# REVIEWS

# Digestive and Absorbing Functions of the Intestine and Kidneys of Newborn Animals

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In higher and many species of lower animals, food processing occurs in three steps: luminal digestion, membrane digestion, and absorption. Biopolymers, complex tissues, and cellular structures of consumed food are disaggregated in the intestinal lumen under the action of secretions of gastric, pancreatic, and Brunner's glands and liver. The resultant oligo- and dimers are hydrolyzed on the membrane surface (membrane digestion). The products of hydrolysis are transferred from hydrolytic to transport systems of the membranes. The final stages of hydrolysis and the initial stages of adsorption are spatially coupled [12-14]. Absorbing cells form numerous microvilli, which enormously increases the hydrolyzing and absorbing surface. For instance, there are 4000 microvilli on the enterocyte surface and 6500 on the cells of proximal tubules in the kidney. The distance between the villi is 100 Å. More than 25 hydrolytic enzymes have been identified in the intestinal microvilli. The microvilli of renal proximal epithelium contains less enzymes, predominantly transport phosphatases and dipeptidases. This set of the border brush enzymes coincides with its major function: intense absorption of various compounds (predominantly monomers) from primary urine.

We managed to visualize transport adenosine phosphatases using electron microscopic and histochemical methods. These enzymes are located on the inner osmiophilic layer of apical plasma membrane in the intestine and on the inner layer of basal and lateral membranes in the kidneys [2]. Microvilli increase the absorption surface to 40-50 $m^2$ in proximal tubules of the kidney and 1300 $m^2$ in the intestine. The outer layer of the membrane is covered with glycocalyx. Both in the microvilli in the plasma membrane of intestine and renal cells, the glycocalyx provides high concentrations of hydrolytic enzymes and substrates, modulates hydrolysis and membrane transport, prevents the invasion of large particles and bacteria, determines immunological properties of erythrocytes, and probably increases the persistence of microvilli.

Membrane and luminal digestion has been expensively studied, while the process of absorption (the transcellular step) did not receive the same attention. The use of modern cytophysiological techniques provided more insight into the mechanisms underlying absorption of nutriments. So far, the following mechanisms were identified:

- internalization of nutrients via the apical plasma membrane;
- intracellular transport with consecutive participation of cytoplasmic structures in the transfer and transformation of internalized nutrients;
- transport into the interstitium via lateral or basal plasma membrane;
- transport from the interstitium into blood or lymph vessels.

Internalization of nutrients has been studied in detail. Depending on the substrate, it occurs by diffusion (amino acid isomers in the intestine [37]) with (fructose [12,29]) and without carriers, active transport (glucose and galactose [12,29]), and pynocytosis (absorption of proteins in newborn animals [22,23,31,40,54]).

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There are several hypothesis on the absorption of fats in the intestine. One of them is that pancreatic lipase hydrolyzes only terminal 1,3-ester bonds of triglycerides of fats emulsified by bile salts. Subsequent hydrolysis of 2-monoglycerides presumably occurs after their isomerization [24].

Micellae enter intestinal enterocytes by passive diffusion. However, there is no consensus over the internalization of bile salts and lipid complexes. Recent findings indicate that micellar lipids cross the membrane as individual fatty acids and monoglycerides, while bile acids are involved in solubilization, thus facilitating transport of these compounds through a stationary layer of water at the apical membrane of endothelial cells [56]. In the iliac portion of the intestine, all bile acids are reabsorbed by active transport.

