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## MORPHOLOGICAL AND FUNCTIONAL CRITERIA FOR CHOICE OF DIETARY MIXTURES FOR ENTERAL FEEDING

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UDC 615.874.032.34.074

KEY WORDS: electron microscopy; dietary mixtures; tube feeding.

Clinicians and theoretical medical scientists are currently displaying increased interest in the question of enteral tube feeding. According to current views, enteral administration of the necessary quantity of nutrients must be the method of choice in cases when, in surgical patients or victims of trauma, no disturbances of function of the gastrointestinal tract are present [3, 5]. Meanwhile, reliance on total enteral feeding for patients undergoing abdominal operations, by the use of transintestinal injection of essential nutrients in the composition of high-calorie elementary mixtures or mixtures of natural food products is often accompanied by dyspeptic disorders [4, 6, 7].

The aim of this investigation was to determine the absorptive activity of the intestine in relation to ingredients of nutrient mixtures and to study the state of the morphological structures of the mucosa of the intestinal wall after enteral administration of high-calorie nutrient mixtures of varied composition, as a criterion with which to assess the suitability of their use.

### EXPERIMENTAL METHOD

The preparatory operations used were those developed previously for the formation of multiple fistulas in dogs and for determination of the digestive and absorptive functions of the small intestine [2]. The rate of passage of the nutrients from the intestine to the internal medium of the body, and also the effect of the composition of the test nutrient mixture on evacuatory activity of the small intestine were studied by autoperfusion of the small intestine while temporarily isolated from the digestive tract [1].

The content of sodium, potassium, calcium, proteins, fats, and carbohydrates was determined in samples of the nutrient mixtures administered and in the perfusion fluid by the

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Laboratory of Experimental Pathology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 10, pp. 501-504, October, 1985. Original article submitted January 18, 1985.

