to those of Nachlas *et al*(7), we obtain a value of 17.8 units. Barka and Dallner reported a mean of 7 mg formazan reduced per g wet weight in 30 minutes(8). Our values for 30 minutes would be approximately 35 mg. Kun *et al* reported 1.6 μg dye reduced per mg liver in 10 minutes(9). For this unit, our value would be approximately 12.4 μg. Our values are thus within the wide range as reported by others.

*Summary.* A micro method for quantitative determination of succinic dehydrogenase (SDH) activity was applied to frozen, vacuum-dried sweat gland. SDH activity determinations were made on cystic fibrosis children and controls. No significant difference between the two groups appeared.

1. Gibbs, G. E., Reimer, K., Kollmorgen, R. L., Young, P. G., Am. J. Dis. Child., 1963, v105, 249.
2. Gibbs, G. E., Reimer, K., J. Pediat., 1964, v65, 540.
3. Chamness, J. T., Kayes, J., Hershey, F. B., Traylor, F. A., Surg. Forum, 1955, v6, 573.
4. Padykula, H., Am. J. Anat., 1952, v91, 107.
5. Defendi, V., Pearson, B., J. Histochem. and Cytochem., 1955, v3, 61.
6. Hershey, F. B., Cruickshank, C. N. D., Mullins, L. I., ibid., 1958, v6, 191.
7. Nachlas, M. M., Margulies, S. I., Seligman, A. M., J. Biol. Chem., 1960, v235, 499.
8. Barka, T., Dallner, G., J. Histochem. and Cytochem., 1958, v6, 174.
9. Kun, E., Abood, L. G., Science, 1949, v109, 144.

Received January 5, 1965. P.S.E.B.M., 1965, v119.

## Stimulation of Gastric Acid Secretion by Acetate. (30214)

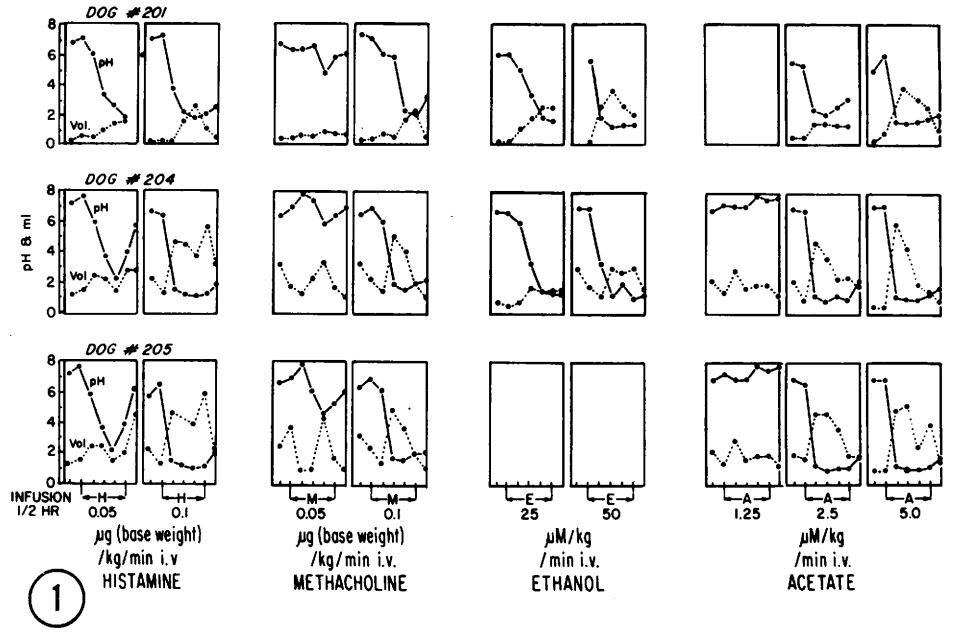
EDWARD C. MCMANUS (Introduced by H. J. Robinson)
*Merck Institute for Therapeutic Research, Rahway, N. J.*