We studied transcellular transport of lipids in adult animals by light and electron microscopy. There were no visible changes in the structure of microvilli during fat absorption. Occasional pinocytotic invaginations containing no lipids were formed between microvilli. There were no structural modifications in the terminal web and connecting tissue. Lipid inclusions (globules 600 Å in diameters) were identified in smooth apical vesicles immediately under the terminal web. Within the first 30-60 min the majority of these globules were localized in over the nucleus and occasionally under it the rough endoplasmic reticulum and Golgi complex. This localization of globules results from resynthesis of triglycerides from monoglycerides and α-glycerophosphate. Acyltransferases of both pathways of fat biosynthesis are located on the inner membranes of smooth vesicles in the rough endoplasmic reticulum [24,32]. Variations of the number of lipid globules in enterocytes observed at the early stages of absorption (30 min) disappear at later (1-3 h) stages. Absorption and resynthesis of fats coincide with an increase in the size of smooth reticulum in the apical cytoplasm and reduction in the profile of rough endoplasmic reticulum. Although the possibility of mutual transformations of these structures cannot be ruled out, hyperplasia of the smooth endoplasmic reticulum occurs not only at the expense of rough reticulum but also due to constant synthesis of membrane structures [18]. Formation of chylomicrons (transported triglycerides) is a subsequent step in the intracellular processing of resynthesized fat. It has been suggested that chylomicrons are formed in the rough endoplasmic reticulum, where their components (proteins, phospholipids, and cholesterol) are synthesized [24]. At the initial stages of absorption, the Golgi apparatus is hypertrophied: the number of flat cisternae decreases, while that of large vacuoles and vesicles with lipid globules increases. Their size and structure are similar to those of smooth vesicles and rough endoplasmic reticulum. In infections or during prolonged lipid loading, lipid drops appear in the cytoplasm of enterocytes 30 min after the start of absorption. They are 10-15-times as large as chylomicrons. Presumably, the lack of material for protein synthesis and regeneration of intracellular structures causes the appearance of lipid drops. The "working capacity" of enterocytes under these conditions may be low, depending on the regeneration of intracellular structures. These observations indicate that the concentration of adsorbed products in the mucosa and the decrease in the volume of washing solution do not adequately reflect the absorption capacity of the intestine. Irrespective of high concentration of products reabsorbed by epithelial cells, their blood and lymph concentrations are low. i.e., the intensity of their transport into extracelluar fluid is high. Our observations point to strong relationships between intracellular structures. For example, there is a dynamic relationship between apical vesicles which migrate to the Golgi apparatus and merge with terminal parts of its flat cisternae. The Golgi apparatus in absorbing cells may act as an intermediate in the transport of absorbed compounds between cytoplasmic reticulum and lateral cell surface. It can be regarded as a valve regulating transport of nutrients into the extracellular fluid. Lipid globules are not just accumulated in its cisternae; they are transported in the form of vesicles to the lateral plasma membrane and discharged into the extracellular space by reverse pinocytosis at the level of the apical nuclear pole. The absence of lipids above the Golgi apparatus indicates that they are not discharged from vesicles of rough endoplasmic reticulum. Discharge of chylomicrons leads to reduction of the Golgi complex. In this case, although lipids are internalized and lipid drops are formed, transcellular transport is impaired due to the lack of plastic material and unfeasible *de novo* synthesis of intracellular membranes.

Absorption in enterocytes requires considerable expenditures of energy. Complex intracellular processes associated with the transported substrates (chylomicrons) involve substantial amounts of the mitochondria to meet the energy demands that increase each hour. For discharge of chylomicrons into the extracellular space, the lateral cytoplasmic membrane has numerous interdigitations. As chylomicrons are accumulated between epithelial cells of the microvilli, the interdigitations disappear, and the space between them increases toward the basal membrane. Globules cross the membrane, appear in the loose connective tissue, and then enter lymph vessels by transendothelial transport. This pathway is typical of

long-chain fatty acids, while short-chain fatty acids are absorbed directly into blood vessels [1].

Thus, under normal conditions absorption of nutrients in the animal organism is a complex process involving luminal and membrane hydrolysis, intracellular transport with subsequent transformation, discharge from the cells into the interstitium, and entering the lymph.

