

10. Cabrera AJR. Zinc, aging, and immunosenescence: an overview. Pathobiol Aging Age Relat Dis. 2015 Feb; 5: 10.
11. Desa K, Peric M, Husedzinovic I, Sustic A, Korusic A, Karadza V, et al. Prognostic performance of the Simplified Acute Physiology Score II in major Croatian hospitals: a prospective multicenter study. Croat Med J. 2012 Oct; 53(5): 442-9.
12. Ghasemi A, Zahediasl S, Hosseini-Esfahani F, Azizi F. Gender differences in the relationship between serum zinc concentration and metabolic syndrome. Ann Hum Biol. 2014 Sep-Oct; 41(5): 436-42.
13. Kartheek K, Baliga BS, Subodhshetty, Mithra P, Yadav C. Nutrient deficiencies (Copper, Zinc, Iron, Magnesium) among children with SIRS/sepsis—a hospital based cross sectional study. Int J Contemp Pediatr. 2017 May; 4(3): 933-8.
14. Khazdouz M, Mazidi M, Ehsaei MR, Ferns G, Kengne AP, Norouzy AR. Impact of Zinc Supplementation on the Clinical Outcomes of Patients with Severe Head Trauma: A Double-Blind Randomized Clinical Trial. J Diet Suppl. 2018 Jan; 15(1): 1-10.
15. Reintam BA, Malbrain MLNG, Starkopf J, Fruhwald S, Jakob SM, De Waele J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. Intensive Care Medicine. 2012; 38(3): 384-94.

#### Реферати

#### ДЕФИЦИТ ЦИНКУ У ПАЦІЄНТІВ З ГОСТРОЮ ЦЕРЕБРАЛЬНОЮ НЕДОСТАТНІСТЮ, ЯКІ ПОТРЕБУЮТЬ ІНТЕНСИВНОЇ ТЕРАПІЇ: ФАКТОРИ РИЗИКУ І ПРОГНОСТИЧНІ МАРКЕРИ

Терів П.С., Удовицька Н.О.

Проведене подвійне констатуюче обсерваційне клінічне дослідження за участю 60 пацієнтів з гострою церебральною недостатністю які потребували інтенсивної терапії. У всіх пацієнтів фіксували стать, вік, клінічні характеристики пацієнта, медикаментозну підтримку, вміст цинку в крові. Серед обстежених пацієнтів частота реєстрації гіпоцинкемії становила 35%. Встановлено, що у зазначених хворих стать, вік, оцінки глибини порушень свідомості, тяжкості стану пацієнта, наявність ознак синдрому системної запальної відповіді, гастроінтестинальної недостатності, артеріальний перфузійний тиск, потребу в штучній вентиляції легень і призначенні атарактиків є факторами ризику виникнення цинкового дефіциту, на основі яких було створено модель прогнозування розвитку цинк-дефіцитного стану.

**Ключові слова:** цинк, гостра церебральна недостатність, інтенсивна терапія, прогноз.

Стаття надійшла 13.07.18 р.

#### ДЕФИЦИТ ЦИНКА У ПАЦИЕНТОВ С ОСТРОЙ ЦЕРЕБРАЛЬНОЙ НЕДОСТАТОЧНОСТЮ, НУЖДАЮЩИХСЯ В ИНТЕНСИВНОЙ ТЕРАПИИ: ФАКТОРЫ РИСКА И ПРОГНОСТИЧЕСКИХ МАРКЕРЫ

Терив П.С., Удовицкая Н.А.

Проведенное двойное констатирующее обсервационное клиническое исследование с участием 60 пациентов с острой церебральной недостаточностью, нуждающихся в интенсивной терапии. У всех пациентов фиксировали пол, возраст, клинические характеристики пациента, медикаментозную поддержку, содержание цинка в крови. Среди обследованных пациентов частота регистрации гипоцинкемии составляла 35%. Установлено, что у указанных больных пол, возраст, оценки глубины нарушений сознания, тяжести состояния пациента, наличие признаков синдрома системного воспалительного ответа, гастроинтестинальной недостаточности, артериальное перфузионное давление, потребность в искусственной вентиляции легких и назначении атарактиков являются факторами риска возникновения цинкового дефицита, на основе которых была создана модель прогнозирования развития цинк-дефицитного состояния.

