ORIGINAL ARTICLE

PECULIARITIES OF THE SOURCES OF ORIGIN AND MORPHOGENESIS OF THE HUMAN MANDIBLE

DOI: 10.36740/WLek202204114

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ABSTRACT

The aim: To determine the sources and terms of origin, developmental peculiarities and dynamics of ossification of the mandible during the prenatal period of human ontogenesis.
Materials and methods: The research was carried out on the specimens of 30 embryos, 30 pre-fetuses and 60 human fetuses at the period from the 9th to the 12th weeks of the intrauterine development, which were studied by microscopic examination. Three-dimensional computer reconstructions of the human pre-fetal head were made.
Results: During the 7th week of development the maxillary processes maximum approach the lateral and medial nasal ones; in pre-fetuses 20,0 mm of PCL they join the frontal spindle forming the facial structures (upper jaw and lip, vestibule of the oral cavity, rudiments of dental laminas, and rudiments of dental buds in its distal portions). Osteogenous islets, rudiments of the mimic and masticatory muscles, blood vessels are formed. During the 8th week of development the osseous tissue of the mandible is formed, the alveolar processes are formed. The oral and nasal cavities are isolated in 9-10-week pre-fetuses, the mass of the osseous tissue increases in both jaws, the enamel organs are detached, the angles and rami formed by the hyaline cartilaginous tissue of the mandible are determined, the rudiments of the temporomandibular joints are already seen. During the 11th week of development the osseous base of both jaws become formed. Till the end of the 12th week the osseous tissue begins to replace the hyaline cartilage of the mandibular rami, and the articular heads are formed in the portion of their proximal ends.
Conclusions: The mandible in its development is known to be characterized by intra-cartilaginous formation of the bone which starts from the ends of the cartilage gradually displaced by the osseous tissue. It is indicated that both jaws in pre-fetuses 37,0 and 42,0 mm of PCL are presented by the typical cartilaginous tissue, and in pre-fetuses 45,0-50,0 mm of PCL the osseous tissue is already available replacing the cartilaginous one.

KEY WORDS: mandible, morphogenesis, origin, ossification, ontogenesis

Wiad Lek. 2022;75(4 p1):824-830

INTRODUCTION

Learning the sources, terms, chronological sequence of morphological transformations, finding critical periods and developmental peculiarities of the anatomical structure of the stomatognathic system during the prenatal period of human ontogenesis are relevant areas of morphological studies promoting solution of an important medical-social issue – improvement of the methods of prevention, early diagnostics and effective surgical correction of congenital defects and treatment of the acquired diseases of the human mandible. Morphological description of the maxillofacial structures and peculiarities of development of the mandible in particular, does not keep pace with up-to-date requirements of practical medicine. Usually to investigate these issues experimental models are used (laboratory animals) [1]. The methods of development and analysis of two-dimensional reconstructions are applied at the late stages of the craniofacial human development [2]. The data concerning regulations and peculiarities of mandibular morphogenesis during the prenatal period of human ontogenesis are insufficient. Certain fragments of research are known – those concerning morphogenesis of the mandible in human pre-fetuses [3]. Clear understanding of etiopathogenesis of congenital pathology of the human body organs and systems is based on comprehensive morphological examinations of peculiarities of the anatomical structures in the dynamics of the intrauterine development. Embryogenesis of the mandible differs by the formation of Meckel's cartilage followed by its involution and the processes of osteogenesis. Detection of chronological order of mandibular transformations at the early period of ontogenesis will promote development of morphological criteria of the norm, and improve diagnostic algorithms in interpretation of examination of human fetuses.

THE AIM

The aim was to determine the sources and terms of origin, developmental peculiarities and dynamics of ossification of the mandible during the prenatal period of human ontogenesis.

MATERIALS AND METHODS

The research was carried out on the specimens of 30 embryos, 30 pre-fetuses and 60 human fetuses at the Municipal Medical Institution «Chernivtsi Morbid Anatomy Bureau» according to the agreement on collaboration.