At the early stages of postnatal mammalian ontogenesis, the functioning of gastric, pancreatic, Brunner's, and other glands is insufficient. Plasma proteins pass through the renal glomerular filter, enter primary urine, and are then reabsorbed in the proximal tubules [27,30,35,46,50,56]. The concentration of albumins and other low-molecular-weight compounds in the urine is essentially high, while that of high-molecular-weight proteins (globulins) is low [46,52]. The proteins are reabsorbed in proximal tubules and subjected to intercellular proteolysis [9, 17,25,38,39,42,43,51-53]. Proteins enter the cell only by pinocytosis. Protein-containing pinocytotic vesicles are transformed into large light vacuoles. Then these vacuoles are enriched in hydrolytic enzymes by merging with small enzyme-containing vesicles of the Golgi apparatus or secrete their contents into large electron-dense lysosomes. Irrespective of the mechanisms of transformation, large lysosomes with high acid phosphatase, glycuronidase, cathepsin, and ribonuclease activities are formed. Electron microscopy and autoradiography showed that 90% of systemically administered lysozyme is associated with pinocytotic vesicles and lysosomes [21]. Thus, proteins reabsorbed in the proximal tubules are hydrolyzed to oligo- and monomers. It was demonstrated that protein is internalized by pinocytosis and catabolized in lysosomes.

Proteolytic activity of the kidneys is of great importance. Under normal conditions, when the permeability of the glomerular filter provides for the entrance of only low-molecular-weight compounds in primary urine, kidneys are the major site of protein degradation and play a substantial role in protein metabolism. There is evidence that growth hormone [49], adrenocorticotropic hormone [47], insulin [20], glucagon [26,41], and parathyroid hormone [36] are degraded in the kidneys. Since the permeability of glomerular filter for albumin is low, only 10-15% of albumins are degraded in the kidneys [53]. The permeability of glomerular filter increases considerably in renal pathologies and due to changes in plasma protein contents and the presence of even trace amounts of foreign proteins in the blood. Reabsorption and hydrolysis of protein with different molecular mass, including transferring and some immunoglobulins increase [34,48,53,54]. This indicates that the protein degradation activity in renal tubules is associated with glomerular permeability. Presumably, this prevents urinal excretion of proteins urine and modifies their specificity and antigenic properties by degrading them to oligo- and monomers. Thus, this renal function can be defined as protein-homeostatic. Nevertheless, further evidence is necessary, since numerous physiological aspects of this function remain obscure. We attempted to assess proteolytic activity of the kidneys during the early postnatal ontogenesis, when considerable changes in blood protein content occur due to transferring of nondegraded proteins from the intestine into blood [4,15].

The specific feature of the enterocytes of newborn animals is invagination of the microvilli plasma membrane. The microvilli contain formed organelles. The Golgi apparatus consists of 2-3 cisternae and has no vesicles and vacuoles. Lateral membranes form numerous interdigitations. Occasional lysosomes are seen in the supranuclear cytoplasm, they are not identified by the acid phosphatase reaction.

When milk components are absorbed, the number of apical pinocytotic invaginations increases considerably; these invaginations are deep and have an ampule-like widening in the cytoplasmic portion. Their contents has a low electron density. The number of vesicles of varying in increases in the apical cytoplasm; their contents is similar to that of invaginations. The mitochondria are oriented along the lateral membrane; their matrix is clarified. The amount of profiles and the length of cytoplasmic reticulum decrease considerably, while the amounts of ribosomes, polysomes, and smooth vesicles increase. Hypertrophied Golgi complex consists predominantly of vacuoles. A dense round supranuclear body is formed in the cytoplasm, and chylomicrons are observed in the widened extracellular spaces. After 3 h, the supranuclear body is much smaller as well as the extracellular spaces. After 4-6 h, extracellular spaces return to normal, and the mass of absorbed product in the stroma progressively increases. The structure of enterocytes normalizes, and the invaginations in the microvilli basement.

Consequently, in the early postnatal ontogeny absorption of milk by intestinal enterocytes proceeds with the aid of numerous pinocytotic invaginations, which is accompanied by activation of intracellular structures and metabolic processes.

