Theses.
Drewry
Prize
1940

A STUDY OF THE ELECTRICAL POTENTIAL OF THE GASTRIC MEMBRANE IN THE DOG. [1]

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A Submission in Application for the E.L. Drewry Memorial Scholarship and Medal.

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Aided by a grant from the Richardson Research Fund of the Winnipeg General Hospital.

An abstracted version of this submission has been accepted for publication in the American Journal of Physiology under co-authorship of H.V. Rice and R.T. Ross.

In reviewing the literature concerning the electrobiological phenomenon observed in the stomach one finds that some twelve different authors have contributed to the subject.

The first experiments were done in 1927 by Mond, the only worker to use frogs stomachs. Rehm has contributed the greatest number of papers and has directed his work towards discovering the source of the potential and correlating it to the gastric secretion. Goodman, on the other hand, approached the problem from a clinical and diagnostic point of view entirely. His work has been done solely on human subjects.

Mond (1) in 1927 measured the electrical potential of the frog's stomach and found values between 10 and 70 millivolts. He noted that the longer the time spent in the preparation of the experiment and the more handling and trauma incurred by the stomach during the procedure, the greater was the tendency for the resting potential to be low. Using an artificial vascular perfusion apparatus he has caused temporary reductions in the value of the potentials.

There was a marked reduction of potential with the perfusion of .01% potassium cyanide, distilled water, 6.5% NaCl, .65% NaCl, .1% $HgCl_2$, and potassium added to Ringer's saline solution. In every case however, the reduction was reversible and the potential difference returned to normal with the reperfusion of oxygenated, heated, normal Ringers. He also found that .03% and .06% heptyl alcohol were without effect and that atropine, acetylcholine and adrenalin were without effect.

In this respect Mond is the only author to report no change in potential difference from acetylcholine and adrenalin. He also reports that hydrogen ion increases in the perfusion fluid caused a reduction in the

potential. On the other hand, within the lumen of the stomach he states that only the actual concentration or normality of the solutions, regardless of their nature, had an effect on potential difference. He concludes that for the salts tested their only effect on potential is when they are applied from the bloodstream side in the perfusion apparatus.

In 1932 Mislowitzer and Silver (2) did a similar piece of work and duplicated Mond's technique fairly accurately with the introduction of several refinements. Using cats under pernoston anaesthesia, they found the potential of the stomach to range from 70 to 80 millivolts. Introducing the mucosal electrode via the oesophagus and placing the serosal one on the center of the anterior wall they found the potential to be substantially lower in the pylorus than in the fundus and cardia. Furthermore they observed that it is of considerable importance to ensure a good contact and a permanent contact between the mucosa and the mucosal electrode and that the position of the mucosal electrode is more important than the position of the serosal electrode. This latter fact has not been mentioned by any other investigator but was found to be of maximum importance in this investigation.

Contrary to Mond they found that differences in the normality of solutions contained in the stomach did not produce changes in the potential difference but noticed various potential responses from equal volumes of solutions of the same degree of normality of chloride, citrate, iodide, and bromide salts. Sodium chloride introduced into the stomach doubled the resting potential in many cases. The increase lasted anywhere up to one hour and then returned to its normal resting level. On the other hand, equal concentrations of sodium citrate and sodium iodide caused a reversible reduction in potential, the citrate salt having the greater effect. A certain number of experiments were also directed towards an evaluation of the effects of other

metals and some of the alkaline earths. A reversible reduction of approximately 20 millivolts was found when N/10 lithium was introduced into the stomach. Similarly they found that N/10 calcium caused a reduction of from 10-15 millivolts, while ammonium was without effect. In each case the chloride salt was used. Mislowitzer and Silver also changed the concentration of hydrogen ions in the vascular perfusion apparatus. They noticed that it required fairly large pH changes (.5 to 1.5 pH) for a considerable length of time before the potential difference was effected. However the potential difference could be decreased by making the perfusion fluid either acid or alkaline and it always returned to normal when the pH of the fluid was brought back to 7.33 $\pm$ .03. Again, contrary to Mond, they found that the addition of alcohol to the perfusion fluid caused a reversible reduction in the potential difference. No mention is made as to the concentration of the alcohol or how much was added. They found reductions in potential with intravenous injection of histamine (.2 - 2.0 mgms.) and also with fairly large doses of adrenalin (.2 to 2 c.cs. of 1: 1000).

They have gone on to conclude that as these large injections produced very small rapidly reversed reductions in potential and, that as a shift of the acid-base balance of the blood to either side did not permanently influence the potential, that the effects from the bloodstream side are secondary. The only direct method of changing the potential is through the nature of the substance within the stomach. They also find that vagal stimulation, both peripheral and intact, is without effect as is vagal section. However they do corroborate Mond's findings concerning the condition of the animal having an important effect on the resting potential and that the magnitude of the recordable potential is indicative of the general metabolic state of the animal. That is, with vomiting, pulmonary edema, bradycardia or a fall in blood pressure there was a marked reduction in potential.

Later in conjunction with Rothschild (3) they found that by placing ionic solutions of substances of different absorbability in the stomach that the potential difference decreased during the periods when the greatest absorption was going on from the stomach.

Sarre (4) in 1934 also worked with cats and used pernoston as an anaesthetic. He successfully demonstrated the fact that there was a definite potential difference across the gastric membrane. He was the first investigator to mention that the mucosal surface was negative with regard to the serosal, a fact which has since been found true by every subsequent worker. Unlike Mislowitzer and Silver he found an increase in potential when the stomach was stimulated to secrete from the injection of histamine.

Adair and Goodman (5) measured the electrical potential in human subjects and reported an accurate description of their apparatus. They used platinum calomel electrodes which showed a constant minute polarization potential difference of 0.4 millivolts. The resistance of the entire galvanometer was only 400 ohms and this was used in conjunction with a potentiometer. The mucosal electrode in each experiment was a string soaked in potassium chloride which was passed by means of an ordinary stomach tube. It made contact with the mucosa at one end and with the platinum calomel electrode at the other. The circuit was completed by means of introducing the other electrode into the ante-cubital vein. The potential they recorded varied from 30 to 50 millivolts. These workers also observed the fact that the mucosal electrode was negative with regard to the skin electrode. Of a short series of 4 experiments they observed in two cases an immediate fall in potential after taking milk, in one case no change, and an increase in potential difference in the remaining subject. They believe the time interval between the last

meal and the initial reading to exert an effect on the response to milk.

Quigley et. al (6) have repeated certain phases of Sarre's work using the apparatus of Adair and Goodman (5) on the stomach and pouch of unanaesthetized Pavlov dogs. They placed a combined stomach tube and electrode via the oesophagus into the stomach and another into the pouch. The tubes were used both as carriers and insulators for the electrodes and also served as a means of administering the test solutions. The circuit was completed by placing the other electrode on the abraded skin. They found the resting potential of the stomach to be from 20 to 30 millivolts and of the pouch to be from 10 to 20 millivolts. The initial resting potential varied with the time interval after the last meal as was observed by Adair and Goodman (5) and apparently was not related to hunger contractions or movements of the stomach from respiration. Unlike Mislowitzer and Silver they observed no change in potential difference following the subcutaneous injection of 0.5 milligrams of histamine. Also 2 milligrams of pilocarpine intravenously or 1 milligram of atropine failed to cause any significant change in the potential. Similarily they observed no change in potential when solutions of a pH range of from 1.08 to 9 were introduced into the stomach. Neither did hypertonic, isotonic or hypotonic NaCl solutions effect the potential when introduced into the stomach or pouch. However, the perfusion of the stomach with 5% dextrose caused an increase in potential difference of both the stomach and the pouch while no change was seen from the intravenous injection of the dextrose. It was observed that the introduction of whole milk into the pouch increased the potential difference of the pouch whereas whole milk in the stomach decreased the electrical state of both stomach and pouch.

Soluble casein was without effect and emulsified fat had the same effect as whole milk in both stomach and pouch. It was observed

that alcohol (7% - 10% ethyl) introduced into the pouch increased the potential difference of the pouch while alcohol of the same concentration in the stomach increased the potential difference or negativity of both the stomach and the pouch. It was found that these increases in potential difference were unrelated to secretion, for although the administration of alcohol both intravenously and directly into the stomach increased the secretion, only the alcohol placed directly into the stomach had an effect on potential.

Rehm (7) in an elucidation of the hypothesis that electro-endosmosis may be the mechanism by which osmosis is performed by living organisms has measured the electrical energy output of the resting stomach. He has used zinc acetate-agar electrodes and shunted the potential of the stomach through a low resistance circuit. Working with dogs under light pernoston anaesthesia, Rehm states that the stomach can maintain a constant potential difference across its wall despite the fact that the maximum current is being withdrawn. He demonstrates almost conclusively that current as high as 200 to 270 microamperes per square centimeter of stomach can be produced continually without any appreciable maintained depolarization of the difference in potential across the gastric mucous membrane. Further, he has gone on to calculate that of the total metabolic energy of the resting, non-secreting stomach, 1.9% to 4.4% of this energy may be obtained and measured as electrical energy. He concludes from this, that as there is no maintained depolarization of the potential during the flow of the maximum current, that the difference in potential across the gastric mucous membrane is capable of producing sufficient energy for the continuous secretion of gastric juice.

Following this (8) in an attempt to correlate the effect of histamine and hydrochloric acid on secretion and potential, Rehm devised an apparatus to include a small area of stomach (21 square centimeters) in

a minature water bath which readily facilitated the measurement of the rate of secretion as well as the potential. Again using dogs under pernoston anaesthesia, with zinc acetate and saturated potassium chloride electrodes; the potential was decreased to a relatively constant level with a progressive increase in secretion from repeated subcutaneous doses of histamine. Rehm determined the effect of pH changes due to gastric secretion on the potential and found that when a histamine induced secretion had reached its maximum quantity and the pH of the saline in the water bath chamber had changed from approximately 6 to a pH of 1.9 to 2.6, the replacement of this fluid with fresh saline never altered the potential by more than 3 millivolts. Therefore, the effect of the acid secretion of the stomach on the recordable potential is insignificant. This was demonstrated again by placing an isotonic phosphate buffer of a pH of 7.2 to 7.5 in the chamber. After histamine stimulation the potential decreased to the same extent as with saline in the chamber, while the pH remained practically unchanged due to the presence of the phosphate buffer.

