ACID-BASE COMPOSITION OF PANCREATIC JUICE AND BILE.

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The measurements of fixed base in gastric secretions given in the preceding paper, explain a rapid depletion of blood plasma base when these secretions are continuously lost from the stomach. It has been pointed out that this loss of fixed base, rather than the larger loss of chloride ion, is the significant factor in the accompanying dehydration of the plasma (1). The alkaline digestive juices entering the duodenum presumably contain more of fixed base than of chloride ion. Under normal circumstances the inorganic substances contained in these secretions are in chief part returned to the blood plasma. If the concentrations of these substances in the digestive juices are appreciable in terms of their blood plasma values, continued failure of reabsorption due to abnormal circumstances such as upper intestinal obstruction, fistula, or diarrheal disease, may be expected to produce dehydration of the plasma and, also, distortion of acid-base structure, unless the amounts of the individual substances lost are proportional to their plasma concentrations. In this study it was undertaken to establish the concentrations of the chief plasma substances, fixed base and chloride ion, in pancreatic juice, in bile from the hepatic duct and from the gall bladder, and in secretions accumulating in an upper intestinal loop. The materials studied were obtained from dogs and from cats by the operative procedures described below. Two specimens of human pancreatic juice were obtained from a patient with a pancreatic fistula.

Collection Methods.

Pancreatic Juice.—An unusual surgical situation provided the opportunity of collecting two samples of human pancreatic juice. This material was obtained from a patient at the Massachusetts General Hospital, who had undergone an operation for removal of the contents of a large pancreatic cyst. The walls of the cyst were stitched to an opening in the anterior abdominal wall and for a time a sinus tract discharging a clear mucoid fluid persisted. In addition to this material, a clear, watery fluid was noted to leave the sinus after meals. Two small collections of this latter material were obtained following breakfasts of milk, cream, tea, and toast. Tests for the specific ferments of pancreatic juice in the fluid were positive.

A few samples of juice were obtained from the cat, but this animal was found to be unsatisfactory both as regards the establishment of a fistula and the subsequent withdrawal of juice. In the formation of the fistula, it is necessary to use the main pancreatic duct. Since this duct opens into the duodenum at the papilla of Vater close to the bile duct, it is necessary to side-track the bile in order to obtain the pancreatic juice alone. Furthermore, the lumen of the intestine is so small that it is not possible to excise the portion containing the pancreatic duct and then close the wall, so that the intestinal stream, as well as the bile, must be diverted from the first portion of the duodenum. This was done in stages as follows: Under ether anesthesia, an anastomosis was made between the gall bladder and the stomach, and a posterior gastroenterostomy between the stomach and the jejunum was carried out. 4 weeks later, the animal having completely recovered from the operation, the common duct was divided, the bile now passing from the gall bladder into the stomach. The portion of the duodenum containing the pancreatic duct was then excised for transplantation into the abdominal wall as a permanent fistula. The distal end of the duodenum was closed by suture. The stomach contents then entered the intestine through the posterior gastroenterostomy. Except for loss of weight, the animals remained for 2 weeks in fair condition. There appeared to be a continuous slight secretion of pancreatic juice from the fistula which greatly increased on taking food.

The dog with us, as with other investigators, proved in all respects satisfactory. The fistula was established by two methods. The first, that of Pawlow (2), is as follows: A small section of the duodenal wall containing the accessory pancreatic duct is excised; the opening in the duodenum is closed, and the section of the duodenum containing the mouth of the duct transplanted into the abdominal wall.

The second method is an adaptation by Elman and McCaughan (3) of the Rous and McMaster method (4) for collecting sterile bile, and is practically identical with the latter, except that the pancreatic duct is used. Briefly, it consists in cannulation of the pancreatic duct and collection of the secretion in a balloon outside the abdomen. The connection between the cannula and the balloon is made by a somewhat elaborate series of rubber tubes which insures collection of the juice under aseptic conditions. It has the disadvantage, pointed out by Pawlow (2), in regard to methods involving cannulation of the duct, that the cannula acts as a constant irritant, perhaps stimulating abnormal secretion.

