

**OFFICIAL JOURNAL OF THE SCIENTIFIC SOCIETY OF  
ANATOMISTS, HISTOLOGISTS, EMBRYOLOGISTS AND  
TOPOGRAPHIC ANATOMISTS OF UKRAINE**

**DOI: 10.31393  
ISSN 1818-1295  
eISSN 2616-6194**

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# **ВІСНИК МОРФОЛОГІЇ REPORTS OF MORPHOLOGY**

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**Vol. 26, №4, 2020**

**Scientific peer-reviewed journal in the fields of normal and pathological anatomy, histology, cytology and embryology, topographical anatomy and operative surgery, biomedical anthropology, ecology, molecular biology, biology of development**

**Published since 1993  
Periodicity: 4 times a year**

**Vinnytsya · 2020**

# ВІСНИК МОРФОЛОГІЇ - REPORTS OF MORPHOLOGY

Founded by the "Scientific Society of Anatomists, Histologists, Embryologists, and Topographic Anatomists of Ukraine" and National Pyrogov Memorial Medical University, Vinnytsya in 1993

Certificate of state registration KB №9310 from 02.11.2004

Professional scientific publication of Ukraine in the field of medical sciences in specialties 221, 222, 228, 229  
According to the list of professional scientific publications of Ukraine, approved by the order of the Ministry of Education and Science of Ukraine No. 1188 of 24.09.2020 (Annex 5)

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Approved by the Academic Council of National Pyrogov Memorial Medical University, Vinnytsya, protocol №6 from 24.12.2020.

**Indexation:** CrossRef, Index Copernicus, Google Scholar Metrics, National Library of Ukraine Vernadsky

## **Address editors and publisher:**

Pyrogov Str. 56,  
Vinnytsya, Ukraine - 21018  
Tel.: +38 (0432) 553959  
E-mail: nila@vnmue.edu.ua

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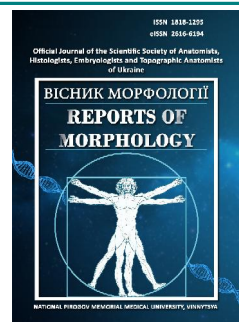




## REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>



## Forensic medical evaluation of dental-jaw injuries in cases of traffic accidents

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### ARTICLE INFO

Received: 31 July, 2020

Accepted: 7 September, 2020

UDC: 616-001.4/6-036.88-079.6

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*Information about the differential diagnosis of human bodily injuries, which were formed when the body, wheel and bottom of a modern car came into contact with the body of a pedestrian; a person on the road surface, in the cabin of a modern car (driver and passengers), when a cyclist comes into contact with a car, in cases of combined types of car injury, is not enough. The purpose of the study is to increase the objectivity of forensic examinations by determining the criteria for assessing damage to the dental system in cases of the most common types of accidents: collision of moving vehicle with man; run over the body with a wheels or the bottom of vehicle; at an injury inside the vehicle on the basis of the analysis of morphological features and the mechanism of the specified damages. The archival materials of 130 forensic medical examinations of the municipal institution "Odessa Regional Bureau of Forensic Medical Examination" concerning victims of living persons and corpses as a result of traffic accidents that were accompanied by their injuries in the period 2015-2020 were used. The following research methods were used: anthropometric, morphometric, photographic, radiological, statistical. The article presents our own experience of improving the objectivity and provability of forensic examinations by determining the criteria for assessing damage to the dental system in cases of the most common types of vehicle: collision of moving vehicle with man; run over the body with a wheels or the bottom of vehicle; at an injury inside the vehicle on the basis of the analysis of morphological features and the mechanism of the specified damages. It is proved that according to the degree of gravity of physical injuries (health disorder or disability), damage to the dental apparatus in traffic accidents should be investigated only in cases of isolated injuries. In this case, fractures of the jaws, regardless of their nature, should be assessed as moderate injuries according to the criterion of long-term health disorders; Crown fractures, traumatic tooth dislocations, and soft tissue fatal wounds should be considered simple injuries that have caused short-term health disorders. Abrasions, bruises should be attributed to simple injuries. Thus, it is impractical to separately determine the severity of the injury of the dental system in cases run over the head with a wheels or the bottom of vehicle - in these cases, we always deal with gross, massive destruction of the bones of the skull.*

**Keywords:** physical injuries, dental apparatus, traffic accident, vehicle injury, forensic examination.

### Introduction

Traffic injuries are one of the most pressing problems of today, because, according to official statistics of the SAI of the Ministry of Internal Affairs of Ukraine, every day there are an average of 477 traffic accidents in which about 12 people die and about 100 people are injured. the number of people killed in road accidents in Ukraine fluctuated

annually within 4 thousand people [13]. Accident statistics remain at about the same level today.

The main causes of traffic accidents are disregard for traffic rules, including collisions due to speeding, non-compliance with the distance, violation of maneuvering rules, collision with standing vehicles or various obstacles,

poor road conditions, etc. In addition, according to the Center for Traffic Safety SAI UMIA, more than 40 % of all accidents occurred when the participants of the accident were in a state of alcohol intoxication, in particular, in 2015 there were 2358 (9.7%) cases of accidents with victims, committed by drivers in a state of alcohol intoxication, which killed 317 people and injured 3203 [13].

It is clear that one of the most important pieces of evidence in road accident cases is the opinion of a forensic expert. Of course, the most important objects of study in performing such examinations are the victims (corpses or living persons). In general, these issues have been carefully studied by both domestic [11, 22, 23] and foreign authors [1, 10, 17, 18, 19, 24, 25]. Particular attention in cases of accidents was paid to comprehensive studies [1, 3, 4, 5, 7]. However, in the study of injuries in victims of traffic accidents traditionally paid attention primarily to damage to the lower extremities (due to the action of the car bumper), torso, skull bones and brain [5, 6, 10, 15, 17, 19, 26]. Therefore, accordingly, in the forensic literature there are very few works related to other injuries received by victims of traffic accidents, in particular, injuries of the dental apparatus [3, 8, 12, 20, 24, 25, 27]. Meanwhile, the assessment of such injuries by their severity is extremely important, especially in situations where injuries in victims are limited to damage to the bones of the facial skeleton [16, 26].

Given the above, this work aims to address this shortcoming.

The aim of the study was to increase the objectivity of forensic examinations by determining the criteria for assessing damage to the dental system in cases of the most common types of accidents: collision of moving vehicle with man; run over the body with a wheels or the bottom of vehicle; injury inside the vehicle on the basis of the analysis of morphological features and the mechanism of the specified damages.

### Materials and methods

The objects of the study were archival materials of the municipal institution "Odessa Regional Bureau of Forensic Medical Examination" for 2015-2020, namely: 1) 30 "Expert Conclusions" on traffic accidents that were accompanied by injuries and deaths; 2) 73 "Expert conclusions" on traffic accidents that were accompanied by injuries to survivors; 3) 20 "Expert conclusions" (complex forensic medical and transport-trasological examinations on the facts of traffic accidents, which were accompanied by death and injury).

All 130 victims had injuries to the dental apparatus. The distribution of the number of all victims studied by us as a result of traffic accidents with injuries of the dental apparatus for different types of injuries is shown in table 1.

It should be noted that during forensic examinations of corpses conducted research and analysis:

a - a description of the damage to the dental apparatus in the victims (corpses), which was made by an expert

**Table 1.** Distribution of the number of victims who received injuries of the dental apparatus for different types of injuries

№	Type of injury	Number of victims
1	collision of moving vehicle with man	40
2	inside the vehicle	62
3	run over the body with a wheels or the bottom of vehicle	21
Total		123

directly "at the section table";

b - photographic images of the relevant damage;

c - schematic images of injuries of the dental apparatus in the victims (corpses), which were made by an expert who performed a forensic autopsy;

d - the results made by the expert who carried out autopsy of the corpse of the victim in traffic accident.

In the study of forensic examinations of victims, accused and other persons conducted research and analysis:

a - a description of the damage to the dental apparatus in the victims, which was made by an expert who examined the victim in the accident;

b - schematic images of injuries of the dental apparatus in the victims, which was made by an expert who examined the victim;

c - the results of radiological examinations of the bones of the facial skeleton in the victims;

d - dental cards of victims and other medical documentation;

e - the results made by the expert who conducted the examination of the victim.

In the study of complex forensic and transport-trasological examinations on the facts of the accident studied and analyzed:

a - a description of the injuries of the victims, which was made by an expert directly "at the section table", or during the examination of the surviving victim by an expert;

b - photographic images of bodily injuries in the victims;

c - schematic images of bodily injuries in the victims, which were made by an expert who performed a forensic autopsy or examined a living person;

d - the results of forensic examination of objects that were seized during a forensic autopsy;

e - results of X-ray examinations of victims (radiography, CT and MRI examinations) - during the examination of living persons;

f - results of the commission of experts.

The research results are processed by standard methods of variation statistics.

Anthropometric, morphometric, photographic, radiological and statistical research methods are used in the work.

### Results

During the forensic analysis of injuries of the dental system in cases of various types of traffic accidents, the following was established. *In cases of collision of moving*

**Table 2.** Distribution of the nature of injuries of the dental system depending on the types of injuries in the number of cases.

№	The nature of the damage	Injury due to collision of moving vehicle with man	Injury inside the vehicle	Injury due to run over the body with a wheels or the bottom of vehicle
1	Fractures of tooth crowns	11	38	Massive destruction
2	Traumatic dislocations of teeth	14	8	Massive destruction
3	Fractures of the lower jaw	10	7	Massive destruction
4	Fractures of the upper jaw	5	9	Massive destruction
Total		40	62	

vehicle with man, the most typical were the following injuries of the dental system:

- fractures of the crowns of the 1st and 2nd teeth of the upper jaw and the 1st, 2nd, 3rd teeth of the lower jaw, which were accompanied by hemorrhage and stab wounds of the mucous membrane of the upper and lower lips, as well as large abrasions and stab wounds to the skin face in the area of these injuries (11 cases);

- closed and open fractures of the mandibular bones in the area of its body (4 cases) or corners of the jaw (6 cases);

- closed fractures of the bones of the upper jaw LeFort (LeFort, 1901) type II (5 cases);

- complete and incomplete traumatic dislocations of the 1st, 2nd, 3rd teeth of the upper and lower jaws with hemorrhages, fatal wounds of the mucous membrane of the upper and lower lips of the victims, as well as accompanied by facial skin injuries in the area of these injuries (14 cases);

- these injuries were combined with each other in different variants - fractures or traumatic dislocations of the teeth were combined with fractures of the jaw bones, or only with injuries of the soft tissues of the face;

- it should be noted that in this type of accident in no case we found isolated damage to the dental system - they were all accompanied by damage to the bones of the skull or injury to other parts of the body (fractures of limbs, ribs, internal injuries, etc.).

In cases of injury inside the vehicle there were the following injuries of the dental system:

- fractures of crowns of 1st, 2nd, 3rd teeth of the upper and lower jaw with hemorrhages and fatal wounds of the mucous membrane of the upper and lower lips, bruises and small abrasions of the face (38 cases);

- closed and open fractures of the mandible in the body (3 cases) or corners (4 cases);

- closed fractures of the upper jaw bones LeFort (LeFort, 1901) type II (6 cases), LeFort (LeFort, 1901) type III (3 cases);

- in 8 cases there were complete and incomplete traumatic dislocations of the 1st, 2nd, 3rd teeth of the upper and lower jaws, which were accompanied by hemorrhages, fatal wounds of the mucous membrane of the upper and lower lips of the victims, as well as facial skin lesions in the area of injuries;

- in contrast to the cases of collision of moving vehicle with man, in cases of injury inside the vehicle in about half

of the cases (30 cases) there were isolated injuries of the dental system - only teeth, jaw bones, soft tissues of the face not accompanied by trauma to the bones of the skull, other parts of the victim's body (we deliberately did not take into account the diagnosis of concussion, which, in our opinion, is not always justified and is not informative to establish the mechanism of injury). All cases of isolated injuries of the dental system concerned living persons and did not occur in cases of examination of corpses;

- other cases (combined damage to the dental system and bones of neurocranium, as well as other parts of the body) occurred in both cases of examinations of living persons and corpses.

In the case of injuries to the victim by run over the body with a wheels or the bottom of vehicle, all cases concerned the rolling of the wheel (or injury to the bottom of the car) of the victim's head. In these cases, we encountered only gross damage to the dental apparatus in the form of multifracture fractures of the jaws, the destruction of the dentition, which was *always accompanied by the same gross damage to the bones of the skull and brain.*

The distribution of the nature of the damage depending on the conditions of injury is shown in table 2.