**Ключевые слова:** цинк, острая церебральная недостаточность, интенсивная терапия, прогноз.

Рецензент Дельва М.Ю.

DOI 10.26724/2079-8334-2019-1-67-102

UDC 616.315-007.254-089

P.I. Tkachenko, O.B. Dolenko, N.M. Lakhmatova, S.O. Bilokon, V.O. Dobroskok  
Ukrainian Medical Stomatological Academy, Poltava

#### CLINICOMORPHOLOGICAL CHARACTERISTICS OF THE WOUND PROCESS AT THE EARLY POSTOPERATIVE PERIOD AFTER RADICAL URANOSTAPHYLOPLASTY

E-mail: vitalinadobroskok87@gmail.com

The purpose of the paper was to study the clinical situation and the morphological structure of the biopsy material of the hard palate mucoperiosteal grafts in children with the congenital cleft palate before surgery and at the early postoperative period after radical uranostaphyloplasty. The study of clinical characteristics and general somatic state of children with this pathology before operative intervention enables to reveal the marked anatomical and functional disorders. The study of the wound process at the early postoperative period after radical uranostaphyloplasty with the help of morphological structure of the biopsy material of the hard palate mucoperiosteal grafts enables to predict the degree of probability of the formation of dense scar and make individual plan of treatment-and-prophylactic and rehabilitation measures for this category of patients.

**Keywords:** children, congenital cleft palate, reparative regeneration.

*The work is a fragment of the research project "Integrative-differentiated substantiation of selecting the best methods for surgical interventions and the volume of therapeutic measures in the surgical pathology of the maxillofacial area", state registration No. 0116U003821.*

Congenital malformations of the maxillofacial area are the most common among other facial defects where congenital cleft lip and palate account for 90% of all cases. The degree of severity of anatomical abnormalities of the palate significantly affects the progress of the postoperative period, the frequency of occurrence and severity of complications, differentiation of the upper jaw bone frame [1, 2, 6, 9].

Postoperative complications, related to the nature of the wound healing, worsen the general condition of the patient, prolong the time period of inpatient treatment and contribute to the development of the residual defects, which requires repeated surgeries. It is often associated with the type and size of the cleft defects and sufficient availability of soft tissue component, associated with concomitant somatic diseases of a child. Unfortunately, no clear tactics in relation to the definition of the conceptual approach to the prevention and treatment of undesired aftermaths exists to date [4, 7, 8].

Therefore, when planning a surgical intervention the clinical situation of every specific case should be thoroughly studied at the preoperational period to prevent postoperative complications; the objective estimation of anatomical and functional disorders that formed within the tissues of the nasolabial complex and the upper jaw should be made in advance. In addition to a careful and rational examination of the ability of the wound surfaces to reparative regeneration around the hard palate mucoperiosteal grafts should be considered. The study of their morphological features can be the basis for the creation of optimal conditions for wound healing, promote the opportunity to study the complex of preventive measures at all stages of observation, actions aimed at improving the metabolic processes, better proliferation of regional blood vessels and microcirculation in them. It may be a prerequisite to ground the importance of the use of pharmacological drugs that are able to influence the process of scarring and, at the final stage, on the density of the scar and its potential tendency to direct participation in the formation of cicatricial deformation of the palate.

**The purpose** of the paper was to study the clinical situation and morphological structure of the biopsy material of the hard palate mucoperiosteal grafts in children with cleft palate before surgery and at the early postoperative period after radical uranostaphyloplasty.

