TASHKENT MEDICAL ACADEMY
TERMEZ BRANCH OF TASHKENT MEDICAL ACADEMY
FIRST MOSCOW STATE MEDICAL UNIVERSITY NAMED AFTER I.M.SECHENOV

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STRUCTURAL AND FUNCTIONAL CHARACTERISTICS OF THE THE SMALL INTESTINE MUCOUS MEMBRANE DURING NATURAL AND ARTIFICIAL FEEDING IN THE EARLY POSTNATAL PERIOD OF LIFE

(monograph)

Termez- 2024

Structural and functional characteristics of the the small intestine mucous membrane during natural and artificial feeding in the early postnatal period of life – monograph

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ABOUT THE CHAPTER

INTRODUCTION

Relevance. According to modern concepts, the small intestine of humans and animals performs digestive-absorptive, exo-endocrine, immunological, motor-evacuatory, excretory functions. This wide range of activities of the body determines close attention to the study of its structure and function, and the clarification of adaptive capabilities. Modern concepts of the functional morphology of the small intestine have been developed based on the fundamental research of I. P. Pavlov, K. M. Bykov, and I. P. Razenkov. The successful development of this field has been contributed to by the works of A. M. Ugolev, K. A. Zufarov, M. V. Voyno-Yasenetsky, V. A. Shakhlamov, J. Trier, K. Leblond, J. Bienenstock, and others. However, the inaccessibility of the small intestine for endoscopic studies, its considerable length, architectural polymorphism in different periods of ontogenesis, and the conjugation of various functions allow solving many questions of structure and function. In particular, until today there are no complete representations of the regularities of its development and formation, nor the clarification of the features of adaptive reconstructions in the early postnatal ontogeny. As a result of these studies, the concept of the norm in the dynamics of the development and formation of the body, adaptation to the character can be substantiated. It is still difficult to understand the process of absorption in the mucous membrane of the thin layer, its participation in the structure regulation of homeostasis internal environment fragments. Issues of rapid (during functional loads) and slow (age) changes in the structure of the mucous membrane of the small intestine, topographical organization system of the crypt-villi along the organ turned out to be insufficiently studied. The issues of interrelationship of cytoplasmic structures in the regulation of the process of absorption turned out to be insufficiently developed. Meanwhile, the study of these issues, the structure relationships and some functions of the small intestine is important for the development of regularities of its age adaptation, determination of adaptive capabilities. Concepts of the processes of adaptation and adaptive capabilities of the early postnatal ontogenesis are contradictory, their mechanisms are poorly understood. In early postnatal ontogeny, intensive growth is observed in mammals. Naturally, this requires relatively large (compared to adults) amounts of nutrients. For a newborn child, the protein requirement is 2.7–2.8 g, fats are 6–6.5 g, and carbohydrates are 12–15 g per kg of body weight. However, as it has been established by numerous studies, the growth of mammals, the satisfaction of their needs in nutrients is possible during natural (breastfeeding) feeding. Artificial feeding disrupts not only the development of mammals, but also causes an increase in the incidence of disease. Therefore, the question of mechanisms of impaired digestion and absorption is of both theoretical and practical interest.

Chapter I. MORPHO-FUNCTIONAL FEATURES OF THE SMALL INTESTINE IN AGE-RELATED ASPECTS (literature review)

The deposit of the digestive organs, and in particular the intestines, is noted at a very early stage of embryonic development. On the 7-8th day, the endoderm begins to separate into the primary cyst, which on the 12th day is divided into 2 parts: intraembryonic - yolk sac. The endoderm is very early connected with the visceral layer of the mesoderm, and both fleshy layers are called the splanchnopleura. Mesenchyme forms between endo and mesoderm.

Epithelium, mesenchyme - connective tissue with blood vessels and muscular sheath develops from the endoderm. From the inner leaf mesoderm - the serous membrane to the intestine.

By the end of the first month of embryonic development, 3 parts of the primary kidney are formed: head (front), middle and back (caudal). From the anterior part of the intestinal tube, the pharynx, esophagus, stomach and part of the duodenum with rudiments of the pancreas and liver are formed; from the middle hip - the distal part of the 12-tip, knee and iliac muscles; from the back - all parts are thick.

Due to the fact that the small intestine develops from the middle skin, let's consider the features of histogenesis in it.

Histogenesis begins in the midbrain, starting with the 12th digit of the brain and extending in a caudal direction. At the earliest stages of embryonic development, it is lined from the inside by flattened cells of endodermal origin. The index of labeled nuclei (ILI) here is 50% with a single and 70% with a double introduction of H3-thymidine. The outer layer is formed laterally by randomly arranged mesodermal cells. In parallel with the formation of the tubule, the mitotic activity of its constituent cells increases. Epithelial cells, which proliferate intensively, exert mutual pressure on each other and change their flat shape to cubic and prismatic. Cell nuclei are oriented perpendicular to the plane of the plate. For some time, they are located in one row, however, over time, as the cells are stretched in length and, apparently, purely mechanically, they separate each other, they form 2-3 irregular rows. H3-thymidine injection in the intestinal epithelial cells increases from 70% to 85-90%.

Cells and nuclei in the epithelial layer are arranged very closely, as a result of which they give the impression of a simple, multi-layered epithelium. In fact, the epithelium passes through the mid-late stage in the true symplast. All cells, located on the basal membrane, reach the free surface layer. Therefore, despite the assertion of some authors, the epithelium should be characterized as a single-row cell composition of the epithelial layer in this period of development completely uniform, in which there are no signs of differentiation yet. Therefore, endodermal cells are not yet considered tissue.

Intensively proliferating epithelial cells in the middle late, forming significant growths, can completely or partially fill the lumen of the organ . This is called physiological atresia and is most often observed in the 12-thirtyline, less often in the lower parts of the intestinal layer. Rarely, physiological atresia can cause congenital atresia or stenoses at various levels in the pelvis.

At 6-8 weeks of embryonic development (10-25mm), the development and differentiation of different layers of the small intestine layer begins. When the thickness of the epithelial layer reaches 80-90 μm, at the border between the epithelial and the future connective tissues in the 12-tip layer, small compactions of mesenchymal cells appear, which extrude the epithelium into the lumen of the organ. Actively proliferating mesenchymal cells, which are still separated by significant gaps, form aggregates that closely adhere to the base of epithelial cells. The basal membrane at the base of the epithelial cells is continuous and smooth.

From the very beginning of the formation of epithelial tubercles, primary longitudinal folds, blood capillaries are found under them, which are important in the process of villi formation. The development of blood vessels, the formation of various units of the microcirculatory channel, is probably the factor that leads to the appearance of villi in mice, chickens, marine pig, dog. According to N.G.Grigoriev, who studied the formation of villi in a number of vertebrates, blood vessels and interlayers of connective tissue and mesenchyme are involved in this process, possibly laying the structural and functional units of the organ.

At 8–10 weeks of embryonic development, the process of villus formation involves the ileum. The formation of new generations of villi between the earlier ones occurs identically in the first and fourth months of prenatal human development, they reach a height of 500 μm. In areas located between the bases of villi or protrusions, the epithelium still retains a multi-row structure. Among the epithelial cells lining the surface folds and primary villi, the nuclei are arranged in one row. Mitoses are found throughout the entire length of the epithelial lining, but the IMR at the base of the folds and on the surface of the villi is 2 times higher than at their apex.

Thus, with the beginning of the formation of specialized structures in the epithelial outer organ, clear changes in the processes of reproduction of cells are noted. A significant part of them at the top of the folds and villi comes out of reproduction and stops dividing. In the well-differentiated areas of the epithelium (between the folds and the basal villi), the rate of cell division is simultaneously intensified due to the reduction of the interphase.

As a result of the exit of some epithelial cells from reproduction and the increase in the specific value of differentiated cells, the NAME drops sharply. Electronmicroscopically, the epithelial cells of the forming villi of mammals are connected to each other by numerous desmosomes. On the free surface of the cell there are single cytoplasmic outgrowths, single microvilli about 0.3μm in length and 0.07μm in width. In the apical part of the cytoplasm, in addition to growths, there are invaginations of the plasmolemma, sometimes quite deep. Cytoplasm is rich in ribosomes and polysomes. Smooth and rough reticulum are found in all cells, in significant quantities. The structures of the Golgi complex are located above the nucleus and, as a rule, consist of 1-2 flattened tanks, 3-4 small vesicles. Mitochondria are small with oriented cristae. Nuclei large with distinct nucleolus. Deren describes epithelial cells with numerous pinocytotic invaginations and electron-dense round formations in the supranuclear region at this stage of development. According to Schmidt, Parat M., Patzelt, Biering et al., supranuclear bodies arise as a result of resorption of amniotic fluid from the lumen.

An autoradiographic study of the proliferation of the epithelium of the mucous membrane of the small intestine during this period of embryonic development of rats and mice showed that marked cells are found throughout the organ, however, the mitotic index (MI) of the apex of the forming villi is noticeably lower than at their base. 2 hours after a single injection of H3-thymidine at the tip of the villi, half of the cells were labeled, and on that basis - 69%. After three injections, the amount of H3-thymidine in the corresponding areas is equal to 75-97%.

Thus, during the period of villus formation, certain shifts in cell reproduction occur. About 25% of epithelial cells exit the reproduction cycle and stop dividing. In the well-differentiated areas, the rate of cell division intensifies due to the reduction of interphase periods.

When the diameter of late human embryos is 0.5 mm, 6-8 villi up to 100 μm in height are visible on the cross section. Epithelium on the upper surface is single-layer prismatic with a brush layer on the apical surface. Electron microscopy shows a strong development of microvilli with a small number of filaments. Plasmolemma has microvilli 11nm thick. The number and size of mitochondria, the length of the membrane of the rough and smooth reticulum changed slightly. In the cytoplasm, electron-shielding granules are found, in which the activity of acid phosphatase is established. Acid phosphatase is also found near the nucleus and in the zone of the Golgi complex.

As well as the development of villi, the first embryonic crypts are revealed relatively early: the human is already at 8 weeks, and the rat is at 20-21 days of embryonic development. This process begins with the adhesion of intensively proliferating epithelium to the underlying mesenchyme. Initially, it is a collection of intensively proliferating epithelial cells. Therefore, the clearance of the crypt is either absent or very high. Simultaneously with the immersion, the epithelial cell grows towards and separates the mesenchyme it is a series of independent formations that have the shape of a cylinder. As a result of these complex epitheliomesenchymal interactions, crypts appear in the future laminar mucosa. The rate of development of the crypt during a certain period of time is relatively intensive, in the late prenatal ontogeny it decreases somewhat. The absolute amount of rapidly proliferating epithelial cells during the formation of villi and crypts is sufficient for the formation of structural and functional units of the organ, differentiated cells. This process does not stop even in the early life of mammals.

Thus, in mammals, even before birth, intensive education and formation of structural and functional units of the small intestine, long organ as a whole takes place. This is considered to be the result of a complex integration of the activity of epithelial and connective tissues, the processes of reproduction and differentiation of cells.

If at the beginning of the formation of the crypt H3 - thymidine is included in practically all epithelial cells, meanwhile, with its topographic establishment, the label is detected mainly in its lower and middle third. The upper third crypt is considered as a zone of differentiation of epithelial cells before their exit to the surface of the villi. In this period of development of mammals, when the linear parameters of villi and crypts, their number in the mucous membrane of the small intestine, are progressively increasing, the renewal of epitheliocytes occurs 2 times slower than in newborn animals.

An increase in the number of crypts occurs either due to the splitting of previously formed crypts or from the opening of primary crypts. This mechanism is recognized by the majority of researchers as part of the formation of the crypt. However, O. V. Volkova and co. suggests that crypts of small intestine are formed as a result of fusion of villi in its lower half.

At the time of birth, the basic mass of the crypt of the 12-thirtyline human has a depth of about 180 µm. Whereas in the lower parts they are still at the stage of implantation in the epithelial cells in the underlying connective tissue.

At the beginning of crypt formation, proliferating cells are concentrated only in the. At this stage of development, the index of primary mesenchymal cells is equal to 52% in mice, with a triple injection of H3-thymidine it reaches 96%. Intensive proliferation of cells in the crypts provides an increase in the number and size of villi and crypts, the absorbent surface of which is thin.

At the 9th week of human embryonic development, goblet cells are differentiated from the cells of the tubular epithelium, which are visible on the lateral surface of the forming villi. First, they appear in the proximal part, and then in the distal part of the 10th part of the thin layer. At the same time, a network of blood capillaries is formed from the mesenchyme of villi in the stroma.

In parallel with the formation of the mucous membrane, at the 8th week of development, smooth muscle cells and neuroblasts appear in the mesenchyme. At the 10th week of human development, nerve fibers sprout into the intestinal wall and differentiate adrenergic and cholinergic.

Endocrine cells appear at 12 weeks, Paneth cells at 17 weeks. At the same time, the epithelial villi take a cylindrical (prismatic) shape with a brush-like layer. Non-specific esterase (10-12 weeks), alpha-glucosidase, lipase, sucrase, dipeptidase, maltase (10-14 weeks) are detected in its cytoplasm. With K 17, the activity of these enzymes increases significantly.

In this period, for example, the differentiation of other elements of the wall is observed. According to some data, by the end of 12 weeks, according to others - in 13-19 weeks, Brunner's glands begin to form from the epithelium of the crypt of the 12-tiered intestine.

At the age of 16-20 weeks, separate clusters of lymphoblasts appear in the mesenchyme, which is located between the epithelium and the muscular membrane of the organ, from which lymphatic follicles (Peyer's plaques) are formed later (24 weeks).

K 6 months The development of the human fetus involves all the layers that form in the intestine. In the course of 8 months. The mucous membrane begins to thin more quickly than the rest of the mucosa. The consequence of this is the formation of transverse folds of the mucous membrane. The formation of the body, as well as the structural and functional units of the organ, begins in the 12th tip and spreads in the caudal direction. In the muscular shell, the more developed inner circular and outer longitudinal layers are clearly distinguished.

Auerbach's nerve plexus is found between them. The largest ganglia of this plexus are found on the side of the mesenteric attachment. Part of the nerve fibers eventually grow into the submucosa, where they form Meissner's plexus. Initially, it is formed in the 12-thirty line, later in the lower and iliac regions, etc. e. the establishment and development of the nervous system occurs in the dorsocaudal direction, in close connection with the development of other tissues and structural small intestine.

Therefore, already in the period of embryonic development of mammals, the laying and development of villi and crypts, the formation of populations of proliferating, differentiating and differentiated (panetov, absorbing, goblet and endocrine) cells occurs. Histo- and organogenesis is carried out due to very low (almost 2 times less than in adults) physiological renewal of epithelial cells. Cambial, proliferating epitheliocytes, concentrated in forming and forming crypts, become part of complex differentiated system crypt-villus, a part specialized in reproduction and differentiation of cells.

According to the data of the literature, the histogenesis of the intestine of higher vertebrates and its variation from one species to another relate only to absolute terms and secondary signs related to the peculiarities of life and nutrition of the animal.

The development and formation of the small intestine as an organ is a long way of prenatal and postnatal development. Postnatal development and establishment of a thin layer, its structural and functional units is a logical continuation of intrauterine and a component of a single process. Significant restructuring of the structure and functions of organs after birth, apparently, is the result of evolution.

The human small intestine, like that of other mammals, begins to function very early. A normal fetus swallows a large amount of amniotic fluid. They penetrate through the stomach into the intestines and undergo absorption, and individual components are even hydrolyzed. It is assumed that in the intestines of the fetus, the products of excretion of nutrients from its blood are also absorbed. Only part of the swallowed substances is not absorbed and does not undergo decomposition and forms meconium. During the first 6 months Amniotic fluid of pregnancy contains 6-18g/l protein, later 2-3g/l. Concentration of glucose at 14-15 weeks of pregnancy - 0.40g/l, from 35 to 40 - 0.22g/l.

If you take into account that during the day the human fetus swallows about 450 ml. amniotic fluid, the daily content of protein entering the digestive tract, even in the last months of pregnancy, is about 1g. It has been shown by electron microscopy that the villi enterocytes at birth absorb not only proteins but also carbohydrates from the lumen by pinocytosis.

Therefore, the small intestine of mammals before birth, despite intensive implementation of processes of formation and development of structural and functional units, participates in digestion and absorption of nutrients from amniotic fluid.

After birth, the length of the intestine is relatively longer than that of older children and adults. The ratio between the length of the intestine and the body in newborns is 8, 3: 1, in the first year of life 6, 6: 1, at the age of 16 years - 7, 6: 1, in adults - 5, 4: 1.

The length of the thin hair of a 1-year-old child is 1.2-2.8m, which is almost 2 times less than that of an adult. When calculated per 1 kg of body weight, a newborn has 1 m, an adult - 10 cm, the length is thin. The physiological length of the thin posterior is 4 times less than the anatomical length. A similar observation was made on the side of the large intestine. Probably, the relatively small absorbent surface of the thin mucous membrane is compensated by the length and lactotrophic nutrition, in which the main mechanism of assimilation of nutrients is pinocytosis.

Despite its relatively small diameter, the wall is thin and has a mucous, submucosa, muscular and serous membrane. The mucous membrane throughout the body is not yet formed at birth. Along with tall, finger-shaped villi, short, forming ones are seen. The crypt is relatively short. In the iliac crest, the number and linear parameters of the crypts and villi are less than in the proximal parts of the thin cecum. The main part of striated enterocytes, which cover the surface of the villi, in all parts of the thin dark cylindrical (prismatic) shape, have a single-row homogeneous cytoplasm with a slight lightening above the nucleus. Only some of them may be vacuolated due to absorption from the lumen of late nutrients contained in the contaminated amniotic fluid. Between the striated cells there are goblet cells, the secretion of which is HIC and Hale-positive. The amount increases in the caudal direction, active secretion is not yet observed.

In the crypts, the epithelial cells are low-prismatic in shape, closely adjacent to each other, and have basophilic and pyroninophilic cytoplasm. The brush is not contoured. Single goblet cells and mitotically dividing cells are found among these cells. Behind the thin basophilic membrane, both the crypts and the villi reveal their own connective tissue plate, which at birth consists of blood and lymphatic capillaries and a small number of blast cells. The density of blood vessels is relatively insignificant. At the border of the mucous and submucous membranes there is a muscular plate, individual cells of which are directed towards the crypt and villi. The submucosa is thin, consisting of a wide loop network of vessels and blast cells.

Electron microscopic enterocytes of thin villi have a characteristic structure late after birth. They differ from enterocytes of sexually mature mammals by the absence of a terminal network, low activity of hydrolytic-transporting enzymes of the brush border, and the presence of pinocytotic formations between the bases of microvilli.

Consequently, histogenesis is late at birth. In its mucous membrane, villi are formed at different stages, surface absorption is insignificant. Enterocytes in the crypt-villi system are topographically and functionally heterogeneous: on the surface of the villi, they are specialized for the implementation of absorption and secretion processes; proliferation and differentiation in crypts. Extremely low activity of hydrolytic-transporting enzymes of the brush coat, lack of specialized cells in the lamina propria mucosa indicate imperfection of membrane digestion and immune function in the early postnatal period of life.

According to numerous studies, the most intensive growth of the mammalian organism is observed in the early postnatal period of life. According to A.V. Mazurina, body mass of a newborn child for 4-4.5 months. doubles to 10-11 months. triples Its size increases twice a week after birth, and four times after two weeks. Such high rates of development require relatively large (compared to adults) amounts of nutrients. For a newborn baby, the need for protein is 2.7-2.8 g. fat 6-6.5g, carbohydrates 12-15g/kg body weight.

However, during the period of milk feeding of mammals, the degree of structural and functional development of digestive organs is relatively low. According to numerous studies of our colleagues, as well as other authors in the mucous membrane of mice, the main source of pepsin activity is absent until the 7th day after birth - the main cells, parietal cells are at the stage of differentiation. Pancreas is characterized by intensive proliferation of acinar cells, increase of structural and functional units - acini. The activity of trypsinogen, chemotrypsinogen, amylase, lipase is very low. The same is observed in other animals.

Determination of the activity of some hydrolytic transport enzymes involved in the assimilation of proteins, fats and carbohydrates in the mucous membrane of the proximal and distal parts of the small intestine showed that the rat in other immature mammals during lactation, the activity of invertase is almost absent, and monoglyceridlipase and amylase are extremely insignificant. Very low activities of trypsin and chymotrypsin were found in fractional brush paste. The high activity of peptidase proteolytic enzymes in the homogenate mucous membrane, especially in the distal part of the small intestine, revealed by a number of researcher, today can be said to represent the activity of intracellular lysosomes.

However, on the basis of a number of works of domestic researchers, in many textbooks, manuals it is stated that in infancy, not pepsin, but a number of other proteases are involved in protein digestion. Pancreatic proteases (trypsin, chymotrypsin) are primarily involved in the digestion of peptides in the thin layer. Fat is digested under the influence of milk lipase and pancreatic lipase.

Hydrolysis of carbohydrates mainly occurs in the thin layer. Lactose is broken down into monosaccharides b-glucosidase, sucrose and maltose by alpha-glycosidase. According to A. M. Ugolev, this process is carried out in the zone of brush-like enterocides.

Based on these results, the authors of the above studies believe that membrane digestion is carried out both by enzymes synthesized by enterocytes and enzymes of pancreatic origin.

Therefore, there are two points of view about the process of digestion and absorption of proteins, fats and carbohydrates. However, the relatively small absorbent surface of the small intestine, the incompleteness of its morphological formation, the high activity of trypsin inhibitors and other proteolytic enzymes in breast milk, as well as the results of the research of our colleagues allow us to consider that during the period of breastfeeding, cavity and membrane digestion is not effective. Naturally, then the question arises about the biological relevance of this phenomenon in the assimilation of complex biopolymers, which provide the most intensive growth of the organism in the postnatal period of the life of mammals.

According to numerous studies, breast milk (colostrum-intermediate-mature milk) contains significant amounts of proteins, fats and carbohydrates, all classes of immunoglobulins, components of complement, lactoferrin, lysozyme, factors inhibiting migration of lymphocytes, differentiation of B-lymphocytes, synthesis of own antibodies, proteolytic enzymes and their inhibitors. In milk, macrophages, monocytes, T- and B-lymphocytes, plasma cells, polymorphonuclear leukocytes, which contribute to the development of non-pathogenic lactobacilli and the establishment of colonization resistance, preventing the development of pathogenic microorganisms.

When breastfeeding newborns, mammalian immunoglobulins of all classes, being absorbed from the small intestine into the blood, participate in the creation of passive immunity. Secretory immunoglobulin A, as in adult mammals, covering the surface of the mucous membranes of the digestive tract, prevents the interaction of microorganisms with the membranes of epitheliocytes, thanks to which the pathogenicity of various microbes is not realized (antimicrobial, antiviral action). Breast milk hormones, which are absorbed as well as immunoglobulins, regulate the interconnected activity of organs and systems, their structural and functional establishment, because in this period there is no close relationship between the endocrine glands. These and other unique properties of breast milk allow us to consider it not only as a valuable and irreplaceable food product, but also as a natural regulator of the physiological development of mammals. The biological and plastic properties of breast milk in the early period of life, which are explained above, as well as still unclear, can be preserved only under the condition (however paradoxical) of structural and functional immaturity of organs and systems, and, in particular, digestive, inefficiency of cavity and membrane digestion. Boiling, sterilization of breast milk, especially the effect of enzymes of gastric juice, pancreas and intestines after the formation of digestive organs, deprives breast milk of species specificity, practically all biological properties.

On this basis, the structural and functional immaturity of the small intestine, as well as other organs and systems (immune, hormonal, etc.), should be considered a relative, genetically determined, general biological regularity for a certain stage of the ontogenesis of mammals.

During millions of years of evolution, in order to preserve the unique biological properties, the complex structure of milk, and to provide optimal conditions for the relationship between the mother and the child, a special pinocytotic suction mechanism was formed. As a result, the intact components of milk penetrate into the internal environment of the body of mammals hydrolysis.

Previously, there was an opinion that pinocytosis of small enterocytes in the early postnatal period of the life of mammals is not able to satisfy the nutritional needs of the body. However, B. Morris, K. Morris et al., Walker showed that 18 to 60% of the total mass of orally administered proteins are absorbed with preservation and immunological specificity in the thin layer of mammals. V. K. Mazo et al., and V. A. Shaterniko, V. A. Shaternikov and V. K. Mazo point out that when determining the mass of absorbed undegraded protein, their constant capture from circulating blood and deposition in internal organs is not taken into account. We absorb cleavage, as established by SL Clark, Vollrath, Gossrau, colloidal iron, ferritin, peroxidase, polyvinylpyrrolidone, various carbohydrates, fat.

Employees of our department K. A. Zufarov, V. M. Hontmacherom and A. Yu. Yuldashev, based on the results of his own research, made a scientific discovery about a new property of the kidneys to digest orally administered proteins when they are absorbed from the small intestine into the blood.

Based on the above data, there is now reason to reconsider the presentation, digestion, and absorption of nutrients in the liver. A. A. Pokrovsky and V. A. Tutelyan believes that the evolution of natural breastfeeding in each species occurred somewhat "convergently," that is, through the mechanisms of lactation and the adaptation of newborns to its composition. The surface structure that individual biological species receive from the environment over the course of many millennia forms perfect mechanisms for their utilization. In the future, these relationships were established as formulas of balanced nutrition, characteristic of individual biological species. It is natural that for humans, or other mammals, a specific mechanism of breastfeeding has developed, which reflects the specifics of individual pre- and postnatal development and formation of the body, providing nutrients and biologically active substances. Feeding with milk of the second type, with artificial mixtures, which are not ideal, close to the composition of breast milk, is a forced, extreme measure, because the negative impact of this is very large.

During artificial feeding, there is a violation of the formation of the microbiocenosis of the goat, colonization resistance, which has a significant effect on the formation of local and general immunity, damage to intestines, kidneys and other internal organs. Naturally, there is a need to study the mechanisms of breast milk suction, as well as the components of artificial breast during the newborn period and the influence of artificial feeding on the development and formation of the small intestine. Despite the fact that in ontogenesis each period represents a physiologically mature form of existence, nevertheless the period breastfeeding is a stage of preparing the body for independent existence. Therefore, the task is to clarify its mechanism, the possibility of its regulation.

After the period of lactation in mammals, there is a period of mixed nutrition. According to K. R. Rakhimova, A.I. Demidova, deep structural and functional restructuring during the considered period is caused by a change in the character of nutrition, vol. e. transition to food with a higher quality composition and content of proteins, fats and carbohydrates. He is Chris G. F. Karimova, B. A. Sadykova, K. R. Rakhimov, A. I. Demidova, A. Yu. Yuldashev, Robberecht et al., Henning, Kretchmer noted a sharp increase in the activity of invertase, amylase, trypsin, and chymotrypsin in the zone of the brush border of enterocytes of the villi of the small intestine from the 14th day after birth. However, there are many examples in the literature that indicate that exogenous factors, in particular nutritional ones, regulate the structural and functional restructuring of internal organs during postnatal ontogenesis. Bone ontogenetic development of structure and function, like other internal organ, is controlled by genetic factors. As shown by the researches of our colleagues, as well as other authors, mammals structurally - functional establishment of internal organs and systems is completed mainly at the time of transition to final (definitive) nutrition. Structural and functional restructuring ends at the time of puberty. At this age, the mucosal architectonics do not change under late physiological conditions. Our colleagues note the same when studying the morphology of the stomach, pancreas, Brunner's glands, and liver in the postnatal ontogeny. Numerous data on the stabilization of age-related structural and functional changes in the internal organs of mammals during puberty are also given in the works of domestic and foreign researchers. However, the peculiarities of the structure and function of the thin layer during artificial feeding at the time of puberty have been studied only fragmentarily. They need a comprehensive study.