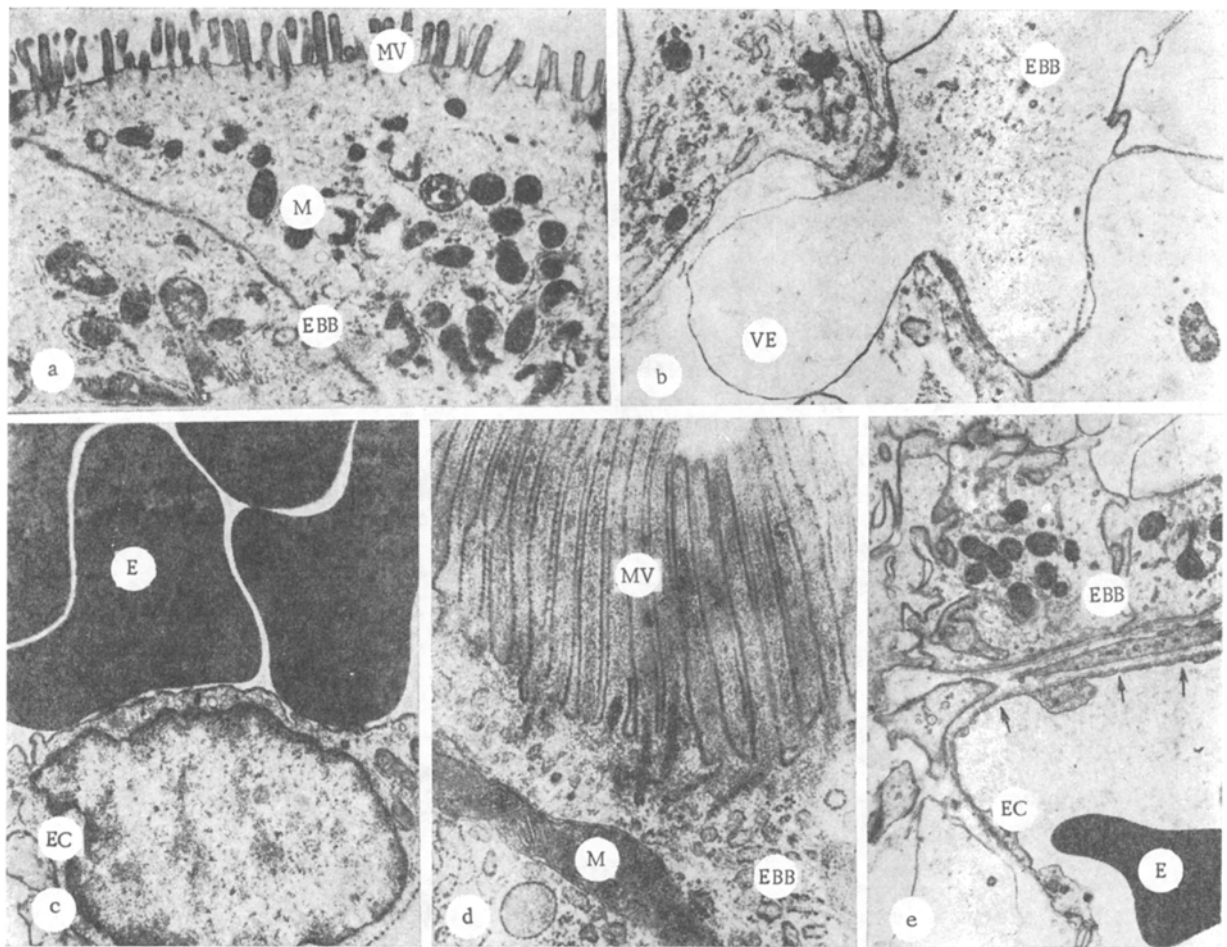


Fig. 1. Ultrastructural changes in epitheliocytes with brush border and capillaries of intestinal villi after enteral administration of "Vivonex" elementary nutrient mixture (a-c) and of special high-calorie mixture (d, e). a) Shortening and reduction of density of microvilli (MV) of epitheliocytes with brush border (EBB), swelling of matrix of mitochondria (M); b) edema of cytoplasm of basal portions of EBB with formation of vesicular evaginations (VE); c) dense distribution of erythrocytes (E) in lumen of subepithelial capillary (erythrostasis), EC endotheliocyte; d) regular arrangement of MV of brush border in cytoplasm of EBB — smooth and granular vesicles; e) thinning of cytoplasm of EC of a capillary with formation of fenestrations (arrow), narrowing of intercellular spaces of EBB. Magnification: a, b, c, e) 18,000, d) 42,000  $\times$ .

ordinary biochemical methods of investigation. Biopsy material from the mucosa of the small intestine, after the end of perfusion, was subjected to histological investigation after fixation by Carnoy's method, and to electron-microscopic study on the ÉVM-100B electron microscope.

The mixtures used included the "Vivonex" elementary mixture (USA), a 20% solution of a protein "enteral food," consisting of a specially prepared high-calorie nutrient mixture (1 kcal/ml), with proteins, fats, carbohydrates, and also poly-, oligo-, and monomers in their composition which corresponded to that of the natural intestinal medium (chyme) on a mixed diet. Experiments were carried out on 14 dogs with multiple fistulas (51 experiments).

#### EXPERIMENTAL RESULTS

Depending on the composition of the mixture, the character of its assimilation in the proximal part of the jejunum and the state of the morphological substrate after the end of autoperfusion varied widely. For instance, the mixture "Vivonex," which is well known and often used in medical practice, and which contains the principal nutrients in the form of monomers, with a high proportion of the carbohydrate components, was assimilated after 10 to 11 passages. It was noted that the high osmotic pressure of the mixture led to the out-

flow of a large quantity of endogenous water into the intestinal lumen, and during the whole period of assimilation of a standard volume of the mixture (400 ml) this outflow exceeded the original volume by 3-5 times.

Analysis of the average rate of passage of the nutrients from the enteral to the internal medium showed a sharp decrease in the rate of entry of all ingredients studied with the exception of carbohydrates, the rate of absorption of which was quite high, namely  $147.35 \pm 5.40$  mg/min. The considerable rise in the coefficient of evacuation (up to  $25.5 \pm 5.69$ ) is evidence of a marked hyperosmolar effect of the mixture, with disturbance of the evacuatory activity of the part of the small intestine studied. The results of morphological investigations of the biopsy material of the mucous membrane taken after autoperfusion with "Vivonex" nutrient mixture, also indicate disturbance of the conditions of assimilation of the nutrients.

Ultrastructural analysis revealed evidence of swelling of the brush-border epitheliocytes of the intestinal villi, straightening out of the folds of the lateral membranes, narrowing of the intercellular spaces, a reduction in density of the cytoplasmic organelles in the basal zones with the formation of vesicular evaginations (clasmatosis), and the pinching off of cell fragments into the interstices. Evidence of congestion of the subepithelial capillaries, plasmorrhagia, and erythrostasis also was found (Fig. 1a, b).

Ultrastructural changes in the epitheliocytes indicate growth of intracellular edema, a decrease in intracellular transport of nutrients, and also increased vascular permeability, leading to intravascular rheologic disorders.