Rehm also made the astute observation that as the HCl secreted by the stomach diffuses into the fluid in the chamber that there might well be a diffusion potential that would be orientated toward the mucosal electrode i.e. opposite to the potential of the stomach, and thereby the apparent reduction of the stomach potential difference following histamine might merely be the effect of a greater diffusion potential in an opposite direction overcoming the constant potential of the stomach. In an attempt to determine to what extent this diffusion potential contributes to the decrease in the potential after histamine stimulation, the effect of a synthetic diffusion of HCl on the potential was tried. The experiments were performed with solutions of HCl varying in pH from 0.64 to 1.03. After the stomach had been stimulated with repeated injections of histamine and the potential had reached

its new level, approximately 200 c.cs. of HCl were run into the chamber and the pH of the last 50 c.cs. of the solution leaving the chamber was found to equal that of the original HCl to within 0.02 of a pH. The fact that the potential remained at the maximum low level for some time after the flow had ceased is evident that the decrease in potential is not due to a diffusion potential.

Histamine stimulation, while the potential was still depressed from previous histamine was followed by secretion and comparatively little change in the magnitude of the potential.

In a subsequent paper (9) Rehm demonstrated that electric current applied to the secreting stomachs of pernostonized dogs from serosa to mucosa resulted in an increase in the secretion of HCl. This was not found however in non-secreting stomachs. When current is applied in the reverse direction, i.e. from mucosa to serosa, there is a decrease in secretion along with depression of the potential. With the cessation of the current the secretion slowly returns accompanied by the potential. It was also found that histamine stimulation, following the depression of the potential from the application of current from mucosa to serosa in the non-secreting stomach, resulted in secretion and was associated with a relatively small change in the potential. In these experiments the level of the potential, after secretion was well established was essentially the same as that found in secreting stomachs not initially depressed by applied current.

Later in collaboration with Enelow (10) Rehm found that when small amounts of sodium thiocyanate were administered to dogs to completely inhibit the gastric secretion, that the potential remained unchanged and constant at the resting level. When given in larger amounts it was found that as the drug took effect the potential slowly increased to a new level where it remained for the duration of the experiment.

In his most recent paper (12) Rehm has presented rather con-

clusive evidence that the major part of the gastric potential originates between the submucosa and mucosa. By developing an apparatus which employs three electrodes; one on the mucosa (m), one in the sub-mucosa (S-M), and one on the serosa (S), recordings were made of the difference in potential between M and S electrodes in the usual manner. It was found that the potential difference in the resting stomach between the sub-mucosal and mucosal electrodes was esentially of the same magnitude as that between the serosal and mucosal electrodes. It was also found that the changes in potential that occur following histamine injection are only recorded from the mucosal-submucosal electrodes or the mucosal-serosal electrodes. The submucosal-serosal electrodes show no change. Further, the difference of potential in the resting stomach recorded from the submucosal-serosal electrodes is only a small fraction of the total potential difference of the stomach. Rehm concluded that the electromotive force originates in the secretory portion of the stomach.

Finally, Goodman (11) using a Leeds and Northrop special micromax recorder, which is in effect a high resistance potentiometer, and electrodes employing liquid junctions which prevented the actual electrode from making contact with the living tissues, studied a series of known normal stomachs and known cases of duodenal ulcer, gastric ulcer and gastric carcinoma. Data is presented on the various lesions indicating a characteristic response to milk in the normal and in each of the conditions mentioned above.

APPARATUS

It was seen at an early stage in the investigation of this problem that it was necessary to develop recording equipment that provided both stability and sensitivity. It was also desirable that the apparatus would faithfully record voltage changes as fast as one per second. The apparatus consists essentially of three parts, viz: electrodes, amplifier, and recording galvanometer.

The amplifier was designed so that the actual current drawn from the stomach was nil and it merely amplified the difference in potential across the gastric mucous membrane. This was facilitated by having a high input impedance (1 megohm) to the amplifier. By this means a recording galvanometer of high resistance was operated from the amplifier. It was found that this high resistance of the electrodes, amplifier and galvanometer in no way interfered with the recording of the potential differences.

ELECTRODES

There are three necessary features in any recording electrodes all of which must be present and constant. These are (a) constant (and in this case high) resistance, (b) contact with the tissue without injury to them and (c) absence of polarization at the point of contact with the tissues. The electrode system as shown in Figure 2. consists of two saline bridges connected at one end with the silver input leads of the amplifier, and making contact at the other end with the stomach. Plastic tubing of 2.5 m.m. inside diameter was used. These proved to be more comfortable than standard naso-gastric tubes being more flexible and having a relatively smaller outside diameter for their bore due to the thinness of the wall; they were therefore easier to insert. They are also unaffected by moisture. The concentration of the

electrolyte used to fill the tubes was not critical, provided it was great enough to provide sufficient conductivity; 10% NaCl proved satisfactory. It was essential however, for the concentration at the two silver junctions to be identical. Connections between the saline bridges and the amplifier input leads were made through chlorided silver wire in a glass T. tube which permitted replacement of the electrolyte by flushing (Figure 2.).

The distal end of each bridge was closed with a spruce plug $\frac{1}{2}$" long. This provided a mechanical obstruction to the escape of saline from the tubing but did not significantly decrease the electrical conductivity. This procedure was adapted because it was found in the early experiments that pinching the tubing during insertion or even swallowing expelled a small amount of electrolyte which was replaced by a bubble of air; and a sudden drop in voltage occurred due to the resulting high increase in resistance of the lead. It was also found necessary to boil the saline, since gas bubbles were driven off in the tubing by the heat of the body if this were not done, and again a high resistance was imposed in the bridge with a consequent reduction in recorded potential. To ensure that the end of the gastric electrode did not become occluded by end on pressure against the gastric wall, small windows were cut in the wall of the tubing for a distance of 1" from the end and distal to the wooden plug. The space in the tip of the tubing (distal to the plug) was filled with a wick of cotton wool moistened with saline. This ensured contact with the mucosa and therefore electrical conductivity with a minimum chance of damage to the mucosa from electrode pressure or stomach movements.

By following the foregoing description, the electrodes were found to be of constant resistance, of good conductivity and had no detrimental effect on the tissues that they came in contact with. The subject of polarization must be gone into in some detail. Polarization, which may be described as an extraneous current resulting from the contact of electrode and

tissue, is capable of causing entirely spurious results. A current of polarization may occur at one or both electrodes and may be equal or greater than the original difference of potential which is properly being recorded. Similarily the current of polarization may be in the same direction or in the opposite direction to the potential difference being recorded. It is obvious therefore, that any current of polarization must be small, ideally less than 1% of the recorded potential, must be constant, and must at all times be recognized and considered in the results. For these reasons electrodes were devised which minimized or obliterated any polarization. The contact with the tissues by cotton soaked in saline, the use of saline bridges and the silver-silver-chloride junctions at the galvanometer input, along with the fact that both sides of the saline bridge were filled with saline of the identical concentration, all helped towards this end. As is shown in Figure 2. the upper set of glass T. tubes are provided with rubber tops. These facilitated the flushing out of the entire electrode with fresh saline. It was possible by means of the clamps shown to close off the electrode when filled and maintain the bridge as an air free closed system.

AMPLIFIER (Figure 1.)

The purpose of this amplifier is to amplify minute direct current differences of potential. As was stated earlier the difference in the electrical condition (actually, the number of electrons) of the mucosal as opposed to the serosal side of the stomach is described as a difference of electrical potential. As these differences are very small it is necessary to have the amplifier to exaggerate them. The circuit diagram of the amplifier is shown in Figure 1. It is a balanced, single stage, push pull, pentode, Class A amplifier. The input impedance is high being 1 megohm.

The input is represented by the two points A and B, coming

from the silver-silver-chloride junctions of the electrodes. After passing through the two variable resistors R9 and R10 which are each 500,000 ohms, the input is fed to the control grids of the two 3Q5GT. tubes. The 250 ohm resistor, R11, between the filament and the ground provides a small standing negative bias on the grids with respect to the filaments.

The output is represented on photographic paper by means of a moving coil galvanometer, and is also balanced. The screen grids are connected directly to 45 volts positive. The plates receive this 45 volts via a balanced load network, resistors R12, R13, R14, R15, and the shunting effect of the galvanometer coil. The resistances are made variable so that when there is "no input", the current through the two tubes may be balanced. When this occurs there is no difference in potential between the two points "X" and "Y", and therefore, no current flowing through the galvanometer coil and consequently there are no deflections. When however, a minute difference in potential exists between the input terminals "A" and "B", the more positive terminal causes one tube to conduct more than normal, and the negative terminal causes the other tube to conduct less than normal. The net result of these conditions is an unbalance in the load resistors R12, R13, R14, R15, causing a difference in potential to exist between "X" and "Y". This in turn allows a current to flow through the galvanometer coil causing it to swing between the poles of its magnet. Very slight changes in potential on the control grids of these tubes produce relatively large changes in the current flowing through them. The deflection of the galvanometer mirror is a highly magnified undistorted replica of the input voltage. Although this is a simple explanation of the purpose and function of the amplifier, there are still a few technical points that need mentioning. The two tubes used provided economy of operation and had sufficient gain and a low enough plate impedance to match the galvanometer used. The problem of drift or base line instability

was dealt with by using a common cathode bias resistor. Drift due to varying radiation and conduction of heat from the tubes to the chasis was practically eliminated by raising the tubes slightly in their sockets so that there was no physical contact between the base of the tubes and the chasis. The galvanometer was connected from plate to plate of the two tubes and the voltage across it equalized (with no potential difference across the input of the amplifier) by adjusting the center top of a wire wound potentiometer connected to the high voltage source.

GALVANOMETER

The galvanometer was of d'Arsonval type using two 2 inch permanent magnets of the type used in small loud speakers. The moving coil was wound with 2,000 turns of number 42 enamel covered wire and had a D.C. resistance of 4,000 ohms. It was suspended vertically by a fine phosphor-bronze wire allowing a linear torque movement. Records were taken on slow moving velox paper, by means of a light beam reflected from a silvered microscope cover slip attached to the galvanometer coil. A second light beam reflected from the galvanometer mirror was focused on a red glass viewing screen, and provided opportunity to observe the voltage being recorded. Maximum gain of the amplifier with the saline-bridge electrodes used, provided full-scale deflection (5 inches) of the light beam with 30 millivolts input. A dual potentiometer in the grid circuits provided any gain required up to the maximum without changing the impedance of the input system.

