J. Membrane Biol. 16, 163–174 (1974)

Properties of the Passive Conductance Pathway Across *in Vitro* Rat Jejunum

B. G. Munck and Stanley G. Schultz*

Department of Physiology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261

Received 15 October 1973

Summary. The unidirectional influxes of several monovalent ions into the epithelium of *in vitro* rat jejunum were determined as a function of the transepithelial electrical potential difference using the technique described by Frizzell and Schultz (*J. Gen. Physiol.* **59**:318, 1972). The results indicate that the passive conductance pathway accounts for approximately 80% of the total tissue conductance and is cation-selective. The relative ionic permeabilities of this pathway, which is in all likelihood largely if not entirely extracellular, is $P^{K} \geqq P^{Rb} > P^{Na} \gg P^{Cl}$. The sequence of relative cation permeabilities corresponds most closely to Eisenman's sequence V suggesting that the route possesses a negative electrical field strength of intermediate intensity. The unidirectional influxes of lysine and tetraethylammonium (TEA) were unaffected over the range of ± 50 mV. These findings are consistent with the notion that the passive conductance pathway is impermeable to solutes with an equivalent diameter greater than 8 Å; however, the possibility that factors other than ionic size are responsible for the exclusion of TEA and lysine from the shunt pathway cannot be excluded. The diffusional influx of Na closely agrees with the transepithelial serosa-to-mucosa flux of Na suggesting that the latter is largely, if not entirely, mediated by the passive conductance pathway and may circumvent the limiting membranes of the epithelial cells.

Studies on *in vitro* rabbit ileum (Frizzell & Schultz, 1972) as well as on a variety of other epithelia that are characterized by low transepithelial electrical potential differences (p.d.'s), low transepithelial resistances, relatively high hydraulic conductivities and isotonic absorbates or secretions have suggested that many of these properties can be attributed to the presence of relatively high conductance extracellular or "shunt" pathways that circumvent the limiting membranes of the epithelial cells (Frömter & Diamond, 1972). That is, in these tissues, the resistance to ionic diffusion through the shunt pathway is much lower than the resistance to flow through the transcellular pathway, and, in general, all of these epithelia are

* Reprint requests.

characterized by large bidirectional transepithelial ion fluxes. It follows that a quantitative description of the shunt pathway in these tissues is a prerequisite to any effort to define the role(s) of the epithelial cells themselves in the movements of ions and small nonelectrolytes. Data collected on rat jejunum suggest that this tissue possesses many of the properties displayed by other epithelia characterized by high conductance shunt pathways (Frömter & Diamond, 1972; Munck, 1972). The purpose of the present study was to examine the permselective properties of the passive conductance[1] pathway across *in vitro* rat jejunum and to relate these findings to previous studies of ion transport across this preparation.

Materials and Methods

Male, Sprague-Dawley rats (approximately 150 to 200 g), fed *ad libitum*, were anesthetized by intraperitoneal injection of sodium pentobarbital. A segment of mid-jejunum was removed and the rat was then sacrificed. The segment was opened along the mesenteric border, rinsed free of intestinal contents and mounted in a modified version of the influx apparatus described by Frizzell and Schultz (1972, Fig. 1). The principal modifications were that (i) the area of mucosal surface exposed to the radioactive *test* solution was reduced to 0.62 cm^2; and (ii) aeration and stirring of the serosal solution was accomplished by means of a gas-lift circulating system employing 100% O_2. The serosal fluid in the gas-lift system was level with the mucosal solution so that no hydrostatic pressure difference was generated across the tissue. Aeration and stirring of the mucosal solution was accomplished by vigorous bubbling with humidified 100% O_2.

Two Ringer's-agar bridges adjacent to the tissue were employed to monitor the transepithelial p.d. (Ψ_{ms}) via a pair of matched calomel electrodes leading to a Kiethly (Model 610) electrometer. External current from a variable electromotive source was passed across the tissue employing Ringer's-agar bridges inserted into the mucosal and serosal reservoirs. This permitted clamping the tissue at any predetermined Ψ_{ms}; all values for the Ψ_{ms} are expressed with reference to the mucosal solution and were corrected for the fluid resistance between the agar bridges adjacent to the tissue. Because the tissue behaves as an ohmic resistor, tissue conductance was simply calculated from the linear current-voltage relation.

The steady-state unidirectional influx from the mucosal solution into the epithelium was determined as a function of Ψ_{ms} precisely using the method described by Frizzell and Schultz (1972). All experiments were performed in a warm-room at 37 °C.