The investigations were performed keeping to the major regulations of the Resolution of the First National Congress

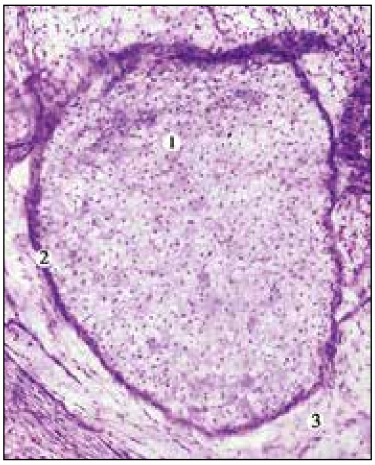

Fig. 1. Transverse section of Meckel's cartilage of the human embryo 13,5 mm of PCL. Staining with hematoxylin and eosin. Microphotograph. Magnification: 80x. Signs: 1 – Meckel's cartilage; 2 – perichondrium; 3 – mesenchyme.

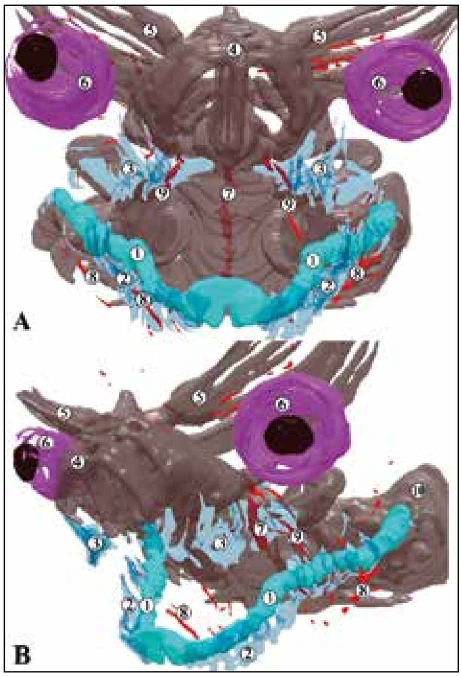

Fig. 2. Three-dimensional computer reconstruction of the human pre-fetal head 19,0 mm of PCL. A – anterior projection, Б – left anterior-lateral projection. Magnification: 15x. Signs:
1 – Meckel's cartilage; 2 – foci of mandibular osteogenesis; 3 – foci of the maxillary osteogenesis; 4 – nasal capsule; 5 – rudiment of the cranial bones; 6 – eyeballs; 7 – basilar artery; 8 – inferior alveolar artery; 9 – maxillary artery; 10 – auricular cartilage.

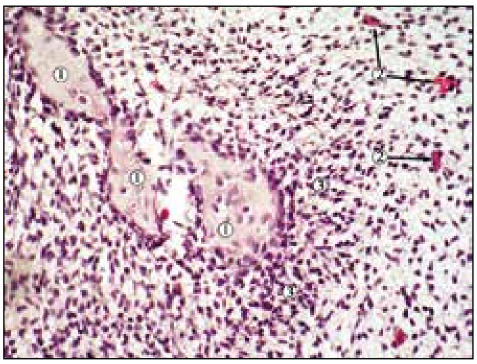

Fig. 3. Histological section of the pre-fetal mandible 18,0 mm of PCL. Staining with hematoxylin and eosin. Microphotograph. Magnification: 190x. Signs:
1 – osteogenous islets, 2 – condensed mesenchyme around the osteogenous islets, 3 – blood islets.