Bile.—The bile studied was obtained from cats, collections being made from both the gall bladder and the hepatic duct. The gall bladder collections were made as follows: After a 24 hour fast, the animal was etherized, the abdomen opened and the cystic duct occluded by a clamp. A needle attached to a syringe was then introduced into the bladder and the contents aspirated. The hepatic duct collections were made by an adaptation of the method of Rous and McMaster (4). The gall bladder was first removed and the cystic duct ligated. The hepatic duct was divided and a cannula placed in the proximal end, the end towards the duodenum being ligated. The cannula was connected, by a system of rubber tubing, with a balloon outside the abdomen, an arrangement permitting collection of the entire biliary secretion.

Upper Intestinal Secretions.—A loop about 20 cm. from the pylorus was selected and the bowel divided. A second cut was made through the bowel about 25 cm. distal to the first one, leaving the loop attached by the mesentery only. Great care was used not to interfere with the blood supply. The continuity of the gastrointestinal tract was then restored by an end to end anastomosis and the ends of the isolated loop closed. A small opening into the lumen of the loop was made, and a catheter inserted and held in place by purse string sutures, the free end being brought out through a stab wound in the abdominal wall and connecting with a balloon.

All operations were carried out under ether anesthesia and with aseptic technic. The animals were then cared for in comfortable cages and at the end of the experimental period were killed by etherization.

Methods of Analysis.

The methods used for measuring total fixed base, chloride, inorganic phosphate and calcium, were those cited in the preceding paper. The measurements of sodium and potassium given in Table II were obtained by the method of Stoddard (5) for determining sodium plus potassium and the method of Fiske (6) for potassium.

RESULTS.

The measurements of the two chief factors, fixed base and chloride ion, in the acid-base composition of the secretions studied are given in Table I. The diagrams in Fig. 1 were constructed from average values from these data. The figure also contains for comparison, diagrams representing the acid-base composition of gastric juice and of blood plasma. In the specimens of pancreatic juice, the concentration of fixed base was found to be double or more that of chloride ion. The single measurement of fixed base in human pancreatic juice gave a value only slightly above that usually found for fixed base in human blood plasma (158 cc. 0.1 N per 100 cc.). The averages for fixed base in the series of samples from Dog 3 and from Dog 4, showed a rather wide difference, being respectively 182 cc. 0.1 N and 159 cc. 0.1 N per 100 cc. Measurements of fixed base in the blood plasma of these animals, however, gave approximately corresponding levels, the values found being for Dog 3, 175 cc. 0.1 N per 100 cc., and for Dog 4, 159 cc. 0.1 N per 100 cc. This degree of difference in the blood plasma level of fixed base in these two animals is surprising and, we believe, unusual. The fixed base found in

TABLE I.

Measurements of Fixed Base and of Chloride Ion.

Material	Number of specimens analyzed	B˙, cc. 0.1 N per 100 cc.			Cl′, cc. 0.1 N per 100 cc.		
		Min.	Max.	Av.	Min.	Max.	Av.
Pancreatic juice, human	2	—	—	164	86	88	87
" " dog, No. 3	19	170	189	182	28	66	42
" " " " 4	6	152	163	159	55	89	73
" " cats (two)	2	192	200	196	67	93	80
Bile, hepatic duct, cats	11	157	194	172	100	130	120
" gall bladder "	8	261	318	274	0	20	5
Upper jejunal loop, cat*	2	169	172	170	129	131	130
Blood plasma, cat**		—		175	—	—	119

* Inflammation due to infection was a factor in production of fluid taken from the jejunal loop.

** From measurements published by Baumann and Kurland (7).

single samples from each of the two cats, 192 cc. 0.1 N and 200 cc. 0.1 N per 100 cc., is considerably above the usual plasma concentration in this animal, 175 cc. 0.1 N per 100 cc., established by the data of Baumann and Kurland (7). The specimens of pancreatic juice, however, were small, and the measurements obtained from them cannot be taken as dependably defining the usual concentration of fixed base in pancreatic juice from the cat.

