THE EFFECT OF VARIED OXYGEN SUPPLY AND OF FOOD INTAKE ON WATER MOVEMENT IN SURVIVING LIVER TISSUE

By EUGENE L OPIE

(*From The Rockefeller Institute*)

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In a preceding publication, evidence was cited to show that the movement of water in immersed slices of liver varied widely when liver tissue was obtained from animals in different stages of gastrointestinal digestion (1). It was noted that liver slices from animals with stomach distended with food took up more water than those obtained from animals with advanced digestion and smaller stomach contents.

Slices of liver usually weighing from 50 to 100 mg. have been immersed in buffered Krebs-Ringer solution and exposed with rhythmic shaking to streaming oxygen with varied partial pressure. The procedure has been described in detail in the preceding publication (1). In liver slices, obtained from white rats at different intervals after the ingestion of food, changes in the water contents of the tissue have been measured during the period of immersion.

In animals that have received no food during 20 to 24 hours the stomach is empty save for a minute quantity of insoluble residue. The small intestine contains a variable quantity of yellowish translucent mucoid material. After ingestion of 15 to 25 gm. of food, consisting of bread with milk, stomach contents diminishes to 3 or 4 gm., remains at this level during several hours and then decreases so that after 12 hours the stomach contains from 0.2 to 1.2 gm. of soft, far-digested material. The contents of the small intestine have increased and chiefly in the distal part have become semisolid, opaque, and greenish brown. This opaque soft material is still present in decreased quantity after 12 hours but is absent after 20 hours. In the period between 4 and 8 hours the cecum and proximal part of the colon contain abundant soft material somewhat more fluid than that in the distal part of the small intestine.

It has been found desirable to control the feeding of animals by a mechanical timing device which has been constructed for the purpose by Mr. N. A. Jernberg, The Rockfeller Institute. Access to a food cup is prevented by a plunger moved by an electric motor which is controlled by two timers. Each has a range of 24 hours so that at a chosen time the plunger can be raised to give access to the food or dropped in order to close the cup. It has been necessary to provide the plunger with a mechanical lock which acts when the plunger falls, as otherwise animals have almost invariably succeeded in raising the plunger. The feeding device has been attached to a cage having a floor of wire grating with wide mesh so that the ingestion of fecal material is unlikely to occur. With unusual exceptions, animals that had consumed at least 15 gm. of food were used.

Water intake of liver slices has been measured, on the one hand, in the presence of streaming oxygen supplied by air and with 5 per cent carbon dioxide;

on the other hand, it has been measured with complete anoxia caused by gassing with nitrogen 95 per cent and carbon dioxide 5 per cent. The former contains oxygen with partial pressure of about 140 mm. Hg and carbon dioxide with partial pressure of about 35 mm. Hg (1). With the progress of digestion, water movement within the corresponding liver slices varies widely (Table I, Fig. 1). The greatest water intake in the presence of the two gas mixtures and the widest deviation between the two has occurred with liver of animals that have received no food during 20 to 24 hours. Liver of animals that had ingested food took up less water both with anoxia and in the presence of air. The quantity was less after 2 to 5 hours of feeding and still less after 5 to 7 hours, and after 7 to 9 hours. After 12 hours water was lost by liver slices in the presence of both

TABLE I

Water Movement in Immersed Liver Slices from Animals at Different Intervals after Ingestion of Food

Time with no food	Food eaten	Stomach contents	Air 95 per cent			Nitrogen 95 per cent		
			After 60 min.	After 120 min.	After 180 min.	After 60 min.	After 120 min.	After 180 min.
hrs.	*gm.*	*gm.*						
20 to 24		0.4	128.1	128.0	123.9	140.4	137.0	130.9
2 to 5	16	7.6	114.0	102.2	101.5	124.7	116.8	119.1
5 to 7	20	4.2	107.1	96.1	94.9	116.1	113.5	111.9
7 to 9	21	2.1	105.3	90.2	92.2	105.3	90.2	92.2
12	21	0.5	81.9	86.2	82.9	96.4	99.4	93.9
11	18	0.7	125.9	122.8	116.7	135.5	130.8	129.2

nitrogen and air. Nevertheless, liver slices exposed to anoxias or to air reached highest level of water intake about 20 hours after feeding with an intermediate stage after 16 hours (Fig. 1).

The maximum partial pressure of oxygen brought to the tissues by the arterial blood and hence in the tissues themselves is about 100 mm. Hg. With this relation in view (Table II), liver slices from animals at different intervals after the ingestion of food have been exposed to oxygen 14 per cent which in mixtures with carbon dioxide 5 per cent, nitrogen, and water vapor provides a partial pressure of about 100 mm. Hg. (1).

In the experiments with oxygen 14 per cent (Table II) water movement in liver slices has followed with relation to gastrointestinal digestion a course similar to that of liver tissue exposed to air or to nitrogen (Table I, Fig. 1), being greatest after a period of fasting and diminishing to a low level after ingestion of food.