Unless otherwise indicated the incubation medium consisted of a Krebs-phosphate buffer at pH 7.4 and contained 28 mM glucose (Munck, 1972). ^{22}Na, ^{36}Cl, ^{42}K, ^{85}Rb, ^{14}C-lysine, ^{14}C-tetraethylammonium (TEA)-bromide and ^{3}H-inulin were obtained from the New England Nuclear Corp.

1 The term *passive conductance pathway* refers to the transepithelial pathway(s) through which ionic movements conform to the laws of strict ionic diffusion and is thereby distinguished from transepithelial conductance resulting from nondiffusional ion transport processes.

Results

Frizzell and Schultz (1972) have demonstrated that the total unidirectional influx (J_i) of a charged species i from the mucosal solution into the epithelium can be operationally subdivided into two parallel components. The first, J^i_{mc}, is independent of Ψ_{ms} over the range studied, whereas the second, ${}_dJ^i_{ms}$, obeys the laws of strict ionic diffusion. Under these conditions

$$ {}_dJ^i_{ms} = {}_{0\,d}J^i_{ms}\,\xi^{-\frac{1}{2}} \tag{1} $$

where ${}_{0\,d}J^i_{ms}$ is the rate of unidirectional diffusion of i from the mucosal solution to the serosal solution under short-circuit conditions (i.e. when

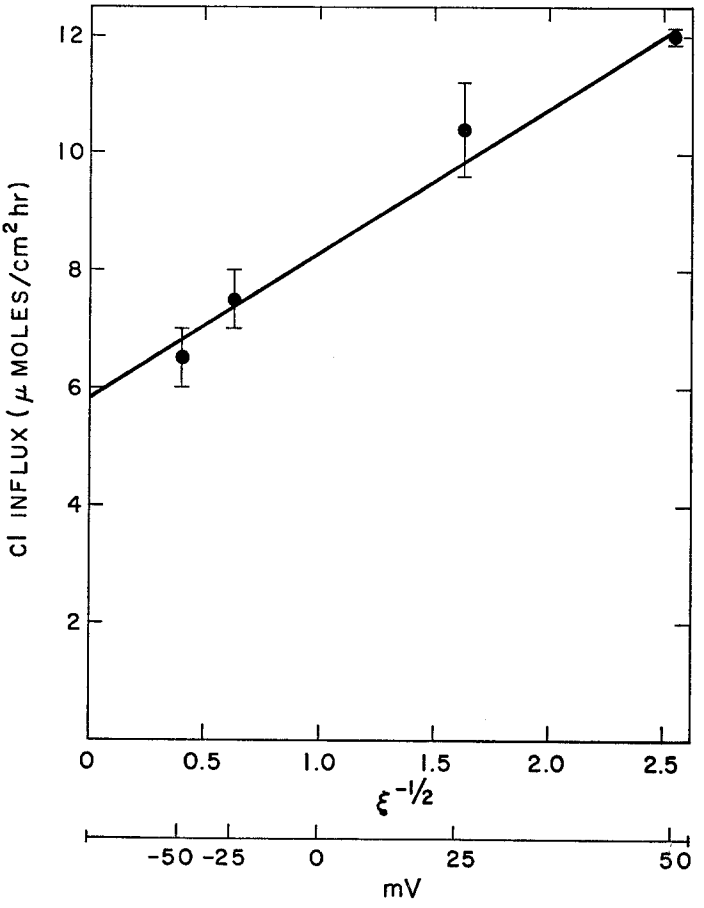

Fig. 1. Cl influx as a function of $\xi^{-\frac{1}{2}}$; the lower abscissa indicates the transepithelial p.d. corresponding to various values of $\xi^{-\frac{1}{2}}$. The Cl concentration in both bathing media was 140 mM and both media contained 28 mM glucose. Each value is the mean ±SEM of 20 determinations