It is known that one of the fundamental properties of any biological system, including the digestive system, is the ability to adapt. Adaptation is considered as the most important characteristic of normal functioning of all levels of organization of living matter. Taking this into account, the task is to study its mechanism in the thin layer under natural and artificial feeding.

Thus, despite the significant success of gastroenterology, the questions of its functional morphology in different periods of postnatal ontogenesis remain unsolved. In particular, there is not a sufficiently complete understanding of the participation of the structural organ in the regulation of homeostasis of the internal environment in newborn mammals, the issues of rapid (functional) and slow age adaptations, topographical organization of the crypt-villus system are considered to be insufficiently clarified. Knowledge of these issues is important for the regularities of age adaptation of mammals, determination of ability to adapt to functional loads, prevention of diseases.

CHAPTER II. RESULT OF THE RESEARCH.

2.1 Features of the structure of the mucous membrane of the small intestine of puppies during natural feeding.

At birth, the thin penis has a length of 68, 6±4.1 cm and a diameter of 3.7±0.1, 3.0±0.2 mm, respectively, in the iliac and pelvic sections. Its wall, consisting of mucosa, submucosa, muscular and serous membranes, is relatively thin and decreases in the distal direction. In the mucous membrane there are few villi, which are at different stages of formation (Fig. 1.) and short cylindrical crypts. The linear parameters of the formed villi can vary from 100 to 700 μm and are 602.1±25.2 and 403.1±30.4 μm, respectively, in the thoracic and iliac regions. It should be noted that the height of the villi decreases towards the iliac crest and they become more variable. This testifies to the greater expression of histogenetic processes in the distal part of the organ.

The depth of the crypt also clearly decreases towards the iliac crest: from 60.0±9.8 in the left to 41.2±10.1 μm in the iliac. The crypt is separated by significant layers of loose connective tissue.

The surface of the villi is lined with a single-layered high-prismatic striated epithelium with distinct polarity (Fig. 2). The oval nucleus is elongated and located in the basal part of the cell. The apical surface has an intensely eosinophilic brush layer. At the beginning of feeding, the ultranuclear cytoplasm is uniform, homogeneous, slightly brightened above the upper pole. At the base of the villi, the cytoplasm of enterocytes is more basophilic. After the beginning of natural feeding, the cytoplasm of striated enterocytes of the villi over the nucleus is vacuolated. The degree of its expression increases from the base to the apex of the villi (Fig. 3a, b). This is observed up to 3 weeks after birth. When newborn puppies are starved for more than 6 hours, vacuolization gradually decreases and the cytoplasm of striated enterocytes becomes homogeneous, homogeneously eosinophilic.

In the ileum, vacuolation of the supranuclear cytoplasm of striated enterocytes is observed for a longer time.

On the first day after the birth of puppies, 11.5±1.4% and 12.6±1.6% of typical goblet cells are found between the lamellar enterocytes on the surface of the villi. The secretion is intensively SIK-positive (Fig. 4.); The Hale reaction is moderate. The density of the secretion and the intensity of the goblet reaction of the goblet cells are more significant in the iliac crest.

The incompleteness of structural and functional reconstructions in the mucous membrane is the reason that the mucosal index (ratio of linear parameters of villi and crypts) is 9.6 and 9.3 on average in the lower and lower part of the small intestine. The ratio of enterocytes in the crypt-villus system is on average 6 and 7, respectively

Fig. 1 Villi at different stages of formation in the mucous membrane of the breast of newborn puppies before feeding Chem. - eosin. Increase in 8x10

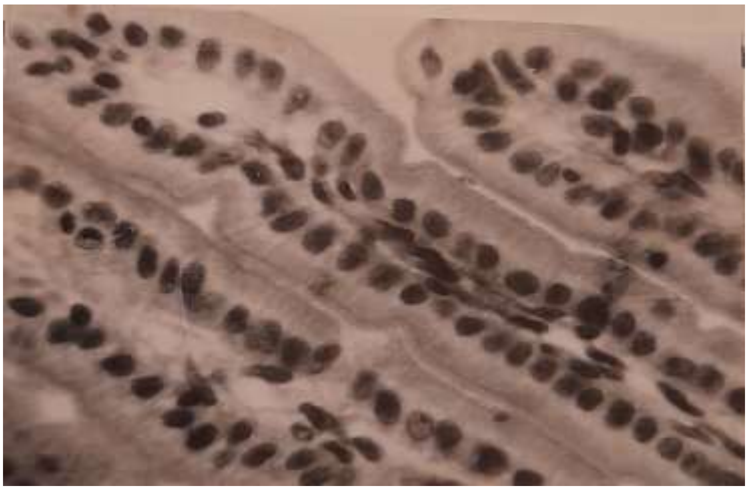


Fig. 2 Single-layered high-prismatic lamellar epithelium on the surface of the formed villi of the breast of newborn puppies before feeding. Hematoxylin - eosin. Magnification: 10x20

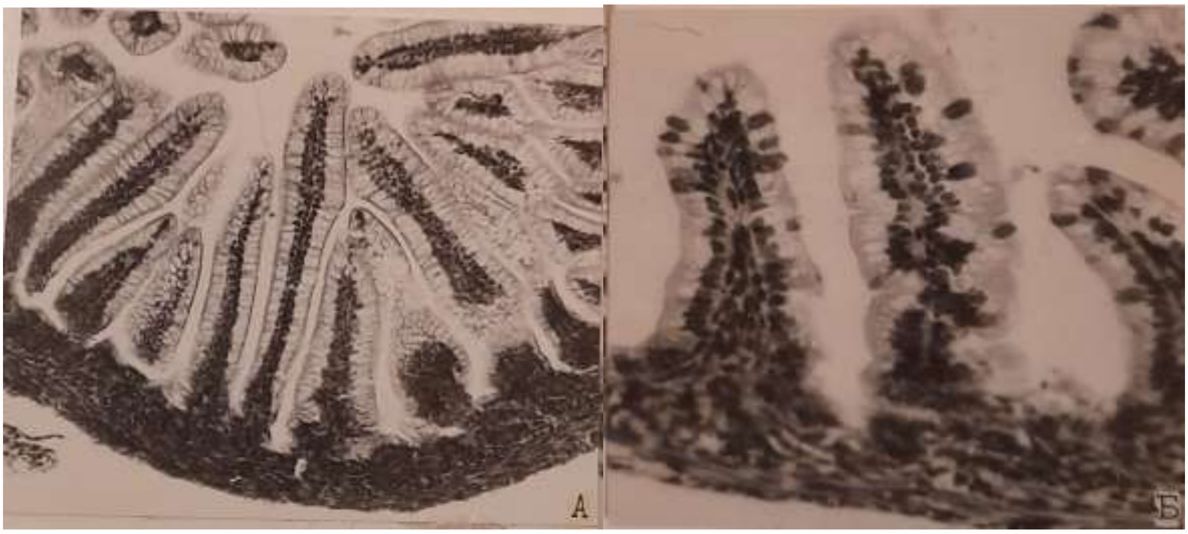


Fig. 3. Vacuolation of the supranuclear cytoplasm of the striated enterocytes of the villi of the calf /A/ and the iliac /B/ pouch of newborn puppies after the start of natural feeding. Hematoxylin-eosin. Magnification: 8x10

Fig. 4 PAS-positive reaction of the secretion of individual goblet cells in the villi of the ileum of 1-day-old newborn puppies after natural feeding. Hematoxylin - PAS reaction. Magnification: 20x10.

The crypt is lined with a single-layered low-prismatic epithelium (20.1±1.7 μm on the surface of the villi, 15.4±0.2 μm in the middle third of the crypt). Below the crypt, their number is 21.1 ± 1.7 and 15.1 ± 3.5 in the studied areas. The number of epithelial cells in the cross-section and sections is equal to 20.1±0.5 and 17.4±0.2. Their nuclei are round in shape and are located in the middle part of the cells. Cytoplasm is homogeneous, basophilic. The brush border is almost non-contouring. Goblet cells are not detected in the crypts. Mitotically dividing enterocytes are frequently found throughout the crypts. Between the epithelial cell crypt and villi thin late lymphocytes or other infiltrating blood cells (connective tissue) are practically not detected. The stroma of the villi has few capillaries, blast connective tissue cells. Smooth muscle cells are single, elongated longitudinal villi. Under the crypts, they are embedded in the still poorly developed muscular plate of the mucous membrane. The submucosa consists of loose connective tissue, where vessels of various calibers and nerve elements are distinguished. In the muscular shell, the inner circular layer is relatively more developed than the outer longitudinal layer. Consequently, already at the birth of puppies there is a proximo-distal gradient formation and formation of the structural-functional unit system crypt-villus, the number of enterocytes and other structures. These data also indicate a decrease in the distal direction, the suction surface is thin.

Table 1

Morphometric parameters of the small intestinal mucosa of puppies after birth with natural feeding. /M±m, n=3/.

Parameters	Jejunum	Ileum
Height of villi, µm	602.1±25.2	403.1±30.4
Crypt depth, µm	60.0±9.8	41.2±10.1
Intestinal mucosa index	9.6	9.3
Number of enterocytes on one side of the longitudinal section:		
Villi	132.1±5.4	91.2±12.4
Crypt	21.1±1.7	15.1±3.5
Number of enterocytes in the cross section of the crypts	20.1±0.5	17.4±0.2
Height of enterocytes of the middle third:		
Villi, µm	22.1±0.2	25.1±0.2
Crypt, µm	15.4±0.2	15.1±0.2
Relative number of goblet cells:		
On the villi /%/	11.5±1.4	12.6±1.6
On the crypt /%/	—	—
Mitotic index /%/	38.1±1.6	36.1±2.0

Both in the first and in the following days after the birth of puppies, in the mucous membrane of the small intestine, separate stages of the laying of villi and crypts, intensive increase of structural and functional units are observed. Electron-microscopically, enterocytes have fine villi on the luminal surface, tightly adhering microvilli with a length of about 1.0 and a width of 0.1 μm; the distance between them is 0.01 μm (Fig. 5). The core of microvilli is formed by longitudinally oriented thin fibrils, freely ending in the apical part of the cytoplasm. From the plasmolemma of the microvilli, the thinnest filamentous structures that form the glycocalyx move outward. However, it is less expressed than in adult mammals. A homogeneous structureless zone 0.5-1.0 μm wide is revealed at the base of the microvilli of the enterocytes of the microvilli of the stomach or ileum, where single endocytic vesicles and shallow indentations of the plasmolemma are found (Fig. 6). The terminal network, which in sexually mature mammals is a specialized structure of the apical part of the cytoplasm of enterocytes, is not detected in the cells of newborns. Mitochondria of different shapes and sizes are found in the supranuclear cytoplasm of striated enterocytes of the stomach or ileal cell. The matrix is of medium electron density, with a moderate amount of crystals.

Fig. 5 High-prismatic lamellar enterocytes and goblet cells of thin villi of newborn puppies before feeding. Magnification: in 7500

Fig. 6 Single endocytic vesicles and thickening of the cytolemma at the base of microvilli of ciliated enterocytes of the villi of the stomach of newborn kittens before feeding. Magnification: in 17500

Profiles of the granular endoplasmic reticulum are moderately developed, rarely contact mitochondria, and are located around. Profiles of smooth endoplasmic reticulum are few. The Golgi complex is located above the upper pole of the nucleus, and consists of flattened short cisternae and single vesicles (Fig. 7). After feeding, it is sharply hyperplastic and consists of enlarged cisterns, vacuoles; vesicle malo. Mitochondria, free ribosomes and polysomes in enterocytes of villi in moderate amounts are found everywhere (Fig. 8). Round small mitochondria, short profiles of granular reticulum, relatively few free ribosomes can be seen under the nucleus.

Nuclei of absorbent cells are oval in shape, located in the basal part. The nuclear envelope is of normal structure, occasionally forming shallow intussusceptions. Nuclear pores in moderate quantity (Fig. 9). Karyoplasm of moderate electron density, formed mainly by euchromatin. One or two electron-dense cores are located eccentrically.

The lateral plasmolemma of lamellar enterocytes forms a connective complex, deep interdigitation and desmosomes (Fig. 10). The connective complex is marked in the apical part, below the level of the base of the cells there are numerous interdigitations of considerable length. Desmosomes are observed only at the level of the upper third of the cells. Goblet cells of thin villi of newborn puppies have a typical shape, as a rule, they contain numerous secretory granules of moderate density in the supranuclear region. The core is cut to the core

Fig. 7 Flattened short cisternae and few vesicles of the Golgi complex of the villi of lamellar enterocytes of late feeding puppies. Magnification: in 17500

Fig. 8 Mitochondria, ribosomes, and polysomes of the supranuclear cytoplasm of ciliated enterocytes of the villi of the stomach of newborn puppies before feeding. Magnification: in 12000

Fig. 9 Oval-shaped nuclei of striated enterocytes of the villi of the breast of newborn puppies before feeding. Magnification: in 12500

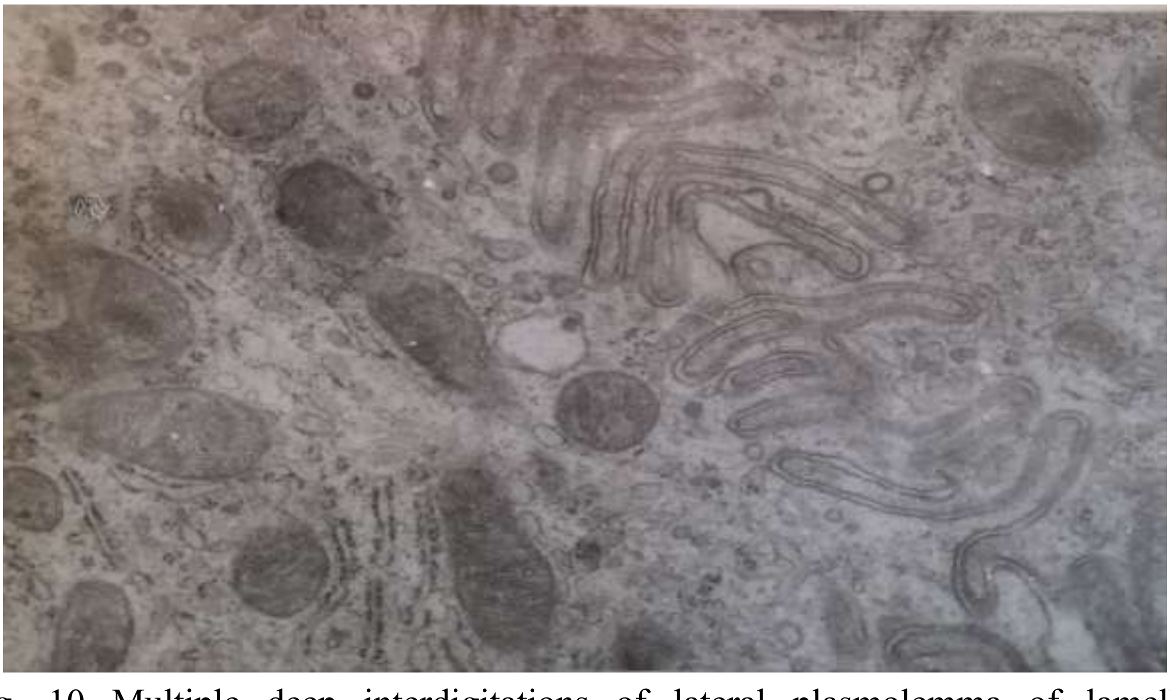


Fig. 10 Multiple deep interdigitations of lateral plasmolemma of lamellar enterocytes of villi of breast milk of newborn puppies before feeding. Magnification: in 15000

cells, oval in shape. A granular endoplasmic reticulum concentrically surrounds the nucleus. The Golgi complex is located above the nucleus, occupies a significant area, consists of numerous tanks, vacuoles, vesicles (Fig. 11).

Epithelial cells are crypts of low-prismatic form, with single short microvilli (Fig. 12). The glycocalyx is visible on the surface of the membrane. Below the apical plasmolemma, the terminal network of microvilli at the base of the lower level is absent; endocytic vesicles or other formations are not detected. Cytoplasm of enterocytes is more electron-dense than cells of villi due to significant content of free ribosomes. Mitochondria are relatively small, they are small, with a moderately dense matrix, and are located, as a rule, above the nucleus. Profiles of the granular endoplasmic reticulum unit. The Golgi complex consists of single short cisternae and vesicles. The nucleus is relatively large and occupies the lower half of the cell. Nucleoplasm is of moderate density and mainly consists of euchromatin. Nuclei (one or two) are electron dense, located eccentrically. Among these cells, a rare form of mitosis is seen (Fig. 13). Lateral plasmolemma of epithelial cells forms crypt complex junctions.

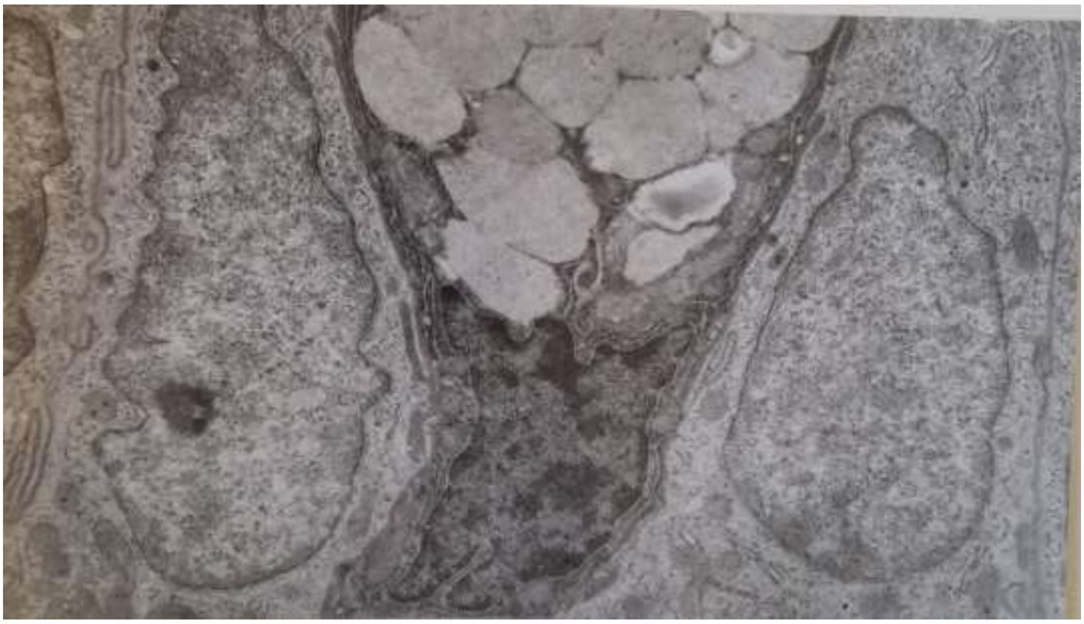


Fig. 11 The Golgi complex over the nucleus of goblet cells fills the villi of late feeding newborn puppies. Magnification: in 15000

Fig. 12 Epitheliocytes of the low-prismatic form of the crypt of late-term newborn puppies. Magnification: 7500

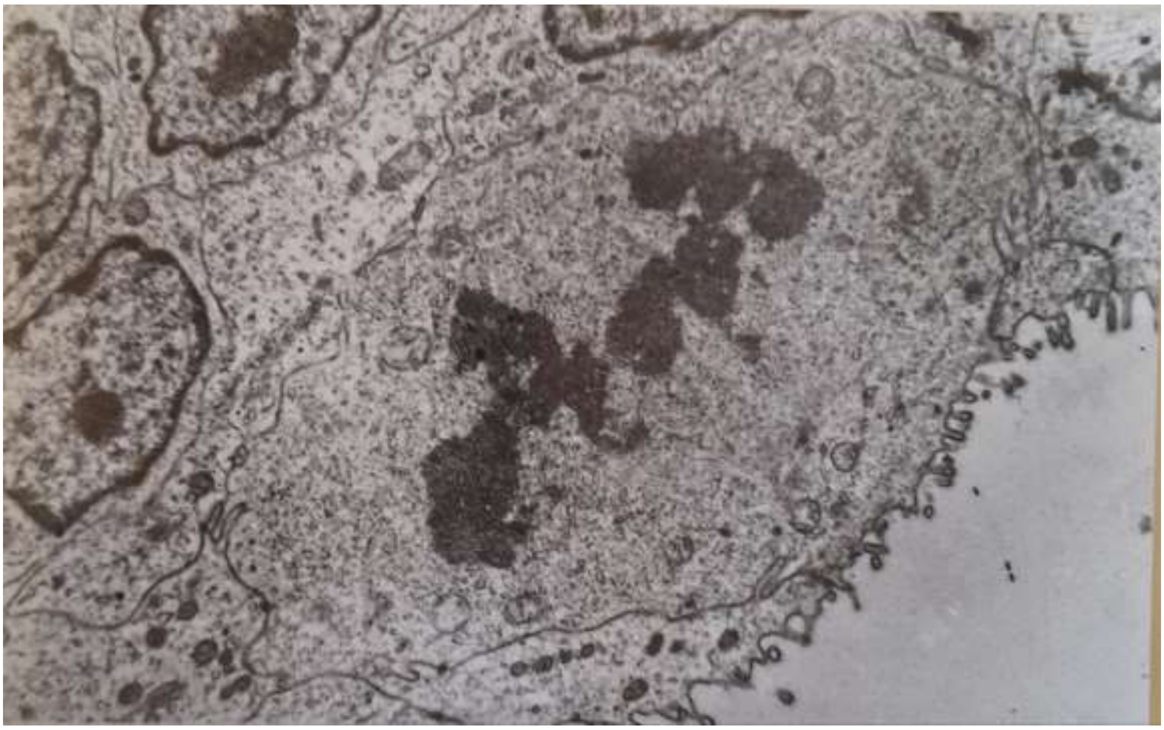


Fig. 13 Mitotically dividing epithelial cells in the crypts of late-term newborn puppies. Magnification: 7500

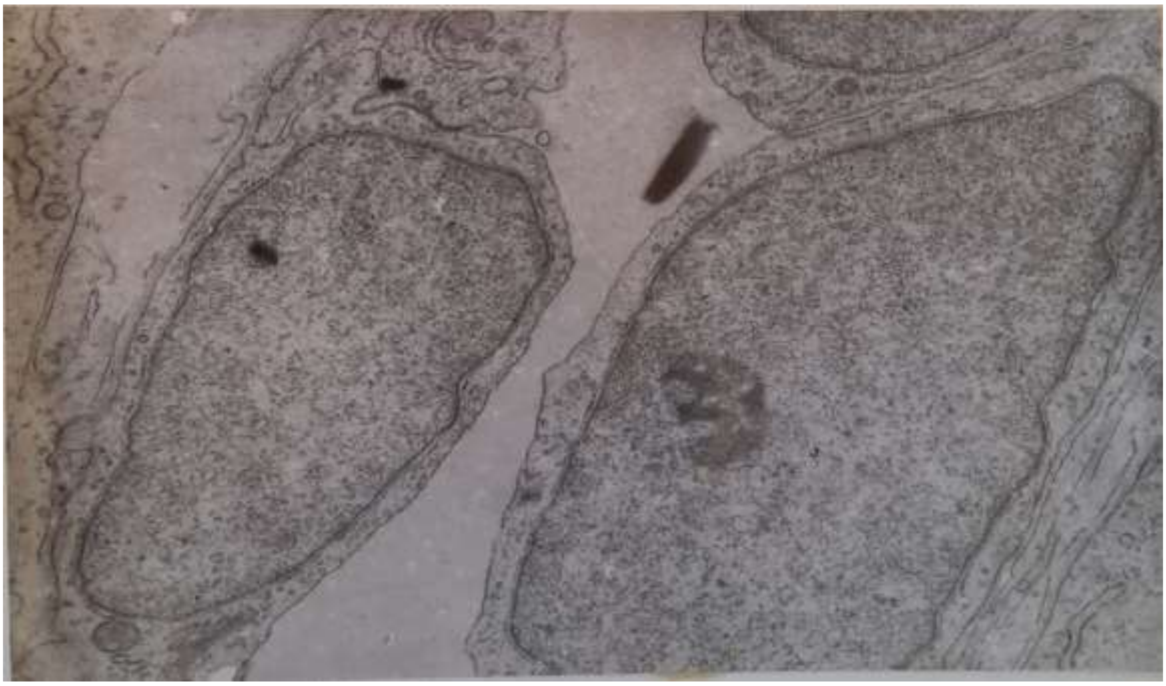


Fig. 14 Blood capillaries stroma of villi with 2-3 flattened endotheliocytes. Magnification: 15000

Capillaries, blast cells, and fibroblasts extending along the epithelial layer are visible in the stroma of villi and crypts. Blood capillaries, located under the epithelium of the villi, have a small diameter, lined by 2-3 flattened endothelial cells (Fig. 14). The lumen of some capillaries is barely visible; apparently, they represent themselves neoplastic vessels. Single nerve fibers and nerve endings are found near the crypt vessels and villi, between the differentiating cellular stroma.

Thus, at birth, all shell-thin puppies are morphologically distinct. However, the process of morphogenesis, which began before birth, is observed after birth and spreads in the distal direction. Enterocytes of villi and crypts are topographically functionally heterogeneous: they can perform absorption, secretory and generative functions, respectively. The presence of figures of mitosis among the cells of the crypt indicates spatial separation already at the birth of the processes of proliferation and differentiation, functioning of enterocytes in the crypt-villus system. Absence of own lamellar mucous membrane along thin layer of differentiated cells (plasmacytes, lymphocytes, macrophages, white cells, etc.) indicates immaturity of one of its important functions - immune.

Intensive formative processes that occur in the thin layer after birth cause an increase in structural and functional units on the surface of the mucous membrane, especially in the iliac layer, less in the 12-tip and left layer. Accordingly, the number of epithelial cells increases, the absorbent surface of the organ increases.

3 days after birth, intensive formation of villi and crypts, thickening of all membranes is observed photooptically throughout the thin layer. New education villi are marked between the previously formed ones and have either a short finger-like or a conical shape. The large surface, like a villi, is lined with a single layer of cylindrical striated enterocytes, the cytoplasm of which is vacuolated (Fig. 15).

Neoformation of the crypt occurs as a result of adhesion of the connective tissue of the own plate to the base of the forming crypts, or at the base of the villi, where the epithelium adheres to the underlying tissue. The rate of new formation of structural and functional units is the same as at the birth of animals.

