Scientific Papers. Series D. Animal Science. Vol. LXVI, No. 1, 2023
ISSN 2285-5750; ISSN CD-ROM 2285-5769; ISSN Online 2393-2260; ISSN-L 2285-5750

MORPHOFUNCTIONAL FEATURES OF MECKEL'S DIVERTICULUM OF GEESE

Olena BYRKA, Viktoriia YURCHENKO, Mykola KUSHCH, Liubov LIAKHOVICH

State Biotechnological University, 44 Alchevskikh Str., Kharkiv, Ukraine

Corresponding author email: histology@ukr.net

Abstract

The parameters and dynamics of the development of Meckel's diverticulum in large gray geese aged one day to 5 years were determined. The changes in the length, cross-sectional area and wall area of the Meckel's diverticulum indicate that its growth stops by 3 months of age. The age-related morphofunctional indicators of lymphoid tissue formation in the wall of Meckel's diverticulum were determined. Diffuse lymphoid tissue is predominant in the composition of lymphoid tissue. Full morphofunctional maturity of the lymphoid tissue with the development of four levels of its structural organization is observed at the age of 21 days in geese. The lymphoid tissue in the wall of Meckel's diverticulum reaches its maximum development by the age of 3 months, which must be taken into account when raising large gray geese and conducting experimental studies.

Key words*: geese, lymphocytes, lymphoid tissue, Meckel's diverticulum.*

INTRODUCTION

The lymphoid tissue of the mucous membranes makes up more than half of the body's lymphoid tissue, forming their unified immune system (Schuh, 2020; Junior et al., 2018; Kang et al., 2014; Cesta, 2006; Ciriaco et al., 2003; Jeurissen et al., 1994; Kendall, 1980). The lymphoid tissue of the mucous membrane of the digestive tube contains the largest pool of immunocompetent cells: up to 80% of B-lymphocytes, macrophages, antigen-stimulated T-helpers, plasma cells. The formation of immunoglobulin molecules in mucous membranes occurs on the surface of epitheliocytes, where they provide local antibacterial and antiviral protection (Meek et al., 2022; Rehfeld et al., 2017; Day & Schultz, 2014; Rehfeld et al., 2013; Korver, 2006; Friedman et al., 2003). In lymphoid formations of the digestive tube of birds, lymphoid tissue can be located diffusely, forming clusters in the form of lymphoid nodules, tonsils, Peyer's patches, Meckel's diverticulum - lymphoid diverticulum of the jejunum (Khomich et al., 2020; Makhotina et al., 2020; Kushch et al., 2019; Dishluk & Orlova, 2017; Al-Juboury et al., 2016; Kaspers & Göbel, 2016; Kharchenko & Lykova, 2013; Brandtzaeg et al., 2008; Besoluk et al., 2002; Jeurissen et al., 1989).

In 1809, Johann-Friedrich Meckel Jr. (Meckel J.F., 1781-1833) first described the embryonic yolk duct in humans, named Meckel's diverticulum in his honor (Meckel diverticulum) (Ibrahim & Mohamed, 2023; Kafshgari et al., 2023; Farrell & Zimmerman, 2020; Lindeman & Søreide, 2020; Hamilton & Arnason, 2015; Farah et al., 2015; Opitz et al., 2006).

The first reports on the origin, structure and functional significance of Meckel's diverticulum, published in 1984, laid the foundation for its morphological studies in birds (Olah & Glick, 1984; Olah et al., 1984). Features of the morphogenesis of Meckel's diverticulum in the postembryonic period of ontogeny have been studied only in chickens and ducks (Mazurkevych & Khomych, 2017; Khomych & Mazurkevych, 2015; Mazurkevych, 2013a; Mazurkevych, 2013b; Mazurkevych, 2012; Jamroz et al., 2004; Kalynovska, 2004; Bar-Shira et al., 2003; Friedman et al., 2003; Besoluk et al., 2002; Jeurissen et al., 1994; Jeurissen et al., 1989; Olah et al., 1984; Olah & Glick, 1984). In this regard, the features of the development of Meckel's diverticulum in geese, its lymphoid tissue and the levels of its structural organization require in-depth study.

MATERIALS AND METHODS

The material for the study was Meckel's diverticulum from clinically healthy large gray geese 1-, 3-, 7-, 14-, 21-day-old, 1-, 2-, 3-, 6-, 8-month-old and 1-, 2- , 3- and 5-year-old (n = 5). The material was fixed in 8% aqueous neutral formalin and embedded in paraffin. Serial sections 7-8 µm thick were stained with H&E, aniline-blau-orange according to Mallory, Kelemen, Brachet. The total population of endocrinocytes was detected by the Grimelius method. Enterochromaffin EC cells were identified by the Masson-Gamperl method modified by I. Singh. Lymphoid cells were determined on Pappenheim-stained imprint preparations (Horalskyi et al., 2019).
The cross-sectional area of Meckel's diverticulum, its walls, membranes, crypts, and lymphoid formations was defined using a *Jenamed-2* light microscope. *Image Tools 3.6* software was used to determine the morphometric parameters of the microstructure of Meckel's diverticulum. Endocrinocytes were counted using an eyepiece grid, in terms of 1 mm^2 of the mucous membrane. Obtained digital indicators were processed using one-way ANOVA and Student's t-test. The data obtained in the tables are presented as a standard deviation. The reliability of the difference in indicators was determined by the reliability criterion (td) and Student's tables.
The experiment was conducted in accordance with generally accepted principles of humane treatment of animals (Law of Ukraine "On the Protection of Animals from Cruelty Treatment", No. 3447-IV as of 21.02.2006, Kyiv; European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Strasbourg, 1986). The work was done at the Department of Normal and Pathological Morphology of the State Biotechnological University (Kharkiv, Ukraine).

