method II: As shown in Fig. 26, the current began to decrease later in 5 cm than in 2 cm long segments. However, it began to decrease within 15 to 20 min. in all cases. In this method, also, the current began to decrease when the segments were totally discolored. Two of 3 followed-up segments were totally occluded on the second postoperative day.

Method III: As shown in Fig. 27, the I-t curves were not of the descending type seen with Method I, and total discoloration of the segments was not seen within 15 to 20 min. Of the 3 dogs treated for 15 min. only one developed complete occlusion.

Method IV: No decrease of the current was observed within 15 to 20 min. (Fig. 28), and follow-up studies (3 dogs) were all negative.

Method V: The I-t curves fluctuated, and there was no tendency for the current to decrease with time (Fig. 29). No thrombus formation was observed in any of the 3 dogs.

Method VI: The I-t curves were almost flat (Fig. 30), and minimal discoloration of the segments and appearance of bubbles of gas around the electrode were noted. The vessels of all 3 dogs were patent on the second postoperative day.

Method VII: The I-t curves were almost

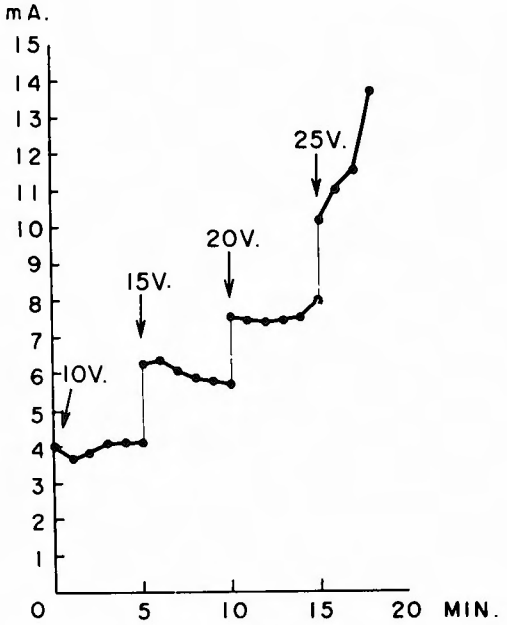

Fig. 29 Negative controlled potential electrolysis.

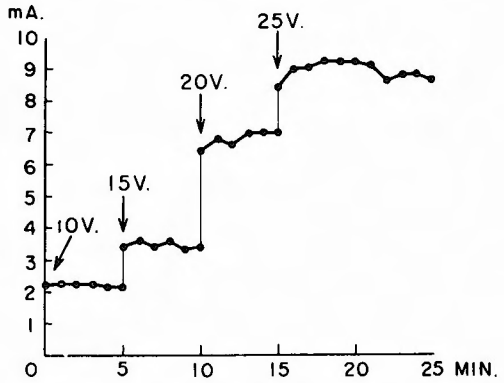

Fig. 30 Controlled potential electrolysis with an alternating current.

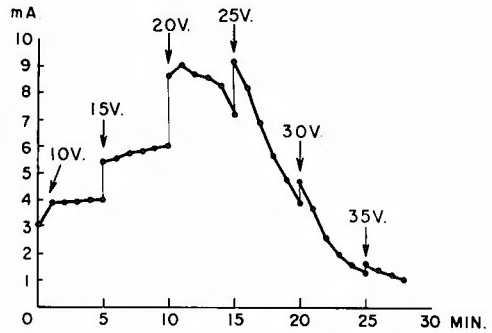

Fig. 31 Controlled potential electrolysis in mechanically injured segment.

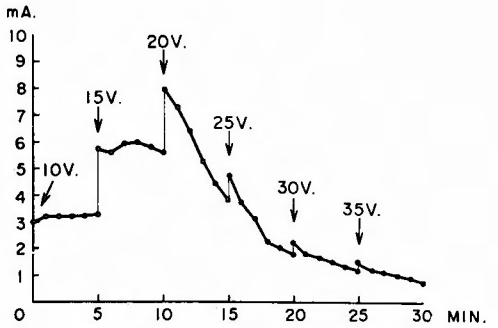

Fig. 32 Controlled potential electrolysis in segment containing heparin solution.

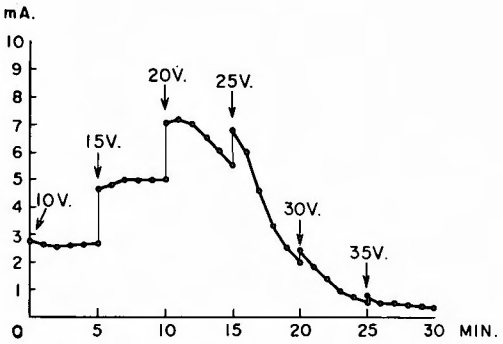

Fig. 33 Controlled potential electrolysis in segment containing protamine solution.

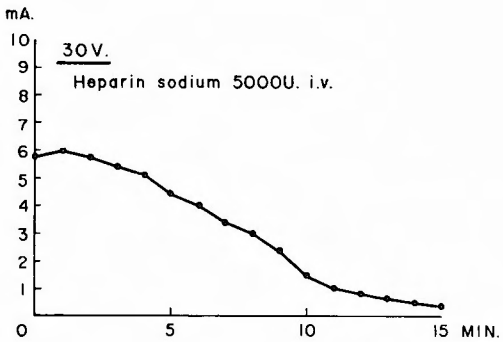

Fig. 34 Controlled potential electrolysis immediately after intravenous injection of heparin.