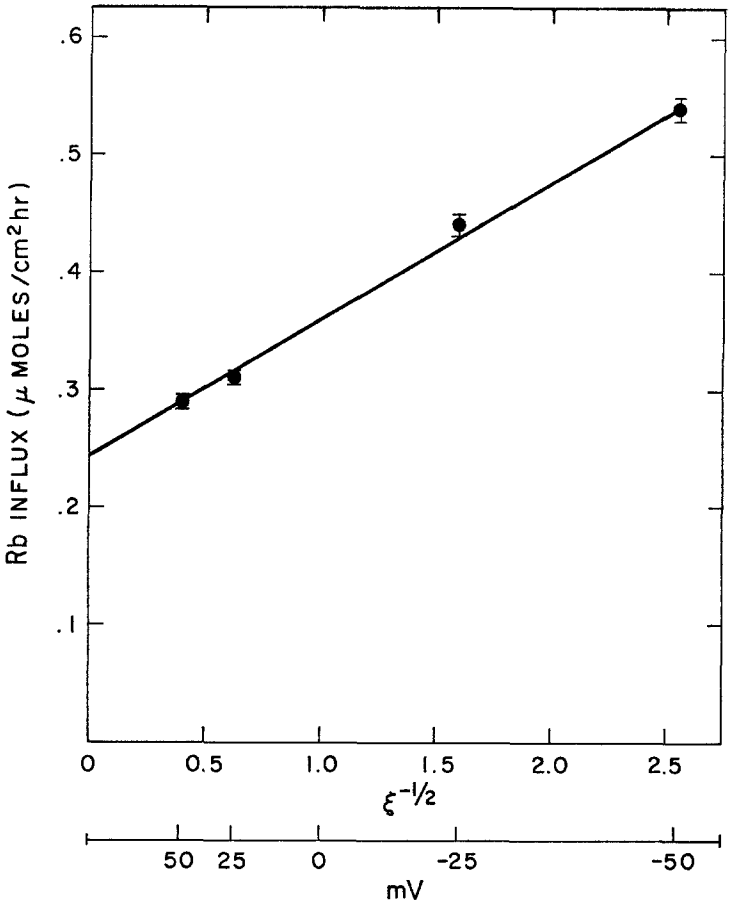

Fig. 2. Rb influx as a function of $\xi^{-\frac{1}{2}}$. The Rb concentration in both bathing media was 1 mM. Each point represents the mean ±SEM of 14 determinations

$\Psi_{ms}=0$), $\xi^{-\frac{1}{2}}=\exp(-zF\Psi_{ms}/2RT)$, and z, F, R and T have their usual meanings. Similar expressions for a unidirectional diffusional ionic flux have been derived by Parlin and Eyring (1954), Kimizuka and Koketsu (1964) and Mullins (1961) and may be readily derived from the Goldman-Hodgkin-Katz equation (Schultz, 1974). Thus, the total measured influx is given by

$$J_i^i = J_{mc}^i + {}_{0d}J_{ms}^i \xi^{-\frac{1}{2}}. \tag{2}$$

A plot of J_i^i *vs.* $\xi^{-\frac{1}{2}}$ should, therefore, yield a straight line whose intercept on the ordinate represents the influx component that is independent of Ψ_{ms}, over the range studied, and whose slope represents ${}_{0d}J_{ms}^i$, the diffusional component under short-circuit conditions. Further, in a tissue where the

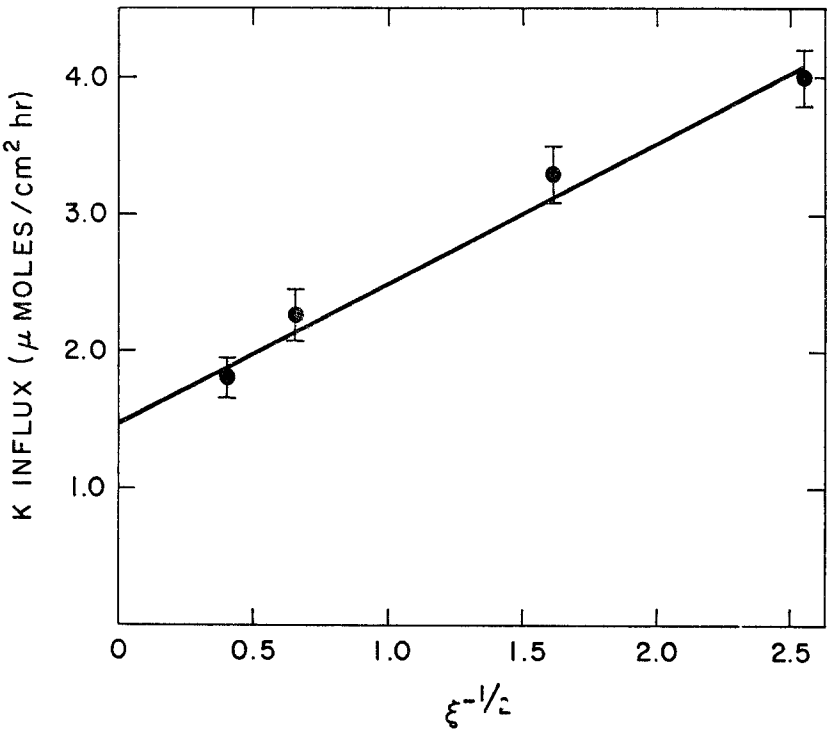

Fig. 3. K influx as a function of $\xi^{-\frac{1}{2}}$. The K concentration in both bathing media was 8 mM. Each point represents the mean ±SEM of eight determinations

passive conductance of the extracellular route is many times greater than that of the transcellular route, it is not unreasonable to assume that most if not all of the observed ${}_dJ^i_{ms}$ traverses the shunt pathway.