CALIBRATION

Calibration of the apparatus was carried out by applying potential differences of 10-60 millivolts, from a voltage divider in 10 millivolt steps. The calibrator voltages were applied through the saline bridges from a second pair of low resistance silver-silver-chloride junctions con-

nected to the calibrator. The arrangement of the calibrator is shown on the left hand side of Figure 1.

In some experiments gastric secretions were recorded simultaneously with potentials. The secretions were collected in a 2 c.c. plastic thimble held in a loop on the arm of a spring balance. The latter was connected with a pivoted mirror which recorded the secretions by means of a reflected light beam onto the same paper as was used to record the potentials. The spring balance gave linear displacement of the light beam as the weight of the secretion in the thimble increased from its zero position. Several thimbles of identical weight were provided so that when one thimble had filled it could be replaced instantly by another with the return of the light beam to its former base line. The quantity of secretion per unit of time is indicated therefore by the total upward excursion of the light beam, and the rate of secretion is apparent from the slope of the graphic record. The more rapid the secretion, the closer to the perpendicular is the photograph of the light beam representing the secretion. The spring balance was calibrated from time to time with known weights and the actual secretion was also weighed in many instances. The photographic tracing also actually provided an accurate record of the weight of the secretion.

PROCEDURE

The early experiments in this work concerned an effort to record gastric potentials in humans using the technique outlined by Goodman (12) with slight modifications. This series proved to be unsatisfactory mainly because it was impossible to obtain consistent records. There was almost continuous variation in the recorded potential to an extent which prevented any conclusions being reached concerning either the steady state or the reasons for the variations. It appeared that the instability was partly due to technical error, e.g. changing electrical contact in the stomach, and partly due to physiological variations which were not understood. Furthermore the evidence was fairly strong that the emotional state or the condition of rest or alertness of the patient materially effected the gastric potential being recorded from minute to minute. For example, a sudden noise caused a rapid decrease in potential lasting several minutes.

In one patient a change in potential produced by such an interruption was characteristically reproduced on more than one occasion. Since such variations in potential difference occurred, the causes of which were not understood, it seemed unlikely that the investigation of patients with gastric lesions would provide results which could be interpreted. Therefore a series of animal experiments were undertaken in an effort to clarify further the more fundamental control of the gastric potentials.

In all cases dogs were used weighing from 5 to 15 kilogrammes. They were anaesthetized with soluble barbitone, 225 milligrams per kilo give intraperitoneally. The neck and abdomen were clipped and a mid-line incision was made in the neck and a tracheal cannula inserted. A venous tap cannula for the administration of drugs was inserted in the internal jugular vein. The stomach was then brought into a mid-line abdominal incision and a flanged

glass gastroenterostomy tube 1.5 c.m. in diameter and 15 c.m. long was tied into the anterior wall of the stomach by a pursestring suture. All bleeders were caught and carefully tied. The gastrostomy tube protruded through the abdominal opening and was held vertically in a clamp. This tube provided means of introducing solutions and the recording electrode into the lumen of the stomach. To prevent salivary secretion from entering and gastric contents from leaving the stomach, the oesophagus was tied in the neck and the pylorus ligated just distal to the sphincter. In tying the pylorus, care was taken to exclude all the arcurate vessels from the ligature.

The stomach was then filled with physiological saline at body temperature and the electrode dipped into the saline filled lumen of the stomach. Various liquids were tried for this purpose among them, various saline solutions up to 10% NaCl, physiological saline, tap water, and dilute hydrochloric acid. It was decided that as far as conductivity and stability were concerned, normal saline was the most satisfactory. The level of the saline was brought half way up the glass gastrostomy tubing and this offered a visual record of peristaltic contractions of the stomach wall and movements of the stomach due to respiration. In this way the potential difference of the gastric mucosa as a whole was measured and artefacts caused by a variable contact between the mucosa and gastric electrode from respiratory movements, peristalsis etc., were eliminated.

The foregoing technique was adhered to rigidly in the first series of dog experiments where only gastric potentials were recorded.

A second series of experiments were conducted in which efforts were made to record and correlate gastric potential differences, and secretion. For the latter the following procedure was used. Tracheal and internal jugular cannulae were inserted as before. A mid-line abdominal incision was made and the stomach was exposed. A gastrostomy opening was made

on the anterior stomach wall about 2 c.ms. proximal to the proximal border of the pyloric antrum. Bleeders were caught and tied. Through this opening a spiral of 3 millimeter glass rod was inserted in to the stomach.

This served to separate and prevent opposition of the mucosal surfaces so that peristaltic waves were ineffective, and the steady flow of gastric secretion could be recorded. The size of the glass spiral in each dog was carefully chosen to avoid stretching of the stomach and possible interference with its secretory function. A straight glass tube of 1.5 c.m. diameter, to serve as a collecting tube, was then tied into the gastrostomy opening with a purse string suture. This tube was arranged so that its long axis was parallel to the long axis of the glass spiral and therefore of the body of the stomach. The dog was placed on its right side, and the collecting tube brought out through a small skin incision over the right rectus. The table was tilted and the position of the tubing adjusted in a clamp, until the long axis of the stomach and the collecting tube were in alignment and almost vertical. The gastric secretions were thus permitted to flow steadily out of the collecting tube. The gastric electrode was inserted through the collecting tube and a cotton wick in the end of it was allowed to lie on the mucosa. This gave good electrical contact. The other electrode was fixed subcutaneously as before.

All drugs and solutions given were administered either intravenously via the tap cannula, subcutaneously or directly into the stomach as noted in each instance.

RESULTS

The initial recorded potential difference ranged between 50 and 100 millivolts. This potential was steady, in that it did not show any fluctuation or wave pattern. It did show, however, a progressive and gradual increase from the beginning of the record for a variable period of 10 minutes to ½ an hour. At the end of this time when this increase was complete the potential difference remained at this new level until experimental procedure was started. It would appear that this represents a gradual return to a state of absolute basal conditions following the disturbance created by reflexes aroused during the preparation of the animal. The extent of the gradual increase of potential, until a constant level was attained ranged from 3 to 10 millivolts. These findings are in accord with those of Mislowitzer and Silver (2) and other early investigators who found that the gastric potential difference was greatest when the animal was in a resting state. They are also in accord with our early observations in humans, e.g. when the patient was disturbed the potential difference was reduced.

It was also found that in all experiments the electrode within the stomach was negative with respect to the extra-gastric lead. In none of the animal experiments was the intragastric electrode positive to the extra-gastric lead except as a terminal phenomenon following the death of the animal. Sarre (4) on the contrary recorded some instances in frogs in which the gastric lead was positive.

ADRENALIN - EFFECT ON POTENTIAL

From the observations of the effect which a sudden scare and a subsequent adrenalin release had on the potential in human subjects it was determined to try the effect of injections of intravenous adrenalin in vary-

ying doses on dogs. Thirty nine dogs were experimented on for this purpose and a total of 81 injections of adrenalin were given. Both soluble barbitone and pentobarbital were used as anaesthetics. There is no distinguishable difference in the recorded results from the use of either agent. All drugs given were made up in a solution of physiological saline. Saline given by itself as a control was without effect on repeated trial.

The response from adrenalin falls characteristically into one of two types. The first response (Figure 4A) to the larger dose (the size of the dose, and weight of the animal is given with the illustration) reaches it maximum in 2 to 3 minutes and is usually complete within 10 minutes. There is a rapid fall in potential of from 5 to 20 millivolts to a new level within 2 or 3 minutes. Having reached this point there is a return to approximately 75% of the original level in the next 2 to 3 minutes. At this point the return of the potential becomes more gradual and may take 10 minutes for complete recovery. The result, as shown in Figure 4A is an asymmetrical downward spike.

On the other hand a small dose elicits a bi-phasic response. As is shown in Figure 4B, the response to .05 c.cs. of 1: 1000 adrenalin in a 6.5 kilogramme dog is an immediate fall of about 10 millivolts within a period of of about 1 minute. Having reached this point at the end of this time there is an immediate return to the normal level at the same rate forming a symmetrical downward spike. At this point there is again a reduction in potential but slower, requiring about twice as long as previously to reach this second low point, and then a slow recovery to normal requiring as long as 20 minutes on occasion. As is shown in Figure 4B, the last two responses are typical of the effect of a small dose while the first response with a dose of .15 c.c of 1: 1000 adrenalin shows some of the characteristics of the small dosage in

the small upward spike at the peak of the response, while the long gradual recovery is characteristic of a larger dose. The critical dose would appear to be 0.0295 $\pm$ .006 c.cs. of 1: 1000 adrenalin per kilogramme. With doses larger than this the response is of the type shown in Figure 4A. This has been found to be the case almost without exception in the adrenalin response in this work.

It was also observed, that with adrenalin as many as 6 or 9 consecutive doses could be given, within a period of two hours and the response was apparently not in any way influenced by the preceding injections.

PILOCARPINE - EFFECT ON POTENTIAL

To determine the effect of pilocarpine, 25 experimental dogs were employed and a total of 45 doses of pilocarpine were given ranging from 0.1 c.c. to 1.0 c.c. of a 1% aqueous solution.

The result again followed a definite pattern in each case, the only variation being the size and duration of the response which was definitely related to the size of the dose.

Figure 5A represents a typical response to pilocarpine. In the space of 5 or 6 minutes there is a drop in potential difference of 35 millivolts to what appears to be a new permanent level of potential. This new level of approximately 40 millivolts was maintained for $\frac{1}{2}$ hour and then the potential difference slowly began to increase and after 1 hour was back to the pre-pilocarpine level. Figure 5C is another typical response in which the dose of pilocarpine is smaller. The potential begins to return to normal much sooner than the previous case and the response was complete within one hour without the period of plateau which was present with the larger dose. Figure 5B represents the response of the electrical potential to an even smaller dose. There is a small biphasic element in this response which is seen immediately after the drug is given. This increase in potential, before it was completely

decreased from the effect of the pilocarpine causes a small spike in the downward curve and cannot be explained on the basis of dosage as it was commonly found with both small and large doses. It is seen in both Figures 5B and 6 and is much more marked in 6.

