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Effect of Close Arterial Injections of KCl on Gastric Potential Difference.* (25830)

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Numerous studies on a variety of organisms have shown that there is in general an inverse relationship between K^+ ion concentration of ambient fluid and magnitude of transmembrane potential difference (P.D.). In the frog skin(1), resting nerve and other tissues, it has been suggested that the potential difference is due primarily to K^+ ion gradient from inside of cell to the nutrient medium. There are exceptions to this general rule, for example, the findings of Tasaki *et al.*(2) with respect to K^+ ion gradient in fluids of inner ear, where the gradient is opposite to that predicted by the classical scheme. In the gastric mucosa, it has been suggested that the P.D. arises from EMF's associated with active transport of Cl^- ion(3,4). However, the possibility exists that the actual EMF of gastric mucosa is dependent on K^+ ion gradient from the cell to the interstitial fluid (ISF). Our primary purpose was to determine the effect of increasing K^+ ion concentration in ISF on gastric P.D. Because of systemic toxic effects of elevated plasma K^+ ion concentration, the method of close arterial injection was used. A preliminary report has been published(5).

Methods. Amytalized dogs were used with chambered gastric segment technic(6). Approximately 20 cm^2 of the secretory portion of stomach with blood supply intact, is placed in a lucite chamber. Two pairs of reversible electrodes were used, one pair for measuring P.D. and the other pair for sending current (1 ma/20 cm^2). P.D. was measured with Brown recording potentiometer. Direct current resistance was determined as change in P.D./unit of applied current(7). One branch of splenic artery was canulated for close arterial injections. All other branches except those going to stomach were ligated. Injections were made with motor driven syringe. All experiments were performed on resting stomachs with 0.16 M NaCl solution bathing the mucosal surface.

Results. Fig. 1 illustrates a typical experiment showing effect of injection of several iso-

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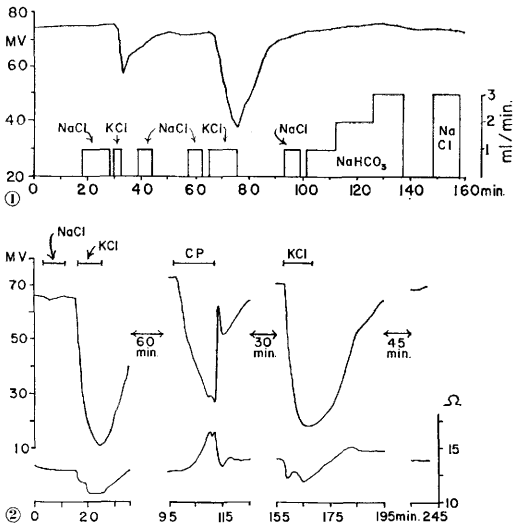

FIG. 1. Potential difference across the mucosa (serosa positive in an external circuit) as a function of time is shown by solid curve. Block denotes close intra-arterial inj. of isotonic electrolytes with the height denoting rate.

FIG. 2. Upper curves show potential difference as a function of time and the lower the direct current resistance in ohms for 20 cm². Lines at the top indicate periods of close arterial inj. (1 ml/min. for each experiment) or occlusion of blood supply (CP).

tonic (0.16 M) solutions on P.D. The right hand ordinate gives rate of close arterial injection in ml/min. NaCl and $NaHCO_3$ injections did not result in significant change in P.D. but KCl injections resulted in marked decrease in P.D.

Injection of KCl resulted in very marked blanching of mucosa not observed with other electrolytes even at rates of 5 ml/min. Blanching occurred when the P.D. started to fall. Following termination of KCl injection, the normal pink color of the mucosa usually returned immediately and P.D. started rising. In some experiments, the stomach remained blanched for varying periods following cessation of KCl injection and P.D. did not start increasing until pink color returned. On the assumption that blanching indicates drastic decrease in blood flow through the mucosa, the possibility was considered that decrease in P.D. was due to anoxia since it has been shown that interruption of blood supply results in decrease in P.D.(8). Following interruption of blood supply, the direct current resistance of the stomach increases. Obviously if the effect of KCl injections is due solely to lack of blood flow, then resistance should increase. Fig. 2 shows that the effect of KCl injections was a decrease in resistance. The magnitude of decrease in resistance was a function of the magnitude of decrease in P.D. For those experiments in which injection was continued until the P.D. fell below 20 mv. average decrease in resistance was 2 ohms for 20 cm² (8 experiments range 1.2 to 3.2). During recovery, P.D. and resistance increase and return to approximately their original levels.