The unidirectional influxes of Cl, Rb and K from the mucosal solution into rat jejunum are plotted as a function of $\xi^{-\frac{1}{2}}$ in Figs. 1–3; the experimental details are given in the legends to these figures. The relations shown conform to Eq. (2).

The unidirectional influx of Na in the presence and absence of 28 mM glucose is plotted as a function of $\xi^{-\frac{1}{2}}$ in Fig. 4. Clearly, the presence of glucose markedly enhanced the influx component that is independent of Ψ_{ms} (the intercept on the ordinate) but did not affect the diffusional permeability since the slopes of the two lines are identical. These data strongly suggest that the enhancement of Na influx by glucose reported previously for rabbit ileum (Goldner, Schultz & Curran, 1969) is not a consequence of an increase in the Na permeability of extracellular or transcellular diffusional pathways. Instead, these data corroborate the observations of

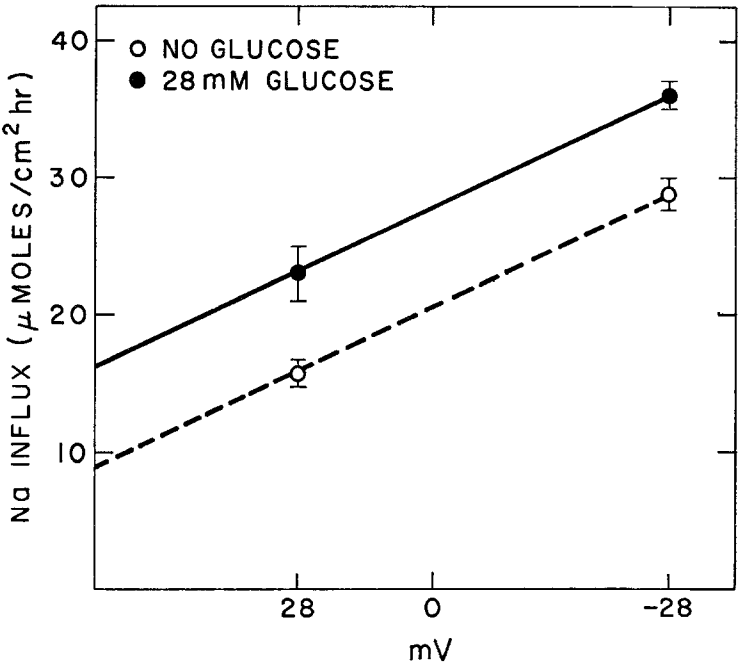

Fig. 4. Paired determinations of Na influx when the Ψ_{ms} was clamped at +28 mV or −28 mV in the presence (●) and absence (○) of 28 mM glucose. The Na concentration in both bathing media was 140 mM. Each point represents the mean ±SEM of 10 determinations

Frizzell, Nellans and Schultz (1973) and add to the evidence that the increase in Na influx in the presence of actively transported sugars is the result of a carrier-mediated co-transport process located at the brush border of the villus absorptive cells (Kinter & Wilson, 1965).

The effect of Ψ_{ms} on lysine influx is illustrated in Fig. 5. Clearly, the unidirectional influx of this monovalent cation averages approximately 0.4 μmoles/cm² hr and is not affected by Ψ_{ms} over the range of ± 50 mV. These observations are consistent with those of Munck and Schultz (1969) that the transepithelial flux of lysine from mucosa-to-serosa across rabbit ileum under short-circuit conditions does not differ significantly from that observed when the transepithelial electrical potential difference is clamped at 35 mV, mucosa negative with respect to serosa. Further, eight experiments evaluating the effect of Ψ_{ms} on the influx of TEA indicated that the average influx in the presence of 1 mM TEA was 0.016 ± 0.006 μmoles/cm² hr and was independent of Ψ_{ms} over the range of ± 50 mV. Thus, neither lysine influx nor TEA influx displayed a significant diffusional component.