RESULTS AND DISCUSSIONS

Resulting from the conducted study, it was established that Meckel's diverticulum (MD) in geese in embryogenesis is a derivative of the yolk stalk. In the postembryonic period of ontogenesis, MD is a permanent peripheral organ of the immune system, has a conical shape, and is tubular in structure. It is located on the antimesenteric surface of the loop of the jejunum, its apex is directed caudo-ventrally, and its base communicates with the lumen of the jejunum (Figure 1).

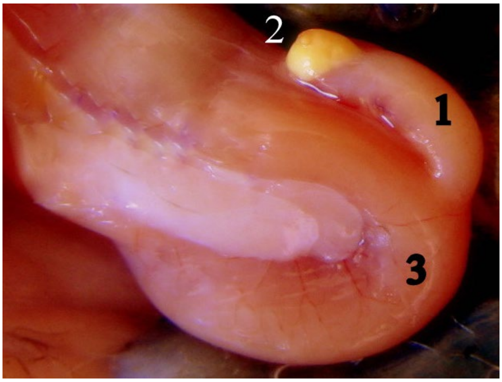

Figure 1. Loop of jejunum with Meckel's diverticulum of a 14-day-old gosling (macropreparation): 1 - Meckel's diverticulum; 2 - the rest of the yolk; 3 - jejunal loop

The length of the segments of the small intestine before and after the MD in geese of all the studied age groups is stable at an average ratio of 0.59: 0.41 cm. The length of the MD from a day- to 2-month-old geese increases in direct proportion to body weight, the total length of the intestine and, especially, the thin section. In the first three months of a bird's life, the length of the MD increases by 3.1 times (17.50 ± 3.50 mm). In 6-month-old geese its length decreases to 13.25 ± 1.55 mm, and from the age of 8 months to 5 years it is in the range of 13.67 ± 0.33 - 12.67 ± 0.33 mm.
The area of the transverse section of the MD by the age of 3 months increases by 34 times (13.84 ± 0.90 mm^2), and the area of the wall of the MD increases by 36 times, reaching a maximum value (12.63 ± 0.82 mm^2). From the age of 3 months to 3 years, the cross-sectional area of the MD decreases by 1.5 times (9.36 ± 0.30 mm^2), and up to 5 years of age - by 1.7 times (7.97 ± 0.12 mm^2). The wall area of the MD of geese up to 3 years of age decreases by 1.4 times (8.92 ± 0.23 mm^2), and up to 5 years of age by 1.8 times (6.84 ± 0.13 mm^2), which indicates a direct correlative dependence in the development of the compared MD structures.
An increase in the area of transverse sections of the MD and its wall up to 3 months of age

occurs due to a more intensive development of the mucosa, the formation of cellular structures of the epithelial layer in it, its own plate and submucosa, as well as the formation of folds and crypts that increase the total area of the mucosa, through which the immune system controls the antigens that fall on its surface (Schuh, 2020; Day & Schultz, 2014; Koutsos & Klasing, 2014; Casteleyn et al., 2010; Friedman et al., 2003; Jamroz et al., 2004; Besoluk et al., 2002; Jeurissen et al., 1989). The absolute area of the mucous membrane of the MD by the age of 3 months increases by 65 times (11.63 ± 0.73 mm^2), and the relative area reaches a maximum value of 92.08%. From 6 months to 5 years of age, the absolute area of the mucous membrane decreases to 5.55 ± 0.27 mm^2. The relative area of the mucous membrane of the MD of 5-year-old geese decreases, but remains at a fairly high level of 81.14%.

With age, structural reorganization of the mucous membrane of the MD occurs. Up to 3 days of age, the epithelial layer is represented by a single-layer prismatic border. It defines prismatic cells with a border, goblet, endocrine and cambial cells with mitotic figures. The number of goblet cells in the epithelial layer prevails in 21-day-old geese and persists up to 2 years of age. The secretion of goblet cells of the epithelium act as a protective barrier, it constantly renews the coating of the mucous membranes, promotes the transport of secretory immunoglobulin to its surface, providing the first line of immune defense (Kushch et al., 2020; Yu et al., 2020; Ross & Pawlina, 2015; Day & Schultz, 2014; Besoluk et al., 2002; Sharma, 1991).

In 21-day-old geese, in the total population of endocrinocytes of the epithelial layer, the number of EC cells has a maximum value of 97.66%. From one month to 2 years of age, it is 84.81% and 83.60%, respectively, and in 3-5-year-olds it is 43.40 and 33.73%. Based on the fact that the biologically active substances of EC cells are involved in the regulation of the processes of proliferation, growth, and differentiation of cells in tissues, these processes are reduced in the MD of geese of older age groups (Kushch et al., 2019; Koutsos & Klasing, 2014; Bar-Shira et al., 2003).