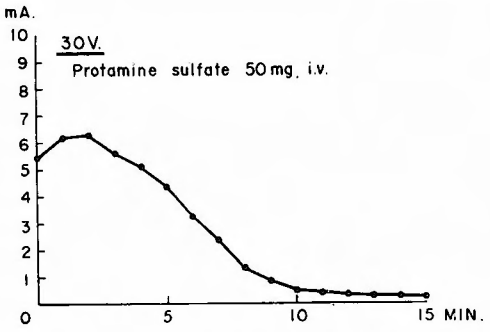

Fig. 35 Controlled potential electrolysis immediately after intravenous injection of protamine.

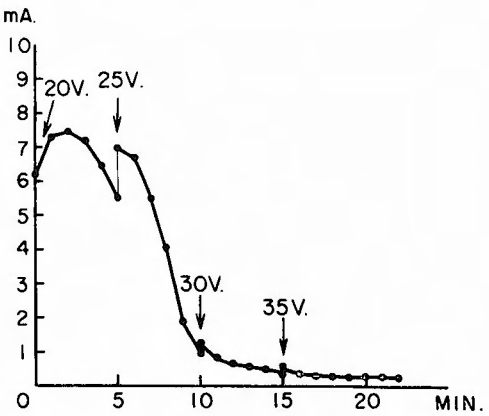

Fig. 37 Controlled potential electrolysis in a segment of dog femoral vein.

the same as with Method I (Fig. 31). The vessels of all 3 dogs were also totally occluded in the follow-up studies.

Method VII and **IX**: Both showed almost the same type of I-t curves (Figs. 32 and 33). Follow-up studies showed occlusion of the vessels of all 6 dogs in which the current had been stopped at less than 1 mA. When heparin sodium (5 ml, 500 U), or protamine sulfate (5 ml, 50 mg) had been injceted intravenously before the electrolysis, the I-t curves were not altered (Figs. 34 and 35), and the follow-up studies were also all positive (Fig. 36).

Method X: No significant differences were observed between the common carotid arteries and the femoral veins in their reaction to controlled potential electrolysis (Figs. 37 and 38).

DISCUSION

The changes in a vascular segment were observed following positive and negative electrolytic polarization with a platinum needle electrode, and the passage of A. C. between the needle electrode and a counter-electrode. Intravascular thrombosis was induced only by positive electrolytic polarization. The phenomenon of thrombus formation by positive electrolysis appeared to be due to electrolysis of the blood followed by adherence of the electrolized blood coagulum to the vessel wall. LAMB et al.[18] showed that the in vitro coagulation of the whole blood of dogs and in vivo thrombosis of blood vessels depended on the strength of the voltage and that below the electrolytic decomposition potential (2.0 V) whole blood was not deposited as a coagulum on the positive electrode even when the amount of charge allowed to flow was greater than that which caused coagulation at higher voltages.

Accroding to studies in organic electrochechemistry, positive electrolysis appears to be more complex and uncontrollable than negative electrolysis. In studying the changes of the formation of membrane around the electrodes by electrolysis, two methods of controlled current and potential electrolysis are used. In electrolysis of the blood, controlled potential electrolysis seemed to be better than controlled current electrolysis. In the latter method, it was difficult to determine the time when electrolysis should be stopped in order to induce thrombosis, since voltage increases progressively with time (Fig. 39). In contrast, in the former method, there is a definite tendency for the strength of the current to charge with time (Fig. 40), making it much easier to study the changes around the electrode.

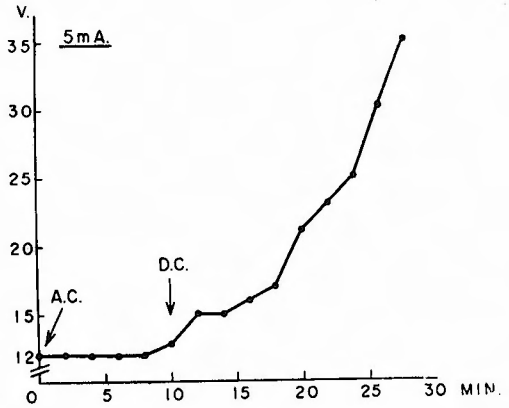

Fig. 39 Controlled current electrolysis in a segment of dog common carotid artery.

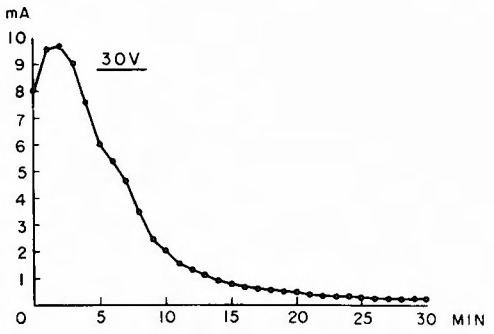

Fig. 40 Controlled potential electrolysis in a segment of dog common carotid artery.

In Method I, with electrolysis with less than 20 V, there were no gross changes in the current. This is probably due to weak electrolysis and electrophoretic action, which will not have enough effect to form compact membranes of blood coagulum around the electrode. The current began to decrease with electrolysis with more than 20 V as time went on. From the electrochemical point of view, this phenomenon might be explained by the following mechanisms; the blood in the segment is completely electrolized and strongly adherent around the electrode electrophoretically, which may lead to the formation of compact membranes of coagulum and increased electrical resistance. The main factors increasing electrical resistance in the positive controlled potential electrolysis of blood are considered to be as follows: (1) evolution of oxygen around the positive electrode; (2) formation of compact membranes of blood coagulum by electric attraction; (3) changes of tissue impedance (IR-drop), etc. With positive controlled potential electrolysis at 10 V, the evoluation of bubbles of gas was already observed. These experimental results indicate that the phenomenon of the decreasing current with electrolysis at more than 20 V is probably due to the compact membranes deposited around the electrode rather than to the resistance caused by the evolved oxygen.