When a 20% solution of the special protein enteral mixture containing a high concentration of protein in the form of polymers was used, a sharp decrease in the rate of assimilation of the mixture also was observed ( $1.61 \pm 0.28$  ml/min). Meanwhile the increased concentration of nitrogenous products resulted in their passage from the enteral into the internal medium of the animal taking place rapidly ( $21.75 \pm 5.91$  mg/min). Nevertheless, the results as a whole are evidence that the selective flow of nitrogenous products from the enteral medium into the internal medium was accompanied by the secretion of a considerable volume of fluid into the intestinal lumen in the composition of endogenous juices and transudate of water, sodium, and chloride. The coefficient of evacuation also increased under these circumstances ( $5.27 \pm 1.44$ ).

Although the results of the morphological investigation demonstrated integrity of absorption processes, nevertheless they also revealed signs of increased functional activity of the epitheliocytes and endotheliocytes of the capillaries. Electron-microscopic investigation showed that the structure of the brush border was intact, and that hypertrophy of the mitochondria was present but without any disturbance of the structure of the matrix and cristae. Changes in the cytoplasm of the basal zones of the brush-border epitheliocytes were heterogeneous; besides a decrease in density of the cytoplasmic organelles in the submembranous zone and narrowing of the intercellular spaces, moderate widening of the intercellular spaces and hyperactivity of elements of the lamellar network could also be observed. In capillaries of the lamina propria of the intestinal villi signs of aggregation of erythrocytes were found with preservation of the plasma flow or of congestion (Fig. 1c). Structural changes in the organelles of the endotheliocytes, in the form of increased pinocytotic activity of some or edema and clasmatosis of others were evidence of differences in functional activity of the cells of the vessel walls.

Different results were obtained by the use of a nutrient mixture corresponding in composition of its basic nutrients and its concentration of poly-, oligo-, and monomers to chyme. The mixture, as a rule, was assimilated in the course of one or two passages. The results are evidence of a high and fairly uniform rate of passage of the components of the mixture from the enteral into the internal medium of the animal without any disturbance of evacuatory activity (rate of absorption of the mixture  $3.01 \pm 0.25$  ml/min, coefficient of evacuation  $1.48 \pm 0.47$ ).

These morphological investigations of the character of assimilation of a mixture corresponding in the proportions of its ingredients to chyme confirm the absence of any structural changes in the epitheliocytes and capillary endotheliocytes. The microvilli of the brush border were regularly arranged, and a layer of glycocalyx was preserved on their surface. Numerous smooth vesicles were found in the cytoplasm of the apical zones, as a manifestation of intracellular transport of nutrients. Intercellular spaces in the basal zones

of the epitheliocytes were moderately widened. Capillary endotheliocytes in the zone of contact with the epitheliocytes formed multiple fenestrations over a large area (Fig. 1d, e). Structural changes discovered in the epitheliocytes and the capillary network indicates an enhanced absorptive function.

The results are thus evidence that, if nutrient mixtures of equal and high calorific value, providing 1 kcal/ml of solution, are given optimal conditions, maintaining "coordination" between absorption of all nutrients are created if the calorific value is increased, as a result of an increase in the content of the basic nutrients so that they correspond to their proportions in the chyme, and a constant ratio is maintained between poly-, oligo-, and monomers. Preference must be awarded to mixtures of such a composition when total enteral feeding of surgical patients is indicated.

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#### INVESTIGATION OF EXPERIMENTAL STAPHYLOCOCCAL SEPSIS

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UDC 616.94:579.861.2]-092.9-07

KEY WORDS: sepsis; experimental model.

Despite active research into the problem of sepsis, conflicting opinions are still held on aspects of its pathogenesis, there is no generally accepted terminology and classification, and should the disease arise its mortality remains high. Prospects for the solution of this problem rest on expansion of fundamental theoretical ideas of the nature of this disease and, in particular, the study of microorganism-host interrelationships, which will enable up to date clinical-bacteriologic and morphologic criteria of the development of this infectious process to be established [4].

A detailed study of the mechanism of these interrelationships is possible only experimentally. However, it has not yet proved possible to induce sepsis in animals by introducing bacteria isolated from man. Existing methods reproduce either bacteriemic shock [3] or local suppurative infection with periodic bacteriemia [5]. The main shortcoming of all known methods is the absence of a set of criteria whereby sepsis can be characterized as an independent disease.

In the investigation described below the development of the principal features of sepsis was studied using rats as the model.

#### EXPERIMENTAL METHOD

Experiments were carried out on 230 mature noninbred male albino rats. The infectious process was induced by a single intramuscular injection of various doses of a culture of

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