[CONTRIBUTION FROM THE LABORATORY OF THE NORTHWESTERN UNIVERSITY MEDICAL SCHOOL AND THE RESEARCH LABORATORY OF ARMOUR AND COMPANY.]

ON THE NORMAL REACTION OF THE INTESTINAL TRACT.

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Received April 20, 1917.

Views of physiologists concerning the reaction of the small intestine with its mixed contents of partially digested food, bile and ferment juices have materially changed since the introduction of more delicate methods of research. Reactions were measured by the aid of indicators and while there could be no doubt of the behavior of media appreciably acid or appreciably alkaline, of the chyme for example, as it passes the pylorus, on the one hand, or of the active flow of the pancreatic juice from a fistula, on the other, there was always uncertainty about the reaction of body fluids near neutrality, such as the saliva or even the blood.

This uncertainty was augmented by the introduction of new indicators, before the range of their efficiency was established, or before the relation to hydrogen-ion concentration was known. This was especially true of the methyl orange group of indicators, according to the indications of which a mild degree of alkalinity could be ascribed to fluids which in reaction were indeed weakly acid. Possibly in this manner the notion of "zones" of reaction in the small intestine came into existence. Below the pylorus there was, of course, a distinctly acid stretch but this was assumed to be followed by a recognizably alkaline zone due to the influx of alkaline juices from the pancreas and other glands and from the bile. The alkaline zone, in turn, would be followed by another zone where the acids resulting from fermentation would come into play.

Three series of observations, not very recent, may be cited as showing points of view of different authors which are still frequently quoted in the text-books. One of the first important papers containing observations on the reaction of the intestinal contents was published by Macfadgen, Nencki and Sieber.[1] Following a surgical operation it was necessary to excise a short piece of the small intestine, just above the caecum, and temporarily lead the end of the ileum to the surface of the abdomen for the discharge of the intestinal contents. The reaction of this liquid was found to be normally acid, and not because of the presence of lactic or butyric acid. Observations were carried through weeks.

Experimenting with dogs and other animals, Moore and Rockwood[2] came to the conclusion that the reaction of the small intestine throughout its length may be generally alkaline. They drew the conclusion from the animal experiments that the small intestine in man cannot have an acid reaction in any considerable part of its length, and in addition criticize

[1] *Arch. exp. Pharm.*, **28**, 311 (1891); *Jahresber. Tierchem.*, **21**, 269 (1891).

[2] *J. Physiol.*, **21**, 58 and 373 (1897); *J. Chem. Soc.*, **52**, 151 and 331 (1897).

the work of the preceding investigators as insufficient to prove their conclusions. Moore and Rockwood employed mainly litmus and methyl orange in noting reactions of the fluids in the intestines of the animals as they were opened, and it is evident that they attached much importance to the behavior of the latter indicator. Unfortunately the real basis of many of their conclusions is not clearly explained.

Later experiments by Munk[1] led to the conclusion that to indicators sensitive to weak acids the small intestine is always acid. In these observations dogs and young pigs were killed and the small intestine tied in loups to have three or four changes from pylorus to caecum. While the general differences in indicators are recognized in these tests it is not recognized that in presence of proteins the apparent results may be obscure. Among the indicators employed importance was attached to rosolic acid. The color change here, in presence of protein and near the neutral point, is not very distinct.

The conclusions reached by all these authors, and others, are based on the interpretation of the reaction of indicators and were apparently reached without due regard to the [H] range in which the indicators act. As Moore and Rockwood point out it is very important to know just how the small intestine reacts with reference to acidity or alkalinity. Our artificial digestion experiments are based on the assumption that the intestinal chyme is always slightly alkaline and experimental media are made accordingly.

We have thought it important to attempt an answer to the question through the electrometric determination of the hydrogen-ion concentration of the intestinal contents of man and animals. There are very few such observations on record and we present some data in this direction.

Experiments on Man.

The difficulties in the collection of the intestinal fluid have to be overcome here. In the few cases referred to observations were made on human subjects on whom some surgical operation involving the intestine had been performed. We have not depended on this source for the contents tested but have employed the fluid withdrawn by aid of a narrow Rehfuss tube which was always taken into the intestinal tract to a considerable length. The position of the open end of the tube was controlled by radiographic observations as well as by the length of tube swallowed. We have been able to watch the reaction in subjects who had retained the tube some hours or even days, and in whom we knew that the duodenum had been passed

The amount of fluid which may be secured in this way is not large, since the chyme trickles through the duodenum but slowly, never filling it.