Experiments were carried out on the assumption that clips could be applied temporarily approximately 2 cm apart in clinical cases. It seems to be possible to place the temporary clips as far as 5 cm apart, even when the dissection and isolation of the parent vessel near the aneurysms is difficult. In Method II, the time at which the current begins to decrease became longer as the length of the segment increased. So, the distance between the temporary clips influences the I-t curve. Even with longer segments, the I-t curve will reflect the changes around the electrode. When the current begins to decrease, the blood in the segment will be completely electrolized, and compact membranes of coagulum will be deposited around the electrode. During clinical application, discoloration of the aneurysmal sac by electrolysis will be seen around the needle electrode within the sac at first, then extending to the entire lumen as the strength of the current decreases. Hence, a thrombus can always be induced in an aneurysmal sac; it is not necessary to see the discoloration, but only to note when the strength of the current begins to decrease. Although

the length of the portion of the needle electrode within the vessel also influences electrolysis, these experiments were all carried out with 1 cm of needle inserted, in consideration of the actual size of intracranial aneurysms.

In Method III, no definite decrease of the current was observed. This may be explained by the assumption that the membranes deposited around the electrode are partially separated and removed by the blood flow. The membranes around the electrode are readily separated by the summation of effects of the evolved oxygen and of the blood flow, and become somewhat loose even after deposition around the electrode. The results of Method IV also show the influence of the blood flow upon the formation of the membranes which will be the nidus of thrombus formation.

In Method V, marked evolution of bubbles of gas was noted, but no blackish-brown discoloration. With the passage of A. C., in Method VI, the occurrence of electrolysis could not be observed because there were almost no bubbles of gas or discoloration of the segment, and the I-t curves were all flat.

Experiences in vascular surgery, especially surgery on the small vessels have taught us that any type of injury (mechanical, chemical, etc.) to the vessel wall often leads to thrombus formation. In Method VII, the segment was injured mechanically by a Kocher clamp, but the I-t curve showed no significant difference between intact and injured segments. However, the same reaction of injured and non-injured segments to controlled potential electrolysis is not always reflected in similar results following electrolysis. Electrolysis could induce the initiating process of thrombus formation, but could not influence the entire process of thrombus formation. The mechanism by which electrolized blood coagulum adheres to the inner wall of the vessels must be studied further from various approaches. Certain chemical substances released from the injured vessel wall may activate the surface of the inner wall and change its potential difference so that an electric attraction developes between the injured vessel wall and the blood cell elements, resulting in thrombus formation around the injured areas of the vessel wall. Anyway, the absence of gross differences in the I-t curve between normal and injured segments cannot be explained unless we assume that the released substances have minimal influence in the earliest stage of thrombus formation by electrolysis.

The results of other studies[43] have shown that the negativity of the inner wall of the vessels with respect to the adventitia is increased by the administration of heparin, and decreased by protamine. Hence, the former protects against thrombus formation, and the latter promotes it. However, in Methods VIII and IX, no significant difference was observed in the I-t curve between the two methods. The same type of I-t curves does not always mean that the process after electrolysis is the same, but it is apparent that the typical descending type of the I-t curve always reflects thrombus formation.

It is obvious that many differences between the artery and the vein are present, especially in the nature of the vessel wall and the blood in the lumen. Method X was performed to detect whether or not significant differences are present in controlled positive potential electrolysis. Since no definite differences were noted, it is probable that in the initiating process of thrombus formation by electrolysis, the type of vessel does not significantly influence the response to electrolysis.

It is clear from these experimental studies that thrombosis induced by controlled

potential electrolysis with a rather strong current has the following characteristics: (1) a thrombus can be produced easily, and the recognition of whether or not a thrombus will be induced is quite possible in the early stage; (2), as already shown in the thrombus induced by bipolar electrodes[48], no tendency toward spontaneous dissolution or absorbability is observed, in contrast to thrombi induced by other methods; and (3) there is no possibility of extension or embolism of the induced thrombus. In clinical application, the membranes of the blood coagulum are compact around the needle within the sac, and become looser as the distance from the electrode increases. The loosely electrolized blood in the parent vessel may be removed away without causing embolism. Moreover, the processes of thrombus formation are interrupted at the mouth of the aneurysmal sac by the flushing action of the blood flow in the parent vessel.