Electron microscopy reveals a significant number of endocytic invaginations of the plasmolemma, tubulo-vesicular structures, the content of which is of low electron density, at the base of the microvilli of the striated enterocytes of the villi of the stomach. The Golgi complex is moderately developed: along with vacuoles, numerous vesicles, expanded cisternae are noted (Fig. 16). Chylomicron-like particles are rarely found in their cavities. In identical cells of the iliac crest, endocytic formations, tubulo-vesicular structures are constantly revealed from the beginning of natural feeding to the transition to definitive nutrition. A number of tubulo-vesicular structures in the apical part of striated enterocytes directly interact with a large supranuclear body surrounded by a smooth membrane.

Fig. 15. Vacuolization of the cytoplasm of striated enterocytes, formed villi, is late. Hematoxylin. - eosin. Magnification: in 20x10

Fig. 16 Enlarged cisternae, vesicles, and vacuoles of the Golgi complex in striated enterocytes of villous mats of late control 3-day-old puppies. Magnification: in 12000

The structure of the supranuclear body is heterogeneous: it contains substances of different electron density, sometimes it is attached to small lysosome-like formations (Fig. 17). Photo-optical this manifests as vacuolization of enterocyte villi. After 7 days, the structure of the mucous membrane of the small intestine of puppies is almost similar to that of 3-day-old animals. It should only be noted the further deepening of the crypt, the increase of structural and functional units. New formation of crypts and villi is more intense in the distal part of the small intestine. A gradual thickening of all layers due to new formation of blood vessels, increase in the mass of connective and muscle tissues is noted along the small intestine. Electron microscopic enterocytes of villi and crypts are similar to those of 1-3 day old puppies. As in previous studies, endocytic formations at the base of microvilli and the apical part of cells are clearly visible in striated enterocytes (Fig. 18). In the supranuclear zone, ultrastructural signs of the transport of absorbed ingredients of breast milk are noted. In the lower third of the crypt, low-prismatic enterocytes are located at various stages of the interphase cell cycle. In the upper third, high differentiation into absorptive and goblet cells is observed. 2 weeks after the birth of the puppies, all the membranes thicken evenly. The mucous membrane consists of tall finger-like villi with pronounced folds on the lateral surfaces (Fig. 19). The height of the lower leg is 623.1±21.3 μm, and the iliac height is 501.4±25.1 μm (Table 2). During this period of research, the formative process also continues: short and medium-sized finger-shaped villi are observed (Fig. 20 a, b), the crypts are separated by connective tissue growing from below.

Fig. 17 A large supranuclear body in the cytoplasm of striated enterocytes of iliac villi of 3-day-old puppies. Natural feeding. Magnification: 22500

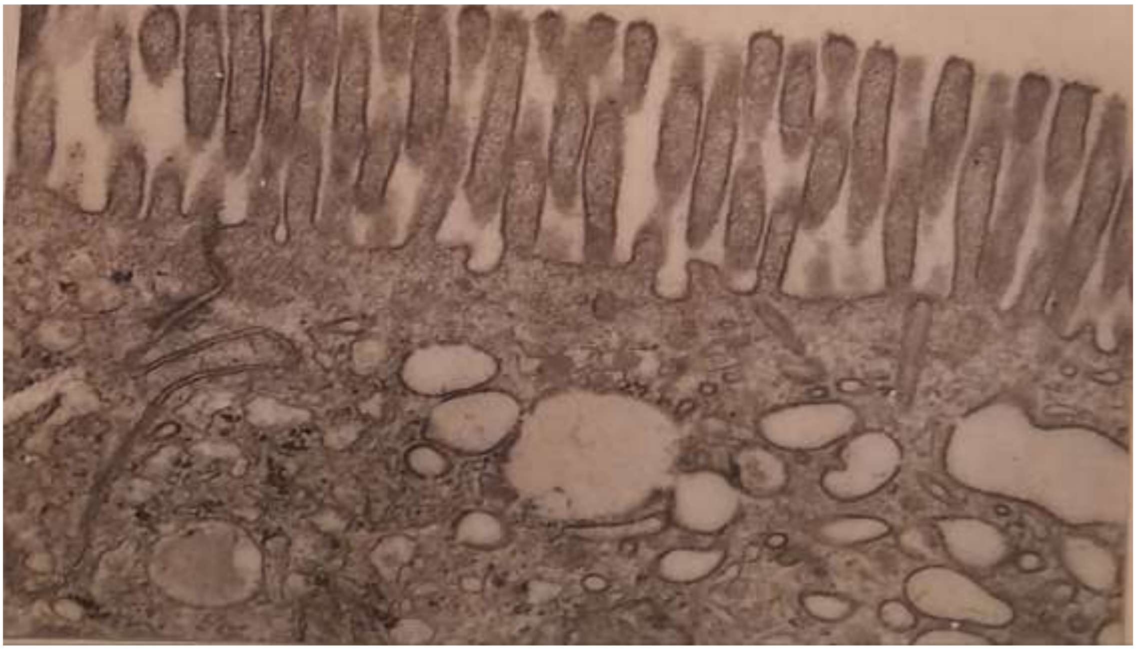


Fig. 18 Tuburo-vesicular endocytic formations at the base of microvilli of striated enterocytes of villi of 7-day-old control puppies. Magnification: 30000

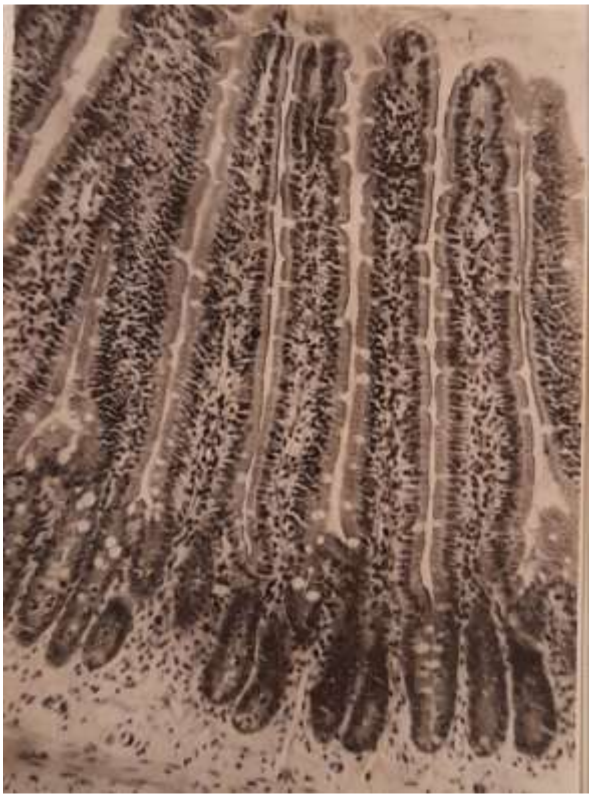
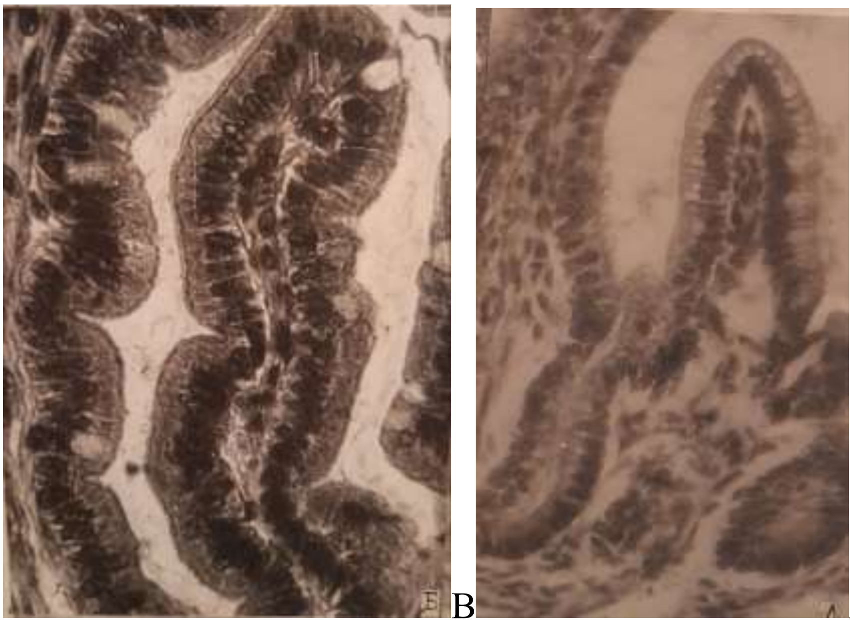


Fig. 19 Long finger-shaped villi without protruding folds on the lateral surfaces in the mucous membrane of a 14-day-old puppy. Hematoxylin - eosin. Magnification: 8x10



B A

Fig. 20 Short / A / and medium size / B / developing villi of 2-week-old puppies. Hematoxylin. - eosin. Magnification: 20x10

Tapered enterocytes of villi have a high-prismatic shape and are arranged in one row on a thin basement membrane. The luminal surface is intensely eosinophilic throughout the villi and partially on cells forming crypts. Cytoplasm of enterocytes of villi is vacuolated, the nucleus is in the basal part. In the middle third, the height of villi of epithelial cells is 25.0±0.2; 25.0±0.1, respectively, in the upper and lower back, t. e. decreases towards the distal part of the organ. On the surface of the villi, between the lamellar enterocytes, typical goblet-shaped cells (Fig. 21) are noted, intensively staining neutral and acidic glycosaminoglycans. The number increases towards the iliac crest. Crypts increase in number and length by 2 weeks of postnatal life. As a result, they have a straight and cylindrical shape, are located close to each other (Fig. 23), have a depth of 229.2±7.4 and 183.2±12.4 µm, respectively, in the lower and lower parts (P<0.001). Compared to one-day-old puppies, the depth of the crypt increased in the studied sections of the thin layer by an average of 2.5 and 4 times.

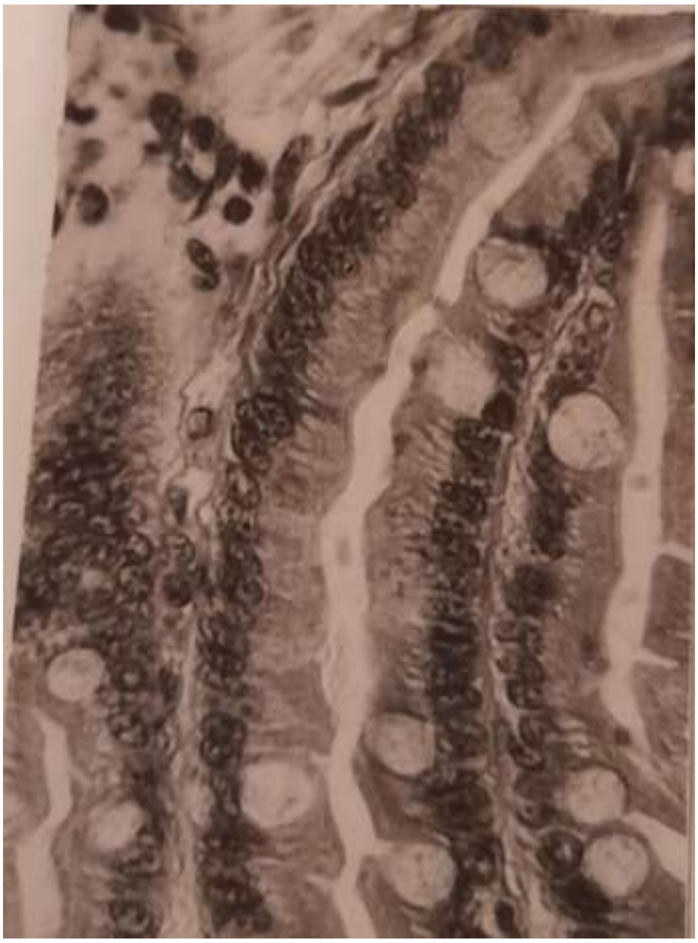


Fig. 21 typical goblet-shaped cells on the surface of the villi in the evening of 2-week-old puppies. Hematoxylin. - eosin. Magnification: 20x10

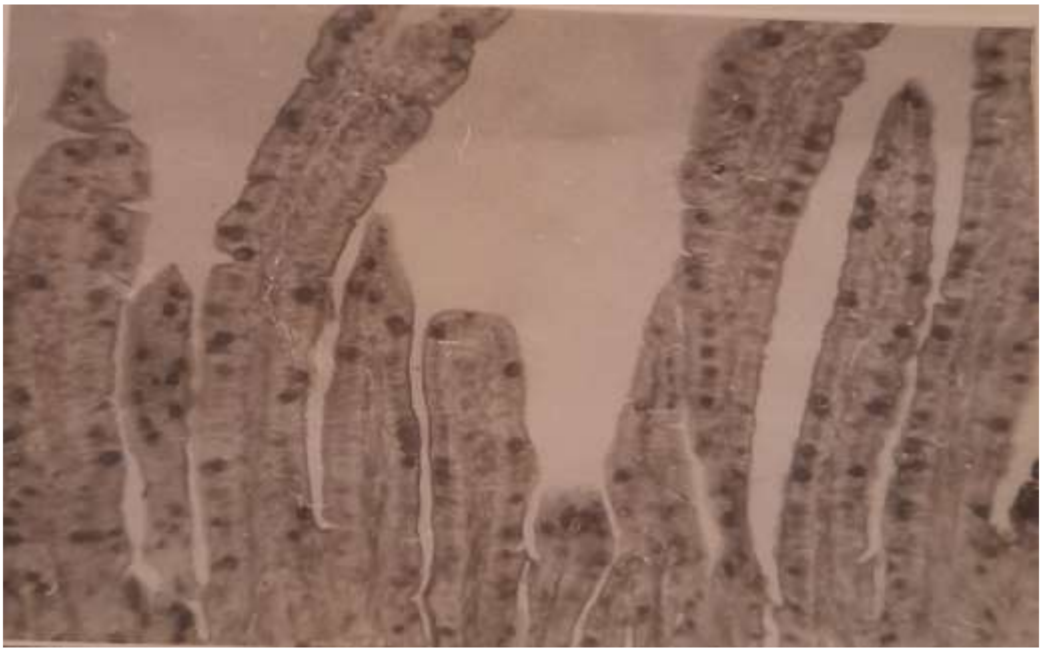


Fig. 22 Relatively greater number of goblet cells on the villi surface of the iliac crest of 2-week-old puppies. CHIC-reaction-hematoxylin. Magnification: 10x10

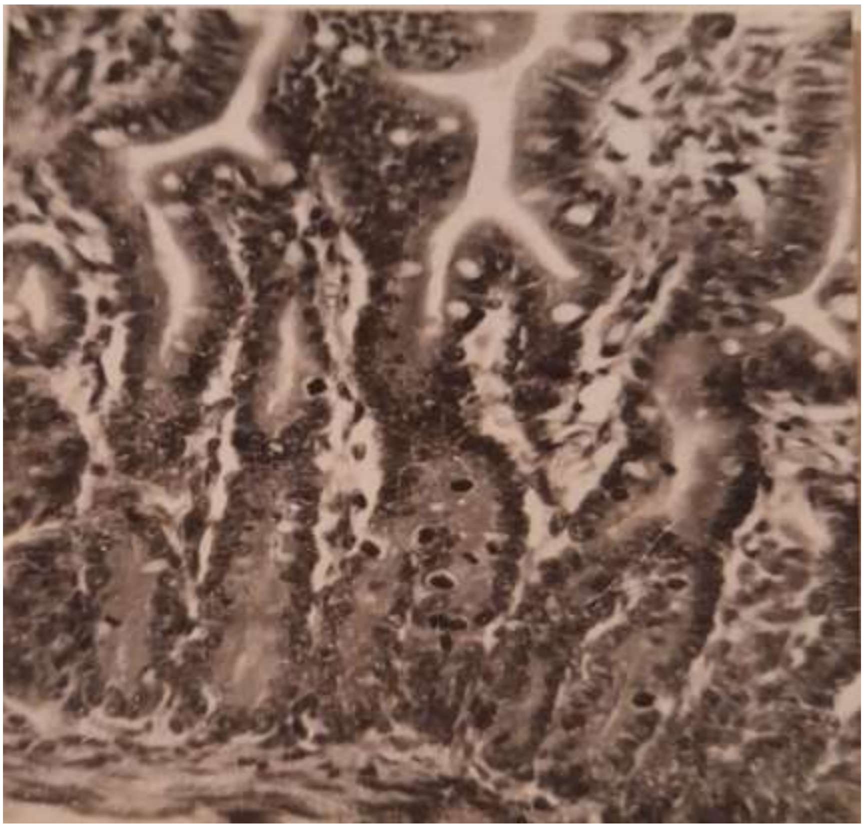


Fig. 23 Cylindrical crypts of 2-week-old puppies. Hematoxylin - eosin. Magnification: 10x10

Fig. 24 PAS-positive material in the goblet cells of the crypts of the jejunum in 2-week-old puppies. PAS reaction - hematoxylin. Magnification: 10x10.

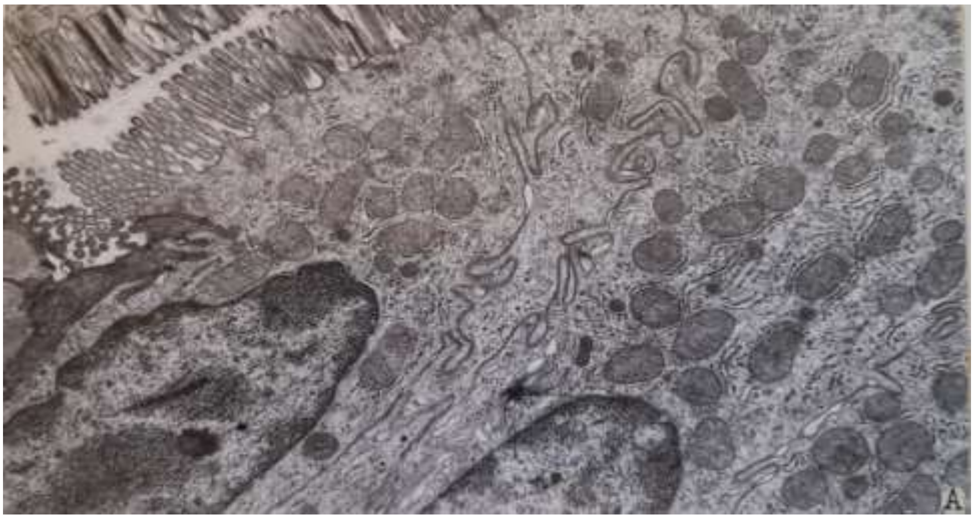
The number of cells on the surface increased accordingly. From the 3rd day after birth, goblet cells with intensely Hale-positive secretion are identified in the upper third of the crypts; the PAS reaction is moderate (Fig. 24). Electron microscopically, 14 days after birth, the epithelial cells of the villi and crypt small intestine have almost the same structure as in 1-3-day-old puppies (Fig. 25 a, b).

Table 2

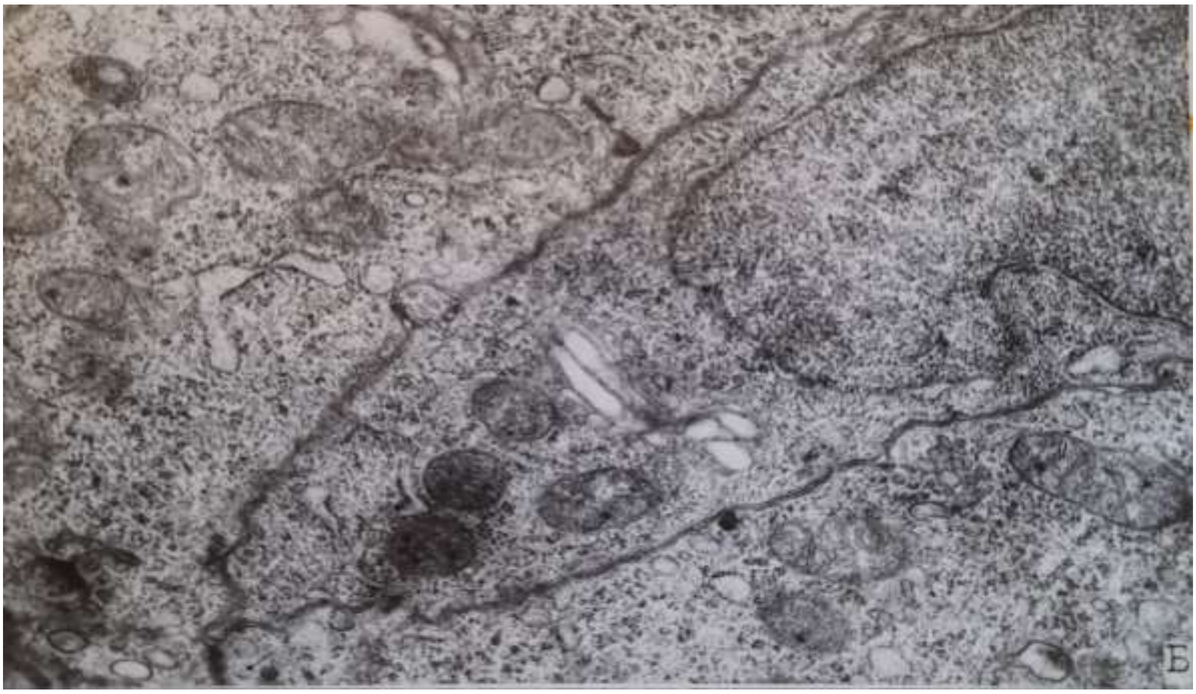
Morphometric parameters (mucous membrane) of the small intestine of puppies 14 days after birth with natural and artificial feeding. /M±m, n=3/.

Parameters	Jejunum	Ileum
Height of villi, µm.	623.±21.3 601.6±35.7	501.4±25.1 490.8±42.9
Crypt depth, µm	229.2±7.4 203.1±11.2	183.2±12.4 162.4±23.1
Number of enterocytes on one side of the longitudinal section:		
Villi	146.2±4.4 74.1±7.8	115.2±10.1 70.3±6.9
Crypt	60.1±2.5 31.6±1.7	47.2±2.4 30.6±2.1
Number of enterocytes in the cross section of the crypts	20.1±0.2 20.4±0.3	20.2±0.2 20.3±0.3
Height of enterocytes of the middle third:		
Villi, µm	25.1±0.2 23.2±0.2	25.0±0.1 22.7±0.2
Crypt, µm	15.3±0.2 15.1±0.2	15.5±0.1 15.4±0.2
Relative number of goblet cells:		
On the villi /%/	15.1±1.1 19.8±1.2	18.9±1.3 24.3±1.9
On the crypt /%/	11.4±1.7 13.5±1.0	7.0±2.0 14.2±2.7
Mitotic index /%/	11.6±1.5 15.7±2.1	13.1±1.8 15.1±1.9

Note: in the numerator – values for natural feeding, in the denominator - for artificial feeding.



A



B

Fig. 25 Ultrastructure of epithelial cells of villi (A) and crypt (B) of control 2-week-old puppies in the interdigestive phase during natural feeding. Magnification: 12000

The index of the mucous membrane in the upper and lower part of the pelvis is 2.6, respectively; 2.7. the height of enterocytes in the middle third of the crypt and their number on the cross section of the crypt almost did not change during two weeks of development of puppies (Table 2). C is determined 3 days after birth in the upper third of the crypt.

The stroma of the villi and the crypt consists of loose fibrous connective tissue, in which there are numerous blast cells, formed and forming capillaries, and nerve endings (Fig. 26).

By the end of the second week of life, the puppies have a total length of 94.3±4.6 cm. the diameter and thickness of its membranes gradually decrease in the distal direction (Table 2). The thickness of the mucous membrane, in particular, decreases by an average of 220 µm: from 925 µm in the thigh to 708 µm in the iliac crest.

Thus, within two weeks after birth, puppies undergo intense neoplasia and growth of villi and crypts. Histogenesis of structural and functional units is observed along the entire organ. As well as at birth, a number of morphological parameters in the thoracic and iliac regions are significantly different, indicating the existence of a proximo-distal gradient along the fallopian tube.

Apparently, the physical characteristics are genetically determined. If in natural conditions during 4 weeks of life puppies are fed only mother's milk, then after 1 month they switch to final nutrition. The total length of the slender body reaches 122.6±5.7 cm, diameter - 7.3±0.7 and 6.8±0.4 mm on average in the lower and lower parts of the body (Table 3). With uniform thickening of all membranes of the organ, the villi in the mucous membrane have a length of 645.3±11.5 and 558.0±15.5 µm, respectively, in the thoracic and pelvic sections. In the lower part, it is finger-shaped, thinly leaf-shaped with intussusception along the lateral surface.

The number of newly formed villi is significantly less than in the previous study periods. In the iliac crest, the villi are more often leaf-shaped. The crypt has a cylindrical shape with a thin longitudinal axis, the depth of which is 266.7±6.1 and 227.3±9.8 µm, respectively, in the lower and iliac sections (Table 3).

As a result, the index becomes equal to 2.4 along the entire thin layer of the mucosa. In view of the fact that for 2 weeks, the crypts of the iliac compartment have deepened, the number of enterocytes on the longitudinal section and the cell pool in them increases accordingly.

The average late mitotic index along the thin layer is 20.8±1.3%. It should be noted that not only the mucosal index approaches that of adult animals, but also the crypts complete the topographic establishment. In its lower and middle thirds, mitotically dividing cells are located, and in the upper part, they differentiate into absorptive, goblet and endocrine cells.

Electron microscopic signs of cells are shown very distinctly. Enterocytes, covering the villi, are highly prismatic in shape. The large brush-like layer is intensely eosinophilic, the cytoplasm is homogeneous, oxyphilic, slightly brightened above the nucleus.

Table 3

Morphometric parameters (mucous membrane) of the small intestine of puppies 1 month after birth with natural and artificial feeding. /M±m, n=3/.

Parameters	Jejunum	Ileum
Height of villi, µm.	645.3±11.5 332.1±17.3	558.0±15.5 282.0±10.1
Crypt depth, µm	266.7±6.1 285.1±8.0	227.3±9.8 302.8±8.0
Intestinal mucosa index	2.4 1.2	2.4 1.0
Number of enterocytes on one side of the longitudinal section:		
Villi	140.3±6.4 76.7±2.5	129.3±5.1 61.3±3.2
Crypt	65.1±2.7 51.2±1.9	56.2±2.1 41.1±1.2
Number of enterocytes in the cross section of the crypts	20.8±0.2 24.1±0.5	20.6±0.2 20.1±0.3
Height of enterocytes of the middle third:		
Villi, µm	25.4±0.1 23.0±0.2	25.3±0.2 22.1±0.1
Crypt, µm	15.8±0.1 15.0±0.1	15.9±0.2 14.7±0.2
Relative number of goblet cells:		
On the villi /%/	18.4±1.3 26.5±0.1	24.4±1.3 28.6±1.4
On the crypt /%/	17.9±1.7 25.8±0.8	32.6±2.1 37.1±2.4
Mitotic index /%/	20.8±1.3 26.1±1.2	20.4±1.4 27.7±1.3

Note: the numerator shows the values for natural feeding, the denominator shows the values for artificial feeding.