In geese up to 3 months of age, branched folds predominate in the MD mucosa, which is associated with the process of crypt formation. Thus, in 21-day-old geese, compared with 1-day-old geese, the area of crypts increases by 11 times, and in 2-month-old geese - by 17.9 times. From the age of 6 months, the folds of the mucous membrane acquire a columnar and triangular shape. The area of crypts in 6-month-old geese, compared to 3-month-old ones, decreases by 1.7 times. At the same time, individual crypts are expanded, their wall is lined with squamous epithelium, they are filled with a thickened oxyphilic secret, which contains lymphocytes, eosinophils and cellular detritus. In geese from 1 to 5 years of age, the crypts are solitary, their lumen is narrowed, and some take the form of cysts. All this leads to a decrease in the source of regeneration of the integumentary epithelium and the total area of the mucous membrane (Doneley, 2016; Samour, 2015; Bar-Shira et al., 2003; Besoluk et al., 2002).

The epithelium of the folds and crypts of the mucous membrane of the MD of geese in the postnatal period of ontogenesis is unevenly infiltrated with lymphocytes. They interact with antigens, performing the function of the first protective barrier, which is typical for lymphoid formations associated with mucous membranes (Junior et al., 2018; Davison, 2014; Ruddle & Akirav, 2009; Bar-Shira et al., 2003; Friedman et al., 2003).

In the lamina propria of the mucous membrane of the MD of 1-day-old geese, diffuse lymphoid tissue (LT) is formed, structures of loose fibrous connective tissue and vessels of the microvasculature are formed. Reticulocytes, lymphocytes, macrophages, eosinophils, reticular fibers and single fibroblast cells are detected in the lamina propria. Lymphocytes are predominant in the cell population. Single lymphocytes are found intraepithelially and on the surface of the mucous membrane. The absolute area of the LT is 0.176 ± 0.009 mm^2, and the relative area is 50.30%. (Figures 2, 3).

With the age of geese, diffuse LT gradually occupies the entire area of the mucosal lamina propria. In 3-day-old geese, compared to 1-day-old geese, the LT occupies 58.00% of the wall area of the MD. Its absolute area increases by 4.3 times (0.76 ± 0.02 mm^2).

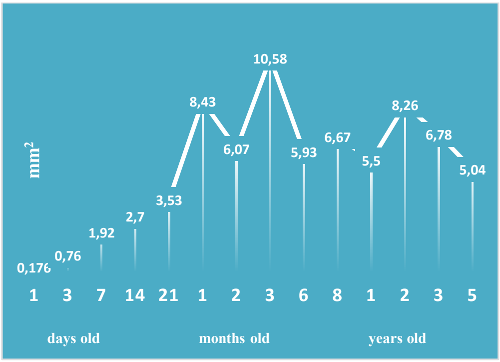

Figure 2. The absolute area of lymphoid tissue in the wall area of Meckel's diverticulum of geese, mm^2

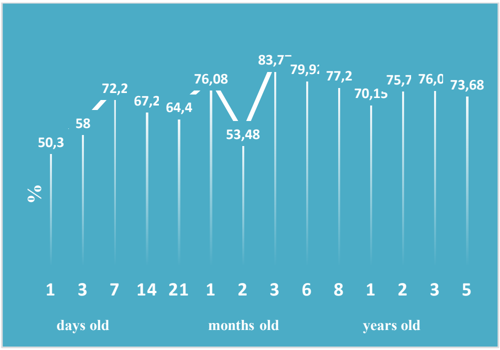

Figure 3. The relative area of lymphoid tissue in the wall area of Meckel's diverticulum of geese, %

As part of diffuse LT denser accumulations of lymphocytes in the form of prenodules (3-4 per section area) are detected for the first time. Around the crypts, single primary lymphoid nodules are formed, which are an integral part of the immune structures associated with the mucous membrane (Nochi et al., 2018; Kaspers & Göbel, 2016; Day & Schultz, 2014; Randall et al., 2008; Friedman et al., 2003). They are based on reticular tissue populated by small lymphocytes, eosinophils and single macrophages. The periphery of primary lymphoid nodules is surrounded by fibroblasts and single collagen fibers.

From the age of 7 days, LT is detected in the mucous, muscular and serous membranes of the MD. Diffuse LT, prenodules and primary lymphoid nodules continue to be formed in the mucosa. The absolute area of the lymphoid tissue increases by 11 times (1.92 ± 0.04 mm^2), and the relative area by 14.20%, up to 72.20%. Lymphocytes are detected both intraepithelially and on the surface of the mucous membrane of the MD. Diffuse LT fills the subepithelial areas of the main mucosal lamina. In the deep layer of the lamina propria around the crypts, prenodules and primary lymphoid nodules are formed, surrounded by a connective tissue membrane. In the muscular and serous membranes, diffuse LT is detected around the blood vessels.

In 14-day-old geese, LT is represented by a diffuse form, prenodules, and emerging primary lymphoid nodules. The relative area of LT decreases to 67.20%, which is due to an increase in the area of the crypts (17.93%). The absolute area of LT increases by 1.4 times (2.70 ± 0.12 mm^2). Lymphocytes are detected intraepithelially, on the surface of the mucous membrane, as well as in the secretion of crypts. Primary lymphoid nodules are found in the deep layer of the lamina propria of the MD mucosa. In the muscle membrane, diffuse LT is detected between the muscle layers. Primary lymphoid nodules appear in the serous membrane of the MD.

In 21-day-old geese, LT in the MD wall is represented by a diffuse form with prenodules, primary and secondary lymphoid nodules, which is an indicator of the full morphofunctional maturity of the MD as a peripheral organ of immunogenesis. The absolute area of LT increases (3.53 ± 0.21 mm^2), while the relative area decreases (64.40%), which is associated with an increase in the area of the crypts. Lymphocytes are detected on the surface of the mucous membrane, interepithelially and as part of the secretion of crypts. In the surface layer of the main plate of the mucous membrane, lymphocytes are located diffusely, in some places very densely. The total area of diffuse LT (87.00%) significantly exceeds the area of lymphoid nodules (13.00%). Formed primary and solitary secondary lymphoid nodules are revealed in the deep layer of the lamina propria (Figure 4).