## Discussion

Thus, the analysis of archival material of the municipal institution "Odessa Regional Bureau of Forensic Medical Examination", including materials of the departments: forensic medical examination of corpses, forensic medical examination of victims, accused and others, as well as forensic medical examinations of injuries of the dental apparatus in automobile injury to 130 people, indicates that in the most common types of traffic accidents (collision of moving vehicle with man, injury inside the vehicle, run over the body with a wheels or the bottom of vehicle) damage to the dental system is quite common.

Of the 130 cases, these injuries were most common in victims of the first two types of traffic accidents and are fractures of dental crowns (49 people), traumatic dislocations of the teeth (usually 1st - 2nd) (22 people), closed and open fractures of the mandible (usually in the area of the body or corners of the jaw) (17 people), closed fractures of the upper jaw bones LeFort (LeFort, 1901) type II and III (14 people) and various soft tissue injuries of the face.

We believe that damage to the dental system when the

car comes into contact with a pedestrian could be formed either by throwing the body on the car, or by falling the body on the road surface, which coincides with the results of research P.V. Plevinskis [11, 21, 22, 23].

Damage to the dental system due to injury in the car could occur when the person comes into contact with parts of the car, usually in frontal collisions, namely with the steering wheel, front panel, front windshield. This assumption of the mechanism of damage is consistent with the results of other similar studies [1, 5, 12, 14, 20, 24, 25].

The use of modern methods of control and diagnosis of changes in dental status and maxillofacial area in general helps to increase the level of objectification of the consequences and disorders arising from traffic accidents [3, 4, 5, 8, 12, 24]. The relevant task is to develop criteria for assessing the state of the dental system (level of dental health) before the direct impact of traumatic factors on the victim's body, and after completion of all necessary iatrogenic manipulations during rehabilitation after a traffic accident - thus, it will be possible to achieve proper stratification of the parameters of loss of dental health, differentiating them into those associated with previous violations of dental status, those that are directly related to the fact of injury, those associated with the residual compensation available at the time of injury range, and those that depend on the effectiveness of the chosen method of treatment [10, 20, 25, 27].

Specific forensic dental criteria can be used as reference points for assessing changes in dental status as a result of traffic accidents, the design of which provides unambiguous interpretation and clear identification orientation [2, 3, 5, 6, 7, 9, 10, 28].

Based on specific forensic dental criteria, it is possible to develop clear protocols for assessing the loss of dental health in the future, which can be used as additional parameters to verify the severity of the injury and the predicted effectiveness of dental rehabilitation.

## Conclusions

1. Analysis of morphological features and mechanism of damage to the dental system of victims in cases of the most common types of traffic accidents (collision of moving vehicle with man; run over the body with a wheels or the bottom of vehicle; at an injury inside the vehicle) and determination criteria by which it is advisable to assess these injuries, increase the objectivity and accuracy of forensic examinations and increase the provability of expert results.

2. According to the degree of severity of damage to the dental apparatus in traffic accidents, it is advisable to investigate only in cases of isolated injuries. In this case, fractures of the jaws, regardless of their nature, should be assessed as moderate injuries according to the criterion of long-term health disorders; crown fractures, traumatic tooth dislocations, and soft tissue contused wound should be considered minor injuries that have caused short-term health problems. Abrasions, bruises should be classified as minor injuries.

3. It is impractical to separately determine the injury of the dental system in cases of run over the body with a wheels or the bottom of vehicle by its severity - in these cases we always deal with gross, massive destruction of bones of the victim's skull, which automatically qualifies as serious injuries.

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#### СУДОВО-МЕДИЧНА ОЦІНКА УШКОДЖЕНЬ ЗУБОЩЕЛЕПНОГО АПАРАТА У ВИПАДКАХ ДОРОЖНЬО-ТРАНСПОРТНИХ ПРИГОД

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Відомостей щодо диференційної діагностики тілесних ушкоджень людини, що утворились при контакті кузова, колеса та днища сучасного автомобіля з тілом пішохода; людини, що знаходиться на дорожньому покритті, у салоні сучасного автомобіля (водія та пасажирів), при контакті велосипедиста з автомобілем, у випадках комбінованих видів автомобільної травми - недостатньо. Мета дослідження - підвищення об'єктивності виконання судово-медичних експертиз шляхом визначення критеріїв оцінювання ушкоджень зубощелепної системи у випадках найбільш розповсюджених видів ДТП: при контакті автомобіля, що рухається, із пішоходом; при перекочуванні через тіло потерпілого колеса та днищевої частини автомобіля; при травмі у салоні автомобіля на основі аналізу морфологічних особливостей і механізму вказаних ушкоджень. У роботі були використані архівні матеріали 130 судово-медичних експертиз комунального закладу "Одеське обласне бюро судово-медичної експертизи" стосовно потерпілих живих осіб і трупів внаслідок дорожньо-транспортних подій, що супроводжувалися їх травмуванням у період 2015-2020 р.р. Використані наступні методи дослідження: антропометричний, морфометричний, фотографічний, рентгенологічний, статистичний. У статті наведений власний досвід підвищення об'єктивності і доказовості судово-медичних експертиз шляхом визначення критеріїв оцінювання ушкоджень зубощелепної системи у випадках найбільш розповсюджених видів ДТП: при контакті автомобіля, що рухається, із пішоходом; при перекочуванні через тіло потерпілого колеса та днищевої частини автомобіля; при травмі у салоні автомобіля на основі аналізу морфологічних особливостей і механізму вказаних ушкоджень. Доведено, що за ступенем тяжкості (розладом здоров'я чи втратою працездатності) ушкодження зубощелепного апарата при дорожньо-транспортних пригодах доцільно досліджувати виключно у випадках ізольованих ушкоджень. При цьому, переломи щелеп, незалежно від їх характеру, слід

*оцінювати як тілесні ушкодження середнього ступеня тяжкості за критерієм тривалого розладу здоров'я; переломи коронок, травматичні вивихи зубів, забійні рани м'яких тканин слід оцінювати як легкі тілесні ушкодження, що спричинили короточасний розлад здоров'я. Садна і синці слід відносити до легких тілесних ушкоджень. Таким чином, недоцільно окремо визначати за ступенем тяжкості травму зубощелепної системи у випадках перекочування через голову колеса автомобіля або травмування дніщевою частиною - у цих випадках ми завжди маємо справу із грубими, масивними руйнуваннями кісток усього черепа потерпілого.*

**Ключові слова:** *тілесні ушкодження, зубощелепний апарат, дорожньо-транспортна подія, автомобільна травма, судово-медична експертиза.*

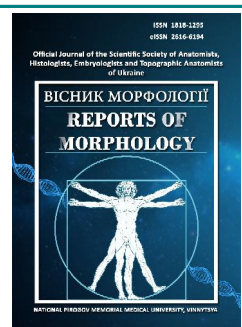
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## REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>



## Positive trend of Ukrainian surgeons' attitude to simultaneous operations: analysis of survey results

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### ARTICLE INFO

Received: 4 August, 2020

Accepted: 9 September, 2020

UDC: 616-089(477):303.621.3

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*In recent years, there has been an increase in attention to simultaneous operations, but their frequency does not meet real needs. The aim of the study was to determine the dynamics of surgeons' awareness of simultaneous surgery in combined abdominal pathology. The results of the survey of surgeons of surgical inpatient departments of regional, district and city hospitals, as well as institutes and university clinics of Poltava, Sumy, Rivne, Kharkiv, Luhansk and Donetsk regions (except for territories not controlled by the Ukrainian authorities) were analyzed. The sample was random within a homogeneous general population of surgeons. The first survey, which included 724 doctors, was conducted in 2016. The re-survey, conducted in 2020, involved 153 doctors. The subject of the survey was the state of simultaneous surgical interventions in surgical departments and the personal attitude of specialists to this type of intervention. The comparison of the survey results in 2016 and in 2020 was carried out using the criterion  $\chi^2$ . In response to questions about the feasibility of simultaneous implementation, there is an increase in the proportion of doctors who consider these losses appropriate - from 86.3% to 96.7%. The following questions show that practicing surgeons are more likely to perform simultaneous interventions themselves - their share has increased from 66.3% to 86.3%. At the same time, the number of doctors with skills and knowledge of a related specialty increased by 20% (from 27% to 47.1%), however, it is still less than half of doctors. The share of physicians who consider it appropriate to master a related specialty to be able to perform a wider range of simultaneous interventions increased from 68.0% to 80.4%. The share of physicians with minimally invasive techniques to perform simultaneous operations increased from 26.0% to 55.6%. There is a positive trend in the attitude of practitioners to simultaneous operations. For the further development of simultaneous operations in combined pathology, it is necessary to train "endoscopic surgeons", who must have the skills of related specialties.*

**Key words:** simultaneous operations, abdominal pathology, interrogation, dynamics of subjective attitude.

### Introduction

Simultaneous operations (SO) for combined diseases requiring surgical treatment are performed in many surgical, gynecological, urological and other departments, but have not yet become routine. Moreover, the number of such operations is much smaller than the prevalence of combined pathology - 1.5-6% vs. 10-20% [20]. In the publications devoted to this problem, among the advantages of simultaneous operations are mentioned the SO of two or more diseases, each of which has a risk of

complications; eliminates the danger of the operation in the conditions of the adhesion process during the second operation; high economic efficiency; getting rid of repeated preoperative stress in anticipation of the second operation. It is reported that there is no difference between their direct results with the results of isolated operations, but with a decrease in the number of complications after simultaneous operations is less compared to their total number after staged interventions [8, 14, 15, 20]. The most

common arguments against simultaneous operations are an increase in the volume and duration of surgery, which increases the degree of surgical aggression and the risk of complications [10, 12, 20], but these shortcomings are offset by the introduction of new surgical techniques [1].

Therefore, often a small number of simultaneous interventions can be explained by purely subjective factors - the attitude of practicing surgeons and, possibly, incomplete examination of patients before surgery.

The aim of the study was to determine the dynamics of surgeons' awareness of simultaneous operations in combined abdominal pathology.

### Materials and methods

Connection of work with scientific programs, plans and topics: The work was performed within the planned research work of Kharkiv National Medical University "Development of surgical technologies for diagnosis and treatment of diseases and injuries of the digestive system using hybrid (open and minimally invasive) operations" (state registration № 0119U002909).

The results of a survey of surgeons of surgical inpatient departments of regional, district and city hospitals, as well

as institutes and university clinics of Poltava, Sumy, Rivne, Kharkiv, Luhansk and Donetsk regions (except for areas not controlled by the Ukrainian authorities) were analyzed. The sample was random within a homogeneous general population of surgeons. Respondents participated in the survey on a voluntary basis. The first survey, which included 724 doctors, was conducted in 2016. The re-survey, conducted in 2020, involved 153 doctors.

The questions of the questionnaire were developed independently. The subject of the survey was the state of conducting SO in these departments and the personal attitude of specialists to this type of intervention.

Processing of survey results was carried out using a program for processing sociological questionnaires [17]. The comparison of the results of the survey conducted in 2016 and in 2020 was carried out using the criterion  $\chi^2$  [16].

### Results

The questions included in the questionnaire and the answers of the respondents are given in Table 1.

A comparative analysis of the structure of answers to the main questions revealed the following. In the answers

**Table 1.** Survey results of surgeons in 2016 and 2020.

Questions and answers	2016 (n=724)	2020 (n=153)	p
Do you consider it appropriate to implement SO? - yes - no	625 (86.3%) 99 (13.7%)	148 (96.7%) 5 (3.3%)	<0.001
Actually, do you perform SO? - yes - no	480 (66.3%) 244 (33.7%)	132 (86.3%) 21 (15.7%)	<0.001
Do you now have the relevant skills and knowledge of a related specialty (documented) which help you perform SO on your own? - yes - no	195 (27.0%) 529 (73.0%)	72 (47.1%) 81 (52.9%)	<0.001
Do you consider it appropriate to master a related specialty to be able to perform SO on your own? - yes - no	492 (68.0%) 232 (32.0%)	123 (80.4%) 20 (19.6%)	<0.001
Do you currently (at the time of the survey) have techniques for performing SO in a minimally invasive way? - yes - no	188 (26.0%) 536 (74.0%)	85 (55.6%) 68 (44.4%)	<0,001
Have you ever actually worked as a "guest consultant" to help colleagues in another specialty in their SO performing? - yes - no	637 (88.0%) 87 (12.0%)	112 (73.2%) 41 (26.8%)	<0.001
What is the most significant advantage of SO you can highlight? - getting rid of several diseases - economic benefits - avoiding the risk of repeated interventions	32 (4.4%) 148 (20.4%) 544 (75.1%)	3 (1.9%) 31 (20.3%) 119 (77.8%)	>0,05
What, in your opinion, can be attributed to the most significant disadvantage of SO? - change the location of the operating team during the intervention - increased risk of complications - increased duration of intervention	44 (6.0%) 175 (24.2%) 505 (69.8%)	14 (9.2%) 28 (18.3%) 111 (72.5%)	>0,05

**Notes:** p - the reliability of the difference between 2016 and 2020 by criterion  $\chi^2$ .

to the first question regarding the opinion of doctors about the expediency of SO, there is an increase in the proportion of doctors who consider these interventions appropriate - from 86.3% to 96.7%. The following questions showed that practicing surgeons more often perform SO themselves - their share increased from 66.3% to 86.3%. At the same time, the number of doctors with skills and knowledge of a related specialty increased by 20% (from 27% to 47.1%), however, it is still less than half of doctors. The share of physicians who consider it appropriate to master a related specialty to be able to perform a wider range of SO has increased from 68.0% to 80.4%.