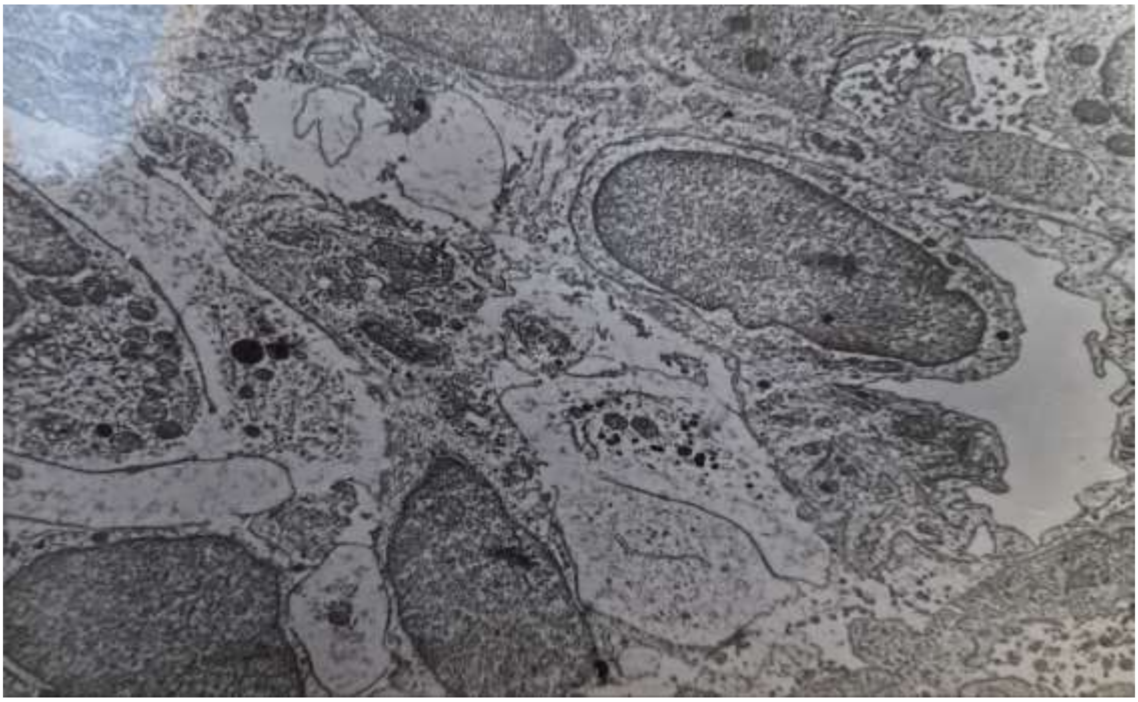


Fig. 26 Blast cells and capillary stroma lining the villi of 2-week-old control puppies. Magnification: 7500

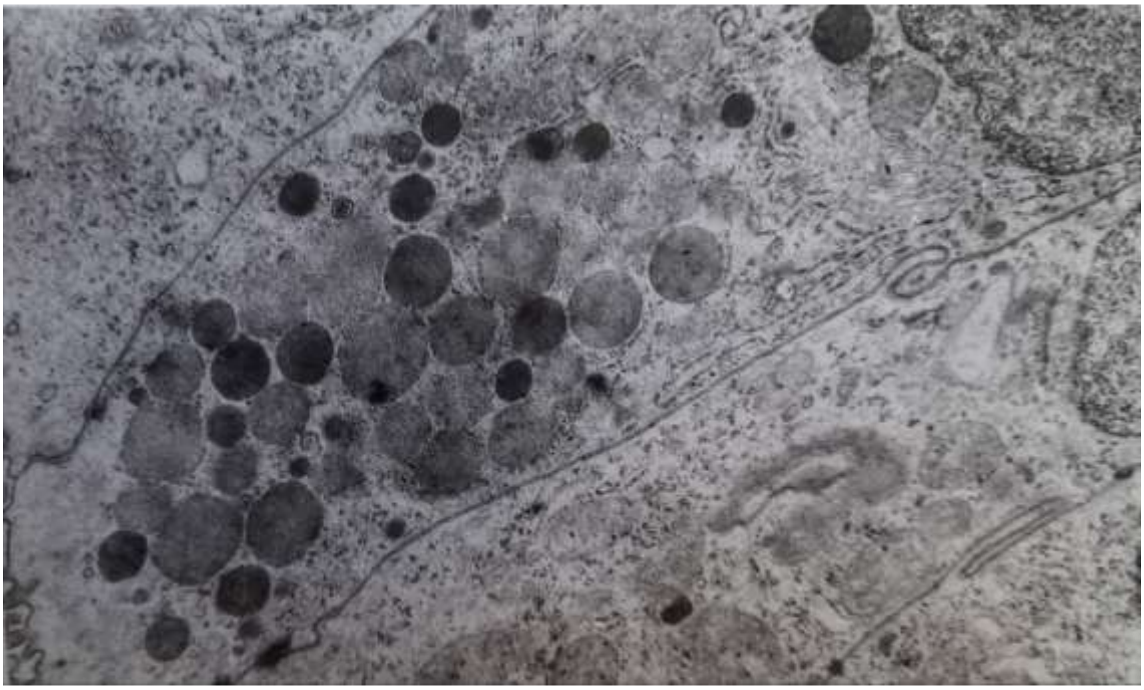


Fig. 27 Differentiation of epithelial cells into absorptive and goblet cells in the upper third of the thin crypt of late control 1-month-old puppies. Magnification: 10500

Oval-shaped nuclei, intensely basophilic, are located in the basal part of the cells. Electron-microscopically, a brush-like layer of enterocytes of villi form typical microvilli with a well-developed glycocalyx. Longitudinally oriented fibrils inside the microvilli intertwine with fibrils located transversely in the area of their base, in the apical cytoplasm. The apical plasmolemma forms endocytic vesicles between the bases of microvilli. Organelles of striated enterocytes are located below the well-developed terminal network. In the period of the so-called relative functional rest, 6 hours after the last feeding, the profile of the granular endoplasmic reticulum has a moderate extension in the supranuclear cytoplasm (Fig. 28). The profiles of the smooth reticulum are few in number and are found in the apical part of the cells. Mitochondria of various shapes, typical in structure, are located in the supranuclear cytoplasm. Under the nucleus, they often have a rounded shape and interact with the profiles of the reticulum. The Golgi complex is a nucleus above the upper pole, there are many vacuoles, the cisterns are not expanded, and there are moderate amounts of vesicles (Fig. 29). Free ribosomes and polysomes are ubiquitous. Occasionally, in the supranuclear cytoplasm, there are individual small electron-dense lysosome-like formations that have a specific localization. The number and sometimes the size may increase after feeding, apparently due to the absorption of some insufficiently broken down substances (Fig. 30).

Fig. 28 Moderate elongation of the Golgi membrane complex, profiles of the granular endoplasmic reticulum, and their relationship with mitochondria in the supranuclear cytoplasm of striated enterocytes of breast villi of late control puppies of 1 month of age. Magnification: 17500

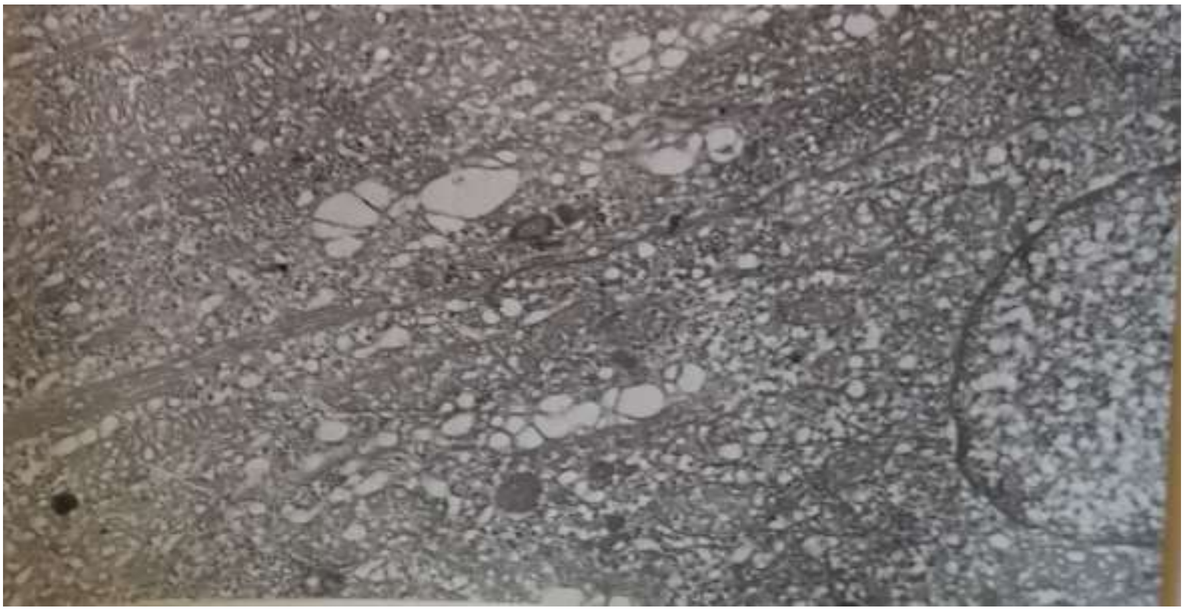


Fig. 29 moderately developed complex of Golgi lamellae of enterocyte villi of 1-month-old control puppies. Magnification: 12500

The nuclei of the cells are oval in shape and are visible in their basal part. One or two electron-dense nuclei are located eccentrically, with the ratio of euchromatin to heterochromatin being approximately the same. Heterochromatin is concentrated in the peripheral nucleus. Nuclear pores are moderate. The outer nuclear membrane contacts the profiles of the granular endoplasmic reticulum in some areas. The lateral plasmolemma of the epithelial cells of the villi forms a connective complex, numerous interdigitations of moderate character, desmosomes. In the middle and lower third of the crypt epithelial cells are low-prismatic in shape with a relatively large centrally located round nucleus. The nucleoplasm consists mainly of euchromatin and has many pores. In the cytoplasm, the organelles are small, and profiles of the granular endoplasmic reticulum are practically not visible. Golgi complex is represented by single short cisternae, vesicles, vacuoles are absent. Mitochondria are single, small, round in shape, distributed evenly throughout the cytoplasm. There are many free ribosomes and they are found everywhere. On the apical surface, the plasmolemma forms single short microvilli. Along the lateral surface, the plasmolemma forms complex junctions and deep intussusceptions.

In the upper third of the crypt, epithelial cells differentiate, acquiring characteristics of absorbent or secretory mucus-forming cells (Fig. 31). This is accompanied by a progressive increase in the length of the membrane of the granular endoplasmic reticulum with a decrease in the number of free ribosomes.

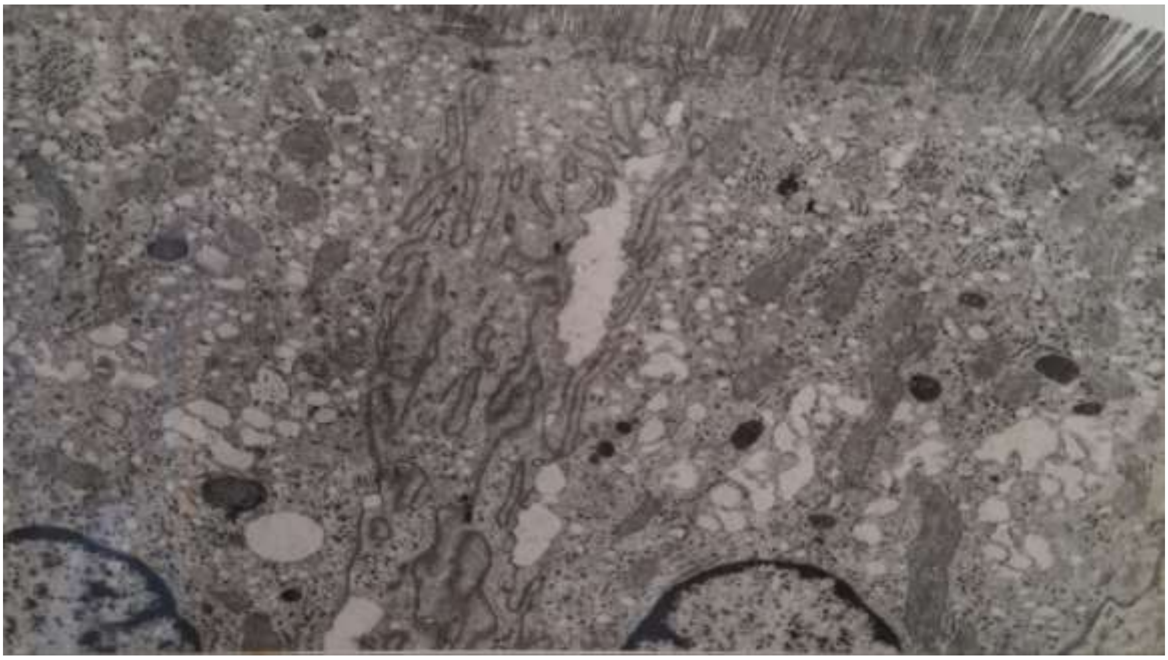


Fig. 30 Single small lysosome-like formations in the supranuclear cytoplasm of striated enterocytes of the villi of the breast of control puppies of 1 month of age. Magnification: 12500

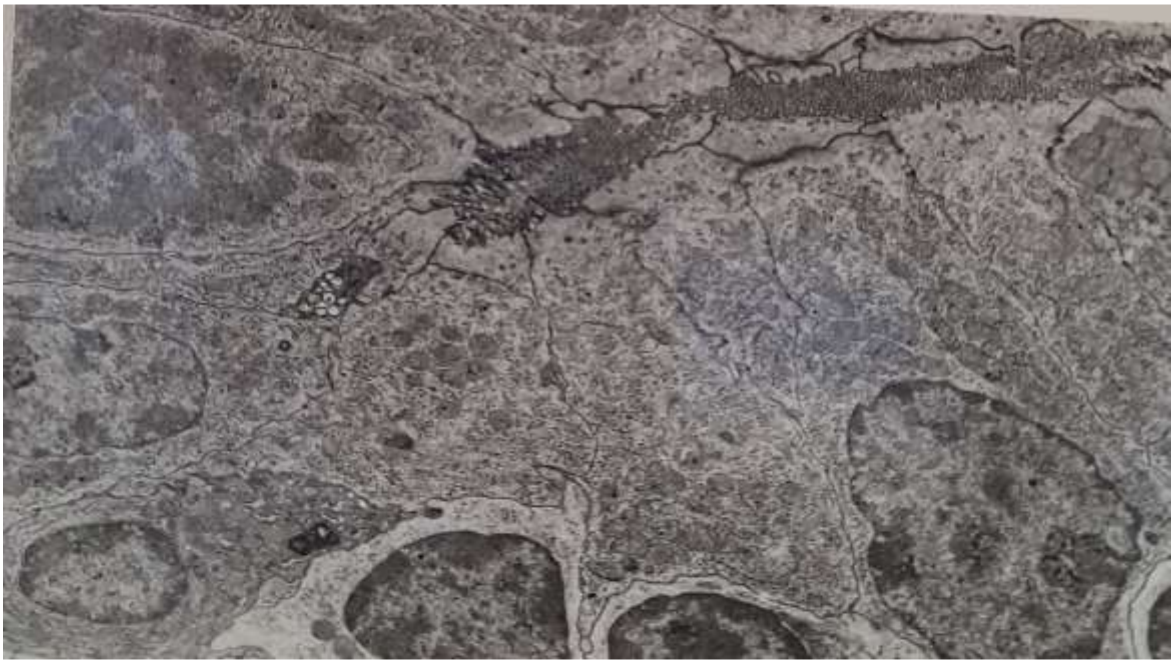


Fig. 31 Ultrastructure of differentiating epitheltocytes in the upper third of the crypt of the late control puppies of 1 month of age. Magnification: 7500

Thus, during the transition to the final nutrition, the structural and functional establishment of the thin layer of the mucous membrane is observed: in the crypts, the middle and lower thirds are topographically different - the zone of polyfiring, poorly differentiated cells. The upper third is the zone of differentiation into absorbent and goblet. Such a division of the crypt zone reflects the complexity of its structure during the transition to the final feeding. This is an important and necessary step in the formation of a crypto-vortex system. At this time, the number of interepithelial lymphocytes on the villi increases sharply (Fig. 32).
Glycosaminoglycan staining allows establishing the crypt villous and proximal-distal gradient of their distribution in goblet cells and on the surface of the mucous membrane of the small intestine.

Blood and lymphatic capillaries, numerous lymphocytes, fibroblasts, plasma cells, mast cells, eosinophilic cells, and macrophages are found in the lamina propria mucosa of small intestine thin layer of puppies 1 month after birth (Fig. 33). Visible restructuring of the stroma of the villi and the crypt also indicates its formation during the transition to final feeding.

After the transition to the final nutrition is 3-6 months. after birth, the length and diameter of the thin layer increases (Table 4). While preserving the general architectonic mucosa, this causes a proportional increase in the number of villi and crypts and, consequently, digestive-absorptive

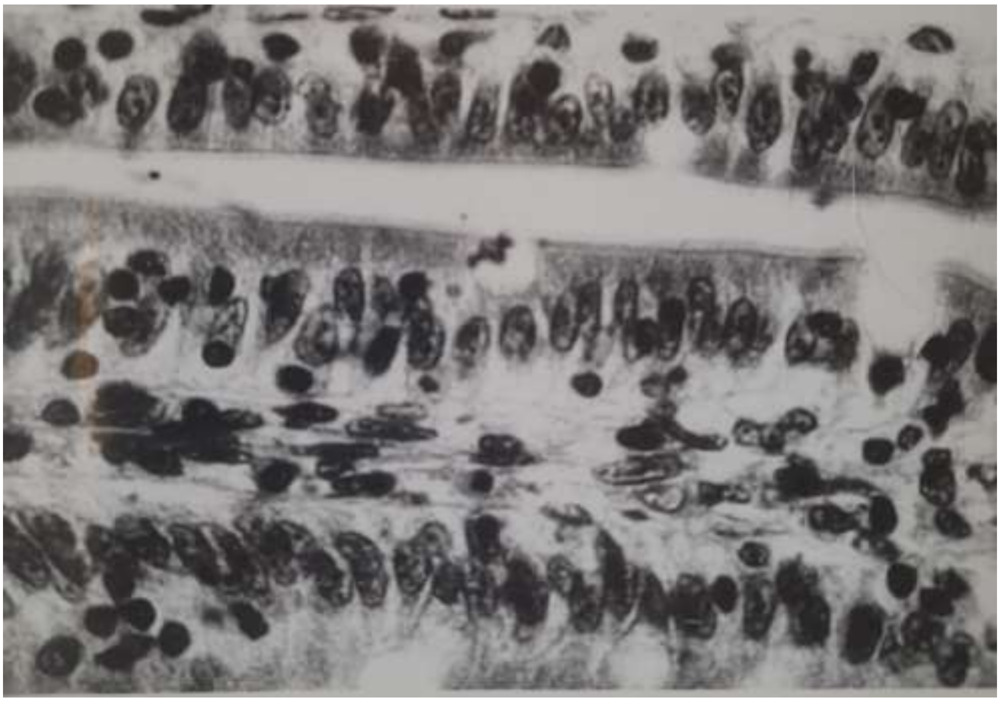


Fig. 32 Increase in the number of interepithelial lymphocytes on the surface of the villi of the mucous membrane of puppies after 1 month. birthday Hematoxylin. - eosin. Magnification: 40x10

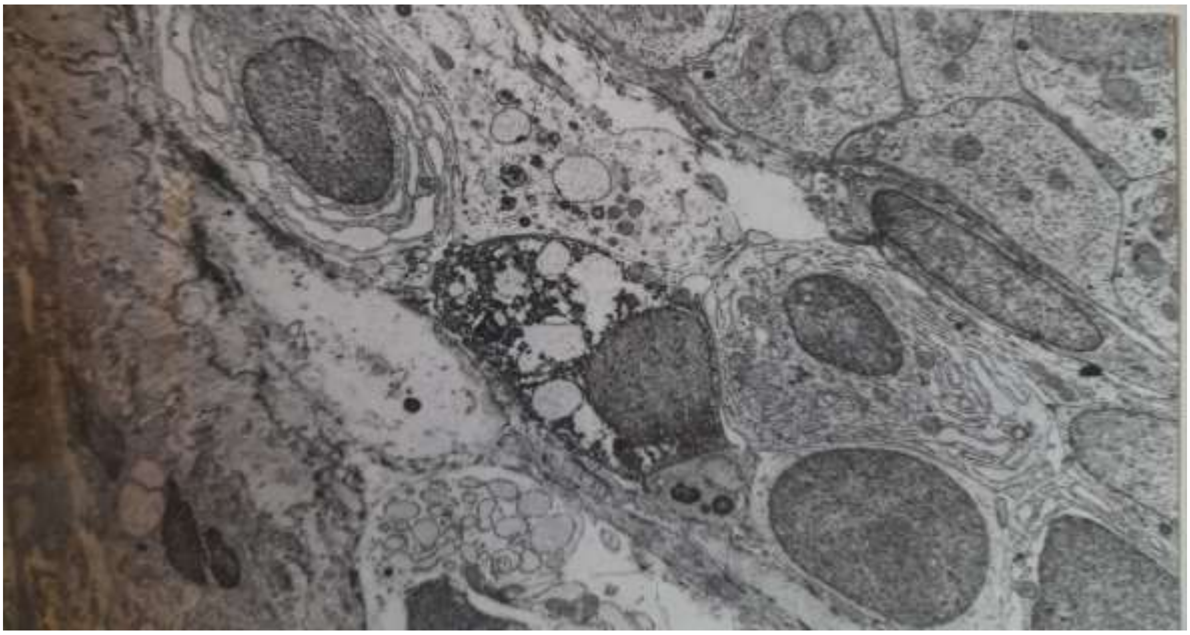


Fig. 33 different connective tissue cells in the stroma of villous mats of pups at 1 mo. after birth Magnification: 7500
surface organ.

The thickness of the mucous membrane gradually decreases as it descends to the iliac crest. A similar proximal-distal gradient is established in relation to the height of villi, the number and height of enterocytes and, consequently, the hydrolytic surface. Towards the iliac crest, the proportion of goblet cells and the mitotic activity of epithelial cells increases in the mucous membrane (Table 4).
Throughout the organ, the villi are mostly finger-shaped, rarely leaf-shaped with numerous invaginations along the surface (Fig. 34 a, b). In the evening of the pelvis, it is more tender, juicy and tender than in the evening. Cylindrical crypts with a narrow lumen, as a rule, do not branch; the muscular plate and the mucous membrane are separated from each other by a thin layer of loose connective tissue.
Mucous-forming goblet cells are most numerous in the upper third of the crypt and the lower half of the villi, gradually increasing towards the iliac crest.

The crypt is lined with a single-layer low-prismatic epithelium, the height of which gradually increases towards the base of the crypt, on average it is 16.0 µm (Table 4).

Table 4

Morphometric parameters (mucous membrane) of the small intestine of puppies 3 months after birth with natural and artificial feeding. /M±m, n=3/.

Parameters	Jejunum	Ileum
Height of villi, µm.	649.6±7.9 550.0±1.4	559.7±7.3 373.1±1.2
Crypt depth, µm	283.3±6.1 623.6±9.0	225.7±6.6 520.1±2.0
Number of enterocytes on one side of the longitudinal section:		
Villi	141.4±3.7 99.3±1.0	125.0±1.4 73.1±3.2
Crypt	75.1±1.5 66.0±3.5	56.5±1.5 49.3±4.1
Number of enterocytes in the cross section of the crypts	21.4±0.2 23.1±1.3	21.4±0.1 20.1±1.2
Height of enterocytes of the middle third:		
Villi, µm	27.0±0.2 23.7±0.2	25.6±0.1 22.9±0.1
Crypt, µm	15.9±0.2 14.1±0.1	16.0±0.2 14.0±0.2
Relative number of goblet cells:		
On the villi /%/	16.6±0.8 26.1±0.7	21.1±0.8 27.2±1.1
On the crypt /%/	21.3±0.9 30.1±1.1	27.0±1.1 32.6±1.7
Mitotic index /%/	24.4±0.8 28.6±1.0	28.1±0.8 31.8±1.2

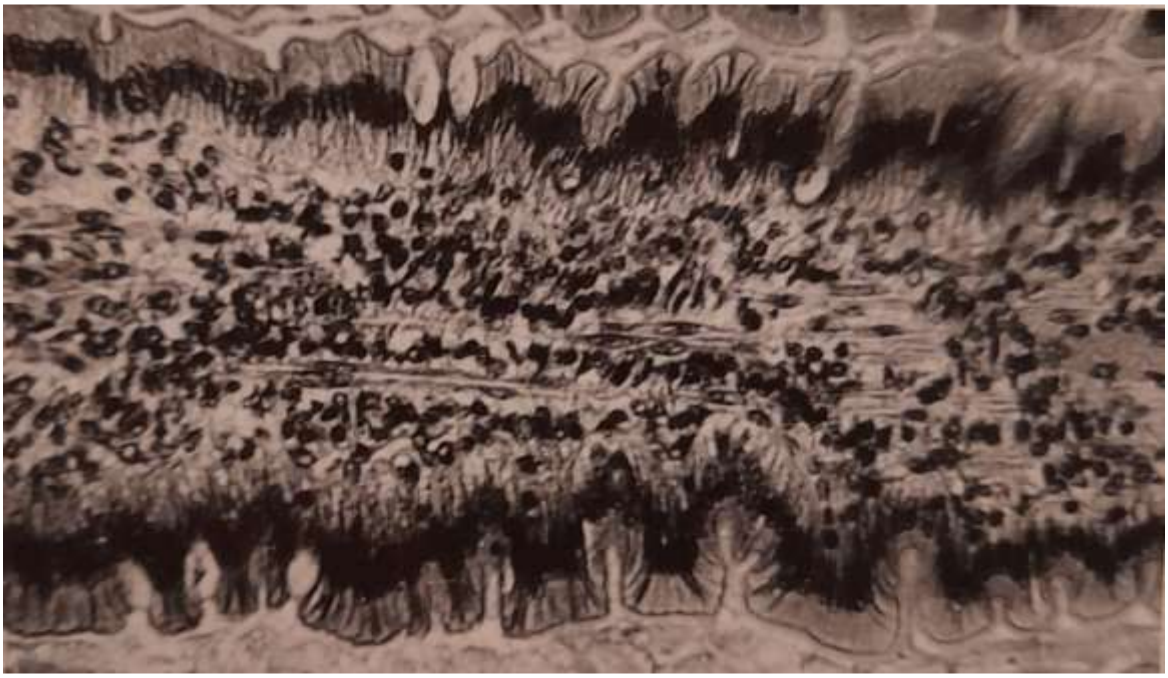


Fig. 34 A. Finger-shaped with multiple intussusception villi of the mucous membrane of the intestine of a dog after 1 month. after birth Hematoxylin. - eosin. Magnification: 20x10

Fig. 34 B Finger-shaped and leaf-shaped villi, cylindrical shape of the iliac crypt of a dog after 1 month. after birth Hematoxylin. - eosin. Magnification: 8x10

Fig. 35 Cylindrical crypts closely adjacent to each other, separated by thin layers of connective tissue. Hematoxylin. - eosin. Magnification: 8x10

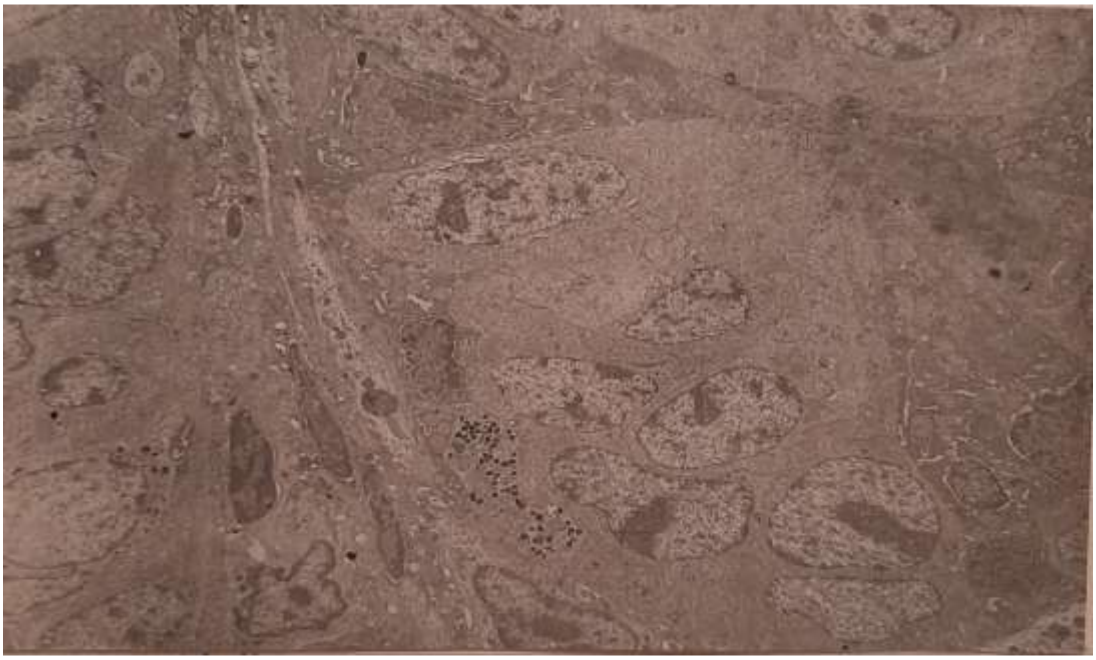


Fig. 36 Low-prismatic epitheliocytes of the crypt breast of 6-month-old control dogs. Magnification: 3500

Electron microscopically, in the lower and middle parts of the crypt, the apical surface of enterocytes consists of short and rare microvilli (Fig. 36). At the end of differentiation, the microvilli elongate and gradually take the correct cylindrical shape. The maximum length is 0.4-0.6 µm, the glycocalyx is poorly developed. There are few organelles in the cytoplasm, many free ribosomes. The nucleus is oval, rounded, and occupies a large area part cells Nucleoplasm consists mainly of euchromatin, one or two electron-dense nuclei (Fig. 37).