Although ethyl alcohol has long been known to stimulate gastric acid secretion, there is no agreement concerning the mode of action. Dragstedt *et al*(2) observed that perfusion of organs with dilute alcohol solution resulted in histamine-like activity in the perfusate. They considered histamine release to be a possible mechanism. However, Irvine, Watkin and Williams(6) did not detect a rise in free histamine concentration in the urine during alcohol stimulation but a histamine infusion producing equivalent acid response raised urinary histamine levels. Woodward, Slotten and Tillmanns(12) reported that alcohol applied directly to antral mucosa was a powerful stimulant for the antral gastrin mechanism. Irvine, Watkin and Williams(6), although confirming the gastrin releasing effect of ethanol, did not believe that gastrin was the major factor mediating the acid response to oral or intravenous alcohol. Hirschowitz *et al*(5) interpreted results of experiments with human subjects to indicate a central mechanism for alcohol stimulation of gastric secretion mediated through the vagus nerve.

The stimulatory effect of acetate, a metabolic product of ethanol, was reported by McManus(11). Gastric stimulation by acetate was used by Zawoiski, Braunschweig and Beyer(13) in experiments with steroids. Certain similarities between acetate and ethanol stimulation were observed. In this paper are presented in more detail some of these observations.

*Methods.* Six female Heidenhain gastric pouch dogs with total antrum resections were used in the experiments. The dogs ranged in weight from 10.0-12.7 kg. The animals were prepared surgically several months before they were used experimentally. Test meals determined the adequacy of resection of antrum. The animals had been trained to stand in a loose sling and were not anesthetized during experiments. Collections of gastric secretion were made into 12 ml graduated centrifuge tubes attached to stainless steel gastric cannulas. Acidity of collections was measured with a Beckman glass electrode pH meter. Since the small volumes of some of the collections limited the analysis, gastric acidity was expressed in terms of pH. The

gastric acid stimulants were administered intravenously by a constant velocity infusion pump at the rate of 2 ml/minute. Before stimulation, the control phase secretion was measured at ½-hour intervals for 1 hour. During a 2-hour period of intravenous in-



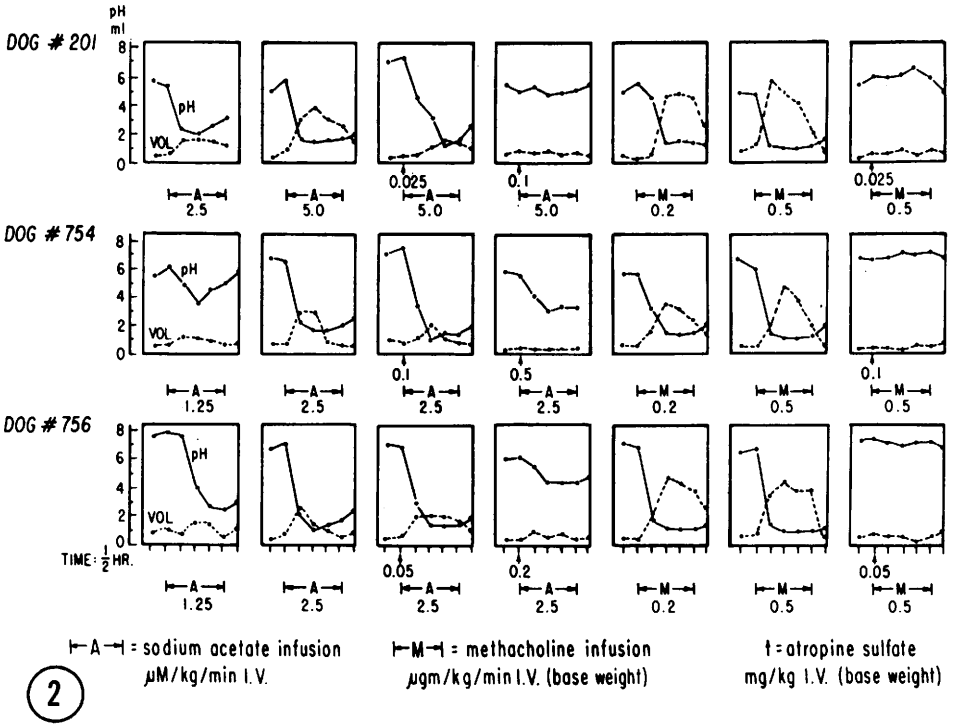




FIG. 1. Response of 3 dogs to stimulants of gastric acid secretion.
FIG. 2. Inhibitory effect of atropine.

fusion which followed immediately after the control phase, four ½-hour collections were made. An additional ½-hour sample was collected after termination of the infusion. Mett's method(4) was used for determination of pepsin.

