THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

INFLUENCE OF VARIOUS STIMULI ON THE DC RESTING POTENTIALS OF THE LARGE ARTERIES

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

DOCTOR OF PHILOSOPHY

BY

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Oklahoma City, Oklahoma

1965

INFLUENCE OF VARIOUS STIMULI ON THE DC RESTING POTENTIALS

OF THE LARGE ARTERIES

APPROVED BY

DISSERTATION COMMITTEE

ACKNOWLEDGEMENT

Full appreciation is expressed to Doctor Chesterfield G. Gunn, Doctor Francis J. Haddy, Doctor M. Jack Keyl, Doctor Garmon Harlow Daron, and Doctor Clinton M. Miller, III, for their advice and help in the execution of this research problem. This investigation was supported in part by a Public Health Service Fellowship (Number GPM 16,956) from the National Institutes of Health, and in part by a Public Health Service Grant (Number He 3111) from the National Institutes of Health.

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INFLUENCE OF VARIOUS STIMULI ON THE DC RESTING POTENTIALS OF THE LARGE ARTERIES

CHAPTER I

INTRODUCTION

Blood cells and other formed elements in the blood carry a negative charge when at the pH of blood. The sign and magnitude of this charge have been extensively investigated using electrophoretic techniques with the formed elements in plasma or blood substitutes (1 to 11). What is probably the first recorded reference to the electrical nature of blood is the observation, by Scudamore in 1824, that blood precipitated on the anode but not on the cathode (12). No further observations of this nature were reported until Dineur investigated the electrical characteristics of leucocytes in 1893 (33), and Poore, in 1895, suggested the possibility of taking advantage of these electrical characteristics by catalyzing coagulation with an electric current (13). This was again mentioned as a possibility by Skene in 1899 (14).

Abramson (1 to 8) was probably the most active investigator of the electrical characteristics of blood elements in the 1920's and 1930's. In one of his first papers (1) he hypothesized that the migration of leucocytes to an injury was due to the attractive force of the positive injury potentials (15) exerted on the negative blood cell. This was also

the hypothesized mechanism by which the clot was caused to form on the intimal wall following arterial injury (16 to 19). The basis for this thesis was that the sludging in arterioles and capillaries of the rat mesentery which is supposedly caused by the injury potential of a cut muscle applied to the mesentery is identical to the sludging which is induced in the same arterioles and capillaries by passing a direct current from one side of the vessels to the other (20). Sawyer and his group (16 to 19) reported a large resting potential, lumen negative, across the wall of the aorta. This potential changed polarity following injury, making the lumen positive with respect to the adventitia. This work now fit into the picture of an electrophoretic genesis of thrombus formation. The direction of the current flow is the causal factor in electrically induced coagulation since a beginning clot, precipitated onto the intimal surface which is at the more positive potential in the electric field, will lyse and the elements will go back into solution when the direction of the current flow is reversed. A clumping of formed elements will now occur on the intimal surface which was at the less positive potential but is now at the more positive potential in the field.

It has thus been shown that minute amounts of direct current will induce clotting.

A blood pressure increase, <u>per se</u>, may by its hydraulic pressure on the walls of the artery, collapse the vasa vasorum, thus leading to ischemia of the vessel wall. Vasoconstriction could also lead to ischemia by forcing the vasa vasorum closed as the smooth muscle in the vessel wall contracts.

Many reports of central nervous system stimulation leading to

blood pressure changes and vasoconstriction have been made (21 to 27). Stimulation in the same areas of the hypothalamus cited in these papers was followed by increased atherosclerotic plaque formation in rabbits fed a cholesterol diet (28).

These three facts: stimulation leading to plaques, stimulation leading to blood pressure changes, and the electrical induction of thrombi, led to the following hypothesis: 1) the changes in blood pressure following hypothalamic stimulation may have been caused in part by vasoconstriction and in part by cardiac changes, 2) this blood pressure change could cause local vessel wall ischemia, 3) this ischemia could cause edema of the vessel wall, 4) this edema could lead to the production of an injury potential, 5) this injury potential would attract the fat moieties and formed elements of the blood and thereby enhance thrombus formation, and subsequently plaques.

An experiment was designed to test this hypothesis at the arterial level of description by measuring the potential from lumen to adventitia, and the changes in this potential which followed various stimuli: blood pressure changes, total wall damage (by crushing), intimal and adventitial damage, and local vasoconstriction.

CHAPTER II

MATERIALS AND METHODS

Equipment Considerations

Many processes in the living organism are accompanied by the production of an electric potential (15, 29). Most commonly only those potentials which change rapidly in magnitude are studied. There are two main reasons for this: the difficulty in making electrodes which are stable enough and which will not introduce into the measuring circuit more potential change than is arising from the system being measured and, until recently, the difficulty in manufacturing and using amplifiers which will follow slow, small changes in potential (29).

Reference, or reversible, electrodes can be used to measure small DC potentials in an electrolyte milieu (30). These electrodes consist of an active portion, in contact with the system being measured, which contains at least two ions. One of these ions is in equilibrium with the system being measured and the other is in equilibrium with the metal in the inactive portion of the electrode. In most cases concerned with living organisms the ion in equilibrium with the organism is chloride and the ion in equilibrium with the measuring system is either silver or mercury. Thus there are two basic types of reversible electrodes used in biological work: silver-silver chloride and mercury-mercury chloride (calomel). Both

of these function in the same manner--the active layer (silver or mercury chloride) is nearly insoluble in the electrolyte milieu and therefore does not dissolve. An electric current caused to flow in the one direction will remove the negative ions (chloride) from the electrode layer and put them into solution with the concomitant deposition of positive ions (silver or mercury) onto the metal of the electrode. An electric current caused to flow in the other direction causes the negative ion (chloride) from the electrolyte to associate with the positive ion (silver or mercury) from the metal of the electrode thus increasing the amount of metal-chloride layer. These two actions of the reversible silver-silver chloride electrode are connected and controlled by the solubility equilibrium constant of the solid silver chloride. Thus:

$$K_s = ({}^{a}Ag^{+})\ ({}^{a}Cl^{-})$$

where: ${}^{a}Ag^{+}$ is the activity coefficient of silver ion and ${}^{a}Cl^{-}$ is the activity coefficient of chloride ion and K_s is the activity solubility product of silver chloride. For best results, the amount of current passed through the electrodes should be very small.

The commonly available electrodes cannot be used with assurance at potentials below approximately one millivolt because they drift an appreciable fraction of this amount over a relatively short period of time. This drift is almost non-existent if the electrodes are isolated by means of a plastic, sintered glass, asbestos, or other porous plug from the ionic milieu which they are measuring. These sealed electrodes, however, cannot be used in contact with blood, since clot formation on the end of the electrode produces spurious potentials (31,32). Therefore some means of removing these clots must be provided.

These problems become much more important when the potentials

being measured are well below the one millivolt level. The potentials which appear to be generated by clots on the end of the electrode are as large as one millivolt. The drift of most unsealed electrodes is sometimes more than a few hundred microvolts per hour, and the drift of most DC amplifiers is usually more than one millivolt per hour referred to the input of the amplifier.

The drift of the unsealed electrodes is caused mainly by diffusion of the electrolyte being measured into the electrolyte used in the electrodes. This diffusion can be made as small as desired by using small bore catheters for the electrode tubing. However, a small bore catheter filled with electrolyte is a poor conductor, having a resistance of several hundred megohms if very long. In addition, it is very difficult to flush clots out of a small bore. The use of a saturated potassium chloride solution for the electrolyte will decrease the resistance of the electrodes but this solution is toxic to living organisms. Since its effect in this preparation was unknown, a 0.85% sodium chloride solution would be preferable in this experiment.

High resistance electrodes may be used if the input resistance of the amplifier being used is many times the resistance of the electrodes. High input resistance amplifiers are usually unstable and therefore difficult to use. In addition to having a high input resistance the amplifier must have a low input current so as not to introduce more signal into the measuring circuit than is being introduced by the measured system.

Potentials are induced into long, high resistance electrodes by changes in the electrostatic field in which they are placed. These field changes may be caused by movements of the investigator, movements of the

animal or movements of other people in the room. The potentials induced by these movements in this experiment were many times larger than the potentials being measured. Therefore the animal, the electrodes, and the input circuit of the amplifier should be shielded from the investigator.

All electrically operated equipment in contact with the animal: infusion pump, blood pressure transducer, stimulator, and amplifier must have virtually complete isolation from the electric mains as any additional ground introduced by any of this equipment will produce large and variable potentials.

The DC resting potential difference between the lumen and the adventitia of the aorta, the common iliac, and the femoral arteries was measured in the unstimulated, anesthetized animal. For this measurement the two electrodes were carefully juxtaposed, one inside, and the other outside, the artery. Following this measurement various stimuli were applied to the animal and the potential changes following the stimuli were recorded. The stimuli were of four types: 1) arterial wall damage, 2) changes in blood pressure, 3) local vasoconstriction, and 4) interruption of blood flow.

Electrode Fabrication

Silver-silver chloride electrodes were chosen for the experiment because mercury-mercury chloride electrodes are unstable mechanically and thermally and are relatively difficult to manufacture.

All glassware used in the preparation of the electrodes was soaked for at least twenty-four hours in a saturated solution of potassium dichromate and technical grade sulphuric acid to remove foreign ions from the surface. All reagents used were the purest available commercially and

the water used was freshly distilled using a triple distillation Pyrex still. The resistivity of this water was not measured, but it was higher than the best commercially available water which was greater than one million ohm-centimeters. The silver wire used exceeded 99.999% purity.

The wire was filed and polished to a mirror finish thus eliminating all surface irregularities. Number 10 B & S gauge silver wire was used for the electrodes because smaller diameter wire bent with the small stresses attendant upon mounting it and this bending cracked the very brittle silver chloride layer rendering the electrode unstable. The larger diameter wire did not suffer thus and approximately ten square centimeters of active area per electrode was prepared.