[1] *Zentr. Physiol.*, 16, 37 (1902); *Maly's Jahresb.*, 32, 420 (1902).

The liquids collected and examined were all from men in hospital but who were not suffering from any disorder of the alimentary tract. In this respect they were normal individuals and the contents tested represented normal products. In most cases the subjects were convalescent from physical accidents. As a rule the fluids were brought to the laboratory for the ion concentration test within a few minutes of the time of collection as the hospital is in the same block. In the second set of observations recorded below the fluids were secured very early in the morning and had to be held a few hours for the special tests.[1]

Subject No. 1.—This man was on an abundant diet of toast, figs, milk and coffee. The Rehfuss tube was taken soon after breakfast and allowed to work down through the pylorus. An hour after this the tip was about six inches below the pylorus. The intestinal chyme secured at this point was 20 cc. in volume and was thick and not much colored. In the Hasselbalch cell we found

$$P_H = 4.56;\ C_H = 2.75 \times 10^{-5}.$$

This is a pronounced degree of acidity and indicates that at this point the stomach chyme had not yet been neutralized by the bile or pancreatic juice.

Subject No. 2.—This was a different man and furnished the next three portions of liquid examined. The samples were collected in the early morning after a meal consisting of meat, potatoes, bread and milk. This meal was taken at midnight and the tube immediately swallowed. It worked down rapidly and by 4 o'clock was well through the duodenum, the tip showing some seven or eight centimeters beyond the duodenal-jejunal bend. Collections were then begun and continued with the following results:

	4 A.M.	6 A.M.	6.30 A.M.	7.15 A.M.	7.45 A.M.
P_H =	5.36	3.80	5.78	7.30	7.81
C_H =	4.4×10^{-6}	1.4×10^{-4}	1.7×10^{-6}	5×10^{-8}	1.5×10^{-8}

This is a very singular series of reactions. There are two which are faintly acid, but the second one is decidedly acid. It is possible that here, on account of some sudden movement on the part of the subject, a more marked opening of the pylorus followed and a larger flow of acid chyme passed suddenly into the duodenum. A lapse of the flow of the alkaline bile or pancreatic juice from any cause would likewise give rise to an acid content. It is further to be noted that after the 4 o'clock collection a drink of water was taken by the subject.

The last collection was made over seven hours after the meal, when the stomach digestion was probably completed and the flow of the acid chyme, therefore, small. The pancreas and bile flows continued, with the latter

[1] Our thanks are due to Dr. Achilles Davis and assistants for their kindness in making these collections, and precautions taken to secure the fluids from the desired location.

in evidence, as shown by the color. The last portions of liquid collected were rather scanty, and much below the amounts secured earlier.

Three days later; same subject and same diet. The fluid was taken after the tube had been in position some three hours with the tip beyond the duodenum. We found:

$$P_H = 5.12; C_H = 7.6 \times 10^{-6}$$

Five days after last; same subject and same diet. The fluid was collected under the same conditions. We found:

$$P_H = 5.69; C_H = 2 \times 10^{-6}$$

The amount of liquid secured for these tests was not over 20 cc. in each case; later efforts failed to yield more. But little liquid was consumed at the morning meal and it appears that nearly everything had left this part of the intestine before the time of the collection. In both cases there is a marked degree of acidity, but if examined by the aid of methyl orange the result would suggest alkaline reaction.

Subject No. 3.—A normal individual as far as digestive functions are concerned. The tube was passed into the duodenum immediately following an ample breakfast consisting of meat, potato and bread. Four hours after the introduction of the tube the tip was in position about five inches below the pylorus when the first sample of contents was brought up. There was no marked bile color in evidence. We found:

$$P_H = 2.27; C_H = 5.4 \times 10^{-3}$$

It is quite clear that the chyme is but slightly neutralized at this point and that we are not dealing with a characteristic duodenal fluid.