CLINICAL CASE

CASE 4: A 52-year-old male was admitted with complaints of pulsating tortuous dilatation of the vessels extending from around the right ear to the temporal, parietal and frontal regions, and a dark reddish, easily bleeding, diffuse swelling around the right ear (Fig. 41 and 42). At about ten years of age, he had developed a small, easily bleeding swelling in the right supraauricular region, which gradually increased in size and began to resemble a cavernous hemiangioma. He had been treated by ligation of the vessels flowing into the lesion several times and by radiation therapy at other clinics. However,

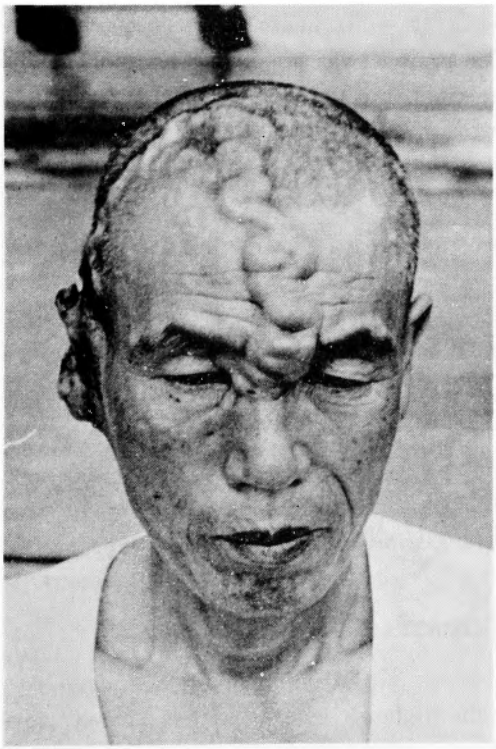

Fig. 41

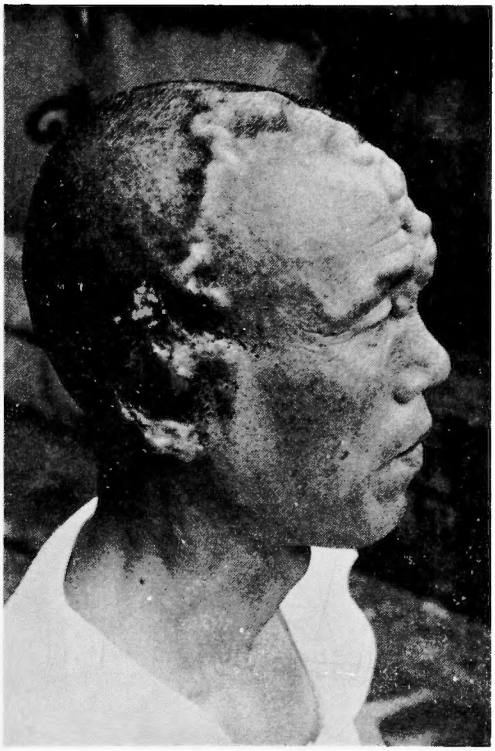

Fig. 42

despite these procedures, the lesion continued to increase in size and extended to the right temporal, parietal and frontal regions. Then, the left superficial temporal artery also started to show totuous dilatation. Because of the presence of abundant anomalous feeding arteries seen in right vertebral angiography (Fig. 43), ligation of the external carotid artery and as extensive resection of the arterial branches as possible were performed by right neck dissection. These procedures lessened the pulsation of the lesion fairly well, but could not cause it to disappear (Fig. 44). So, segmental obstruction of the lumen in the exposed vessels in the right preauricular, frontal and left temporal regions was attempted by controlled potential electrolysis (Fig. 45). The patient tolerated the procedures well and the pulsating tortuous dilatations over the scalp disappeared (Figs. 46 and 47).

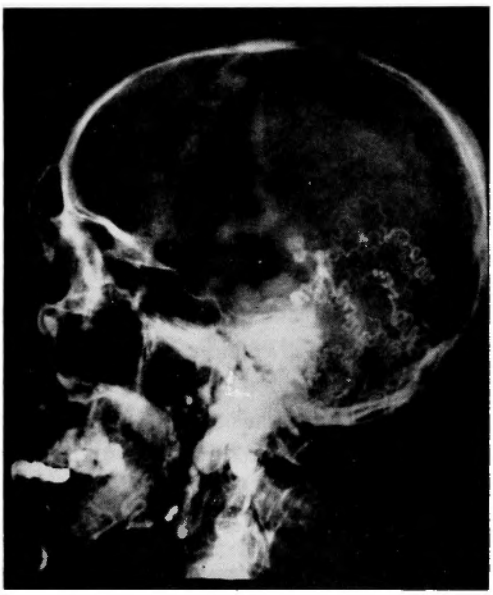

Fig. 43

Comments: In the left temporal region, a segment about 5 mm long and 2 mm in diameter, was ligated off temporarily with two silk ligatures, and electrolized with 35 volts. The current decreased rapidly and fell below 1 milliampere within two minutes. The current was stopped at ten minutes. In the right preauricular region, two segments were made. Each segment was elctrolized as shown in Fig. 45. It required much more