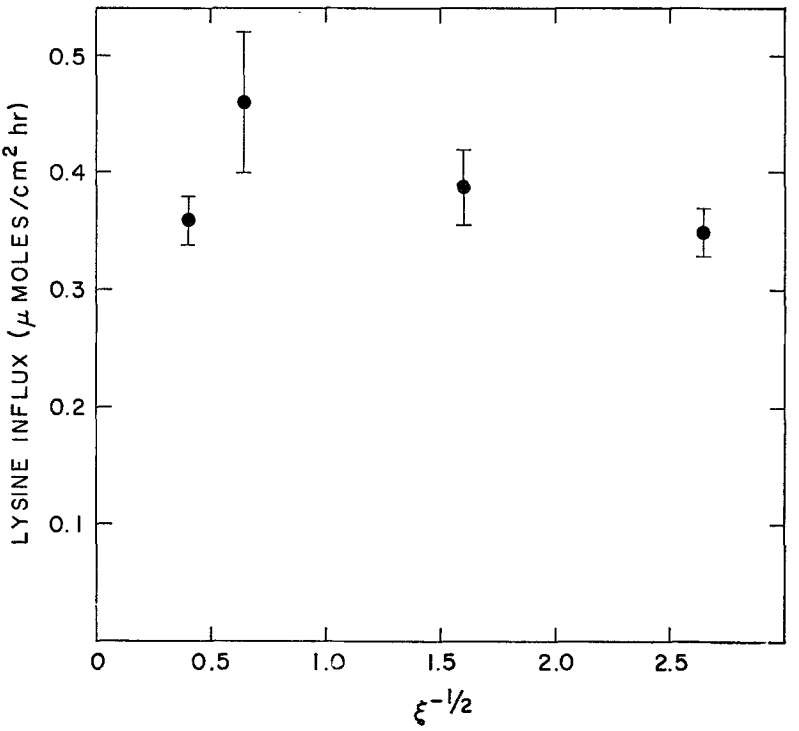

Fig. 5. Lysine influx as a function of $\xi^{-\frac{1}{2}}$. The lysine concentration in both bathing media was 1 mM and the glucose concentration was 17 mM. Each point represents the mean ±SEM of four determinations

Discussion

The purpose of the present investigation was to define some of the properties of the passive conductance pathway across *in vitro* rat jejunum, a tissue that can be grouped among other low resistance epithelia such as renal proximal tubule, rabbit and *Necturus* gallbladder, and rabbit ileum (Frömter & Diamond, 1972). It seems quite likely from studies on the latter tissues that extracellular shunt pathways, whose anatomic counterparts appear to be the junctional complexes and the lateral intercellular spaces (Whittembury & Rawlins, 1971; Frömter, 1972; Machen, Erlij & Wooding, 1972), are largely, if not entirely, responsible for transepithelial diffusion of small hydrophilic solutes across rat jejunum.

The average data derived from the relations shown in Figs. 1–4, and Eq. (2) are summarized in Table 1. P^i is the permeability of the passive conductance pathway to the species i defined by $P^i = {}_{0d}J^i_{ms}/[i]$ where the brackets indicate the concentration of i in the mucosal and serosal solutions.

Table 1. Unidirectional influxes into passive conductance pathway and across mucosal membranes

Ion (i)	i (mM)	J^i_{mc} (μmoles/cm^2 hr)	${}_{0d}J^i_{ms}$ (μmoles/cm^2 hr)	P^i (cm/hr)	G_t (mmhos/cm^2)	R_t (Ω cm^2)	r^i_s (Å)
K (4)	8	1.45	1.05	0.13	14.7	68±3	1.29
Rb (7)	1	0.25	0.12	0.12	16.2	62±4	1.24
Na (5)	140	9.0	11.5	0.08	22.3	44±2	1.85
Na + Glucose (5)	140	16.0	11.5	0.08	22.3	44±2	—
Cl (10)	140	5.9	2.4	0.02	19.5	51±2	1.24

All data for K, Rb and Cl were obtained in the presence of 28 mM glucose. The data for Na were determined on paired tissues from the same animal in the absence of glucose or the presence of 28 mM glucose. The Stokes radius (r^i_s) was obtained from the limiting equivalent conductivities in water at 35 °C given in Appendix 6.2 of Robinson and Stokes (1959). The numbers in parentheses indicate the number of experiments and each experiment involved the determination of eight influxes at different Ψ_{ms}.