*Results.* Infusion of sodium acetate in doses of 2.5-5.0 μM/kg/minute had an immediate pronounced stimulatory effect on secretion of acid. Volume rose sharply and the pH dropped to about 1. Data that compare the stimulatory effect of histamine, methacholine, ethanol and sodium acetate on three dogs are summarized in Fig. 1. Each plot is the average of results for 2 separate experiments.

A large number of acids were tested for similar action. Sodium propionate was approximately as potent as sodium acetate. β-Alanine and sodium hydracrylate(7,8) were moderately active in doses of 10 μM/kg/minute. The following sodium salts were inactive when infused in a dose of 50 μM/kg/minute: butyrate, pyruvate, lactate, oxalacetate, α ketoglutarate, fumarate, succinate, glutamate and acetoacetate.

The effects of atropine on secretion stimulated by methacholine and by sodium acetate were compared. In these experiments, the dose of methacholine was determined which produced equivalent or greater stimulation than the minimally effective doses of acetate. Then the inhibitory effect of atropine was determined. The doses of atropine required to suppress the effect of acetate were higher than those required to inhibit methacholine. Fig. 2 summarizes the results of the tests with atropine. The plots are averaged values for 2 experiments.

The peptic activity of secretion evoked by sodium acetate and by methacholine were compared. During a 1½-hour period of stimulation with sodium acetate, 5.0 μM/kg/minute, the peptic activity tended to decrease slightly. Methacholine, 0.2 μg/kg/minute, produced an equivalent secretion in respect to pH and volume but with very much higher peptic power. Results of experiments with 3 dogs are summarized in Fig. 3. One experiment was performed with dog #204. The data for dogs #756 and 705 are averaged

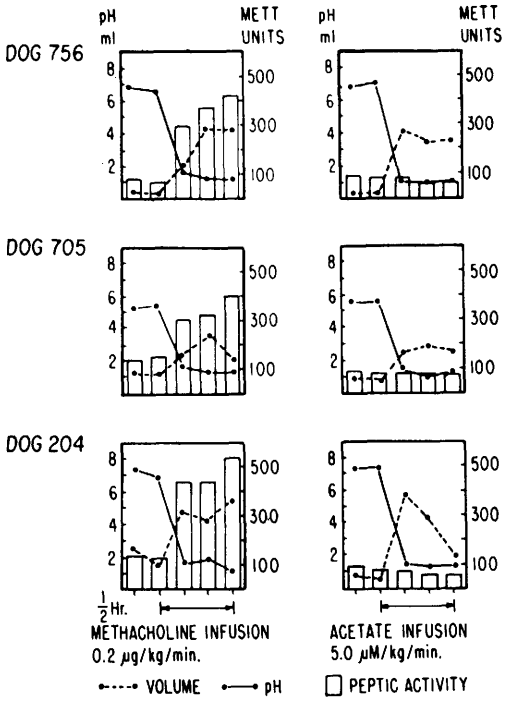



FIG. 3. Peptic activity of gastric secretion stimulated by acetate and methacholine.

values for 2 experiments with each animal.

*Discussion.* In regard to 2 parameters, acid secretion stimulated by acetate and ethanol were similar. Secretion stimulated by ethanol is known to be relatively low in peptic activity(9). This was also found for acetate stimulated secretion. Secondly, ethanol stimulation in the dog is readily inhibited by atropine but in a dose higher than required to inhibit secretion mediated by cholinergic stimulation(3). The acetate effect was likewise inhibited by atropine but in a dose higher than that required to block stimulation by methacholine.

The effect of infusion of acetate on plasma levels of the compound was not determined. Annison(1) reported normal plasma acetate levels of approximately 0.1 to 0.25 mM/l for the dog. For man, the levels were approximately 0.2 mM/l. Lundquist(10) using a different method, reported normal levels of about 0.05 to 0.1 mM/l for the human.