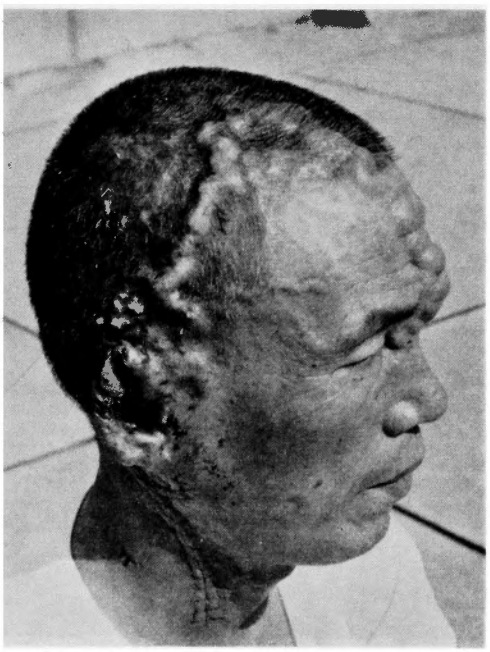

Fig. 44

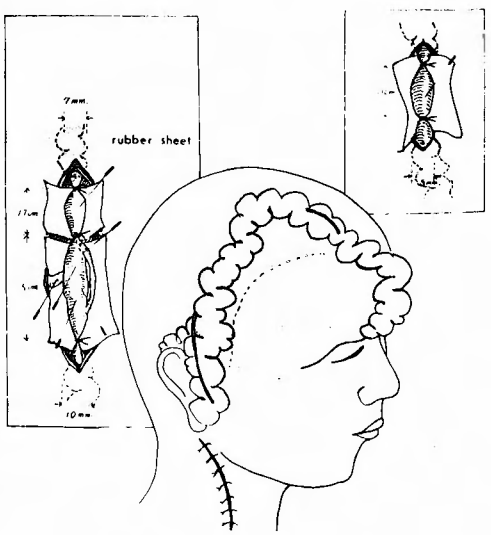

Fig. 45

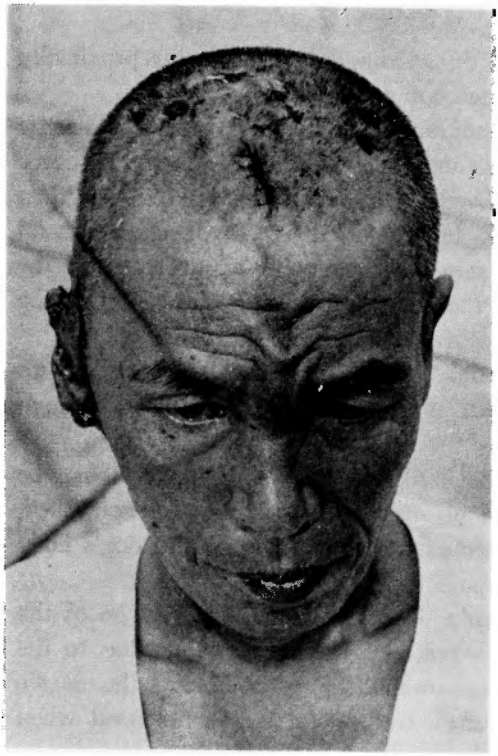

Fig. 46

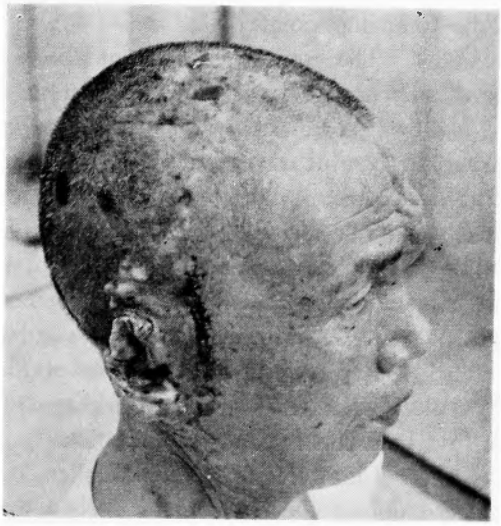

Fig. 47

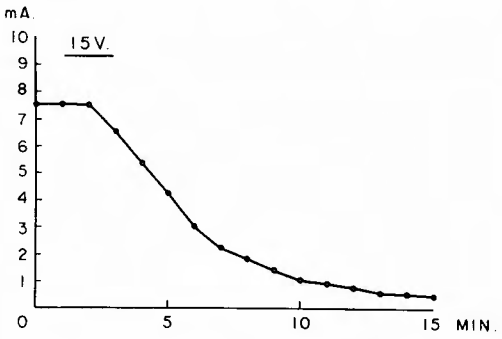

Fig. 48

time for the current to begin to decrease in the lower unusually large segment which was fed by a non-ligated branch. With 5 volts, the current began to decrease at forty minutes and stopped after one hour. A segment in the frontal region, approximately 1.0 cm in length and 5 mm in diameter, which resembled an intracranial aneurysm, could be electrolized with 15 volts within ten minutes (Fig. 48). After removal of the ligatures, no migration of the electrolized coagulum was observed in any of the segments.

The results of controlled potential electrolysis in these three segments indicate that electrolysis occurred at a high voltage for a short duration in the smaller segment, while in the large segment a low voltage of long duration was needed. The response of human vessels to controlled potential electrolysis agreed satisfactorily with the experimental results. This clinical trial establishes the applicability of this new method to intracranial vascular malformations.

MATTERS REQUIRING ATTENTION DURING CLINICAL APPLICATION

Even when discoloration of the aneurysmal sac by the application of a positive electric current cannot be ascertained through adherent brain tissue, one can determine whether or not a thrombus is forming within the aneurysmal sac by carefully examining the I-t curve. However, in order to obtain accurate information, one must be especially careful

of the following points:

(1) The parent vessel should be carefully dissected and isolated as far proximally and distally as possible for the application of the temporary clips.

(2) Before the passage of the current, great care must be taken to avoid electric leakage by careful control of the bleeding points and the application of rubber sheets. Controlled potential electrolysis at a voltage which allows a flow of over 5 mA is then started, and the current is stopped when becomes less than 1 mA. In the experimental studies, incomplete isolation and oozing of blood from the surrounding tissues between the segment and the rubber sheets during passage of the current caused the insulation of the segment to be incomplete, and the I-t curve showed oscillation and fluctuation.