Also indicated are the average total tissue resistances (R_t) and conductances (G_t) for each series of experiments and the Stokes radii of the ions studied. Clearly, $P^K:P^{Rb}:P^{Na}:P^{Cl} = 1.6:1.4:1.0:0.2$.[2] The finding that $P^K/P^{Cl} = 8$ indicates that the passive conductance pathway is cation selective since the ratio of the mobilities of K and Cl in free solution is close to unity. This observation together with finding that $P^K \geqq P^{Rb} > P^{Na}$ is consistent with an anionic field strength of intermediate intensity and corresponds to Eisenman's sequence V (Eisenman, 1961). Barry, Diamond and Wright (1971) also found that the relative cationic permeabilities of rabbit gallbladder determined from dilution potentials correspond to Eisenman's sequence V. The relative permeabilities determined in these studies are in fair agreement with those determined by Wright (1966) from studies of diffusion potentials across rat jejunum. Assuming that these diffusion potentials can be described by the modification of the Goldman equation (Goldman, 1943) by Hodgkin and Katz (1949), Wright found that $P^K:P^{Na}:P^{Cl} = 1.2:1.0:0.1$. Agreement between the relative permeabilities of Na, K and Cl determined directly by the influx technique (as in the present studies) and by analysis of transepithelial diffusion potentials using the Goldman-Hodgkin-Katz equation has been demonstrated for rabbit ileum (Frizzell & Schultz, 1972). The findings that P^K does not differ markedly from P^{Na} and that transepithelial

2 If ${}_{0d}J^i_{ms}$ is normalized to the average tissue conductance observed in the experiments on Na influx, the relative ionic permeabilities would be $P^K:P^{Rb}:P^{Na}:P^{Cl} = 2.4:2.0:1.0:0.2$. The relative cation permeabilities resulting from this normalization are in close agreement with those determined by Barry *et al.* (1971) from dilution potentials across rabbit gallbladder.

diffusion potentials conform reasonably well with the Goldman-Hodgkin-Katz equation suggest that ionic diffusion takes place predominantly via aqueous, extracellular pathways. These observations also *suggest* that, as for rabbit ileum and rabbit gallbladder, the diffusional pathway is electrically neutral and that cation selectivity is a consequence of the fact that the pathway is lined with either fixed dipolar molecules or fixed Zwitterions (i.e., dissociated anions and cations in approximately equivalent amounts) aligned so that the electronegative group restricts the partition coefficient and/or mobility of anions. (Sandblom & Eisenman, 1967; Barry *et al.*, 1971; Frizzell & Schultz, 1972; Schultz, 1974). However, additional study is necessary to verify this notion.

The observations that Ψ_{ms} does not affect the influxes of lysine or TEA are not amenable to definitive interpretations at this time. The equivalent molecular diameter of lysine is approximately 10 Å. TEA is a spherical cation with a Stokes radius of 2.8 Å. However, as pointed out by Robinson and Stokes (1959) this value is an underestimate resulting from the fact that Stokes' law is not strictly applicable to solutes whose dimensions significantly exceed that of H_2O; the unhydrated diameter of TEA determined from "Catalin" atomic models based on bond lengths calculated by Pauling is approximately 8 Å. Thus, it is quite possible that the limiting dimensions of the passive conductance pathway restrict the diffusion of hydrophilic solutes with equivalent diameters greater than 8 Å. If this interpretation is correct, the diffusional pathway would be essentially impermeable to hexoses (Schultz & Solomon, 1961) and amino acids larger than leucine.

However, as pointed out by several authors (Eisenman, 1961; Diamond & Wright, 1969) the notion that the permeability of hydrophilic solutes (particularly ions) is determined *exclusively* by steric factors is incorrect. Clearly, if the dimensions of the solute exceed the limiting dimensions of the diffusional pathway, permeation is impossible. However, a solute whose dimensions are smaller than those of the diffusional pathway may also be excluded because of unfavorable Coulombic and/or non-Coulombic interactions with the groups that line the pathway. For these reasons, even in a cation-selective pathway, it is quite possible for the size of an impermeant cation to be considerably smaller than other highly permeant cations. These considerations have been discussed in detail by Diamond and Wright (1969). Suffice it to say that although our findings with respect to lysine and TEA *may* have some bearing on the dimensions of the shunt pathway a definitive conclusion is unwarranted and awaits additional studies, currently in progress, using larger cations with varied chemical (reactive) properties.