Figure 6 represents a biphasic response to 3.0 milligrams of pilocarpine and a decrease in potential of 25-30 millivolts. The potential remained at this level for 10 minutes, and when 5 milligrams of atropine were given, the potential difference immediately began to increase. It reached its old level and remained steady at this level. It was observed that with the intravenous administration of atropine there was a much more rapid return to normal than if the pilocarpine response was left to recover for itself. Atropine after pilocarpine did not always produce as rapid a return as is shown in Figure 6 but almost without exception it reduced the time for the recovery from pilocarpine to occur. This, in several instances, brought the effect of the drug and the complete recovery within a space of 40 minutes, whereas if the pilocarpine had not been followed by atropine it would have required from an hour to 2 hours for the complete recovery and response to the same dose. The dose of atropine given was approximately twice the size of the dose of pilocarpine and within 2 minutes of its injection the potential difference was rising in a straight line to the pre-pilocarpine level.

HISTAMINE - EFFECT ON POTENTIAL AND SECRETION

To determine the effect of histamine on potential and secretion, experiments were carried out on 30 dogs. The secretions were collected in the plastic cup on the end of the arm of the spring balance and the rate and amount were measured and recorded simultaneously with the recording of the electrical potential. The details of this part of the apparatus and the surgical preparation of the dogs was alluded to in the discussion of apparatus and procedure. The anaesthesia used in these experiments was changed. In-

stead of soluble barbitone, eighteen dogs were anaesthetized with morphine, urethane and chloralose and twelve with pentobarbital. There was no significant difference in the results with either anaesthesia.

In every case the histamine used was a fresh aqueous solution of Ergamine Acid Phosphate (B. & W.) made up at the time of injection. The effect of a subcutaneous injection of histamine on potential was constant in all the experiments and is shown in Figure 11. Although larger doses causes a longer and greater depression of the potential, essentially the response was of the same type in all cases.

There was always a definite electrical response within less than one minute of the time of injection. There was a gradual drop in potential which was usually complete within 5 to 20 minutes of the injection and the return of the potential began as soon as the new low point was reached without any period of maintained decreased potential. The return to the pre-histamine level required from 20 minutes to one hour. In Figure 11B the time required was 20 minutes. The amount of decrease in potential difference varied from a drop of 5 millivolts in response to .02 milligrams of histamine / kilogram. to a drop of 15 to 20 millivolts in response to 0.12 milligrams of histamine per kilogram. In Figure 11A the dose of histamine was sufficient to decrease the potential 30 millivolts in 20 minutes. Although not shown there was a subsequent return of potential within the next hour to its pre-histamine level.

The effect of histamine on secretion however, produced far from constant results. In some instances, Figure 11A, the amount of secretion in a given time was increased considerably. In other such instances, as shown in Figure 11B, there was no change and the rate of secretion was the same before and after the histamine, and in other non-secreting stomachs no secretion was initiated.

After each experiment a careful post mortem was performed on the animal in the exact position that was held during the experiment. The position and drainage of each stomach considered in the results was such that all secretion formed could be collected without any mechanical or technical impedance.

Despite the variations in secretory responses from histamine, it is possible to show the same electrical response in every case. When an increase in secretion did occur (Figure 11A), the onset of the increase followed the drug approximately 5 minutes after injection while the electrical response was usually initiated within less than one minute.

PILOCARPINE - EFFECT ON SECRETION

In an attempt to determine the effect of pilocarpine on secretion and to correlate this with the potential changes, 13 experiments were performed. In every case dogs were used with intraperitoneal sodium pentobarbital as the anaesthetic agent. In 7 of these experiments there was a definite increase in secretion (Figure 10A) along with the characteristic electrical response (See Figure 5). In 6 experiments there was no change in secretion (Figure 10B) but there was the same characteristic electrical response.

When an increase in secretion did occur (Figure 10A) it did not last as long as that induced by histamine, but usually appeared within 5 minutes after the injection of the drug and had returned to the normal rate within 45 minutes to 1 hour.

ADRENALIN - EFFECT ON SECRETION

In 10 experimental animals the effect of adrenalin on secretion was determined using both the secreting and non-secreting stomach. In no instance could any change in the rate of secretion be credited to the adrenalin although in each case there was the characteristic adrenalin electrical response, seen in Figure 4.

THE EFFECT OF PERIPHERAL NERVE STIMULATION BY INDUCTORIUM ON THE ELECTRICAL POTENTIAL DIFFERENCE

Nineteen experiments were devoted to the stimulation of the vagus and the femoral nerves, intact and sectioned. The results at best are confusing. Stimulation of the central end of either the right or left vagus with the opposite one intact produced no constant effect on gastric potential difference. Also, the same is true for the central end of the sectioned femoral.

It was found that the short, quick, inconstant reduction in potential resulting from stimulation of the peripheral end of the sectioned vagus, could be reproduced by similar stimulation of fascia or muscles in the neck. It is quite apparent that some further work should be done on this aspect of the problem.

THE EFFECT OF FOOD SUBSTANCES IN THE STOMACH ON POTENTIAL

Of 17 experiments in which 25 c.cs. of a 5% sucrose solution were put into the stomach, 15 failed to produce any change in the potential difference. The change evoked in the other two was permanent and resulted in a new lower level of potential which was maintained throughout the remainder of these two experiments. This is possibly explained on the basis of conduction changes in the electrolyte within the stomach. Corn oil and alcohol were also without any immediate effect when placed directly into the stomach.

THE EFFECT OF DEATH OF THE ANIMAL ON THE ELECTRICAL POTENTIAL DIFFERENCE

In 38 experiments the condition of the electrical potential difference was recorded while the animal was dying and for some time after death. A typical record is shown in Figure 9. The dogs were usually killed with intravenous air or chloroform. The result of this embolus was death of the animal usually within 3 to 5 minutes after injection. The electrical

potential difference underwent an immediate vertical drop of from 5 to 15 millivolts. At this point the drop became more gradual and the potential then slowly approached the base line or the iso-electric zero requiring about 30 minutes in the experiment shown in Figure 9. In three instances the potential went below the base line, indicating a positive or reverse potential. A suggested explanation for this is included in the discussion.

To elaborate on the statement of Mislowitzer and Silver (2) that the recorded electrical potential difference was lower in the pylorus than other parts of the stomach, 17 experiments were performed to record the potential from the two areas of the same stomach using the same degree of amplification.

In every case the potential difference was found to be greater in the fundus than in the pylorus, the lowest potential of all being recorded from the gastric side of the pyloric sphincter.

As is shown in Figures 8A and B the response to equal doses of histamine in the same stomach is approximately the same in pylorus as in fundus. The initial potential in the pylorus was 40 millivolts while in the fundus was 60 millivolts.

DISCUSSION

Before discussing the actual results found in the investigation it was thought that a few remarks might be properly directed toward the reports of some of the contributing authors.

When one considers the report of Mond (1), it hardly seems feasible that his results can be interpreted with any accuracy. His method of a vascular perfusion apparatus was used by other workers (2) and (3) and they encountered little difficulty in this respect so that one may exclude technical errors for the apparent discrepancies that he reports. He states that the intravenous injection of acetylcholine and adrenalin produce no effect on the electrical potential difference of the stomach! Not only is he the only worker to report these negative results but he states that the changes in potential difference from various substances introduced into the stomach are dependent only on the osmotic tension of these substances and independent of their nature. This latter fact has been shown to be otherwise by four subsequent works (2), (5), (11), and (10).

One observation of Mond's that has been corroborated by almost every subsequent investigator however, is that the poorer the physiological state, fluid balance, etc., of the animal, the lower the resting potential difference. There can be little doubt in the fact that Mond actually was recording a difference of potential from the stomach but there must have been a large element of spurious polarization current in his results. Nevertheless, he did record a potential difference which could be lowered by the vascular perfusion of specific substances and which in every case was reversible when the apparatus was reperfused with Ringers.

Several of the results of Mislowitzer and Silver were borne out in this present investigation. Their findings of a higher potential dif-

ference in the pylorus than in the cardia, and of the importance of a good connection between mucosa and mucosal electrode were demonstrated on many occasions by us. Contrary to Mond (1) they found that the differences in the osmotic pressure of solutions contained in the stomach did not produce changes in the potential difference but that the actual nature of the substance was of first importance.

Mislowitzer and Silver (2) are the only workers to extensively investigate the effect of various ionic and molar solutions of different salts on the potential difference. While their results seem logical enough they make no attempt to explain them nor have they been repeated by subsequent workers. Again, contrary to Mond they found reductions in potential difference from the intravenous injection of adrenalin, and like a good many subsequent workers found that the potential difference was markedly reduced when the stomach was stimulated to secrete with histamine. Similar to our own findings, they observed that vagal stimulation, both peripheral and intact was without effect and similarily they noted that the physiological state of the animal has a direct effect on the resting electrical potential difference of the stomach.

A rather unique finding of Rothschild and Silver (3), in that it has not been repeated or mentioned by others, is that the potential difference of the stomach decreases when the greatest absorption is going on within the stomach. This fact will be mentioned again when the possible sources of the electrical potential difference of the stomach are considered.

The work of Sarre (4) is only of importance in that it should be mentioned as one of the early contributions. His finding of an increase in potential difference upon injection of histamine is accompanied by no explanation nor has it been found to be true by subsequent workers.

Adair and Goodman (5) have given an excellent description of their apparatus and the details of their electrodes. They made the first attempt at recording human stomach potentials and it is unfortunate that their results are practically non-contributory. However, despite the fact that only four subjects were experimented upon their one conclusion that the more active the process of digestion is, the lower will be the recorded potential difference from the stomach, appears sound.

Quigley et. al. (6) repeated certain phases of Sarre's work and were benefited by the adoption of Adair and Goodman's apparatus. The fact that they also found no change in potential difference following the injection of histamine makes one inclined to question their technical procedure.

The great strides in this field of experimental physiology made by Rehm are discussed to best advantage when considering the source of the electrical potential difference of the stomach. Goodman's report (11) on the diagnostic possibilities of the recorded electrical potential difference of the stomach must be viewed with some criticism. In the first instance his knowledge of the normal is limited. He has recorded electrical potential differences from 25 cases of duodenal ulcer, 30 cases of gastric ulcer, 46 cases of gastric carcinomas and 10 normals.