By means of calculations based on the oxygen content of blood entering and leaving the submaxillary gland of dogs, Verzár (2) reached the conclusion that diminished respiratory oxygen failed to diminish the oxygen used by the gland, but under similar conditions skeletal muscle used less oxygen. The method was not found applicable to other tissues. Kûthy (3) fed raw meat to rats and measured by Kjeldahl determination of nitrogen the per cent of protein that disappeared from the gastrointestinal tract. Protein had diminished to about 90 per cent after 8 hours. Amino acid nitrogen of the blood increased for a time and reached a maximum after 3 hours at a time when the protein in the gastrointestinal tract had diminished to 50 per cent. Its

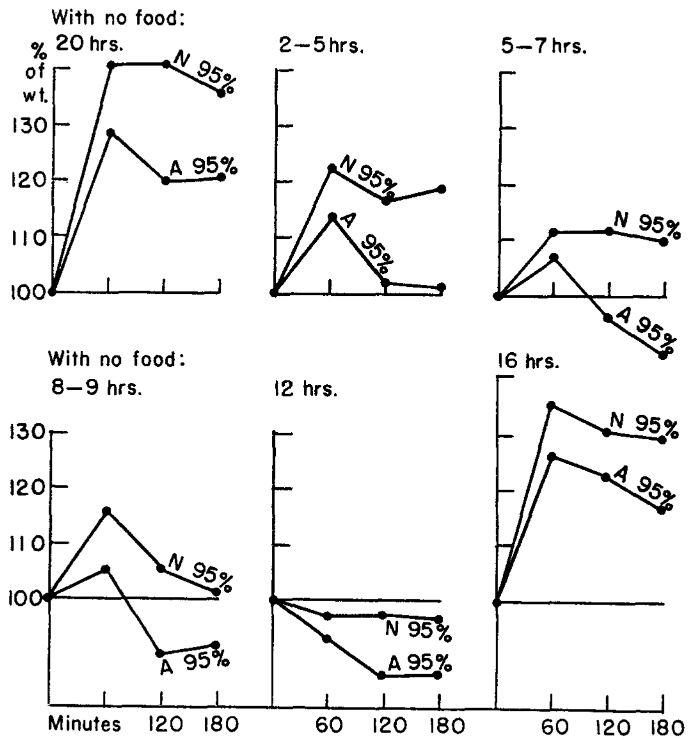

FIG. 1. Water movement in immersed liver slices from white rats at different intervals after the ingestion of food.

quantity remained about the same for 2 hours, and then, with most of the protein from the intestine lost, diminished to a normal value. Respiratory exchange followed a course parallel to that of amino acid nitrogen in the blood, the respiratory quotient being greatest between 3 and 5 hours after feeding. This increase was attributed to the specific dynamic action of the ingested protein.

After the ingestion of different proteins by dogs, Denton and Elvehjem (4) found that the amino acids of the blood usually increased in proportion to those supplied by the food. Longenecker and Hause (5) obtained evidence that this proportion was modified by removal of amino acids from the blood in accord with the characteristic requirements of the animal.

With protein digestion amino acids are passing from the intestine by way of the blood to the liver and here undergo deaminization with formation of urea. In animals with food withheld during 20 to 24 hours amino acids have reached their normal low level but with ingestion of food they enter the blood in increasing quantity during several hours and then diminish. Their fate in the liver presumably depends upon oxidation with formation of urea.

In a preceding publication (6) evidence has been assembled to show that water movement in liver cells is dependent upon the formation of amino acids and related substances, notably arginine and substances derived from it. They raise the osmotic pressure to a level above that of the surrounding extracellular fluid but with oxidation form urea which readily leaves the cell. Oxidation under physiological conditions is limited by the oxygen supply available to the tissue and cannot exceed a level proportionate to that of the oxygen brought to the

TABLE II

Water Movement with Oxygen 14 Per Cent in Immersed Liver Slices at Different Intervals after the Ingestion of Food

Time with no food	Food eaten	Stomach contents	Oxygen 14 per cent		
			After 60 min.	After 120 min.	After 180 min.
hrs.	*gm.*	*gm.*			
20	20	0.04	129.6	128.0	122.6
12	17	0.10	104.7	99.9	93.3
6	17	4.68	106.7	102.0	93.1

tissue by the arterial blood which has a partial pressure of approximately 100 mm. Hg. Between this limit and anoxia is a zone in which water movement may adjust itself to functional requirements. It is not improbable that movement of water favors both the entrance of dissolved nitrogenous substances into the liver and the diffusion of oxygen: oxygen, in turn, promotes deaminization.

SUMMARY AND CONCLUSIONS

Water movement in liver slices has been measured in the presence of varied oxygen supply and during the progress of gastrointestinal digestion.

Maximum water intake occurs both with anoxia and with exposure to oxygen when animals have received no food during 20 to 24 hours. It diminishes almost immediately after the ingestion of food and is least after 8 to 10 hours when digestion is nearly complete. These changes coincide with the passage of amino acids from the gastrointestinal tract to the liver by way of the blood.

Movement of water into the liver cells is favorable to the entrance of dissolved substances and when it is greatest with approaching anoxia the movement promotes the diffusion of oxygen into the cells.

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