Among these poorly differentiated cells, mitotically dividing epithelial cells are often found. They are usually found in pro- and metaphase mitosis.

The villi are lined with a single-layered high-prismatic epithelium, among which the absorbent and goblet cells are clearly distinguished (Fig. 38). Large ultrastructure is 3-6 months. and oni one-month-old animals are practically identical. Therefore, they are not described.

The stroma of the villi consists of cells of loose connective tissue, blood leukocytes, collagen, reticulin fibers and intercellular substance. Blood and lymphatic capillaries forming a microcircular channel, nerve fibers and their terminals are located here.

Thus, after the transition to final nutrition, the small intestine, which performs a number of highly specialized functions under physiological conditions, is the most complex in terms of architecture and structural heterogeneity, polymorphism of tissues and cells that are part of it.

Fig. 37 Relationship between eu- and heterochromatin in oval nuclei of epitheliocytes of 6-month-old control dogs. Magnification: 12000

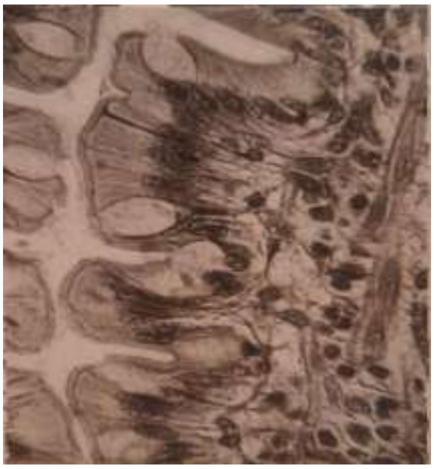


Fig. 38 High-prismatic striated enterocytes and goblet-like epithelial cells of thin villi of control 6-month-old dogs. Hematoxylin. - eosin. Magnification: 40x10

2.2. Structural features of the thin mucous membrane of puppies during artificial feeding.

As it was described earlier in the section "Materials and methods of research", each litter after 3 days of natural feeding is divided into 2 groups: one control group (usually 2 puppies) was left on breast milk, the other experimental group (2-3 puppies) transferred to artificial feeding.

The light-optical mucous membrane of the experimental puppies on the 7th day after birth (4 days of artificial feeding) does not undergo significant changes in the evening. Throughout the organ, the villi are finger-shaped and elongated, filled with a single layer of cylindrical enterocytes with a well-defined brush layer. The nucleus is located in the basal part of the cells, oval, has 1-2 eccentrically located nuclei. Above the nucleus, the cytoplasm is vacuolated, especially in the cells of the middle and upper third of the villi. In most striated enterocytes, the vacuoles are large and occupy almost the entire supranuclear cytoplasm (Fig. 39). Only at the base of the microvilli are very small. If the vacuolization is moderate in naturally fed animals, it progressively decreases within 3 hours after feeding, while in artificial feeding it is more pronounced and is observed for 6 hours after the last feeding. The enterocytes of the villi are closely adjacent to each other, intercellular expansions are noted. Single goblet cells are detected between them, SHIK- and Heil positive and are in a state of accumulation of secretion or overflow.

Single short finger-shaped villi forming between the described villi are visible. The surface of the enterocyte is also vacuolated, i.e. e. they take part in the absorption of substances that are in the cavity of the stomach.

Crypts are short, separated by significant layers of connective tissue and filled with low columnar epithelial cells (Fig. 40). The large nucleus is round or slightly oval, occupying the lower half of the cells. Cytoplasm is homogeneous, basophilic. Throughout the crypt, mitosis figures are noted.

The stroma of the villi consists of loose connective tissue. Muscle cells and capillaries are located behind the basal membrane of striated enterocytes. In the stroma of individual villi behind the basal membrane, especially the upper part of the villi, there are a structureless zone. (Fig. 41)

The connective tissue between the crypts is relatively noncellular. As a rule, blood capillaries are found here, leading to the stroma of the villi.

The submucosa is relatively well developed and consists of loose fibrous connective tissue. In addition to the fibers, numerous blood vessels with different diameters and wall thicknesses are found between the poorly differentiated cells. As a rule, the blood vessels are dilated, filled with blood, and the endothelium is swollen.

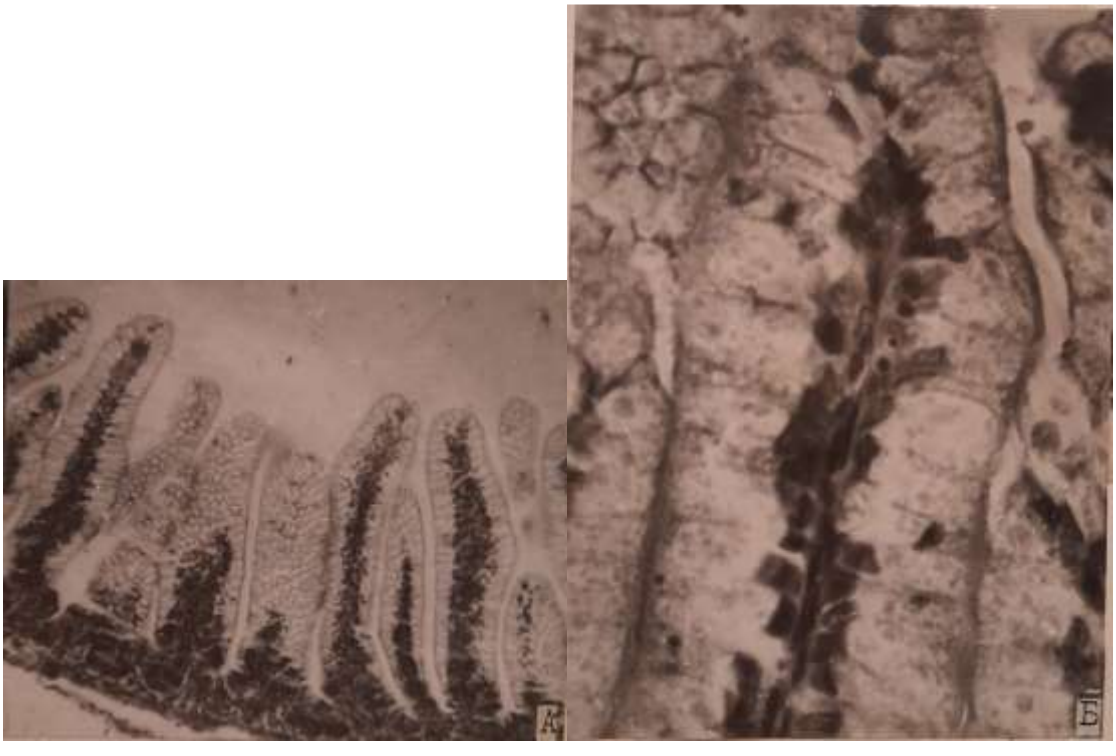


Fig. 39 Pronounced vacuolization of the supranuclear cytoplasm of the striated enterocytes of the villi of the mouse /A/. Fragment of upper third whorl /B/. 7 days after the birth of experimental puppies. Hematoxylin. - eosin. Magnification: A - 8x10, B - 40x10

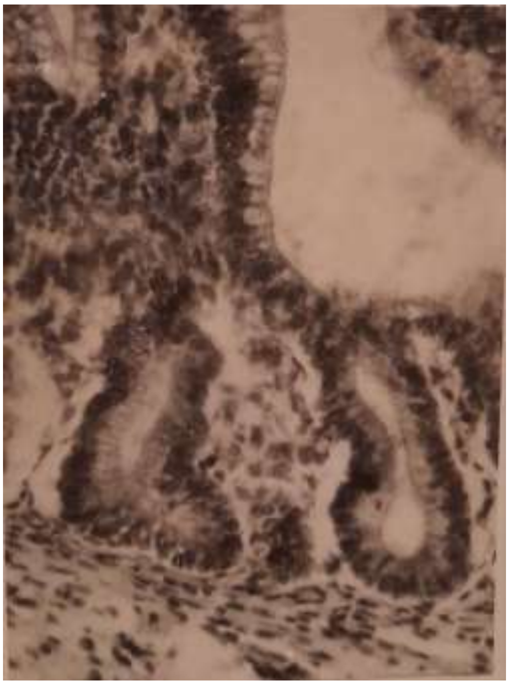


Fig. 40 Short crypts separated by significant layers of connective tissue. 7 days after the birth of experimental puppies. Hematoxylin. - eosin. Magnification: 20x10

B separate the arterioles of the areas pierce the muscular plate and pass into the mucous membrane.

Electron-microscopically, a large supranuclear vacuole with a substance of moderate or low density (Fig. 42), a mass of small vacuoles and endocytic vacuoles of various shapes and sizes and secondary lysosomes are revealed in the cytoplasm of the villi. At the base of the microvilli are endocytic formations of various shapes and sizes. The Golgi complex consists of single vacuoles and numerous vesicles. Mitochondria are separated by vacuoles at the periphery of cells, which have a typical structure. Profiles of granular endoplasmic reticulum are few, relatively more profiles of smooth reticulum. The nucleus is oval-shaped, has numerous pores, and the nucleoplasm is mainly represented by euchromatin.

In the stroma of the upper third of the villi, between poorly differentiated cells and capillaries, under the basal membrane of enterocytes, there is a significant accumulation of chylomicron-like substances (Fig. 43), which move through the mesendothelial spaces, as a rule, into the lumen of lymphatic capillaries.

After 14 days after birth (11 days of artificial feeding), the mucous membrane becomes thinner, relatively few villi are long, thin, without folds on the lateral surface (Fig. 44). The upper surface is lined with a single-layer cylindrical epithelium consisting of 2 types of cells - absorbent and mucus-forming goblet cells.

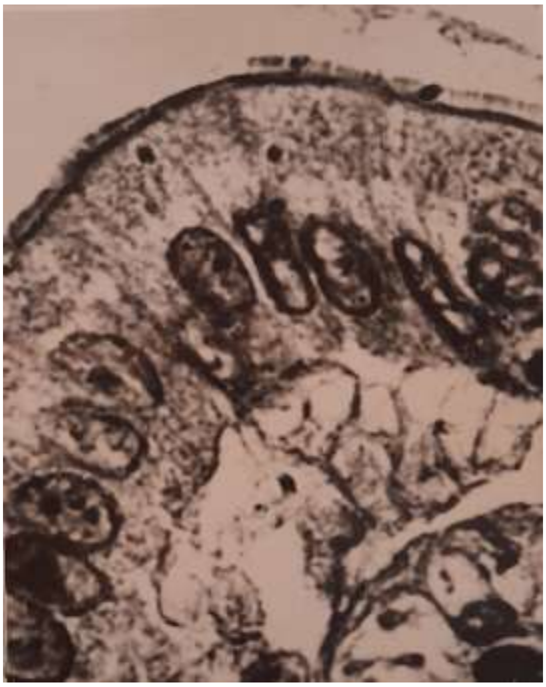


Fig. 41 Structureless zone in the region of the apical villi in the evening of experimental 7-day-old puppies. Hematoxylin. - eosin. Magnification: 40x10

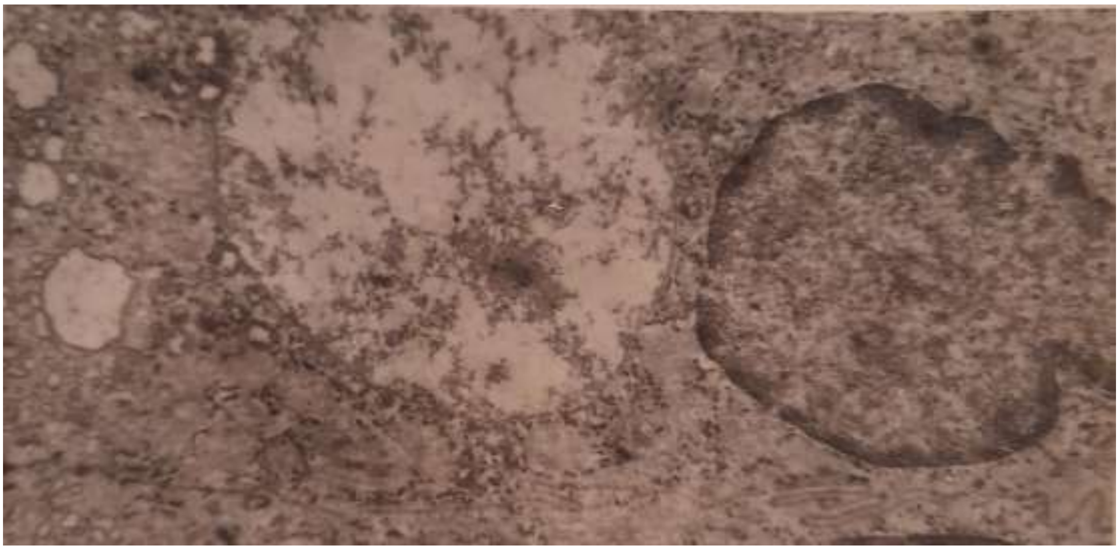


Fig. 42 A large supranuclear vacuole of moderate electron density in the cytoplasm of striated enterocytes of villous mats in the evening of 7-day-old experimental puppies. Magnification: 22000

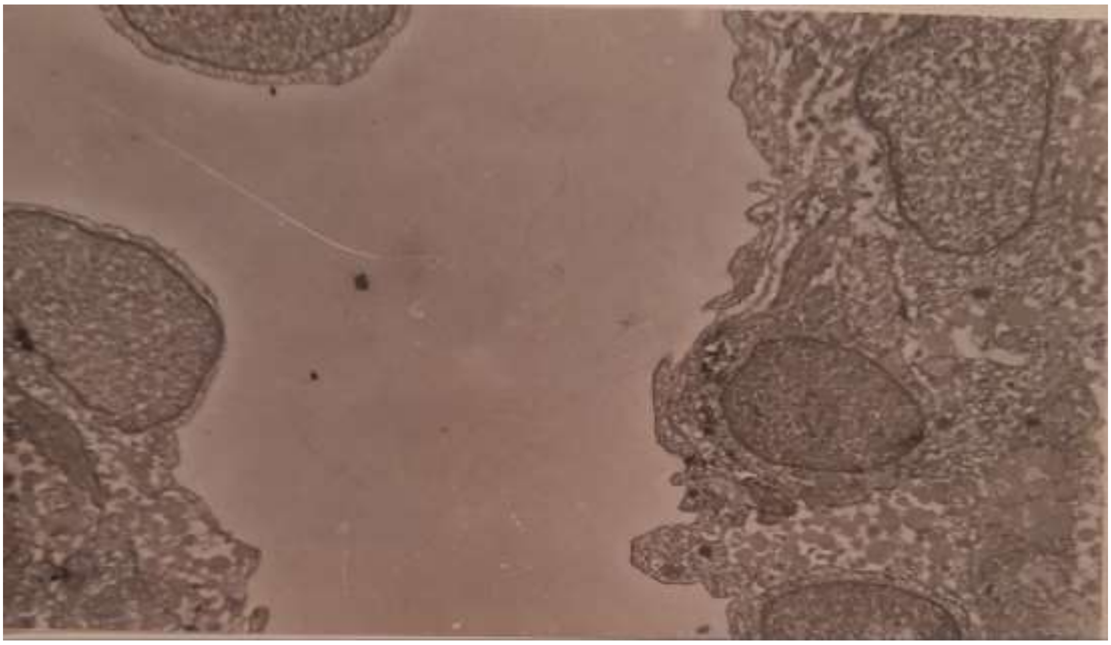


Fig. 43 Significant accumulations of chylomicron-like substances above and below the basement membrane of enterocyte villi in the evening of 7-day-old experimental puppies. Magnification: 20000

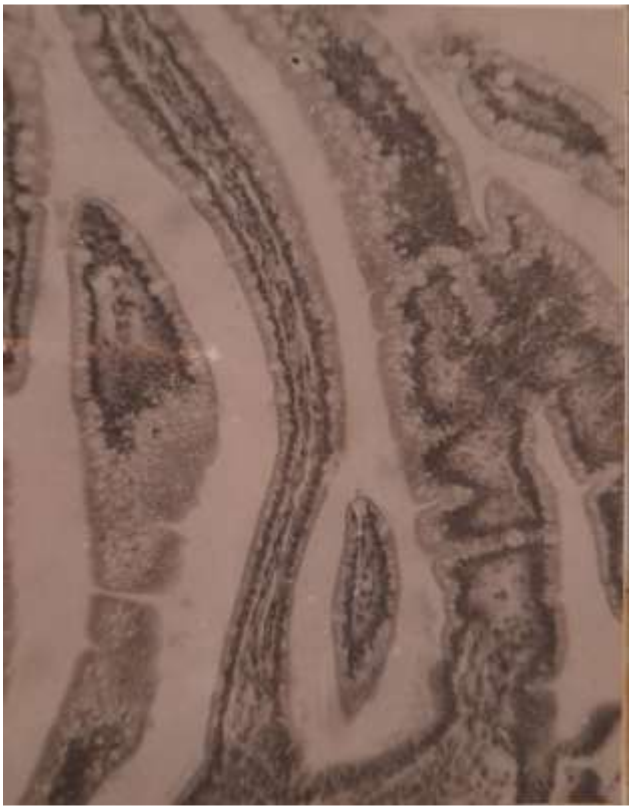


Fig. 44 Stinified folds on the lateral surfaces of the villi in the evening of 14-day-old experimental puppies. Hematoxylin. - eosin. Magnification: 8x10

In the absorbing cells, the brush layer is thin, the cytoplasm is fine-grained, and has a slight lightening above the upper pole of the nucleus. Goblet cells are relatively numerous both in the breast and in the iliac crest, and contain a moderate amount of SHIK- and Heil-positive material (Fig. 45). On the surface of the villi and in the intervilli space there is a crimson or turquoise mucous deposit. Lymphocytes are detected between the enterocytes during this period of research. Due to the fact that the villi cells are relatively poorly developed, the stroma contains fewer capillaries and cellular elements.

Blood stasis is detected in the subepithelial capillaries. Between the capillaries there are longitudinally oriented 2-3 bundles of smooth muscle cells. Crypts are a type of narrow, relatively short cylinders that fit closely together. Vystles do not have low-prismatic cells. Mitosis is frequent and occurs in the lower third of the crypt: differentiation into goblet-like and absorptive cells is carried out in its upper third.

Thus, after 10-11 days after the start of artificial feeding, a decrease in the number and surface of villi, and accordingly, enterocytes, is observed, which causes a significant change in the absorbent surface of the thin stomach. This, of course, affects the development of the body of a newborn mammal, internal organs, in particular, the intestine itself.

After 1 month after birth, when the control animals are switched to definitive feeding, the total length is thinexperimental animals is 96.3±5.2 cm. ($P<0.05$); diameter 7.1±0.4; 6.5±0.4 mm on average, respectively, in the upper and lower parts of it (Table 3). When visible even microscopically, the entire wall of the thin villi of the mucous membrane has a length of 332.1±17.3 ($P<0.001$) and 282.0±10.1 ($P<0.001$) μm, respectively, in the breast and iliac parts of the organ, which is on average two times less than control animals (Table 3). Along the entire small intestine, it is more often leaf-shaped, rarely finger-shaped with invagination along the lateral surface. Neonatal villi are practically not detected. The crypt has a cylindrical shape, the depth is 285.1±8.0 ($P<0.05$), 302.8±8.0 μm ($P<0.05$), respectively, in the left and iliac crests. Due to the specified features of the structural and functional unit of the small intestine- the crypt-villus system - the mucous index is equal to 1.2 - 1.0. the surface of the villi is lined with a single-layer high-prismatic striated epithelium, however, both in the breast and in the iliac crest, it is smaller in size than in control animals ($P<0.001$, table 3). The oval nucleus is located along the cell in the basal part. The supranuclear cytoplasm is uniform, homogeneous, slightly lightened above the upper pole of the nucleus (Fig. 46). Between the absorptive enterocytes of the villi there are typical SHIK- and

Heil-positive goblet cells. The relative number of artificially fed animals is greater along the entire length (Table 3).

Fig. 45 Moderate content of SHIK-positive substance in the goblet cells of the villi in the evening of 2-week-old experimental puppies. SHIK-reaction. Magnification: 20x10

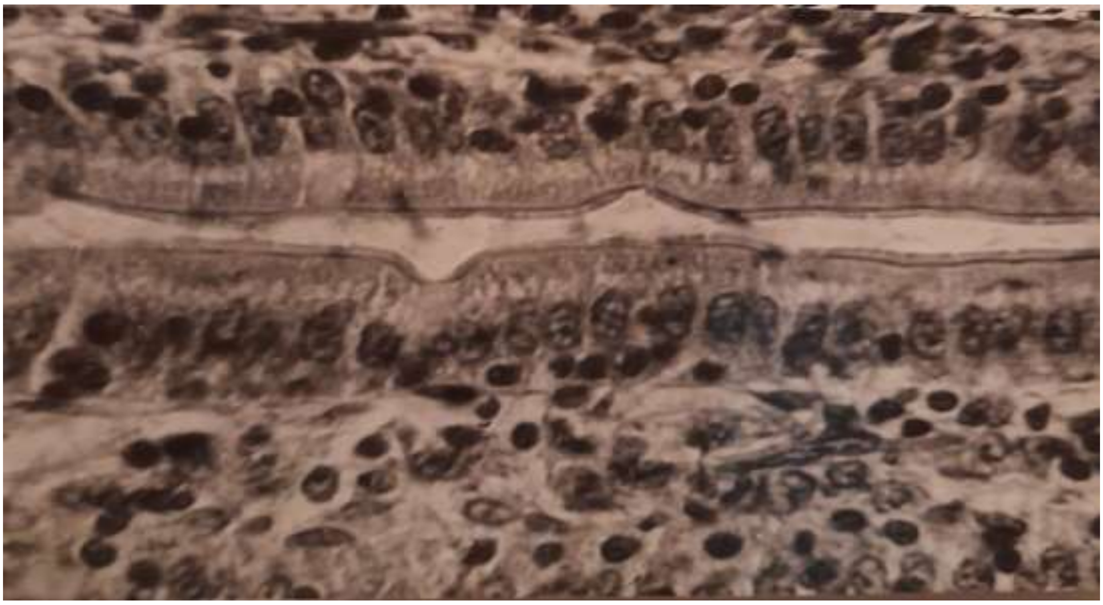


Fig. 46 Slight lightening above the nucleus of high-prismatic striated enterocytes of the villi of 1-month-old experimental puppies. Between enterocytes at different levels - lymphocytes. Hematoxylin. - eosin. Magnification: 20x10

It should also be noted that experimental animals have a significant number of interepithelial lymphocytes between the lamellar enterocytes located at different levels in relation to the basement membrane. Crypts have the form of narrow cylindrical tubes lined with single-layer low-prismatic epithelium. Topographically, the zone of mitotically dividing cells (lower and middle third) and their differentiation in the process of migration (upper third) is distinctly different.

A comparison of the morphological parameters of the control and experiment showed that in the middle third of the studied sections, the height of the thin layer of epitheliocytes is significantly ($P<0.05$) lower than that of the artificially fed ones (Table 3). The cell pool of epithelial crypts (the total number of epitheliocytes lining the average crypt) in experimental puppies is significantly ($P<0.05$) smaller only in the distal part of the small intestine. In the proximal part of the organ, the number of crypt epitheliocytes in experimental puppies is provided by a large increase in the cross-section of the crypt compared to control values. In the crypts of the whole thin layer of the experimental animals, compared to the control ones, a relatively larger number of goblet and mitotically dividing cells is noted ($P<0.05$: table 3).