Before any chemical treatment of the electrodes was carried out the two polished electrodes were soldered together by a cross-wire to facilitate handling and to connect the two together electrically. This cross-wire extended between the two unfinished ends of the two electrodes. The electrodes were then soaked and scrubbed in carbon tetrachloride, then water, then a mixture of one to one ethyl alcohol and acetone, and finally water. These solvents were considered sufficient to remove all traces of organic material from the wire and thus allow an even, complete attack of the surface in the etching process. This etching process produced clean metal surfaces to which the plate would adhere. All fluids were poured over the electrodes with the polished ends up so that any foreign material washed off the unfinished ends would not contaminate the clean surfaces. Better electrodes resulted from freshly prepared wire.

The etching process consisted of dipping the electrodes into a 50% nitric acid solution and leaving them there until a thick, even layer

of bubbles formed on the surface. This took approximately thirty seconds. The electrodes were then withdrawn from the acid and immediately washed with water many times before plating.

The plating bath was a 0.1 normal solution of hydrochloric acid. The plating was done in the system as shown in Figure 1. The electrodes were cut apart to be connected into the plating system. If any substance but the water or the plating solution touched the etched surface a poor plate would result and this would result in an erratic, unstable electrode. This meant that the electrodes had to be suspended in the water during soaking.

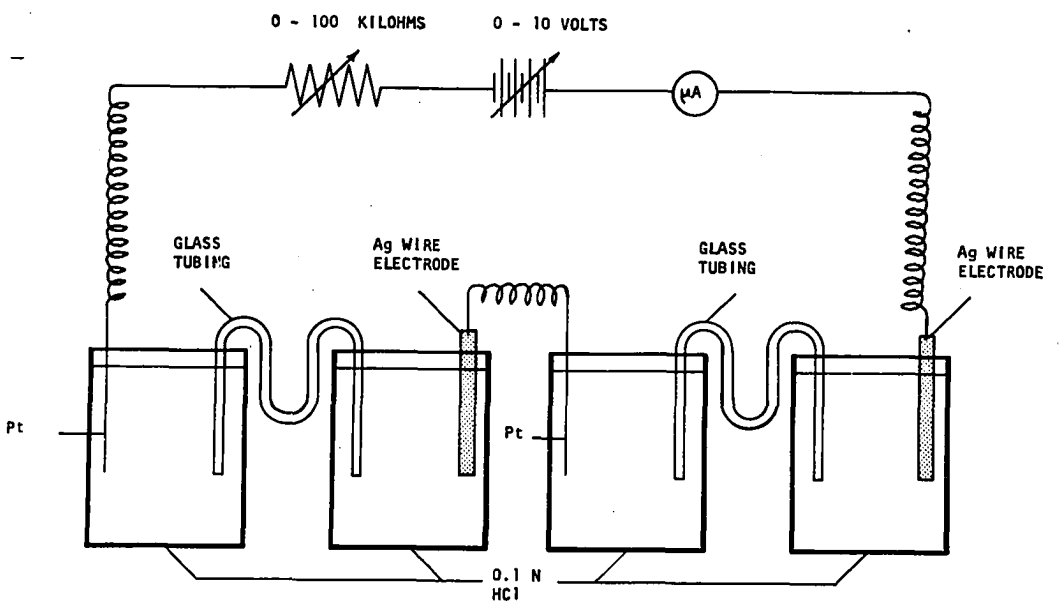


Fig. 1.--Electrode plating system

The plating circuit shown in Figure 1 in which all the current flowing through one electrode must also flow through the other electrode, produces more evenly matched electrodes than if the electrodes are connected together and plated in parallel. The amount of electrode area exposed to the bath must be identical for each of the two electrodes so that the silver chloride layer is the same thickness on each electrode. A current of approximately 100 microamperes per square centimeter for a period of approximately one half hour was used for the plating. The electrodes were watched and when the plate appeared to be smooth and satiny the electrodes were removed, connected together electrically, washed thoroughly in water, soaked for at least one hour in several changes of water, then soaked overnight in 0.85% sodium chloride solution. The interelectrode potential was measured in the 0.85% sodium chloride bath and if greater than ten microvolts the electrodes were discarded.

It was found that the treatment of the two electrodes had to be identical from the time they were cut from the wire stock until they were finished in order that the interelectrode potential be small. During any chemical treatment they had to be electrically connected, the areas exposed to the plating bath had to be identical, and, most important, everything that contacted the water, the plating bath and the electrodes had to be scrupulously clean.

A semischematic diagram of the apparatus is shown in Figure 2.

Polyethylene or polyvinyl tubing large enough to accommodate the electrodes was washed with detergent and rinsed with water then inserted into glass tubing. The electrodes were carefully inserted into the plastic tubing and the whole was glued together with epoxy cement, ensuring that

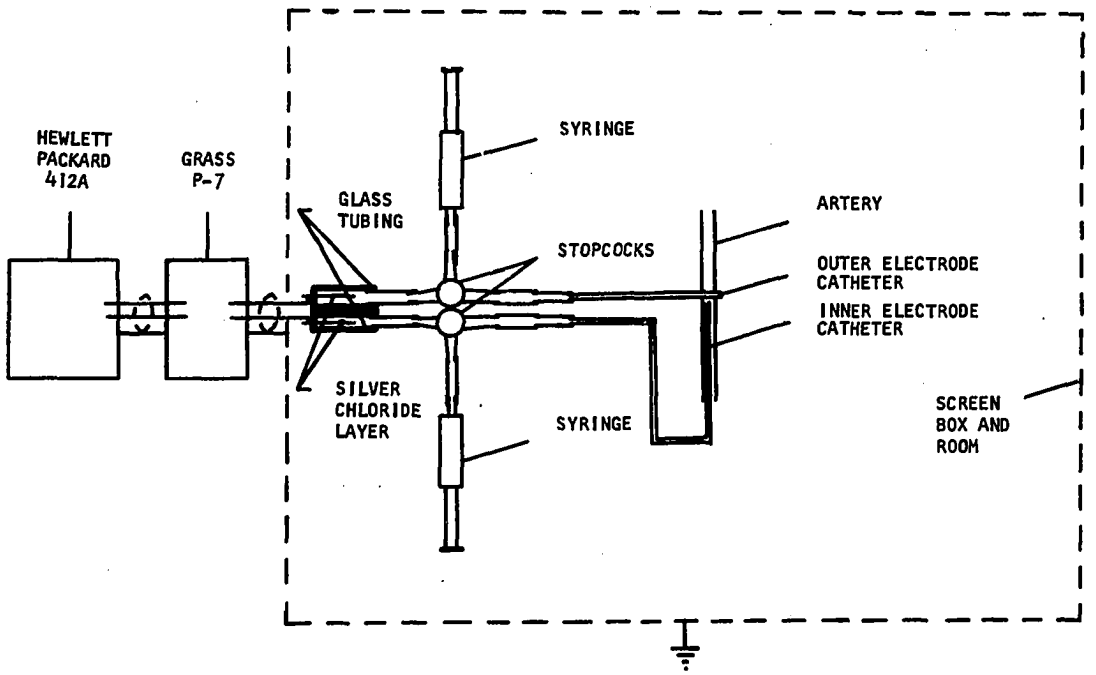


Fig. 2.--Semischematic diagram of apparatus

no bare silver could come into contact with the electrolyte (Figure 3). The plastic tubing prevented the glass from scratching the silver chloride layer and the glass provided rigidity to the structure, preventing any mechanical stress from being applied to the silver chloride layer.

Enough 0.85% sodium chloride solution was prepared for each set of electrodes to soak the electrodes, to fill the electrode catheters and to flush out the catheters. Any change in the electrolyte solution after the electrodes had been equilibrated resulted in spurious potentials.

The plastic tubing leading from the electrodes was attached to one arm of a three-way Teflon and glass stopcock, another arm of which was

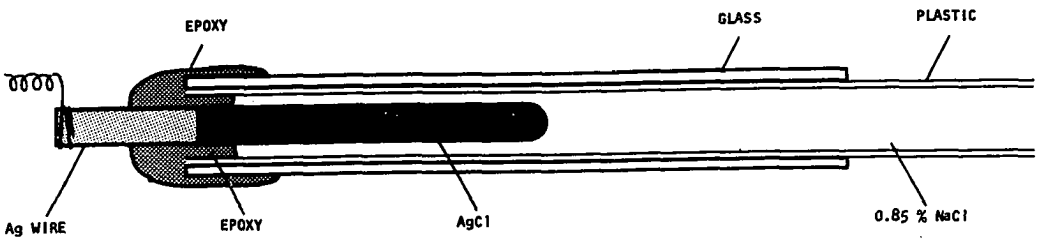


Fig. 3.--Mounted electrode

connected to a syringe and the third arm led through several size reductions of plastic tubing to the electrode catheter (Figure 4). The inner electrode was a polyethylene catheter (PE 10 or PE 20). The outer electrode catheter took two forms (Figure 5).

The helix (Figure 5a) was made by wrapping the polyvinyl tubing (approximately of PE 10 size) around a wire and heating it to 125° centigrade. The end of the tubing was sealed and a pinhole was made on the inner aspect of one of the turns. This small hole allowed the electrolyte in the catheter to conduct the current but reduced the electrolyte diffusion to a negligible amount. The helical configuration allowed the artery to dilate and constrict without losing electrical contact with the electrode.

The sealed electrode (Figure 5b) was formed of polyethylene tubing by heating and forming the end into a cup shape. This shape allowed the electrode to be glued to the outside of the artery with Methyl-2-Cyanoacrylate (Eastman 910) in order that changes in the pH of the tissue fluid which followed the application of the phenol used to damage the adventitia

would not register as potential changes.