The kidneys of newborn rats contain nephrons at different stages of differentiation: from nephrogenic cells to renal corpuscles and tubules. Proximal segments of formed nephrons have a well-developed brush-border, pinocytotic invaginations, and vesicles, and elongated mitochondria contacting with the creases of the basal plasma membrane. The cells

contains considerable amounts of ribosomes and polysomes, formed Golgi complexes, and individual profiles of endoplasmic reticulum. Occasional bodies with acid phosphatase activity were observed in some cells.

One hour after suckling, pinocytotic absorption and activity of the Golgi apparatus increase considerably. Electron-dense cytosomes with acid phosphatase activity are evenly distributed over the cytoplasm.

Consequently, the first suckling is reflected in the ultrastructure of cells in the proximal segment of the nephron as activation of intracellular organelles and hyperactivation of lysosomes. Similar activation of intracellular structures was observed 3-6 h after the first suckling, which is accompanied by an increase in the number of lysosomes with high proteolytic activity. We assessed this activity biochemically.

From our experiments is can be concluded that the first suckling is an important biological factor activating epithelial cells in the intestine and kidneys as well as lytic processes in renal cells.

Similar to mild, peroral protein loading leads to invagination of the microvilli basement. All organelles of the enterocyte participate in transendothelial protein transport. The absorbed material was seen in smooth apical vesicles, cytoplasmic reticulum, and Golgi apparatus. The Golgi apparatus plays an important role in the evacuation of protein into the extracellular space. Then the material enters the connective tissue stroma and lymph nodules. Lysosomes adjacent to the Golgi apparatus were observed in the supranuclear area of some cells. Sometimes these lysosomes were rather large. First, their contents was homogenous, then clarified foci (presumably, of lytic origin) appeared. Acid phosphatase activity was detected in these lysosomes by electron microscopy and quantitated biochemically. After protein loading, acid phosphatase activity in intestinal homogenate increased about 2-fold compared with the control.

Consequently, absorbed protein enters the blood soon after peroral loading: the first portions of absorbed material were detected after 10 min, the maximum being attained after 1 h. The major portion of absorbed and transported protein is not degraded. An inconsiderable amount of protein is hydrolyzed in enterocytic lysosomes. Similar to the processes occurring din adult animals after lipid loading, proteins from the stroma enter lymphatic capillaries by transendothelial transport.

Circulated nondegraded protein is filtered through renal glomeruli and reabsorbed by epithelial cells of proximal tubules. This is accompanied by an increase in the number of pinocytotic invaginations and vesicles, activation of Golgi apparatus, and stimulation of proteolytic activity of cytoplasmic bodies. From these findings, it can be concluded that at the early stages of postnatal ontogeny, in the absence of luminal and membrane digestion food biopolymers are uptaken through pinocytotic invaginations at the basement of microvilli. At late stages of ontogeny, this is observed only in the kidneys. Protein loading stimulates absorptive and mitotic activities of intestinal and renal cells. The intensity of proteolysis in the kidney markedly increases, while in enterocytes this increase is inconsiderable.

Thus, there is obvious difference between proteolytic capacities of renal and intestinal cells. In adults, intestinal epithelial cells contain few lysosomes, while in kidney cells lysosomes are abundant. Consequently, hydrolytic function of adult enterocytes is confined to the apical membrane, while in the endothelium of proximal tubules it is associated with the cytoplasm. This phenomenon seems reasonable, providing for passive immunity via mother's milk. Nevertheless, membrane hydrolysis is more effective than intracellular hydrolysis, since the intestine and kidneys cannot be compared by the degree of hydrolysis. It should be noted that in neonatal animals, intracellular hydrolysis maintains homeostasis strictly determined by physiological parameters.

Cytological analysis of intracellular digestion reveals the functions of cell organelles, which provide not only for transcellular transport but also for the necessary protein transformations. After being uptaken via the system of numerous pinocytotic vesicles, protein is concentrated in large apical vacuoles. These vacuoles are then transformed in the Golgi apparatus, where acid proteases are concentrated in small lysosomal vesicles. Fusion of protein-containing vacuoles with lysosomal vesicle results in the formation of secondary lysosomes, in which proteolysis occurs. Products of hydrolysis diffuse via lysosomal membrane and then are transported in to the interstitium. Thus, intracellular protein transport in the proximal segment of nephron is associated with complex proteolytic transformations of substrates.