In the stroma, the capillaries of the villi are moderately developed, and in some of them, stasis is noted. Smooth muscle cells increase in number over time, and after their contraction, fixation causes the appearance of folds of different depths on the lateral surfaces of the villi. In the proximal part of the thin layer, where the villi are relatively long, the expression of folds is greater than in the distal part.

Thus, after 1 month after birth, experimental puppies have significantly significant differences in the length and diameter of the thin layer, the parameters of the structural-functional unit - crypts and villi, and the number of epitheliocytes on their surface. This is the morphological equivalent of the influence of artificial feeding and is considered as one of the causes of the development of hypotrophy due to the decrease of the absorbent surface of the organ.

Electron-microscopic studies of the functional state of the mucous membrane, enterocytes of thin villi of experimental animals are dynamic after a single injection into the stomach of 1.5-2 ml. cottonseed oil Although the ultrastructure of enterocyte villi is similar to those of adult animals, in the cytoplasm of cells of artificially fed animals, chylomicrons and lipid caps of different sizes appear after 0.5 hours (Fig. 47). A profile of smooth endoplasmic reticulum, which probably takes part in the formation of chylomicron, is detected around the fat capsule 1 hour after feeding. Due to this process, the intracellular transport of absorbed fat is prolonged by an average of 1-2 hours compared to its transport in control animals. Due to this, the process of transport of fat chylomicrons from expansions between enterocytes and interstitium lasts up to 7-8 hours after a single feeding (in control animals - no more than 6 hours).

On the basis of these data, we come to the conclusion that the functional state of enterocytes of the villi is late experimental animals are insufficient to achieve optimal transport of absorbed substances into the blood or lymphatic system. Therefore, the peculiarities of growing puppies have a significant impact not only on the development and establishment of the thin stomach, its structural and functional unit, but also on the functional state of striated enterocytes, which take part in the transport of nutrients from the external to the internal environment. After 3 months after the birth of experimental puppies, the length of the small intestine is 135.6±17.1 cm. c average (c control 224.1±20.3 cm. $P<0.01$); diameter 8.7±0.3 and 7.4±0.4 mm respectively in the thoracic and lumbar sections (in control 11.4±0.3 and 10.6±0.25 mm respectively $P<0.05$).

The length of the villi is 550.0±1.4 with a thin layer of the mucous membrane; 373.1±1.2 μm in the average in the thigh and iliac regions, respectively, which is significantly less than the values in the control animals ($P<0.01$ in the average). Along the entire organ, they gradually decrease in the distal direction. The large surface with numerous folds is lined with a corresponding number of highly prismatic epithelial cells. Crypts, as well as in other terms of research, are narrow cylindrical formations that tightly adhere to each other. During the last two months, the depth increased in the proximal part of the thin layer by 2.2 times, and in the distal part by 1.7 times (Table 4). The number of epitheliocytes in each crypt increased in accordance with this rearrangement.

However, in experimental animals, the height of epithelial cells in the crypt-villus system of the iliac and iliac regions is significantly lower than in control dogs of the same age. Despite the fact that experimental and control animals are already 2 months old. are on the final diet, the relative number of goblet cells in the crypts and villi, as well as the mitotic index is significantly ($P<0.05$) higher than artificially fed dogs. A moderate number of lymphocytes are found between the villi-shaped enterocytes.

The stroma of the villi contains various types of connective tissue cells, blood and lymphatic capillaries. The submucosal and muscular layers of the experimental animals have practically the same amount of small fine fibers as those of the control dogs.

Electron-microscopic striated enterocytes of villi have a typical ultrastructure (Fig. 48, 49), which differs little from that described for adult individuals. However, the functional capabilities of the absorptive cells of control and experimental animals are not the same. This is expressed in the fact that during the transport of fat in the cytoplasm of the cells of fasting experimental dogs, individual lipid droplets are still visible (Fig. 50). They slowly disappear, eventually turning into chylomicrons. With the help of the Golgi structural complex, they are discharged into the intercellular space and then into the interstitium of the villi.

After 6 months After the birth of experimental dogs, the structure of the mucous membrane of the small intestine is almost identical, both optically and electron-microscopically, after 3 months. animals

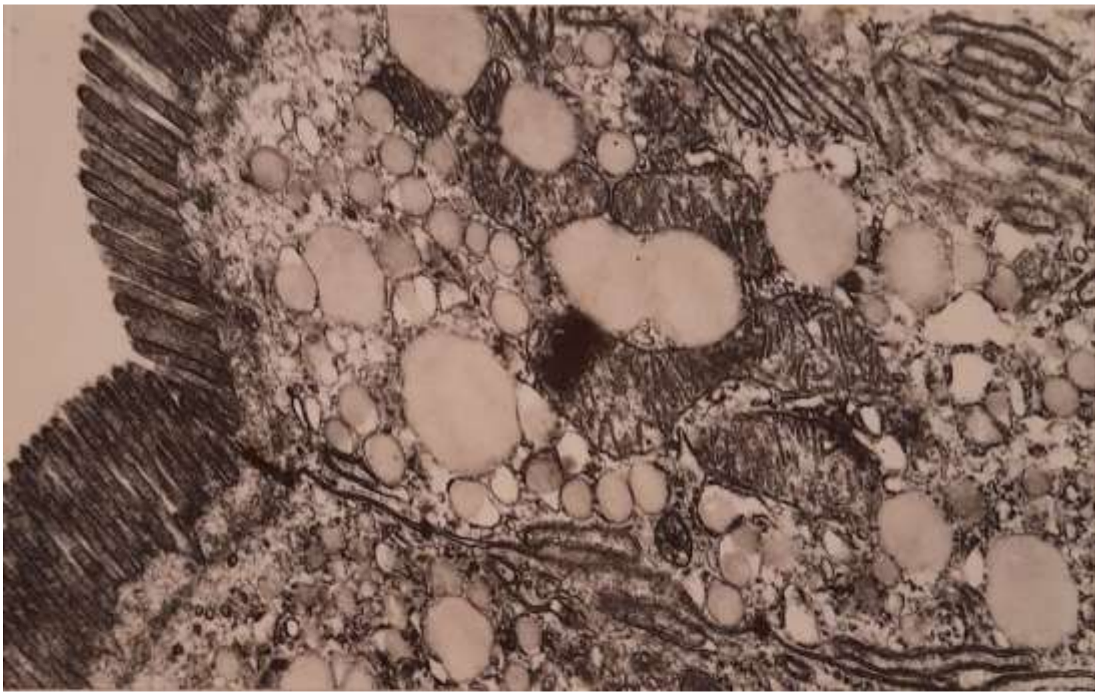


Fig. 47 Lipid droplets and chylomicrons of different sizes in the supranuclear cytoplasm of striated enterocytes of 1-month-old experimental dogs. Magnification: 17000

Fig. 48 Ultrastructure of striated enterocytes of the villi of 3-6-month-old experimental dogs. Magnification: 10500

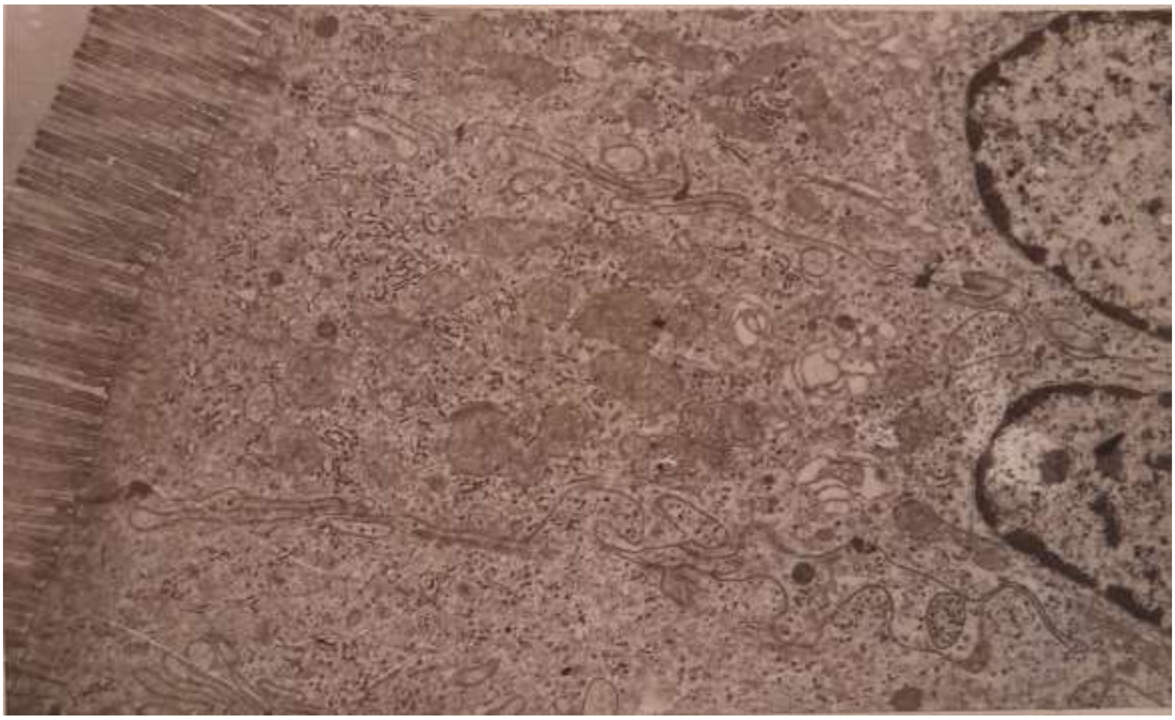


Fig. 49 High-prismatic enterocytes of iliac villi of 6-month-old experimental dogs. Magnification: 10000

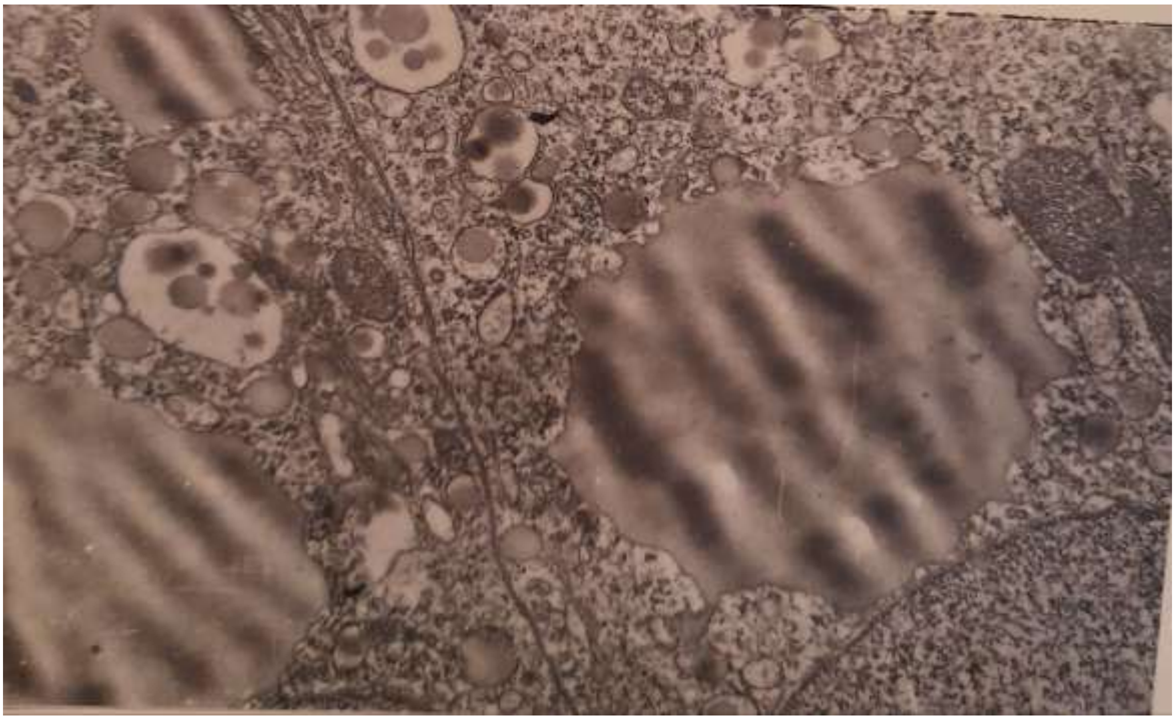


Fig. 50 Single lipid droplets in the supranuclear cytoplasm of striated enterocytes of the villi of 6-month-old experimental dogs. Magnification: 17000

Thus, artificial feeding in the early period after the birth of animals causes a delay in the development of the organ, structural and functional units, lamellar enterocytes, changes in the ratio of goblet cells, relationships in the crypt-villi system, and functional capabilities of absorbing cells. Such pronounced differences in the structural and functional parameters of the thin layer in the dynamics of age during artificial feeding allow to scientifically substantiate the negative influence of artificial feeding on newborns.

2.3 Dynamics of microbiocenosis in late evening with different types of feeding in the morning

Life in the postnatal period. When studying the qualitative and quantitative indicators of different groups of microorganisms contained in the small and large intestines during natural feeding, it was established (table. 5) that lactobacilli, asporogenic anaerobes (bifidobacteria and bacteriocides), gradually increasing, reach a maximum by 30 days after the birth of puppies.

Table 5

Quantitative relationships of lactobacilli, bifidobacterium and bacteriotide in the intestines of puppies with natural (control) and artificial (experiment) feeding (M_{min}-M_{Max}, Ig)

Types of microbes	**AGE, DAYS AFTER BIRTH**					
	6	10	17	30	90	180
JEJUNUM						
Bifidobacterium	1,7-2,9	2,1-2,4	2,1-2,8	3,0-3,8	3,1-3,7	3,1-3,7
	0.8-1.2	0.8-1.1	1.4-1.6	2.9-3.2	2.6-3.0	2.8-3.3
Bacteriotide	0.3-0.9	0.3-0.6	0.3-0.7	-	-	-
	0.4-1.1	0.7-1.3	0.5-1.4	3.0-4.0	3.6-4.0	4.0-4.1
Lactobacillus	1.3-1.9	1.8-2.1	1.8-2.8	3.3-4.2	3.1-3.6	3.0-3.6
	1.4-2.1	1.4-1.7	1.7-1.5	3.0-3.9	3.2-3.5	2.2-2.9
ILEUM						
Bifidobacterium	6.0-7.2	6.2-7.0	6.3-7.0	6.6-7.0	6.3-7.1	6.0-7.2
	4.3-4.8	4.6-5.9	4.3-5.1	4.2-4.8	5.1-5.3	4.0-5.2
Bacteriotide	2.3-2.7	2.6-3.0	3.0-4.3	2.7-3.6	3.1-3.3	3.1-3.9
	3.0-3.6	3.0-3.9	3.3-4.0	3.0-4.2	3.4-4.3	3.6-4.8
Lactobacillus	4.3-6.5	5.7-6.5	5.8-6.5	5.1-5.8	5.2-5.4	5.4-5.9
	5.0-6.1	4.0-4.8	3.1-3.8	3.4-3.9	3.1-3.9	2.9-3.9
COLON						
Bifidobacterium	8.5-10.5	8.7-10.1	10.1-10.5	9.5-10.7	10.3-11.3	10.5-11.3
	5.4-8.1	5.8-7.2	7.1-8.1	5.0-6.0	7.8-9.0	8.0-9.1
Bacteriotide	2.0-3.5	3.8-4.5	-	-	-	2.4-3.1
	2.5-3.5	3.9-4.2	4.1-5.9	5.0-6.0	5.1-6.3	5.3-5.7
Lactobacillus	3.5-8.4	7.1-8.9	7.5-9.0	7.7-8.9	6.8-7.4	7.1-7.7
	2.1-5.9	4.4-6.3	5.1-6.2	4.8-6.3	4.3-5.0	6.0-6.7

Note: the numerator shows the results of studies with natural feeding (control), the denominator shows the results of studies with artificial feeding (experiment).

At this level, they practically do not change until the end of the research, ie. e. do 6 months after birth animals The number of aerobes during breast milk feeding is several orders of magnitude smaller. Big differences from term to term are unreliable.

Bifidum bacteria make up 90-92% of all micro-organisms in puppies on the 6th day after birth. Only in the colon the ratio of anaerobes and aerobes is approximately the same. Subsequently, anaerobic microflora begins to prevail here.

The total amount of microorganisms, gradually increasing, by the 10th day after birth is an average of 1 billion viable cells per 1 g. The content is thick.

Bacteroidetes are detected in the blood of newborn puppies up to 30 days of life. In fat, the amount increases in the evening after the transition to the final meal. After 180 days

Bifidobacteria predominate in all parts of the intestine. After 6 days of birth, this flora becomes predominant, especially in the content of large intestine (from 10.1 to 11.3 years). (Table 5). After establishing a high level of bifidoflora, the number of coliforms and enterococci in the colon decreases. At the same time, their ratio does not change significantly in the thin evening.

Proteus during natural feeding is sown in the iliac crest up to 10 days (0.8 - 1.4 1g.), in the fat and 10 days inclusive (0.3 - 1.7 1g.). In the subsequent periods of the study, it was sown in the control animals throughout the intestine until the end of the study (Table 6).

The total number of lactobacilli increases significantly from day 10 in fat and day 30 - in fat. In the pelvic cavity, its quantity does not change significantly (Table 7).

The total number of staphylococci increases from the 30th day after the birth of puppies (2.1 - 3.0 1g on average). In the pelvis, their number practically does not change. In fat evening they increase to 5.7-6.1 g. (17 days of life), and then sharply decrease to 0.9 - 1.4 1g. (30-180 days of research).

After the transition to definitive nutrition (1 month after birth) and until the end of the experiment (6 months after birth), completely specific ratios of different groups of microorganisms are established throughout the intestines. Bifidobacteria from the contents of the colon of all control animals were cultured from a dilution of 108-1010. 103-107 were sown in breedings also typical coliforms, enterococci and non-pathogenic staphylococci. Naturally, a large proportion of the biocenosis is non-specific. (Table 6).

Candida et al. Fungi do not grow in the intestines of puppies during breastfeeding. After the transition to final nutrition, they are determined in a small amount (0.5 - 2.3 1g.) in the content of fat.

Thus, in the intestines of naturally fed animals (control), asporogenous anaerobes and, in particular, bifidobacteria, stably predominate from the 17th day after the birth of puppies. This position is preserved until the end of the research. At the same time, lactobacilli, enterococci and staphylococci are determined in the contents of the intestine from the 6th day after birth. The specific weight of the intestine in the biocenosis is insignificant and remains approximately at the same level only in the iliac crest. Bacteroidetes are detected in the transition of animals to final feeding after dinner. They are found in small quantities in the pelvic and colon.

Yeast-like fungi in the stomach and in the ileum are not sown during the entire period of research. Microbes of the protease type in the intestines of puppies are found in small quantities only in the first stages of the study. The above indicates that the process of formation of symbiotic microflora in the intestines of naturally fed animals is characterized by a gradual and stable increase in the intensity of colonization by obligate microorganisms and a decrease in these indicators for optional representatives. If the animals of all 3 groups - control and experimental - were on natural feeding until 3 days after birth, it should be assumed that the initial state of microbiocenosis in thin and thick chickens is approximately the same.

Artificial feeding with boiled cow's milk, being non-specific, devoid of immunoglobulins of all classes, leukocytes, macrophages, bifidum bacteria, etc. of the most valuable biological properties of native one-species milk, already 3 days after the start of the experiment causes a significant reduction of lactobacilli and asporogenic anaerobes (mainly bifidobacteria) in the ileum and large intestine (table 5). At the same time, there is a tendency to increase aerobic activity. Late protein is determined in the amount of 0.1 - 0.3 in the chest, pelvis and thick parts; 0.8-1.9; 4.1-4.4 1g respectively. Candida et al. mushrooms in the iliac and thick parts, which are not determined in the control, are sown in the amount of 0.5-1.2; 1.2-2.2 1g respectively.

The decrease in the number of bifidobacteria and lactobacilli in the ileum and colon, revealed in the experimental animals, persists not only until day 30, when the control puppies switch from breastfeeding to final nutrition, but also until the end of the experiment, i.e. e. do 6 months after birth The number of experimental animals is 4.0-5.2; 8.0-9.1 (in control 6.0-7.2; 10.5-11.3) in the ileum and colon, respectively (Table 6).

Table 6

Quantitative relationships between different types of aerobic intestinal autoflora during natural (control) and artificial (experiment) feeding (M_{min}-M_{Max},Ig)

Types of microbes	**AGE, DAYS AFTER BIRTH**					
	6	10	17	30	90	180
JEJUNUM						
Enterococcus	0.2-1.0	0.9-1.4	1.5-2.5	3.3-3.8	3.0-3.4	3.3-3.8
	0.9-2.3	1,3-2,4	1,6-2,7	3,3-4,0	3,1-3,2	2,7-3,0
Staphylococcus	0,5-1,1	0,7-1,4	0,9-1,8	2,6-2,8	2,7-3,0	2,1-2,6
	1.4-2.8	1.5-2.9	1.5-3.0	2.1-3.5	3.0-3.3	2.7-3.4
E. coli	0.3-1.4	1.1-1.8	0.8-1.8	0.7-1.1	0.3-0.7	0.7-1.3
	0.8-1.7	2.1-3.8	2.3-3.8	2.3-3.8	1.6-2.7	0.9-1.8
Proteus	-	-	-	-	-	-
	0.1-0.3	0.2-0.7	0.4-1.1	3.3-4.3	3.0-4.1	5.8
and others	-	-	-	-	-	-
	-	-	0.7-1.6	-	-	-
ILEUM						
Enterococcus	1.7-3.1	1.8-2.8	2.0-2.6	2.1-2.5	2.2-2.4	3.0-3.3
	1.7-3.3	1.9-3.8	2.2-3.8	3.3-3.9	3.0-3.4	3.6-4.0
Staphylococcus	0.8-2.1	0.9-2.6	1.7-2.7	1.4-2.1	1.4-2.0	1.7-2.3
	1.1-3.0	1.19-3.7	2.1-3.7	3.0-3.4	2.9-3.2	4.4-4.7
E. coli	1.6-3.5	2.3-2.8	1.7-2.1	3.0-3.6	3.0-3.3	3.3-4.1
	2.4-4.3	3.3-4.5	3.3-5.9	6.8-6.9	5.4-6.7	6.6-6.8
Proteus	0.8-1.4	-	-	-	-	-
	0.8-1.9	1.4-2.7	2.5-2.9	3.0-3.3	-	3.0-3.2
and others	-	-	-	-	-	-
	0.5-1.2	0.5-1.7	0.7-1.2	-	-	-
COLON						
Enterococcus	5.6-1.2	5.8-7.2	5.4-7.2	4.1-6.5	4.8-5.4	5.0-6.0
	6.7-6.9	6.9-7.4	7.8-8.6	6.0-7.8	7.0-8.1	6.0-7.1
Staphylococcus	2.4-3.4	4.7-5.2	5.7-6.7	0.9-1.4	1.4-1.7	0.8-1.4
	3.1-3.6	5.5-6.0	6.0-6.7	3.3-4.8	3.1-4.0	3.4-4.8
E. coli	3.0-7.2	6.8-7.2	6.8-7.5	4.5-5.6	4.4-5.1	4.7-5.3
	3.7-7.7	6.0-7.8	6.3-7.3	7.7-7.9	6.2-6.8	7.8-7.9
Proteus	1.5-5.3	0.3-1.7	-	-	-	-
	1.1-4.4	4.4-5.0	4.0-5.1	3.0-3.4	2.4-3.2	3.0-4.0
and others	-	0.8-1.4	-	1.7-1.9	2.1-2.3	0.5-1.7
	1.2-2.2	1.6-1.9	1.9-2.6	3.3-4.4	3.1-3.7	3.4-4.8

After the introduction of artificial nutrition, the amount of all representatives of the aerobic microflora increases by 1.4-4;

0.9-2 1g in ileum and colon. In the evening, the number of anaerobes increases significantly. The number of aerobes throughout the intestine increases due to the growth of Escherichia coli, Staphylococcus, Proteus and fungi. Special attention should be paid to sowing of staphylococcus aureus, hemolytic, lactose-negative Escherichia coli, Protea. Artificial feeding causes a significant development of Candida and others. in the hip and fat. Thus, artificial feeding gives way to natural in its regulatory influence on both anaerobic and aerobic intestinal microflora.

Table 7

Quantitative ratios of lactobacilli, asporogenous anaerobic and aerobic intestinal microorganisms of puppies with natural (control) and artificial (experiment) feeding (M_{min}-M_{Max}, Ig)

Types of microbes	AGE, DAYS AFTER BIRTH					
	6	10	17	30	90	180
	JEJUNUM					
Asporogenous lactobacillus anaerobes	2,1-3,1	2,2-3,6	2,3-3,4	2,7-3,8	3,0-3,9	3,2-3,6
	1.2-1.7	1.3-1.9	1.6-2.1	1.8-2.4	2.1-2.9	2.6-2.9
aerobes	1.1-1.5	1.0-1.3	1.6-2.2	1.9-2.1	1.9-3.0	2.3-2.7
	1.7-2.9	2.4-3.9	2.8-3.8	2.6-3.8	3.4-3.8	3.0-3.8
	ILEUM					
Asporogenous lactobacillus anaerobes	6.4-6.6	6.5-6.9	6.4-7.2	6.6-7.3	6.1-7.4	6.2-7.0
	4.5-4.7	4.6-4.8	4.2-5.0	4.0-4.9	4.9-5.2	3.2-4.9
aerobes	2.0-2.8	2.2-2.9	2.1-2.8	2.0-2.9	2.3-3.1	2.6-3.7
	2.4-4.8	3.6-4.7	3.3-5.6	6.1-6.6	3.9-6.2	4.8-6.4
	COLON					
Asporogenous lactobacillus anaerobes	4.7-7.1	9.6-10.0	10.0-10.8	10.1-11.3	10.3-11.2	10.5-11.4
	2.2-4.1	6.0-7.4	6.9-8.3	7.1-9.3	8.7-9.9	8.4-9.7
aerobes	6.9-8.4	6.7-8.1	7.2-8.1	7.0-8.1	7.0-7.4	7.1-8.3
	8.3-9.1	8.1-9.0	7.8-9.8	7.9-9.1	7.0-9.4	7.9-9.7

During artificial feeding and in the subsequent periods of research on the formation of symbiont microflora of various biotypes, it is characterized by a stable increase in obligate microorganisms and a decrease in these indicators for facultative, non-constantly occurring representatives.

The presence of facultative aerobes (enterococci, staphylococci, Candida, proteus) in the contents of the ileum and large intestine is characteristic for experimental puppies. Quantitative content of 1-2 orders of magnitude prevails shifts in the quantitative composition of the microflora of the small and large intestines, their fluctuations during the experiment allow us to come to the conclusion of the development and formation of dysbacteriosis during artificial feeding of animals.

2.4 Influence of natural and artificial feeding in the early postnatal period of life on dynamic body mass.

The mammalian organism and its microflora represent a single ecological system in a state of dynamic equilibrium. When changing any parameter that ensures this balance, interrelated changes are observed: microecological changes lead to a violation of the functioning of the body's protective forces, the state of health of the macroorganism as a whole. Qualitative and quantitative changes in the aerobic and anaerobic microflora of the intestines cause structural and functional changes in the activity of the immune system organs, reduce the body's protective capabilities.