The following day; same subject and diet. The tube had not been removed but had been allowed to work down lower by the general peristaltic action with the tip of the tube well beyond the duodenum. There was much bile in the liquid brought up and this reaction was found:

$$P_H = 5.62; C_H = 2.4 \times 10^{-6}$$

A day later; same subject, same diet. The tube not moved from last position. Plenty of bile in the liquid secured. The tests gave:

$$P_H = 6.26; C_H = 5.5 \times 10^{-7}$$

Subject No. 4.—This was also a normal man with a good appetite. A tube was swallowed and allowed to drop to the beginning of the jejunum before any observations were made. The first liquid brought up some three hours after finishing breakfast showed presence of bile. The tests gave:

$$P_H = 7.69; C_H = 2.1 \times 10^{-8}$$

The same man a day later with the tube still in position. Bile present.

$$P_H = 7.15; C_H = 7.1 \times 10^{-8}.$$

These observations probably give a fair picture of the usual variations

in the reaction of the small intestine. There seem to be few experiments that throw much light on the subject of the reaction in adults. Some are reported by McClendon for the infant duodenal tract where an acid reaction appeared to be the rule. The tests were made by aid of papers with indicator colors. He reports one case of alkaline reaction in an adult.[1] Our experience leads us to believe that in collections with the Einhorn or Rehfuss tube much depends on the depth to which it is allowed to pass. If the end is just below the pylorus the contents brought up may give a strongly acid reaction, as shown in one of the cases reported and found in many instances not reported here, while if at a slightly lower level the pancreatic juice and bile, entering at the same point, may give a distinctly alkaline reaction because of incomplete mixture with the acid chyme. Some time is necessary for this mixing and it is therefore desirable to drop the tube to a lower point and control this with the shadow picture. It may be necessary to leave the tube in the intestine two or three days to secure trustworthy results.

Under these conditions the intestinal contents in man are frequently found to be acid to a distinct degree, but there seem to be individual variations which may call for special study. The results with subjects 3 and 4 who had essentially the same diet and other conditions support the view as to individual peculiarity.

Experiments on Animals.

We have carried out a considerable number of observations on the intestines of certain animals, and essentially in this manner. With the exception of the dog referred to below all the animals observed were killed for food purposes in the packing houses of Armour & Company, of this city. Immediately after slaughtering the abdomen was opened and the small intestine ligatured at each end. Then two more loups were tied so as to divide the whole tract into three equal sections, in the case of hogs each being from 18 to 20 feet in length. The intestines were then removed from the body, taken to the laboratory, washed off, and the contents of each loup or section poured into a vessel which had been washed with toluene. For each set of observations the contents of the intestines of three animals was taken and a composite made from the fluids from each section. This is justified because the animals taken had had the same feed and at the same time, but animals killed on different days would not necessarily show this regularity.

The upper thirds, containing the duodenum and part of the jejunum, were usually nearly empty, the following thirds often so, while the lower sections always contained considerable quantities of food remains, mainly corn and hay in the case of the hogs. In order to effect a separation of

[1] *Am. J. Physiol.*, 38, 191 (1915).

fluid for the tests the composite mixtures, with some toluene added, were transferred to active centrifugal machines and rotated a few minutes. In a few instances an equal volume of distilled water was added to aid in making a separation. It was always easy to secure enough clear liquid for the concentration cell test and this preliminary work was done with the least possible delay in the research laboratory of Armour & Company.

The clarified liquids were then brought immediately to the Medical School laboratory where the ion concentration tests were made, the cells being in readiness for the purpose. The various precautions taken were for the purpose of preventing as far as possible any ferment changes in the organ contents between the time of opening the intestine and the actual determination of the reaction. That these precautions were sufficient is shown by the fact that the liquids in the cells gave a constant value, when once equilibrium was reached, which did not change appreciably in hours. We believe, therefore, that the recorded results represent practically the conditions in the intestines when opened.

Occasionally the reaction of the freshly opened intestine is so distinctly acid or alkaline that it may be recognized with good litmus paper; but often it is obscure because of proximity to the neutral point or because of turbidity of the fluid.

Observations on Hogs.—The following results were obtained from hog intestines examined on different days:

February 7th. Composite from intestines of three hogs. As the contents were too thick to centrifuge an equal volume of water was added.