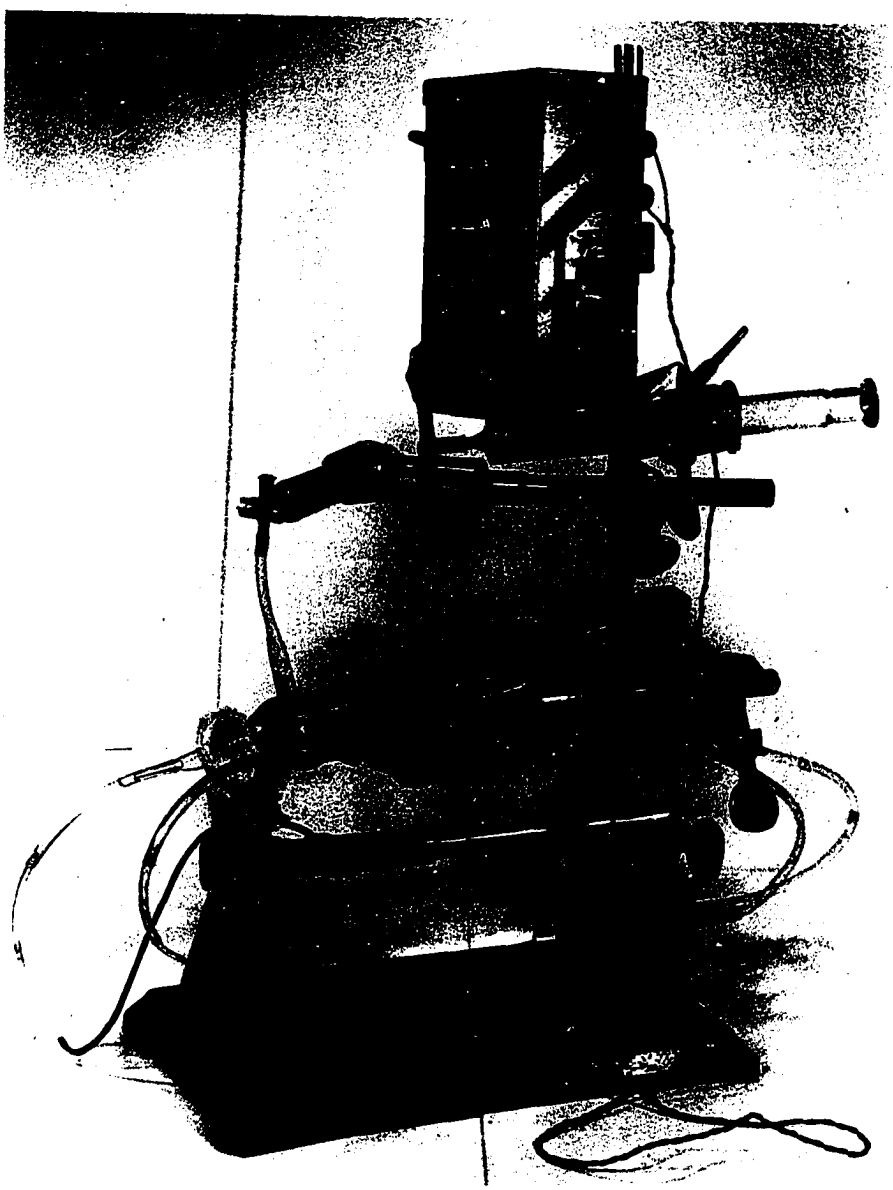
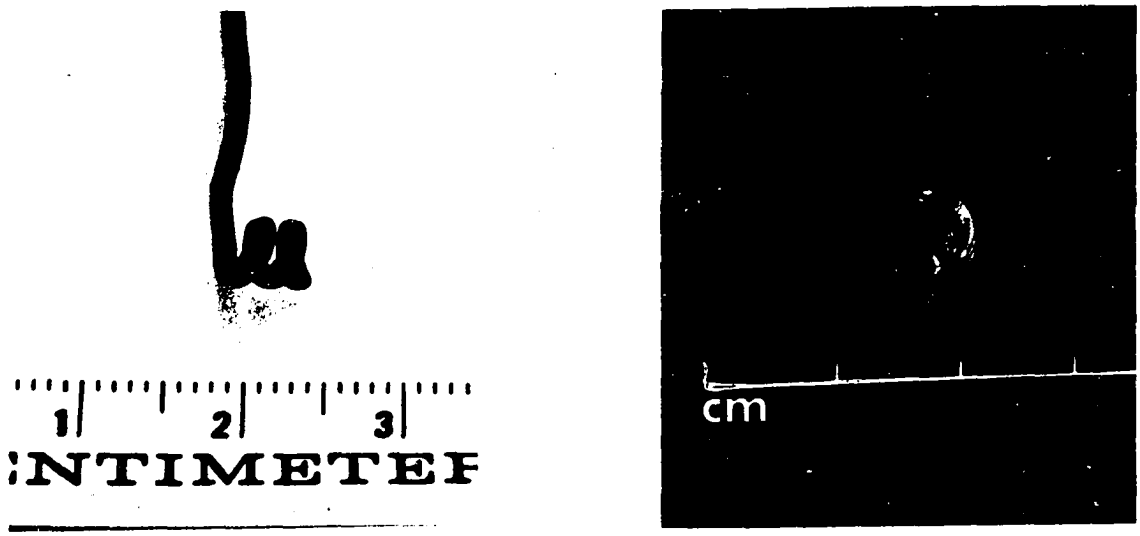


Fig. 4.--Electrodes, stopcocks and stand

When finished the two electrode catheters had a combined resistance of four megohms. The syringe was used to force electrolyte through the electrode catheters to flush out clots and to prevent changes in the composition of the electrolyte resulting from diffusion. The stopcocks closed off the system so that the blood pressure would not open the

syringe and fill the system with blood (Figure 4).



(a) (b)

Fig. 5.--Outer electrode catheters

Amplifying Apparatus

Ordinary twisted pair copper wire was used to lead the potential being measured from the silver electrodes to the input of the amplifier. No thermocouple, triboelectric or piezoelectric effects were noticed. This amplifier served as an impedance matching device and as an isolation unit between the animal and the recording instrument. The investigation began using a Bioelectronics DS2C electrometer input amplifier but the very small potentials found demanded such high amplification in the following recording device that the small base-line drift of the amplifier made it impossible to keep the trace on the scale of the recorder. A Hewlett Packard Model 412A DC Voltmeter proved to be adequate for the job. This amplifier has an input resistance of one hundred megohms. The over-all sensitivity of the system could be increased beyond 10 microvolts per

centimeter of pen deflection referred to the input of the amplifier. Increasing the sensitivity beyond this point revealed no further information because the signal to noise ratio became so small. The first part of the experiment was an investigation of the sign and magnitude of the resting potentials and for this a sensitivity of up to 10 microvolts per centimeter was used. The biggest problem with this sensitivity was the drift in the interelectrode potential. After aging the electrodes this potential can change as much as 30 microvolts in the course of a 3 hour experiment. This drift, unlike the drift of the amplifier and recorder, cannot be checked during the experiment and allowed for in the results.

Recording Apparatus

The amplified potential was led from the amplifier to a DC Pre-amplifier in a Grass Model 7 Polygraph. The record resulting was a standard ink-drawn recording. The Statham Pressure Transducer, Model P23A or P23G, used to measure the blood pressure was filled with mineral oil to isolate the animal from the ground in the metal case and the blood pressure catheter was filled with heparinized 0.85% sodium chloride solution. The electrical output from this transducer was led to another Low-level DC Pre-amplifier in the Polygraph.

Miscellaneous Equipment

A Harvard Apparatus infusion pump was used to either infuse the vasoactive agents into the vena cava or to drop the vasoconstrictor onto the artery.

The electrical stimulation of the artery was carried out using an Electronics for Life Sciences Constant Current Stimulator Model CCS-1.

This device has an input-output resistance of 10^{11} ohms and an input-output capacitance of 50 picro-farads. It was driven by a Grass Model S-5 Stimulator.

The animal, electrodes, and amplifier input circuits were placed in a screened box and the whole within a radio frequency shielded room (Figure 6).

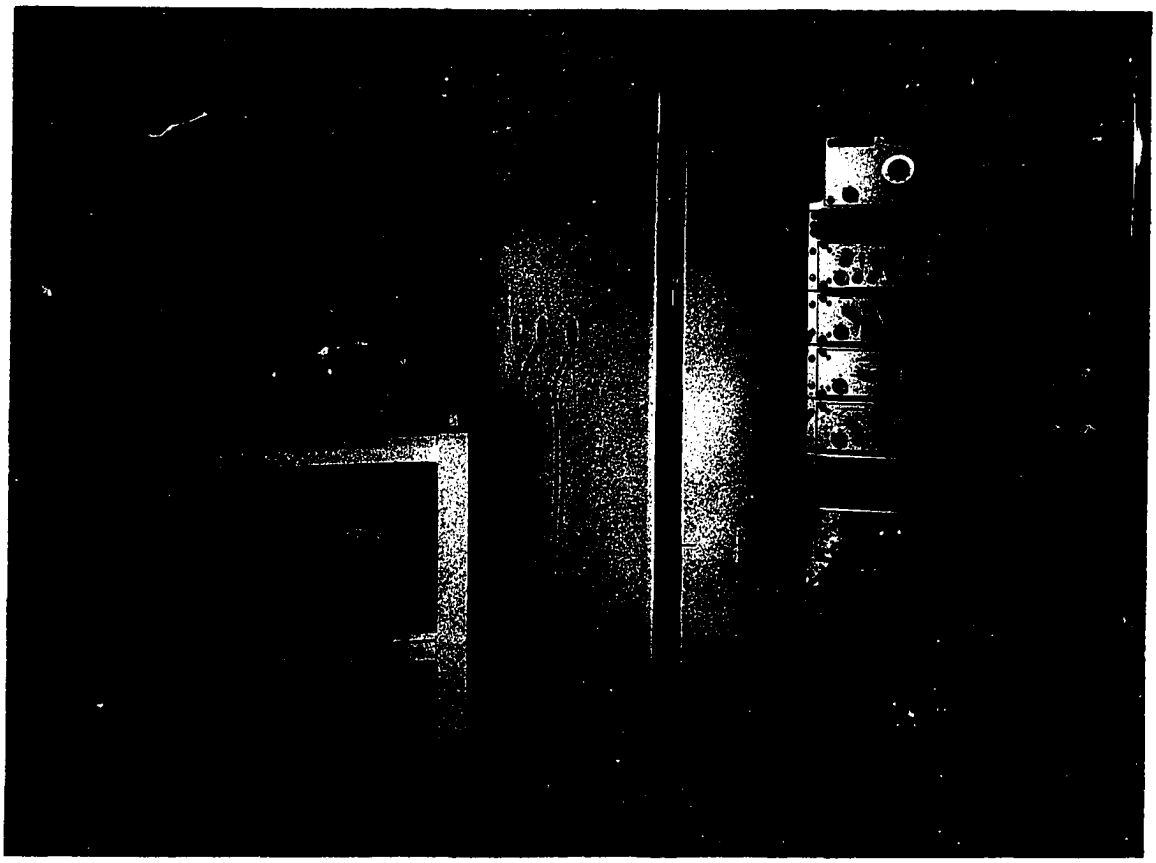


Fig. 6.--Screened room and instrument set-up

CHAPTER III

EXPERIMENTAL PROCEDURES

Preliminary Experiments

The potential field in a saline bath was compared to the theoretical field. This was done by placing two silver-silver chloride electrodes, one at either end of a six inch long plastic trough $\frac{1}{4}$ inch wide and $\frac{1}{4}$ inch deep, in a bath of 0.85% sodium chloride solution, passing a small direct current between these two electrodes and plotting the potential field as measured by the two catheter electrodes. The theoretical potential field was then computed, assuming parallel flux lines in the bath and assuming no polarization at the two end electrodes. Further *in vitro* experiments were performed to measure the polygraph and amplifier and electrode drifts. The effects on the interelectrode potential of the large potentials induced into the electrodes by movements in their vicinity and of the large potentials measured during electrical stimulation were determined.

