

after the astrophysical developments have been carried somewhat further so that more is known about the internal temperature, pressure and density during the various stages of the developing planets. Reference is made also to an article now in press<sup>9</sup> discussing the evaporation process somewhat more fully.

<sup>1</sup> Kuiper, G. P., These PROCEEDINGS, **37**, 1 (1951). For a more detailed and somewhat improved account, see reference 4.

<sup>2</sup> Suess, H. E., *J. Geology*, **57**, 600 (1949).

<sup>3</sup> Brown, H., Chap. IX of *The Atmospheres of the Earth and Planets*, edited by G. P. Kuiper, U. of Chicago Press, Chicago (1949).

<sup>4</sup> Kuiper, G. P., Chap. 8 of *Astrophysics*, edited by J. A. Hynek, McGraw-Hill Book Co. (1951); *Astrophys. J.* (in press).

<sup>5</sup> Baade, W., and Pauli, W., *Naturwissenschaften*, **15**, 49 (1927).

<sup>6</sup> Jung, B., *Z. Astrophys.*, **9**, 1 (1934).

<sup>7</sup> Eucken, A., *Nachr. Akad. Wiss. Göttingen, Math.-Phys. Kl. Heft*, **1** (1944). A summary appeared in *Naturwissenschaften*, **32**, 112(1944).

<sup>8</sup> Latimer, W. R., *Science*, **112**, 101 (1950). Urey, H. C. (in press).

<sup>9</sup> Kuiper, G. P., Chap. XII of *The Atmospheres of the Earth and Planets*, second edition, Chicago (1951).

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## THE CHLORIDE TRANSPORT SYSTEM OF THE GASTRIC MUCOSA

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Investigation of electrolyte transfer across the gastric mucosa has resulted in definitive demonstration of a new cellular mechanism for electrolyte transport: the active chloride transport system.

Productive study of electrolyte transfer across biological membranes has been possible since Ussing formulated a systematic analysis of flux. Flux is the movement of a given ion species crossing a membrane in one direction. Flux is conveniently measured with isotopes. In brief, "flux analysis" embraces: (a) the law of passive diffusion,<sup>1</sup> (b) quantitative measurement of active transport in the short-circuited membrane,<sup>2</sup> (c) the concept of exchange diffusion<sup>3</sup> and (d) expression of passive diffusion in terms of electrical conductance.<sup>2</sup> Two points are critical in the interpretation of the data presented below. The behavior of a passive ion,<sup>1</sup> under specified conditions, is given by:

$$\log \frac{\text{influx}}{\text{outflux}} = \frac{(\text{valence})(Vm)}{60}$$

A membrane can be simply short-circuited by applying an external potential so that the potential difference across the membrane becomes zero.<sup>2</sup> The current necessary to maintain a 0 potential difference is equal though opposite in sign, to the current continuously generated by the membrane.

Data reported here were obtained with the surviving isolated frog gastric mucosa which spontaneously secretes HCl. Approximately 1 sq. cm. of mucosa dissected from the serosal coat was mounted between suitable flux chambers. The mucosa was bathed by a modified Ringer's solution: (110 NaCl, 2.5 KCl, 2.5 CaCl, 1.0 MgSO<sub>4</sub> meq./l. and glucose 100 mg./100 ml.; the nutrient solution being slightly buffered by 3 meq. of buffered phosphate replacing 3 meq. NaCl; aeration 100% O<sub>2</sub>). Fluxes were measured with radioisotopes Na-24, K-42 and Cl-36. To avoid confusion, it is necessary to emphasize that outflux refers to movement from serosa to mucosa and influx, mucosa to serosa.

The flux data are summarized in the tabulation.

Movement of sodium across the gastric mucosa approaches the behavior of a passive ion. Although at P. D. 56 mV, the observed flux ratio was 5.1 against a calculated ratio of 8.5, a better agreement may be anticipated with more adequate provision for equilibration. Probably sodium is crossing the mucosa intercellularly rather than transcellularly. Because of sodium's passive character, it is quantitatively impossible to account for the secretion of H ions (some 0.5-1.0 microeq./hr.) by a Na-H exchange system. An incomplete study has shown that potassium fluxes are about one-fifth those of sodium. The total passive conductivity attributable to sodium and potassium is approximately 30% of the total membrane conductivity under these conditions.

Flux data of chloride present a remarkably different picture from those obtained with sodium. First, the magnitude of the fluxes is unexpectedly great; second, the movement of chloride is certainly not simply passive; and third, there is an appreciable discrepancy between outflux and influx across the short-circuited membrane (0 mV). The mean difference between chloride fluxes at 0 P. D. was 1.4 microeq./hr. when the mean observed current generated by the mucosa was 1.7 microeq./hr. This agreement is sufficiently close, considering that fluxes were measured on separate membranes, to suggest an identity of active chloride transport and mucosal current. Under conditions of these experiments, a combination of unidirectional active transport and passive diffusion cannot alone account for the total chloride flux. Passive chloride flux must be less than 70% of the total membrane conductivity, i.e., less than 1.4 microeq./hr. As both fluxes are considerably greater than this value, a high proportion of the chloride transfer partakes of an exchange diffusion. Hence there is ample demonstration that chloride crosses the gastric mucosa in a combined state.

Chloride flux data suggested that the gastric mucosal current is active chloride transport. Influx and outflux had been measured on different membranes, introducing membrane variability. Membrane variability can be eliminated by comparing net chloride transfer with the sum of mucosal current and hydrochloric acid secretion in a single membrane. Flux chambers have been designed in this laboratory<sup>4</sup> which allow measurement of volume changes of  $\pm 10$  microl. This is sufficiently precise when supplemented by the analytic method of Keys<sup>5</sup> to measure net chloride transfer. The net chloride transfer in the short-circuited membrane is actually equivalent to the sum of the mucosal current and HCl secreted during an experiment. In six experiments net transfer checked within  $+6.9\%$  and  $-7.6\%$  of the sum, current and HCl. Therefore, the source of the distinctive current and potential maintained by the gastric mucosa is active chloride transport.

*Summary.*—1. Study of electrolyte transfer across the gastric mucosa in terms of flux has led to demonstration of an active transport system for chloride.

2. Active transport of chloride is the source of the distinctive current and potential maintained across the gastric mucosa.

TABULATION OF FLUX DATA

mV	SODIUM		mV	CHLORIDE	
	OUTFLUX	INFLUX		OUTFLUX	INFLUX
0	0.52	0.47	0	5.8	4.4
Spont. (25)	0.42	0.81	Spont. (30)	7.1	6.4
30	0.34	0.83	...	...	...
56	0.25	1.28	56	4.8	4.7

(microeq./sq. cm./hr.)

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<sup>1</sup> Ussing, H. H., *Acta Physiol. Scand.*, **19**, 43-56 (1949).

<sup>2</sup> Ussing, H. H., and Zerahn, K., *Ibid.* (in press).

<sup>3</sup> Ussing, H. H., *Nature*, **160**, 262 (1947).

<sup>4</sup> Ussing, H. H., Personal communication.

<sup>5</sup> Keys, A. B., *J. Chem. Soc.*, **1931**, pp. 2440-2447.