After 4-6 h of protein or 6-8 h of fat transport, the membrane structures of enterocytes are markedly reduced. The Golgi apparatus is represented by small vesicles. The profiles of both smooth and rough endoplasmic reticulum are diminished. The mitochondria are clarified and have several short cristae. Accumulation of the mitochondria in the Golgi apparatus zone is probably associated with their involvement in the energy-transforming processes occurring during absorption. Enterocytes are free from rat or protein after 6 h. However, some cells still contain lysosomes with hydrolysis products. Mitochondria with clarified matrix and few short cristae form concentric cristae round these lysosomes.

Without intracellular digestion, the initial structure of the majority of absorbing cells is restored 3-4 h after consuming milk and 4-6 h after consuming fat and proteins; with intracellular digestion, after 10-15 h. The structure is restored after complete disappearance of lysosomes. The length of membrane structure increases simultaneously with formation of invaginations in the basement of microvilli. The number and size of the invaginations increase with time.

The ultrastructure of enterocytes is normalized in rat pups deprived of mother's milk for 3 h. The cytoplasm becomes dense and the length of the both smooth and rough endoplasmic reticulum increases. Mitochondria with moderately dense matrix and oriented cristae are evenly distributed in the apical and basal cytoplasm. The Golgi apparatus is represented by several flat cisternae and small vesicles. In the cytoplasm of absorbing cells protein is not detected 4-6 h and fat 6-8 h after feeding, while in the extracelluar space, stroma, and around blood and lymph capillaries the absorbed product can be seen for long time, indicating that absorption is not eventuated by transepitheial transport. Chylomicrons and proteins are accumulated in the stroma along the entire length of the villus and between the criptae and in the borderline with submucosa, i.e. the absorbed material is moves along villi between the component of loose connective tissue.

Thus, it was found that after a single feeding active functioning of enterocytes during a 3-4-h period is followed by a period of rest, during which restoring processes predominate. Oscillations in functional activity of mitochondria, Golgi apparatus, and cytoplasmic reticulum occur not only upon absorption of nutrients but also in other physiological processes [3,5,7,10].

Discrete activity was particularly pronounced upon absorption of protein by intestinal enterocytes of rat pups. It should be mentioned that formation of pinocytotic invaginations in the apical cytoplasm of enterocytes prior to restoration of intercellular structure, when considerable amounts of protein are in the interstitium, testify to heterogenic activity of cytoplasmic structures. Due to restoration of the initial step of transport absorption may start long before the completion of this process. Asynchronous at the first sight activity of cytoplasmic structures is the most important condition of enterocyte functioning. This principle was defined by G. N. Kryzhanovskii as the law of structural and functional discreteness of biological processes and alternate activity of functioning structures [5,6].

Absorption of milk components in the intestinal enterocytes of rat pups lasts 6 h [16]. This is comparable to the duration of secretory cycle in the pancreas [7] and in hormone-producing cells of the intestine [11]. Proteins and fats are internalized via the apical membrane for 3-6 min, while their intracellular transport and transformation are accomplished in about 3 h. The Golgi apparatus is involved in the transport of these compounds from cell into the interstitium. Electron microcopy showed that the Golgi apparatus prevents the digestion of absorbed proteins in lysosomes. From the stroma fat and protein are transported for about 6 h. Their reabsorption in the kidneys also lasts about 6 h.

The slow transport of these compounds into blood and lymph capillaries is probably due to the necessity of maintaining constant compositions of blood and other biological fluids. We think that this is regulated by the activities of hepatic, renal, intestinal and pulmonary cells. We have revealed a relationship between intestinal and renal absorbing cells. In newborn rats, renal function compensates insufficient function of the intestine, i.e., fats and proteins partially digested in intestinal enterocytes are further degraded to oligo- and monomers in epithelial cells of proximal tubules. This provides a new insight into the metabolism of milk protein in early ontogeny. It can be stated that during this period the kidneys act not only as a protein-homeostatic but also as a digestive organ. This should be taken into account when artificial feeding is prescribed to infants with renal disturbances.