Detail of the acid-base composition of a sample of pancreatic juice from Dog 4 is given in Table II. As may be seen, the fixed base is

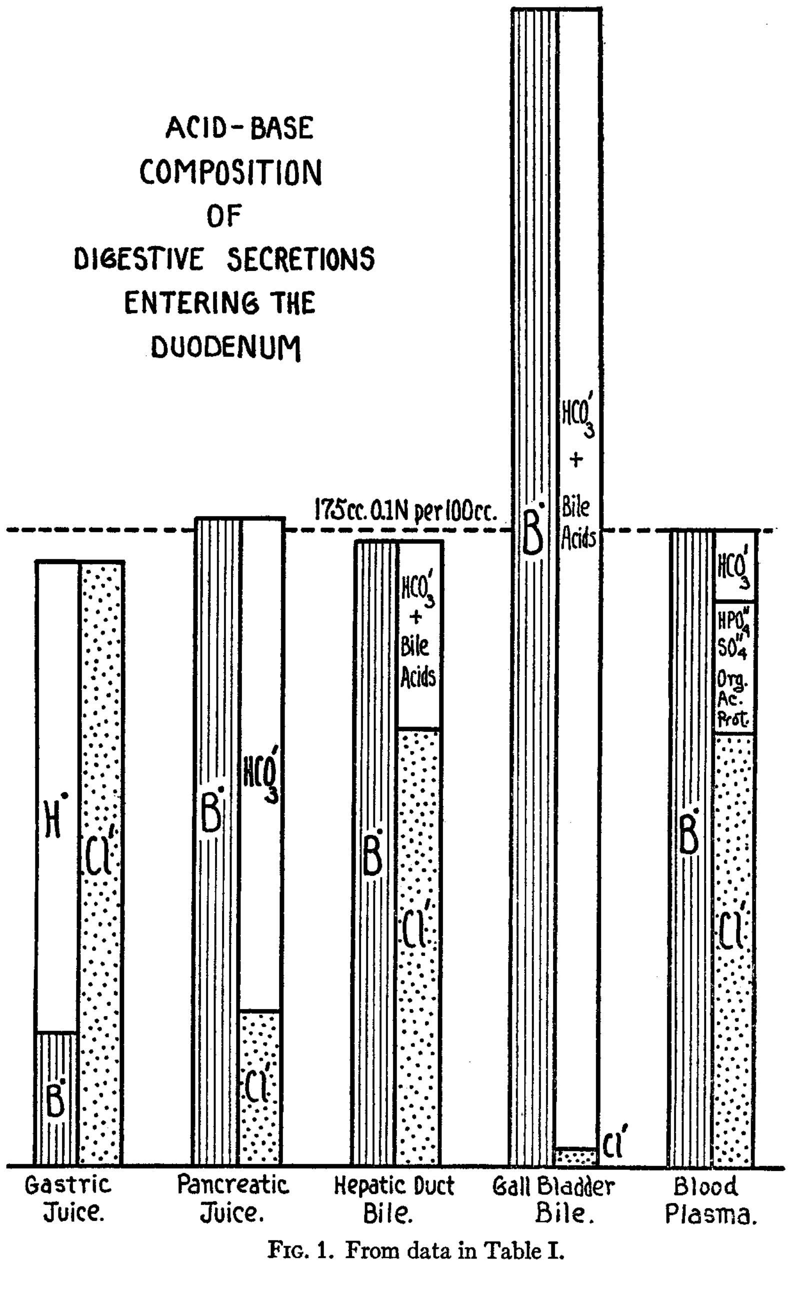

FIG. 1. From data in Table I.

composed almost entirely of sodium, potassium and calcium being found at relatively small values. Magnesium was not measured. Except for a minute concentration of phosphate, the acid factors are chloride ion and bicarbonate ion. In this table the concentration of HCO_3' is assumed to be measured by the extent to which fixed base is in excess of $Cl' + HPO_4''$. That this surmise is approximately correct is indicated by several measurements of bicarbonate obtained

TABLE II.

Acid-Base Composition of Pancreatic Juice from Dog.

HCO_3' taken as total base—($Cl' + HPO_4''$). Magnesium not measured.

Base		Acid	
	cc. 0.1 N per 100 cc.		*cc. 0.1 N per 100 cc.*
$Na^{\cdot}$	148	Cl'	81
$K^{\cdot}$	7	HPO_4''	1
$Ca^{\cdot\cdot}$	6	HCO_3'	79
	161		161

TABLE III.

Measurements of Bicarbonate in Pancreatic Juice after Equilibration with Alveolar Air Compared with Values for Total Fixed Base Minus Chloride.

Material from Dog 4.