Interestingly, the proportion of physicians with minimally invasive techniques for performing SO increased from 26.0% to 55.6%, which coincides with the answers to the third question (regarding the possession of skills in a related specialty). At the same time, the share of doctors who were invited as a consultant by other specialists, on the contrary, decreased from 88.0% to 73.2%. This is indirect evidence of an increase in the list of surgical interventions performed by other specialists and a decrease in the need for external consultants.

The smallest difference in the answers of doctors between 2016 and 2020 is observed in the latest questions regarding the advantages and disadvantages. There is only a slight tendency to increase the proportion of doctors, who consider the main advantage of avoiding repeated surgical interventions, and the disadvantage - the increased duration of the operation. There is no clear answer to these questions among researchers who specifically deal with this problem.

## Discussion

The data obtained indicate a positive trend in the attitude of practitioners to simultaneous operations and the number of physicians with relevant skills. On the other hand, discussions on the safety of simultaneous interventions are still ongoing. Some authors report that they do not increase the duration of inpatient treatment and the frequency of early and late complications, but improve the quality of life compared to isolated hernioplasty [11, 13], according to other data, the number of complications increases significantly [10, 12]. W. Ueland and co-authors in 2020 found that additional surgical procedures are a risk factor for increasing the duration of hospitalization [24]. A large-scale study found that after simultaneous surgery for breast cancer combined with genital pathology, patients had a longer duration of inpatient treatment, the frequency of complications, re-hospitalizations and surgeries. The authors believe that this may delay the necessary adjuvant chemotherapy [23]. Among the negative consequences of simultaneous operations, the increase in the duration of the operation is most often mentioned. Thus, hernioplasty of ventral hernias with the use of a grid during colorectal interventions increased the duration of surgery (195.8±98.7 vs. 164.3±84.4 minutes in isolated colorectal interventions).

However, this did not affect postoperative mortality, the frequency of complications and the duration of inpatient treatment, which indicated the feasibility of such interventions [3]. In addition, the results of individual studies indicate that simultaneous operations lead to an increase in the duration of surgery and anesthesia, as well as to an increase in the frequency of adverse events and the duration of hospitalization. In particular, this was observed in simultaneous laparoscopic cholecystectomy and laparoscopic bariatric surgery [6].

It should be noted that there are many more reports of positive results of simultaneous operations. Simultaneous laparoscopic cholecystectomy with other operations, in particular, with hernioplasty, is especially often performed [2, 5, 18, 25]. In addition to good results, there are enough reports of significant economic impact. Thus, a study by S. Hayakawa and co-authors conducted in 2018 found that the average cost of treatment for simultaneous laparoscopic cholecystectomy and inguinal plastic surgery was \$7,673, while the cost of separate hernioplasty and laparoscopic cholecystectomy is more than \$10,000 [9]. Other authors present data from 22 similar operations performed, which resulted in 1 case of gallbladder perforation, 1 case of ipsilateral testicular atrophy and 1 case of seroma. There were no infectious complications [18]. Simultaneous operations during laparoscopic cholecystectomy did not result in conversion in any way, did not affect the frequency of postoperative complications and length of stay in the hospital. The authors consider these operations as a good alternative to two separate interventions [5]. Simultaneous operations are often performed in patients with hiatal hernias, in whom hernioplasty is combined with bariatric surgery and antireflux intervention is recommended [7, 21]. In addition, hernioplasty is considered appropriate in urological surgeries [19, 22] and in colorectal surgery [3, 4].

Thus, the results of the work of many scientists also confirm the unresolved problem of expediency and safety of simultaneous interventions, and therefore research in this direction does not stop.

The range of simultaneous operations is very large. Further development of technologies for their implementation and methods of perioperative support, aimed at reducing the risk of adverse events after surgery, is an important area of further research.

## Conclusions

Thus, the vast majority of respondents note that the implementation of simultaneous operations in everyday surgical practice is appropriate and this opinion grows with the years and experience of surgeons in laparoscopic surgery. More than half of the respondents perform such interventions in their surgical practice.

The majority of respondents believe that the main advantage of simultaneous operations is the avoidance of repeated interventions and general anesthesia.

For the further development of simultaneous operations in combined pathology it is necessary to train "endoscopic surgeons", who must have many surgical techniques, be familiar with all possible intra- and postoperative

complications and be able to control them at each stage of intervention, have experience in open surgical interventions to convert in a timely and professional manner with certain complications.

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**ПОЗИТИВНИЙ ТРЕНД ВІДНОШЕННЯ ХІРУРГІВ УКРАЇНИ ДО СИМУЛЬТАННИХ ОПЕРАЦІЙ: АНАЛІЗ РЕЗУЛЬТАТІВ ОПИТУВАНЬ**  
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*В останні роки спостерігається збільшення уваги до симультанних операцій, але їх частота не відповідає дійсним потребам. Мета дослідження - з'ясувати динаміку інформованості хірургів про симультанні операції при поєднаній абдомінальній патології. Проаналізовані результати анкетування лікарів-хірургів хірургічних стаціонарних відділень обласних, районних та міських лікарень, а також інститутів та університетських клінік Полтавської, Сумської, Рівненської, Харківської, Луганської та Донецької областей (за виключенням непідконтрольних українській владі територій). Вибірка була випадковою в межах однорідної генеральної сукупності лікарів-хірургів. Перше опитування, до якого увійшли 724 лікаря, здійснено у 2016 році. У повторному опитуванні (проведено у 2020 році) брали участь 153 лікаря. Предметом опитування був стан проведення симультанних оперативних втручань у хірургічних відділеннях та особисте відношення спеціалістів до цього виду втручань. Порівняння результатів опитування 2016 та 2020 років здійснено із застосуванням критерію  $\chi^2$ . У відповідях на питання про доцільність здійснення симультанних операцій спостерігається збільшення питомої ваги лікарів, які вважають таке втручання доцільним - з 86,3% до 96,7%. Наступні питання демонструють, що практикуючі хірурги частіше самі виконують симультанні втручання - їх питома вага зросла з 66,3% до 86,3%. При цьому кількість лікарів, що володіють навичками та знаннями суміжної спеціальності, зросла на 20% (з 27% до 47,1%), однак, це все ще менше половини лікарів. Частка лікарів, що вважають доцільним оволодіти суміжною спеціальністю для можливості здійснення більшого спектру симультанних втручань, зросла з 68,0% до 80,4%. Питома вага лікарів, що володіють мініінвазивними методиками для виконання симультанних операцій зросла з 26,0% до 55,6%. Спостерігається позитивний тренд відношення практикуючих лікарів до симультанних операцій. Для подальшого розвитку симультанних операцій при поєднаній патології необхідна підготовка "ендоскопічних хірургів", які повинні володіти навичками суміжних спеціальностей.*

**Ключові слова:** симультанні операції, абдомінальна патологія, опитування, динаміка суб'єктивного відношення.

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## REPORTS OF MORPHOLOGY

**Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine**

journal homepage: <https://morphology-journal.com>



## Features of longitudinal and transverse body sizes in men with various forms of eczema

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### ARTICLE INFO

Received: 25 August, 2020

Accepted: 28 September, 2020

**UDC:** 616.379-

008.64:577.112:616.61-07-084

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*Consideration of the aspect of adaptation, in particular morphological, is expedient with obligatory comparison of morphometric indicators in healthy and sick patients and between groups of patients with different degrees of severity of dermatosis. The aim of the study was to investigate the differences between longitudinal and transverse body sizes between healthy and/or patients with eczema men depending on the severity of the dermatosis. Patients with idiopathic (n=34) and microbial (n=38) eczema men of the first mature age underwent an anthropometric examination according to Bunak. The diagnosis of eczema was made according to the nomenclature of ICD-10. As a control from the data bank of the research center of National Pirogov Memorial Medical University, Vinnytsya anthropometric data of 82 practically healthy men of the same age group were selected. Statistical data processing was performed in the license package "Statistica 5.5" using non-parametric methods of evaluation of the obtained results. In healthy men, compared with patients, higher values were found for: the height of the pubic anthropometric point by 3.5-5.7% and the height of the acetabular anthropometric point by 4.9-7.5% compared with sick men with idiopathic mild and severe eczema and mild and severe microbial eczema and lower values for: height of the suprathoracic anthropometric point by 1.7-2.6% for idiopathic eczema of mild, severe course and microbial eczema of mild course; height of the acromial anthropometric point by 1.6-2.3% compared with men with idiopathic eczema of mild and severe course; height of the finger anthropometric point by 3.0-5.9% compared with men with idiopathic eczema of mild and severe course and microbial eczema of mild and severe course. In healthy men, compared with patients, higher values were found: mid-thoracic diameter - by 3.1-11.1%, 5.5-14.4%, transverse lower thoracic diameter - by 8.6-14.1% and anterior-posterior mid-thoracic diameter - by 10.2-16.6% and smaller values: width of shoulders by 15.3-21.1% compared with men with idiopathic eczema of mild and severe course and microbial eczema of mild and severe course. In healthy individuals, the width of the distal epiphysis of the forearm is greater by 3.14% compared with patients with idiopathic severe eczema and the width of the distal epiphysis of the crus by 3.1% compared with patients with microbial eczema of mild course; smaller - the width of the distal epiphysis of the shoulder by 3.0% compared with patients with idiopathic eczema of severe course and the width of the distal epiphysis of the thigh by 5.2-7.6% compared with patients with idiopathic eczema of mild and severe course and microbial eczema of mild course. In healthy individuals, the values of the size of the pelvis are lower: interspinous distance - by 8.3-11.6%, intercrystal distance - by 8.7-12.5% and intertrochanteric distance - by 7.7-10.5% compared with sick men with idiopathic mild and severe eczema and microbial eczema of the mild and severe course. Differences in longitudinal body size in patients with different forms and severity of eczema. When comparing anthropometric indicators between sick men, the following were found: the height of pubic and acetabular anthropometric points in sick men with idiopathic eczema of mild course is higher by 1.8% and 1.7%, respectively, compared with sick men with microbial eczema of similar severity; shoulder width in patients with idiopathic eczema of mild course is 4.8% less than in patients with idiopathic eczema of severe course. Thus, men with eczema have a subpathological constitutional type, which is*



*characterized by an elongated "cylindrical" torso, shortened lower extremities, as well as more massive distal and less massive proximal epiphyses of the upper and lower extremities.*

**Keywords:** *eczema, longitudinal and transverse body sizes, men.*

## Introduction

Eczema is a dermatosis that is often registered in the clinical practice of a dermatovenereologist. The disease is characterized by a chronic course with frequent, prolonged relapses, the difficulty of choosing effective treatment measures. Despite the significant amount of work on the study of this disease, eczema remains an urgent medical and social problem, as it is often the cause of disability, reducing the quality of life of patients [1, 6, 23].

Many researchers [2, 14] consider eczema as a disease of multifactorial nature, the morphological manifestations of which are characterized by increased intercellular spaces, and thus the formation of increased permeability of the epidermal barrier to microorganisms, their toxins, development and maintenance of chronic inflammation. In the process of long-term and comprehensive study of various aspects of the pathogenesis of chronic dermatoses, the dominant role of constitutional, metabolic, mental and immunological components have been determined [8, 10].

The study of the relationship between the types of constitution and various diseases creates the preconditions for understanding the peculiarities of their course and risk factors or resistance. It is known that the standard effect causes different adaptive responses in people of different typological categories [9, 20, 22]. However, in clinical medicine, the average approach to the patient is still widely used without taking into account his constitutional affiliation, which significantly reduces the effectiveness of implemented treatment and prevention programs.

Therefore, it is advisable to consider the aspect of adaptation, in particular morphological, with the mandatory comparison of morphometric parameters in healthy and sick patients and between groups of patients with different degrees of severity of dermatosis.