**Material and methods.** The findings of the clinical study are based on examination of 27 children with congenital dipnoous unilateral cleft palate, aged from 2 to 5 years (girls n=11, boys n=16). Cleft defect on the left side was found in 15 (55.5%) children and in 12 (44,4%) children it was on the right side. The control group comprised of 10 children who underwent surgery with regard of dystopia and retention of maxillary teeth or with the presence of benign tumors in this area.

Biopsy material of the soft tissue of the palate, collected from the area of the neurovascular fascicle output from the pterygopalatine foramen during the uranostaphyloplasty, was used. Their repeated sampling was carried out on the 6-7 day after surgery, using the proposed needle for taking biopsy material. The research was conducted in accordance with the ethical standards of the bioethics committee, developed in accordance with the Helsinki Declaration of the World Medical Association (1964), supplemented by the 59th General Assembly of WMA, Seoul, 2008.

Once the biopsy material was fixed, the follow-up 60 min prefixing in the phosphate buffer 4% glutaraldehyde solution (pH 7.4) was made at a temperature of 4°C. Semi-thin sections obtained from the soft tissue of the palate, embedded into EPON-812 were made on the rotational microtome MPS-2 and stained with fresh and twice filtered 0,1% methylene blue solution [3].

Uranostaphyloplasty was carried out by one surgeon according to the method suggested by Prof. Kharkov L.V. [5] to ensure the validity of the study. One and the same suture material was used in all cases.

**Results of the study and their discussion.** In patients with dipnoous unilateral cleft the main clinical signs were the presence of the linear scar on the upper lip, remaining from the previous cheiloplasty and combined defect, extended on the alveolar process, hard and soft palate. In 3 cases (11.1%) a narrow septum, continuous with the cleft, was detected at the base of the nostril.

In 22 cases (81.5%) the cleft passed through the alveolar process between the lateral incisor and canine or between the central and lateral incisors (5 children; 18.5%). In 25 patients (92.5%) the width of the cleft defect at the level of the alveolar process ranged from 2 to 8 cm and in 2 cases (7.4%) a dense fuse of the margins of cleft was found. The defect split the palate into two unequal halves. Anteriorly, a well developed intermaxillary bone, rotated and protruded in 7 (25.9%) children, was fused with a larger fragment. Palatine process was somewhat elevated and joined with vomer on the margin of the defect. In all cases a smaller fragment looked like hypoplastic and significantly shifted medioposteriorly. The width of the cleft on the border of hard and soft palate ranged from 8 to 23 mm. All patients experienced swelling and hyperemia of mucous membranes on the margins of the cleft.

In 7 children (25.9%) uneven shortening of the halves of the soft palate was noted; in 11 patients (40,7%) shifting of the smaller fragment posteriorly was detected, leading to elongation of this half of the soft palate, whereas in another 9 patients (33.3%) the smaller fragment was hypoplastic due to osseous fragment and soft tissues.

Deformation of the nose cartilaginous section, expressed differently, was detected in all patients with this nosological form. Commonly, the front pole of the tip of the nose on the side of the defect was significantly retracted and a deformed nosewing was descended. The medial peduncles of the wing

cartilages were displaced in relation to each other, and the inner corner of the deformed cartilage was lower than on the healthy side. This led to the reduction of the height of the anterior portion of the nasal septum on the affected side and contributed to its deformation.

In 20 patients (74%) S-shaped nasal septum deviation (in the inferior section it was in the direction opposite to the cleft, and in the superior section it was in the direction to the defect) was observed, which was accompanied by the hypertrophy of the nasal turbinates. Mucous membrane of the turbinates was cyanotic with irregular contours and in 3 cases (11.1%) it was hypertrophy and partially obturated the cleft and inferior nasal meatus in the anterior or posterior sections.

Examination of the oro- and nasopharynx revealed the enlargement of the palatine and pharyngeal tonsils, hypertrophy of the mucous membrane of the posterior wall of the pharynx (granular adenoid infiltration) in patients aged 4-5 years, and shortening of the anterior palatine arch was detected in all patients. Adenoid hypertrophy was noted in 12 cases (44.4%).