Upper loups, $P_H = 7.40$; $C_H = 4 \times 10^{-8}$
Middle loups, $P_H = 7.14$; $C_H = 7.2 \times 10^{-8}$
Lower loups, $P_H = 6.86$; $C_H = 1.4 \times 10^{-7}$

February 8th. Composite from three hogs. No water added.

Upper loups, $P_H = 6.61$; $C_H = 2.4 \times 10^{-7}$
Middle loups, $P_H = 6.48$; $C_H = 3.3 \times 10^{-7}$
Lower loups, $P_H = 6.39$; $C_H = 4.1 \times 10^{-7}$

February 20th. Composite from three hogs but no water added for aid in clearing.

Upper loups, $P_H = 6.48$; $C_H = 3.3 \times 10^{-7}$
Middle loups, $P_H = 6.66$; $C_H = 2.2 \times 10^{-7}$
Lower loups, $P_H = 7.43$; $C_H = 3.7 \times 10^{-8}$

There was considerable gas in the intestines of these hogs. It was largely nitrogen and carbon dioxide. No hydrogen or methane.

March 22nd. Composite from three hogs which had been without food 12 hours when killed.

Upper loups, 504 cc.; $P_H = 6.69$; $C_H = 2.0 \times 10^{-7}$
Middle loups, 150 cc.; $P_H = 6.81$; $C_H = 1.5 \times 10^{-7}$
Lower loups, 810 cc.; $P_H = 7.07$; $C_H = 8.5 \times 10^{-8}$

March 28th. Composite from five hogs.

Upper loups, $P_H = 7.01$; $C_H = 1.0 \times 10^{-7}$
Middle loups, $P_H = 7.02$; $C_H = 9.5 \times 10^{-8}$
Lower loups, $P_H = 6.79$; $C_H = 1.6 \times 10^{-7}$

April 6th. Composite from three hogs.

Upper loups, 220 cc.; $P_H = 6.67$; $C_H = 2.1 \times 10^{-7}$
Middle loups, 460 cc.; $P_H = 7.63$; $C_H = 2.3 \times 10^{-8}$
Lower loups, 600 cc.; $P_H = 8.05$; $C_H = 8.9 \times 10^{-9}$

Observations on Calves.—March 22nd. Composite from three yearling calves. They had had no food for 18 hours when killed, but water.

Upper loups, $P_H = 6.57$; $C_H = 2.7 \times 10^{-7}$
Middle loups, $P_H = 6.52$; $C_H = 3.0 \times 10^{-7}$
Lower loups, $P_H = 6.99$; $C_H = 1.0 \times 10^{-7}$

Observations on Lambs.—March 23rd. Composite from three yearling lambs. Deep bile color in all loups.

Upper loups, 200 cc.; $P_H = 6.42$; $C_H = 3.8 \times 10^{-7}$
Middle loups, 170 cc.; $P_H = 6.95$; $C_H = 1.1 \times 10^{-7}$
Lower loups, 570 cc.; $P_H = 7.76$; $C_H = 1.7 \times 10^{-8}$

All of the above results are from animals essentially herbivorous in their diet, and which were killed at periods showing some range in the stage of digestion. Below we have the results from the intestine of a dog which had been abundantly fed on meat and milk. The animal was killed during the progress of digestion, when there was some food in the stomach and plenty of the intestinal chyme, as was found when the tract was opened. The whole of the small intestine was removed, after tying, washed thoroughly so as to avoid contamination and opened at once. The contents of the whole loup was transferred to the centrifuge and separated into a thin and a thick layer, the latter of which was watery enough to put into the concentration cell, all of which operations were carried out within a few minutes. This result was found:

$$P_H = 6.79;\ C_H = 1.6 \times 10^{-7}$$

We have here a slight degree of acidity in a case where the whole of the intestinal contents was used, and where tryptic digestion was undoubtedly in progress. Few similar observations seem to be recorded. According to Foá, quoted by McClendon,[1] a reaction of $P_H = 9.28$ was found in the intestinal contents of a dog, while Auerbach and Pick,[2] for the intestinal juice of dogs report a reaction varying between 0.2×10^{-8} and 5×10^{-8}. While this represents the true juice rather than the duodenal contents during digestion, and has no direct bearing on the question, it shows a much lower alkalinity than formerly assumed.

