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The Fatal Effect of the Complete Loss of Pancreatic Juice.

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In order to collect the total external secretion of the pancreas, a new method seemed necessary. The older procedures,[1, 2] by which an open fistula was made, permitted the licking of the juice by the animal, and always led to infection of the secretion followed by inflammatory changes in the gland. Such a method was devised in 1923 by Rous and McMaster[3] and was used by them for the collection of the total bile under sterile conditions. We have employed the same technique for the collection of the total pancreatic juice. In brief, a cannula was placed in the large duct of the pancreas in dogs, connected with long rubber tubes leading to the outside and joined to a closed rubber balloon provided with an opening for the periodic collection of the accumulated secretion. The smaller duct or ducts were ligated and cut and omentum interposed between the head of the pancreas and the duodenum to insure against reconstitution.

When mechanical obstruction or accidental infection did not occur the pancreatic juice flowed uninterruptedly and on the fifth to eighth day, quite to our surprise, the animals died with evidences of marked asthenia. The course was similar in all 12 instances studied. For a day or two after operation they appeared normal and ate well. The appetite soon diminished and by the fourth day only water was taken. Vomiting was first noted on the third or fourth day and became gradually worse. They drank large quantities of water which was promptly returned. Asthenia was noted early and increased steadily. The temperature, pulse rate, and respirations remained normal.

The secretion of pancreatic juice continued up to the end, varying, with the size of the animal, between 200 and 500 cc. per 24 hours, In one instance for example (Dog 9, weighing 15 kg.) the amounts collected each morning were 175, 275, 300, 325, and 320 cc. The juice was slightly opalescent, colorless and entirely without odor.

At autopsy, performed in most instances immediately after death, no gross changes were noted. The peritoneum was everywhere smooth and glistening, the outlet tube was firmly bound by omentum, and no infection was anywhere made out. The pancreas seemed a little smaller than normal but was soft and pink. The glass cannula was firmly fixed in the duct. Microscopically the acini of the pancreas were small and surrounded by rather wide clear spaces. The islets appeared normal.

The changes observed in the blood in many instances will be recounted in another communication. Marked dehydration was revealed by hematocrit readings which showed an increase in the proportion of red cells to whole blood as high as 80 per cent, the normal being between 40 and 50 per cent. In addition there was a decrease in blood chlorides and an increase in pH. Blood sugar values were within normal limits and the urine, though repeatedly examined, never contained reducing bodies.

Similar blood findings have been observed after acute pyloric obstruction and death occurs in this condition in about the same time. But the final persistent vomiting in our experiments may alone have been responsible for the alkalosis as, it probably is, in acute pyloric obstruction. But with the loss of so much alkaline fluid it is difficult to understand why alkalosis should occur. Whether the condition bears any relation to that following the establishment of a duodenal fistula where similar findings have been reported must likewise remain unanswered.

It is of interest to note that some of the older observers,[2] even with the open pancreatic fistula, noted the occasional development of hypersecretion followed by death. In our experiments it was the rule. The nature of this insistent and powerful stimulus, which must be one quite apart from the ingestion and digestion of food, may be connected with an unopposed secretion of HCl by the stomach, since acid within the duodenum is a most powerful stimulant of pancreatic flow. This taken with the persistent vomiting may indicate that we are dealing with a condition due to the elimination of the normal regurgitation of alkaline pancreatic juice into the stomach. The partial neutralization of the acid gastric contents is thus prevented. This phenomenon, while long known to occur, has never achieved any great recognition and its existence as a normal phenomenon has even been denied. From these findings and others to follow, it would seem that such a relationship may be of vital significance.

It is a pleasure to acknowledge the helpful criticism and suggestions of Dr. Evarts A. Graham during the course of these experiments.

[1] Tigerstedt, R., *Handbuch der physiologische Methodik*, 1911, Bd. II, Abt. 2, 174.

[2] Babkin, B. P., *Die äussere Sekretion der Verdauungdrüsen*, 1924, 234.

[3] Rous, P., and McMaster, P. D., *J. Exp. Med.*, 1923, xxxvii, 11.

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The Bactericidal Influence of Various Substances Upon Gram-Positive and Gram-Negative Bacteria.

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We have found that ether is more rapidly bactericidal in relation to gram-negative organisms *(Escherichia coli, Eberthellia typhi, Eberthellia dysenteriae, Eberthellia paradysenteriae* (Flexner), *Alcaligines fecalis, Salmonella paratyphi, Salmonella Schotmulleri, Pseudomonas aeruginosa, Pseudomonas fluorescens, Proteus vulgaris, Serratia marcescens, Encapsulatus pneumoniae, Neisseria intracellularis)* than in relation to a number of gram-positive organisms *(Staphylococcus albus, Staphylococcus aureus, Staphylococcus tetragenus, Diplococcus pneumoniae* (Types II and III), *Streptococcus pyogenes).* It appears at present that acid fast gram-positive organisms (Mycobacteria), diphtheroids (Corynebacteria) and possibly the Lactobacilli, stand midway between the two first mentioned groups in sensitiveness to this reagent.

We further tested a number of substances containing hydrocarbon chains and possessing varying degrees of lipoid solvent activity on gram-negative and gram-positive bacteria. Our results are shown in Table I.

In general it will be seen that all of these substances act in much the same manner as does ether.

From Table II, it is seen that alkalis act as do the substances containing hydrocarbon chains, but acids act more rapidly on