Noteworthy, the pronounced nasal septum deviation, hypertrophy of nasal turbinates and lymphoid substance of the nasopharynx was most often manifested in patients over 4 yrs and were more significant from the side of the cleft location. Moreover, all examined patients experienced speech disturbances in the form of open rhinolalia, rhinology, unclear pronunciation of certain sounds.

The resulting morphological studies have revealed stratified squamous keratinized epithelium of the palatine mucosa in children of control group who underwent surgery about dystopia and retention, or benign tumors in the anterior maxilla. The lamina propria of the mucosa in the area of the neurovascular fascicles output consisted of loose fibrous shapeless connective tissue without papillae and separated from the epithelium by the basal membrane. A well-developed layer of the elastic fibers and well-marked submucous layer, rich in lipocytes and fine salivary glands, was located behind it (fig. 1). The resulting data of our study concur with finding of other authors [4].

Morphological study of the biopsy material of children with congenital cleft palate, collected just before the surgical intervention, revealed the specific changes of the epithelium in the area of the neurovascular fascicles output. Intracellular edema of the medial and outer layers of the acanthocytes and presence of vacuoles in the cytoplasm of the cells that occupied the entire cell, driven back the nucleus to the periphery, was specific. Moreover, in all specimens it was represented by the oblate cells with elongated nuclei, indicating the parakeratosis. In 9 children (33.3%) epithelium was thickened to 15-17 layers of the acanthocytes, epithelial ridges were elongated, indicating about the events of acanthosis. At the same time the nuclei of epithelial cells were reduced in size and stained more intensively (fig. 2).

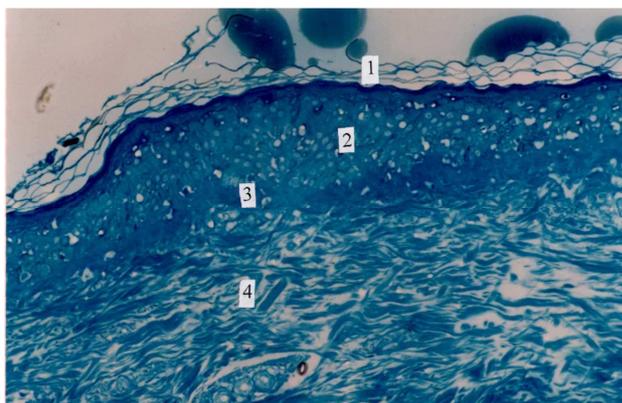


Fig. 1. Microphotogram of the fragment of biopsy material of palatine mucosa in the 4 year-old child M.; control group; medical history No.744. Semi-thin section.  $\times 900$  magnification. Methylene blue stain. Horny layer (1), cells of the granular layer (2), epithelial basal layer (3), connective tissue fibers (4).

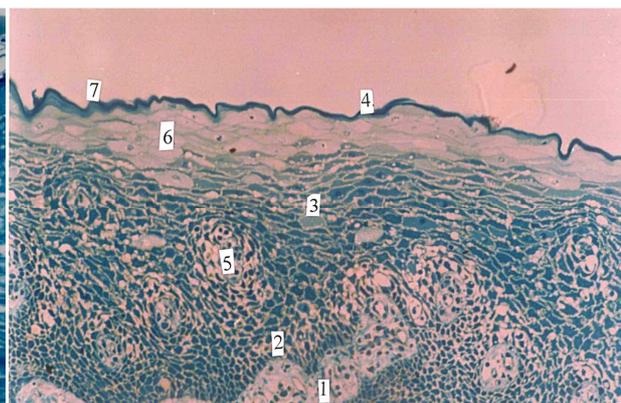


Fig. 2. Microphotogram of the fragment of biopsy material of mucous membrane of a child with congenital cleft palate on the left side before surgery. Patient G.; medical history No. 835. Semi-thin section.  $\times 900$  magnification. Methylene blue stain. Connective tissue (1), epithelial basal layer (2), vacuolar degeneration in the granular layer (3), horny layer (4), connective tissue papillae (5), superficial layer of the epithelium with the events of parakeratosis (6), acanthoma (7).