In the central, light part of the secondary lymphoid nodules, the cells are concentrated in groups, in the form of "rosettes". In the center of each of them is a macrophage surrounded by lymphocytes, which indicates antigen presentation (Figure 5).

Between the rosettes, a reticular skeleton is clearly visible, in which small, medium and large lymphocytes with pyroninophilic cytoplasm are located. The periphery of secondary lymphoid nodules is populated with small lymphocytes in 4-5 rows. In the muscle membrane, diffuse LT is detected between the layers of muscle bundles. In places, lymphocytes surround the blood vessels, forming clusters in the form of "couplings". Single primary lymphoid nodules are formed on the mesenteric surface of the serous membrane of the MD, around the blood vessels.

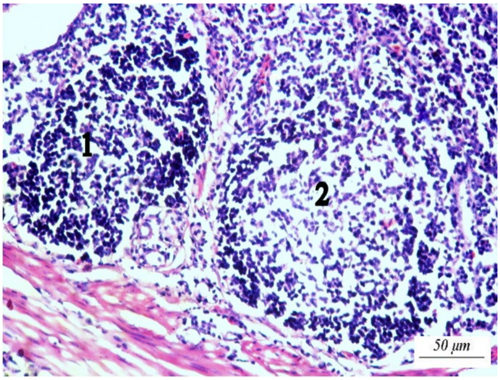

Figure 4. Primary (1) and secondary (2) lymphoid nodules in the lamina propria of the mucosa of Meckel's diverticulum of a 21-day-old gosling (H & E)

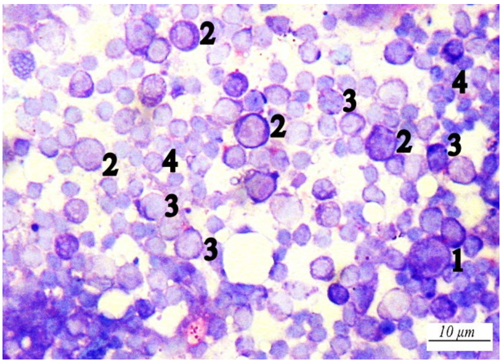

Figure 5. The central part of the secondary lymphoid nodule: 1 - a macrophage in the center of the "rosette"; 2 - large lymphocytes; 3 - medium lymphocytes; 4 - small lymphocytes. Pappenheim staining

In one-month-old geese, the absolute (8.43 ± 0.48 mm^2) and relative (76.08%) area of LT in the MD wall increases. Diffuse LT predominates in the proper layer of the mucous membrane and around the crypts (82.90%) with denser accumulations in the form of prenodules. Lymphoid nodules (17.10%) are detected in the deep layer of the lamina propria of the mucous membrane, the submucosa, between the layers in the muscular and serous membranes. In the center of individual lymphoid nodules, cells with mitotic figures, as well as plasma blasts and plasma cells, are detected. There is antigen presentation, proliferation and differentiation of cells characteristic of the antigenic response and the formation of secondary lymphoid nodules.

In two-month-old geese, compared to one-month-old geese, the absolute (6.07 ± 0.31 mm^2) and relative area of LT (53.48%) decreases, which is associated with an increase in the area of crypts (39.66%). Diffuse LT and lymphoid nodules account for 85.60% and 14.40% of the total LT area, respectively. Diffuse LT is formed subepithelially in its own layer of the mucous membrane and around the crypts. Primary lymphoid nodules are located in the deep layer of the lamina propria, and secondary, in addition to the deep layer of the lamina propria, are concentrated in the submucosal layer of the mucosa, between the layers in the muscular and serous membranes.

In three-month-old geese, the absolute (10.58 ± 0.65 mm^2) and relative area (83.77%) of LT increase. At the same time, the area of diffuse LT decreases (54.90%), while the area of lymphoid nodules increases (45.10%). An increase in these morphological components is considered an indicator of the activation of the main function of the organ (Kaspers & Göbel, 2016; Fellah et al., 2014; Ruddle & Akirav, 2009; Bar-Shira et al., 2003). Diffuse lymphoid tissue with prenodules is concentrated in the lamina propria. Primary lymphoid nodules (17.00%) are located in the deep layer of the lamina propria, in the submucosa of the mucous membrane, as well as in the muscular and serous membranes (Figure 6).

Secondary lymphoid nodules (28.10%) are concentrated mainly in the deep layer of the lamina propria and the submucosa of the mucosa. In 3-month-old geese, the structures of immune protection in the wall of the MD reach full and maximum development, which must be taken into account when growing large gray geese.

From the age of 6 months, both quantitative and qualitative indicators of LT noticeably change. Its absolute (5.93 ± 0.29 mm^2) and relative (79.92%) area decreases. The relative area of diffuse LT increases (85.50%). It is concentrated in its own layer of the mucous membrane subepithelially and around the crypts. The relative area of lymphoid nodules is 14.50%. Primary lymphoid nodules predominate in number, located in the deep layer of the lamina propria, the submucosa of the mucosa, and between the layers in the muscle membrane. Secondary lymphoid nodules are longitudinally oval in shape, concentrated in the deep layer of the lamina propria and the submucosa of the mucosa.