Surgical Procedures

A single intraperitoneal injection of 45 milligrams sodium pentobarbital per kilogram of body weight was administered for the anesthetic in each of the thirty cats and six rats used as the experimental animals. Further anesthetic was given as necessary throughout the

experiment. In most animals a large midline incision was made extending from the xiphoid process to the pubic bone, the viscera were then removed from the abdominal cavity and placed on the table and covered with warm saline sponges. The aorta or other artery was bluntly dissected free, and the electrodes were then positioned in and around the artery (Figure 7).

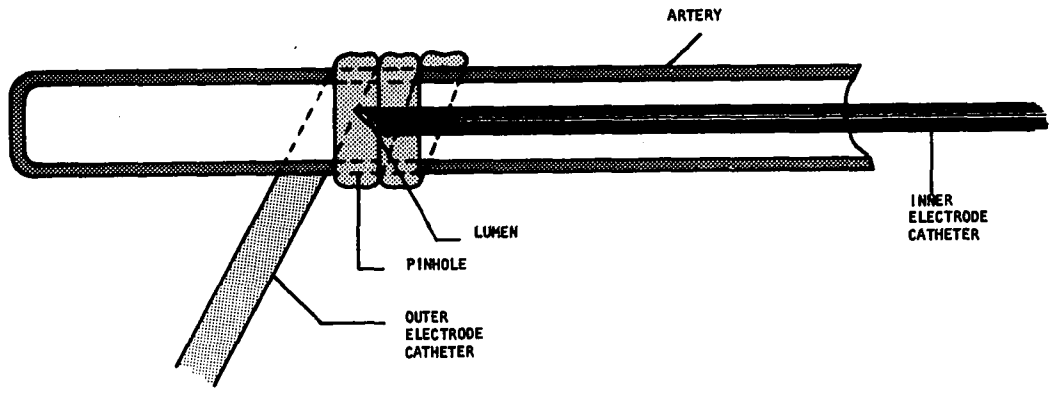


Fig. 7.--Electrode catheters on artery

The first experiments were performed using rats as the experimental animals in order to develop the form of the electrodes, to discover the best routes of entry into the vascular tree and to develop a protocol for the subsequent experiments using cats.

Several different approaches were used to investigate the resting potentials and the changes following a stimulus and each of these approaches utilized the same inner electrode catheter. The helical outer electrode

catheter was also used in each of these except for the phenol experiment when the cup-shaped electrode catheter was used. For most of the experiments the inner electrode catheter was inserted into the vascular tree through a small slit in the wall of the femoral artery and slid up the femoral artery into the aorta. The outer electrode catheter was usually passed through the large abdominal incision and wrapped around the aorta just caudal to the renal arteries. The inner electrode catheter was positioned so that the end of this catheter was immediately adjacent to the pinhole in the outer electrode catheter (Figure 7).

Resting Potential

The resting potential was measured twenty-eight times in twenty different cats. Care was taken in these measurements to ensure that the inner and outer catheters were exactly juxtaposed. The potential was recorded in each instance for a sufficient period to allow equilibrium to be achieved after the manipulations attendant upon placing the catheters.

To discover whether the trauma inflicted by the large abdominal incision and the evisceration had eradicated the resting potential, the outer electrode catheter was wrapped around the femoral artery at the point of incision on the leg of one animal and the inner electrode catheter was positioned in the lumen of the femoral artery immediately adjacent to the pinhole in the helix. This animal had suffered the least amount of trauma consonant with performing the experiment--there was only the intraperitoneal injection of anesthetic, a half inch skin incision, and the small slit in the femoral artery wall.

To investigate whether the direction of the flow of blood relative

to the lumen of the electrode catheter had any effect on the potential measured by the electrode the left common iliac artery was tied off and a small incision was made in the wall of this artery. The inner electrode catheter was passed through this slit, up the left common iliac artery and down the right. The helix was wrapped around the right common iliac artery immediately adjacent to the end of the inner catheter. This question was further investigated by passing the inner electrode catheter up the left renal artery and down the aorta a short distance. As usual the outer electrode catheter was wrapped around the aorta with the pinhole juxtaposed to the end of the inner electrode catheter.

Pressor and Depressor Agents

To discover the effects of blood pressure changes on the potential the inner electrode catheter was inserted via the femoral artery, as before described, or via the left common iliac artery, as before described, in order to investigate a more vasoactive artery than is the aorta. The infusion catheter was passed into the vena cava via the femoral vein. All infusions were given at the rate of one cubic centimeter per minute. Four vasopressors--epinephrine, ten micrograms per minute, angiotensin, five micrograms per minute, vasopressin, twenty micrograms per minute, and norepinephrine, fifteen micrograms per minute--and four vasodepressors--adenosine triphosphate, one hundred micrograms per minute, acetylcholine, fifteen micrograms per minute, bradykinin, four micrograms per minute, and histamine, ten micrograms per minute--were used to change the blood pressure. Infusions of 0.85% sodium chloride solution were given to measure the effect of the dummy infusion on the potential. Epinephrine, angiotensin, norepinephrine and acetylcholine

were each administered eight times as these four agents produced the most marked and most prolonged changes in blood pressure. The remaining four agents were each administered four times.

Vasoconstriction

The effect of chemically and electrically induced vasoconstriction on the potential was investigated by passing the inner electrode catheter into the left common iliac artery and down the right, as before described. The helix was wrapped around the right common iliac artery. Epinephrine was dropped onto the right common iliac artery, where it passed through the helix, at the rate of approximately six drops per minute.

Vasoconstriction was also produced by electrical stimulation. The platinum electrodes used for this stimulation were placed one on either side of the artery immediately upstream from the helix. The stimulus frequency was ten pulses per second, the pulse duration was one millisecond, and the pulse amplitude was 10 milliamperes.

Trauma

To investigate the effect of trauma on the potential of the arterial wall, the inner electrode catheter was inserted via the femoral artery into the aorta: 1) a hematoma was effected by injecting whole blood into the artery wall, and the helix was wrapped around the aorta in such a manner that the hematoma was between the pinhole and the end of the inner electrode catheter, 2) phenol was painted on the adventitia all around the cup-shaped outer electrode catheter in order to coagulate the artery wall, 3) a needle was inserted into the right renal artery and the intima of the

aorta opposite the root of this artery was scraped, the inner electrode catheter was inserted into the right renal artery until it abutted against the damaged intimal surface, and the helix was wrapped around the aorta so that the damaged area was between the end of the inner electrode catheter and the pinhole, 4) massive trauma to all artery wall layers was caused, after placement of the electrode catheters, by crushing the aorta, with a Kelly clamp, six times all around the helix.

Stasis

Stasis of the blood was brought about in two different ways: 1) rubber-shod hemostats were used to occlude the aorta approximately two centimeters upstream from the electrode catheters and 2) the animal was killed by a pneumothorax with the electrode catheters *in situ*. In the latter case the potential was followed for several minutes following the last heart beat.

CHAPTER IV

RESULTS

Electrode Evaluation

The potential field as computed and the potential field as measured with the electrodes corresponded exactly, indicating that the electrodes were sampling accurately.

Measuring System Drift

The drift of the Hewlett Packard Model 412A amplifier and the Grass Model 7 Polygraph was checked on five occasions and found to be less than minus 5 microvolts referred to the input of the amplifier over a period of 100 minutes, with the input open or shorted. The drift of the electrodes, amplifier, and polygraph was checked on five occasions with the electrode catheters in a 0.85% sodium chloride bath and the mean drift in three hour periods was plus 3 microvolts with a range of plus 30 to minus 30 microvolts. No thermoelectric, triboelectric or piezoelectric effects were noticed.

The *in vivo* drift of the electrodes was checked in fourteen animals and the mean drift was plus 0.4 microvolts, with a range of plus 100 to minus 100 microvolts in 30 minute periods. The difference between this drift and that of the electrodes *in vitro* is a reflection of the increased noise level *in vivo*. This drift is caused by changes in the elec-

trodes, potential changes arising from the animal itself and alterations in the electrolyte in the catheters caused by diffusion.

All potentials measured in vivo are referred to the outer electrode both in sign and magnitude.

Electrical "Noise" in Animal

There is a rather large, slowly changing DC potential field in the animal which interferes with measurements of small potentials. This field varies with a periodicity of from three to five minutes and in magnitude as much as 200 microvolts peak to peak. This periodicity and magnitude is not constant but can vary considerably from one wave to the next (Figure 8). If measured between the axillary space and the abdominal cavity this potential was as much as 11 millivolts, with the axilla positive with respect to the abdominal cavity. If measured from the femoral region to the abdominal cavity the potential was as much as 4 millivolts, with the femoral region positive with respect to the abdominal cavity. These potentials were measured in the partially eviscerated animal and thus probably do not obtain normally.

