of time elapsed between adjuvant treatment and collection of the donors' serums (Fig. 2). The similarity between the curve so obtained and that formed by the peak antibody titers of the various groups of recipients is apparent.

The finding that adjuvant action can be passively transferred, in part, by serum does not contradict the widely held view that Freund's adjuvant acts by slowly releasing antigen over a prolonged time. Such a mechanism of action and the one proposed here are not mutually exclusive. The most important implication of the passive transfer experiments is that they provide additional support for an extracellular control of antibody production exerted by antibody itself. This role of antibody was originally proposed by Jerne (*1*) and further elaborated by Karush, and by Eisen and Karush (*4*). Eisen and Karush postulated that the equimolar antigen-antibody complex constitutes the only effective stimulus for antibody formation. Complexes formed in antigen excess or in antibody excess would not stimulate the antibody-producing cells. The former would cause immunologic tolerance, whereas the latter would "shut off" antibody production when antibody concentration has become sufficiently great (*12*). The concentration of equimolar antigen-antibody complexes would control the magnitude of the antibody response. Such concentration, in turn, depends on the concentration of antibody present in circulation as either natural or immune antibodies. Work from this laboratory has demonstrated enhancement of antibody production in colostrum-deprived baby pigs by low concentrations of homologous and heterologous immune antibodies (*2*) and by large quantities of normal colostrum (*2*) and normal γ-globulin (*13*) which presumably contained natural antibodies. The results reported here suggest that the enhancement of antibody response caused by Freund's adjuvant may also be explained on the basis of an increase in concentration of natural antibodies.

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Pancreatic Secretion Induced by Stimulation of the Pyloric Gland Area of the Stomach

Abstract. *Pure gastrin I of Gregory and Tracy stimulated secretion not only of gastric acid but also of pancreatic fluid and protein material. Similarly, endogenous release of gastrin from a transplanted pouch of the pyloric gland area of the stomach, initiated by irrigation with solutions of acetylcholine, stimulated gastric acid secretion and pancreatic flow and protein output in dogs with fistulas of both organs. The effect on the pancreas, like that on the stomach, was inhibited by acidification of the acetylcholine solution.*

The external secretion of the pancreas in man and other mammals is thought to be controlled by (i) the release of two hormones, secretin and pancreozymin, from the mucosa of the small intestine, and (ii) the nerve supply to the gland (*1*). Although it has been known for several years that extracts of the mucosa of the pyloric gland area of the stomach also possess some stimulatory properties for pancreatic secretion (*2*), the effect has simply been ascribed to the presence of some secretin-like material in this region.

Recently, Gregory and Tracy (*3*) described the isolation of two pure polypeptides from the mucosa of the pyloric gland area, which, by reason of their effects in stimulating gastric secretion, are thought to represent gastrin, the hormone of the gastric phase of gastric secretion. These polypeptides stimulate pancreatic secretion (*3*), suggesting that in the intact animal liberation of gastrin by the presence of food in the pyloric gland area provides a third humoral stimulus for external pancreatic secretion.

If this hypothesis, based upon the pharmacological effects of mucosal extracts on pancreatic secretion, is to be accepted, it is necessary to demonstrate that stimulation of the pyloric gland area in the living animal will release a humoral stimulant of pancreatic secretion. Blair *et al.* (*4*) found that the presence of various stimulants in the pyloric gland area of the anesthetized cat caused an increase in enzyme secretion by the pancreas after the vagus nerves and the splanchnic nerves were cut. These results suggest that stimulation of the pyloric gland area results in the release of a humoral stimulus for pancreatic secretion.

The results of our experiments with conscious dogs offer proof of the existence of a humoral stimulant of pancreatic secretion originating in the pyloric gland area. In these animals a permanent pancreatic fistula was created surgically according to a method we have described (*5*). A pouch was made of the pyloric gland area and drained to the exterior by a mucocutaneous fistula on the abdominal wall. Several weeks later the mesenteric attachments of this pouch were divided, and it became dependent on new vessels growing from the abdominal wall for its blood supply. Thus the pouch could be considered totally denervated. The dogs were also equipped with a gastric fistula draining the remainder of the stomach. With the gastric fistula open, an intravenous infusion of histamine dihydrochloride (4.0 mg/hr) caused a marked increase in gastric secretion but no sustained increase in pancreatic secretion. This demonstrated to our satisfaction that, with the gastric fistula draining freely, any increase in pancreatic secretion in those instances in which gastric secretion was stimulated could not be attributed to the escape of gastric juice into the intestine with subsequent release of secretin.

The effect in these animals of a single subcutaneous injection of pure gastrin I (*6*), 2 μg/kg body weight, is

shown in Fig. 1. This confirms the experience of Gregory and Tracy that pure gastrin stimulates both the protein and bicarbonate output by the pancreas in doses which are also effective stimulants of gastric secretion. In these experiments no attempt was made to stimulate the pyloric pouch.