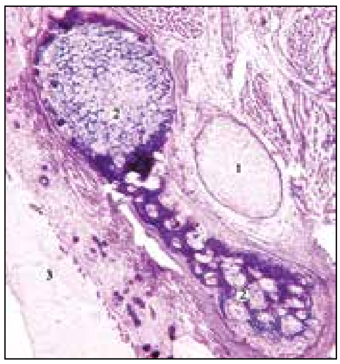

Fig. 4. Frontal section of the right mandible of the human pre-fetus 25,0 mm of PCL. Staining with hematoxylin and eosin. Microphotograph. Magnification: 50x. Signs:
1 – Meckel's cartilage; 2 – rudiment of the mandible; 3 – skin.

Fig. 5. Fragment of head section of the human pre-fetus 23,0 mm of PCL. The vestibule of the oral cavity lines the stratified epithelium. Staining with hematoxylin and eosin. Magnification: 30x. Signs:
1 – upper lip; 2 – lower lip; 3 – lateral palatine lamina; 4 – Meckel's cartilage; 5 – dental laminas; 6 – tongue; 7 – osteogenesis foci.

on Bioethics «General Ethic Principles of Experiments on Animals» (2001), ICH GCP (1996), the European Union Convention on Human Rights and Biomedicine (04.04.1997), and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (18.03.1986), the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (1964-2008), EU Directives №609 (24.11.1986), the Orders of the Ministry of Health of Ukraine № 690 dated 23.09.2009, №944 dated 14.12.2009, № 616 dated 03.08.2012.

RESULTS

At the beginning of the 6th week of the intrauterine development (embryos 8,0-11,0 mm of the parieto-coccygeal length (PCL)) the anlage of Meckel's cartilage is clearly determined. Its central part is formed by oval cells densely packed. These cells are visually smaller than those surrounding cartilages (Fig. 1). They present a distinctive center for the beginning of the cartilage formation. The perichondrium begins to form along the periphery of Meckel's cartilage at the end of the 6th week of the intrauterine development.

Osteogenous islets are found in embryos 10,0-11,0 mm of PCL (the middle of the 6th week of the intrauterine development). These are the areas of mesenchyme hardening located on both sides of the cartilaginous mandibular anlages. The cellular elements in their content are characterized by other forms of cells and nuclear-cytoplasmic correlation in them. The degree of intensity of the osteogenous anlages

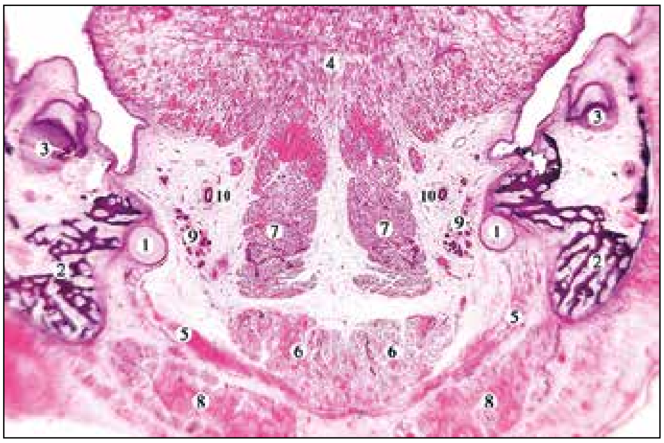

Fig. 6. Frontal section of the mandible of the human pre-fetus 35,0 mm of PCL. Staining with hematoxylin and eosin. Microphotograph. Magnification: 50x. Signs:
1 – Meckel's cartilage; 2 – mandible rudiment; 3 – rudiments of teeth; 4 – tongue; 5 – mandibular-sublingual muscles; 6 – submental- sublingual muscles; 7 – submental-lingual muscles; 8 – anterior ventricles of the digastric muscles; 9 – sublingual glands; 10 – lingual arteries.

