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Influence of Changes in Serum Phosphorus and Creatinine on Respective Concentration in Pancreatic Juice. (25491)

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Few studies have been devoted to the relation between chemical composition of plasma and of secretions of the gastrointestinal tract. This report concerns the influence of changes in plasma content of inorganic phosphorus and creatinine upon their respective concentrations in pancreatic juice. Both elements can be elevated artificially to a high level in blood without danger for the laboratory animal. Ball(1) has shown that calcium, phosphorus and magnesium in pancreatic secretion are much lower than in serum (¼ to 1/20th). Normally, inorganic phosphorus concentration in pancreatic juice equals 1/20 of its plasma value. When plasma phosphorus concentration is raised to 6 times greater than normal, there is a 12 fold increase in concentration of this ion in the pancreatic secretion, this being 1/10 of plasma value.

Technic. Experiments were performed on dogs (20 kg) with duodenal fistula. A modification of the Thomas(2) method was used, by which a fine glass cannula may be introduced to collect pure pancreatic juice. In fasted dogs, amount of juice so collected is minimal; it increases when secretin is injected intravenously. To establish a constant rate of secretion, secretin (Boots) was injected at constant rate with syringe for continuous injection. Rate of pancreatic juice secretion was adjusted betwen 1 and 1.5 cc/min. This was considered sufficient to avoid errors due to pancreatic dead-space. Extreme limits for each individual pancreatic juice collection period were 0.54 cc and 2.6 cc/min. The first 10 cc of pancreatic juice were discarded. Each experiment consisted in measuring output and concentration of inorganic phosphorus (Exp. 1-4) or creatinine (Exp. 2-4) in pancreatic juice at various levels of plasma inorganic phosphorus or creatinine. In Exp. 1 and 2, phosphorus excretion was measured at normal level of serum phosphorus and at various degrees of increased phosphorus levels, in Exp. 3 and 4 only at various levels of hyperphosphoremia. Increased serum phosphorus was induced by injection of buffered solution of inorganic phosphates at first in concentrated, then in diluted form. Rate of injection was such as to obtain levels as constant as possible. In Exp. 2-4, creatinine was added to the liquid of perfusion. Each collection period lasted 4 to 10 minutes. Blood samples were taken at brief and regular intervals throughout experiment. After each induced change in blood level of phosphorus and creatinine, the new pancreatic collection was begun only after at least 5 cc of

TABLE IA. Effect of Increase of Plasma Inorganic Phosphorus on Ratio between Phosphorus Concentration in Pancreatic Juice and in Plasma of Dogs (4 Exp.).

Exp.	Phosphorus in plasma, mg/l	P. conc. in pancreatic juice / P. conc. in plasma	
1	49	.014	
	49	.010	
	49	.011	
	100	.015	
	108	.015	
	201	.021	
	276	.011	
	309	.012	
	337	.010	
	382	.008	
	385	.008	
		mean = .012	σ = .00381
2	53	.009	
	53	.008	
	117	.009	
	131	.010	
	207	.014	
	216	.009	
		mean = .010	σ = .00214
3	123	.008	
	128	.011	
	129	.009	
	205	.010	
	210	.011	
	213	.011	
	214	.011	
		mean = .010	σ = .00122
4	111	.007	
	113	.008	
	114	.007	
	111	.009	
	213	.008	
	218	.007	
	219	.006	
	219	.006	
	260	.007	
		mean = .007	σ = .001

TABLE IB. Effect of Increase of Plasma Creatinine on Ratio between Creatinine Concentration in Pancreatic Juice and in Plasma of Dogs (3 Exp.).

Exp.	Creatinine in plasma, mg/l	Creat. conc. in pancr'tic juice / Creat. conc. in plasma	
2	7.7	(Creat. in pancreatic juice unmeasurable)	
	7.7		
	30.4	.17	
	36.4	.17	
	74.	.18	
	78.	.14	
		mean = .165	σ = .0173
3	50.2	.06	
	52.	.06	
	53.5	.06	
	108.	.08	
	115.	.08	
	119.5	.08	
	123.	.09	
		mean = .07	σ = .0129
4	54.	.06	
	55.5	.07	
	56.	.09	
	53.	.06	
	123.	.06	
	132.	.06	
	133.	.05	
	134.	.06	
	173.	.07	
		mean = .065	σ = .0113

pancreatic juice were obtained and discarded. After intravenous injection of radioactive phosphorus (P 32) radioactivity appears in the pancreatic secretion within 2 minutes or less. It may be concluded that the pancreatic "dead-space" is unimportant. To minimize error due to pancreatic "dead-space" in calculation of clearance of creatinine and inorganic phosphorus for each collection period, we divided the output of these substances by their plasma concentrations at mean time, less 3 minutes of each collection period. Inorganic phosphorus in plasma and pancreatic juice was measured by the technic of Berenblum and Chain(3); creatinine was measured by the method of Bonsnes and Taussky (4).

