

УДК 611.367.013

DOI: 10.24061/1727-0847.17.1.2018.16

**S.I.Riabyi, I.G.Biriuk\*, T.B.Sykyrytska\*\*, I.L.Kukovska\*, D.V.Proniaiev***Department of Nursing and Higher Nursing Education (head – prof. I.A. Plesh), \*Department of Disasters Medicine and Military Medicine (head – doc. I.G. Biriuk), Department of Ophthalmology (head – prof. Ya.I. Penishkevych), Department of anatomy, topographical anatomy and operative surgery (head – prof. O.M. Slobodian) Bukovinian State Medical University, city Chernivtsi***MORPHOGENESIS OF HUMAN BILE DUCTS IN EMBRYONIC PERIOD****МОРФОГЕНЕЗ ЖОВЧНИХ ПРОТОК ЛЮДИНИ В ЕМБРІОНАЛЬНОМУ ПЕРІОДІ**

**Резюме.** Численні публікації в науковій періодичній пресі свідчать про надзвичайну зацікавленість науковців проблемою внутрішньоутробного морфогенезу. Дослідження присвячене проблемі пренатального морфогенезу позапечінкових жовчних проток, адже вади розвитку цього сегмента травної системи складають близько 6-8 % від усіх вад розвитку. Метою дослідження є з'ясування закономірностей просторово-часової динаміки пренатального морфогенезу позапечінкових жовчних проток. В результаті дослідження встановлено: у зародків 4,0-5,0 мм тім'яно-куприкової довжини зачаток спільної жовчної протоки являє собою порожнистий епітеліальний тяж, який з'єднує печінковий дивертикул з венетральною стінкою первинної кишки. Фізіологічна атрезія спільної жовчної протоки виникає в зародків 8,5-11,0 мм тім'яно-куприкової довжини в наслідок інтенсивної проліферації епітелію. Реканалізація спільної жовчної протоки завершується на пізніших етапах внутрішньоутробного розвитку.

**Ключові слова:** спільна жовчна протока; ембріон; анатомія; людина.

Nowadays scientists have a great deal of knowledge concerning anatomical peculiarities and regularities of prenatal morphogenesis of the human structures and organs. However, this fact does not help doctors to reduce the rate of congenital pathology, perinatal mortality and post-operative complications. Numerous publications in scientific periodical press are indicative of an extraordinary interest of scientists in the issues of intrauterine morphogenesis, since disorders of morphogenesis processes at this period result in growth of congenital pathology. Our study deals with the issue of prenatal morphogenesis of extrahepatic biliary ducts, since developmental defects of this segment of the digestive system constitute approximately 6-8 % out of all developmental defects including agenesis, hypoplasia, dysplasia, atresia, cystic dilatation, spontaneous perforation. This is only a small amount of possible variants of congenital pathology, and their main part belongs to developmental defects of the common bile duct.

According to the information of embryological examinations concerning the sources of bile duct rudiments, scientists are not of mutual opinion. The common bile duct (CBD) rudiment is considered to originate from the proximal part of the hepatic diverticulum caudal portion, which is an evagination of the primary intestine ventral wall endoderm at the end of the first month of the human embryo development. A part of the hepatic diverticulum is detached from the

intestinal wall, and its distal part forms hepatic node. The proximal part of the elongated diverticulum (closer to the intestine) originates the common bile duct. The hepatic inlet is formed on the border of the future common bile duct and hepatic node. Meanwhile there are certain data that the hepatic node is completely detached from the primary intestine, and later extrahepatic bile ducts grow into the liver parenchyma.

As to the anatomical peculiarities of the CBD there is no concerted opinion concerning the dynamics of spatial-temporal processes of its canalization. Certain data evidence, that the duct lumen is formed at the end of the 6<sup>th</sup> week of the embryonic development. Still others – open duct is seen at the 3<sup>rd</sup> week of the embryonic development. It should be noted that prevailing majority of scientists consider that the processes of attenuation of CBD physiological atresia begin at the 7<sup>th</sup> week of the embryonic period and during pre-fetal period – at the end of the 9<sup>th</sup> week of development.

In pre-fetuses CBD can be called as an extension of the gallbladder duct passing from the fusion of the hepatic ducts to the ventral surface of the duodenum. Topography of the common bile duct in pre-fetuses differs by its wide variability of a spatial location, which can be explained by syntopic influence of the adjacent structures and organs.