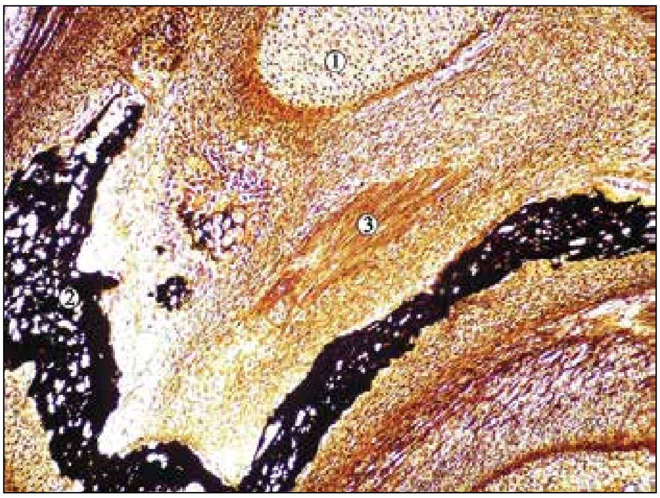

Fig. 7. Fragment of the mandible of the human fetus 55,0 mm of PCL. Silver impregnation. Microphotograph. Magnification.: 50x. Signs:
1 – Meckel's cartilage; 2 – osseous tissue trabecule; 3 – muscular elements.

decreases in the distal direction, and they are lacking in the areas of ventral extremities of Meckel's cartilage.

At the beginning of the pre-fetal period of the intrauterine development the submental nerve is detected close to the inferior border of Meckel's cartilage in the point of the primary ossification center of the mandible. Meckel's cartilages are delimited along the median line in the area of the chin by a thin mesenchyme layer.

At the end of the 7th week of intrauterine development (pre-fetuses 17,0-22,0 mm of PCL) the rudiment of the mandible is found externally from Meckel's cartilages occurring from the adjacent mesenchyme. A small concavity of the cartilage is seen into the center of the primary ossification of the mandible, followed by its ossification along the whole cartilage. At the end of the 7th week of intrauterine development mandible ossification occurs not only distally from the primary center, but in the submental area as well. Due to this process Meckel's cartilage becomes surrounded by the bone along the anterior and posterior surfaces (Fig. 2). At the same time, the process of impression of the dental lamina in the space between the cartilage and anterior bony surface of the mandible is observed.

Special attention is drawn to the fact that the foci of osteogenesis localized externally from Meckel's cartilage in the shape of separate islets with clear signs of mineralization are found among the structures of the mandibular rudiments more clearly than in the objects of preliminary stages. This mineralization becomes especially visible at the end of the 7th week of the intrauterine development. Mineralized islets of the osseous tissue are surrounded by osteoblasts closely adjacent one to another. Their shape is various – from oval to trapezoid (Fig. 3).

Comparing the morphology of certain osteogenic islets our attention was drawn to the fact that they differed in the course of their development by their size, number of cells in the unit of volume of the intercellular matrix, degree of mineralization of osteogenesis centers, which is indicated by the difference of the tinctorial properties of their structures.

Mineralization of osteogenous islets was found to occur nonsynchronous repeating the dynamics of the processes of formation of the mandibular processes. We have found that those areas located closer to Meckel's cartilage are stained more intensively. We consider it is associated with reciprocal relations established between the structures of Meckel's cartilage participating in the formation of the mandible, and osteogenous components in the process of differentiation. Compact mesenchyme participating in osteogenesis is located around osteogenous islets.

The nuclei of osteoblasts are oval by shape. They are most often located eccentrically, dislocating to the apical pole, and the cytoplasm demonstrates pronounced basophilia in different degrees.

The cells located inside of the osteogenous islets become of an elongated stellate shape with various numbers of short processes. The cytoplasm of these cells is stained with the major dyes less intensively than in the area surrounding the islets of osteoblasts. They are located one by one in the so-called lacunas which outlines imitate the shape of cells. Due to the action of a fixing agent the sizes of cells become smaller than lacunar formations, therefore, light colorless cavities are found around them. Considering a specific shape of such cells isolated one from another by intercellular substance, they may be called osteocytes on their different stages of maturation.