*The aim of the study was to examine the differences between longitudinal and transverse body sizes between healthy and/or patients with eczema men depending on the severity of the dermatosis.*

## Materials and methods

Men of the first mature age (22-35 years) patients with idiopathic (n=34, including 16 with mild and 18 with severe) and microbial (n=38, including 28 with mild and 10 with severe) eczema, who were examined on the basis of the Military Medical Clinical Center of the Central Region and the Department of Skin and Venereal Diseases with a course of postgraduate education of National Pirogov Memorial Medical University, Vinnytsya, conducted an anthropometric survey in accordance with the scheme of V.V. Bunak (longitudinal and transverse body sizes - cm) [3].

The diagnosis of eczema was performed according to

the nomenclature ICD-10 ([https://zakononline.com.ua/documents/show/116857\\_531218](https://zakononline.com.ua/documents/show/116857_531218)).

As a control from the data bank of the research center of National Pirogov Memorial Medical University, Vinnytsya anthropometric data of 82 practically healthy men of the same age group were selected.

Statistical data processing was performed in the license package "Statistica 5.5" using non-parametric methods of evaluation of the obtained results. The reliability of the difference between the values between the independent quantitative values was determined using the Mann-Whitney U-test.

## Results

In healthy men, compared with patients, lower values were found for:

height of the thoracic anthropometric point ( $143.8 \pm 6.1$ ) compared with men suffering from idiopathic eczema of the mild ( $147.0 \pm 3.8$ ;  $p < 0.05$ ), severe course ( $147.7 \pm 4.1$ ;  $p < 0.01$ ) and microbial eczema of the mild ( $146.3 \pm 8.0$ ;  $p = 0.063$ ) course;

the height of the acromial anthropometric point ( $146.9 \pm 7.1$ ) compared with men with idiopathic eczema of mild ( $149.3 \pm 3.4$ ;  $p < 0.01$ ) and severe course ( $150.3 \pm 4.5$ ;  $p < 0.01$ );

height of the finger anthropometric point ( $65.85 \pm 4.95$ ) compared with men with idiopathic eczema of the mild ( $68.56 \pm 3.22$ ;  $p < 0.05$ ) and severe course ( $69.94 \pm 3.08$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $67.89 \pm 4.02$ ;  $p < 0.05$ ) and severe course ( $69.00 \pm 4.50$ ;  $p = 0.052$ );

width of the distal shoulder epiphysis ( $6.899 \pm 0.438$ ) compared with men with idiopathic severe eczema ( $7.111 \pm 0.582$ ;  $p = 0.076$ );

width of the distal thigh epiphysis ( $8.917 \pm 0.437$ ) compared with men with idiopathic eczema of mild ( $9.406 \pm 0.733$ ;  $p < 0.05$ ) and severe course ( $9.500 \pm 0.668$ ;  $p < 0.001$ ) and microbial eczema of mild course ( $9.646 \pm 0.914$ ;  $p < 0.001$ );

mid-thoracic diameter ( $28.35 \pm 2.19$ ) compared with men with idiopathic eczema of the mild ( $31.88 \pm 2.31$ ;  $p < 0.001$ ) and severe course ( $33.39 \pm 2.91$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $32.64 \pm 4.47$ ;  $p < 0.001$ ) and severe course ( $33.10 \pm 6.15$ ;  $p < 0.01$ );

transverse lower thoracic diameter ( $25.30 \pm 2.26$ ) compared with men with idiopathic eczema of the mild ( $27.69 \pm 2.12$ ;  $p < 0.001$ ) and severe course ( $29.28 \pm 3.06$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $29.11 \pm 3.62$ ;  $p < 0.001$ ) and severe course ( $29.40 \pm 4.81$ ;  $p < 0.01$ );

anterior-posterior mid-thoracic diameter ( $19.93 \pm 2.12$ ) compared with men with idiopathic eczema of the mild ( $22.19 \pm 3.53$ ;  $p < 0.01$ ) and severe course ( $23.44 \pm 3.38$ ;

$p < 0.001$ ) and microbial eczema of the mild ( $23.89 \pm 4.77$ ;  $p < 0.001$ ) and severe course ( $23.30 \pm 3.68$ ;  $p < 0.01$ );

interspinous distance ( $26.33 \pm 1.98$ ) compared with men with idiopathic eczema of the mild ( $29.00 \pm 1.93$ ;  $p < 0.01$ ) and severe course ( $29.78 \pm 1.86$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $28.89 \pm 2.82$ ;  $p < 0.001$ ) and severe course ( $28.70 \pm 2.54$ ;  $p < 0.01$ );

intercrystal distance ( $29.38 \pm 2.02$ ) compared with men with idiopathic eczema of the mild ( $32.38 \pm 2.25$ ;  $p < 0.01$ ) and severe course ( $33.56 \pm 2.06$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $32.18 \pm 3.10$ ;  $p < 0.001$ ) and severe course ( $32.70 \pm 2.83$ ;  $p < 0.01$ );

intertrochanteric distance ( $32.96 \pm 2.10$ ) compared with men with idiopathic eczema of the mild ( $36.00 \pm 2.00$ ;  $p < 0.01$ ) and severe course ( $36.83 \pm 2.60$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $36.21 \pm 2.81$ ;  $p < 0.001$ ) and severe course ( $35.70 \pm 2.75$ ;  $p < 0.01$ ).

In healthy men, compared with patients, greater values were found:

height of pubic anthropometric point ( $90.57 \pm 5.04$ ) compared with men with idiopathic eczema of the mild ( $87.53 \pm 2.45$ ;  $p < 0.01$ ) and severe course ( $87.83 \pm 3.68$ ;  $p < 0.01$ ) and microbial eczema of the mild ( $85.95 \pm 3.46$ ;  $p < 0.001$ ) and severe course ( $85.65 \pm 5.86$ ;  $p < 0.01$ );

height of the acetabular anthropometric point ( $94.04 \pm 5.40$ ) compared with men with idiopathic eczema of the mild ( $88.94 \pm 2.14$ ;  $p < 0.001$ ) and severe course ( $89.67 \pm 2.85$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $87.50 \pm 3.88$ ;  $p < 0.001$ ) and severe course ( $88.30 \pm 6.34$ ;  $p < 0.01$ );

width of the distal epiphysis of the forearm ( $5.724 \pm 0.327$ ) compared with patients with idiopathic severe eczema ( $5.550 \pm 0.333$ ;  $p < 0.05$ );

the width of the distal epiphysis of the crus ( $7.277 \pm 0.469$ ) compared with men with microbial eczema of mild course ( $6.964 \pm 0.606$ ;  $p < 0.01$ );

shoulder width ( $42.02 \pm 2.64$ ) compared with men with idiopathic eczema of the mild ( $34.69 \pm 2.15$ ;  $p < 0.001$ ) and severe course ( $36.44 \pm 2.06$ ;  $p < 0.001$ ) and microbial eczema of the mild ( $35.46 \pm 2.43$ ;  $p < 0.001$ ) and severe course ( $36.20 \pm 3.55$ ;  $p < 0.001$ );

The height of the pubic anthropometric point in sick men with idiopathic eczema of mild course ( $87.53 \pm 2.45$ ) is greater compared with sick men with microbial eczema of mild course ( $85.95 \pm 3.46$ ;  $p < 0.05$ ).

Shoulder width in patients with idiopathic eczema of mild course ( $34.69 \pm 2.15$ ) is less compared with patients with idiopathic eczema of severe course ( $36.44 \pm 2.06$ ;  $p < 0.05$ ).

The height of the acetabular anthropometric point in men with idiopathic eczema of mild course ( $88.94 \pm 2.14$ ) is greater compared with men with microbial eczema of mild course ( $87.50 \pm 3.88$ ;  $p = 0.077$ ).

## Discussion

Traditionally, the basis of individual-typological diagnosis is the morphological criterion in the form of

somatotype, considered as the main "informant" about the nature of the human constitution [11, 12]. A certain set of constitutional features allows to state not only the existing, but also to predict the quantitative and qualitative level of adaptive reactions of the organism. According to many authors, constitutional features precede the disease, not its result. One of the absolute signs of markers of hereditary determinism is the longitudinal size of the body, they are usually the basis of the leading types of constitution. The transverse dimensions of the body are not so strictly inherited and are more closely related to sex, age and environmental influences on the body [17, 21].

It is established that the extreme manifestations of stress of the homeostasis system in the process of adaptation - the basis for the development of certain diseases. Thus, in patients with severe and prolonged forms of dermatitis, extreme and subpathological constitutional types are more often identified [13].

We found higher values in healthy men compared to patients: the height of the pubic anthropometric point by 3.5%, 3.1%, 5.5% and 5.7% and the height of the acetabular anthropometric point by 5.7%, 4.9%, 7.5% and 6.5% compared with sick men with idiopathic eczema of mild and severe course and microbial eczema of mild and severe course; and lower values: suprathoracic anthropometric point height by 2.6%, 2.6 and 1.7% for idiopathic mild eczema, severe eczema and mild microbial eczema; height of acromial anthropometric point by 1.6% and 2.3% compared with men with idiopathic eczema of mild and severe course; height of the finger anthropometric point by 4.0%, 5.9%, 3.0% and 4.6% compared with men with idiopathic eczema of mild and severe course and microbial eczema of mild and severe course.

In healthy men, lower values of mid-thoracic diameter (by 11.1%, 3.1%, 5.5% and 14.4%), transverse lower thoracic diameter (by 8.6%, 13.6%, 13.1% and 14.1%) and anterior-posterior mid-thoracic diameter (by 10.2%, 15.1%, 16.6% and 14.5%) were found and higher values of shoulder width (by 21.1%, 15.3%, 18.5% and 16.1%) compared with men with idiopathic mild and severe eczema and mild and severe microbial eczema.

The following regularity was established for the width of the epiphyses of the bones: in healthy subjects the value of these dimensions is larger for the more distal, and smaller - for the more proximal segments of the upper and lower extremities. Thus, in healthy individuals the width of the distal epiphysis of the forearm is greater by 3.14% compared with patients with idiopathic severe eczema and the width of the distal epiphysis of the crus by 3.1% compared with patients with microbial eczema of mild course; smaller - the width of the distal epiphysis of the shoulder by 3.0% compared with patients with idiopathic eczema of severe course and the width of the distal epiphysis of the thigh by 5.2%, 6.1% and 7.6% compared with patients with idiopathic eczema of mild and severe eczema and microbial eczema of mild course.

The level of physical development of men directly affects the degree of variability of morphometric parameters. It is shown that the wider the shoulders and the narrower pelvis, the more pronounced the signs of andromorphism, and, conversely, the wide pelvis and narrow shoulders indicate gynecomorphism [19].

In healthy individuals, we found lower values of pelvic size: interspinous distance - by 9.2%, 11.6%, 8.9% and 8.3%, intercrystal distance - by 9.3%, 12.5%, 8.7% and 10.2% and intertrochanteric distance - by 8.4%, 10.5%, 9.0% and 7.7% compared with men with idiopathic eczema of mild and severe course and microbial eczema of mild and severe course.

Summarizing the differences in longitudinal and transverse body size between healthy and patients with idiopathic and microbial eczema of mild and severe course, we found a subpathological constitutional type, characterized by elongated "cylindrical" torso, shortened lower extremities and smaller masses, as well as more massive distal and less massive proximal epiphysis of upper and lower limbs.

Depending on the type of eczema, the disease has its own characteristics. Microbial eczema usually has clear boundaries, develops in places of injury, in places of fungal development, on the crus in varicose veins. Idiopathic eczema occurs after nervous stress or for no apparent reason. Unlike microbial, idiopathic eczema is always symmetrical, and has foci without clear boundaries. The course of idiopathic eczema is chronic or recurrent [18].

It was found that one or another constitutional type is accompanied by a more frequent occurrence, faster development, more severe course and worse outcome of the corresponding pathology. Even the intensity of the development of only one group of constitutional features reveals certain correlations with the development of certain diseases. Thus, it has been shown that both asthenics and hypersthenics are more likely to develop chronic diseases of the skin and its appendages with a tendency to recur [7].

Makarchuk I.M. [15, 16] in young men with acne without taking into account the severity and with mild and moderate severity of the disease found quite similar to our changes in longitudinal and transverse body size. Thus, in patients with acne, the values of the height of the thoracic point, the transverse middle and lower thoracic dimensions, the width of the distal epiphysis of the thigh, and smaller values of the height of the acetabulum and shoulder width are established.