Implications Regarding Transepithelial Ion Transport

The data in Table 1 indicate that the average total tissue conductance in these experiments was 19.7 mmhos/cm^2 and the sum of the partial ionic conductances ($_dG^i$) of K, Na and Cl through the passive conductance pathway ($_{0\,d}J^{K}_{ms} + {}_{0\,d}J^{Na}_{ms} + {}_{0\,d}J^{Cl}_{ms}$) is equal to 15.0 mmhos/cm^2. Thus, the passive conductance pathway accounts for *at least* 76% of the total tissue conductance; the contribution from the diffusional flows of other ions present in the incubation medium is unknown but would certainly increase the fraction of the total tissue conductance attributable to diffusion through the passive conductance pathway. The estimate of 76% attributable to $_dG^K + {}_dG^{Na} + {}_dG^{Cl}$ is in good agreement with the value of 82% reported by Frizzell and Schultz (1972) for rabbit ileum. Thus, ionic diffusion through the passive conductance pathway, which is probably entirely, or almost entirely, extracellular, accounts for at least 80% of the total transepithelial conductance.

In the present studies, $_{0\,d}J^{Na}_{ms}$ averaged 11.5 μmoles/cm^2 hr both in the presence and absence of glucose and accounted for 51% of the total tissue conductance. Previous studies by Munck (1972) indicated that in the presence of 28 mM glucose, the serosa-to-mucosa unidirectional flux of Na, J^{Na}_{sm}, averaged 12.4 ± 0.6 μmoles/cm^2 hr, a value that does not differ significantly from the $_{0\,d}J^{Na}_{ms}$ found in the present investigation. Further, in the presence of glucose the average tissue conductance reported by Munck was 27 mmhos/cm^2 so that J^{Na}_{sm} accounted for 45% of the G_t. In the absence of glucose, J^{Na}_{ms} averaged 7.4 μmoles/cm^2 hr and the average G_t was 15.2 mmhos/cm^2 so that $J^{Na}_{sm}/G_t = 0.49$. Thus, the lower J^{Na}_{sm} reported by Munck in the absence of glucose parallels the decreased G_t observed in those experiments. All of these observations suggest that most if not all of the J^{Na}_{sm} is mediated by the passive conductance pathway and parallels total tissue conductance. Frizzell and Schultz (1972) have arrived at a similar conclusion with respect to whole thickness rabbit ileum and the studies of Nellans, Frizzell and Schultz (1974) corroborate this conclusion for *in vitro* rabbit ileum stripped of the serosal musculature. In the studies by Frizzell and Schultz (1972), the $_{0\,d}J^{Na}_{ms}$ accounted for 49% of the total tissue conductance, a value that is in excellent agreement with those observed for $_{0\,d}J^{Na}_{ms}/G_t$ in the present investigation and J^{Na}_{sm}/G_t in the studies by Munck (1972).

In contrast, $_{0\,d}J^{Cl}_{ms}$ is only 20% of J^{Cl}_{sm} in the presence of 28 mM glucose under short-circuit conditions. Thus, at least 80% of the "back-flux" of Cl is nondiffusional and is mediated by the transcellular route.

The foregoing considerations illustrate that, apart from providing some insights into the permselective properties of the transepithelial passive conductance pathways, information regarding the absolute contributions of these pathways to transepithelial ion movements have profound implications with respect to ion transport by the epithelial cells. Thus, if as suggested by the present results, and the results reported by Frizzell and Schultz (1972) and Nellans *et al.* (1974) for rabbit ileum, J_{sm}^{Na} is strictly diffusional, active Na secretion by these two epithelia would be precluded unless the perturbation that elicits active Na secretion alters the properties of the limiting membranes of the epithelial cells. That is, if J_{sm}^{Na} is entirely attributable to ionic diffusion, under short-circuit conditions J_{sm}^{Na} cannot exceed J_{ms}^{Na}. This conclusion is valid regardless of the anatomic pathways involved in passive transepithelial Na diffusion; it is not contingent upon the presumption that J_{sm}^{Na} is restricted to the extracellular shunt pathway. Further, *if* the passive conductance pathway is entirely extracellular and *if*, as suggested by the data of Munck (1972) and Nellans *et al.* (1974) the mucosal membranes of rat jejunum and rabbit ileum permit bidirectional movements of Na, the baso-lateral membranes of these epithelia must be essentially impermeable to Na and the active Na extrusion mechanism located at these membranes must be essentially rectified (i.e., the mechanism must be capable of mediating movement of Na from the cell into the serosal solution but incapable of mediating Na movement in the opposite direction). Thus, there are two central questions that require unequivocal resolutions: (a) Is J_{sm}^{Na} entirely attributable to strict ionic diffusion?; and (b) if so, is this diffusional process mediated entirely by the extracellular shunt pathway? The answers to these questions would permit important inferences regarding Na transport across the limiting membranes of the epithelial cells.