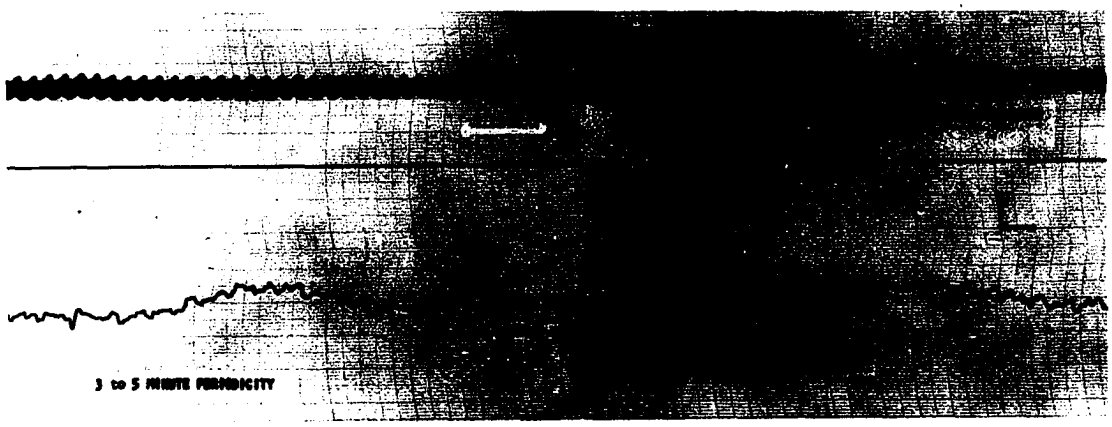


Fig. 8.--Sample trace of normal resting potential near renal arteries

Figure 9 is a plot of the potentials found on the vascular tree of one animal. These measurements were made with the outer electrode catheter around the aorta, just caudal to the renal arteries, and the inner electrode catheter was slid, one centimeter at a time, from the femoral artery to the heart. All potentials are in millivolts. This plot shows that if one electrode catheter was moved within the artery relative to the other a potential change was measured. This was an indication that the catheters were moving in the DC potential field. Movements of the animal, be they peristalsis, respiration, pulse or skeletal muscle in origin, could result in the movement of the electrode catheters relative to one another and thus result in a change in the potential.

Resting Potentials

The resting potential found between the lumen and the adventitia of the aorta, common iliac and femoral arteries, with the electrodes juxtaposed, was relatively small--the mean of twenty-eight measurements in twenty cats was plus 276 microvolts, lumen positive, with a range of plus 550 to minus 150 microvolts. Table 1 is a list of the potentials found and Figure 10 is a histogram of these potentials. In this figure the height of the bar is proportional to the number of potentials found to be within the 100 microvolt range designated on the abscissa.

Heparin Effect

The first experiments were performed in non-heparinized animals and, after the measuring system had been evaluated and some resting potentials had been measured, heparin, in doses of from one microgram to seven milligrams was injected into the femoral vein of cats weighing

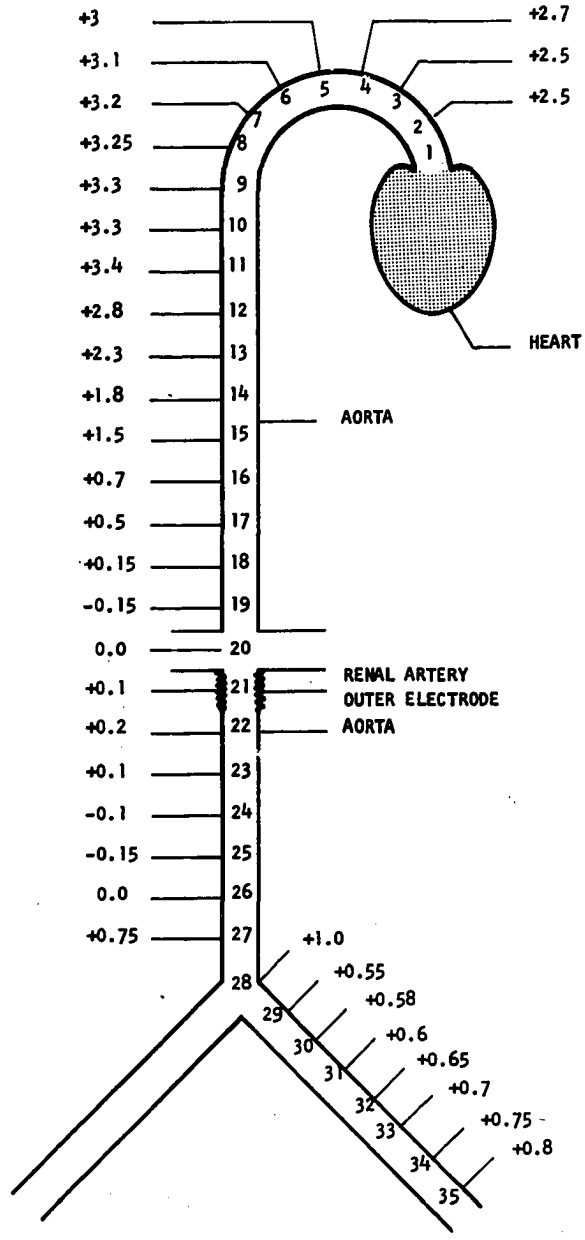


Fig. 9.--Pattern of resting potentials on aorta, in millivolts, in one animal

TABLE 1

RESTING POTENTIAL DIFFERENCES BETWEEN ARTERY LUMEN AND ADVENTITIA, WITH ELECTRODE CATHETERS JUXTAPOSED, OVER TEN MINUTE PERIODS IN TWENTY DIFFERENT CATS

Measured Potential	Fluctuation
- 150	± 50 microvolts
- 50	± 15 microvolts
+ 30	± 80 microvolts
+ 40	± 80 microvolts
+ 75	± 10 microvolts
+ 100	± 20 microvolts
+ 100	± 25 microvolts
+ 100	± 20 microvolts
+ 100	± 10 microvolts
+ 180	± 10 microvolts
+ 200	± 50 microvolts
+ 250	± 20 microvolts
+ 300	± 50 microvolts
+ 300	± 50 microvolts
+ 325	± 50 microvolts
+ 350	± 50 microvolts
+ 350	± 50 microvolts
+ 350	± 30 microvolts
+ 370	± 20 microvolts
+ 400	± 50 microvolts
+ 400	± 50 microvolts
+ 450	± 50 microvolts
+ 475	± 40 microvolts
+ 500	± 50 microvolts
+ 500	± 50 microvolts
+ 500	± 100 microvolts
+ 525	± 25 microvolts
+ 550	± 50 microvolts
+ 7670	± 1155
$\bar{x}$ = + 276	± 42 microvolts

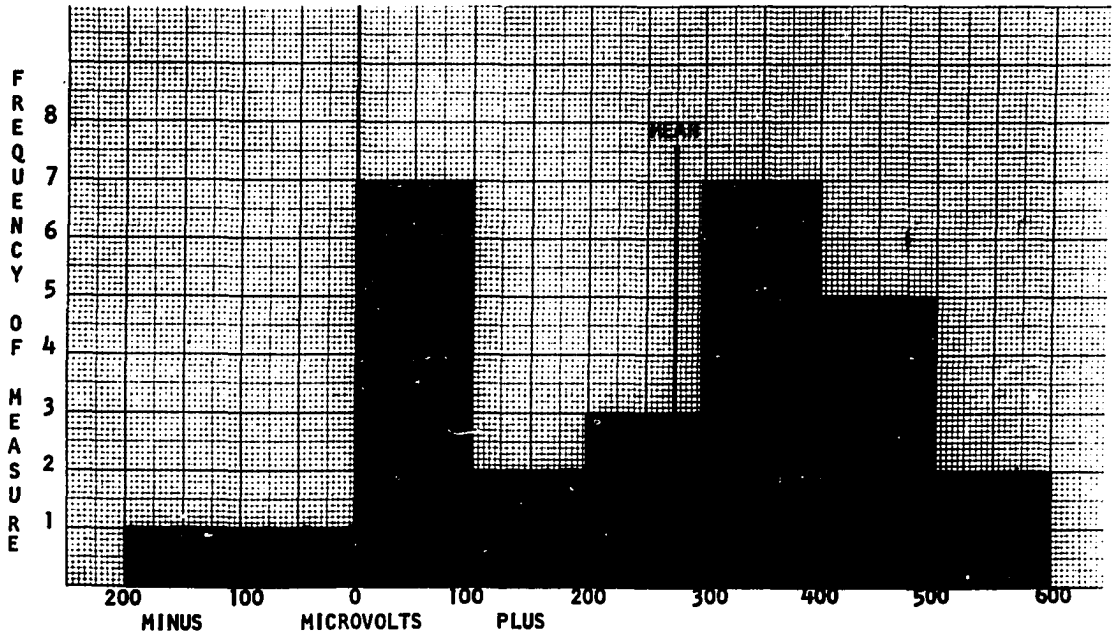


Fig. 10.--Histogram of resting potentials found in twenty cats approximately three and a half kilograms. These injections caused changes in the potential of from plus 70 to minus 25 microvolts with a mean potential change of plus 15 microvolts, when given in doses of one milligram or larger per cat (Table 2). These changes occurred within five minutes and are significant at the 0.2 level of confidence.

Blood Pressure Change Effect

All infusions were at the rate of one cubic centimeter of solution per minute. The concentrations of the agents were adjusted until a significant change in blood pressure followed this infusion rate. Nine control infusions of 0.85% sodium chloride solution (the solvent for all of the agents) were followed by a change in potential of from plus 25 to minus 25 microvolts with a mean change of 0 microvolts (Table 3).