Chaplyk-Chizho I.O. [4, 5] in men with chronic pyoderma of the general group and with an acute course, as well as with deep pyoderma established only greater than in healthy men, the value of the intercrystal size of the pelvis; and in

patients of the general group and with chronic pyoderma only a greater height of the acetabulum point.

When comparing anthropometric parameters between sick men, we found only some differences in longitudinal and transverse body size in patients with different forms and severity of eczema. Thus, the height of pubic and acetabular anthropometric points in patients with idiopathic mild eczema is higher by 1.8% and 1.7%, respectively, compared with patients with microbial eczema of similar severity. Shoulder width in patients with idiopathic eczema of mild course is 4.8% less than in patients with idiopathic eczema of severe course.

Makarchuk I.M. [15, 16] also found virtually no differences in longitudinal and transverse body size between patients with varying degrees of acne in young men.

Chaplyk-Chizho I.O. [4] in patients with chronic pyoderma in men found lower values of transverse medium and lower thoracic size than in men with acute pyoderma, both in general and separately, when divided into superficial and deep.

Thus, as a result of the work, for the first time differences in longitudinal and transverse dimensions were revealed between healthy and patients with idiopathic and microbial eczema by Ukrainian men of the first mature age and between patients with different forms and degrees of eczema severity.

## Conclusions

1. In men with idiopathic and microbial eczema of mild and severe course a comparative analysis of longitudinal and transverse body size compared to healthy men, the following manifestations of subpathological constitutional types were found: against the background of higher values of the height of the suprathoracic and acromial anthropometric points (by 1.7-2.6% and 1.6-2.3%, respectively), lower values of the height of the pubic and acetabular anthropometric points were established (by 3.1-5.7% and 4.9-7.5%, respectively); against the background of larger values of mid-thoracic, transverse lower thoracic, anterior-posterior mid-thoracic diameters (by 3.1-14.4%, 8.6-14.1% and 10.2-16.6%, respectively) and pelvic sizes (by 7.7-12.5%) smaller values of shoulder width (by 15.3-21.1%) were found; against the background of larger values of the width of the distal epiphysis of the shoulder (by 3.0% only idiopathic severe eczema) and thighs (by 5.2-7.6%) lower values of the distal epiphysis of the forearm (by 3.14% only idiopathic eczema of severe course) and crus (by 3.1% only microbial eczema of mild course) were established.

2. Between patients with idiopathic eczema and/or microbial eczema of varying severity found only a few significant differences in longitudinal and transverse body size.

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#### ОСОБЛИВОСТІ ПОЗДОВЖНИХ І ПОПЕРЕЧНИХ РОЗМІРІВ ТІЛА У ЧОЛОВІКІВ, ХВОРИХ НА РІЗНІ ФОРМИ ЕКЗЕМИ

**Дмитренко С.В., Al-Omary Ala'a Osata Ahmad, Дзевульська І.В., Скорук Р.В., Гунас І.В.**

Розгляд аспекту адаптації, зокрема морфологічної, є доцільним з обов'язковим порівнянням морфометричних показників у здорових та хворих пацієнтів та між групами пацієнтів з різними ступенями важкості дерматозу. Мета дослідження - вивчити відмінності поздовжніх і поперечних розмірів тіла між здоровими та/або хворими на екзему чоловіками в залежності від тяжкості перебігу дерматоза. Хворим на істинну (n=34) та мікробну (n=38) екзему чоловікам першого зрілого віку проведено антропометричне обстеження за Бунаком. Встановлення діагнозу екземи проведено згідно номенклатури МКХ-10. В якості контролю з банку даних науково-дослідного центру Вінницького національного медичного університету ім. М.І. Пирогова були відібрані антропометричні дані 82 практично здорових чоловіків аналогічної вікової групи. Статистичну обробку даних проведено в ліцензійному пакеті "Statistica 5.5" із використанням непараметричних методів оцінки отриманих результатів. У здорових чоловіків встановлено більші значення: висоти лобкової антропометричної точки на 3,5-5,7% та висоти вертлюгової антропометричної точки на 4,9-7,5% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу та мікробну екзему легкого і тяжкого перебігу та менші значення: висоти надгрудниної антропометричної точки на 1,7-2,6%, ніж у чоловіків, хворих на істинну екзему легкого і тяжкого перебігу, а також на мікробну екзему легкого перебігу; висоти акроміальної антропометричної точки на 1,6-2,3% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу; висоти пальцевої антропометричної точки на 3,0-5,9% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу та мікробну екзему легкого і тяжкого перебігу. У здорових чоловіків встановлено

більші значення: середньогруднинного діаметра - на 3,1-11,1%, 5,5-14,4%, поперечного нижньогруднинного діаметра - на 8,6-14,1% і передньо-заднього середньогруднинного діаметра - на 10,2-16,6% та менші значення: ширини плечей на 15,3-21,1% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу та мікробну екзему легкого і тяжкого перебігу. У здорових осіб більші були: ширина дистального епіфіза передпліччя на 3,14% порівняно з хворими на істинну екзему тяжкого перебігу і ширина дистального епіфіза гомілки на 3,1% порівняно з хворими на мікробну екзему легкого перебігу; менші - ширина дистального епіфіза плеча на 3,0% порівняно з хворими на істинну екзему тяжкого перебігу і ширина дистального епіфіза стегна на 5,2-7,6% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу та мікробну екзему легкого перебігу. У здорових осіб менші значення розмірів таза: міжкостьової відстані - на 8,3-11,6%, міжребеневої відстані - на 8,7-12,5% і міжвертлюгової відстані - на 7,7-10,5% порівняно з хворими чоловіками на істинну екзему легкого і тяжкого перебігу та мікробну екзему легкого і тяжкого перебігу. Встановлені відмінності поздовжніх розмірів тіла у хворих з різними формами і ступенями важкості екземи. При порівнянні антропометричних показників між хворими чоловіками встановлено: висота лобкової і вертлюгової антропометричних точок у хворих чоловіків на істинну екзему легкого перебігу більша (відповідно) на 1,8% і 1,7% порівняно з хворими чоловіками на мікробну екзему аналогічної важкості; ширина плечей у хворих чоловіків на істинну екзему легкого перебігу на 4,8% менша порівняно з хворими чоловіками на істинну екзему тяжкого перебігу. Таким чином, у хворих на екзему чоловіків встановлений субпатологічний конституціональний тип, який характеризується витягнутим "циліндроподібним" тулубом, укороченими нижніми кінцівками, більш масивними дистальними, а також менш масивними проксимальними епіфізами верхніх і нижніх кінцівок.

**Ключові слова:** екзема, поздовжні і поперечні розміри тіла, чоловіки.

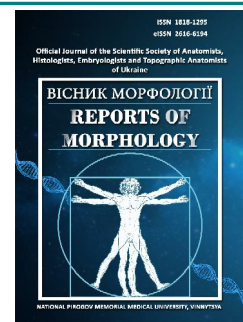
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## REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>



# Dynamics of morphological changes in the heart of rats after serial systemic administration of Doxorubicin

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### ARTICLE INFO

Received: 25 August, 2020

Accepted: 28 September, 2020

UDC: 616-006:615.277.3 + 591.412 + 59.089

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*Along with a good antitumor effect, Doxorubicin has a systemic effect with damage to vital organs, in particular the heart. The lack of a unified approach to dosing and the frequency of administration of Doxorubicin in the experiment prompts the search for an optimal model of Doxorubicin cardiomyopathy. The aim of the study was to develop a method of serial administration of Doxorubicin in medium therapeutic doses in an experiment and to evaluate the cardiotoxic effect of the drug. 42 female Wistar rats were included in the study. The control group consisted of 7 intact rats. The experimental group consisted of 35 rats who received systemic chemotherapy with Doxorubicin at a dose of 5 mg/kg once a week for 5 weeks. On days 7th, 14th, 21st, 28th, 35th, the hearts of experimental animals were taken for morphological examination. Histomorphometrically determined: the diameter of cardiomyocytes (in the middle part) and the transverse diameter of their nucleus, the width of the interstitial space (endo- and perimysia). The data of histomorphological and histomorphometric examination of the myocardium testified that all animals of the experimental group had a circulatory disorder in the heart muscle at the level of hemomicrocirculation. Such changes led to cardiomyocyte hypotrophy, interstitial edema and fibrosis. During systemic chemotherapy, the animals showed marked changes in the myocardium, such as expansion of the endomysial zone, due to capillary congestion and edema, in comparison with animals of the intact group. At the end of the experiment, the animals of the experimental group retained the expansion of the endomysial zone, mainly due to interstitial fibrosis. Such changes indicate myocardial hypoxemia with damage and death of cardiomyocytes, activation of interstitial and replacement collagen formation. The obtained morphological data indicate the development of dilated cardiomyopathy in experimental animals. Serial intraperitoneal administration of Doxorubicin at a dose of 5 mg/kg once a week for 5 weeks causes morphological changes in the myocardium of experimental animals, similar to changes in the heart of people undergoing chemotherapy with this drug.*

**Keywords:** Doxorubicin, cardiomyopathy, morphology, experiment, rats.

### Introduction

Despite constant scientific and technological progress, the incidence and mortality from cancer are increasing rapidly worldwide [5, 18].

Cancer treatments include surgery, radiation therapy, and systemic treatment, which includes chemotherapy, targeted therapy, hormone therapy, and immunotherapy [5]. Among all methods, pharmacological drugs are the most common means of influencing tumor growth and metastasis and are used in almost all malignant cancers, even in the early stages [6, 8, 9, 10, 11, 22, 23].

Affecting tumor cells, chemotherapeutics creates a systemic toxic effect, which is one of the most significant disadvantages of the use of chemotherapeutics, and even with local administration of drugs [16, 27]. A large number of anticancer drugs affect vital organs, including the heart. The list of cardiotoxic therapeutic agents against cancer includes anthracyclines, trastuzumab, alkylating agents, antimetabolites, tyrosine kinase inhibitors, angiogenesis inhibitors, checkpoint inhibitors and proteasome inhibitors [1, 4, 12].

One of the long-term and widely used drugs with pronounced cardiotoxic effects is a drug of the anthracycline series - Doxorubicin [2, 14, 21]. Good tumor regression with the use of Doxorubicin in both mono and chemotherapy regimens encourages the search for ways to prevent the development of Doxorubicin-induced cardiomyopathy.

The development and implementation of new approaches to the treatment and prevention of pathological conditions, first of all, requires pre-clinical research.

The literature describes a large number of experimental studies related to Doxorubicin-induced cardiomyopathy, but they all differ significantly in the parameters of drug administration [3, 13, 26].

In our opinion, the dosage of Doxorubicin and the frequency of its introduction in the study of its systemic effects, in particular, cardiotoxic effects, should be as close as possible to similar in clinical practice.

The aim of the study was to develop a method of serial administration of Doxorubicin in moderate therapeutic doses in the experiment and to evaluate the cardiotoxic effect of the drug.

### Materials and methods

The experimental study was performed on the basis of a research laboratory of preclinical study of pharmacological substances of National Pirogov Memorial Medical University, Vinnytsya. All experiments were performed in accordance with the "Regulations on the Use of Animals in Biomedical Experiments" with the permission of the Bioethics Committee.

The study involved 42 female Wistar rats under 1 year of age and weighing 120 to 220 grams ( $187.3 \pm 13.6$  grams). The control group consisted of 7 intact rats, which were selected to determine the main studied morphological and morphometric parameters in the norm. The experimental group consisted of 35 rats, which underwent systemic chemotherapy with Doxorubicin according to the author's method (Patent of Ukraine for utility model № 138091 from 25.11.2019).

The technique consisted of intraperitoneal administration of Doxorubicin at a dose of 5 mg/kg once a week for 5 weeks. The dose of 5 mg/kg was determined by recalculating the average therapeutic dose of the drug for humans in the treatment of superficial bladder cancer. The recalculation was performed according to the method proposed by Anroop B. Nair and Shery Jacob [19].

One week after each administration of the drug (7, 14, 21, 28, 35 days), 7 rats were randomly selected and removed from the experiment by dislocation of the cervical vertebrae under ketamine anesthesia at the rate of 0.22 ml per 100 grams of weight of the experimental animal.