Results. I. *Effect of increased plasma inorganic phosphorus on its concentration in pancreatic juice* (Table IA). *a*—At a normal level of serum phosphorus, concentration of inorganic phosphorus in pancreatic juice is approximately 1% of its plasma concentration. These figures were obtained from measurements in 5 dogs. (In other experiments not included in Table I percentages up to 6% were found.)

b—Concentration of phosphorus in pancre-

atic juice is proportional to its concentration in plasma. The ratio between concentrations of inorganic phosphorus in plasma and pancreatic secretion remains constant even when there is 8-fold increase of plasma inorganic phosphorus (Exp. 1).

c—In another group of 3 experiments, parathyroid hormone was injected into the animal to study its effect on passage of phosphorus into the pancreatic secretion. After intravenous administration of 100 Collip units of Parathormone (Lilly), there was no change in amount of inorganic phosphorus passing into the pancreatic juice. These experiments lasted at least one hour after injection of parathormone.

II. *Effect of increased plasma creatinine on its concentration in pancreatic secretion.* (Table IB). *a*. At a normal level of creatinine, amount of creatinine in pancreatic juice is too slight to be measured by the method used.

b. When level of creatinine in blood is increased, amount of creatinine in pancreatic secretion is much less than its plasma value. Ratio between concentrations in juice and plasma is respectively 0.165-0.07-0.065 in Exp. 2, 3 and 4.

c. As with phosphorus, there is a definite relationship between concentrations of creatinine in plasma and pancreatic juice. Their ratio remains constant whatever the creatinine content of plasma may be.

Comment. We were interested in the study of permeability of digestive glands to various substances normally present in plasma. Our investigation appears to be the only study of transfer of creatinine through the pancreas at various levels of serum creatinine. Other studies have been directed to permeability of this gland to urea and uric acid. These too, are found in much lower concentration in pancreatic juice than in plasma (Agren 5).

The relative lack of permeability for these products of protein metabolism seems to be a characteristic of the pancreas as compared to other digestive glands. The transfer of non-protein nitrogen, urea, uric acid and creatinine in saliva(6 to 12), stomach juice(7,10, 13 to 20), bile(5,7,13,18,21-24) and intestinal juice(7,25 to 27) has been investigated by various authors, each studying usually one aspect of the problem. There are some differences of opinion; however, concentrations of these compounds in plasma and in digestive secretions, except pancreas, are of the same order of magnitude. Uric acid seems to pass less readily in saliva(12) and especially in gastric juice(20) where it reaches, on the average, one-third of its plasma value. This difference is still much lower than that observed at pancreatic level for each derivative of protein metabolism, creatinine, urea, uric acid.

This relative lack of permeability of the pancreas to products of protein metabolism cannot be explained at present. More extensive research is needed concerning permeability of the digestive tract to ions and other plasma elements and the influence of changes in their plasma levels upon their concentrations in glandular secretion. How intestinal absorption of an element is affected by change in its concentration on one side of the intestinal barrier is a corollary problem, as yet insufficiently studied.

Summary. 1) Concentrations of inorganic phosphorus and creatinine in pancreatic secretion are much lower than their respective concentrations in plasma. 2) Any increase in inorganic phosphorus or creatinine content of plasma leads to proportional increase of their respective concentrations in the pancreatic secretion. 3) Ratios between concentrations of inorganic phosphorus in pancreatic secretion and in plasma remain constant, whatever the inorganic phosphorus content of plasma may be. The same is true for creatinine. 4) Relative lack of permeability for products of protein metabolism seems to be a characteristic of the pancreas, as compared to other digestive glands.

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Association of Resistance to Bile Salts and Virulence in *Salmonella typhimurium* Strains* (25492)

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A number of factors have been reported to influence virulence of various *Salmonella* species. Among these are endotoxins(1), Vi antigens(2), and resistance to action of complement(3). Certain nutritionally deficient strains have also been shown to be less virulent than those from which they were derived (4,5). Results of our study with *Salmonella typhimurium* indicate that in some cases ability to tolerate high concentrations of bile salts is accompanied by increased ability of the organism to persist in tissues of mice.

Methods. S. typhimurium strains used were differentiated by ability to form colonies on SS agar (Difco) which contains 0.85% Bacto Bile Salts No. 3 (Difco). Experiments in which individual components of this medium were tested showed that bile salts were responsible for the inhibitory effect. A brief description of the *S. typhimurium* strains follows: RIA, a relatively avirulent strain unable to form colonies on SS agar, obtained from H. A. Schneider, Rockefeller Inst. for Med. Research; RIA/SS_1, RIA/SS_2, mutants of RIA able to grow on SS agar, isolated by selection on bile agar made by adding 1.5% agar to liquid bile medium described under *in vitro* tests; RIA/SS_3, mutant of RIA able to grow on SS agar, isolated from a mouse inoculated with 4 x 10^6 cells of parent strain; *rev*, SS sensitive reversion of RIA/SS_1, unable to grow on SS agar. Bacteria for use in mouse virulence tests were grown overnight in penassay broth (Difco) at 37°C with aeration and diluted in saline. Assays for viable cell count were made on nutrient agar with control platings on SS agar. Mice were inoculated intraperitoneally with 0.2 ml of various dilutions. Animals employed in all virulence tests were from a colony of *Salmonella* free white Swiss mice maintained in this laboratory. They were originally obtained from Ft. Detrick, Frederick, Md. Equal numbers of males and females 5 to 8 weeks old were used in each experiment. Animals which died were examined for necrotic foci on liver, and spleen

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