(3) Repeated insertion of the needle electrode must be avoided. Even if the tip of needle is sharpened smoothly, leakage of bubbles of gas and sometimes blood through the first hole can impair the insulation.

(4) Care should also be taken to fix the needle securely so that it will not be displaced during the procedures. When the depth of anesthesia was not well-controlled, the I-t curve often fluctuated because of displacement of the needle by the dog's body movements or by deep respiration.

(5) The descending I-t curve may suddenly fluctuate during the passage of the current even when hemostasis and insulation are complete. This is probably due to the separation of the membranes of the coagulum formed around the electrode from the needle by the bubbles of gas in the segment. In such cases, the current may be stopped when it is estimated that the extending curve would cross the level of 1 mA.

(6) When the distance between the temporary clips is more than 2 cm because of difficulty in dissection or separation of the parent vessel due to firm adherence to the surrounding tissues, the current may be stopped when the I-t curve begins to descend.

(7) However, when the I-t curve does not descend in 15 min, the current may be stopped at 15 to 20 min. Since the hemodynamics in the lumen of an intracranial aneurysm differs from that in experimental segments, the formed membranes of the coagulum around the electrode, even if loose because of incomplete electrolysis, can probably not be washed away so easily as in the experimental segment. It is probable that partially occluding thrombosis in the lumen will facilitate further thrombosis as a nidus, so that lateral pressure against the wall of the aneurysm will be diminished and the possibility of rupture greatly reduced. The experimental results indicate that perfect procedures will cause the production of a thrombus in the lumen by controlled potential electrolysis for 15 to 20 min. even when the distance between the temporary clips is not always constant.

SUMMARY

(1) A new method of treating intracranial aneurysms which are difficult to ligate them because of firm adherence to the surrounding brain tissue or dangerous to expose them completely has been devised: electrically induced thrombosis, either alone or in combination with EDH-Adhesive. This method may be used to treat intracranial vascular malformations which are not suitable for other established methods, or as an additional procedure following clipping or coating.

(2) Thrombi were produced experimentally in segments of dog carotid arteries and

veins rapidly and in a narrow operative field by controlled positive current. The insertion of a fine needle type electrode, 0.2 mm in diameter, by the "Acupuncture" technique or manual manipulation and the application of a positive electric current of 5 mA for 15 to 20 min. produced thrombi at a rate of 100%.

(3) Thrombosis was induced by positive electrolysis of the blood vessel.

(4) The relationship between thrombus formation and the potential difference changes caused by the application of electric current was investigated by measuring the P. D. changes of the vessel wall in vivo. These potential changes could be determined qualitatively, but not quantitatively.

(5) Electrochemically, controlled potential electrolysis instead of controlled current electrolysis was used to determine whether or not a thrombus can be induced in the aneurysmal sac and, if so, its quality and gross quantity during the passage of the current or immediately after. A standard thrombus could be induced in all cases by this method; the electrolysis was started under controlled voltage allowing a flow of over 5 mA, then the current was gradually decreased and stopped when it reached less than 1 mA.

(6) In the initiating process of thrombus formation by electrolysis, the kind and nature of the vessel wall did not significantly affect the response to electrolysis. The major role seems to be played by the blood itself, not by the vessel wall.

(7) Electrically induced thrombosis by controlled potential electrolysis was applied successfully in a clinical case.

ACKNOWLEDGEMENT

Grateful acknowledgement is made to Professor Dr. HAJIME HANDA for his constant interest and guidance in this research. Thanks are also due Dr. SHIRO YOSHIZAWA, Professor in Industrial chemistry, Kyoto University and his assistant Mr. ISAO TARI for valuable suggestion, and to Mr. HIROAKI OKUTANI, a student in technology, Kansai University for his helpful assistance throughout the course of this work.

A part of this work was presented at the Third International Congress of Neurological Surgery held at Copenhagen, August 23-27, 1965.

REFERENCES

1) Alksne, J. F., Fingerhut, A., and Rand, R. W.: Stereotaxic Magnetically Controlled Metallic Thrombosis of Intracranial Aneurysms. Presented at the Thirty-fourth Annual Meeting of the Harvey Cushig Society held at Missouri, April 17-21, 1966.
2) Araki, C., Handa, H., and Ohta, T.: Coating and Reinforcement of Intracranial Aneurysms with Synthetic Resins and Rubbers. Neurochir., **6** : 123, 1963.
3) Brooks, B. : Discussion of Noland and Taylor. Noland, L., and Taylor, A .S. : Pulsating Exophthalmos, Result of Injury. Trans. South Surg. Ass., **43** : 176, 1931.
4) Dandy, W. E. : Arterial Aneurysms. In Practice of Surgery. Originally Edited by the Late Dean Lewis. Vol. 12, Hagerstown, Maryland W. F. Prior Company, INC. 1953, p. 405.
5) Deaton, H. L., and Anlyan, W. G. : A Study of Experimental Method for Producing Thrombosis in Small Arteries. S. G. O., **111** : 131, 1960.
6) DeBakey, M. E., Jordan, G. L., Beall, Jr., G. L., O'Neal, R. M., Abbott, J. P., and Halpert, B. : Basic Biologic Reactions to Vascular Grafts and Protheses. Surg. Clin. North Amer., **45** · 477, 1965.
7) Eisner, G. M.. Berrian, J. H., Carter, E. L., Huggins, C. E., and Sewell, W. H.: Electric Potentials Across the Aorta of Dogs. Am. J. Physiol., **189** : 587, 1957.
8) Fukai, H., Kawakami, K., and Tomita, T. : Surgery of Intracranial Aneurysms and Arteriovenous Malformations. Nerve and Brain, **16** : 244, 1964.
9) Gallagher, J. P. : Obliteration of Intracranial Aneurysms by Pilojection. J. A. M. A., **183** : 231, 1963.