## REFERENCES

1. N. U. Bazanova, K. T. Tashenov, and R. O. Faitel'berg, *Absorption in the Gastrointestinal Tract* [in Russian], Alma-Ata (1985).
2. K. A. Zufarov, In: *Ultrastructural Basis of Systemic Organization of Organs and Tissues* [in Russian], Tashkent (1983), pp. 51-73.
3. K. A. Zufarov and A. Yu. Yuldashev, *Arkh. Anat.*, **78**, No. 6, 76-83 (1980).
4. K. A. Zufarov and A. Yu. Yuldashev, *Uzb. Biol. Zh.*, No. 3, 9-14 (1993).
5. G. N. Kryzhanovskii, *Arkh. Patol.*, **40**, No. 1, 3-13 (1978).
6. G. N. Kryzhanovskii, *Vestn Akad. Med. Sci. SSSR*, No. 8, 3-12 (1985).
7. N. G. Permyakov, A. E. Podol'skii, and G. P. Tizhova, *Ultrastructural Analysis of Secretory Cycle of the Pancreas* [in Russian], Moscow (1973).
8. A. A. Pokrovskii and V. A. Tutel'yan, *Lysosomes* [in Russian], Moscow (1976).
9. Z. Z. Sagdullaev, *Compensatory Hypertrophy of the Kidney in Different Periods of Postnatal Ontogeny and Its Dependence on Resection*, Abstr. MD Thesis, Tashkent (1992).
10. D. S. Sarkisov, A. A. Pal'tsyn, and B. V. Vtyurin, *Adaptive Transformation of Biorhythms* [in Russian], Moscow (1975).
11. E. S. Starkova, *Morphofunctional Analysis of the State of Local Endocrine Apparatus of Intestinal Mucosa in Health and after Vagotomy*, Abstr. PhD Thesis, Moscow (1977).
12. A. M. Ugolev, *Membrane Digestion. Polysusbstrate Processes* [in Russian], Leningrad (1972).

