Alkaline Tide of the Alligator. (18072)

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In a study of the biochemistry of *A. mississipiensis* in the fasting state(1) a reference was made to the magnitude of the variation in certain blood constituents which occurred after feeding the animals. It was deemed advisable to study this phenomenon and report the results in some detail.

The animals thrive in captivity and through all of the warmer months they desire large amounts of food every 3 or 4 days. It is not uncommon for them to consume as much as one-fourth their body weight at one meal. Blood glucose and electrolyte studies indicate that about 3 days are required for the complete digestion of any one meal after which time the blood constituents are again at fasting levels. Although the individual variations are considerable, available evidence indicates that the food remains in the stomach from 24 to 36 hours. The plasma becomes lipemic during the second day and the lipemia is usually absent by the sixtieth hour after feeding. During the period of gastric digestion the bolus is subjected both to the action of the muscles of the stomach wall and to a large volume of hydrochloric acid at a pH of 2 or less. The secretion of this acid produces the typical qualitative picture of an "alkaline tide" but the duration and intensity of this phenomenon is far greater than that reported for the human(2,3). Although the general picture of the electrolytes of the fasting alligator is quite similar to that found in the human, the plasma changes after feeding are so great that the pH often becomes as alkaline as 7.8 and a few values of over 8 have been observed. Along with the marked rise in pH the chloride falls to a low level and the bicarbonate rises to a correspondingly high level. In one instance the chloride level of an animal declined from the normal fasting level to 7 m.eq./liter. Plasma bicarbonates as high as 88 m.eq./liter have also been observed.

Eleven alligators of undetermined sex from 3 to 5 years of age and weighing from 1.5 to 7.0 kg were used in the present study. Six smaller alligators weighing 85.8 to 177.5 g were ashed to determine their composition. The analytical methods employed for the estimation of plasma pH, CO_2, chloride, sodium, calcium, and phosphorus were reported in an earlier report on the results of blood and urine analyses(1). A limiting factor in all of the experiments was the large amount of blood required for the different simultaneous analyses, and several experiments had to be concluded prematurely to avoid severe anemia in the animals.

The following procedure was used in the acid-base studies. Blood was obtained by cardiac puncture using a No. 19 gauge needle and a 10 ml hypodermic syringe. About 2 ml of blood were drawn into the syringe, the syringe was detached with the needle left in the heart, and a Beckman blood glass electrode was quickly inserted in the needle. About one-half ml of blood was allowed to well up in the electrode chamber, the needle was withdrawn from the heart, and the pH was determined within 20 seconds. The temperature of the alligator is within 2°C of room temperature which enables one to determine the pH directly without making any correction for temperature changes. Although it was not found necessary to cover the heparinized blood specimens for the sodium, chloride, calcium, or phosphorus determinations, the specimens for CO_2 analyses were placed under oil immediately and the total plasma CO_2 content estimations were done as soon as possible.

Table I presents a more or less typical

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TABLE I.
Changes in Plasma Composition Following Feeding.

	Fasting				9 hr				19 hr			
No.	pH	Cl meq/l	CO_2 mM/l	Na meq/l	pH	Cl meq/l	CO_2 mM/l	Na meq/l	pH	Cl meq/l	CO_2 mM/l	Na meq/l
3	7.36	111	19.4	151	7.67	93	34.6	144	7.64	96	37.7	146
4	7.36	115	15.3	153	7.56	96	26.2	148	7.47	92	35.4	150
6	7.34	112	20.1	151	7.83	88	44.6	149	7.75	47	88.6	150
7	7.32	109	19.9	151	7.48	100	27.4	144	7.26	99	29.4	147
8	7.32	113	21.1	151	7.96	76	45.5	148	7.56	87	37.1	144
9	7.33	102	25.2	150	7.33	93	29.8	153	7.52	88	32.2	152
11	7.30	107	24.1	151	7.56	91	30.1	144	7.41	90	32.0	151
13	7.58	87	30.2	151	8.09	49	74.1	147	7.69	72	44.0	150
	24 hr				180 hr							
3	7.64	98	38.8	150	7.38	115	19.4	152				
4	7.60	93	36.3	155	7.21	117	14.3	148				
6	7.53	81	40.8	152	7.22	113	17.6	151				
7	7.43	99	26.7	150	7.27	109	19.2	153				
8	7.57	89	25.7	154	7.29	115	19.7	154				
9	7.59	81	41.2	148	7.17	109	26.9	150				
11	7.57	92	34.0	150	7.45	99	26.3	144				
13	7.53	70	48.0	150	7.57	87	39.3	147				