From his recordings of these the response in any type of disease is seen to vary within fairly wide limits. In evaluating his results he considers the response of the electrical potential difference of the stomach to milk. In none of the cases illustrated in his paper was the potential in a resting or steady state before the milk was given. Aside from this, there are other technical factors of which he makes no mention, either of their occurrence or control, that must certainly have appeared during the

course of the experiments. There are two other facts pertaining to the contributing investigators that must be mentioned. First, in a majority of cases, a relatively low impedance recording system has been used. This fact is significant because the low resistance of the electrodes may significantly affect the potentials recorded. Secondly, all the reported results to date have been illustrated by graphs drawn from serial visual records, while in this present investigation actual photographs of the results have been made. There can be little doubt that minute changes, as well as time relationships suffer loss of some detail when records are presented by the former methods.

From this investigation it is concluded that the maximum electrical potential of the stomach is recorded when the animal is at rest. Any procedure that produced results, produced a decrease in potential. The results from adrenalin, histamine, and pilocarpine are all of the same type. Each of these drugs resulted in a decrease of potential of a varying degree. The proposed theory behind this uniformity of response from three drugs of no similarity whatsoever is briefly as follows:

It has been a constant observation in this work as well as in the reports of others (1), (2), (3), (4), (6), and (7), that the recorded electrical potential difference of the stomach is an astute indication of the physiological state of the animal. That is, operative manipulation of the gut, heat loss, fluid loss, bradycardia, or a drop in blood pressure are all accompanied at their very onset with a drop in the electrical potential difference of the stomach. It was found that if for no apparent reason the electrical potential difference began to drop very slowly during the course of an experiment that it was futile to go ahead with the injection of drugs or similar experimental procedure. In these instances the response from the

the drug would be superimposed on the already decreasing electrical potential difference. In some cases, in which no cause could be found for the falling off of the potential, and where supportive measures were of no avail in restoring or maintaining potential, death inevitably resulted after $\frac{1}{2}$ to $\frac{3}{4}$ of an hour, by which time the potential difference was usually somewhere close to the base line or zero.

Similarily it was found that different stages of anaesthetia had a variable effect on the electrical potential difference of the stomach. With surgically deep anaesthesis, (i.e. stage 3, plane 3) the secretion of the stomach was found to be practically nil and with these conditions the electrical potential difference of the stomach was found to be high and constant. On the other hand, when the animal was found to be coming out of the anaesthetic (i.e. stage 1. and 2.) the potential became progressively lower. By increasing the anaesthesia the electrical potential difference could be returned to its former high level.

There are two extrinsic factors then, aside from any drugs that influence the magnitude of the recorded electrical potential difference of the stomach, viz: (a) the closer to the normal the physiological balance and

(b) the deeper the anaesthetia of the animal the higher will be the electrical potential difference of the resting stomach. This latter condition is subject to qualification. By deep anaesthesia is meant "surgically" deep without respiratory or cardiac embarassment.

With these two points in mind one can consider the effect of the intravenous injection of adrenalin.

As was outlined in Results, adrenalin produces, a rapid, short lived decrease in electrical potential difference. Large doses produced a simple downward deflection in the form of an inverted spike, while smaller

doses were found to result in a biphasic response. On the basis of the fact that adrenalin is a metabolic stimulant, the resulting drop in electrical potential difference subsequent to the injection of the drug may be explained. It has been demonstrated that the electrical potential difference is highest when the secreting cells of the stomach are completely at rest. Consequently a drug increasing oxygen consumption and promoting the combustion of carbohydrate with a consequent increase in the respiratory quotient will lower the electrical potential difference. In addition it was found in the human experiment that surprise, fear, or mental activity reduced the electrical potential difference. It would appear then that the symatho-adrenal system is capable of producing actual metabolic changes in the secretory cells of the stomach. This change may work through the medium of specific stimulation of certain gastric cells by the sympathetic system, or may be a non-specific metabolic increase, or may be due to circulatory changes.

Our results with adrenalin were similar to those found by Mislowitzer and Silver (2) and Rehm (8) while Sarre (4) reported an increase in potential difference and Quigley (6) and Mond (1) found no change. It is beyond this author to offer an explanation for the failure of voltage change to occur with adrenalin in the work of Mond and Quigley, or the increase as reported by Sarre. There are two possible sites of error however. The first is that their doses were inadequate and the second is the perfusion apparatus they describe. In the early part of this investigation attempts were made to study the isolated stomach in a perfusion apparatus. It was found that even the shortest period of anoxia to the mucosa resulted in no voltage when the apparatus was set up.

As pilocarpine and histamine are both specific stimulants of gastric cells, the decrease in potential subsequent to their injection is understandable. When the stimulant effect of pilocarpine is counteracted by atropine,

the voltage commences to increase again. These findings with histamine are in keeping with those of Mislowitzer and Silver (2), while Sarre (4) described an increase in potential.

The fact that on occasion pilocarpine and histamine did not produce a secretory response must be mentioned. As was pointed out in results in no case did a potential response fail to occur. It would appear from these facts then, that the formed secretory products are the end result of a series of reactions occurring within the gastric cells.

The secretion itself may be negligible, but from the stimulation of specific drugs the cells in every case would appear to undergo a certain amount of activity. This activity which apparently is a far more fundamental thing than the secretion itself occurred in every case and is represented by the potential respons

It was observed in this work, as it was by Mislowitzer and Silver (2) that the potential was higher in the fundus than in the pyloric region of the stomach. It is also interesting to note that Goodman (11) who puts great emphasis on the magnitude of the resting potential difference in humans makes no note as to whether he is recording from fundus or pylorus. It is obvious therefore that the recorded electrical potential differences of the stomach are influenced not only by a wide variety of nervous and other factors but that the actual position of the mucosal electrode is of great importance. These factors prohibit the accurate interpretation of electrical potential recordings from human subjects in light of our present knowledge.

It has not been the purpose of this investigation to identify the source of the electrical potential and therefore little first hand information can be offered. Nevertheless it can be pointed out with some degree of certainity that the potential is a property of the living gastric cell. The recordings taken during the time while the animal was dying from large intravenous emboli show a reduction in the potential to zero or the isoelectric point (Figure 9). If the potential difference was due to an artefact such as the contact of the electrode and the acid gastric juice, or a current of polarization at either end of the electrodes, it would be expected that it would

persist for a considerable time after death. However in every instance in which a recording was taken of the dying animal, it was observed that the potential began to drop coincident with the onset of myocardial failure and a drop in blood pressure. From this fact alone then it can be stated the potential difference is a property of the living cell.

The potential difference is apparently independent of stomach muscle contractions and peristalsis. Quigley et. al. (6) and other workers have observed this fact. In every experiment in this series peristaltic movements of the stomach were seen and in no instance was there any relation between these contractions and a decrease or increase of potentials. Quigley et. al. (6) used unanaesthetized Pavlov Pouch dogs and observed hunger contractions repeatedly.

In Rehm's first paper (7) he has contributed two valuable fundamental facts. First he has shown that current as high as 200 to 270 microamperes per square centimeter of stomach can be produced continually and that a difference of potential can still be measured. In other words, the recordings that he and the other workers in the subject are reporting are true potential recordings and are independent of current. With the apparatus that he describes one may measure the accumulation of electrons (positive potential) against the deficit of electrons (negative potential) on opposing sides of an intact mucous membrane completely independent of any current (amperes) in that mucous membrane.

The second fact that Rehm has stressed concerns energy equivalents. By repeatedly accurate measurements he has shown that of the total metabolic energy of the resting, non-secreting, stomach, 2% to 4% of this energy may be measured as electrical energy. Although he does not state that the difference in potential across the gastric mucous membrane is the source

of the energy for the secretion of gastric juice, he believes that in view of the two facts presented above it is capable of producing sufficient energy for this secretion.

Rehm (8) has also done much to determine what effect HCl ~~acid~~ has on the potential. He has found a negligible change in potential difference from acid added to the contents of the non-secreting stomach and by buffering the secretions with a phosphate buffer. He has also eliminated the possibility that the reduction in potential difference might in reality be the effect of a diffusion potential due to the flow of hydrogen ions through the stomach contents.

Rehm's latest paper (12) gives an account of a technique whereby means of interposing an electrode between the layers of the stomach wall the source of the potential has been identified as being superficial (i.e. towards the lumen) to the submucosa.

It is the belief of this author and the accumulated experimental data would tend to bear this out, that the electrical potential difference recorded from the living stomach originates in the secreting cells, whether acid, mucous, or peptic, of the mucous membrane. Further, the potential difference would seem to be an indication of the physiological state of the cells and is highest when the cells are in a resting condition and lowest when the cells are depleted following secretion.

Mislowitzer, Silver and Rothschild (3) reported similar findings. They observed that when substances of greatest absorbability were in the stomach that the potential difference was lowest. When one considers the vast number of factors which influence the potential, the technical factors involved in recording it, it is perhaps doubtful if a practical application of these findings can be found. Nevertheless, there may be some possible

fields of usefulness worked out through the application of known influences on the gastric potentials.

Firstly, there is the relationship of emotional background on the stability of the potentials. It has been found in this work that there are voltage changes which are a measure of the emotional stability of the individual and are quite independent of the amount of acid or other secretions.

Secondly, it would appear from this investigation that the electrical potential is a more fundamental property of the gastric cell than the actual secretion. It is possible therefore, that changes in recorded electrical potential difference might reveal changes in function much earlier than would gastric analysis or other present-day means of investigation.

Further, it would seem from the death curves that a decrease or reduction in circulation with its co-existant anoxaemia has an extremely marked effect on the electrical potential difference. This poses the question as to whether or not adrenalin and the other drugs have a direct effect on the cells or whether they produce their changes through the medium of the vasomotor system. From this investigation this question cannot be answered.

However, if it were subsequently found that the recordable changes in potential difference were due to the circulatory state of the stomach, a means would thus be at hand to assess this state.

Although this is a rather brief presentation of a fundamental problem, it is justifiable to point out that the subject is worthy of further study. The aspect of recording from humans with fluroscopic placement of the mucosal electrode is of considerable importance and would demonstrate more fully the diagnostic potentialities of the apparatus. It is to be hoped that this work will be continued in the Department of Physiology or elsewhere.