Due to the fact that the digestive-absorptive and immune system is integrated in the mucous membrane of the small intestine, changes in the microbiocenosis not only disrupt the activity of the immune system, but also the digestion and absorption of the main classes of nutrients. A chronic disorder of nutrition and trophic tissue that disrupts the proper harmonious development of a mammal, in particular a puppy, is considered dystrophy. One type of dystrophy is hypotrophy. Clinically, there are 3 grades: mild, moderate-severe, and severe. With hypotrophy of the 1st degree, the body weight deficit is 10-20% compared to the norm (the same-age control), dysporteinemia and a decrease in the level are noted digestive enzymes. With hypotrophy of the 2nd degree - deficit of body mass is 20-30%. Hypotrophy of the 2nd degree is characterized by a decrease in emotional tone, activity, and appetite. Skin elasticity and tissue turgor decrease, muscle hypotonia is expressed. Subcutaneous adipose tissue is noticeably reduced. These symptoms are accompanied by hypochromic anemia, hypo- and dysproteinemia, and a significant decrease in the activity of digestive enzymes. With hypotrophy of the 3rd degree, the mass deficit is 30% or more, the growth curve of the mass is flat. In appearance, lipo is "senile", wrinkled, muscle atrophic, but turgor is increased due to disorders of the electrolyte balance, signs of dehydration are expressed. The stomach is stretched or, on the contrary, inflated, tense. Liver and spleen are reduced in size, dyskinetic disorders are almost always observed: drooling, liquid stool. In our experiment, the cause of chronic malnutrition and development of hypotrophy of 1-2 degrees was the replacement of breast milk with artificial (cow's) milk and intestinal dysbacteriosis. There were 3 litters of 5 puppies under my supervision. 3 of them in each group were fed artificially, 2 - naturally and served as control. The study of the dynamics of the mass and the state of the intestinal biocenosis allows to clarify the direct relationship between them. The condition of the intestinal microflora of puppies is evaluated according to the following criteria: - dysbiosis 1 - degree - anaerobic prevails over aerobic; bifido- and lactobacilli are allocated in dilutions 107-108 or conditionally pathogenic bacteria (no more than 2 species) were grown in dilutions 102-104. - dysbacteriosis of the 2nd degree is characterized by suppression of the growth of anaerobic bacteria, conditionally pathogenic ones are isolated in dilutions 106-107, full-fledged coliforms were replaced by their atypical forms (lactose-negative, hemolyzing); - grade 3 dysbacteriosis is characterized by an almost complete absence of bifido- and lactobacilli, a sharp increase in the amount of conditionally pathogenic flora, especially pathogenic staphylococcus, proteus, yeast-like fungi of the genus Candida. Normally (Table 5), the colon of (control) puppies, which are on natural feeding, is inhabited by bifidum bacteria, the specific weight of other obligate microbes (intestinal and lactic acid microbes, enterococci and staphylococci) is small and in total exceeds 10-15%. During artificial feeding in all animals from the first days of the study, violations of biocenosis are noted, which are considered as dysbacteriosis of the 2nd degree.

During all 6 months, the analysis of the flora showed that most often the medium-severe form of dysbacteriosis was characterized by the release of microbes of the genus Proteus, Staphylococcus aureus, hemolyzing Escherichia coli, and yeast-like fungi of the genus Candida. The development of dysbacteriosis and its severity are closely related to the degree of chronic nutritional disorders. As shown by the results of determining the weight of control and experimental animals, a decrease occurs immediately after the introduction of artificial feeding 25-30% of body weight on average. According to the clinical picture and based on the classification of L.K. Bajenov should be considered hypotrophy grade 3. Next, from the 10th day after birth, a normal increase in the body mass curve of such puppies is noted. The weight loss of experimental puppies is more than 30%, which is hypotrophy of the 3rd degree. A chronic disorder of the process and absorption, dysbacteriosis has a significant influence on its development. A similar clear correlation between the degree of hypotrophy and dysbacteriosis was noted earlier in puppies in the study of I.S. Smiyan, O.E. Fedortsiv. According to the authors, the main mass of puppies with dysbacteriosis was on artificial feeding

(87.6%). Dysbacteriosis developed in almost all puppies regardless of whether they received adapted formulas, whole cow's milk or diluted milk. The inclusion of bacteroid drugs (bifidum-bacterin, bificol, lactobacterin) in the complex therapy of puppies with hypotrophy contributed to the normalization of the condition of puppies. Thus, all experimental puppies have grade 2 dysbacteriosis and grade 3 hypotrophy. Taking into account the important role of microbiocenosis in the development of immune, digestive and absorption functions, their integration (170) in complex therapy should include bacterial preparations that contribute to the normalization or improvement of the condition of the intestinal microflora. Before the appointment of appropriate bacterial therapy, it is necessary to examine the state of the intestinal biocenosis.

Table 8

Dynamics of relative weight of animals with natural and artificial feeding.

AGE, DAYS AFTER BIRTH										
	At birth	6	10	14	17	24	30	90	180	
1	1	1,041	1.083	1.125	1.200	1.270	1.666	3.125		I gr
2	1	1.006	0.938	1.111	1.022	1.289	1.800	3.111		
3	1	1.150	1.050	1.150	1.250	1.300	1.475	3.0		
4	1cont.	1.467	1.667	2.833	4.4	6.267	6.0	10		
5	1cont.	1.130	1.260	1.957	2.826	3.913	4.130	6.739		
1	1	1.286	1.085	1.143	1.429	1.657	1.714	3.743		II gr
2	1	1.270	1.081	1.135	1.946	2.162	2.216	4.595		
3	1	1.312	1.062	1.093	2.125	2.375	2.563	5.312		
4	1cont.	1.074	1.111	1.389	1.815	2.222	2.593	5.370		
5	1cont.	1.395	1.462	1.795	2.308	3.077	4.103	7.641		
6	1cont.	1.250	1.275	1.450	1.950	2.500	3.500	6.500		
1	1	1.190	1.071	1.083	1.250	1.452	1.738	3.810	4.833	III gr
2	1	1.297	1.108	1.162	1.378	1.622	1.892	3.784	5.432	
3	1	1.232	1.098	1.073	1.220	1.463	1.744	3.537	5.122	
4	1cont.	1.225	1.625	2.025	2.475	3.25	3.763	7.375	11.25	
5	1cont.	1.289	1.763	2.079	2.500	3.684	4.237	8.157	12.368	

2.4.1 Weight of animals under natural feeding.

In order to clarify the influence of different types of feeding on the growth and development of mammals during 3-6 months. After birth, the weight of the puppies was determined in three litters. In each group, at least 2 puppies were controls and they were nursed for 1 month. only with breast milk. According to studies, the birth weight of each litter fluctuated between 380-480 g. /1/, 350-540 AD. /2/, 370-420 AD. /3/. After 3 days of birth, this difference became more pronounced 460-520 g. /1/, 420-540 AD. /2/, 480-505 /3/.

With natural feeding, an intensive increase in the weight of animals from term to term is noted. After 2 months the mass of animals in 1 litter increased by 4-5, 2-3-4, 3-4 times on average compared to that at birth. Next 2 months the increase in the weight of the animals was more intensive: in all 3 litters it increased by 1.5-2 times on average compared to that in the previous period of observation. After 3 months the mass of animals is 5-8 times more than at birth (table. 8). Do 6 months. only 3 litters of animals were under observation. Due to this growth, the initial mass increased on average by 10-11 times, that is, in 3 months it increased by 1.5 times or by 1550-1600 g. If you pay attention to the characteristic graph of the growth mass, it has a straight line, which forms an abscissa angle of 55-60° with the axis. Thus, a mass of puppies with natural feeding increases most intensively during the first month. And then every 3 months. increases by 1.5 times on average.

2.4.2. Mass of animals under artificial feeding.

Under supervision in each of 3 gr. The animals were 3 puppies, which were fed cow's milk from the 3rd day after birth. The weight of experimental puppies either did not increase (1 puppy from 1 group) or decreased by 20-100 g during 3 days. on average 7 days after the start of artificial feeding (10 days after birth) some puppies' body mass either remained at the same reduced level (N1 - 1g., N3 - 2g., N1;3 - 3g.), or had a tendency to increase it (tab.). 14 days after the start of the experiment (17 days after the birth of the animals), the body weight of the puppies grew to 40 g. (1 gr.), 100-300 g (2 gr.), 60-80 g. (3 gr.).

Skin turgor is reduced, subcutaneous adipose tissue is not determined, stool is liquid. Stomach bloating is more common due to gas. Peristalsis intensifies, urticaria is noted. The animals are slow moving and moan weakly. The temperature of the body decreases by 0.5-1°, so apparently, despite the temperature in the room (27°-28°), they close to each other. After 1 month after birth, the general condition of the animals is somewhat better - they are more mobile, the body temperature has normalized. The stool is too liquid or pasty. The skin remains wrinkled, subcutaneous fat is absent. As a result, the ribs and other bones of the skeleton stand out. The nose of the animals is wrinkled and less compared to the control animals. The weight of puppies in all three groups gradually increased along a gentle curve and differed from that of the control 2 times on average. According to the modern classification (14), the difference in mass is more than 30% and the above-mentioned signs allow us to consider that the puppy has hypotrophy of the 3rd degree. In the later periods of the study (3-6 months after birth), the mass of puppies increases, but everything also follows a gentle curve.

Table 9

Dynamics of absolute weight of animals with natural and artificial feeding.

AGE, DAYS AFTER BIRTH										
	At birth	**3**	**6**	**10**	**17**	**24**	**30**	**90**	**180**	
1	0.480	0.500	0.520	0.540	0.580	0.610	0.800	1.500		
2	0.450	0.480	0.420	0.500	0.460	0.580	0.810	1.400		
3	0.400	0.460	0.420	0.460	0.500	0.520	0.590	1.200		
4 control	0.380	0.440	0.500	0.850	1.320	1.880	1.990	3.000		I gr.
5 control	0.460	0.520	0.580	0.900	1.300	1.800	1.900	3.100		
1	0.350	0.450	0.380	0.400	0.500	0.580	0.600	1.310		
2	0.370	0.470	0.400	0.420	0.720	0.800	0.850	1.440		
3	0.320	0.420	0.340	0.350	0.680	0.760	0.820	1.700		
4 control	0.540	0.580	0.620	0.750	0.980	1.200	1.400	2.900		II gr.
5 control	0.390	0.540	0.570	0.700	0.900	1.200	1.600	2.980		
6 control	0.400	0.500	0.540	0.580	0.780	1.000	1.400	2.600		
1	0.420	0.500	0.450	0.455	0.525	0.610	0.730	1.600	2.030	
2	0.370	0.480	0.410	0.430	0.510	0.600	0.700	1.400	2.010	
3	0.410	0.505	0.450	0.440	0.500	0.600	0.715	1.450	2.100	
4 control	0.400	0.490	0.650	0.810	0.990	1.300	1.505	2.950	4.500	III gr.
5 control	0.380	0.490	0670	0.790	0.950	1.400	1.610	3.100	4.700	

After 3 months in 1 gr. the mass of puppies increased by 3.0-3.1, 2-3.7-5.2, 3-3.5-3.8 times compared to that at birth. It increased by 6.7-10, 6.5-7.6, 7.3-8.2 times on average. After 6 months after birth, a significant difference in the development of control and experimental animals was preserved. If the initial body weight of the control puppies increased by 11.3-12.3 times, then the experimental ones - by 4.8-5.4 times. Puppies raised on cow's milk show not only a delay in physical development, but also a dense hair cover, no subcutaneous fat, and a wrinkled (senile) expression on the face. They are all my assets. Stools may be loose from time to time. Thus, it is naturally reared animals during 6 months. relatively intensive physical development is noted, which is accompanied by a constant intensive increase in body mass. After 6 months after birth, the body mass increases by an average of 11-12 times compared to that at birth. During artificial feeding, physical development and rate of weight gain are significantly different. The clinical picture of hypotrophy of the 3rd degree is noted during the entire observation period. Through 6 months After birth, artificial pups' body weight gain is only 4.8-5.4 times, which is more than 2 times less than that of control animals.

CHAPTER III. DISCUSSION OF RESEARCH RESULTS

The early postnatal period in the life of a mammalian organism is widely recognized as a time of the most intensive growth and development. This period is marked by significant physical changes and rapid increases in body mass and organ development. According to available literature, the body mass of a newborn puppy undergoes substantial changes during the first months of life. By 4–4.5 months, the body mass doubles, and by 10–11 months, it triples (82). These observations align with earlier findings indicating that body size doubles within just seven days of birth and quadruples by two weeks. These impressive growth rates highlight the biological efficiency of nutrient absorption mechanisms during this crucial period.

Further supporting these findings, studies on puppies fed naturally reveal similar results: within 10 days of birth, their body mass doubles, and by 17 days, it triples. This accelerated rate of development demonstrates the remarkable ability of newborns to process and utilize nutrients efficiently. The high nutrient intake required for such growth underscores the importance of natural feeding during this period, as it enables newborns to meet their substantial energy and metabolic demands.

Extensive literature data confirm that newborn mammals, including humans, have significantly higher nutritional requirements than adults. For instance, a human newborn requires approximately 2.7–2.8 g of protein, 6.0–6.5 g of fat, and 12–15 g of carbohydrates per kilogram of body weight daily. These requirements are several times greater than those of an adult, emphasizing the vital role of breast milk in meeting these demands. The composition of breast milk, which is rich in essential nutrients, allows newborns to thrive and achieve significant weight gain. Consequently, naturally fed puppies exhibit consistent growth, surpassing their birth weight by 3.5–4.6 times within one month, 6.5–7 times within three months, and 11–12 times within six months.

In contrast, artificially fed animals demonstrate considerably slower growth, particularly during the first 24 days of life. The initial phase of artificial feeding reveals limited weight gain, indicating that the replacement of breast milk with artificial substitutes may not provide adequate nutrition for optimal growth. However, after transitioning both groups of animals to a standard diet, the body weight of artificially fed animals begins to increase more rapidly than in the earlier period. Despite this improvement, the overall growth trajectory of artificially fed animals remains significantly lower than that of their naturally fed counterparts. For example, after one month, the body mass of artificially fed animals increases only 1.4–2.5 times, compared to 4.1–6.0 times in naturally fed controls. A similar twofold difference in body weight is observed at three and six months, further highlighting the limitations of artificial feeding.

Chronic nutritional disorders, which impede harmonious development, are clinically classified as dystrophies. Among these, hypotrophy is a well-documented condition characterized by inadequate weight gain and impaired development. Hypotrophy is divided into three degrees of severity:

1. **Mild Hypotrophy (Grade 1):** In this condition, the body weight deficit is 10–20% compared to age-matched controls. Associated symptoms include dysproteinemia and reduced levels of digestive enzymes, reflecting mild disruptions in metabolic and digestive functions.
2. **Moderate Hypotrophy (Grade 2):** Here, the weight deficit increases to 20–30%, accompanied by decreased emotional tone, reduced activity, and diminished appetite. Other notable features include reduced skin elasticity, muscle hypotonia, and visibly diminished subcutaneous fat. Hypochromic anemia, hypo- and dysproteinemia, and significant reductions in digestive enzyme activity are also evident.
3. **Severe Hypotrophy (Grade 3):** This stage is marked by a body weight deficit exceeding 30%. The growth curve becomes flat, indicating stagnation in weight gain. Affected animals often exhibit a "senile" appearance, characterized by wrinkled skin and atrophic muscles. Despite the muscle atrophy, tissue turgor may increase due to

electrolyte imbalances. Additional symptoms include dehydration, reduced liver and spleen size, and frequent dyskinetic disorders such as drooling and diarrhea.

Our experimental findings identify chronic malnutrition as a primary contributor to the development of hypotrophy across all three degrees. This condition is closely linked to the replacement of breast milk with artificial substitutes, such as cow's milk, and the resulting intestinal dysbacteriosis. The mammalian organism and its intestinal microflora form an interconnected ecological system that must maintain dynamic equilibrium for optimal health. Any disruption in this balance triggers a cascade of changes, including microecological shifts that impair the body's protective mechanisms and overall health.

The relationship between body mass dynamics and intestinal biocenosis was explored in our study, revealing a direct correlation between the two. The evaluation of intestinal microflora in puppies was conducted using specific criteria for dysbacteriosis:

4. **Dysbacteriosis Grade 1:** This stage is characterized by a predominance of anaerobes over aerobes. Bifidobacteria and lactobacilli are isolated in dilutions of 10^7–10^8, while conditionally pathogenic bacteria (no more than two species) are detected at dilutions of 10^2–10^4.
5. **Dysbacteriosis Grade 2:** In this stage, the growth of anaerobic bacteria is suppressed. Conditionally pathogenic bacteria are detected in dilutions of 10^6–10^7, and typical coliforms are replaced by atypical forms, such as lactose-negative or hemolyzing strains.
6. **Dysbacteriosis Grade 3:** This advanced stage is marked by an almost complete absence of bifidobacteria and lactobacilli. There is a sharp increase in pathogenic flora, including Staphylococcus aureus, Proteus, and yeast-like fungi of the genus Candida.

Under natural feeding conditions, the large intestines of control animals were predominantly colonized by bifidobacteria, with other obligatory microbes accounting for less than 15% of the total flora. In contrast, artificially fed animals consistently exhibited Grade 2 dysbacteriosis from the earliest stages of observation. Over a six-month period, moderate to severe dysbiosis was consistently associated with the proliferation of pathogenic microorganisms, such as Proteus, Staphylococcus aureus, and hemolyzing Escherichia coli.

Body weight measurements further corroborated these findings. Artificial feeding resulted in an average weight reduction of 25–30%, corresponding to

Grade 3 hypotrophy. Despite some weight recovery beginning on the 10th day after birth, the growth trajectory of artificially fed puppies remained significantly below that of naturally fed controls.

In conclusion, our study underscores the critical importance of natural feeding during the early postnatal period. Breast milk, with its unique composition and bioactive components, supports optimal growth, immune development, and metabolic balance. In contrast, artificial feeding disrupts intestinal microflora, impairs nutrient absorption, and compromises overall development, highlighting the irreplaceable role of natural feeding in early life.

Normally, the large intestine of control puppies, which are on natural feeding, is predominantly inhabited by bifidum bacteria, which play a vital role in maintaining the health of the intestinal microflora. These beneficial microorganisms are crucial for the proper functioning of the gut. The specific weight of other obligate microbes, such as bacteria and lactic acid bacteria, enterococci, and staphylococci, is relatively small, collectively accounting for no more than 10-15% of the total intestinal flora. This delicate balance of intestinal microflora ensures optimal digestive and immune system functioning in naturally fed animals.

In contrast, during artificial feeding, a significant disruption in the intestinal biocenosis is observed from the very first days of the study. This imbalance in the gut microbiome is classified as dysbacteriosis of the 2nd degree. Dysbacteriosis of this degree is characterized by a notable reduction in the population of beneficial bacteria, leading to the overgrowth of opportunistic and pathogenic microbes. Throughout the six-month observation period, the analysis of the intestinal flora consistently revealed that animals subjected to artificial feeding exhibited moderate to severe dysbiosis. This condition was most commonly associated with the proliferation of harmful microorganisms, including species of the genus Proteus, Staphylococcus aureus, hemolyzing strains of Escherichia coli, and yeast-like fungi of the genus Candida.

The progression and severity of dysbacteriosis are closely linked to chronic nutritional disorders. These disorders not only affect the gut microbiome but also lead to systemic issues that impair the overall health and growth of the organism. For example, the results of weight measurements in both control and experimental animals showed a clear impact of artificial feeding. With the introduction of artificial feeding, the body weight of the experimental animals decreased by an average of 25-30%. According to the clinical classification proposed by V.K.Bajenov a, such a significant reduction in body weight corresponds to grade 3 hypotrophy, a severe form of malnutrition characterized by a marked deficiency in body mass and systemic dysfunctions.

Following the initial weight loss, a gradual increase in the body weight of the experimental puppies was observed beginning on the 10th day after birth. However, the overall weight gain in these animals remained insufficient to compensate for the earlier loss. The weight deficit exceeded 30%, reinforcing the diagnosis of grade 3 hypotrophy. This chronic disorder of digestion and absorption, compounded by severe dysbiosis, had a profound impact on the growth and overall health of the artificially fed animals.

A similar and well-documented correlation between the degree of hypotrophy and dysbacteriosis has been observed in children. Studies conducted by O.S.Mahmudova and Simyan, O.E. Fedortsiv highlighted this relationship, emphasizing that the majority of children with dysbacteriosis (87.6%) were on artificial feeding. Dysbacteriosis developed in nearly all children, regardless of the type of artificial nutrition they received—whether adapted formulas, whole cow's milk, or diluted milk. These findings underscore the significant impact of artificial feeding on the gut microbiome and the overall health of children.

The inclusion of bacteriotherapy, involving the administration of beneficial bacterial preparations such as bifidum-bacterin, bificol, and lactobacterin, has been shown to mitigate the adverse effects of artificial feeding. These preparations help restore the balance of the intestinal microflora, improving digestive and immune functions and promoting healthy growth and development in children with hypotrophy.

Thus, based on the results of our study, it can be concluded that all experimental puppies exhibited grade 2 dysbacteriosis and grade 3 hypotrophy. These conditions highlight the critical role of microbiocenosis in the proper functioning of immune, digestive, and absorptive systems. Microbiocenosis is a key factor in the integration and regulation of these essential physiological functions (170). Consequently, the inclusion of bacterial preparations in the complex therapy of artificially fed animals is imperative. These preparations can significantly contribute to the normalization and improvement of intestinal microflora, thereby addressing the underlying causes of dysbacteriosis and its systemic effects.

Before initiating appropriate bacterial therapy, however, it is essential to conduct a thorough examination of the state of the intestinal biocenosis. This step is crucial for determining the specific imbalances in the gut microbiome and tailoring the treatment to address the unique needs of the affected animals. By restoring the balance of intestinal microflora, it is possible to improve the overall health and growth trajectory of artificially fed animals, thereby mitigating the negative impacts of artificial feeding on their development.

As in cattle and humans, the histogenetic processes in the thin-skinned dog, which began at the end of embryonic development, intensively continue even after birth, persisting until the period of puberty. These processes are of paramount importance as they ensure the progressive maturation and functional optimization of the digestive system. During this critical postnatal period, the absorbent surface of the organ progressively increases, reflecting the ongoing structural and functional differentiation necessary for efficient digestion and nutrient absorption.

However, during the period of breastfeeding in mammals, the degree of structural and functional development of the digestive organs remains relatively low. This phenomenon has been extensively documented in numerous studies conducted by employees of the problematic biophysical laboratory, as well as by other researchers. According to these studies, the gastric mucosa of newborn mammals lacks fully formed main cells, and parietal cells are observed to be at the stage of differentiation. This developmental stage reflects the immaturity of the stomach's secretory apparatus at birth, which is a characteristic feature of many mammalian species.

In addition to these observations, the pancreas in newborns is characterized by intensive proliferation of acinar cells, which are essential for the development of the organ's structural and functional units. However, the enzymatic activity in the pancreas, including trypsin, hypotrypsin, amylase, and lipase, is notably low during this early period. This underlines the relative functional immaturity of the pancreas, which only becomes fully operational as the animal grows and transitions to more complex diets.

At birth, the small intestine of puppies, like that of many other mammals, is marked by insufficient formation of the mucous membrane, its morphofunctional units, as well as epithelial and connective tissues. The mucosal layer is irregular, and its structural and enzymatic components are not fully developed, resulting in a small absorbent surface. The hydrolytic transport enzymes, which are critical for nutrient digestion and absorption, exhibit low activity. Consequently, both cavity and membrane digestion are inefficient in this early stage of development.

On the basis of the above observations, it can be concluded that at birth and during the period of natural breastfeeding, the small intestine of puppies, as well as that of other mammals, has a limited functional capacity due to the incomplete morphological and enzymatic development of its mucous membrane. This limitation is further compounded by the low activity of hydrolytic enzymes and the inefficiency of both cavity and membrane digestion, which restricts the absorption capacity of the small intestine.

Based on the results of our own research and extensive data from the literature, it is reasonable to consider the biological feasibility of this phenomenon. The apparent underdevelopment of the digestive organs during this stage may have evolved as an adaptive mechanism to accommodate the specific dietary and metabolic demands of breastfeeding. After all, it is during the period of natural feeding that mammals exhibit their most intensive growth. This suggests that the nutritional composition of maternal milk is ideally suited to support this rapid growth, compensating for the underdeveloped digestive capacity of the newborn. This biological design, while seemingly inefficient, ensures that the organism receives all the necessary nutrients for development while minimizing the metabolic burden on its immature digestive system.

The relationship between the incomplete development of the digestive organs and the reliance on maternal milk during the breastfeeding period is a topic of great interest. The nutrients provided by maternal milk are highly bioavailable and tailored to the needs of the growing organism. This alignment of physiological immaturity with nutritional adequacy highlights the intricate biological strategies that have evolved to optimize early mammalian development. The limited absorbent surface of the small intestine, coupled with the low enzymatic activity, reflects a developmental stage designed to accommodate the nutritional and physiological needs of the organism during this crucial period of growth.

This phenomenon underscores the importance of understanding the interplay between structural development and functional demands in the context of postnatal growth, offering insights into the biological strategies that ensure survival and optimal development in mammals.

According to the literature, breast milk (colostrum-intermediate milk - mature milk)contains a significant amount of nutrients, all classes of immunoglobulins, components of complement, lactoferrin, growth factor, proteolytic enzymes and their inhibitors, leukocytes, plasma cells. During breastfeeding, immunoglobulins, absorbed from the small intestine without cleavage, participate in the creation of passive immunity. Only secretory immunoglobulin A is not absorbed, it covers the surface of mucous membranes and prevents their interaction with pathogenic microorganisms. Polymorphonuclear leukocytes contribute to the development of non-pathogenic lactobacilli and the establishment of colonization resistance, which prevents the development of pathogenic microorganisms in the thin layer. Breast milk hormones absorbed into the blood of newborn mammals without cleavage regulate the interrelated activity of internal organs and systems, their structural and functional formation, because in the early postnatal period of life between the endocrine glands connection is established. These and other unique properties of breast milk make it possible to consider it as an ideal food, a natural regulator of optimal developmentmammals.

Therefore, the structural and functional "immaturity" of the mucous membrane of the small intestine, as well as other organs and systems, is genetically programmed, is a general biologicalregularity for a certain stage of development of some mammals. A dynamic relationship between the type of feeding and the structural and functional features of the organs of the newborn has evolved. Breast milk is a perfectly balanced nutritional product, corresponding to the individual characteristics of each child, it is completely absorbed with the least expenditure of energy, providing ideal metabolism, homeostasis of the internal environment of the body. Research into the mechanism of transport of milk ingredients through the laminar enterocytes of villi showed that it is carried out by endocytosis. Endocytosis (pinocytosis) is a process that constantly occurs in macrophages, endothelium, and epithelial cells of the proximal nephron. In the early 1970s, the presence of receptors on the outer surface of cells was shown - specific structures that ensure selective and rapid capture of macromolecules from the external environment. Endocytosis, which is carried out by receptors of the plasma membrane, are called receptors and is based on the interaction of the ligand with the receptor. Its mechanisms are being studied both in vivo and in vitro. Studies of this process in vivo in newborn rats and breast-fed dogs in various Macromolecules (bovine serum albumin, sunflower oil) made it possible to study its mechanism in the dynamics of the process of absorption by enterocytes of empty stomach.