The common bile duct gets morphological signs

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similar to that of the definite form at the end of the 3<sup>rd</sup> month of the human intrauterine development. At the early fetal period together with increasing size of the CBD and further differentiation of the hepatic-duodenal ligament structures topographic-anatomical interrelations peculiar for the last weeks of the pre-fetal period are retained. In particular, the CBD of the 4-month fetuses is described to occupy the last right position in the depth of the hepatic-duodenal ligament, pass downward posteriorly from the upper part of the duodenum through the pancreatic parenchyma, penetrates into the dorsal-medial wall of the duodenum.

At the end of the fetal period in the wall of the extrahepatic bile ducts 3 layers can be differentiated: mucous, muscular and external. Their mucous layer is covered with one-row cylindrical epithelium, the muscular one is formed by the bundles of the smooth muscular fibers, and the external layer is in the form of loose connective tissue.

**Objective:** to specify regularities of the spatial-temporal dynamics of the prenatal morphogenesis of the extrahepatic bile ducts.

**Material and methods.** *Histological and histotopographic sections and specimens of fetuses and pre-fetuses from the Museum of M.H. Turkevych Department of Human Anatomy, Higher State Educational Establishment of Ukraine "Bukovinian State Medical University" were used in the study. To achieve the purpose the following methods of anatomical examination were applied: microscopy of the series of histological sections to study the rudiment and structure of the common bile duct, its muscular contactors and bloodstream; graphic and plastic reconstruction to clarify the shape and formation of the topography of the common bile duct and sources of its blood supply in the embryos and pre-fetuses; macro- and microdissection to study the structure and topographic changes of the common bile duct in fetuses and newborns; injection with further X-ray to specify the topographic details of the common bile duct and peculiarities of its bloodstream structure in fetuses and newborns; morphometry to clarify the dynamics of changes of the common bile duct size in fetuses and newborns. Numerical data were processed by means of the variation-statistical method.*

**Results and discussion.** Examination of the specimens of the human embryos aged from 4 to 6 weeks of embryonic development determined that at the end of the 4<sup>th</sup> week evagination of the endodermal epithelium – hepatic diverticulum on the ventral wall of the primary intestine is found. Its cells are located in the shape of wide cords in the direction of the transverse septum of the embryo. At this stage cranial and caudal parts can be differentiated in the hepatic diver-

ticulum. The cranial part is liver rudiment, and the caudal one – the rudiment of the gallbladder. Cavities are seen among the cells of the liver rudiment. The largest one is located on level of the caudal part of the hepatic diverticulum and presents the rudiment of the portal hepatic vein. Dorsally from it peduncle of the hepatic diverticulum forms cone-shaped dilation – hepatic inlet. In this part epithelia cord is found connecting the hepatic diverticulum with the primary intestine and presents the rudiment of the CBD. The latter one passes from the lumen of the primary intestine in the ventral-caudal direction and consists of compact located high epithelial cells of an oval shape with eccentric located nuclei. Between the two layers of the epithelial cells forming the walls of the CBD rudiment there is a lumen 15-20 mcm thick in the proximal part. The place of location of the CBD rudiment itself is a reference point to determine the duodenal rudiment, which does not have clear borders at this stage. In the cranial part the CBD rudiment borders on the rudiment of the portal hepatic vein, and in the caudal part the ventral rudiment of the pancreas branches off from it. At the beginning of the 5<sup>th</sup> week of the intrauterine development the CBD rudiment 175 mcm thick is located on the border of the rudiments of the liver and duodenum in the caudal direction from the portal hepatic vein. In the ascending direction the CBD continues into the rudiment of the gallbladder. Its walls are formed by two layers of the cylindrical epithelium with a visible slit-like lumen 15 mcm thick between them. In the embryos 8,0-8,5 mm of the PCL due to rapid enlargement of the size of the hepatic diverticulum the CBD rudiment is surrounded from all the sides by the liver rudiment. In the cranial-ventral direction from the CBD rudiment the gallbladder and hepatic ducts are branched off in the shape of separate solid epithelial cords. Due to duodenal curve to the right, the position of the CBD rudiment dislocates to the cranial semicircle of the upper part of the intestine. The CBD length reaches 180 mcm. Its walls are formed by the one-layer cylindrical epithelium 20 mcm high with basal location of the nuclei, externally surrounded by the mesenchymal cells of the primitive ventral mesentery. Between the epithelial walls of the duct a lumen of an oval shape 25-30 mcm wide is determined except its caudal portion. The latter closes blindly in the part of the duodenal wall evagination formed by multinucleated epithelium. In embryos 8,5 mm of the PCL the proximal part of the common bile duct in the point of junction with the duct of the ventral rudiment of the pancreas widens to 150 mcm, forming the hepatic-pancreatic duct, in which lumen there is aggregation of the epithelial cells in the form of epithelial plug. The portal

hepatic vein is located in the cranial direction from the CBD rudiment. Posteriorly from the liver rudiment the aortic branch grows in the direction of the dorsal mesogastrium (the rudiment of the upper mesenteric artery).