10) Gallagher, J. P. . Pilojection for Intracranial Aneurysms. Report of Progress. J. Neurosurg., **21** : 129, 1964.
11) Gallagher, J. P. : The Closure of Intracranial Aneurysms by Pilojection. In Intracranial Aneurysms and Subarachnoid Hemorrhage. Compiled and Edited by William S. Field and Adolph L. Sahs. Charles C Thomas Publisher, Springfield, Illinois, 1965, p. 444-458.
12) Genest, A. S. : Experimental Use of Intraluminal Plastics in the Treatment of Carotid Aneurysms. J. Neurosurg., **22** : 136, 1965.
13) Gilsdorf, R., Bina, P. C., and Abrolon, K. B. : Investigations on Thrombosis Using a New Experimental Model. J. A. M. A., **186** : 32, 1963.
14) Handa, H. : The Neurosurgical Treatment of Intracranial Vascular Malformation, Particulary with the Use of Plastics and Polarographic Measurements. Clin. Neurosurg., **9** : 223, 1964.
15) Handa, H. : Discussion following Dr. Poppen's Speech. Intracranial Arteriovenous Malformations. Nerve and Brain, **17** : 358, 1965.
16) Harshaw, D. H., Ziskind, H., Mazlen, R., and Sawyer, P N. : Electrical Potential Difference Across Blood Vessels. Cir. Res., **11** : 360, 1962.
17) Harshaw, Jr., D. H., and Sawyer, P. N. : Electroosmotic Characteristics of Mammalian Aorta and Vena Cava. In Biophysical Mechanisms in Vascular Homeostasis and Intravascular Thrombosis. Edited by Philip N. Sawyer, Appleton-Century-Crofts Division of Meredith Publishing Company, New York. 1965, p. 61-68.
18) Lamb, J. C., Isaacs, J. P., Bloom, W. L., and Harmer, D. S. : Electrical Thrombosis of Blood Vessels : A Voltage-dependent Phenomenon. Am. J. Physiol., **208** : 1006, 1965.
19) Luessenhop, A. J., and Spence, W. T. : Artificial Embolization of Cerebral Arteries. Report of Use in a Case of Arteriovenous Malformation. J. A. M. A., **172** : 1153, 1960.
20) Luessenhop, A. J., and Velasquez, A. C. : Observations on the Tolerance of the Intracranial Arteries to Catheterization. J. Neurosurg., **21** : 85, 1964.
21) Mullan, S., Beckman, F., and Vailati, G. : Simplified Thrombosis of a Large, Hypertrophic Hemangioma of the Scalp. J. Neurosurg., **21** : 68, 1964.
22) Mullan, S., Vailati, G., Reyes, C., and Beckman, F. : Induced Thrombosis of Intracranial Aneurysms. Exhibited at the VII Symposium Neuroradiologicum Held at New York, Sept., 1964.
23) Mullan, S., Beckman, F., Vailati, G., Karasick, J., and Dobben, G. : An Experimental Approach to the Problem of Cerebral Aneurysm. J. Neurosurg., **21** : 838, 1964.
24) Mullan, S., Raimondi, A. J., Dobben, G., Vailati, G., and Hekmatpanah, J. : Electrically Induced Thrombosis in Intracranial Aneurysms, J. Neurosurg., **22** : 539, 1965.
25) Ohta, T. : Coating and Reinforcement of the Intracranial Aneurysm with Synthetic Resins and Rubbers. Arch. Jap. Chir., **30** : 753, 1961.
26) Richardson, J. W. : Prevention of Thrombosis Using a Negative Electric Current. Surg., **52** : 636, 1962.
27) Sano, K. : Intracranial Arteriovenous Malformation with Special Reference to its Treatment. Nerve and Brain, **17** : 360, 1965.
28) Sawyer, P. N., and Pate, J. W. : Bioelectric Phenomena as an Etiologic Factor in Intravascular Thrombosis. Am. J. Physiol., **175** : 103, 1953.
29) Sawyer, P. N., Pate, J. W., and Weldon, C. H. : Relation of Abnormal and Injury Electric Potential Differences to Intravascular Thrombosis. Am. J. Physiol., **175** : 108, 1953.
30) Sawyer, P. N., and Pate, J. W. : Electric Potential Differences Across the Normal Aorta and Aortic Grafts of Dogs. Am. J. Physiol., **175** : 118, 1953.
31) Sawyer, P. N., and Deutsch, B. : The Experimental Use of Oriented Electric Fields to Delay and Prevent Intravascular Thrombosis. S. Forum, **5** : 173, 1955.
32) Sawyer, P. N., and Deutsch, B. : Use of Electrical Currents to Delay Intravascular Thrombosis in Experimental Animals. Am. J. Physiol., **187** : 473, 1956.
33) Sawyer, P. N., and Wesolowski, S. A. : The Electric Current of Injured Tissue and Vascular Occlusion. Ann. Surg., **153** : 34, 1961.
34) Sawyer, P. N., Dennis, C., and Wesolowski, S. A. : Electrical Hemostasis in Uncontrollable Bleeding States. Ann. Surg., **154** : 556, 1961.
35) Sawyer, P. N., and Wesolowski, S. A. : Studies in Direct Current Coagulation. Surg., **49** : 486, 1961.
36) Sawyer, P. N., Levine, J., Mazlen, R., and Valmont, I. : Active Ion Transport Across Canine Blood Vessel Walls. J. Gen. Physiol., **45** : 181, 1961.
37) Sawyer, P. N., Ziskind, H. S., and Harshaw, D. H. : Ion Metabolism of the Blood Vessel Wall. In Fundamentals of Vascular Grafting. Edited by Wesolowski, S. A. and Dennis, C. D. New York, McGraw-Hill