Eight infusions of epinephrine at ten micrograms per minute raised the blood pressure as much as 70 millimeters of mercury for as long as six

TABLE 2

EFFECT OF HEPARIN ON THE POTENTIAL IN NINE CATS

Dose	Potential Change Within First Five Minutes
1 milligram	- 25 microvolts
1 milligram	- 5 microvolts
1 milligram	+ 5 microvolts
5 milligrams	- 5 microvolts
5 milligrams	+ 25 microvolts
5 milligrams	+ 50 microvolts
5 milligrams	+ 70 microvolts
7 milligrams	0 microvolts
7 milligrams	+ 5 microvolts
	+ 145

$\bar{x}$ = +15 microvolts, +70 to -25 microvolts

$p < 0.2$ that this change is due to chance

TABLE 3

EFFECT OF CONTROL SOLUTION, 0.85% SODIUM CHLORIDE, ON THE POTENTIAL IN NINE CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
- 2	- 15 microvolts
0	- 10 microvolts
0	- 10 microvolts
0	+ 5 microvolts
0	+ 10 microvolts
0	+ 10 microvolts
0	+ 25 microvolts
+ 2	- 25 microvolts
+ 2	+ 10 microvolts
	0

$\bar{x}$ = 0 microvolts, +25 to -25 microvolts

minutes and were followed by a change in potential of from plus 100 to minus 75 microvolts, with a mean change of plus 25 microvolts (Table 4 and Figure 11). This change is significant at the 0.4 level of confidence.

TABLE 4

EFFECT OF EPINEPHRINE ON THE POTENTIAL IN EIGHT CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
+ 50	- 75 microvolts
+ 60	+ 50 microvolts
+ 60	+ 150 microvolts
+ 70	+ 20 microvolts
+ 70	+ 100 microvolts
+ 70	- 20 microvolts
+ 75	- 20 microvolts
+ 75	+ 20 microvolts
	+ 200 microvolts

$\bar{x}$ = +25 microvolts, +150 to -75 microvolts

$p < 0.4$ that this change is due to chance

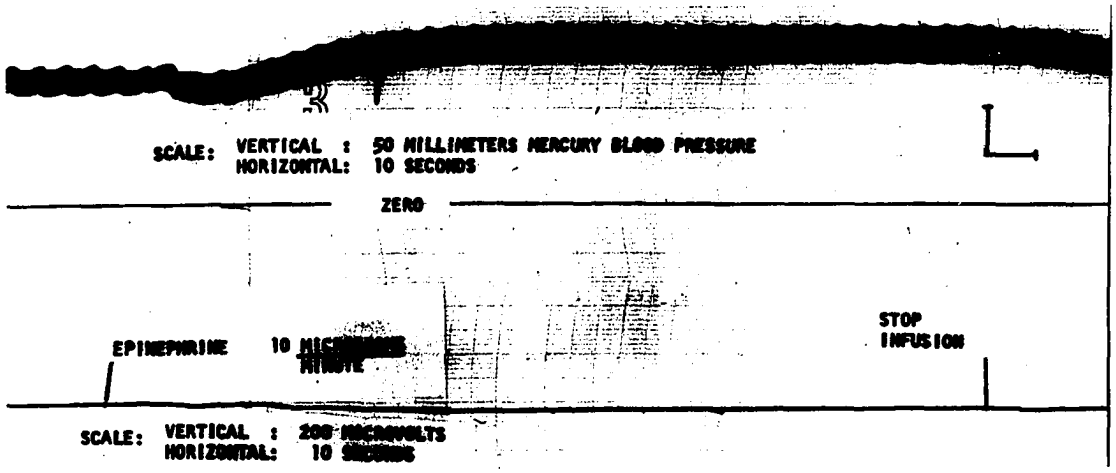


Fig. 11.--Sample trace of response to epinephrine

Eight infusions of angiotensin at five micrograms per minute

raised the blood pressure as much as 115 millimeters of mercury for as long as six minutes and were followed by a change in potential of from plus 40 to minus 40 microvolts, with a mean change of minus 2 microvolts (Table 5). This change is not significant.

TABLE 5

EFFECT OF ANGIOTENSIN ON THE POTENTIAL IN EIGHT CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
+ 100	+ 5 microvolts
+ 100	+ 20 microvolts
+ 110	- 40 microvolts
+ 110	- 25 microvolts
+ 110	- 5 microvolts
+ 110	+ 10 microvolts
+ 115	- 20 microvolts
+ 115	+ 40 microvolts
	- 15

$\bar{x}$ = -2 microvolts, +40 to -40 microvolts

$p > > 0.5$ that this change is due to chance

Four infusions of vasopressin at twenty micrograms per minute either lowered the blood pressure as much as 25 millimeters of mercury for as long as two minutes or the blood pressure did not change, and were followed by a change in potential of from plus 30 to minus 50 microvolts, with a mean change of minus 1 microvolt (Table 6). This change is not significant.

Eight infusions of norepinephrine at fifteen micrograms per minute raised the blood pressure as much as 75 millimeters of mercury for as long as five minutes and were followed by a change in potential of from plus 10 to minus 10 microvolts, with a mean change of minus 1 microvolt

(Table 7). This change is not significant.

TABLE 6

EFFECT OF VASOPRESSIN ON THE POTENTIAL IN FOUR CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
- 25	- 10 microvolts
- 20	- 50 microvolts
- 5	+ 30 microvolts
0	+ 25 microvolts
	- 5

$\bar{x}$ = -1 microvolt, +30 to -50 microvolts

$p > > 0.5$ that this change is due to chance

TABLE 7

EFFECT OF NOREPINEPHRINE ON THE POTENTIAL IN EIGHT CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
+ 40	+ 5 microvolts
+ 50	+ 5 microvolts
+ 60	- 10 microvolts
+ 70	- 10 microvolts
+ 70	- 5 microvolts
+ 70	+ 10 microvolts
+ 75	- 5 microvolts
+ 75	0 microvolts
	- 10

$\bar{x}$ = -1 microvolt, +10 to -10 microvolts

$p > > 0.5$ that this change is due to chance

Four infusions of adenosine triphosphate at one hundred micrograms per minute lowered the blood pressure as much as 20 millimeters of mercury

for as long as one minute and were followed by a change in potential of from plus 30 to plus 5 microvolts, with a mean change of plus 16 microvolts (Table 8). This change is significant at the 0.1 level of confidence.

TABLE 8

EFFECT OF ADENOSINE TRIPHOSPHATE ON THE POTENTIAL IN FOUR CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
- 20	+ 30 microvolts
- 10	+ 5 microvolts
- 10	+ 10 microvolts
0	+ 20 microvolts
	+ 65

$\bar{x}$ = +16 microvolts, +30 to +5 microvolts

$p < 0.1$ that this change is due to chance

Eight infusions of acetylcholine at ten micrograms per minute lowered the blood pressure as much as 75 millimeters of mercury for as long as six minutes and were followed by a change in potential of from plus 350 to minus 100 microvolts with a mean change of plus 90 microvolts (Table 9 and Figure 12). This change is significant at the 0.15 level of confidence.

Four infusions of bradykinin at four micrograms per minute lowered the blood pressure as much as 30 millimeters of mercury for as long as three minutes and were followed by a change in potential of from plus 40 to minus 30 microvolts, with a mean change of plus 3 microvolts (Table 10). This change is not significant.

TABLE 9

EFFECT OF ACETYLCHOLINE ON THE POTENTIAL IN EIGHT CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
- 60	- 20 microvolts
- 60	+ 30 microvolts
- 65	- 100 microvolts
- 65	+ 150 microvolts
- 65	+ 300 microvolts
- 70	- 10 microvolts
- 70	+ 350 microvolts
- 75	+ 20 microvolts
	+ 720

$\bar{x}$ = +90 microvolts, +350 to -100 microvolts

$p < 0.15$ that this change is due to chance

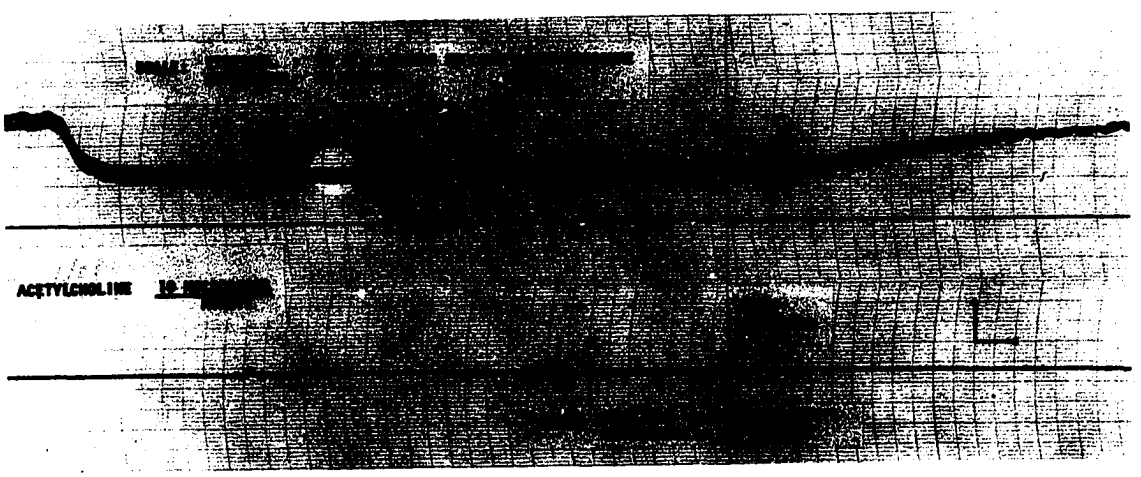


Fig. 12.--Sample trace of response to acetylcholine

Four infusions of histamine at ten micrograms per minute lowered the blood pressure as much as 50 millimeters of mercury for as long as four minutes and were followed by a change in potential of from plus 100 to minus 10 microvolts, with a mean change of plus 35 microvolts (Table

11). This change is significant at the 0.3 level of confidence.