Therefore, on the 7th week of the intrauterine development differentiation of structures participating in the formation of the maxillofacial apparatus occurs more rapidly in comparison with the previous stage of development. Osteogenesis is more active in the mandible. The vestibule of the oral cavity is formed, dental laminas are laid, and till the end of the 7th week dental germs are laid down. The mimic and masticatory muscles are differentiated.

During the 8th week of the intrauterine development (pre-fetuses 21,0-30,0 mm of PCL) further ossification of the mandible occurs. It becomes visible in the area of its rami (Fig. 4).

Meckel's cartilage begins to lose its clear outlines and smooth surfaces, and the distance between the posterior extremities of cartilages enlarges. The cells of the cartilage become vacuolated and lose their nuclei. Ossification process spreads over all the areas of the mandible. Ossified rami of the mandible are the places for attachment of the masticatory muscles, they are located on both sides from the cartilage, and the base of the mandible surrounds it from below and from the side. The body of the mandible becomes U-shaped.

The islets of the osseous tissue are seen laterally from Meckel's cartilage. These islets in comparison with similar formations in the pre-fetuses of the 7th week of the intrauterine development become larger in size at the expense of their growth on the one hand, and on the other – at the expense of fusion between themselves. As a result, the space between osteogenous islets filled by mesenchyme becomes vividly smaller. The foci of ossification spread along Meckel's cartilages both in the proximal and distal directions making up the bony basis of the mandible, and the rudiments of alveolar processes in the shape of grooves open into the side of dental gums in particular.

Similar to the previous stage of development the mesenchyme around the cartilages is characterized by more compact location cell in it, and around the islets of the osseous tissue.

The foci of osteogenesis in the mandible are found in the form of separate osteogenous islets of various size (Fig. 5). They are oxyphil stained, and differentiated osteoblasts are localized along the periphery. Single osteocytes separated one from another by the intercellular matrix, are located in the middle of them. Some of the osteogenous islets are on the initial stages of osteogenesis in the form of osteoid masses surrounded by the osteogenous cells. Cells are still absent inside of such formations. Oxyphilia in the centers of osteogenesis of the maxillary rudiments is less prominent than in the osteogenous islets of the mandible. Thus, morphological peculiarities and tinctorial properties of the intercellular matrix of the osteogenous rudiments are indicative of the heterochronic bone formation in the mandible and maxilla.

During the 9th week of the intrauterine development osteogenesis is implemented actively, and due to this process their bony basis is formed. The osseous septa in the mandible which are located from both the ventral-lateral sides from Meckel's cartilage approach each other in the distal direction. Though in the area of the chin similar to the extremities of Meckel's cartilage they remain divided by the layer of the connective tissue presented by the cellular elements located compact. Due to appositional growth the amount of the osseous tissue in the maxillofacial apparatus increases considerably, and therefore it participates in the formation of the shape of the facial portion of the head.

Morphological structural changes of the osseous tissue are characterized by general biological regularities of osteogenesis in both jaws, but similar to the previous stage of development ossification in the mandible occurs quicker. Thus, if the maxilla does not have compact consolidation of the osseous islets, the latter practically form an integral osseous structure of a trabecular type in the mandible. At the same time, a common feature for both jaws is that the osseous tissue increases in them by means of an appositional way at the expense of active proliferation of osteoblasts located on the surface of the osseous tissue, and their secretion of the intercellular substance components in which they gradually are embedded.

Morphology of the osteoblasts located in the periphery of the osseous basis of the jaws is rather variable. First of all, they are different by their shape. They may be oval and amorphous. Basophilia of their cytoplasm is diverse, which is associated with a different degree of their differentiation. In the course of embedding the cells into the intercellular substance they become of an elongate shape.

At this stage of development the rates of histogenetic formation take place in the mandible. One of the signs is more accelerated osteogenesis in it. Stromal elements of the red bone marrow are formed in the centers of its osseous basis, while it is not observed in the upper jaw.