[1] *Med. Rev. of Rev.*, **22**, 359 (1916).
[2] *Jahresber. Tierchem.*, **42**, 339 (1912).

Intestinal Gases.

In working with the hog intestines, especially, it was noticed that much gas was often present. As the nature of this gas might have a bearing on the character of the acidity observed a number of additional experiments were carried out to throw some light on this point. The greatest importance would be attached to the presence of hydrogen or methane.

It is not possible to determine with any great degree of accuracy the distribution of the gases in different parts of the tract because, in the manipulations of the bodies of the animals, there would be every opportunity for some shifting of the gases, and much more than for the liquid contents. However, the bodies were shifted as little as possible and loups were tied off as for the other work. The gases were collected separately from these loups, composites being made to secure averages following different feedings.

The following results were obtained in a number of trials. Hydrogen and marsh gas were either absent or in such small quantity that they could not be recognized. Nitrogen is given here by difference.

Conditions.		CO_2.	O.	N.
3 hogs, recently fed.....	1st loup	27.6%	5.0%	67.4%
	2nd loup	but little gas present		
	3rd loup	9.0	8.8	82.2
5 hogs, recently fed.....	1st loup	19.0	4.6	76.4
	2nd loup	20.8	2.2	77.0
	3rd loup	18.8	2.6	78.6
2 hogs, not recently fed.....	3rd loup	5.8	14.2	80.0
5 hogs, recently fed.....	1st loup	18.0	7.8	74.2
	2nd loup	5.2	3.2	91.6
	3rd loup	22.4	1.2	76.4

From these results, which are very irregular, only general conclusions may be drawn. Nitrogen is always the main gas present and in amount approximating the atmospheric content. Carbon dioxide is greatest and oxygen lowest during active digestion, as shown in the case of the hogs where the feeding had been recent. In the case of the two hogs not recently fed the small intestine was nearly empty and the upper stretches flat. There was not much gas except in the lower part, and the oxygen is highest here. In some of the cases where digestion was in active progress a trace of hydrogen sulfide could be occasionally recognized by lead paper. No explanation can be offered for the peculiar composition of the middle loup mixture in the last group of animals examined.

Conclusions.

In the human small intestine the reaction may vary from distinctly acid to slightly alkaline on the part which may be reached by the Rehfuss tube. Where the tube is far enough down to secure a uniform mixture of contents the acid reaction is apparently as common as the alkaline, but

the degree of acidity is not sufficient to check the normal tryptic digestion, which in some instances seems to be favored by a reaction on the acid side of neutrality. The reaction found must vary with the state of digestive activity and is simply an equilibrium condition between the chyme and the alkaline juices poured into the duodenum. Any reaction near neutrality may obtain.

In the case of a dog the intestinal contents secured during active digestion was slightly acid with $[H] = 1.6 \times 10^{-7}$, and this after much of the carbon dioxide had escaped.

In working with other animals notable variations in the reaction were found, at different times and in different parts of the small intestine, which for convenience in observation was tied so as to make three loups in each case. No simple relation was found, but for hogs, lambs and calves the reaction was found to be more often acid than alkaline, the measurements in all cases being made by concentration cells. In most cases the upper third of the intestine was found to be the most strongly acid, while the lower third might be alkaline. However, this relation was sometimes found to be reversed. In the case of the hogs some food remains were always found in the middle and lower thirds of the intestine, and the amount would vary with the time which had elapsed since feeding. Digestion would be in active progress, therefore, sometimes under acid and sometimes under an alkaline condition.

In working with the hogs we found the variations in the reaction to be between $[H] = 3.3 \times 10^{-7}$ and 8.9×10^{-9}. The slight degree of alkalinity is more marked than the acidity reached. The range for the other animals is included within these limits, but for man the acidity reached was sometimes lower. But in this case, it must be remembered, we have but little more than the duodenum for comparison.

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THE PLANT FOOD MATERIALS IN THE LEAVES OF FOREST TREES.

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Received March 27, 1917.

Introduction.

This work was undertaken for the purpose of investigating the plant food constituents of the leaves of three typical New England forest trees at the beginning of their activity in the spring and practically at the end of their growth in the fall; to observe the difference in content of these materials in the leaves taken from the branches nearest the soil and those from the very top of the tree; to observe the varying content in the leaves