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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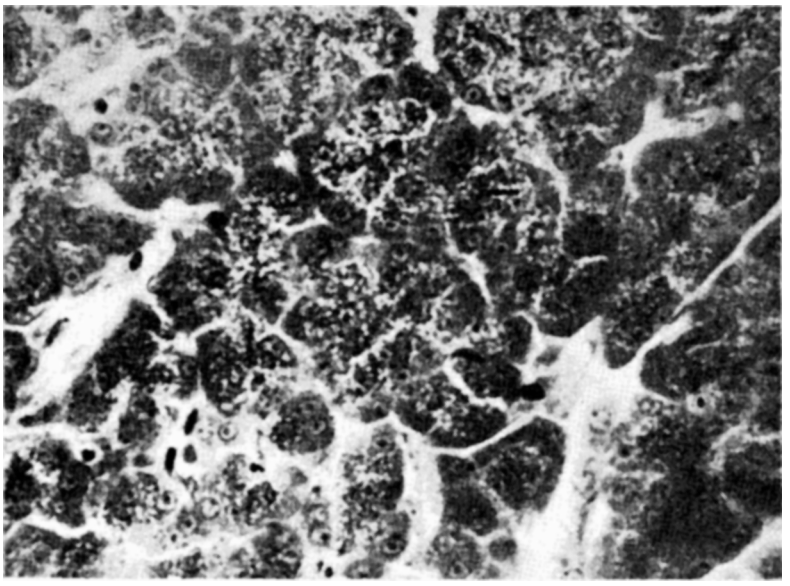

FIG. 1.

Normal rat pancreas. The apical portion of the acinar cells are filled with zymogen granules (black in photograph). Note the cytoplasmic basophilia at the base of the cells. All glands were fixed by intra-arterial injection of Zenker-formol; sectioned at 4 microns. Masson: ×500.

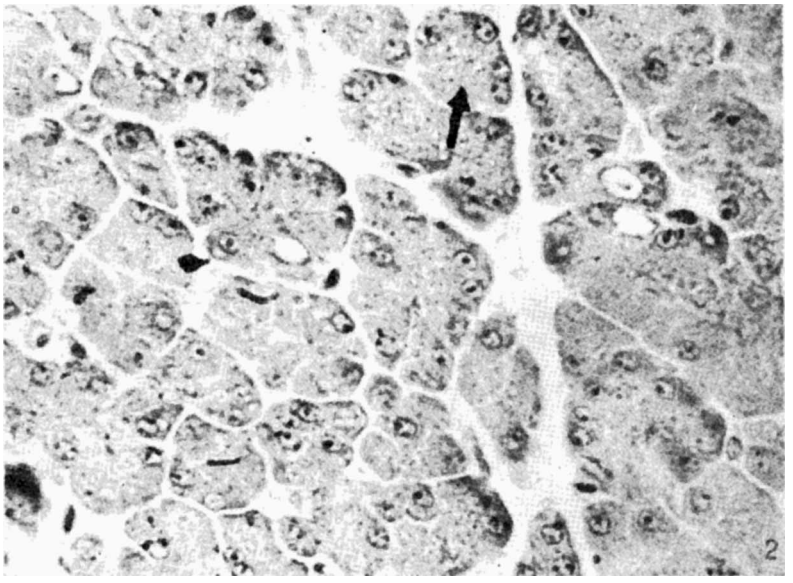

FIG. 2.

Pancreas from rat sacrificed 12 hours after injection of 50 mg DL-ethionine. Note almost complete absence of both zymogen granules and cytoplasmic basophilia. Acinar cells at tip of arrow still are sparsely granulated. Masson: ×500.

the gland. The islet tissue appears histologically normal.

Experimental. Male and female rats, weighing 200-250 g, were injected intraperitoneally, daily, with 50 or 100 mg of DL-ethionine for 1 to 14 days. The rats had ac-