The alveolar processes in the form of osseous laminas connected close to the base are formed in both jaws.

The distal extremities of the osseous laminas form alveolar grooves (Fig. 6). And the thickness and degree of development of the external laminas are more expressed in comparison with the internal ones. The grooves are filled with mesenchyme inside. Bot typical mesenchyme cells and those on the stage of their differentiation are found in its loosely located cells. The structures of the alveolar nerves with basophil staining are clearly seen by their morphological peculiarities between the mesenchyme cells located in the alveolar grooves.

During the 10th week of the intrauterine development the rates of differentiation of the hard and soft tissues of the human maxillofacial apparatus continue to increase compared to the previous stage of development. The upper jaw is modeled by the osseous tissue islets fused between themselves, and the hard basis of the mandible together with the osseous tissue are still formed by Meckel's cartilage.

Osseous rudiments of both jaws are of a typical structure peculiar for the rough fibrous osseous tissue. The signs of periosteum formation are found in some places of their periphery, the external and internal layers can be seen in it. Fuchsine stained collagen fibers are found in the external layer, osteoblasts oriented by their long diameters parallel to the surface of the osseous base are located in the internal layer.

The osseous tissue matrix is unevenly contrasted. Its peripheral area manifests oxyphilic properties, and the central one is stained by the common dyes. Lacunas of various shapes are seen in it. Osteocytes with cytoplasmic processes emerging from them are located in the lacunas. As a result of fixing agent action their bodies become considerably smaller, therefore unstained cavities are visualized around cells. They give the osseous tissue a porous view.

Fusion of the distal extremities of Meckel's cartilage in the area of the chin at the end of the 10th week of the intrauterine development is a specific feature of the mandible development. The osseous formations located in the ventral-lateral position are directed forward coming closer together and are connected along the midline by means of the retention connective tissue ligament, which morphologic features are similar to the 9-week pre-fetuses.

Formation of the alveolar process continues along the whole osseous basis. The borders of its walls are directed to the side of dental rudiments and envelope them Y-shaped. The alveolar groove is filled with mesenchyme containing blood vessels and big trunks of the alveolar nerves.

The rami of the mandible are more visualized at this stage of development. They emerge from its proximal portions at an obtuse angle and decline from Meckel's cartilage cranially into the direction of the temporal bones where the areas of mesenchyme cells condensation are determined. They are rudiments of the heads of the temporomandibular joints.

Contrary to the osseous basis of the mandibular body which is directly formed from the mesenchyme, its rami are formed by the hyaline cartilage which is displaced by the osseous tissue later. Its intercellular matrix manifests pronounced basophilia.

During the 11-12th weeks of the intrauterine development the rami of the mandible continue to form. First they are formed by the hyaline cartilage, but to the end of the 12th week of the intrauterine development narrow deposits of the osseous tissue appear around the cartilage which differ from it by tinctorial features.

Meckel's cartilage is located to the middle from the osseous basis of the mandibular body. Space between it and the osseous tissue is filled with mesenchyme. This space is dilated in the proximal portion and narrowed to minimum in the distal direction.

Argyrophilic fibers are found in the connective tissue structures of the maxillofacial apparatus with silver impregnation. The centers of ossification are impregnated more intensively in comparison with other structures. The intercellular matrix of Meckel's cartilage is non-reactive, but the structural elements of the muscular tissue are found clearly (Fig.7).

Formation of the mandibular rami continues in the 12-week pre-fetuses. These rami emerge from the angles of the mandible in the dorsal-cranial direction. The hard base of the rami consists of the hyaline cartilage in the form of continuous bundles with relatively smooth borders. An amorphous component of the hyaline cartilage forming the mandibular rami and the heads of the temporomandibular joints demonstrate sharply basophilic properties. As far as the hyaline cartilage is replaced by the osseous tissue, tinctorial properties change into oxyphilic ones, and as a result the border between them is clearly visualized in the form of a broken line. Formation of the heads of the temporomandibular joints continues at this stage of development.