On the 6<sup>th</sup> week of the intrauterine development the CBD passes in the depth of the mesenchyme of the ventral mesogastrium from the lower liver surface downwards and forward. The cranial part of the CBD is located intrahepatically, where it forms a small curve to the right continuing into the gallbladder duct. In this portion the common hepatic duct branches off from the CBD. The last dichotomic duct is in the depth of the right semicircle of the upper duodenal curve. In the embryos of this age the CBD is in the form of the continuous epithelial cord formed by two layers of high cylindrical epithelium. The lumen in the duct is absent except small thinning among epithelial cells in the point of ventral pancreatic duct branching off.

In embryos of 11,0-11,8 mm of the PCL topographic-anatomical interrelations of the CBD and adjoining structures change, which is caused by rapid growth of the liver rudiment and reversion of the duodenum. The upper and lower parts are found in the latter. Position of the CBD dislocates from the cranial to the ventral-lateral wall of the upper duodenal part, from which the duct passes in the depth of the ventral mesogastrium in the ventral-cranial direction. The CBD length reaches 475 mcm. Due to its intensive enlargement the curves of the duct are formed in the frontal plane: the cranial one – to the left and backward, and caudal one – to the right and forward. At this stage extra- and intra-intestinal portions can be differentiated in the CBD. Extra-intestinal portion of the CBD 375 mcm long is located in the mesenchymal depth of the ventral mesogastrium and borders on the ventral rudiment of the pancreas in the right and caudal direction. Intra-intestinal portion of the CBD in the depth of the cranial-lateral duodenal wall is joined with the ventral pancreatic duct forming the hepatic-pancreatic duct. At this stage the ventral and dorsal rudiments of the pancreas approach each other. The lumen of the portal hepatic vein filled with primary blood elements is determined in the right side from the CBD. The CBD wall is formed by the one-layer high cylindrical epithelium located on the basal membrane. Externally it is surrounded by the mesenchyme cells of the ventral mesogastrium. Around the intra-intestinal portion of the CBD, especially in the point of connection with the ventral pancreatic duct, certain adjoining mesenchymal cells separating from the surrounding mesenchyme become of a circulatory orientation. It can be indicative of the beginning of

formation of the CBD sphincter rudiment. At this period duodenal wall externally is surrounded by clearly expressed circular layer of the mesenchymal cells. Along the whole length of the CBD the lumen 35 mcm wide is found. In the part of the hepatic-pancreatic duct it reaches 75 mcm. At the end of the embryonic period (embryos of 12,0-13,0 mm of the PCL) the primitive ventral mesentery, stomach and duodenum are surrounded by the liver tissue from both sides. The CBD passes in the depth of the ventral mesogastrium posteriorly from the upper part of the duodenum in the dorsal-cranial direction, where it branches off on the common hepatic and gallbladder ducts. At the same time, the common hepatic duct is located cranially concerning the gallbladder one, and the latter looks like CBD continuation by its direction. According to the prominence of the intestinal wall the CBD forms an arch-like curve backward and reaches 650-700 mcm long. At the distance of 170 mcm from the dorsal intestinal wall the caudal part of the CBD sharply turns to the right and forward, and is connected with the ventral pancreatic duct forming the hepatic-pancreatic duct. The latter is located in the depth of the dorsal-lateral wall of the upper part of the duodenum in the oblique direction.

Extra-intestinal portion of the CBD 450-530 mcm long is located in the mesenchymal depth of the ventral mesogastrium in the right and backward from the ventral rudiment of the pancreas. Cranially and posteriorly the CBD borders on the portal hepatic vein. In the left and anteriorly from the CBD the branch of the hepatic artery is located, which passes along the left wall of the duct. The CBD lumen is well expressed along the whole its length. Its diameter is 60-65 mcm in its cranial part and is narrowing in the shape of a cone to 15-20 mcm in the caudal direction. The walls of the duct are covered with the one-layer high cylindrical epithelium. Externally it is surrounded by the adjoining layer of the mesenchymal cells separated from other cells of the ventral mesogastrium forming the external membrane of the CBD. Intra-intestinal portion of the CBD 120 mcm long is located in the oblique direction in the depth of the dorsal wall of the upper duodenal part. On the level of the external layer of the mesenchymal intestinal membrane the junction of the CBD and ventral pancreatic duct is found with formation of the hepatic-pancreatic duct. The latter is 60 mcm in diameter and closes on the level of aggregation of the epithelial cells in the duodenal lumen. The walls of the intra-intestinal portion of the CBD are covered with high cylindrical epithelium inside. Externally they are surrounded by the adjoining mesenchyme layer up to 50 mcm thick, which cells are of a circular direction