picture of the "alkaline tide" that follows the ingestion of food (whole rats) by the alligator. It will be noted that the individual differences are considerable. Alligator No. 7 showed the least response and No. 6 showed the greatest response. At the time the high blood pH (8.09) was observed in No. 13, the alligator was placed under careful observation to ascertain the effect of extreme alkalemia on respiration, irritability, etc. The animal appeared to be normal in all respects. Curiously enough some alligators show a perennial alkalemia, and there is no evidence that these animals are in poor health or that the continued alkalinity is in any way injurious. Perhaps it represents merely another example of individual variation. With the exception of No. 13 the sum of the principal anions, chloride and CO_2, gives a value which is fairly constant for each alligator throughout the entire experiment. The slight variations in plasma sodium levels are within the experimental error of our method of determination since we could not spare the plasma for duplicate or triplicate analyses on each blood specimen. Although attempts were made to determine the pH of the urine every time blood was withdrawn from an alligator about one-third of the time the urine volume was inadequate for testing. No significant pH changes over the fasting levels were noted in the specimens which were analysed.

In all, 10 experiments were conducted in the months of January, February, April, May, June, August, September, and November to determine the nature and magnitude of the "alkaline tide." These experiments included a total of 360 individual chloride analyses done on blood specimens taken at varying numbers of hours after feeding. In spite of the number of experiments the exact effect of season on the rate of production of HCl is still in doubt. The greatest response observed following feeding occurred in August and September, a fact which may or may not be significant. It is a disappointment to note that the variation in response from animal to animal and indeed in the same animal at different times is very great, and, although the direction of these plasma changes is always the same, the degree of change and the exact time when the lowest plasma chloride level is reached is almost impossible to predict. Technical difficulties have prevented adequate study of the quantity of hydrochloric acid and volume of the gastric contents, although pH values as low as 2 were observed.

Evidence for the fact that all of the alli-

TABLE II.
Effect of Changes in Plasma pH on Plasma Ca and P. (Avg of 6 animals).

	Cl meq/l	CO_2 mM/l	pH	Ca mg%	P mg%
26 hr after feeding	88	31.4	7.45	11.3	3.53
Fasting	109	22.7	7.28	11.5	3.53

TABLE III.
Individual Variations in Fasting Blood pH.

	Time		
All. No.	10:00 A.M.	11:00 A.M.	1:00 P.M.
5	7.18	7.26	7.07
6	7.13	7.36	7.20
7	7.26	7.42	7.47

gators which were used for this study do respond to feeding may be deduced from an examination of the following figures which represent the lowest plasma chloride levels ever found in each of the 11 animals. These values are 40, 75, 46, 45, 57, 27, 50, 13, 7, and 41 milliequivalents per liter. It is possible and even probable that had we known the exact time of maximum response to feeding of all of these experimental animals we might have found chloride values even lower than these reported here. The lowest fasting level ever found was 83 and the average of 98 fasting chloride determinations was 111 milliequivalents per liter.

The high pH levels often observed made it desirable to determine the effect of these drastic pH changes on the plasma calcium and phosphorus contents. Several experiments were conducted and the results of one of these are to be found in Table II. We could find no effect of changes in pH, chloride or CO_2 levels on plasma calcium and phosphorus.

The least reliable information on the acid-base balance of the alligator is furnished by determination of blood pH. Although it is true that the pH of the blood does rise following feeding the amount of this increase is variable. It is possible that the extremely irregular rate of breathing causes wide variations in the amount of free H_2CO_3 in the plasma which results in fluctuations in the $H_2CO_3/NaHCO_3$ buffer ratio. Table III illustrates the variations in the pH change in 3 fasting alligators under conditions in which the environment and temperature were kept constant.