TABLE 10

EFFECT OF BRADYKININ ON THE POTENTIAL IN FOUR CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
0	- 30 microvolts
- 10	- 10 microvolts
- 10	+ 10 microvolts
- 30	+ 40 microvolts
	+ 10

$\bar{x}$ = +3 microvolts, +40 to -30 microvolts

$p > > 0.5$ that this change is due to chance

TABLE 11

EFFECT OF HISTAMINE ON THE POTENTIAL IN FOUR CATS

Blood Pressure Response in Millimeters of Mercury	Potential Change in First Fifteen Minutes
- 25	+ 40 microvolts
- 40	- 10 microvolts
- 45	+ 100 microvolts
- 50	+ 10 microvolts
	+ 140

$\bar{x}$ = +35 microvolts, +100 to -10 microvolts

$p < 0.3$ that this change is due to chance

Local Vasoconstriction Effect

Chemically Induced Vasoconstriction

Epinephrine was dropped on the common iliac artery on six occasions

for periods of up to one hour. The artery constricted to an estimated three fourths of its unstimulated size. This change in artery size was followed by a change in the potential of from minus 20 to minus 40 microvolts, with a mean change of minus 37 microvolts. The potential remained within minus 60 microvolts for an hour after the epinephrine stopped dropping on the artery (Table 12). This change is significant at the 0.001 level of confidence.

TABLE 12

EFFECT OF VASOCONSTRICTION ON THE POTENTIAL IN SIX CATS

Epinephrine	
5 minutes	- 20 microvolts
5 minutes	- 40 microvolts
10 minutes	- 40 microvolts
10 minutes	- 40 microvolts
30 minutes	- 40 microvolts
60 minutes	- 40 microvolts
	- 220

$\bar{x}$ = -37 microvolts, -20 to -40 microvolts

$p < 0.001$ that this change is due to chance

Electricity	
5 minutes	- 20 microvolts
5 minutes	- 20 microvolts
10 minutes	- 20 microvolts
15 minutes	- 20 microvolts
15 minutes	- 20 microvolts
60 minutes	+ 60 microvolts
	- 40

$\bar{x}$ = -7 microvolts, +60 to -20 microvolts

$p > > 0.5$ that this change is due to chance

Electrically Induced Vasoconstriction

The common iliac artery was stimulated electrically on six occasions for periods of up to one hour. The artery constricted to an estimated three fourths of its unstimulated size. This change in artery size was followed by a change in potential of from plus 60 to minus 20 microvolts, with a mean change of minus 7 microvolts. The potential remained within minus 60 microvolts for an hour following cessation of the stimulus (Table 12). This change is not significant.

Artery Wall Damage Effect

The potential change following hematoma in the wall of the artery in six cats was from plus 70 to minus 80 microvolts, with a mean change of minus 7 microvolts (Table 13). The potential was followed for forty minutes after injecting the blood. This change is not significant.

The potential change following coagulation of the artery by phenol on six occasions was from plus 25 to minus 25 microvolts, with a mean of minus 1 microvolt. The potential was followed for thirty minutes following the application of the phenol (Figure 13 and Table 13). This change is not significant.

The potential change following intimal damage sufficient to cause a clot on the intima on six occasions was from plus 80 to minus 100 microvolts, with a mean change of minus 11 microvolts. The potential was followed for forty minutes following the intimal damage (Figure 14 and Table 13). This change is not significant.

The potential change following crushing of the artery on six occasions was from plus 300 to minus 300 microvolts, with a mean change of minus 17 microvolts (Table 13). The potential was followed for one hour

TABLE 13

EFFECT OF TRAUMA ON THE POTENTIAL IN SIX CATS

Hematoma

- 80 microvolts
- 70 microvolts
- 50 microvolts
+ 30 microvolts
+ 60 microvolts
+ 70 microvolts
- 40

$\bar{x}$ = -7 microvolts, +70 to -80 microvolts

$p > > 0.5$ that this change is due to chance

Coagulation

- 25 microvolts
- 20 microvolts
- 10 microvolts
+ 10 microvolts
+ 15 microvolts
+ 25 microvolts
- 5

$\bar{x}$ = -1 microvolt, +25 to -25 microvolts

$p > > 0.5$ that this change is due to chance

TABLE 13--Continued

intimal

- 100 microvolts
- 40 microvolts
- 15 microvolts
0 microvolts
+ 10 microvolts
+ 80 microvolts
+ 65

$\bar{x}$ = -11 microvolts, +80 to -100 microvolts

p >>0.5 that this change is due to chance

Crushing

- 300 microvolts
- 100 microvolts
- 100 microvolts
0 microvolts
+ 100 microvolts
+ 300 microvolts
- 100

$\bar{x}$ = -17 microvolts, +300 to -300 microvolts

p >>0.5 that this change is due to chance

Fig. 13.--Coagulated artery

after the crushing was done. These large potential changes were probably due to movements of the aorta and electrode catheters when the crushing was done. This change is not significant.

Occlusion and Stasis Effect

The potential change following occlusion of the aorta on forty-two occasions was from plus 50 to minus 50 microvolts, with a mean of plus 7 microvolts. This potential change occurred when the aorta was occluded even after death possibly indicating that the change was a reflection of the physical movement of the aorta caused by the hemostat rather than a real change in potential due to stasis (Figure 15 and Table 14). This change is not significant.

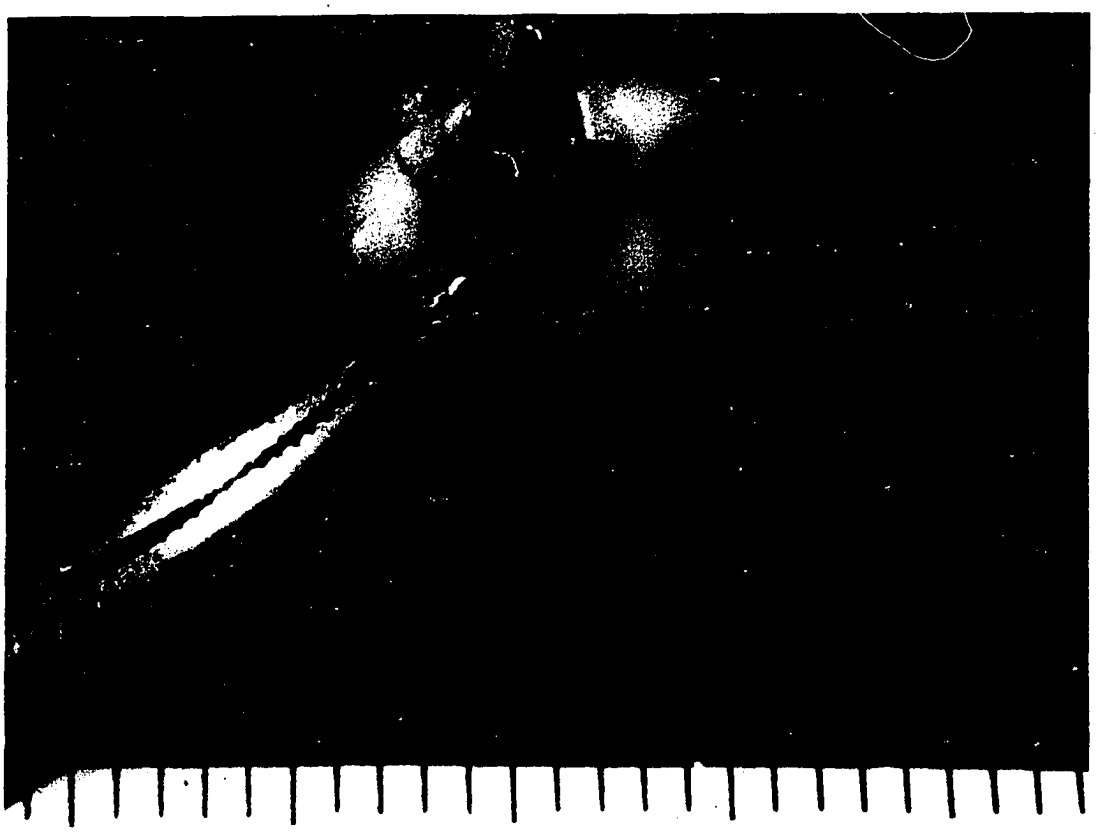


Fig. 14.--Abraded artery

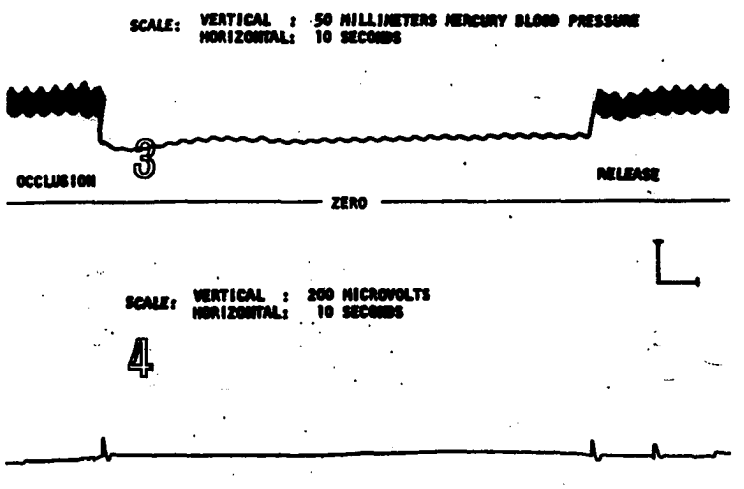


Fig. 15.--Sample trace of response to occlusion

TABLE 14

EFFECT OF OCCLUSION ON THE POTENTIAL IN NINE CATS

-	50 microvolts	
-	50 microvolts	
-	50 microvolts	
-	50 microvolts	after death
-	40 microvolts	after death
-	25 microvolts	after death
-	25 microvolts	
-	20 microvolts	
-	20 microvolts	
-	20 microvolts	
-	15 microvolts	after death
-	10 microvolts	
-	10 microvolts	
-	10 microvolts	
-	10 microvolts	
-	10 microvolts	
-	2 microvolts	
+	2 microvolts	after death
+	5 microvolts	
+	10 microvolts	after death
+	10 microvolts	
+	10 microvolts	
+	10 microvolts	
+	10 microvolts	
+	10 microvolts	
+	20 microvolts	after death
+	20 microvolts	
+	25 microvolts	
+	25 microvolts	
+	25 microvolts	
+	35 microvolts	
+	35 microvolts	
+	35 microvolts	
+	40 microvolts	after death
+	40 microvolts	
+	50 microvolts	after death
+	50 microvolts	
+	50 microvolts	
+	50 microvolts	
+	50 microvolts	
+	50 microvolts	
+	50 microvolts	
+	300	

$\bar{x}$ = + 7 microvolts, +50 to -50 microvolts

p > >0.5 that this change is due to chance

The potential change following pneumothorax and cessation of the heart beat on ten occasions was from plus 85 to minus 75 microvolts, with a mean change of minus 4 microvolts. The potential was followed for fifteen minutes after the last heart beat (Table 15). This change is not significant.