mainly. The indicated layer is clearly isolated from the mesenchymal membrane of the duodenum and it is the rudiment of the CBD sphincter. Among aggregation of the epithelium in the duodenal lumen certain vacuole-like cavities are found, that are the manifestations of its recanalization. Although on the level of the caudal part the aggregation of the epithelial cells is retained in the form of a distinctive epithelial plug. Therefore, direct connection of the lumens of the CBD and duodenum at this stage of development is not found. Thus, at the end of the 4<sup>th</sup> week of the intrauterine development the CBD rudiment is formed from the cells of the endodermal evagination of the primary intestine in the proximal portion of the hepatic diverticulum. In the embryos of 4,0-5,0 mm of PCL the CBD rudiment is presented by the cord of the epithelial cells located in two layers, and between them a slit-like lumen is found. In the embryos of 8,5-10,0 mm of PCL the lumen in the CBD is not found at the expense of aggregation of the epithelial cells (physiological atresia). Recanalization of the CBD lumen is first found in the embryos of 11,0 mm of PCL as a result of a reverse development of physiological atresia. However, on the level of the caudal part epithelial plug in its lumen remains till the end of

the embryonic period. At the end of the embryonic period due to rotation of the duodenum and the junction of the ventral and dorsal pancreatic rudiment caused by it, extra-intestinal and intra-intestinal portions of the CBD are formed. In the embryos of 11,0-13,0 mm of PCL the rudiment of the CBD sphincter begins to form, which develops from the adjoining layer of the mesenchymal cells round its intra-intestinal portion. In the portion of junction with the ventral pancreatic duct they become of a circulatory direction.

**Conclusion.** The rudiment of the common bile duct in embryos of 4,0-5,0 mm of the parietococcygeal length is in the form of a hollow epithelial cord connecting the hepatic diverticulum with the ventral wall of the primary intestine. Physiological atresia of the common bile duct occurs in embryos of 8,5-11,0 mm of the parietococcygeal length due to intensive epithelial proliferation. Recanalization of the common bile duct is completed at the later stages of the intrauterine development.

**Prospects of further studies.** The study of peculiarities of the spatial-temporal dynamics in the morphogenesis of the extrahepatic bile ducts during pre-fetal and fetal periods of morphogenesis is considered to be reasonable.

#### Список використаної літератури

1. Ахтемійчук ЮТ, Слободян ОМ, Юзько РВ. Топографоанатомічні особливості холедохоранкреатичного комплексу в перинатальному періоді онтогенезу. Науковий вісник Ужгородського університету. Серія медицина. 2010;39:42-5.
2. Антонюк ОП, Цигикало ОВ. Кровопостачання замикальних сегментів позапечінкових жовчних проток у пренатальному періоді онтогенезу людини. Вісник проблем біології і медицини. 2015;2(3):294-9.
3. Ахтемійчук ЮТ, Хмара ТВ, Проняєв ДВ. Варіант анатомії органів черевної порожнини. Клінічна анатомія та оперативна хірургія. 2008;7(3):81-2.
4. Козак ІО. Кістозна дилататція внутрішньопечінкових та позапечінкових жовчних протокою Вісник морфології. 2016;22(1):191-5.
5. Cheng-Maw Ho, Po-Huang Lee, Wing Tung Cheng, Rey-Heng Hu, Yao-Ming Wu, Ming-Chih Ho. Succinct guide to liver transplantation for medical students. Ann Med Surg. 2016 Nov 14;12:47-53.
6. Usha Dandekar, Dandekar Kundankumar. Cystic artery: morphological study and surgical significance. Anatomy Res Internat. 2016; Article ID 7201858. <http://dx.doi.org/10.1155/2016/7201858>
7. Цигикало ОВ Морфогенез сфінктерного апарату жовчного міхура та міхурової протоки. Вісник проблем біології і медицини. 2013;4(1):287-91.