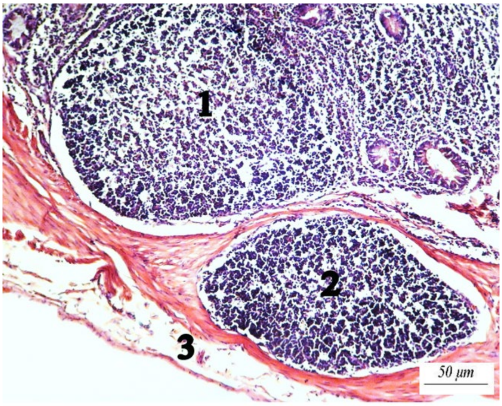

Figure 6. A primary lymphoid nodule (1) in the submucosal base of the mucosa and in the muscle sheath (2) of the wall of Meckel's diverticulum of a 3-month-old gosling; 3 - serous membrane (H & E)

In accordance with the biological characteristics of the large gray geese, 8 months of age is considered to be the period of reaching puberty. The absolute area of LT, compared to 6-month-old ones, slightly increases (6.67 ± 0.41 mm^2), while the relative area decreases (77.20%). The relative area of diffuse LT decreases (84.30%), while that of lymphoid nodules increases (15.70%). Formed primary lymphoid nodules are localized in the deep layer of the lamina propria and the submucosa of the mucous membrane, and in the muscular and serous membranes they are placed one after another, creating ribbon-like formations. The number of secondary lymphoid nodules increases, which are localized in the deep layer of the lamina propria and submucosa. Next to some secondary lymphoid nodules, bud-shaped formations from lymphocytes are determined and are the beginning of the formation of primary lymphoid nodules.

In one-year-old geese, the absolute (5.50 ± 0.29 mm^2) and relative (70.15%) area of LT decreases. Diffuse LT predominates (80.70%) in the main plate of the mucous and muscular membranes of the MD. The quantitative ratio of primary (14.20%) and secondary (5.10%) lymphoid nodules changes. Primary lymphoid nodules are spherical in shape, located in the deep layer of the lamina propria and muscle membranes, and secondary ones are detected in the submucosa of the mucous membrane.

In 2-year-old geese, the absolute (8.26 ± 0.52 mm^2) and relative (75.71%) area of LT in the MD wall slightly increased. However, the relative area of diffuse LT decreases (76.00%), while the area of lymphoid nodules increases (24.00%). The relative area of primary lymphoid nodules (20.60%) prevails over secondary ones (3.40%). Primary and secondary nodules are predominantly oval in shape. In the deep layer of the lamina propria, the mucous membranes are placed singly. They have a ribbon-like placement in the submucosal layer of the mucosa, in the muscular and serous membranes (Figure 7).

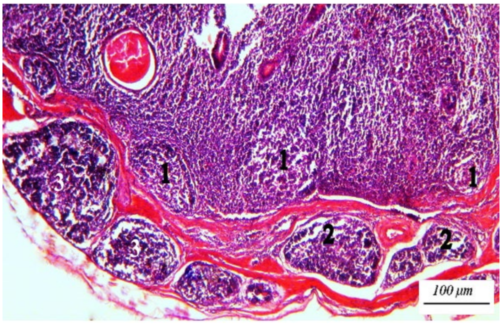

Figure 7. Primary lymphoid nodules in the wall of Meckel's diverticulum of a 2-year-old goose: 1 - in the lamina propria of the mucous membrane; 2 - in the muscular membrane; 3 - in the serous membrane (H & E)

In 3-year-old geese, the absolute LT area in the MD wall slightly decreases (6.78 ± 0.35 mm^2), while the relative area increases (76.01%). Diffuse LT (88.50%) is located in the main lamina of the mucous membrane subepithelially, around the crypts, in the interlayers between the layers of the muscular membrane. Single primary lymphoid nodules (7.08%) of an oval shape are located in the submucosa of the mucosa. Secondary lymphoid nodules (4.42%) are located in the deep layer of the main lamina and the submucosa of the mucosa.

In 5-year-old geese, the absolute (5.04 ± 0.20 mm^2) and relative (73.68%) LT area decreases. In the MD wall, the diffuse form prevails (84.00%) with single prenodules, which in the mucous membrane is located in its own layer, and mainly around the blood vessels in the muscular one. Primary lymphoid nodules (8.90%) are located in the deep layer of the lamina propria, in the submucosal layer of the mucosa, and in groups of 2-3 in the muscular membrane. Secondary lymphoid nodules (7.10%) are longitudinally oval in shape, concentrated in the submucosal base of the mucosa.

CONCLUSIONS

The conducted studies determined the parameters and dynamics of the development of Meckel's diverticulum of the jejunum in large gray geese from 1-day-old to 5 years of age. It has been established that the growth of Meckel's diverticulum stops by the age of 3 months. In the postnatal period of ontogenesis in the Meckel's diverticulum, an age-related structural and functional reorganization occurs, manifested by a change in the structure of crypts and their area, the quantitative composition of cells in the integumentary epithelium, and the form of development of lymphoid tissue. Up to 2 years of age, goblet cells predominate in the integumentary epithelium of the mucous membrane of the Meckel's diverticulum. A decrease in the number of EC cells in the total population of endocrinocytes of the epithelial layer of the mucous membrane in geese of 3 and 5 years of age is associated with a decrease in the processes of proliferation, growth, and differentiation of cells in the tissues of the Meckel's diverticulum wall.