After dissection, the heart was removed, followed by fixation in 10% neutral formalin solution. After fixation for 3 days, cardiac drugs were prepared according to standard

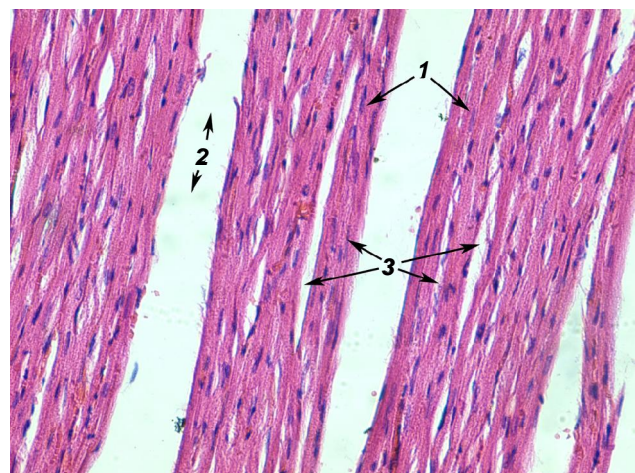
methods. Paraffin sections 5-7  $\mu\text{m}$  thick were stained with hematoxylin and eosin. Microscopy and photographing of histological specimens were performed using a light microscope OLIMPUS BX 41 at magnifications of 40x, 100x, 200x, 400x and 1000x. Microscopy assessed the condition of the myocardium, the presence and nature of pathological and compensatory-adaptive changes in it. Images were obtained and processed, morphometry and statistical processing were performed using the program "Quick PHOTO MICRO 2.3". Histomorphometrically determined: the diameter of cardiomyocytes (in their middle part) and the transverse diameter of their nucleus, the width of the interstitial space (endo- and perimysia).

The obtained data were processed using the statistical software package SPSS 20.0 for Windows.

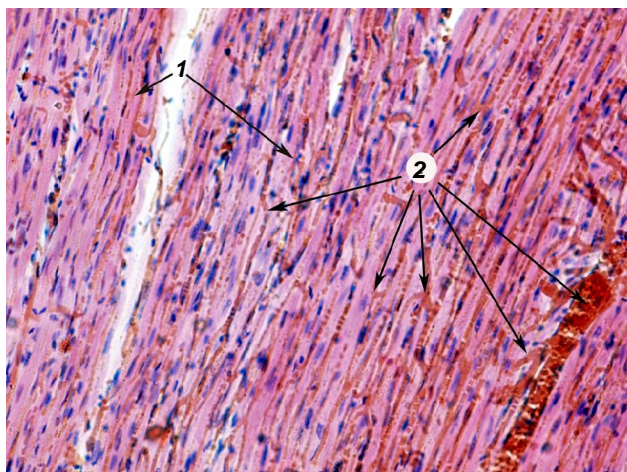
### Results

On microscopic examination, the myocardium of the animals of the control group had a characteristic structure of cardiac muscle tissue, without pathological changes. Functional (typical) elements of the myocardium were represented by integral muscle fibers of cardiomyocytes, which in all fields of view were evenly stained with background stain (hematoxylin and eosin), in their peripheral parts was clearly defined cross-striation, not long and less was traced. Inserted discs and lateral anastomoses were visualized between cardiomyocytes. The diameter of cardiomyocytes averaged  $11.30 \pm 0.10 \mu\text{m}$ . In the central parts of each cardiomyocyte there were 1-2 nuclei of round-oval shape, with evenly distributed chromatin.

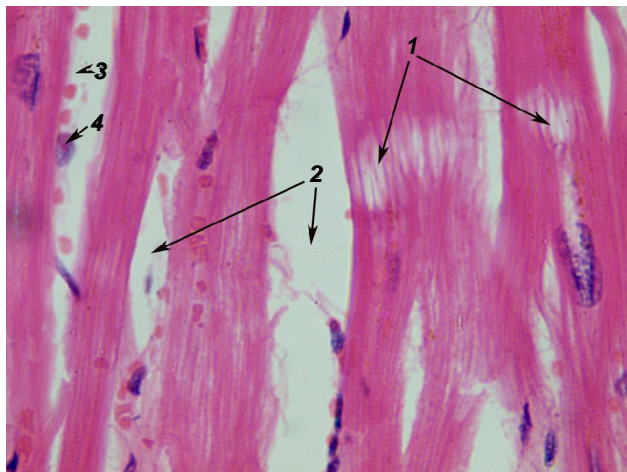
The transverse diameter of the nucleus averaged  $3.50 \pm 0.19 \mu\text{m}$ . The stromal component of the myocardium was represented by loose unformed fibrous tissue with vascular and nerve elements, without inflammatory cellular infiltration. Relatively uniform, moderate blood supply, with insignificant venular-capillary predominance



**Fig. 1.** The rat myocardium of the control group. Hematoxylin-eosin. x200. 1 - cardiomyocytes with a pronounced cross-striation; 2 - perimysium; 3 - endomysium.



**Fig. 2.** The rat myocardium of the experimental group on day 7 after systemic chemotherapy. Hematoxylin-eosin. x400. 1 - cardiomyocytes; 2 - pronounced dilation and fullness of blood vessels of hemomicrocirculation.

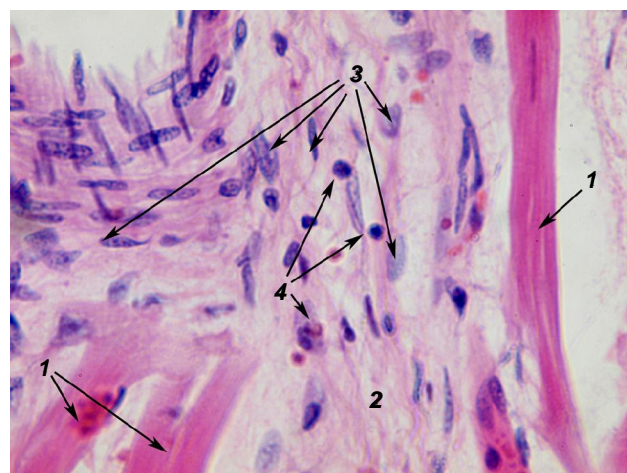


**Fig. 3.** The rat myocardium of the experimental group on day 7 after systemic chemotherapy. Hematoxylin-eosin. x1000. 1 - vacuolation and defibering of cardiomyocytes; 2 - edema; 3 - blood capillary; 4 - swollen endothelium of the hemocapillary.

was noted in vessels of hemomicrocirculation. The vascular endothelium had a flattened nucleus, almost imperceptible, narrow rim of the cytoplasm (Fig. 1). The width of the endomysium zone averaged  $5.40 \pm 0.09 \mu\text{m}$ , perimysium -  $28.90 \pm 0.22 \mu\text{m}$ .

On the 7th day of the experiment in the group of animals treated with systemic chemotherapy, there were pronounced changes in the dyscirculatory nature in the form of a significant uniform expansion of the peri- and endomysial zone ( $33.40 \pm 0.10 \mu\text{m}$  and  $16.33 \pm 0.33 \mu\text{m}$ , respectively), indicating interstitial myocardial edema. In vessels of hemomicrocirculation (mainly in venules and capillaries) signs of hyperemia were observed - the expanded gleam of vessels with an unchanged wall was filled with erythrocytes freely located among plasma, and also a stasis - the endothelium of vessels was swollen,

the expanded gleam distributed mainly on the periphery of the vessel. In addition, in part of the venules there was a sludge phenomenon (Fig. 2). Small focal diapedetic hemorrhages in perimysia were observed irregularly. If the hyperemia was evenly distributed, the phenomena of stasis, sludge phenomenon and diapedetic hemorrhage were observed more often in the subendocardial parts of the myocardium. There was also swelling of the ventricular endothelium, local subendothelial edema. The average diameter of cardiomyocytes was  $8.70 \pm 0.21 \mu\text{m}$ . From a considerable part of cardiomyocytes there was their swelling with the expressed eosinophilic homogenization of a sarcoplasm, basophilic pyknotic nuclei. In this case, more than 50% of the nuclei of preserved cardiomyocytes have condensation of chromatin in the form of a distinct layer with uneven outlines near the nucleus wall, as well as large lumps of chromatin in the center of the nucleus. The transverse diameter of the nuclei averaged  $2.20 \pm 0.13 \mu\text{m}$ . No muscle fiber fragmentation was observed. Areas of myofibrillar degeneration and areas with fibrosis and wavy tortuosity of both single and individual groups of muscle fibers were identified. There was also uneven staining with background dyes, deep decay of myofibrils of cardiomyocytes. Some groups of cardiomyocytes had significantly enlightened sarcoplasm (a sign of myocytolysis). There were also single cardiomyocytes with a sharp weakening of tinctorial properties in the central part of the muscle fiber and the preservation of the color of the sarcoplasm in its peripheral areas. The nuclei in such cells had an irregular oval shape. Small foci of a myocardium with express vacuolation of cardiomyocytes, their disintegration without cellular reaction were found (Fig. 3). Most often, these changes were observed in muscle fibers located directly under or near the endocardium.

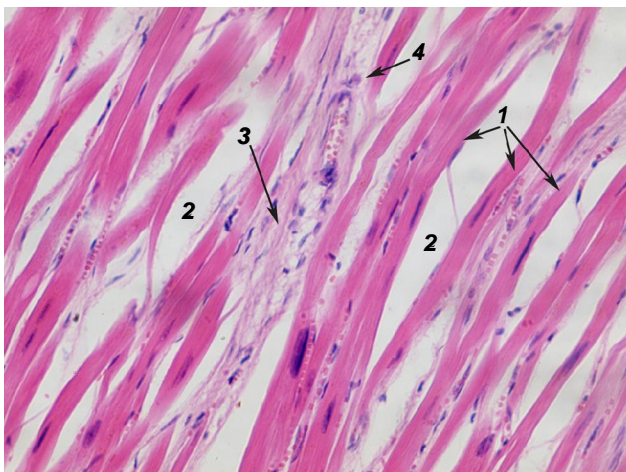


**Fig. 4.** The rat myocardium of the experimental group on the 14th day after systemic chemotherapy. Hematoxylin-eosin. x1000. 1 - cardiomyocytes; 2 - loose unformed connective tissue interstitium; 3 - active fibroblasts; 4 - lympho-histiocytic elements.





**Fig. 5.** The rat myocardium of the experimental group for 21 days after systemic chemotherapy. Hematoxylin-eosin. x100. 1 - cardiomyocytes with pronounced anastomoses; 2 - edema of the interstitium; 3 - small-focal fibrosis of the interstitium; 4 - dilated vessels of hemomicrocirculation; 5 - dilated lymphatic vessel.



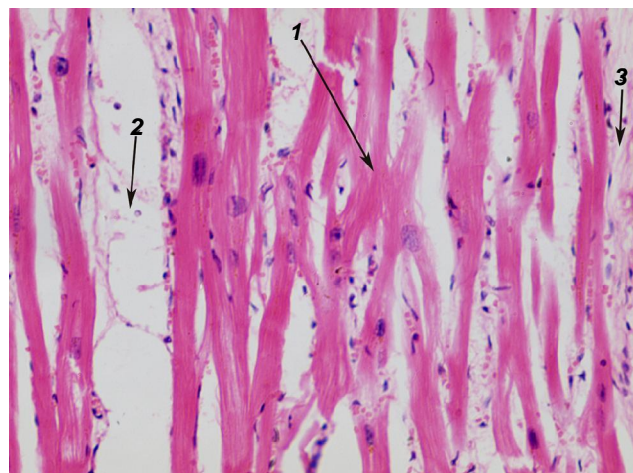
**Fig. 6.** The rat myocardium of the experimental group for 28 days after the application of systemic chemotherapy. Hematoxylin-eosin. x400. 1 - cardiomyocytes with homogenized sarcoplasm and pyknosis of the nucleus; 2 - swollen endomysium; 3 - perivascular interstitial fibrosis; 4 - plasma cell.

On day 14 of the experiment, in the group of animals treated with systemic chemotherapy, dyscirculatory changes in the form of interstitial edema persisted in the myocardium, although less pronounced (relatively uniform expansion of the peri- and endomysial zone to an average of  $39.30 \pm 0.25 \mu\text{m}$  and  $10.23 \pm 0.22 \mu\text{m}$ , respectively), as well as signs of uneven capillary-venular plethora, erythrostatics and sludge phenomenon. These pathomorphological changes were most clearly observed in the subendocardial parts of the myocardium. In the stroma, in addition to signs of edema, mainly perivascularly, small-focal clusters of active fibroblasts and thin fibrous fibers were observed, among which a small number of lympho-histiocytic elements were found

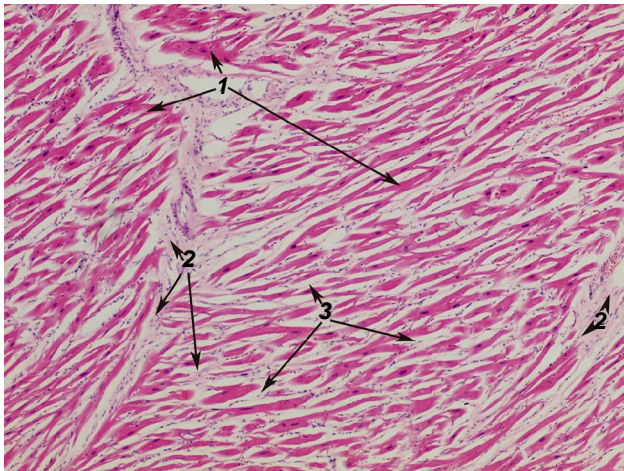
in some places (Fig. 4). On the part of the muscle fibers, there was a focal fragmentation, defibering and wavy tortuosity, their uneven perception of background stains. Eosinophilic homogenization of sarcoplasm, or, on the contrary, its significant enlightenment, basophilia and pyknosis of nuclei, was preserved in some cardiomyocytes. These changes in myocytes were most often observed subendocardially. The average diameter of cardiomyocytes was  $7.30 \pm 0.14 \mu\text{m}$ , the diameter of the nuclei in the cross section was  $2.00 \pm 0.14 \mu\text{m}$ .