13. A. M. Ugolev, *Evolution of Digestion and Principles of Functional Evolution* [in Russian], Moscow (1985).
14. A. M. Ugolev, *Fiziol. Zh. SSSR*, **72**, No. 4, 401-413 (1986).
15. A. Yu. Yuldashev, *Functional Morphology of Intestinal Mucosa in Different Periods of Postnatal Ontogeny*, Abstr. MD Thesis, Novosibirsk (1988).
16. A. Yu. Yuldashev, A. P. Parpiev, and I. Khalelov, *Fiziol. Zh. SSSR*, No. 9, 1240-1244 (1978).
17. A. Yu. Yuldashev, *Cellular Responses of the Early Postnatal and Compensatory Growth of the Kidneys to Low-Frequency Alternate Magnetic Fields*, Abstr. DSci Thesis, Tashkent (1993).
18. D. Alpers and J. Kenzieg, *Gastroenterology*, **77**, No. 3, 471-496 ((1986).
19. G. Bernier and M. Conrad, *Am. J. Physiol.*, **217**, No. 5, 1359-1362 (1974).
20. M. Chamberlain and L. Stymmlez, *J. Clin. Invest.*, **46**, No. 4, 911-919 (1967).
21. E. Christensen and A. Maunsbach, *Kidney Int.*, **6**, No. 6, 396-407 (1974).
22. S. Clarc, *J. Biophys. Biochem. Cytol.*, **5**, No. 1, 41-50 (1959).
23. R. Clarke, *J. Anat.*, **112**, No. 1, 27-33 (1971).
24. J. Clement, *Reprod. Nutr. Dev.*, **20**, No. 48, 1285-1307 (1980).
25. M. Cortney, L. Sawin, and D. Weiss, *J. Clin. Invest.*, **49**, No. 1, 1-4 (1970).
26. W. Duckworth, *Biochem. Biophys.*, **437**, No. 2, 518-530 (1976).
27. E. Exaire, V. Pollak, and A. Pesce, *Nephron*, **9**, No. 1, 42-54 (1972).
28. R. Gossran, *Adv. Anat. Embryol. Cell Biol.*, **5**, No. 5, 1-93 (1975).
29. G. Gray, In: *Physiology of Gastrointestinal Tract*, Ed. L. R. Johnson. Vol. 2, New York (1981), pp. 1063-1072.
30. J. Hardwicke and J. Squire, *Clin. Sci.*, **14**, No. 3, 509-530 (1955).
31. S. Henning and N. Kretchmer, *Enzyme*, **15**, No. 1, 3-23 (1973).
32. J. Higgins and R. Barnett, *J. Cell Biol.*, **50**, No. 1, 102-120 (1971).
33. *Intestinal Transport: Functional and Comparative Aspects*, Eds. M. Gilles *et al.*, Berlin (1987).
34. J. Katz, G. Bonnorris, and A. Sellers, *J. Lab. Clin. Med.*, **62**, No. 3, 910-934 (1963).
35. T. Maack, D. Mackensie, and W. *Kinter, Am. J. Physiol.*, **22**, No. 6, 1609-1616 (1971).
36. T. Martin, R. Melick, and M. Luise, *Clin. Sci.*, **37**, No. 1, 137-142 (1969).
37. D. Matthews, In: *Peptide Transport in Protein Nutrition*, Amsterdam (1975), pp. 61-146.
38. D. Mendel, *J. Physiol.*, **148**, No. 1, 1-13 (1959).
39. Moller, Taugner, *Pflugers Arch.*, **354**, No. 3, 241-248 (1975).
40. J. Morris, In: *Handbook of Physiology*, Sect. 6, Vol. 3, Washington (1968), pp. 1491-1512.
41. H. Narahara, N. Everett, B. Simmons, and R. Williams, *Am. J. Physiol.*, **192**, No. 1, 227-231 (1958).
42. D. Oken, S. Cotes, and C. Mendel, *Kidney Int.*, **1**, No. 1, 3-11 (1972).
43. D. Oken and W. Flamenbaum, *J. Clin. Invest.*, **50**, No. 7, 1498-1505 (1971).
44. K. Ono, Ztschr. Microsk. Anat. Forsch., **89**, No. 5, 870-893 (1975).
45. *Peptide Transport and Hydrolysis*, Eds. K. Iliot, M. O. Connor, Amsterdam, 1977.
46. R. Perassi and A. Martin, *Int. J. Pept. Protein Res.*, **5**, No. 1, 1-6 (1973).
47. J. Richards and G. Sayers, *Proc. Soc. Exp. Biol. Med.*, **77**, No. 1, 87-93 (1951).
48. S. Rosenfeld, J. Katz, and A. Sellers, *J. Lab. Clin. Med.*, **52**, No. 2, 381-386 (1962).
49. S. Salmon, R. Utiger, M. Parker, and S. Rechlin, *Endocrinology*, **70**, No. 3, 459-464 (1962).
50. A. Sellers, A. Griggs, J. Marmozston, and H. Codman, *J. Exp. Med.*, **100**, No. 1, 1-9 (1954).
51. W. Spector, *J. Pathol. Bacteriol.*, **68**, No. 1, 187-196 (1954).
52. W. Straus, *J. Cell Biol.*, **12**, No. 2, 231-246 (1962).
53. W. Strober and T. Waldmann, *Nephron*, **13**, No. 1, 55-66 (1974).
54. T. Waldmann, W. Strober, and R. Mogialnicki, *J. Clin. Invest.*, **51**, No. 6, 2162-2174 (1972).
55. A. Walker and J. Oliver, *Am. J. Physiol.*, **194**, No. 3, 562-57 (1941).
56. R. Williamson, *Scand. J. Gastroenterol.*, **17**, No. 74, 21-29 (1982).