DISCUSSION

We have found that at the end of the 5th week of embryogenesis isolation of Meckel's cartilage is observed in the mandibular rudiments. The cartilage makes up their hard base. Parallel to this process the foci of mesenchyme condensation located in the lateral direction from the cartilage anlages are determined. From the topographic point of view these foci correspond to osteogenous islets which become more apparent during further stages of embryogenesis, that is, during the 6-7 weeks of development. In this respect the data of our study correspond to the data of other researchers [4].

The foci of direct osteogenesis in the upper jaw appear a week later after the fusion of the maxillary processes with the nasal and medial frontal processes. The researchers of this issue state [5] that the foci of the membranous ossification in both jaws are clearly determined in the embryos of the 8th week of development stained with alizarin and cleared in xylene, the parietal-coccygeal length of these embryos is 23,5 mm. At the same time, there are several ossification centers in the upper jaw which develop from the heterogeneous anlages. Thus, its cutting part is formed of the material of the nasal passages, and the rami originate from the maxillary spindles of the mandibular arch. The osseous tissue of these maxillary rami undergoes ossification first, while in the cutting portion this process occurs later.

According to the literary data [6], the human embryos 12,5-13,0 mm of PCL already have the primary palate. It is known to be resulted from the fusion of the distal extremities of the palatine processes [7]. Other sources state that this process occurs during the 8th week of embryogenesis. During the fetal period starting from the 9th week of development [8], the proximal portions of the palatine processes continue to approach each other. Their fusion is over at the end of the 9th week of the intrauterine development (33,0 mm of PCL) resulting in the formation of the secondary palate. These data are confirmed by our investigations as well. Still other sources admit that this process only starts at the 7-8 week and is over during the 10th week [9].

According to the data of the scientific sources [10], the rudiments of the maxillary sinuses in the form of small hollow formations begin to isolate during the 9th week of the intrauterine development. Our studies found that during this period of development the alveolar groove is formed in the mandible. The wall of the groove is formed by the two osseous laminas: internal and external. And the internal osseous lamina first is thinner in comparison with the external one. Free borders of the groove open into the side of enamel rudiments and involve them as Y-shaped. The alveolar groove is filled with poorly differentiated mesenchyme in which alveolar nerves pass and blood vessels are formed that gradually join together, and finally contact the rami of the major alveolar vessels. The process of the alveolar groove formation in the upper jaw is lagging behind in comparison with the mandible.

The osseous formations are the most extensional near the base of the alveolar groves of both jaws. Their amorphous part along the periphery is poorly oxyphile stained, while the central part of the alveolar crests demonstrates besophilia, and morphology of the cellular elements is similar to that of the chondrocytes.

Chondroid is supposed to be the periosteal osseous tissue in the process of formation, and the cells contained in it are similar to those of cartilage by their morphological characteristics. They are modified osteocytes possessing a convergent likelihood with chondrocytes. In the process of differentiation that makes up the basis of embryonic histogenesis the cellular elements of one and the same type are considered to be able to undergo a number of specific qualitative changes. As a result of these changes the cellular elements are specialized to perform certain functions [11].

Our studies demonstrated that in pre-fetuses 40,0 mm of PCL (the end of the 10th – beginning of the 11th weeks of development) the longitudinal fusion of Meckel's cartilage in the mandible results in maximum approach of its distal extremities and their fusion in the area of the chin.

During 11-12th weeks of the intrauterine development paired processes are formed in the area of the proximal ends of the mandibular rami directed upwards: ventral coronary and dorsal condylar ones.