It is known that the luminal surface of enterocytes of villi of newborn mammals is formed by microvilli - finger-like protrusions of the plasmolemma. The maximum number on the surface of one cell is from 1700 to 4000, which increases the total surface of the absorbing cell and organ by 30-40 times on average. Microvilli have a glycoprotein membranelayer (glycocalyx). Glycocalyx is an integral part of plasmalemma and is a carbohydrate-enriched peripheral part of the outer surface of a lamellar enterocyte. It gives a certain rigidity to the entire field of microvilli, carries out chemical and physical protection of the plasmolemma of the enterocyte from the damaging action of chyme; creates a relatively autonomous paramembrane layer of liquid, providing optimal conditions for the transport of substances through the plasmalemma, creates a capillary effect, functions as a molecular sieve, ensuring a directed flow of certain substances to the membrane, ensures the sterility of the paramembrane layer, adsorbs enzymes from the cavity of the stomach, determines the immunobiological properties of enterocytes, being carrier of secretory immunoglobulin A.

Plasmolemma of microvilli is an elementary biological membrane, characterized by a smaller content cholesterol. The matrix of microvilli is a bundle of 20-40 parallel oriented active fibrils with cross-bridges and an amorphous component. At the top of the microvilli, the fibrils are attached to a special seal, and at the base of newborn rats and puppies, they are freely located in the apical part of the cells. In sexually mature mammals, they are woven into transversely arranged bundles of the fibril terminal network. Due to these differences in the organization of the fine structure of the matrix of microvilli, the plasmolemma has increased fluidity between its bases. When interacting with nutrients (breast milk, solutions of proteins, fats, carbohydrates) they provide a special way of endocytosis absorption. Numerous endocytic tubulo-vesicular formations in the base of microvilli, the apical part of the enterocytes of the villi of the stomach of the newborn rat and dog should be considered., in our opinion, as a specialized structure that provides: - preservation of biological (immunoglobulins-growth factors, suppressor factors, hormones, etc., and plastic, various proteins, fat, carbohydrates, phospholipids, a number of saturated fatty acids) properties of breast milk; - selective transport of proteins, fats and carbohydrates; - carries out the transport of a certain mass of substances, proportional to its functional properties.

Absorption of milk ingredients by puppies during period breastfeeding is carried out at the first stage with the help of endocytic tubulo-vesicular formations, which are detected under the bases of microvilli, in the apical part of striated enterocytes. However, they appear for a very short time (3-5 min.), after which they, losing their characteristic membrane, separate from the apical plasmolemma, turn into endosomes, merge with each other and move to the supranuclear zone, to the structures of the Golgi complex.

The endocytic vesicular mechanism is not only characteristic of absorption large-molecular compounds such as peroxidase, ferritin, cyanocobalamin, hemoglobin, and low-molecular compounds - Ca+2, Fe+3.

Matrix microvilli are essential in the formation of endocytosis. Its composition includes actin, fibrin and villin and calmodulin. It is assumed that actin fibrils with the participation of these proteins carry out the retraction of endocytic vesicles and their removal from the apical surface. However, studies Barkan R.S. using cytochalasin B, demonstrated independent endocytosis of the active cytoskeleton. A similar finding was previously made by Kolgett et al.

Vesicles of the Golgi complex can move in several directions: with the ingredients of breast milk at the level of the upper pole of the nucleus, they can fuse with the lateral plasmalemma and discharge the contents of moderate electron density into the intercellular space. Other vesicles, also with contents that are heterologous compared to the ingredients of breast milk, combining with primary lysosomes to form secondary lysosomes. Thus, endocytosis in striated enterocytes allows relatively fast selective transport of nutrients from the intestinal lumen; is a selective concentration mechanism that allows transporting a large amount of macromolecules without absorbing a correspondingly large volume of extracellular fluid; distinguish between homology and heterologity of the absorbed substance.

Electron-microscopically, it can be seen that striated enterocytes contain about 100 lined vesicles. If it is based on anatomical and histological parameters, I.A. Morozov and co., that one pool of endocytic formations, formed by about 50% of enterocytes on villi, can transfer a volume of about 100 ml. Calculations show that during the entire active digestive period, the transported volume of food can be stored in the vesicles, covering all the needs of the body, although A. M. Ugolev was of the opinion that the nutritional needs of mammals cannot be covered by endocytosis.

On the basis of the endocytosis mechanism, it is possible to explain the transport into the internal environment of the body of various biologically active substances that are part of the breast milk of immature mammals. Transporting transcellularly, they carry out the regulation of genetically determined development and establishment of organs and systems, Harmonious physical and intellectual development of a newborn child. On the basis of the endocytosis mechanism, the absorption of hard-to-hydrolyze macromolecular compounds and inert particles, enteral and pancreatic enzymes, di- and oligo-compounds of protein and carbohydrate nature is also understood.

Thus, receptor endocytosis and the subsequent intracellular mechanisms of transport allowed to optimally solve the seemingly insoluble contradiction between the huge needs for all biological ingredients of food, which are characteristic of all immature mammals, and the relatively low degree of structural and functional development of the stomach and pancreas.

Absorption of nutrients is sharply impaired during artificial feeding. It sharply slows down weight gain, disrupts psychomotor and intellectual development, suppresses the function of the hormonal and enzyme system, no matter how ideal the artificial nutritional mixture is, absorption of 60-70% of proteins causes hypoproteinemia, hyperproduction Ig E with a decrease in the level of T and B lymphocytes, acid-base imbalance, metabolic acidosis, azotemia.

This is what our data show, with the introduction of artificially fed girain animals, the enzyme systems of striated enterocytes are not able to effectively carry out vetricellular transport and transformation of absorbed zira to chylomicron. Considering the fat load and chylomicrons as natural markers, it was possible to show a decrease in the functional capabilities of enterocytes, the possibility of cell damage due to the constant formation of lysosomes in the supranuclear region. Based on the comparison of the transport of chylomicrons in naturally and artificially fed, it was also possible to show the slowing down of the supply of nutrients to the internal environment. On the one hand, this is an adaptive reaction of the mucous membrane, on the other hand, it is one of the mechanisms of malnutrition, retardation of the development of organs and systems, and the organism as a whole. The presence of substances absorbed by the transporter in the thin layer of the newborn's complex mechanism is a decisive factor that ensures its unique adaptation to the type of feeding. The need to maintain the concentration of nutrients in a narrow range of values to ensure homeostasis of the internal environment led to the complication and improvement of the mechanisms of absorption and transport of substances through the mucous membrane in postnatal ontogeny. The relationship between the structure of breast milk and the surface of the thin layer, apparently, it is so optimal that only an insignificant amount of nutrients reaches its distal parts, A. A. Pokrovsky and V. A. Tutelyan believes that the evolution of milk nutrition within each species was carried out somewhat "convergently", ie. e. so foreign mechanisms of lactation and adaptation of newborns to the composition of mother's milk. Violation of absorption, formation of late microbiocenosis, colonization resistance during artificial feeding has a significant effect on the establishment of local immunity, development and establishment of structural and functional units small intestine, kidney and other internal organs.

Despite the fact that there is an opinion that in ontogenesis each period represents a physiologically mature form of existence, nevertheless, the period of lactation represents the stage of preparation of the organism for independent existence, definitive nutrition.

How morphological studies show after the birth of puppies during the early postnatal ontogenesis, the highest (compared to other periods of postnatal ontogenesis) dynamic tension of the late growth, formation and formation of structural and functional units of the organ is noted. In two weeks after birth, the depth of the crypt in the studied sections of the thin layer increased by an average of 2.5 and 4 times. The number of cells on the surface increased accordingly. Linear parameters remained unchanged in the evening; The iliac crest increased by approximately 30%. With such intensive processes of crypt growth, new formation of epithelial cells, preservation of the length of villi in the breast and 30% increase in the pelvis is explained, as noted, by intensive new formation of structural-functional units in the early postnatal period of the life of mammals. This is noted by other researchers. However, as shown by morphometric studies, the histogenetic process proceeds unevenly along the thin layer. The formation and formation of villi and crypts occurs earlier and more intensively in the proximal part, and more slowly - in the distal part of the organ. During the lactation period, this difference becomes less pronounced. Therefore, the proximal part of the small intestine, experiencing a greater functional load, has a greater length of villi and depth of the crypt (the suction surface) than the distal, ilium. Morphological differences along the body, although they are formed under the influence of functional load, their existence already at birth indicates their genetic determination.

After 1 month After birth, the puppy is transferred to the final feeding. At this time, the total length of the thin part is 122.6±5.7 μm, the diameter is 7.3±0.7 and 6.8±0.4 μm on average in the lower and iliac sections. With uniform thickening of all membranes, the length of the villi of the organ is 645.3±11.5 and 558.0±15.5 μm. respectively, in the proximal and distal parts of the thin layer. In the lower part, it is finger-shaped, thinly leaf-shaped with intussusception along the lateral surface. The number of short newly formed villi is significantly less than in the previous study periods. In the iliac crest, the villi are more often leaf-shaped, the crypt has a cylindrical shape, the depth is 266.7±6.1 and 227.3±9.8 μm, respectively, in the iliac and iliac sections. As a result, the index becomes equal to 2, 4 along the mucous membrane. The mucous membrane approaches that of sexually mature animals, but the crypts complete the topographic structure. In its lower and middle thirds, mitotically dividing cells are located, and in the upper one, they differentiate into absorbing goblet and endocrine cells. The signs of cell specialization are especially clearly visible during electron microscopy of different levels of the crypt.

After 1 month after the birth of puppies, the apical plasmolemma forms endocytic vesicles of microvilli at the base. Organelles of striated enterocytes are located below the well-formed terminal network. Analogous reconstruction of the structure of the mucous membrane of the small intestine, the temporary transition of enterocytes to definitive nutrition was noted earlier by A. Yu. Yuldashev. The described picture is observed 3 weeks after birth.

Completion of the structural and functional formation of the thin intestine during the transition to final nutrition occurs simultaneously in other organs of the digestive system - stomach, large intestine, liver, pancreas.

Alteration in the stroma of the villi and the crypt also indicates the completion of its formation by 1 month after birth. This structural transformation reflects the dynamic processes taking place during the early stages of postnatal development. According to the findings of K. R. Rakhimova and A. I. Demidova, these changes are characterized by significant structural and functional modifications associated with the transition from neonatal feeding patterns to definitive nutrition. The maturation of the stroma, as well as its integration with surrounding tissues, is a complex process influenced by both endogenous and exogenous factors.

Furthermore, studies by A. Yu. Yuldashev, G. F. Karimova (58), and B. A. Sadykov highlight a marked increase in the enzymatic activity of invertase and amylase during this critical developmental period. This enzymatic enhancement plays a vital role in the digestive capacity of the gastrointestinal system, aiding in the breakdown and absorption of nutrients necessary for growth and development. However, as noted in the literature, exogenous factors, particularly dietary inputs, serve as primary drivers of structural and functional reconstructions within the thin layer of the intestinal lining. These dietary factors interact with the organism's intrinsic developmental pathways to optimize the functionality of the digestive system.

The course of ontogenetic development of the stomach and other internal organs is largely governed by genetic factors. These factors operate in conjunction with the body's immune and endocrine systems, which significantly influence the pace and quality of organ maturation. The development and stabilization of the immune and endocrine systems are intricately linked to the mode of feeding, whether natural breastfeeding or artificial feeding, as well as to the microbiocenosis along the thin layer of the intestine. The nature of the microbiota plays a pivotal role in shaping these systems, thereby affecting the overall health and resilience of the organism.

This intricate relationship is underscored by research conducted by employees of our laboratory in collaboration with the Laboratory of Gnotobiology at the IEM named after N. F. Hamlea RAMS. Their findings, alongside those of other researchers, provide compelling evidence for the interplay between genetic predispositions, immune regulation, and dietary factors in determining the trajectory of gastrointestinal and systemic development. These studies contribute to a deeper understanding of how early nutritional and microbiological environments shape long-term physiological outcomes.

After transition to final nutrition during 3-6 months. After birth, it increases in length and diameter and becomes thinner later. While preserving the general architectonic mucous membrane, this causes a proportional increase in the number of villi and crypts, and, consequently, the digestive-absorptive surface of the organ. As evidenced by the data of our laboratory staff, the homeomorphosis of the organ is maintained in accordance with the processes of proliferation and differentiation of the crypt epitheliocytes at the rate of their functioning and extrusion on the surface of the villi. In case of their inadequacy (for example, in the case of infectious lesions of the intestines), atrophy of the mucous membrane, changes in the linear parameters of the crypts and villi are possible.

Thus, histogenetic processes occur in the mucous membrane of the thin and late complex, correlating with similar processes in the connecting base of the organ. These processes are closely linked to the peculiarities of digestion, absorption, and the functional activity of the small intestine. Such correspondence emphasizes the dynamic interaction between structural and functional development in the gastrointestinal system. This synchronization suggests that the formation of the mucous membrane and the connective tissue foundation is not isolated but rather occurs in a coordinated manner with similar changes in other internal organs. The structural and functional maturation of these organs occurs in parallel and is regulated by organism-wide intersystemic factors. These factors ensure the optimization of the internal organs' activity during various stages of age-related development. The temporal alignment of these processes reflects a highly intricate biological mechanism, where the small intestine's adaptation to functional demands harmonizes with the overall development of the organism, thereby contributing to an efficient and balanced regulatory framework within the body's systems. This dynamic interplay ensures the proper functioning of digestive processes while supporting the broader physiological needs of the organism in different life stages.

After the transition to final nutrition in puppies and other mammals, the length and diameter of the thin intestine, submucosal and muscular membranes, as well as the absorptive surface, increase. Over the course of 3-6 months, the structural and functional parameters in the thin layer remain relatively stable.

Other employees of our laboratory who studied the functional morphology of the stomach, pancreas, liver, and Brunner's glands in the postnatal period of life note the same. Stabilization of structural and functional changes in the internal organs of mammals during puberty is noted in their works by domestic and foreign researchers.

The type of feeding of immature mammals (dogs, cats, cattle, rats, humans) has a significant impact on the growth and development of organs and systems, the vital activity of the organism, and the state of its organism.

Centuries of human experience and modern scientific research have shown that the only food that provides harmonious development of the child
Mother's (breast) milk. It is an indispensable, perfectly balanced nutritional product produced by the mammary gland of each woman according to the individual characteristics of her child. Breast milk should be considered not only as the simplest and most affordable food product for newborns - it contains immune factors (Ig of all classes), factors of non-specific protection, hormones, proteases and their inhibitors, vitamins, etc. d. make it irreplaceable and non-reproducible with the most advanced technologies.

Numerous studies conducted by us, as well as in other laboratories showed that the ingredients of artificial nutritional mixtures are recognized at the level of absorbing cells as heterogeneous.

As a result, endocytic vesicles with their contents induce the formation of primary lysosomes. The specified property of the lamellar enterocytes of the fasting goat was noted earlier in relation to ferritin, carbohydrates, horseradish peroxidase, and albumin. This is shown when studying the absorption of fat. If the receptor endocytosis is important for the absorption of proteins, it allows to distinguish the type of transported substrate and determine the route of intracellular transport, but the mechanism of selective transport of carbohydrates and fats by endocytic vesicles of striated enterocytes is not yet clear.

Induction of lysosomes during the administration of artificial nutrient mixtures causes a sharp, 2-fold increase in activity lysosomal enzymes in the mucosa of the small intestine and kidney.

As a result of this, as well as the absorption of only 60-70% of proteins, fats and carbohydrates, dysbiosis in the lumen of the small and large intestine, there is a delay in the development of the newborn organism, a violation of the structure and function of organs and systems, first of all it's late, it's late.

By the 4th day of artificial feeding (7 days after birth) in puppies, both the development of secondary lysosomes and a slowdown in the transport of absorbed substances can be observed. This slowdown is marked by the vacuolization of enterocytes, a phenomenon that gradually diminishes within 3 hours following feeding. The vacuolization reflects notable changes in the functional behavior of enterocytes, likely triggered by shifts in digestive and absorptive processes associated with artificial feeding practices. Secondary lysosome formation during this phase plays an essential role in intracellular digestion, while the reduced efficiency in substance transport underscores the intestinal cells' adaptation to the artificial feeding regimen. The vacuolization of enterocytes, serving as a morphological indicator of modified metabolic activity, decreases over time after feeding, pointing to the intestinal epithelium's dynamic adaptation to the new dietary conditions. These observations underline the time-dependent adjustments in the digestive system's functionality as it adapts to artificial nutrition in newborn puppies.

Artificial feeding induces more pronounced changes in the mucous membrane of the small intestine. The mucosa and submucosa become thinner, and lymphocytes are observed between the enterocytes of the elongated, slender villi. There is also a relatively high number of goblet cells, along with an increased presence of mucus between the villi and on the surface of absorptive cells. As noted by I. M. Vorontsov and A. V. Mazurin, the physicochemical differences between breast milk and cow's milk explain why the proteins in cow's milk are more challenging for a newborn to digest and absorb. Enzymes present in breast milk play a crucial role: they are essential not only for the digestion of macromolecules in the small intestine but also for protecting the cells of various organs and systems from potential damage.

Those experimental animals after 1 month after birth, the length is thin, the linear parameters of the villi and crypts, the height of the enterocytes significantly less than control pups. Due to the specified features, the mucous index and the suction surface are also reliably reduced. Artificial food in the early postnatal period causes an increase in the number of interepithelial cells. Interepithelial lymphocytes are described in many organs.

Migrating from the own plate, they are located, as a rule, singly, rarely in groups between enterocytes, 90% of all interepithelial lymphocytes, perform pendulum-like movements in the epithelial layer and vice versa when colonized by fine intestinal microflora and thereby regulate the immune response.

A. M. Ugolev proposes that the entry of urine into the body triggers, within a few minutes, the activation and reproduction of microorganisms residing in the gastrointestinal tract. This process leads to the formation of surface antigens and microbial populations. Based on this observation, the author concludes that the presence of antigenic "aggression" should be regarded as a physiological norm. During phylogenetic and ontogenetic development, this phenomenon has driven the organism to enhance the infiltration of the epithelial layer and fortify the immunological barrier between the external and internal environments. T-lymphocytes, thanks to surface receptors, carry out recognition of antigens in the interepithelial space. Migrating back, they activate B-lymphocytes and the production of immunoglobulins. If this reaction is protective and adaptive, particularly during artificial feeding, the involvement of T-lymphocytes in enhancing the extrusion of striated enterocytes from the surface of the villi significantly impacts the architectonic structure of the stomach's mucosa. Thus, the increased infiltration of the epithelial layer in artificially fed animals, on the one hand, indicates an elevated transport of antigens into the internal environment and, on the other hand, an increase in the extrusion of enterocytes from the surface of the mucous membrane.

A comparative, at different ages, study of the kinetics of the thin late epithelium revealed its essential features in each of the periods of postnatal ontogenesis. Received A. A. Zavarzin, K. A. Zufarov and co., A. Yuldashev, the data indicate that the relationship between the reproduction and differentiation of enterocytes in the crypts at the level of their migration and extrusion on the surface of the villi determine the architectonic mucosa of the organ. Under the influence of numerous factors present in the composition of breast milk, the most optimal relationships are established in the crypt-villi system, which determine the typical structure and function of the mucous membrane characteristic of normal mammals. In the absence of these factors, as well as due to the development of dysbacteriosis in the mucous membrane, a thin layer is noted after 1 month. almost 2-fold reduction of linear parameters of crypts and vortices. After 3 moons Mismatch of proliferation-migration processes in the crypt-villus system causes with a significant decrease in the length of the villi, deepening in 2.2-1.7 times the crypt. A similar structure in the mucous membrane of the small intestine of experimental animals is maintained even 6 months after birth. The functional capabilities of the striated enterocytes in the villi also show distinct differences.

Artificial feeding during the early postnatal phase of a dog's life has a profound impact on the body's structural and functional characteristics. This stage is critical for the organism's development, marked by rapid growth and the progressive maturation of internal systems. The introduction of an artificial diet induces significant shifts in physiological functions and the structural configuration of organs, particularly the gastrointestinal system. These alterations are largely determined by the artificial diet's specific composition and texture, which often vary considerably from those of natural feeding. Over time, however, as the dog transitions to its final nutritional regime—characterized by a more balanced and natural dietary profile—a progressive restoration of the body's architectonic structure takes place. This adjustment demonstrates the organism's inherent capacity to adapt and recover its structural coherence and functional stability, supporting optimal growth and the full maturation of its bodily systems.

CONCLUSION

1. The period of natural feeding of newborn puppies is characterized by the most intensive histogenetic processes: the number of villi, the number and depth of crypts, and the thickness of all organ membranes progressively increase. As a result of hypertrophy and hyperplasia of structural and functional units, the increase in diameter and length of the thin absorbent surface of the organ increases dramatically during the transition to final nutrition.
2. The transition to final feeding coincides with the topographic establishment of the proliferation and differentiation zones of the epithelium in the crypts, the disappearance of endocytic formations at the base of the microvilli, and the increase of immunocompetent cells in the lamina propria of the mucous membrane of the small intestine.
3. In the period of final nutrition, structural and functional changes in the mucous membrane of the small intestine stabilize and are characterized by certain proximal-distal gradients of the linear parameters of villi and crypts, enterocytes, the ratio of absorbing and goblet cells.
4. Artificial nutrition causes a delay in the development of the small intestine, structural and functional units, striated

enterocytes, violation of the transport of absorbed substances, changes the ratio in the system of crypt-villi, goblet and absorbing cells.

5. During natural feeding, bifidobacteria stably predominated in control animals from the 17th day after birth. The specific weight of other microorganisms (lactobacillus, enterococci and staphylococci) is insignificant and remains at the same level only in the ileal cavity. Bacteroidetes in the evening after the transition to the final nutrition are revealed. This indicates a gradual and stable increase in the intensity of colonization by obligate microorganisms and a decrease in these indicators for facultative representatives during natural feeding of animals.
6. Artificial feeding, which significantly affects the establishment of anaerobic and aerobic microflora in the intestines, causes the development of dysbacteriosis, the degree of which correlates with the degree of hypotrophic organism.

LITERATURE REFERENCES

1. Абольян Л.В., Новикова С.В., Дерю А.В. Длительность грудного вскармливания младенцев, наблюдавшихся в детских поликлиниках,имеющих и не имеющих звания ВОЗ/ЮНИСЕФ «Больница ,доброжелательная к ребѐнку» . // Педиатрия . - 2015. - №5. - С.89-95.
2. Боровик Т.Е., Гусева И.М., Звонкова Н.Г, Семенова Н.Н., Лукоянова О.Л., Захарова И.Н., Степанова Т.Н., Бушуева Т.В., Суржик А.В., Моз- 162 жухина Л.И., Руссова Т.В. Особенности организации и потребления пищевых веществ детьми в возрасте от 1 года до 3 лет, проживающими в центральном федеральном округе РФ (Москва, Иваново, Ярославль). Вопросы питания. 2016.Т.85.№6.С.86-94.
3. Булатова О.М., Нетребенко О.К.,Богданова Н.М. Влияние применения пробиотических продуктов в период беременности и кормления грудью на становление кишечной микробиоты ребѐнка. // Педиатрия . - 2015. - №3. - С.121-128.
4. Георгиева О.В., Конь И.Я., Абрамова Т.В., Гурченкова М.А. Аспекты питания детей старше первого года жизни и современные специализированные отечественные продукты на молочной основе. Вопросы питания. 2015.Т.84.№53.С.96.
5. Конь И.Я., М.В. Гмошинская, Т.В. Абрамова.Питание беременных женщин,кормящих матерей и детей 1 года жизни.-М.:МЕДпрессинформ,2014.-160с.
6. Кильдиярова Р.Р., Макарова В.И. Пропедевтика детских болезней. –М.: ГЭОТАР-Медиа, 2012. – 587-628 сс.
7. Мачарадзе Д.Ж. О патогенезе пищевой аллергии. Педиатрия. 2016;95(6):151-164.
8. Национальная программа оптимизации питания детей первого года жизни в Российской Федерации / Союз педиатров России [и др.]. 2009.-70 с.
9. Национальная программа оптимизации питания детей в возрасте от 1 года до 3 лет в Российской Федерации / Союз педиатров России [и др.]. 2-е изд., испр. И доп. – М.; ПедиатрЪ, 2016.-36с.
10. Нетребенко О.К., Украинцев С.Е., Дубровская М.И. Профилактическая медицина: питание младенца и программирование. Педиатрия. 2016; 95(2): 124-132.
11. Педиатрия: национальное руководство: в 2 т. – М.: ГЭОТАР - Медиа, 2009. – Т.1. – с.132-147.

12. Романюк Ф.П. Питание детей раннего возраста. Пособие для врачей. – Спб., 2015.- 68с
13. Юлдашев А.Ю. Иммунная система слизистых оболочек как самостоятельная функциональная система организма / А.Ю. Юлдашев, М.А. Юлдашев.// Морфология. - 2006. Т. 129, № 4. – С.145.
14. Юлдашев А.Ю., Каххаров З.А., Юлдашева М.А, Ахмедова Х.Ю. Функциональная морфология системы слизистой оболочки тонкой кишки.- Ташкент, 2008.- 48 с.
15. Рахматова М.Х., Юлдашева С.З., Каххаров З.А., Юсупова Л.Ю. Структурные механизмы формирования интеграции иммунной и пищеварительно-всасывательной функций в тонкой кишке//Матер. научно-практ. конф. «Актуальные проблемы морфологии / Проблемы биологии и медицины, 2013, № 3 (74). – С. 73-74.
16. Rakhmatova M.Kh., Tarinova M.V.,Nugmanova U.T.,Nishanova A.A. Structure of the small Intestinal Mucosa after Acute Hemorrhagic Shock and Reperfusion of the Ischemic Limbs//British.J.of Medicine and Medical Research, 2016, 13(10). – P. 1–6.
17. Рахматова М.Х., Юлдашев А.Ю., Таринова М.В. Функциональная морфология слизистой оболочки тонкой кишки и особенности ее адаптации// International Scientific and Practical Conference «World Science», №4(20), vol.6, April 2017 – Dubai, UAE. – P. 38–43.
18. Юлдашева С.З., Тиллашайхова М.Х. Интеграция пищеварительно-всасывательной и иммунной функции в слизистой оболочки тонкой кишки и регуляции гомеостаза// Европейский журнал биомедицины и наук о жизни, Biomedical.- 2017, №2.- С. 3-7
19. Dommett R. Zilbauer M. Innate immune defense in the human gastrointerstinaltrast //Molec. Immunol.-2015.-Vol.42,№ 8.-P.903-91