On the 21st day of the experiment, in the group of animals treated with systemic chemotherapy, the heart muscle showed uneven moderate blood supply and dilatation of the vessels of hemomicrocirculation, places with stasis and erythrocyte sludge. Significant signs of diffuse interstitial edema endo- and perimysia persisted (width  $9.82 \pm 0.26 \mu\text{m}$  and  $37.40 \pm 0.15 \mu\text{m}$ , respectively). In the latter, the lymphatic vessels had a significantly dilated lumen, with no sign of lymphostasis. In endomysia and perimysia, indistinct foci of excess loose fibrous tissue were observed, represented mainly by a fibrous component with few fibroblasts (including active ones), single lympho-histiocytic elements. Muscle functional fibers of the myocardium, due to endomysia edema, were mostly distant from each other, due to which the anastomoses between them became distinct (Fig. 5).

Some of the fibers and their nuclei had an increased volume (ie, were hypertrophied) and, there was a fragmentation of the fibers, their wavy tortuosity. Most cardiomyocytes had a fuzzy transverse and enhanced longitudinal striation, uneven staining with background stain. In some cardiomyocytes there was their branching and splitting, the presence of vacuolar dystrophy and lysis of the sarcoplasm, condensation of nuclear chromatin and karyopyknosis. In general, the average diameter of cardiomyocytes was  $5.10 \pm 0.08 \mu\text{m}$ , the transverse



**Fig. 7.** The rat myocardium of the experimental group for 35 days after systemic chemotherapy. Hematoxylin-eosin. x400. 1 - cardiomyocytes anastomosing; 2 - moderate edema of the interstitium; 3 - focal interstitial fibrosis.



**Fig. 8.** The rat myocardium of the experimental group for 35 days after systemic chemotherapy. Hematoxylin-eosin. x100. 1 - cardiomyocytes; 2 - fibrous interstitium; 3 - endomysial edema.

diameter of the nuclei -  $2.27 \pm 0.08 \mu\text{m}$ .

On the 28th day of the experiment, in the group of animals treated with systemic chemotherapy, the heart muscle showed uniform moderate blood supply to the blood vessels of hemomicrocirculation, erythrostatics and sludge phenomenon were not observed. Although less pronounced, signs of diffuse interstitial edema of the endomysium persisted (on average, the width of the endomysium was  $7.50 \pm 0.14 \mu\text{m}$ , and the perimysium was  $32.30 \pm 0.37 \mu\text{m}$ ). However, the expansion of the endomysium zone was due, in addition to edema, to the presence of excess loose unformed fibrous tissue. In perimysium, foci of fibrosis were observed mainly perivascularly. At the same time, active fibroblasts were found irregularly and in small quantities in the connective tissue, scattered insignificant histio-plasmacytic infiltration was noted (Fig. 6). The functional fibers of the myocardium show an increase in most of them in volume, focal fragmentation, fuzzy transverse and enhanced longitudinal striation, uneven perception of background dyes. In some cardiomyocytes there was defibering, their wavy tortuosity, greater severity of cellular anastomoses. In addition to the increased volume of cardiomyocytes (and, consequently, their nuclei), mostly individual cardiomyocytes and their groups were observed mainly subendocardially, among which there was eosinophilic homogenization of sarcoplasm, basophilia and pyknosis of nuclei. Lipofuscin grains were located perinuclearly in some myocytes. In general, the average diameter of cardiomyocytes was  $5.20 \pm 0.13 \mu\text{m}$ , the transverse diameter of the nuclei was  $3.30 \pm 0.15 \mu\text{m}$ .

On the 35th day of the experiment in the group of animals treated with systemic chemotherapy, as in the previous period, in the myocardium there was a uniform moderate blood supply to the vessels of hemomicrocirculation, signs of interstitial edema, which was local (mainly in the subendocardial). Dilatation of the

lumen of lymphatic vessels without signs of lymphostasis was preserved. Also in the interstitium there was a growth of fibrous loose tissue, the fibrous structures of which were relatively thickened, acquired an orderly appearance (located mainly along the functional muscle fibers). Its cellular component was represented by a small number of fibroblasts of varying degrees of activity, single lymphohistiocytic elements. The average width of the endomysium was  $7.24 \pm 0.08 \mu\text{m}$ , perimysium -  $30.50 \pm 0.18 \mu\text{m}$ . In cardiomyocytes the morphological changes which were noted in the previous term of experiment remained. Namely, the presence of functional fibers of the myocardium and their nuclei increased in volume, with signs of vacuolar and granular dystrophy, lipofuscinosis. The average diameter of cardiomyocytes was  $5.50 \pm 0.15 \mu\text{m}$ , the diameter of their nuclei was  $3.90 \pm 0.16 \mu\text{m}$ . Focal fragmentation and defibrillation of cardiomyocytes, their wavy tortuosity, the severity of cellular anastomoses due to their dissociation were also preserved (Fig. 7).

At the same time, the number of myocytes with basophilia and nuclear pyknosis decreased. In general, the myocardium retained its structural order. Its architecture was disturbed mainly due to fibrosis and edema of the interstitium (Fig. 8).

## Discussion

Doxorubicin belongs to the anthracycline series and has been used as an antitumor drug for almost half a century [20].

Although the use of this drug has shown excellent results in the treatment of malignant tumors, but its wider use is hindered by its potential cardiotoxicity, which is clinically manifested by cardiomyopathy and congestive heart failure [15, 20, 25].

The mechanism of cardiotoxicity of Doxorubicin has not been fully studied. Summarizing the results of a large number of diverse studies, it can be argued that oxidative stress, inflammation, apoptosis, mitochondrial dysfunction and calcium overload of cardiomyocytes are the main components of the pathogenesis of toxic heart disease [7, 17, 24, 28].

The literature describes a large number of experimental studies in which Doxorubicin is administered to develop Doxorubicin-induced cardiomyopathy [3, 13, 26]. However, they all differ significantly in the parameters of drug administration, such as dosage and frequency of its administration.

In our opinion, a large number of differences in the results of Doxorubicin cardiomyopathy studies are due to the variety of dosing methods and the frequency of administration of Doxorubicin.

That is why, in our opinion, an important task is not only the standardization of the method of modeling Doxorubicin-induced cardiomyopathy, but also the maximum approximation of the parameters of the method to those used in clinical practice.

After analyzing modern techniques and not finding one that would fully meet the requirements, we decided to start from proven effective treatment strategies and try to create our own experimental method for modeling Doxorubicin-induced cardiomyopathy.

Our proposed method was intraperitoneal administration of Doxorubicin at a dose of 5 mg/kg once a week for 5 weeks.

The dose of 5 mg/kg was determined by recalculating the average therapeutic dose of the drug for humans in the treatment of superficial bladder cancer. The recalculation was performed according to the method proposed by Anroop B. Nair and Shery Jacob [19].

In general, analyzing the data of histomorphological and histomorphometric examination of the myocardium, we can conclude that in all animals of the experimental group there was, first of all, circulatory disorders in the heart muscle at the level of hemomicrocirculation, which in turn led injury (mainly to dystrophy), predominant cardiomyocyte malnutrition, interstitial edema and fibrosis. Systemic chemotherapy in animals showed marked myocardial changes, such as a threefold enlargement of the endomyocardial area due to capillary plethora and edema compared with intact animals. At the end of the experiment, the animals of the experimental group maintained an expansion of the endomyocardial zone to

7.24±0.08 μm, mainly due to interstitial fibrosis. In itself, the expansion of the interstitial zone due to fibrosis indicates, first of all, that in the myocardium there was a significant hypoxemia with damage (including death) of cardiomyocytes, activation of interstitial and replacement collagen formation. The presence of the above changes, such as hypertrophy of the cardiomyocytes on the background of their general malnutrition, interstitial fibrosis, give us reason to argue about the development in experimental animals dilated cardiomyopathy.

In the future, experimental studies are planned on the possibility of reducing the cardiotoxic effects of Doxorubicin.

## Conclusions

1. Serial administration of Doxorubicin in medium therapeutic doses according to the proposed method causes changes in the myocardium of experimental animals similar to changes in the heart of people undergoing chemotherapy with this drug.

2. The presence of changes, such as hypertrophy of part of cardiomyocytes against the background of their general malnutrition, interstitial fibrosis, allow to interpret the pathological process in the heart of experimental animals as dilated cardiomyopathy.

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#### ДИНАМІКА МОРФОЛОГІЧНИХ ЗМІН У СЕРЦІ ЩУРІВ ПРИ СЕРІЙНОМУ СИСТЕМНОМУ ВВЕДЕННІ ДОКСОРУБІЦИНУ


Костюк О.Г., Годован Н.Л., Гормаш П.П., Таран І.В., Гребенюк Д.І., Машевська О.В.

Поряд із хорошим протипухлинним ефектом Доксорубіцин спричиняє системний вплив із ураженням життєво важливих органів, зокрема серця. Відсутність єдиного підходу до дозування та кратності введення Доксорубіцину в експерименті спонукає до пошуку оптимальної моделі доксорубіцинової кардіоміопатії. Мета дослідження - розробити спосіб серійного введення Доксорубіцину у середньотерапевтичних дозах в експерименті та оцінити кардіотоксичний ефект препарату. До дослідження було включено 42 самок щурів лінії Wistar. Контрольну групу склали 7 інтактних щурів. Дослідну групу склали 35 щурів, яким проводили системну хіміотерапію Доксорубіцином у дозі 5 мг/кг 1 раз на тиждень протягом 5 тижнів. На 7, 14, 21, 28, 35 добу вилучали серця піддослідних тварин для морфологічного дослідження. Гістоморфометрично визначали: діаметр кардіоміоцитів (в серединній їх частині) і поперечний діаметр їх ядра, ширину інтерстиціального простору (ендо- та перимізія). Дані гістоморфологічного та гістоморфометричного дослідження міокарда свідчили про те, що у всіх тварин дослідної групи мало місце порушення кровообігу в серцевому м'язі на рівні гемомікроциркуляції. Такі зміни призводили до гіпотрофії кардіоміоцитів, інтерстиціального набряку та фіброзу. При проведенні системної хіміотерапії у тварин відмічались виражені зміни міокарда такі, як розширення зони ендомізію, за рахунок капілярного повнокріє'я та набряку, у порівнянні з тваринами інтактної групи. Наприкінці експерименту у тварин дослідної групи зберігалось розширення зони ендомізію в основному за рахунок інтерстиціального фіброзу. Подібні зміни вказують на гіпоксемію міокарда з ушкодженням та загибеллю кардіоміоцитів, активацією інтерстиціального та замісного колагенутворення. Отримані морфологічні дані свідчать про розвиток в експериментальних тварин дилатативної кардіоміопатії. Таким чином, серійне інтраперитонеальне введення

*Доксорубіцину у дозі 5 мг/кг 1 раз на тиждень протягом 5 тижнів викликає морфологічні зміни в міокарді експериментальних тварин аналогічні до змін у серці людей, що проходять хіміотерапію даним препаратом.*

**Ключові слова:** Доксорубіцин, кардіоміопатія, морфологія, експеримент, щури.

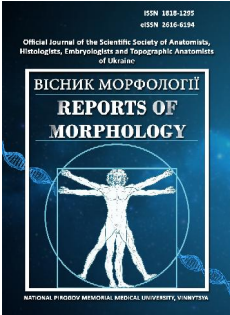
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*Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
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## The structure of morbidity of secondary school children