#### References

1. Akhtemiychuk YuT, Slobodyan OM, Yuz'ko RV. Topografoanatomichni osoblyvosti kholedokho-rankreatychnoho kompleksu v perynatal'nomu periodi ontogenezu [Topographic anatomical features of the choledocho-pancreatic complex in the perinatal period of ontogenesis]. Naukovyy visnyk Uzhhorods'koho universytetu. Seriya medytsyna. 2010;39:42-5. (in Ukrainian).
2. Antonyuk OP, Tsyhykalo OV. Krovopostachannya zamykal'nykh sehmentiv pozapechinkovykh zhovchnykh protok u prenatal'nomu periodi ontogenezu lyudyny [Blood supply of closure segments of extrahepatic bile ducts in the prenatal period of human ontogenesis]. Visnyk problem biolohii i medytsyny [Internet]. 2015;2(3):294-9. Available from: [http://nbuv.gov.ua/UJRN/Vpbm\\_2015\\_3%282%29\\_\\_61](http://nbuv.gov.ua/UJRN/Vpbm_2015_3%282%29__61)
3. Akhtemiychuk YuT, Khmara TV, Pronyayev DV. Variant anatomiyi orhaniv cherevnoyi porozhnyny [Anatomy of an abdominal cavity.]. Klinichna anatomiia ta operatyvna khirurhiia. 2008;7(3):81-2. (in

Ukrainian).

4. Kozak IO. *Kistozna dylyatatsiya vnutrishn'opechinkovykh ta pozapechinkovykh zhovchnykh protok [Cystosal dilatation of intrahepatic and extrahepatic bile ducts]. Visnyk morfolohii. 2016;22(1):191-5. (in Ukrainian).*

5. Cheng-Maw Ho, Po-Huang Lee, Wing Tung Cheng, Rey-Heng Hu, Yao-Ming Wu, Ming-Chih Ho. *Succinct guide to liver transplantation for medical students. Ann Med Surg. 2016 Dec; 12:47-53.*

6. Usha Dandekar, Dandekar Kundankumar. *Cystic artery: morphological study and surgical significance. Anatomy Res [Internet]. 2016; Article ID 7201858. Available from: <http://dx.doi.org/10.1155/2016/7201858>*

7. Tsyhykalo OV. *Morfohenez sfinkternoho aparatu zhovchnoho mikhura ta mikhurovoyi protoky [Morphogenesis of the sphincter apparatus of the gall bladder and bladder duct]. Visnyk problem biolohii i medytsyny. 2013;4(1):287-91. (in Ukrainian).*

### МОРФОГЕНЕЗ ЖЕЛЧНЫХ ПРОТОК ЧЕЛОВЕКА В ЭМБРИОНАЛЬНОМ ПЕРИОДЕ

**Резюме.** Многочисленные публикации в научной периодической прессе свидетельствуют о чрезвычайной заинтересованности ученых проблемой внутриутробного морфогенеза. Исследование посвящено проблеме пренатального морфогенеза внепеченочных желчных путей так как пороки развития этого сегмента пищеварительной системы составляют около 6-8 % от всех пороков рахвития. Целью исследования является выяснение закономерностей пространственно-временной динамики пренатального морфогенеза внепеченочных желчных протоков. В результате исследования установлено: у зародышей 4,0-5,0 мм теменно-копчиковой длинны зачаток общей желчной протоки являет собой полый эпителиальный тяж, который соединяет печеночный дивертикул с вентральной стенкой первичной кишки. Физиологическая атрезия общей желчной протоки возникает у зародышей 8,5-11,0 мм теменно-копчиковой длинны в следствии интенсивной пролиферации эпителия. Реканализация общей желчной протоки заканчивается на более поздних этапах внутриутробного развития.

**Ключові слова:** общий желчный проток; эмбрион; анатомия; человек.

### MORPHOGENESIS OF HUMAN BILE DUCTS IN EMBRYONIC PERIOD

**Abstract.** Numerous publications in scientific periodical press are indicative of an extraordinary interest of scientists in the issues of intrauterine morphogenesis. The study deals with the issue of prenatal morphogenesis of extrahepatic biliary ducts, since developmental defects of this segment of the digestive system constitute approximately 6-8 % out of all developmental defects. The objective of the study is to specify regularities of the spatial-temporal dynamics of the prenatal morphogenesis of the extrahepatic bile ducts. The investigation resulted in the following: the rudiment of the common bile duct in embryos of 4,0-5,0 mm of the parietococcygeal length is in the form of a hollow epithelial cord connecting the hepatic diverticulum with the ventral wall of the primary intestine. Physiological atresia of the common bile duct occurs in embryos of 8,5-11,0 mm of the parietococcygeal length due to intensive epithelial proliferation. Recanalization of the common bile duct is completed at the later stages of the intrauterine development.

**Key words:** common bile duct; embryo; anatomy; man.

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Надійшла 25.12.2017

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