Lymphoid tissue of the mucous membrane of Meckel's diverticulum in its diffuse form is detected from 1-day-old geese. In 3-day-old geese, prenodules appear in diffuse lymphoid tissue, and centers of formation of primary lymphoid nodules appear around the crypts. In 7-day-old geese, lymphoid tissue is represented by a diffuse form with prenodules and emerging primary lymphoid nodules. In 14-day-old geese, the diffuse form, prenodules, and first formed primary lymphoid nodules are detected in the lymphoid tissue of the Meckel's diverticulum. Full morphofunctional maturity of the lymphoid tissue in the Meckel's diverticulum with the development of four levels of its structural organization was recorded in 21-day-old geese. In geese of 3 months of age, the structures of lymphoid tissue reach their maximum development, which must be taken into account when raising geese, forming production groups, carrying out diagnostic, preventive and therapeutic measures, as well as when studying the mechanism of action of immunomodulatory biological products. From 6 months to 5 years of age, the relative area of diffuse lymphoid tissue significantly exceeds the area of lymphoid nodules.

ACKNOWLEDGEMENTS

The authors express their sincere gratitude to Professor V.T. Khomych (National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine).

REFERENCES

Al-Juboury, R., Daoud, H., & Al-Arajy, A. (2016). Comparative anatomical, his- tological and histochemical studies of the oesophagus in two different Iraqi birds (*Columba palumbus* and *Tyto alba*). *International Journal of Advanced Research in Biological Sciences*, *2*(12), 188–199. DOI:10.13140/RG.2.1.2961.2403.

Bar-Shira, E., Sklan, E., & Friedman, A. (2003). Establishment of immune competence in the avian GALT during the immediate post-hatch period. *Develop. Comp. Immunol.,* 27, 147-157.

Besoluk, K., Eken, E., & Boydak, M. (2002). Morphological studies on Meckel's diverticulum in geese (*Anser anser domesticus*). *Anat. Histol. Embryol*., 31(5), 290-292.

Brandtzaeg, P., Kiyono, H., Pabst, R., & Russell, M.W. (2008). Terminology: nomenclature of mucosa-associated lymphoid tissue. *Mucosal Immunology*, 1(1), 31-7. doi: 10.1038/mi.2007.9

Casteleyn, D., Doom, M., Lambrechts, E., Van den Broeck, W., Simoens, P., & Cornillie P. (2010). Locations of gut associated lymphoid tissue in the 3-month-