At this period the structures forming articular heads appear on the ends of the condylar processes. Certain researchers state that isolation of these structures in the form of mesenchyme condensation occurs much earlier – during the 8th week of the intrauterine development. Their further formation continues during subsequent 10-12weeks in the form of rudiments of the hyaline cartilage which later will be replaced by the osseous tissue. Simultaneously with isolation of the articular heads the sockets of the joints begin to form as well. Their endesmal ossification continues as far as the articular heads are isolated. Meanwhile, even in 4-month human fetuses the temporomandibular joints are characterized by their incomplete structure. We did not find the formation of the temporomandibular joints during the 11-12th weeks of the intrauterine development either.

According to our data at this period the structure of the mandibular rami is mostly represented by the hyaline cartilage covered with a thin layer of the osseous tissue. The formation of the tissue occurs by means of appositional overlapping on the cartilaginous anlages modeling the rami. Therefore, the cartilage undergoes degenerative changes and is replaced by the osseous tissue.

Thus, contrary to the formation of the mandibular body, the formation of the osseous base of the mandibular rami results from indirect osteogenesis. And the data found in the course of our investigations correspond with the data of other researchers [12].

The rudiments of the mandibular rami in the distal direction join the osseous formations of its body. These formations from both sides envelope Meckel's cartilage in the form of an arch externally and approach one another in the area of the chin. Though, contrary to Meckel's cartilage they do not join together. Temporary compact connective tissue is formed between them at this period of time performing the role of a connective element at this stage of development. Further it will be replaced by the osseous tissue.

According to our findings, in the process of formation of the mandibular rami as far as their cartilaginous rudiments are replaced by the osseous tissue, the cartilaginous cells swell and enlarge in their sizes, their cytoplasm changes tinctorial properties becoming light and vacuolated. Glycogen is accumulated in it, and the nuclei undergo pyknotic changes and shrink. The major substance of the cartilage becomes harder and undergoes destruction. The mesenchyme grows into these places. A part of its cells are transformed into chondroclasts breaking down the cartilaginous tissue, and on its place mesenchyme cells are differentiated into the osteoblasts and osteocytes. Advance of this process is best observed in the areas of future articular heads.

The mandible in its development is known to be characterized by intra-cartilaginous formation of the bone which starts from the ends of the cartilage gradually displaced by the osseous tissue. It is indicated that [13] both jaws in pre-fetuses 37,0 and 42,0 mm of PCL are presented by the typical cartilaginous tissue, and in pre-fetuses 45,0-50,0 mm of PCL the osseous tissue is already available replacing the cartilaginous one. Although, we did not find enchondral osteogenesis of Meckel's cartilage in the objects examined.

CONCLUSIONS

1. During the 7th week of development (pre-fetuses 14,0-20,0 mm of PCL) the maxillary processes maximum approach the lateral and medial nasal ones; in pre-fetuses 20,0 mm of PCL they join the frontal spindle forming the facial structures (upper jaw and lip, vestibule of the oral cavity, rudiments of dental laminas, and rudiments of dental buds in its distal portions). Osteogenous islets, rudiments of the mimic and masticatory muscles, blood vessels are formed.
2. During the 8th week of development the osseous tissue of the mandible is formed, the alveolar processes are formed.
3. The oral and nasal cavities are isolated in 9-10-week pre-fetuses (33,0-40,0 mm of PCL), the mass of the osseous tissue increases in both jaws, the enamel organs are detached, the angles and rami formed by the hyaline cartilaginous tissue of the mandible are determined, the rudiments of the temporomandibular joints are already seen.
4. During the 11th week of development the osseous base of both jaws become formed. Till the end of the 12th week the osseous tissue begins to replace the hyaline cartilage of the mandibular rami, and the articular heads are formed in the portion of their proximal ends.

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The work is a fragment of the research work of the Department of Histology, Cytology and Embryology of Bukovinian State Medical University "Structural and functional features of tissues and organs in ontogenesis, patterns of variant, constitutional, gender, age and comparative human morphology", state registration number 0121U110121.

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Conflict of interest:

The Authors declare no conflict of interest.

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Received: 05.06.2021
Accepted: 04.03.2022

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article