Dr. Munck was on leave of absence from the Department of Physiology A, University of Copenhagen and was partially supported by a grant from the Danish Research Council.

This investigation was supported by research grants from the U.S.P.H.S., National Institute of Arthritis, Metabolism and Digestive Diseases (AM 16275-02) and the American Heart Association (70-633).

References

Barry, P. H., Diamond, J. M., Wright, E. M. 1971. The mechanism of cation permeation in rabbit gallbladder: Dilution potentials and biionic potentials. *J. Membrane Biol.* **4**:358

Diamond, J. M., Wright, E. M. 1969. Biological membranes: The physical basis of ion and nonelectrolyte selectivity. *Annu. Rev. Physiol.* **31**:581

Eisenman, G. 1961. On the elementary atomic origin of equilibrium ionic specificity. *In:* Membrane Transport and Metabolism. A. Kleinzeller and A. Kotyk, editors. p. 163. Academic Press Inc., New York

Frizzell, R. A., Nellans, H. N., Schultz, S. G. 1973. Effects of sugars and amino acids on sodium and potassium influx in rabbit ileum. *J. Clin. Invest.* **52**:215

Frizzell, R. A., Schultz, S. G. 1972. Ionic conductances of extracellular shunt pathway in rabbit ileum: Influence of shunt on transmural sodium transport and electrical potential differences. *J. Gen. Physiol.* **59**:318

Frömter, E. 1972. The route of passive ion movement through the epithelium of *Necturus* gallbladder. *J. Membrane Biol.* **8**:259

Frömter, E., Diamond, J. 1972. Route of passive ion permeation in epithelia. *Nature, New Biol.* **235**:9

Goldman, D. E. 1943. Potential, impedance and rectification in membranes. *J. Gen. Physiol.* **27**:37

Goldner, A. M., Schultz, S. G., Curran, P. F. 1969. Sodium and sugar fluxes across the mucosal border of rabbit ileum. *J. Gen. Physiol.* **53**:362

Hodgkin, A. L., Katz, B. 1949. The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol.* **108**:37

Kimizuka, H., Koketsu, K. 1964. Ion transport through cell membrane. *J. Theoret. Biol.* **6**:290

Kinter, W. B., Wilson, T. H. 1965. Autoradiographic study of sugar and amino acid absorption by everted sacs of hamster intestine. *J. Cell Biol.* **25**:19

Machen, T. E., Erlij, D., Wooding, F. B. P. 1972. Permeable junctional complexes: The movement of lanthanum across rabbit gallbladder and intestine. *J. Cell Biol.* **54**:302

Mullins, L. J. 1961. The macromolecular properties of excitable membranes. *Ann. N.Y. Acad. Sci.* **94**:390

Munck, B. G. 1972. Effects of sugar and amino acid transport on transepithelial fluxes of sodium and chloride of short circuited rat jejunum. *J. Physiol. (London)* **223**:699

Munck, B. G., Schultz, S. G. 1969. Lysine transport across isolated rabbit ileum. *J. Gen. Physiol.* **53**:157

Nellans, H. N., Frizzell, R. A., Schultz, S. G. 1974. Brush border processes and transepithelial Na and Cl transport by rabbit ileum. *Amer. J. Physiol. (In press)*

Parlin, R. B., Eyring, H. 1954. Membrane permeability and electrical potential. *In:* Ion Transport Across Membranes. H. T. Clark, editor. p. 103. Academic Press Inc., New York

Robinson, R. A., Stokes, R. H. 1959. Electrolyte Solutions. Academic Press Inc., New York. 2nd Edition

Sandblom, J. P., Eisenman, G. 1967. Membrane potentials at zero current: The significance of a constant ionic permeability ratio. *Biophys. J.* **7**:217

Schultz, S. G. 1974. Principles of electrophysiology and their application to epithelial tissues. *In:* Gastrointestinal Physiology. E. D. Jacobson, editor. Butterworth, London *(In press)*

Schultz, S. G., Solomon, A. K. 1961. Determination of the effective hydrodynamic radii of small molecules by viscometry. *J. Gen. Physiol.* **44**:1189

Whittembury, G., Rawlins, F. A. 1971. Evidence of a paracellular pathway for ion flow in the kidney proximal tubule: Electromicroscopic demonstration of lanthanum precipitate in the tight junction. *Pflüg. Arch. Ges. Physiol.* **330**:302

Wright, E. M. 1966. Diffusion potentials across the small intestine. *Nature* **212**:189