In view of the normal plasma levels for acetate cited above, the quantities of acetate required for stimulation of gastric secretion appear to be extremely low. This is all the

more reason to suspect that the results herein reported have significance from a physiological and biochemical standpoint.

*Summary.* Sodium acetate or propionate, administered by venoclysis in a dose of 2.5-5.0 μM/kg/minute, had a pronounced stimulatory effect on secretion of acid from the Heidenhain pouch of the dog with total antrum resection. Higher doses of atropine were required to suppress acetate than methacholine stimulation. Acetate-stimulated secretion was lower in peptic activity than secretion produced in response to methacholine. Similarities of acetate and ethanol stimulation were recognized and discussed.

1. Annison, E. F., Biochem. J., 1954, v58, 670.
2. Dragstedt, C. A., Gray, J. S., Lawton, A. H., DeArellano, M. R., Proc. Soc. Exp. Biol. and Med., 1940, v43, 26.
3. Gray, J. S., Bachrach, W. H., ibid., 1940, v43, 36.
4. Hawk, P. B., Oser, B. L., Summerson, W. H., Blakiston, Philadelphia, 1947, 12 ed., 347.
5. Hirschowitz, B. J., Pollard, H. M., Hartwell, S. W., London, J., Gastroenterology, 1956, v30, 244.
6. Irvine, W. T., Watkin, D. B., Williams, E. J., ibid., 1960, v39, 41.
7. Ivy, A. C., Javois, A. J., Am. J. Physiol., 1924-25, v71, 591.
8. ———, ibid., 1924-25, v71, 604.
9. Krueger, L., MacIntosh, F. C., Am. J. Dig. Dis., 1937, v4, 104.
10. Lundquist, F., Acta Physiol. Scand., 1960, v50, Suppl. 175, 97.
11. McManus, E. C., Fed. Proc., 1955, v14, 368.
12. Woodward, E. R., Slotten, D. S., Tillmanns, V. C., Proc. Soc. Exp. Biol. and Med., 1955, v89, 428.
13. Zawoiski, E. J., Braunschweig, L. W., Beyer, K. H., J. Pharm. Exp. Therap., 1958, v122, 512.

Received January 25, 1965. P.S.E.B.M., 1965, v119.

## Movement of Calcium in Both Directions Across the Primate Placenta.* (30215)

NORMAN S. MACDONALD, DONALD L. HUTCHINSON, MARILYN HEPLER AND ELIZABETH FLYNN
(Introduced by G. V. Taplin)
*Laboratory of Nuclear Medicine and Radiation Biology, Department of Biophysics-Nuclear Medicine; and Departments of Obstetrics and Gynecology, and Radiology, School of Medicine, University of California at Los Angeles*

The continuous movement of a myriad of nutrient substances and metabolic waste products across the placenta from mother to fetus and in the reverse direction is vital to the growth and development of the embryo. Radioactive tracer techniques have been used for the study of placental transport of the essential nutrient, calcium, in mice, rats, rabbits and cattle(1-4). The rapid movement of strontium in both directions across the monkey placenta has been directly demonstrated in monkeys(5). This report concerns the simultaneous transfer of isotopically labeled calcium across the placenta from mother to fetus and in the reverse direction. The primary intent was to estimate the approximate magnitudes of these transfers. Pregnant monkeys were chosen because of the close similarity of their placental structure to that of humans(6,7).

*Method.* Each of 3 pregnant rhesus monkeys was anesthetized with intramuscular piperidine HCl (4 mg/kg supplemented with pentobarbital 10 mg/kg body weight). Polyethylene catheters were placed in a maternal femoral vein, an interplacental vessel of the fetus and the amniotic sac in a manner previously described(6). Five μc of $I^{131}$ labeled human serum albumin in 2 ml of isotonic saline were injected into each fetal and maternal catheter, for estimation of blood vol-

* These investigations were supported by Contract AT(04-1)-GEN-12 between U. S. Atomic Energy Commission and University of California, Los Angeles, and by research grants HD-00402 and HD-00474 from Nat. Inst. Health, Dept. of H.E.W.