old chicken: A review. *Avian Pathology, 39* (3), 143–150. https://doi.org/10.1080/03079451003786105
Cesta, M.F. (2006). Normal structure, function, and histology of mucosa associated lymphoid tissue. *Toxicologic Pathology,* 34(5), 599-608. DOI: 10.1080/01926230600865531
Ciriaco, E., Perez Pinera, P., Díaz-Esnal, B., & Laurà, R. (2003). Age-related changes in the avian primary lymphoid organs (thymus and bursa of Fabricius). *Microscopy Research and Technique, 62* (6), 482–487.
Davison, F. (2014). The importance of the avian immune system and its unique features. In: Schat, K. A., Kaspers, B., & Kaiser, P. (Eds). Avian Immunology. *Academic Press,* London., 1–9.
Day, M.J., & Schultz, R.D. (2014). *Veterinary Immunology*: *Principles and Practice*, Second Edition. E-book.
Dishluk, N. V., & Orlova, A. V. (2017). Osoblyvosti budovy stravokhodu ta yoho imunnykh utvoren' perepeliv [Structure's features of esophagus and it's immune formations of quails]. *Scientific Messenger of Lviv National University of Veterinary Medicine and Biotechnologies named after S. Z. Gzhytskyj, 77* (19), 3–6. [in Ukrainian]. DOI: https://doi.org/10.15421/nvlvet7701.
Doneley, B. (2016). *Avian medicine and surgery in practice: Companion and aviary birds.* Second Edition. CRC Press. https://doi.org/10.1201/9781315371047
European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes. (1986). Strasbourg, France. https://rm.coe.int/1680900466
Farah, R.H., Avala, P., Khaiz, D., Bensardi, F., Elhattabi, K., Lefriyekh, R., Berrada, S., Fadil, A., & Zerouali, N.O. (2015). Spontaneous perforation of Meckel's diverticulum: a case report and review of literature. *Pan African Medical Journal,* 20, 319. doi: 10.11604/pamj.2015.20.319.5980. eCollection 2015.PMID: 26175810
Farrell, M.B., & Zimmerman, J. (2020). Meckel's Diverticulum Imaging. *Journal of Nuclear Medicine Technology*, *48(3),* 210-213.
Fellah, J. S., Jaffredo, T., Nagy, N., & Dunon, D. (2014). Development of the avian immune system. In: Schat, K. A., Kaspers, B., & Kaiser, P. (Eds.). *Avian immunology.* Academic Press, London, 45–63. https://doi.org/10.1016/B978-0-12-396965-1.00003-0
Friedman, A., Bar-Shira, E., & Sklan, D. (2003). Ontogeny of gut associated immune competence in the chick. *World's Poultry Science Journal, 59* (2), 209–219.
Hamilton, C.M., & Arnason, T. (2015). Ileitis associated with Meckel's diverticulum. *Histopathology, 67*(6), 783-91. doi: 10.1111/his.12717.
Horalskyi, L.P., Khomych, V.T., & Kononskyi, O.I. (2019). *Osnovy histolohichnoji tekhniky i morfofunktsionalni metody doslidzhennia u normi ta pry patolohiji [Fundamentals of histological technique and morphofunctional research methods in normal and pathology].* Polissia, Zhytomyr [in Ukrainian].
Ibrahim, A.I., & Mohamed, A.K.A. (2023). Ileal atresia with intraluminal Meckel's diverticulum. *Journal of Pediatric Surgery Case Reports, 89.* https://doi.org/10.1016/j.epsc.2022.102552
Jamroz, D., Wertelecki, T., & Wiliczkiewicz, A. (2004). Dynamics of yolk sac resorption and post-hatching development of the gastrointestinal tract in chickens, ducks and geese. *J. Anim. Physiol. Anim. Nutr. (Berl.).*,88 (5-6), 239-250.
Jeurissen, S.H.M., Janse, E.M., & Koch, G. (1989). Meckel's diverticle: a gut-associated lymphoid organ in chickens. *Advances in Experimental Medicine and Biology*, 237, 599–606.
Jeurissen, S. H. M., Janse E. M., Koch, G., & De Boer, G. F. (1989). Postnatal development of mucosa-associated lymphoid tissues in chickens. *Cell and Tissue Research*, 258, 119–124.
Jeurissen, S. H. M., Vervelde, L., & Janse, E. M. (1994). Structure and function of lymphoid tissues of the chicken. *British Poultry Science*, 5, 183-207.
Junior, A. F., Santos, J. P., Sousa, I. O., Martin, I., Alves, E. G. L., & Rosado, I. R. (2018). *Gallus gallus domesticus*: Immune system and its potential for generation of immunobiologics. *Ciencia Rural*, 48(8), 1–8. https://doi.org/10.1590/0103-8478cr20180250
Kafshgari, R., Majd, A.R., & Ledari, A.T. (2023). Meckel's diverticulum axial torsion: A rare complication case report of a 5-year-old girl. *International Journal of Surgery Case Reports, 103.* https://doi.org/10.1016/j.ijscr.2023.107883
Kalynovska, I.H. (2004). Topohrafiia, makro- i mikrostruktura dyvertykula Mekkelia v postnatalnomu periodi ontohenezu [Topography, macro- and microstructure of Meckel's diverticulum in the postnatal period of ontogenesis]. *Naukovyi visnyk Lvivskoi natsionalnoi akademii veterynarnoi medytsyny im. S.Z.Hzhytskoho,* 6 (1), 2, 28–32 [in Ukrainian].
Kang, H., Yan, M., Yu, Q., & Yang, Q. (2014). Characterization of nasal cavity-associated lymphoid tissue in ducks. *Anatomical Record*, 297(5), 916-24.
Kaspers, B., & Göbel, T. W. F. (2016). The avian immune system. In: Ratcliffe, M. J. H. (Ed). *Encyclopedia of immunobiology*, 1. Elsevier Ltd, 498–503. https://doi.org/10.1016/B978-0-12-374279-7.12013-2
Kendall, M. D. (1980). Avian thymus gland: A review. *Developmental and Comparative Immunology, 4, 191–209.* DOI: 10.1016/s0145-305x(80)80023-1
Kharchenko, L. P., & Lykova, I. A. (2013). Limfoyidni struktury travnoho traktu kulykiv (Charadrii) [Lymphoid structures of the waders' (Charadrii) digestive tract]. *Visnyk Kharkivs'koho Natsional'noho Universytetu imeni V. N. Karazina,* 1056, 123–130 [in Ukrainian].
Khomich, V.T., Usenko, S.I., & Dyshliuk, N.V. (2020). Morphofunctional features of the esophageal tonsil in some wild and domestic bird species. *Regulatory Mechanisms in Biosystems*, *11* (2), 207–213. doi:10.15421/022030 [in Ukrainian].
Khomych, V.T, & Mazurkevych, T. A. (2015). Osoblyvosti lokalizatsii limfoidnoi tkanyny v