SUMMARY AND CONCLUSIONS

1. A brief review of the pertinent literature concerning the electrical potential of the gastric mucosa was presented.

2. Apparatus and procedures for obtaining continuous photographic records of gastric potentials and secretions were described.

3. Limited results of experiments on a small number of human subjects, and detailed results pertaining to gastric potential and secretions in dogs were presented and discussed. These results disclosed that the resting voltage of the stomach ranges between 40 and 100 millivolts. The mucosal surface is negative with respect to the serosal surface. The voltage attains its maximum when the stomach is at rest and the animal quiescent. Interference or trauma to the stomach lowers the potential difference across the mucosa. Systemic disturbance to other parts of the body, as by painful stimulation, also lowers the voltage, as does adrenalin. These observations indicate that the voltage may be modified by the sympatho-adrenal system.

Also, the stimulant drugs pilocarpine and histamine reduced the gastric potential. The decrease caused by these drugs, especially pilocarpine, was prolonged.

4. The reduction of potential caused by pilocarpine and histamine was sometimes associated with increased gastric secretions and sometimes not. Secretory responses of the stomach to these drugs were unreliable, whereas the electrical responses almost invariably occurred.

5. Possible explanations for the results observed were presented and discussed. Some remarks were made relating to the possible diagnostic value of the gastric potentials.

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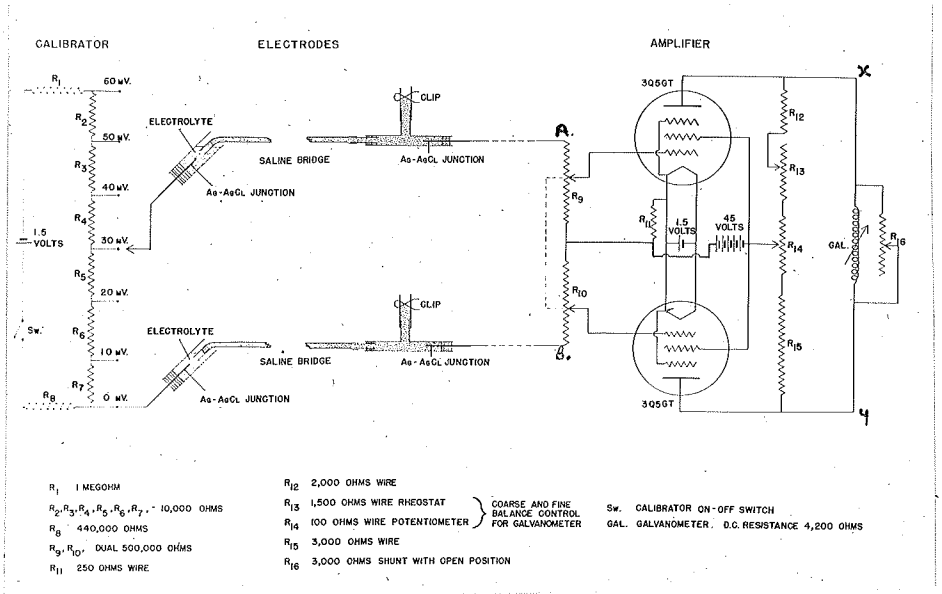
Fig. 1

Schematic Diagram of Calibrator, Electrodes and Amplifier



R_1 1 MEGOHM

$R_2, R_3, R_4, R_5, R_6, R_7$, - 10,000 OHMS

R_8 440,000 OHMS

R_9, R_{10}, DUAL 500,000 OHMS

R_{11} 250 OHMS WIRE

R_{12} 2,000 OHMS WIRE

R_{13} 1,500 OHMS WIRE RHEOSTAT } COARSE AND FINE BALANCE CONTROL FOR GALVANOMETER

R_{14} 100 OHMS WIRE POTENTIOMETER }

R_{15} 3,000 OHMS WIRE

R_{16} 3,000 OHMS SHUNT WITH OPEN POSITION

Sw. CALIBRATOR ON-OFF SWITCH

GAL. GALVANOMETER, D.C. RESISTANCE 4,200 OHMS

Fig. 2

Diagram of Electrode System

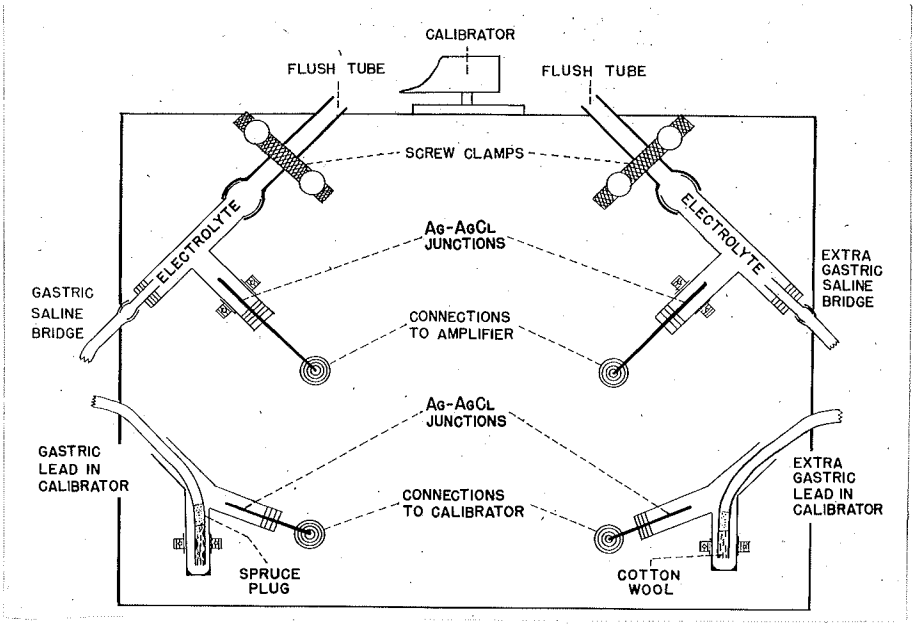


Fig. 2A Detailed diagram of construction and arrangement of electrodes. The mounting was a vertical bakelite plate 10 x 12 inches. The calibrator network was mounted on the back.

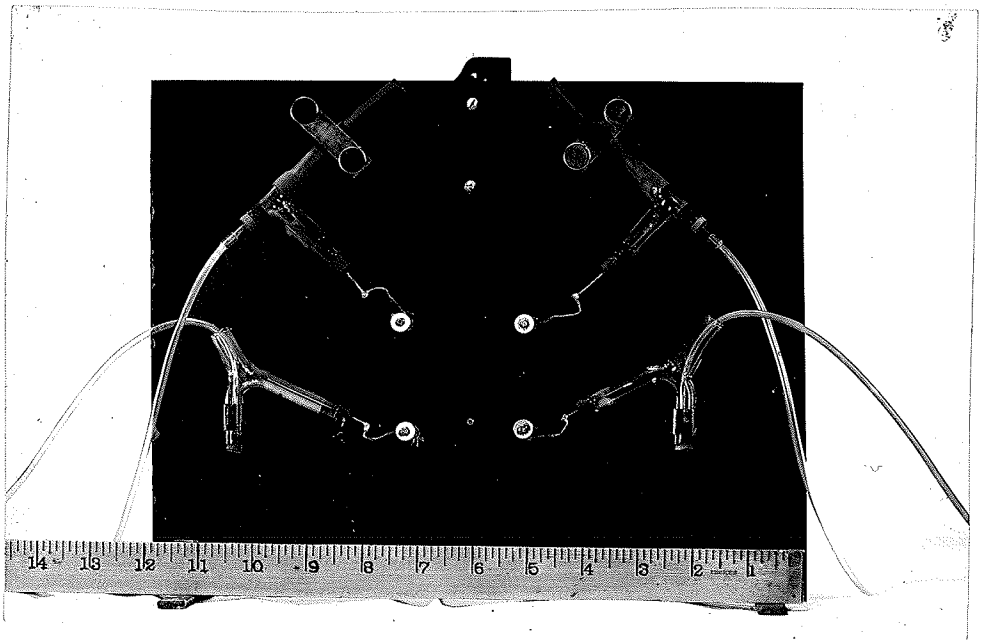


Fig. 2B Photograph of electrodes mounted on bakelite board.

Fig. 3

Photograph of Recording Unit

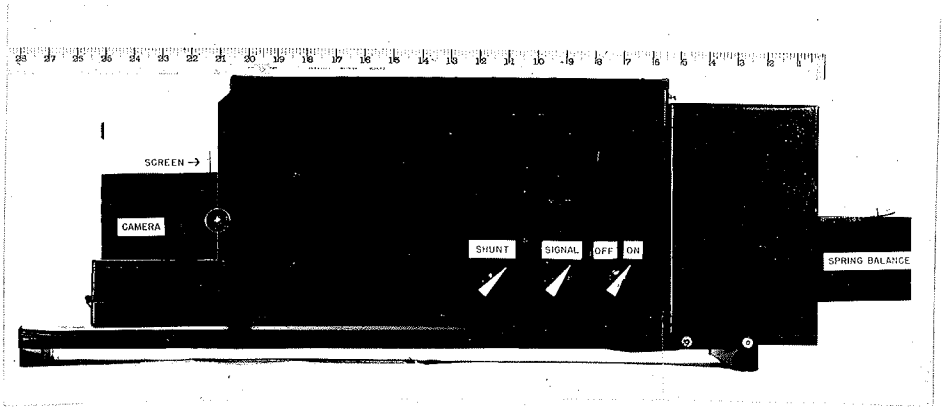


Fig. 3 Photograph of recording unit for gastric potential and secretion, incorporating camera and paper drive mechanism, galvanometer, and spring balance with their optical systems.