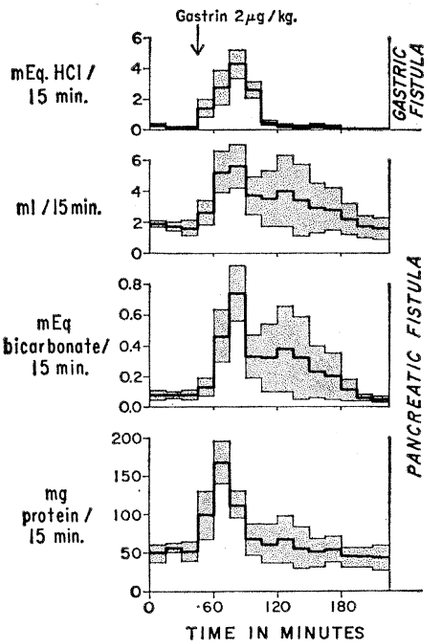

Fig. 1. Gastric and pancreatic responses to a single subcutaneous injection of gastrin I (2 μg/kg body weight). The gastric response is expressed as milliequivalents of hydrochloric acid secreted per 15 minutes; the pancreatic response is expressed in milliliters, milliequivalents of bicarbonate, and milligrams of protein, respectively, secreted per 15 minutes. Each value is the mean plus or minus the standard error of the mean of four experiments in two dogs.

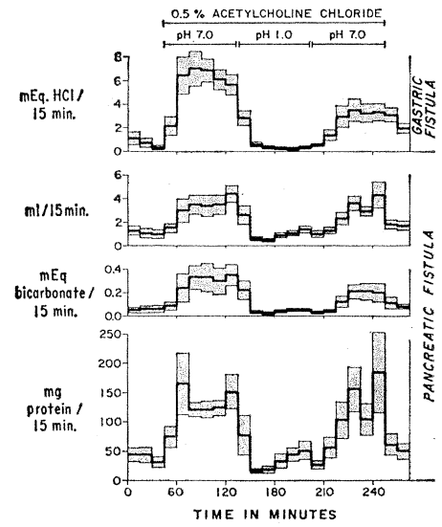

Fig. 2. Gastric and pancreatic responses to irrigation of the pouch of the pyloric gland area with 0.5 percent acetylcholine chloride (60 ml/hr) at *p*H 7.0 and *p*H 1.0. Each value is the mean of six experiments with three dogs.

Figure 2 shows the gastric and pancreatic secretory responses when the pouch of the pyloric gland area was irrigated continuously with a dilute solution of acetylcholine chloride. The irrigating fluid was maintained neutral until a response was evident; it was then acidified to *p*H 1.0, and then returned to *p*H 7.0. Stimulation of both the stomach and pancreas induced by acetylcholine in the pouch was easily inhibited by acidification. We have obtained similar, though smaller, gastric and pancreatic responses by irrigation of the pyloric pouch with a 5-percent solution of a peptone (Bactoprotone, Difco) and also with a 5-percent solution of liver extract. Again both responses were inhibited by acidification of the irrigating solution. Attempts to distend the pouch by means of a balloon were unsuccessful in terms of both gastric and pancreatic responses, possibly because of the mechanical difficulty of distending a pouch almost buried in the muscles of the abdominal wall.

Since the pyloric pouch in these experiments was transplanted and was devoid of any nervous connections with the gastrointestinal tract, the results indicate that a humoral agent, or agents, which excited both a gastric and pancreatic response was released by stimulation of the pouch. Although it is possible that acetylcholine or the protein hydrolysates were absorbed from the pouch and stimulated the stomach and pancreas directly, Robertson *et al.* (*7*) have shown conclusively that the gastric response to acetylcholine placed in a pyloric pouch cannot be attributed to absorption of the stimulant.

The demonstration that the same substances which are known to release gastrin from the pyloric gland area were effective stimulants of pancreatic secretion when introduced into the pouch supports the hypothesis that gastrin is also a pancreatic stimulant. The important observation that the effects were abolished by acidification of the antrum confirms this view; the release of gastrin from the pyloric gland area has been shown to be inhibited by acidification (*8*). If we had caused release of secretion from the pouch, it might have been expected that the pancreatic response would have been augmented rather than inhibited by acidification. The similarity between the gastric and pancreatic responses to both exogenous gastrin and to release of endogenous gastrin by stimulation of the pouch is further evidence for the hypothesis that gastrin is a physiological stimulant of pancreatic as well as gastric secretion.

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Response of the Rabbit Oviduct to a Tissue Adhesive

Abstract. *Sexual sterilization of mammals by the production of an obstruction at the tubo-uterine junction has been reevaluated experimentally. The application of 0.15 ml of methyl 2-cyanoacrylate monomere to the junction in rabbits produced, at intervals from 1 to 6 weeks later, histological, hydrodynamic, and functional evidence of tubal obstruction.*

Current techniques to produce permanent sterilization of the human female require abdominal surgery. A transcervical technique which is simple, safe, acceptable, and reliable would undoubtedly prove useful as a contraceptive method. The first known attempt to achieve this goal was reported in 1849, when a method was described which involved placing sufficient silver nitrate at the uterine cornu to produce scarring and cornual obstruction (*1*). In 1878 Kocks suggested the use of