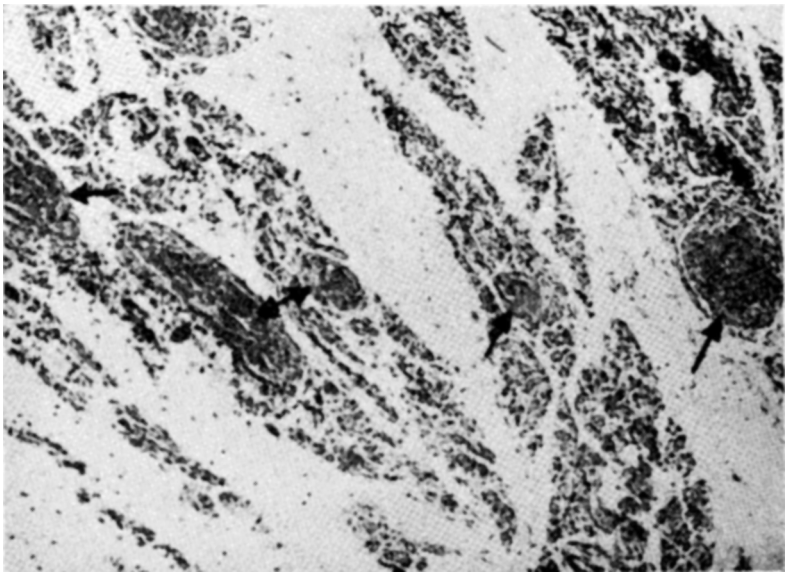

FIG. 3.
Pancreas from rat which received 100 mg DL-ethionine per day for 14 days. Arrows point to islets embedded in the atrophic, fibrotic gland. At this time only a few scattered identifiable acinar cells were observed. Masson: ×100.

cess to food and water until they were sacrificed.

Cytological changes were observed in the pancreas as early as 12 hours after a single injection of 50 mg of DL-ethionine. The acinar cells showed loss of zymogen granules and of cytoplasmic basophilia (Fig. 2). In 24 to 48 hours, the acinar tissue was almost completely degranulated and had lost its cytoplasmic basophilia. The nuclei of these cells exhibited coarser, deeper staining nuclear membranes, and there was clumping of the chromatin material. Distortion of the typical acinar architecture was evident at this time. Dilation of the ducts was prominent; many contained an eosinophilic granular material. No histological alterations were observed in the islets of Langerhans.

Marked pancreatic atrophy and fat necrosis were prominent in rats that had been injected daily with ethionine for one week. Microscopic examination revealed nuclear pyknosis and fragmentation, hydropic degeneration, and cellular disintegration. The tissue was edematous, and a leucocytic infiltration was evident. Exocrine tissue had been gradually replaced by newly laid down connective tissue.

After 2 weeks of ethionine injections, only occasional, scattered single exocrine cells could be identified in the fibrous stroma; some of these contained zymogen-like granules. The dilated ductules appeared unaffected, and the islets still showed no pathological alterations (Fig. 3).

Farber and coworkers(8-10) have shown that the injection of ethionine induces fatty livers in the rat and that this response is much more prominent in the female than in the male. This observation has been confirmed by Jensen in this laboratory (unpublished data). Interestingly enough, the destruction of acinar tissues after injection of ethionine was widespread in both sexes.

The rats suffered marked loss in body weight as a result of the injections. Diarrhea was observed 5-6 days after the start of treatment. An increase in the histologically demonstrable lipid was found in the liver as

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early as 6 to 8 hours after injection, and rose to a maximum in about 48 hours. At that time, the entire liver parenchyma was involved, all hepatic cells being distended with lipid globules. A progressive loss of liver lipids was noted after that time despite continued ethionine injections.

One group of rats was fed the stock diet to which had been added 0.1 per cent DL-ethionine. Although the food intake varied widely (0-14 g per day, average of 5 g per day), the effect on the pancreas was no different from that observed when the ethionine was injected.

Comment. It has been known since 1924 that fatty livers developed slowly in depancreatized dogs kept alive with insulin, and that the addition of raw pancreas prevents this fatty change(11). The finding that a similar type of fatty liver occurs in dogs subjected to complete ligation of their pancreatic ducts has led to the view that the release of pancreatic juice into the intestinal tract is necessary for inhibiting the deposit of excessive amounts of fat in the liver. This led us to question whether the fatty liver found in the DL-ethionine-treated rats resulted from destruction of their pancreatic acinar tissue. However, the rapid onset of this fatty change would appear to cast doubt on the possibility that it results from loss of the external secretion of the pancreas.

The view that ethionine inhibits protein synthesis has been expressed by Simpson *et al.* (12). The rapid depletion of zymogen granules and the loss of cytoplasmic basophilia (presumed to reflect the nucleoprotein content of the cell) might be construed to support this view(13-18). It should be stressed, however, that a direct toxic action of the administered ethionine (or a derivative) upon the acinar tissue is not ruled out.

Summary. 1. The effects of daily administration of 50 or 100 mg of DL-ethionine on the rat pancreas is described.

2. Degenerative changes in the acinar tissue occurred as early as 12 hours after a single injection of 50 mg DL-ethionine.

3. Daily injections of 50 or 100 mg in nonfasted rats, for 2 weeks, resulted in almost complete obliteration of the acinar tissue accompanied by fibrous proliferation.

4. No histological evidence of islet damage was observed with these dosages.

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Passive Transfer of Atopic Hypersensitiveness in Man by Means of Leucocytes.* (18074)

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Lawrence(1) has recently demonstrated, in man, the local passive transfer of the delayed type of cutaneous hypersensitiveness to tuberculin by the intracutaneous injection, into normal recipients, of viable leucocytes obtained from the blood of tuberculin-sensitive

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