The composition of the ashes of several 1-year-old alligators with respect to some of the more important electrolytes involved in acid-base regulation is presented in Table IV. On the assumption that all of the chlorides assume an extracellular position in the body (an assumption which is not necessarily valid) the total extra-cellular fluids may be calculated from the chloride content. The volumes of extra-cellular fluids calculated in this manner vary from about 19 to about 32% of the body weight. The total sodium and potassium contents showed far less deviation than the chlorides which suggested that chloride had been lost in the ashing of No. 5 and No. 14. Since all of the ashings were done at the same temperature (460°C) and in the same oven it seemed plausible to suspect that the excessive chloride loss may have been due to the volatilization of free gastric HCl. No information is available on the plasma chloride or CO_2 contents of alligators 1, 2, 5 and 48 just prior to ashing. The plasma chloride content of 14, which was fed 18 hours before ashing, was 51 m.eq./l and the plasma chloride content of 23, an animal in the fasting state, was 90 m.eq./l. This indicates that some HCl may have been lost in the ashing although the evidence is by no means conclusive. Further studies are necessary to clarify this point.

Experiments with histamine on the "alkaline tide" met with little success. Amounts varying from 0.01 mg/kilo to 10 mg/kilo were given intramuscularly to several different alligators and blood samples were taken at intervals of from as early as 5 minutes to as late as 27 hours after the injection. The lower doses had little apparent effect while with one possible exception the higher doses produced an acidemia instead of an alkalemia. It is possible that the increased acidity of the blood was due to anoxia caused by respiratory depression since the animals appeared to be semi-moribund for a large part of the experiment. It is still possible that our dosage was wrong and that a study

TABLE IV.
Composition of the Alligator.

All. No.	Wet wt, g	Dry wt, g	H_2O, %	Ash wt, g	Cl m.eq.	Na m.eq.	K m.eq.
1	111.0	25.7	76.8	4.658	3.93	5.35	4.69
2	92.7	22.7	77.6	3.660	3.23	4.45	3.88
5	177.5	43.8	75.0	6.803	3.70	7.07	8.29
48	85.8	20.8	75.8	3.488	3.02	3.52	3.53
14	140.0	31.2	77.7	5.547	3.58	5.80	6.16
23	93.0	18.7	79.9	3.900	3.08	4.03	3.72

of several more animals may yet reveal some effect of histamine.

Summary. The alkaline tide of the alligator has been studied. Although the plasma electrolyte changes were qualitatively similar to those reported for other animals the magnitude of these changes was much greater. Some plasma chloride levels as low as 15% of the fasting level were found and some plasma bicarbonates were elevated 5-fold. Although the average fasting blood pH is about 7.3, pH values of over 8 have been observed at the height of the "alkaline tide." Plasma sodium concentrations were unaffected by feeding. No correlation was found between pH and plasma calcium content.

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Destruction of Pancreatic Acinar Tissue by DL-Ethionine.* (18073)

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The liver's dependence upon dietary factors for its structural and functional integrity is now fully accepted. That such factors also influence the exocrine portion of the pancreas is becoming increasingly clear. Chernick *et al.* found that the feeding of raw soy bean meal induced pancreatic hypertrophy and increased proteolytic activity in the chick(1). Grossman *et al.* reported atrophic pancreases in rats fed a low protein-high fat diet(2) whereas chronic cystic fibrosis was observed, by the Gillmans, in rats fed mealie pap and sour milk(3). In this laboratory, pancreatitis, in which the interstitial tissue appeared to be primarily involved, was induced in dogs by feeding them a high fat-low protein diet(4). Interest in these experimental lesions was increased by the recent suggestion of Davies that kwashiorkor, a nutritional disorder widespread in Africa, is essentially of a pancreatic nature(5). Davies' report was quickly followed by two letters in *Lancet* which brought to light further instances, in man, of pancreatic dysfunction accompanying severe nutritional deficiency(6,7).

We have recently observed that the feeding of a high fat-low protein diet in rats resulted in zymogen degranulation of the acinar tissue of the pancreas, and that methionine prevented its occurrence. This protective action of methionine led us to study the effects of DL-ethionine upon the pancreas. It is shown here that the administration of this analogue of methionine destroys the acinar portion of

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