Specimen No.	$B^{\cdot} - Cl'$	HCO_3'
	cc. 0.1 N per 100 cc.	*cc. 0.1 N per 100 cc.*
1	96	99
2	88	98
3	81	87
4	63	69

by a somewhat rough method from samples of pancreatic juice in which fixed base and chloride were also determined. The measurements were obtained by first shaking samples of juice in the Van Slyke CO_2 apparatus with alveolar air from the operator and then determining bicarbonate in the usual manner. As may be seen in Table III, the measurements were somewhat beyond the mark but may be taken as satisfactorily demonstrating that the acid equivalence of the base in pancreatic juice is composed practically entirely of chloride and bicarbonate.

The data from the series of specimens of pancreatic juice from Dog 3 and from Dog 4 (Table I) demonstrate that fixed base is, for the individual, a much more stationary value than is chloride ion. Pawlow (2) and others have stated that the alkalinity of pancreatic juice varies considerably, apparently according to differences in the character of the food intake. Fixed base remaining stationary, adjustment of bicarbonate and thereby degree of alkalinity, is referable to change in the chloride ion concentration. The mechanism establishing reaction is thus the inverse of that found in gastric secretions where, as shown in the preceding paper, chloride ion is stationary and fixed base is the movable factor.

In bile from the hepatic duct, fixed base and chloride were found at approximately the concentrations which obtain in the blood plasma (see Fig. 1). The fixed base concentration in bile from the gall bladder exhibits, interestingly, a wide departure from the blood plasma level, reaching in one of the specimens a value of 318 cc. 0.1 N per 100 cc. The work of Rous and McMaster (4), which has shown us that the gall bladder has the unique function of concentrating a physiological secretion, would lead us to expect this finding. Another striking and ingenious change in the composition of gall bladder bile is the almost complete removal of chloride ion, with presumably, replacement by bile acids.[1]

It is the evidence of these data that, during digestive activity in the upper intestinal tract, much more of fixed base than of chloride ion is required. In the case of pancreatic juice, these materials are directly withdrawn from the blood plasma. The release of gall bladder bile with its large content of fixed base does not, however, involve an immediate and extensive removal of plasma base. Replacement of bladder bile is presumably a gradual process extending over the period of absorption of fixed base from the gastrointestinal tract and

[1] In the diagrams representing the composition of the bile specimens the presence of bicarbonate is indicated. No measurements of bicarbonate were made. From the studies of Rous and McMaster of the reaction of bile, we are informed that gall bladder bile is nearly neutral or even slightly acid, and hepatic duct bile, or "liver bile" to use their more appropriate term, is decidedly alkaline. It may therefore be inferred that the former contains a very small amount and the latter a considerable amount of bicarbonate.

is probably accomplished without disturbing the fixed base content of the plasma. We may thus regard the reservoir mechanism for supplying the digestive secretion of the liver as providing a probably important protection against sudden and large depletions of plasma base. It is to be noted however that, in the presence of circumstances causing continued loss of bile, extensive withdrawal of plasma fixed base must occur unless the food intake provides adequate replacement.

The experiment of constructing a jejunal loop with fistula, continuity of the remainder of the gastrointestinal tract being preserved, was undertaken with the purpose of learning the inorganic composition of the secretions of the upper intestinal mucosa during the digestion of food. The experiment was unsuccessful. It was found that moderate infection and inflammation were undoubtedly factors in the production of the fluid which was obtained from the loop in surprisingly large amounts. The measurements obtained are given in the table for the reason that they probably indicate the composition of the fluid which is so abundantly produced by the intestinal mucosa under obstructive conditions. As may be seen both fixed base and chloride ion are present at approximately their respective concentrations in blood plasma.

SUMMARY.

Pancreatic juice contains fixed base at approximately the concentration found in the blood plasma. Chloride ion is present in concentrations varying from one-fourth to one-half the fixed base value and the remainder of the acid equivalence is composed of bicarbonate ion. Fixed base being a nearly stationary factor, variation of bicarbonate and thereby of alkalinity is referable to change in the concentration of chloride ion.

In bile, as delivered by the liver, both the fixed base and chloride ion values correspond closely with their respective concentrations in blood plasma. In gall bladder bile, however, the concentration of fixed base is, roughly, double that in hepatic duct bile, and chloride ion has been almost entirely removed.

From these data it may be inferred that loss of digestive secretions entering the duodenum will, in the absence of replacement of the

materials contained, cause dehydration of the blood plasma and reduction of the plasma bicarbonate.

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