The effect of clamping the pedicle is illustrated in the middle experiment Fig. 2. Duration of clamping is indicated by the line labelled CP. Following the experiment on interrupting the blood flow, the stomach still behaves in typical fashion with KCl injections as seen in last experiment in this Figure.

The effect of KCl injection differs from that of clamping the pedicle. Apart from the difference in direction of the resistance change, P.D. decreases more rapidly following KCl than with clamping of pedicle. The rate at which both resistance and P.D. return to normal is greater following release of clamped pedicle than following cessation of KCl injection. In spite of these differences, it is not possible to conclude that the effect of KCl injection is not due in part to anoxia. In some experiments, when blanching persisted longer than shown in the Figures, resistance started rising. In one experiment, blanching persisted for 19 minutes after cessation of KCl injection and P.D. fell to approximately zero. After a typical fall in resistance (2 ohms), the resistance 14 min from start of injection started to increase and increased by 15 ohms in the following 19 minutes. At this time, close arterial injection of 0.16 M NaCl resulted in reestablishment of normal color of the mucosa and a response of P.D. and resistance essentially the same as that seen after reestablishing the blood supply following a period of interrupted blood flow, *i.e.*, similar to results shown in middle experiment of Fig. 2.

It is apparent that a quantitative study of the effect of changes in K^+ ion concentration in ISF, in preparations with intact blood supply is beset with difficulties. It was planned

originally to estimate K^+ ion concentration in mucosal ISF by determination of K^+ ion concentration in venous outflow from the segment, after steady state conditions were established. Blood flow through the segment in absence of intra-arterial injection ranges from 7 to 12 ml/min (collection of entire outflow after heparinization). However, because of blanching, it is obvious that K^+ ion concentration in plasma of the venous outflow would not be a reliable index of K^+ ion concentration in ISF of the mucosa. Smaller concentrations of KCl (plus NaCl for isotonicity) and lower injection rates were tried but there was no fall in P.D. until the stomach blanched. With lower concentrations and longer periods of injection, there was a tendency for resistance to increase after the initial decrease (probably the result of prolonged anoxia of mucosa).

An attempt was made to prevent blanching by injection of a vasodilator (histamine, methacholine chloride or sodium nitrite) along with KCl. These agents even in high concentration (when injected close arterially with KCl, resulted in lowering of mean carotid blood pressure) did not prevent blanching.

Discussion. A marked vasoconstrictor action of elevated plasma K^+ ion concentration has been previously reported(9). Although it is not possible to arrive at a clear cut conclusion on the relationship between P.D. and K^+ ion concentration in ISF, the results are compatible with the idea that increase in K^+ ion concentration in ISF results in decrease in both P.D. and resistance. Mond(10) had previously reported that in the perfused frog stomach, an elevation of K^+ ion results in decrease in P.D. However, our results force one to consider the possibility that in Mond's experiment, the high K^+ ion may have diverted the perfusion fluid from the mucosa with a consequent decrease in O_2 supply and that part of the observed effect may have been due to anoxia. Harris and Edelman(11) on the other hand found that P.D. of the secreting *in vitro* frog's stomach is inversely related to K^+ ion concentration over range of 1 to 9 meq of K^+ ion/liter. One might be tempted to assume that K^+ ion gradient from cells to ISF is solely responsible for the P.D. However, other evidence indicates that there may be another EMF dependent on presence of Cl^- ion.

Summary. We determined the effect of increasing K^+ ion concentration of interstitial fluid on the potential difference across the resting dog's stomach. The chambered gastric segment preparation was used and because of toxic systemic effects of elevated plasma K^+ ion concentration, local plasma K^+ ion concentration was elevated by close arterial injection. Close arterial injection of KCl resulted in a decrease in P.D., a decrease in resistance, and a marked blanching of the mucosa. Control experiments with NaCl and $NaHCO_3$ did not result in blanching and had relatively little influence on P.D. or resistance. That the effects of close arterial KCl injections are not the result of anoxia alone is suggested by the occlusion of blood supply producing a decrease in P.D. but an increase in resistance.

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