Fig. 4

Effect of Adrenalin on Gastric Potential

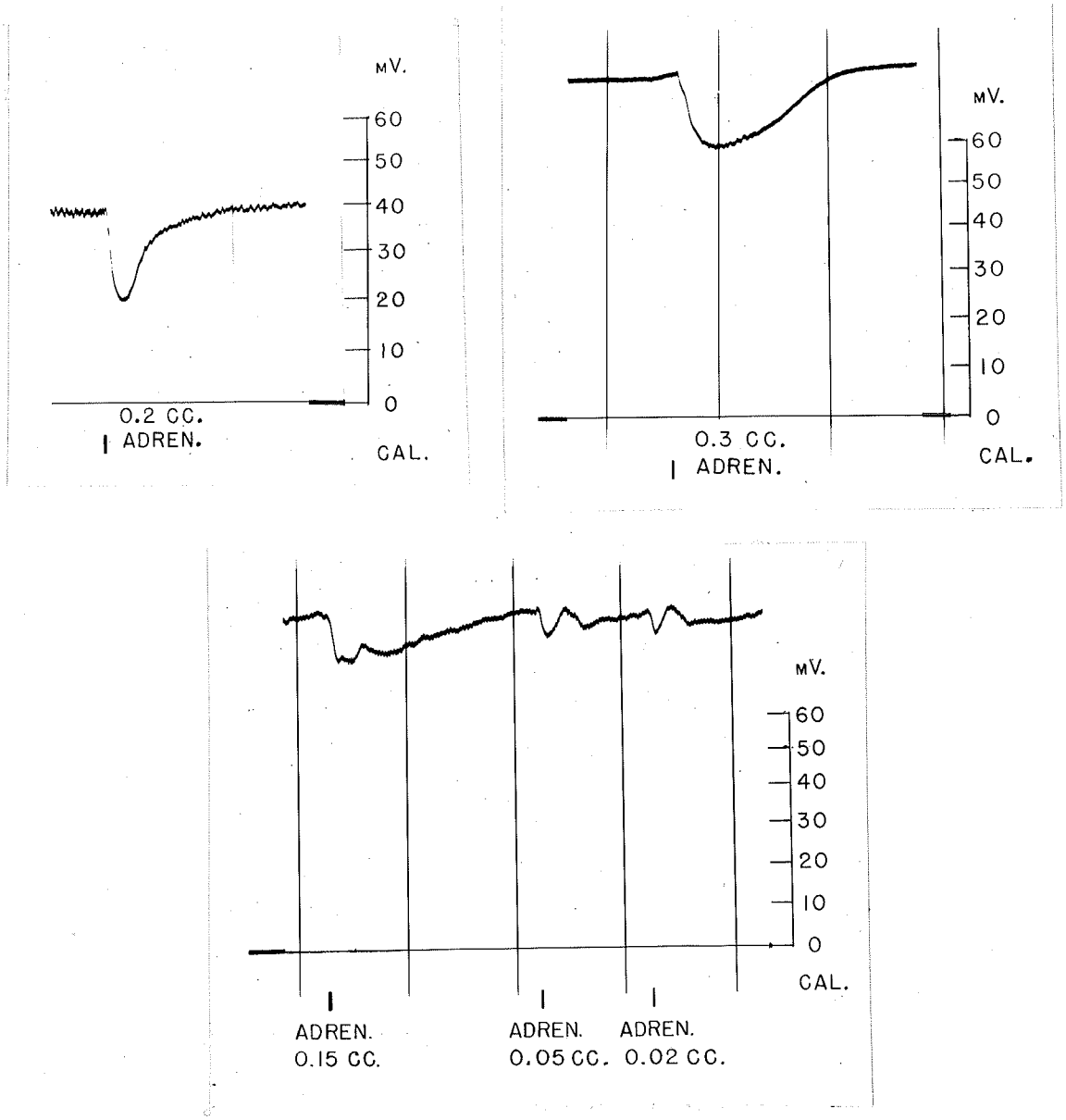


Fig. 4A Effect of 0.2 and 0.3 c.c. 1: 1000 Adrenalin in two dogs. Simple reduction of potential followed by recover.

B Effect of 0.15, 0.05 and 0.02 c.c. 1: 1000 Adrenalin in a dog. Biphasic type of response.

In this and subsequent records, vertical lines mark 10 minute intervals.

Fig. 5

Effect of Pilocarpine on Gastric Potential

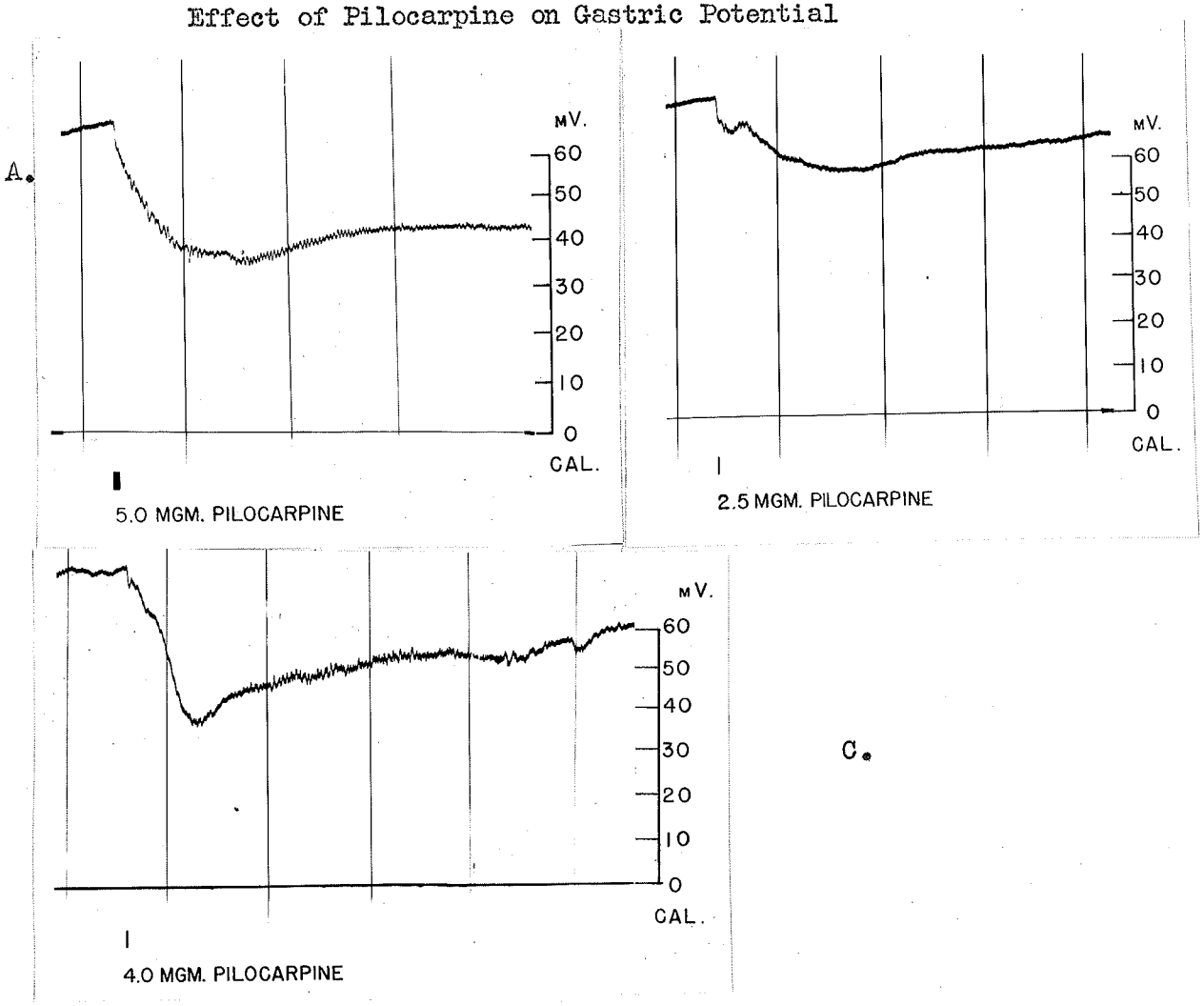


Fig. 5 Effect of pilocarpine in 3 dogs, with doses of 5, 2.5 and 4 milligrams. The prolonged effect of pilocarpine is apparent.

Fig. 6

Effect of Atropine Following Pilocarpine

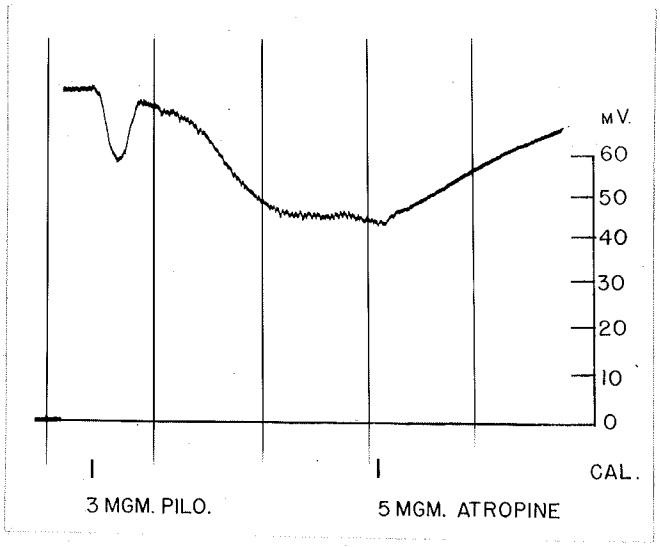


Fig. 6 A dose of 3 milligrams pilocarpine caused a typical reduction of potential which was neutralized by atropine.

Fig. 7

Comparison of Potentials in Pyloric and Fundic Regions of Stomach, and the Effects of Adrenalin.