Book Co., 1963, p. 3-31.
38) Sawyer, P. N. : Bioelectric Phenomena and Intravascular Thrombosis : The First 12 years. Surg., **56** : 1020, 1964.
39) Sawyer, P. N., and Wesolowski, S. A. : Electrical Hemostasis. Conference on Bleeding in the Surgical Patient. Ann. New York Acad. Sc. **115** : 455, 1964.
40) Sawyer, P. N., and Himmelfarb, E. H. : Studies of Streaming Potentials in Large Mammalian Blood Vessels in vivo. In Biophysical Mechanisms in Vascular Homeostasis and Intravascular Thrombosis. Edited by Philip N. Sawyer. Appleton-Century Crofts Division of Meredith Publishing Company, New York. 1965, p. 69-80.
41) Schwartz, S. I. : Prevention and Production of Thrombosis by Alterations in Electric Environment. S. G. O., **108** : 535, 1959.
42) Schwartz, S. I., and Richardson, J. W. : Prevention of Thrombosis with the Use of a Negative Electric Current. S. Forum, **12** : 4, 1961.
43) Schwartz, S. I. : Effects of Electric Environment on Thrombosis. Clin. Neurosurg., **10** : 291, 1964.
44) Speakman, T. J. : Internal Occlusion of a Carotid-Cavernous Fistula. J. Neurosurg., **21** : 303, 1964.
45) Sugar, O. : Plastic Coating of Intracranial Aneurysms with "EDH-Adhesive" J. Neurosurg., **21** : 114, 1964.
46) Williams, R. D., and Carey, L. C. : Studies in the Production of Standard Venous Thrombosis. Ann. Surg., **149** : 381, 1959.
47) Wesolowski, S. A., and Sawyer, P. N. : Major Surgery on Severe Hemophiliac : Lessons in Management. Conf. on Bleeding in the Surgical Patient. Ann. New York Acad. Sc., **115** : 505, 1964.
48) Yoshida, K. . Experimental Studies on the Production and Treatment of Carotid Thrombosis in Dogs — Especially on the Application of Fibrinolytic Treatment—. Arch. Jap. Chir., **33** : 502, 1964.

和文抄録

電気的作成血栓による脳動脈瘤ならびに脳動静脈奇形の治療に関する実験的研究

京都大学医学部脳神経外科学教室（指導：半田　肇教授）

森　　惟　　明

脳動脈瘤の外科的治療法としては，完全切除，頸部の clipping，または ligation，時には trapping を行なうのが理想であるが，これらが出来ない場合には，"EDH-adhesire" による動脈瘤壁補強が行なわれる．ところが，動脈瘤が周囲脳組織と強く癒着している場合には，"EDH-adhesive" による壁補強も時としては不完全にならざるをえない場合がある．このことより電気的作成血栓による嚢内閉塞療法と "EDH-adhesive" との併用療法を創案するにいたつた．

本研究では，犬の総頸動脈を用いて，電気的作成血栓による閉塞療法を細部にわたつて改良，検討を行なうために臨床的応用上の基礎的実験を行ない，ほぼ完成した方式を確立した．

① 陽極通電による血栓形成の機序に関しては，血管の陽極電解が主役を演ずることが判明した．

② 狭い手術野での通電と，temporary clip を使用するために生ずる操作の時間的制限に対しては，"Acupuncture" technique または用手的に直径0.2㎜の細白金針状電極を血管腔内に刺入し，5 mA，15～20分間の定電流陽極電解により確実に実験的血栓を作成することに成功した．

③ 更に，通電中，もしくは通電直後に動脈瘤嚢内に確実に血栓が作成されたかどうか，また作成しえたとすればその大まかな性状までも知る indicator を求めるため，通電による血管壁の電位差の変化と血栓形成の関係を追求した．ところが，血管壁の電位差の変化は定性的につかめても定量的には把握出来なかつた．

④ そこで，新たに定電流電解方式にかえて定電位電解方式を採用するにいたつた．定電位電解においては，時間の経過にともなう電流変化の傾向が割合はつきりしていて，電極周囲の変化がより適確に把握出来る．これによると，通電時 5 mA 以上の電流が流れるような電位のもとで電解を開始すると，時間の経過とともに電流値が低下し，その値が 1 mA を割つたときに通電を中止すれば，確実に血栓を作成しうることが分つた．しかも，電流値が 1 mA を割るまでに要する時間は，10～20分間以内であつた．

⑤ 定電位電解方式による実験結果より，電気的作成血栓の初期過程においては，血管の種類，血管壁の性状よりも，血液自身の電解が主役を演ずるということが判明した．

⑥ 定電位電解方式を臨床例に応用し，満足すべき結果をえた．脳動静脈奇形の場合も，この方法を併用することにより，出血のcontrolがきわめて容易になり全摘出がたやすく行なわれた．

（尚，本論文要旨は第3回国際脳神経外科学会において発表された）．