Such changes are specific to hydropic (another name is vacuolar) degeneration. In 8 cases (29.6%) hydropic degeneration was observed along with acanthosis. Round cell or lymphohistocytic infiltration was also detected in the lamina propria of the mucous membrane in 16 observations (59.5%).

On the 6-7 day after uranostaphyloplasty and removal of protective plate from the palate the healing run in compliance with the patterns of the primary intention on the palatine midline and secondary intention in other areas in all patients.

Microscopically, the tissues of biopsy material were represented by the new granular tissue with big amount of leucocytes and small number of macrophages. Noteworthy, the cellular elements prevailed over the fibrous structures, and a significant number of newly formed capillaries in connective tissue was detected (fig. 3).

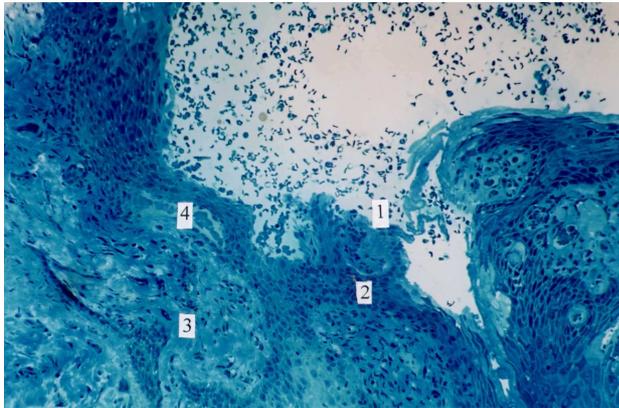


Fig. 3. Microphotogram of the fragment of biopsy material in the area of surgical intervention in a child with congenital cleft palate on the right side on day 6-7. Patient B.; medical history No. 2224. Semi-thin section.  $\times 900$  magnification. Methylene blue stain. Margin of the wound tract with blood clots (1), epithelium with leucocytic infiltration (2), connective tissue with microvessels (3), venous stasis (4), newly formed capillaries (5).

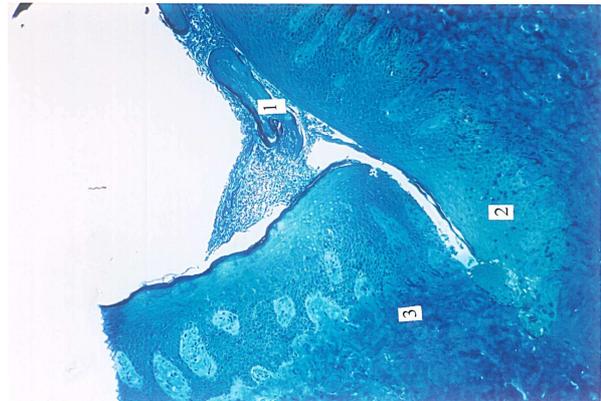


Fig.4. Microphotogram of the wound defect on the area of surgical intervention in a child with congenital cleft palate on the right side; initial epithelization, day 6-7. Patient B.; medical history No.2224. Semi-thin section.  $\times 900$  magnification. Methylene blue stain. Migration of epithelium onto the wound surface (1), infiltration of polymorphonuclear leukocytes and macrophages (2), connective tissue (3).

A marked leucocytic infiltration and enhanced serofibrinous exudates, accompanied by the signs of congestion and local hemorrhages caused by the presence of the red blood cells, as well as small amount of mastocytes with the signs of degranulation, was noted on the wound surface margin in the biopsy material sections of 25 patients (92.5%).