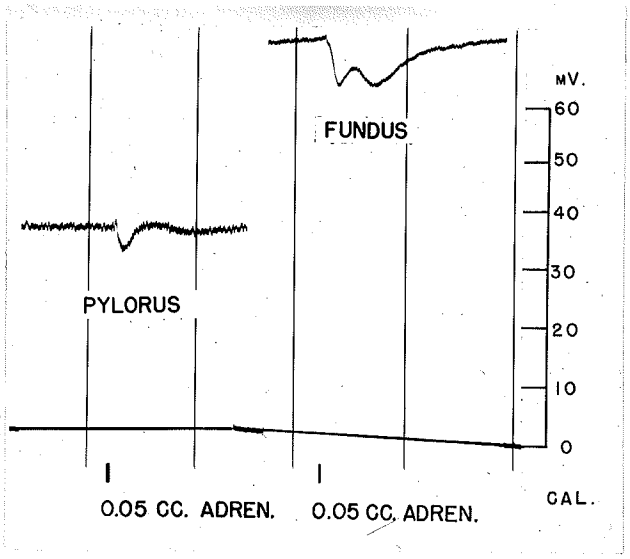
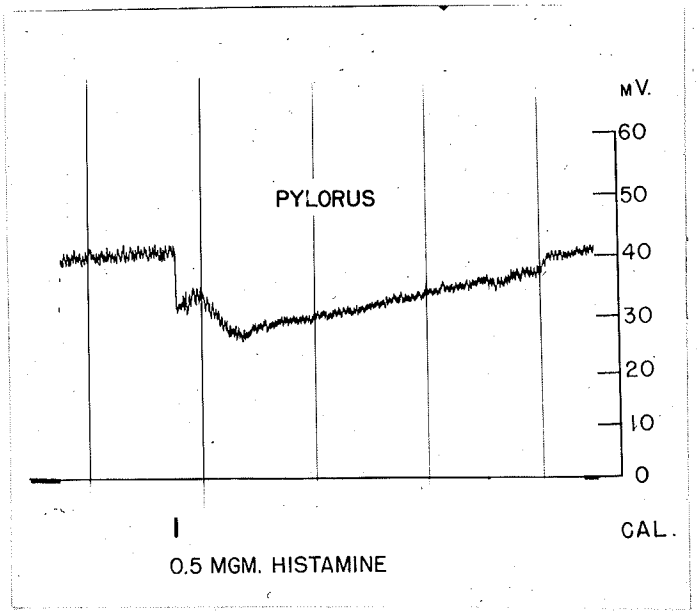


Fig. 7 Voltage at fundus is approximately twice that at pylorus, in the same dog. In each region 0.05 c.c. 1: 1000 adrenalin caused a biphasic response.

Fig. 8

Comparison of Potentials in Pyloric and Fundic Regions, and the Effects of Histamine.



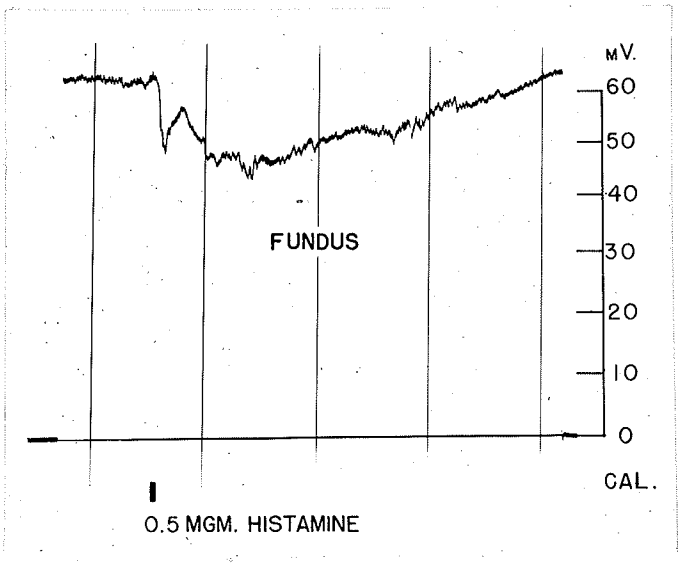


Fig. 8 Voltage at pylorus approximately two-thirds that at fundus in the same dog. Histamine caused a similar response in each region.

Fig. 9

Effect of Death by Air Embolism on Gastric Potential.

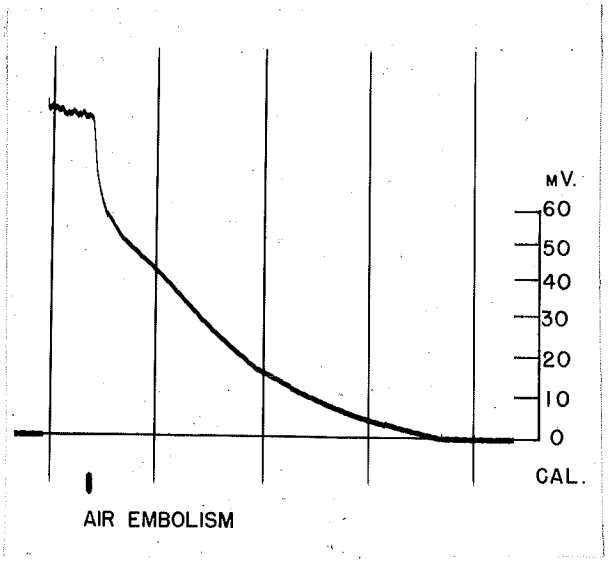
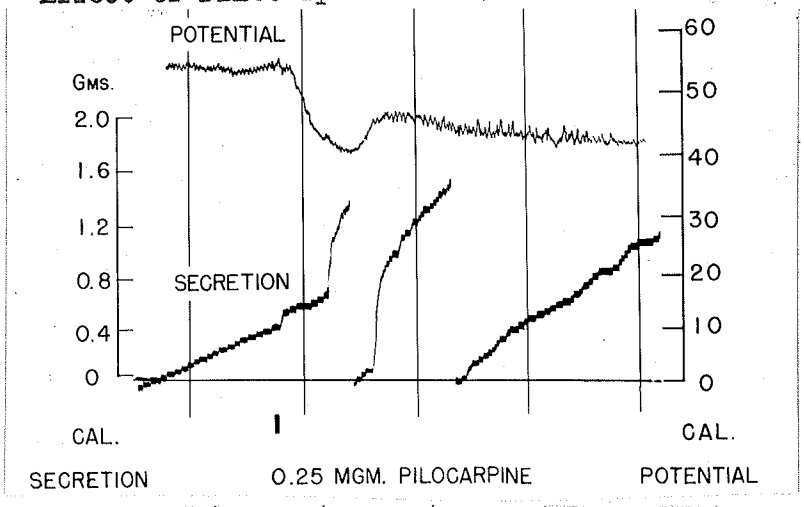


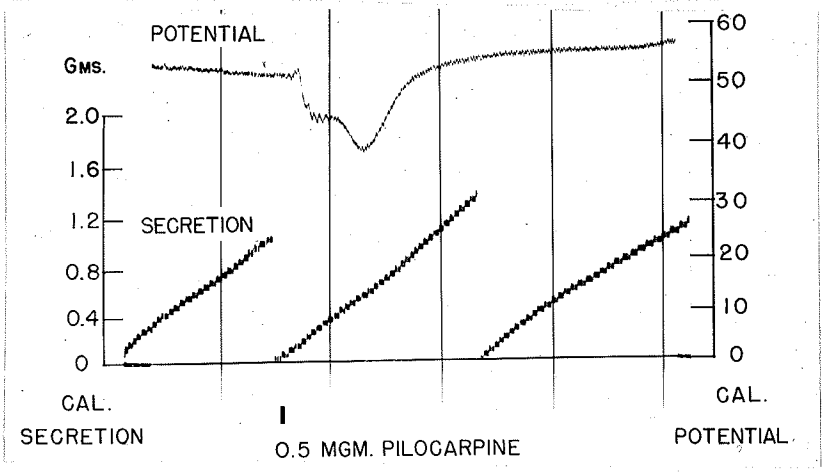
Fig. 9 Air embolism caused a reduction in potential to half the former voltage in 5 minutes. Voltage fell to zero in 30 minutes.

Fig. 10

Effect of Pilocarpine on Potential and Secretions.



A.



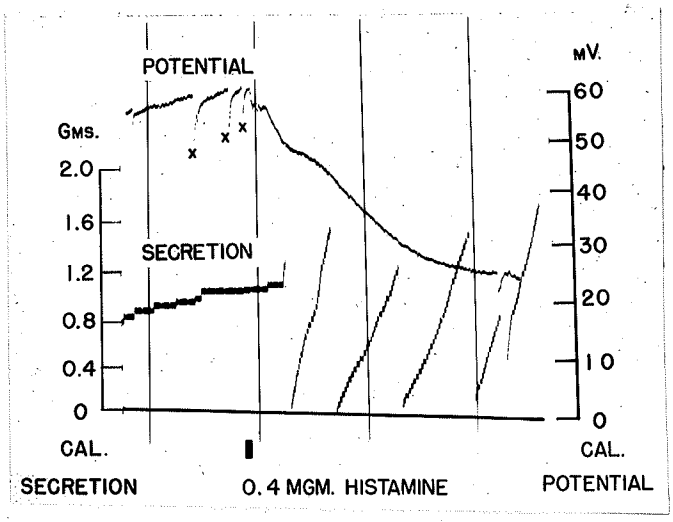
B.

Fig. 10A 0.25 milligrams pilocarpine caused reduction of potential and marked increase of secretion in this dog.

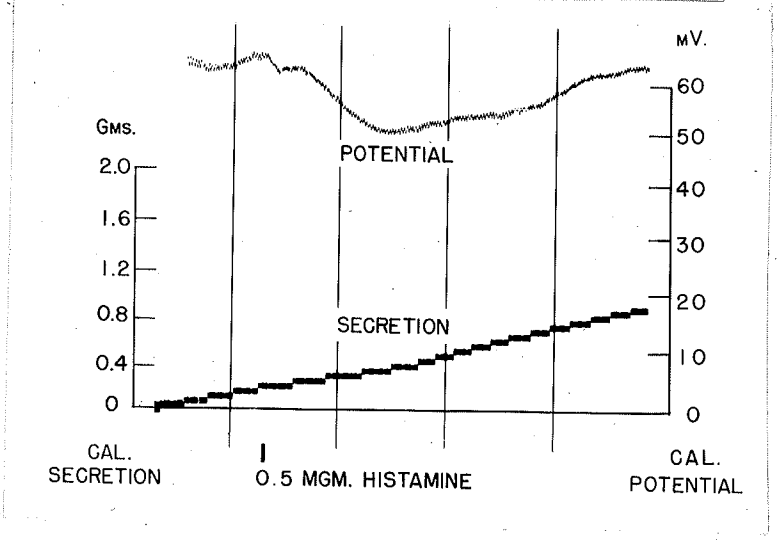
B 0.5 milligrams pilocarpine caused a reduction of potential but insignificant effect on secretion in this animal.

Fig. 11

Effect of Histamine on Potential and Secretion



A.



B.

Fig. 11A — 0.4 milligrams histamine in this dog caused marked reduction of potential and increase of secretion.

B — 0.5 milligrams histamine caused definite reduction of potential and insignificant effect on secretion in this animal.