imunnykh utvorenniakh stinky tonkoi kyshky i dyvertykuli Mekkelia kachok [Features of the localization of lymphoid tissue in immune formations of the wall of the small intestine and Meckel's diverticula of ducks]. *Biolohiia tvaryn*, 17, 2 [in Ukrainian].
Korver, D. R. (2006). Overview of the immune dynamics of the digestive system. *Journal of Applied Poultry Research,* 15(1), 123–135. https://doi.org/10.1093/japr/15.1.123
Koutsos, E. A., & Klasing, K. C. (2014). Factors modulating the avian immune system. In: Schat, K. A., Kaspers, B., & Kaiser, P. (Eds.). *Avian Immunology*. Academic Press, London, 299–313. https://doi.org/10.1016/B978-0-12-396965-1.00017-0
Kushch, M.M., Kushch, L.L., Byrka, E.V., Byrka, V.V., & Yaremchuk, O.S. (2019). Morphological features of the jejunum and ileum of the middle and heavy goose breeds. *Ukrainian Journal of Ecology*, *9* (4), 690–694. doi:10.15421/2019_811 [in Ukrainian].
Kushch, M.M., Mahotina, D.S., & Fesenko, I.A. (2020). Osoblyvosti mikroskopichnoi budovy tonkoho viddilu kyshechnyka kachok u postnatalnomu periodi ontohenezu. *Theoretical and Applied Veterinary Medicine*, 8, 2, 101-110. doi: 10.32819/2020.82014 [in Ukrainian].
Law of Ukraine "On the Protection of Animals from Cruelty" dated February 21, 2006 No. 3447-IV, Kyiv, Ukraine. https://ips.ligazakon.net/document/T063447
Lindeman, R.J. & Søreide, K. (2020). The Many Faces of Meckel's Diverticulum: Update on Management in Incidental and Symptomatic Patients. *Current Gastroenterology Reports, 22(1),* 3. https://doi.org/10.1007/s11894-019-0742-1
Makhotina, D.S., Kushch, M.M., & Miroshnikova, O.S. (2020). Osoblyvosti mikroskopichnoi budovy slipykh kyshok kachok. *Veterynariia, tekhnolohii tvarynnytstva ta pryrodokorystuvannia:* Naukovo-praktychnyi zhurnal, 6, 56–63 [in Ukrainian].
Mazurkevych, T.A. (2012). Topohrafiia i morfolohiia dyvertykula Mekkelia kachok na rannikh etapakh postnatalnoho periodu ontohenezu [Topography and morphology of Meckel's diverticulum of ducks in the early stages of postnatal ontogenesis]. *Visnyk ZhNAEU*, *1*(32), 2, 2, 341–345 [in Ukrainian].
Mazurkevych, T.A. (2013a). Topohrafiia i morfolohiia dyvertykula Mekkelia u kachok vikom vid 25 do 120 dib [Topography and morphology of Meckel's diverticulum in ducks aged 150 to 240 days]. *Naukovyi visnyk Lvivskoho natsionalnoho universytetu veterynarnoi medytsyny ta biotekhnolohii imeni S.Z. Gzhytskoho*, 15, 1(55), 350-355 [in Ukrainian].
Mazurkevych, T.A. (2013b). Topohrafiia i morfolohiia dyvertykula Mekkelia u kachok vikom vid 150 do 240 dib [Topography and morphology of Meckel's diverticulum in ducks aged 150 to 240 days]. *Ukrainskyi chasopys veterynarnykh nauk*, 188 [in Ukrainian].
Mazurkevych, T.A., & Khomych, V.T. (2017). Osoblyvosti lokalizatsii limfoidnoi tkanyny v imunnykh utvorenniakh stinky kyshechnyku, dyvertykuli Mekkelia i slipokyshkovykh dyvertykulakh kachok [Features of the localization of lymphoid tissue in immune formations of the intestinal wall, Meckel's diverticulum and cecal diverticula of ducks]. *Naukovyi visnyk Lvivskoho natsionalnoho universytetu veterynarnoi medytsyny ta biotekhnolohii imeni S.Z. Gzhytskoho*, 19, 82, 30-35. doi:10.15421/nvlvet8207 [in Ukrainian].
Meek, H.C., Stenfeldt, C., & Arzt, J. (2022). Morphological and Phenotypic Characteristics of the Bovine Nasopharyngeal Mucosa and Associated Lymphoid Tissue. *Journal* of *Comparative Pathology*, 198, 62-79. doi:10.1016/j.jcpa.2022.07.011
Nochi, T., Jansen, C. A., Toyomizu, M., & Eden, W. (2018) The well-developed mucosal immune systems of birds and mammals allow for similar approaches of mucosal vaccination in both types of animals. *Frontiers in Nutrition*, 5, 60–65. https://doi.org/10.3389/fnut.2018.00060
Olah, I., & Glick, B. (1984). Meckel's diverticulum. I. Extramedullary myelopoiesis in the yolk sac of hatched chickens (*Gallus domesticus*). *Anatomikal Record*, 208(2), 243-252.
Olah, I., Glick, B., & Taylor, R.L.Jr. (1984). Meckel's diverticulum. II. A novel lymphoepithelial organ in the chicken. *Anatomikal Record*, 208(2), 253-263.
Opitz, J.M., Schultka, R., & Göbbel, L. (2006). Meckel on developmental pathology. *American Journal of Medical Genetics. Part A, 140(2),* 115-28. DOI:10.1002/ajmg.a.31043
Randall, T.D., Carragher, D.M., & Rangel-Moreno, J. (2008). Development of secondary lymphoid organs. *Annual Review of Immunology*, 26, 627-50. doi: 10.1146/annurev.immunol.26.021607.090257
Rehfeld, A., Nylander, M., & Karnov, K. (2017). The Digestive System I: The Alimentary Canal. *Compendium of Histology.* Springer, Cham., 433–473. https://doi.org/10.1007/978-3-319-41873-5_21
Rehfeld, A., Nylander, M., & Karnov, K.K.S. (2013). *Histologikompendium.* 2nd ed. Munksgaard.
Ross, M.H., & Pawlina, W. (2015). *Histology: a text and atlas: with correlated cell and molecular biology.* 7th ed., Philadelphia, USA: Wolter Kluwer Publishing House
Ruddle, N. H., & Akirav, E. M. (2009). Secondary lymphoid organs: Responding to genetic and environmental gues in ontogeny and the immune response. *The Journal of Immunology*, 183(4), 2205–2212.
Samour, J. (2015) *Avian medicine.* 3rd edition. Mosby Ltd. https://doi.org/10.1053/j.jepm.2017.01.020
Schuh, J.C.L. (2020). Mucosa-Associated Lymphoid Tissue and Tertiary Lymphoid Structures of the Eye and Ear in Laboratory Animals. *Toxicologic Pathology*, 49(3), 472-482.
Sharma, J. M. (1991). Overview of the avian immune system. *Veterinary Immunology and Immunopathology*, 30(1), 13–17.
Yu, Y., Wang, Q., Huang, Z., Ding, L., & Xu, Z. (2020). Immunoglobulins, Mucosal Immunity and Vaccination in Teleost Fish. *Frontiers in Immunology, 11,* 567941. DOI: 10.3389/fimmu.2020.567941