In addition, edema in the tissues, manifested by the hydropic degeneration of the cells was detected, as well as rejecting foci of micronecrosis. At that period a partial epithelization on the wound margin was noted on 20 specimens (74%).

It was expressed in migration, i.e. covering of granular tissue by the epithelium from all sides. Initial signs of differentiation of migrating epithelium were found in 14 specimens (51.8%), expressed by diminishing of its nuclei; the pole of the cells was perpendicular to the layer that covered the defect; round cells were changed into polymorphous ones (fig. 4).

Consequently, the study of the clinical characteristics and general somatic state of children with congenital cleft palate prior to surgical intervention has revealed the marked anatomical and functional disorders.

In patients with dipnoous unilateral cleft palate the main clinical signs were the presence of a linear scar on the upper lip, remained from the previous cheiloplasty and combined defect, extended on the alveolar process, hard and soft palate, separating them into two unequal, underdeveloped, deformed fragments. Anatomical abnormalities in the form of deformity of the external nose, narrowing of the nostrils and nasal septum deviation of different severity were detected in all examined patients.

Study of the morphological structure of the hard palate mucoperiosteal grafts in the area of the neurovascular fascicles output in children with congenital cleft before surgery has revealed the presence of the vacuolar degeneration in the acanthocous layer of the epithelium, which, in our opinion, is the outcome of the cumulative impact of microcirculation disorders and antigen load. Moreover, the decrease in the events of keratinization and manifestations of dystrophic processes in epithelium in the form of acanthosis was observed, indicating a modified appropriate response of the palatine tissues on physical load due to the dysfunction of mastication and deteriorated blood circulation. These features in the structure of mucosa in children with congenital defects provide with the prerequisites for inadequate regeneration of the epithelium in this area and create the basis for further formation of scar.

Microscopically, on day 6-7 after uranostaphyloplasty the patients experienced the phase of post-traumatic inflammation. At this time, cellular elements prevailed over the fibrous structures, and white blood cells dominated over the macrophages. The marked leucocytic infiltration indicated the presence of the inflammatory component in the wound, which can cause intensification of the collagen synthesis and stipulate the formation of denser scar.

It is known that macrophages can both phagocytize the red blood cells, destructed forms of leukocytes, fibrin and adipose cells, and secrete specific substance which enhances proliferation of

fibroblasts and plays a certain role in collagen resorption. Therefore, at the period of observation, their small amount definitely affects the quality of the proliferative reaction of fibroblasts and prolongs the process of wound healing. Slowed marginal wound epithelization leads to premature sclerosis of granular tissue and also creates the prerequisites for the formation of denser scars.

### Conclusion

Study of the morphological structure of the biopsy material of hard palate mucoperiosteal grafts in children with cleft palate before surgery and in the early postoperative period enables to predict the degree of probability of the formation of dense scar and make individual plan of treatment-and-prophylactic and rehabilitation measures for this category of patients.