TABLE 15

EFFECT OF STASIS ON THE POTENTIAL IN TEN CATS

- 75 microvolts
- 50 microvolts
- 40 microvolts
- 30 microvolts
- 10 microvolts
0 microvolts
+ 10 microvolts
+ 30 microvolts
+ 40 microvolts
+ 85 microvolts
- 40

$\bar{x}$ = -4 microvolts, +85 to -75 microvolts

$p > > 0.5$ that this change is due to chance

Clotting Effect

Flushing of the inner electrode catheter caused little or no change in the potential measured by the electrodes if only a short time had elapsed since the previous flushing. If, however, sufficient time had elapsed since the previous flushing for a clot to form or for diffusion to have occurred in significant amounts, the change in potential following flushing was considerable. This change in potential was sometimes as much as 1 millivolt either positive or negative.

CHAPTER V

DISCUSSION

The experiments reported in this paper indicate that the resting potential between the lumen and the adventitia of the large arteries is small (mean of twenty-eight measurements plus 276 microvolts), and that this potential is stable. The changes in potential following the various stimuli are all small, with the largest potential changes occurring following the infusion of acetylcholine. This change may be due to the fact that this agent may raise the hydrogen ion concentration thereby raising the potential. This change of 90 microvolts corresponds to a pH change of less than 0.002 pH units, certainly too small a change to be measurable except with a system comparable to the one used in this experiment to measure the resting potentials. Similarly, the potential changes following the infusions of adenosine triphosphate may be due to the same mechanism, as this agent also would release hydrogen ions. The oppositely directed shift in potential during local vasoconstriction induced by epinephrine could be explained by the same mechanism if it is remembered that in this case the outer electrode catheter would be the one affected by the change in pH.

None of the other changes are large enough to unequivocally rule out the possibility that the changes are due to the electrical noise in the animal and to electrode drift. Only three results were significant

to the 0.15 level of significance. Large increases in blood pressure, as occurred during infusion of epinephrine, are followed by changes in potential of the same sign as those which follow large decreases in blood pressure, as occurred during infusion of acetylcholine. These potential changes are not correlated with the blood pressure changes. Practically no change in blood pressure occurred during infusions of bradykinin yet the potential changed in a similar manner. The changes in potential following the infusions of sodium chloride indicate the amount of spurious potential which can be generated by the animal itself.

The frequently seen three to five minute fluctuation in potential of unknown origin further complicates the interpretation of any change which is not of a sufficient size or is not rapid enough to rule out the possibility that it is a spurious potential change. The average change in potential following each type of stimulus is from plus 36 microvolts for the depressor agents to minus 22 microvolts for the vasoconstriction. These changes do not seem large enough to be causative factors in electrophoretic clot formation (Table 16).

These equivocal, and small, changes in potential, most of which are not significant, in response to extreme stimuli would seem to cast doubt upon the hypothesis that the mechanism whereby a clot or plaque is formed is one of an electrophoretic nature. The change in potential following the various stimuli used in the foregoing experiment, of from plus 36 to minus 22 microvolts, would cause a potential gradient across an artery wall of one half a millimeter thickness of less than one millivolt per centimeter. This would cause a current density of less than 10 microamperes per square centimeter, which value is well below the minimum current density required to form intravascular clots (20).

TABLE 16

MEANS OF POTENTIAL CHANGES FOLLOWING THE VARIOUS STIMULI

Stimulus	Mean	Range	p
0.85% Sodium Chloride	0 microvolts	+ 25 to - 25 microvolts	
Heparin	+ 15 microvolts	+ 70 to - 20 microvolts	<0.2
Pressor Agents			
Epinephrine	+ 25 microvolts	+ 100 to - 75 microvolts	<0.4
Angiotensin	- 2 microvolts	+ 40 to - 40 microvolts	>0.5
Vasopressin	- 1 microvolt	+ 30 to - 50 microvolts	>0.5
Norepinephrine	- 1 microvolt	+ 10 to - 10 microvolts	>0.5
	+ 21		
	$\bar{x}$ = + 5 microvolts		
Depressor Agents			
Adenosine Triphosphate	+ 16 microvolts	+ 30 to + 5 microvolts	<0.1
Acetylcholine	+ 90 microvolts	+ 350 to - 100 microvolts	<0.15
Bradykinin	+ 3 microvolts	+ 40 to - 30 microvolts	>0.5
Histamine	+ 35 microvolts	+ 100 to - 10 microvolts	<0.3
	+ 144		
	$\bar{x}$ = + 36 microvolts		

TABLE 16--Continued

Stimulus	Mean	Range	p
Vasoconstriction			
Chemical	- 37 microvolts	- 20 to - 40 microvolts	<0.001
Electrical	- 7 microvolts	+ 60 to - 20 microvolts	>0.5
	- 44		
	$\bar{x}$ = - 22 microvolts		
Arterial Wall Damage			
Hematoma	- 7 microvolts	+ 70 to - 80 microvolts	>0.5
Coagulation	- 1 microvolt	+ 25 to - 25 microvolts	>0.5
Intimal	- 11 microvolts	+ 80 to - 100 microvolts	>0.5
Crushing	- 17 microvolts	+ 300 to - 300 microvolts	>0.5
	- 36		
	$\bar{x}$ = - 9 microvolts		
Occlusion	- 7 microvolts	+ 50 to - 50 microvolts	>0.5
Stasis	- 4 microvolts	+ 85 to - 75 microvolts	>0.5

Sawyer and his group (16 to 19) reported a resting potential of from minus 1 to minus 5 millivolts between the lumen and the adventitia of the aorta. They further reported that this potential changed polarity and magnitude making the lumen to adventitia potential plus 1 to plus 15 millivolts following injury.

On the basis of this report the experiments described in this paper were undertaken. Shortly after these experiments began it became obvious that the previous reports were in error and, after they were nearly completed Sawyer (33) reported that his original results were indeed in error and that the potentials measured were those resulting from streaming potentials. His group has recently measured streaming potentials in the rabbit aorta of from minus 10 to minus 30 millivolts (33).

As these experiments progressed several possible sources of the potentials measured by the original investigators (16 to 19) were found. In these original experiments the electrodes were not juxtaposed, no provision was made to flush the electrodes free of clotted blood, and damaged tissue was allowed, even deliberately interposed, between the two electrodes. In addition, the electrodes were moved relative to one another while potentials were being measured. Each one of these errors in method can account for a considerable potential. In the experiments reported herein the potential between an electrode catheter in the artery lumen and another wrapped firmly around the artery can measure as much as 3.5 millivolts, depending on the placement in the artery of the inner electrode catheter relative to the outer (Figure 9). This potential is not a characteristic of the artery but rather is a characteristic of the tissue in which the artery lies. That is, the same pattern of potentials is measured whether both electrode catheters are simultaneously inside the

artery or simultaneously outside, or if one is inside the artery and the other is outside or if both electrode catheters are in tissue space. Clots inside the catheter lumen or on the end of the catheter can cause a potential of more than a millivolt of either sign. Damaged tissue is well known to produce potentials of anything up to plus 90 millivolts (15). The potentials on the vascular tree (Figure 9) would also be measured as potential changes if the electrode catheters are moved relative to one another up and down the aorta.

Any or all of these sources of potential could account for the erroneous results reported by Sawyer.

There is no doubt that streaming potentials exist in the aorta and other arteries but an accurate measurement would be a difficult procedure as these streaming potentials are superimposed on the large DC potential field in the animal. As an adjunct to the measurements made in this experiment an approximate value of minus 200 microvolts for the streaming potential may be derived. That the DC potential field in the animal is not due to streaming potentials is certain, because this field changes but little in the first few minutes following cessation of the heart beat. The three to five minute periodicity in this potential has no obvious connection with respiratory movements, peristalsis movements, skeletal muscle movements, or changes in blood pressure. The possibility exists, however, that movement of the aorta could have occurred over that long a period of time and not be noticed. A relatively small movement could account for a change in potential of 200 microvolts. This movement of the aorta could be the result of peristalsis or diaphragmatic movements. None of these organs was constrained during the experiment.

CHAPTER VI

SUMMARY

The DC resting potential difference between the lumen and the adventitia of the aorta, the common iliac, and the femoral arteries was measured in the unstimulated, anesthetized animal. For this measurement the two electrodes were carefully juxtaposed, one inside and the other outside, the artery. Following this measurement various stimuli were applied to the animal and the potential changes following this stimulus were recorded. The stimuli used were of four types: 1) arterial wall damage inflicted by crushing with a clamp, by phenol coagulation, by intimal abrasion, and by an intramural injection of blood, 2) increases and decreases in blood pressure induced by vasoactive agents, 3) local vasoconstriction induced by chemicals and by electrical stimulation of the wall muscle, and 4) interruption of blood flow by mechanical occlusion of the artery and by pneumothorax.

The resting potential difference between the lumen and the adventitia was very small--the mean of 28 measurements in 20 different animals was 276 microvolts, lumen positive with respect to the adventitia, with a range of from plus 550 microvolts to minus 150 microvolts. Furthermore, this potential proved to be very stable--the largest changes following the various stimuli were plus 90 microvolts after infusions of

acetylcholine and minus 37 microvolts after chemically induced local vasoconstriction. There was no correlation between the direction of the blood pressure change due to different agents and the direction of the potential change.

The results of this experiment indicate that the large arteries do not exhibit a large injury potential and therefore that the electrophoretic theory of the genesis of intravascular thrombi and perhaps plaques, at least as viewed from a gross, as opposed to a microscopic, level, would seem to be invalid.

Heuristically, this experiment indicates that a further study of the electrical forces in blood and their role in maintaining fluidity and in clotting will involve an investigation of the zeta potential. This potential may assist in maintaining fluidity by preventing clumping and stasis of cells by virtue of the electrostatic repulsion due to this potential. These forces are effective only within a few molecular diameters of the charged surface of the cell.

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