### References

1. Hulyuk AH, Kohan LB, Demyd OI, Kryklyas VH, Dmytriyeva NB. Medyko-sotsialna reabilitatsiya ditey z pryrodzhenoyu patolohiyeyu oblychchya. Visnyk stomatolohiyi. 2015; 2: 54-60. [in Ukrainian]
2. Demid AI, Makarenko OA, Tashchyan AE. Biokhimicheskiye pokazateli rotovoy zhidkosti u detey s nesrashcheniyami noba. Vestnik stomatologii i chelyustno-litsevoy khirurgii (Armeniya). 2014; 11(1-2): 9-11. [in Russian]
3. Karupu VYa. Elektronnyaya mikroskopiya. K.: Vyshcha shkola. 1984; 240s. [in Russian]
4. Tkachenko PI, Bilokon SO, Lokhmatova NM, Dobroskok VO. Vyrashenist psykhoemotsiynoho napruzheniya na sytuatsiynyi stres u ditey iz nezroshchennyamy pidnebinnya. Ukrayinskyi stomatolohichnyy almanakh. 2017; 1: 75-78. [in Ukrainian]
5. Kharkov LV. Khirurgicheskoye lecheniye vrozhdennykh nezarashcheniy noba.- K.: Vyshcha shkola. 1992; 210s. [in Russian]
6. Abdel-Aziz M, Khalifa B, Shawky A. et al. Trans-oral endoscopic partial adenoidectomy does not worsen the speech after cleft palate repair. Braz.J. Otorhinolaryngol. 2016; 83 (4): 422-426.
7. Bhuskute AA, Tollefson TT. Cleft Lip Repair, Nasoalveolar Molding, and Primery Cleft Rhinoplasty. Facial Plast Surg Clin North Am. 2016; 24 (4): 453-466.
8. De Ladeira PRS, Alonso N. Protokols in Cleft Lip and Palate Treatmen: Systematic Review. Plast Surg Int [Internet]. 2012 [cited 2016 Oct 1]; 2012. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3503280/>.
9. Mostafa NZ, Doschak MR, Major PW, Talwar RJ. Reliable critical sized defect rodent model for cleft palate research. Craniomaxillofac. Surg. 2014; 42(8): 1840-1846.

### Реферат

#### КЛІНІКО-МОРФОЛОГІЧНА ХАРАКТЕРИСТИКА РАНОВОГО ПРОЦЕСУ В РАНЬОМУ ПІСЛЯОПЕРАЦІЙНОМУ ПЕРІОДІ ПІСЛЯ РАДИКАЛЬНОЇ УРАНОСТАФІЛОПЛАСТИКИ

Ткаченко П.І., Доленко О.Б., Лохматова Н.М.,  
Білоконь С.О., Доброскок В.О.

Метою роботи було вивчення клінічної ситуації та морфологічної структури біоптатів слизово-окісних клаптів піднебіння у дітей з його вродженими незрощеннями до оперативного втручання та в ранньому післяопераційному періоді після радикальної ураностафілопластики. Дослідження клінічної характеристики та загально соматичного стану у дітей з цією патологією до оперативного втручання дозволило виявити у них виражені анатомічні та функціональні порушення. Вивчення ранового процесу в ранньому післяопераційному періоді після радикальної ураностафілопластики за допомогою морфологічної структури біоптатів слизово-окісних клаптів піднебіння дає змогу спрогнозувати ступінь вірогідності формування щільного рубця, та скласти індивідуальний план лікувально-профілактичних і реабілітаційних заходів для цієї категорії хворих.

**Ключові слова:** діти, вроджені незрощення піднебіння, репаративна регенерація.

Стаття надійшла 21.06.18 р.

#### КЛИНИКО-МОРФОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА РАНЕВОГО ПРОЦЕССА В РАННЕМ ПОСЛЕОПЕРАЦИОННОМ ПЕРИОДЕ ПОСЛЕ РАДИКАЛЬНОЙ УРАНОСТАФИЛОПЛАСТИКИ

Ткаченко П.И., Доленко О.Б., Лохматова Н.М.,  
Белоконь С.А., Доброскок В.А.

Целью работы было изучение клинической ситуации и морфологической структуры биоптатов слизисто-надкостничных лоскутов неба у детей с его врожденными несращениями до оперативного вмешательства и в раннем послеоперационном периоде после радикальной ураностафилопластики. Исследование клинической характеристики и общего соматического состояния у детей с этой патологией до оперативного вмешательства позволило выявить у них выраженные анатомические и функциональные нарушения. Изучение раневого процесса в раннем послеоперационном периоде после радикальной ураностафилопластики с помощью морфологической структуры биоптатов слизисто-надкостничных лоскутов неба позволяет спрогнозировать степень достоверности формирования плотного рубца, и составить индивидуальный план лечебно-профилактических и реабилитационных мероприятий для этой категории больных.

**Ключевые слова:** дети, врожденные несращения неба, репаративная регенерация.

Рецензент Аветіков Д.С.