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### ARTICLE INFO

Received: 31 August, 2020

Accepted: 30 September, 2020

**UDC:** 616.1/9-057.874-055.1/3-071

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*Intensification of the educational process is one of the risk factors for increasing the prevalence of morphofunctional disorders, acute and chronic somatic morbidity, mental and behavioral disorders, maladaptation syndrome. Many researchers have found a negative chronological dynamics of school health and a high incidence among secondary school students. The purpose of the study is a comparative analysis of the structure and dynamics of morbidity of children during secondary school. The study involved more than 266 students of secondary schools aged 10 to 14 years. The state of health was assessed according to preventive medical examinations conducted by specialists of the Institute of Child and Adolescent Health of the National Academy of Medical Sciences of Ukraine with the informed consent of parents and according to the bioethical norms of the Helsinki Declaration (as amended in 2013). Statistical data processing was performed using the licensed package SPSS Statistic v.20 using Student's t test. The highest level of morbidity was found in diseases of the endocrine system (468.4±39.7‰), the organ of vision and the appendix (322.8±37.2‰), the circulatory system (310.1±36.8‰) and respiration (303.8±36.6‰). Among girls, endocrine (520.7±57.7‰) and ophthalmological pathology (386.7±56.2‰) were more often registered, and among boys - mental and behavioral disorders (168.7±39.9‰; p<0.05). During the training, negative dynamics was determined for diseases of the endocrine system (due to a probable increase in their number among boys, at p<0.05), diseases of the digestive system, eye and appendages due to decreased visual acuity (p<0.01). In the structure of endocrine pathology, 60% were thyroid diseases in both sexes, and the prevalence of grade 1 obesity was higher among boys (p<0.05). Mental and behavioral disorders were mainly represented by disorders of activity and attention in adolescent boys, sleep disorders - in girls; hyperkinetic behavioral disorders - in both sex groups. Gender features in the structure and dynamics of morbidity of secondary school students to a greater extent in diseases of the endocrine system, eye and appendix with a general negative tendency to increase the prevalence of these groups of diseases.*

**Keywords:** morbidity, structure of diseases, students, secondary school age, adolescent boys, girls.

### Introduction

Intensification of the educational process is one of the important risk factors for increasing cases of morphofunctional disorders, acute and chronic somatic diseases, mental and behavioral disorders, maladaptation syndrome. Progressive increase of mental disorders and diseases of the nervous, digestive and urogenital system more than 2-3 times, ophthalmological - 4.1 times, endocrine - 7 times during training in general secondary education [3, 6, 9, 22]. Determining the characteristics of the state of health should take into account that nowadays chronic diseases are more and more common in the form of combined pathology, which complicates the diagnosis,

treatment and, moreover, prevention of pathological conditions.

Against the background of increasing the prevalence of morbidity is experiencing significant negative changes and lifestyle of school-age children, which is determined by a significant imbalance of ways of organizing leisure in the direction of passive activities. Decreased physical activity of adolescents is not only a poor physical form, but also a factor in the development of significant somatic and psychological problems in adolescents [5, 7, 21]. A high medical and social problem is the high prevalence of endocrine pathology, including childhood obesity, as

excessive fat deposition is associated with decreased cognitive abilities, school performance and professional achievement in the future [18, 23].

One of the main criteria of health is the level of pathological involvement of children and adolescents. Ukrainian researchers have found a negative chronological dynamics of the health of schoolchildren and the highest incidence among secondary school students. It is during this school period that the formation of certain classes of diseases (so-called "school diseases") is noted [30]. The leading place among them is occupied by pathology of the eye, first of all - myopia. Modern researchers consider the following factors as the main risk factors for the formation and spread of ophthalmic pathology among schoolchildren: intensification of the educational process, increase of school and extracurricular time, uncontrolled screen time, unregulated use of technical teaching aids [3, 10, 11, 19, 20].

The secondary school age is characterized by two physiological crises (prepuberty and puberty), which are deepened by changes in the education system and social maturation. That is why adolescence is considered as a period of increased susceptibility to stress, the leading factors in the formation of which are a large amount of educational material, tight learning schedule, lack of time to repeat and consolidate educational material, too frequent control of knowledge, competitive educational environment. It is at this age that the highest physiological "value" of learning and academic success is determined [15, 26, 29].

*The purpose* of the study is a comparative analysis of the structure and dynamics of morbidity of children during secondary school.

### Materials and methods

The longitudinal study involved 266 students of secondary schools aged 10-14 years. The state of health was assessed according to preventive medical examinations conducted by specialists of the SI "Institute of Child and Adolescent Health of the National Academy of Medical Sciences of Ukraine" with the informed consent of parents and according to the bioethical norms of the Helsinki Declaration (as amended in 2013).

Medical examinations were performed three times: at the beginning, in the middle and at the end of secondary school with the involvement of a pediatrician, endocrinologist, ophthalmologist, psychoneurologist, cardiologist and gastroenterologist. According to the results of the survey of schoolchildren according to the International Classification of Diseases (ICD-10), the following indicators of morbidity were determined: its general level and main classes of diseases of the endocrine, respiratory, nervous, cardiovascular, digestive system, eye disorders, mental and behavioral disorders. Additionally, the internal structural characteristics of morbidity are given with the determination of the percentage contribution of certain groups of diseases to its general

level and by individual nosological groups.

Statistical data processing was performed using the licensed SPSS Statistic v.20 package using Student's t test.

### Results

At the beginning of secondary school, the total pathological incidence was 1683.5‰, and its highest level was found in diseases of the endocrine system (468.4±39.7‰), the organ of vision (322.8±37.2‰), circulatory system (310.1±36.8‰) and respiratory (303.8±36.6‰).

Some sex differences in the structure of diseases have been established (Fig. 1). Thus, if in both sex groups the first rank was occupied by diseases of the endocrine system, then among boys the second and third rank places were occupied by diseases of the respiratory system (361.4±51.9‰) and blood circulation (313.3±51.4‰), and in girls, respectively, ophthalmic (386.7±56.2‰) and cardiovascular pathology (306.7±53.2‰) (Fig. 1).

In addition, the higher prevalence among girls of the endocrine system pathology (520.7±57.7‰ against 421.7±54.7‰ in boys), diseases of the visual organ (respectively 386.7±56.2‰ and 265.1±52.7‰) drew attention. Among boys, mental and behavioral disorders were registered more often than in the group of girls (168.7±39.9‰ and 40.00±22.6‰, respectively;  $p < 0.05$ ). During secondary school, the negative dynamics of endocrine system diseases appearance due to their probable increase in the group of examined boys ( $p < 0.05$ ) was established. It should be noted that the increase in the incidence of diseases of the eye and digestive organs was in both groups ( $p < 0.01$ ). At the same time, there was a decrease in morbidity in diseases of the respiratory system ( $p < 0.05$ ) due to their decrease among girls (Table 1.)

Additionally, the structure of endocrine pathology as the most common class of diseases among secondary school children was analyzed (Fig. 2). It has been established that the leading pathology is thyroid disease, which accounts for more than 60% of schoolchildren of both sexes, regardless of the stage of education, except for boys aged 14-15. The prevalence of diffuse goiter of the 1st degree ranged from 265.1±48.5‰ in boys and 413.3±56.9‰ in girls at the beginning of secondary school to 241.0±46.9‰ and 373.3±55.9‰ respectively at the end of training. The second place was occupied by 1st degree obesity, the prevalence of which was higher among boys, but this figure reached a significant difference only at the end of training: 156.6±39.9‰ against 40.00±22.60‰ in girls ( $p < 0.05$ ) (Fig. 2).

Disorders of growth included only its delay, which was registered in 8.6% of boys at the beginning of training and in 13.2% - in the middle of training. At the end of the study, tallness was found in 4.0% of students, and growth retardation was found in 8.0%. In the female sex group, the inverse ratio of these disorders was determined, namely: there were two to three times more girls with high growth

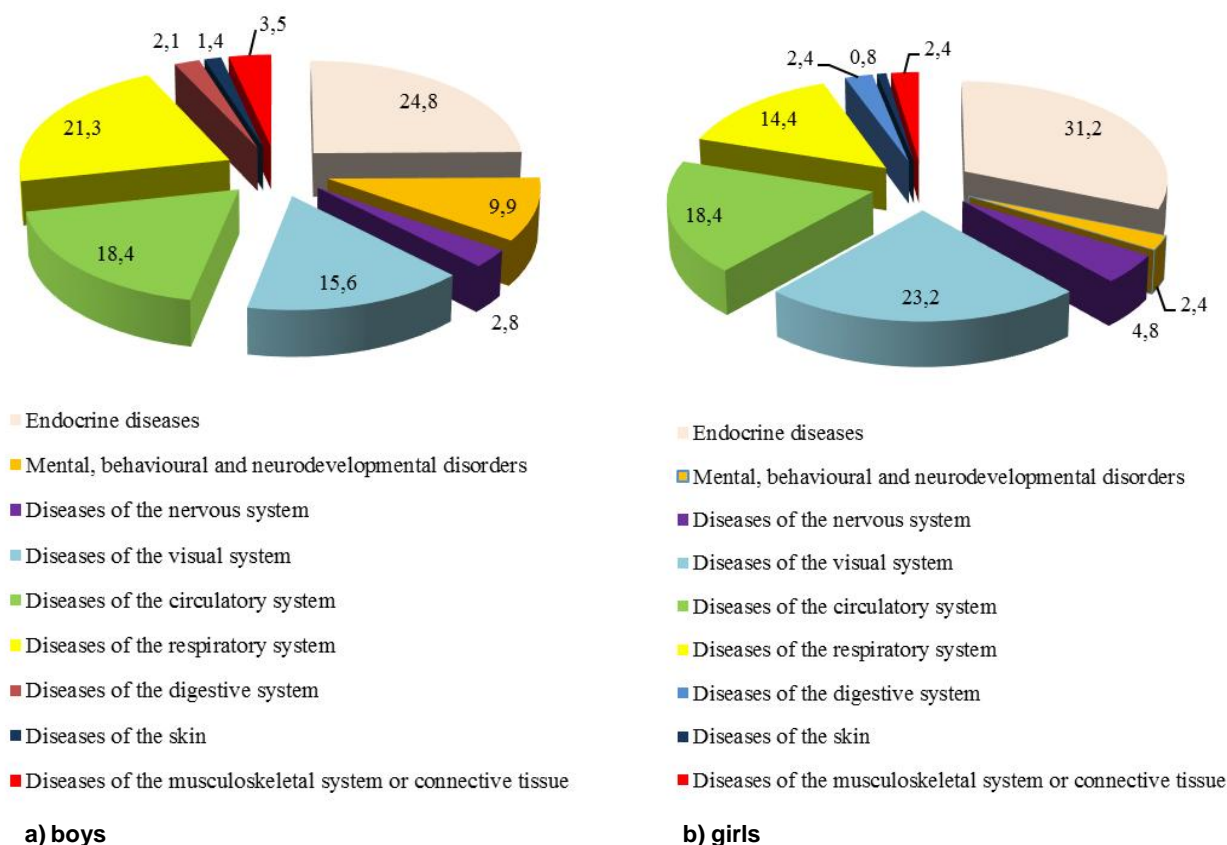


Fig. 1. The structure of the incidence of secondary school age students (%).

Table 1. Sex and age features of morbidity of secondary school students, %, (M±m).

Class of diseases	at the beginning of training		at the end of training	
	boys	girls	boys	girls
Diseases of the endocrine system	421.7±54.2	519.9±57.7	602.4±53.7#	599.9±56.6
Diseases of the eye	265.1±48.4	386.7±56.2	433.7±54.4*#	599.9±56.6#
Diseases of the circulatory system	313.3±50.9	306.7±53.2	373.5±53.1	413.3±56.9
Diseases of the respiratory system	361.4±52.7	239.9±49.3	253.0±47.7*	106.7±35.6#
Mental and behavioral disorders	168.7±41.1*	39.99±22.63*	84.33±30.50	39.99±22.63
Diseases of the nervous system	48.19±23.51	79.99±31.33	60.24±26.11	119.99±37.50
Diseases of the digestive system	36.14±20.49	39.99±22.63	192.8±43.3##	146.7±40.9#

Notes: the presence of statistically significant differences between boys and girls (\* - p<0.05); in the dynamics of learning (# - p<0.05; ## - p<0.01).

than with growth retardation.

In the middle of secondary school, 36.1±20.5% boys and 13.3±13.2% girls were reported to be at risk of sexual delay. It should be noted that at the end of training 6.0% of boys and 6.7% of girls were diagnosed with endocrine pathology, namely: hypothalamic syndrome and dyspituitarism, which led to delayed sexual development.

Mental and behavioral disorders, which were more common in middle school boys, in 1/3 of cases were represented by disorders of activity and attention, and in 20-30% of students - hyperkinetic behavioral disorders. Among girls, the proportion of sleep disorders doubled during

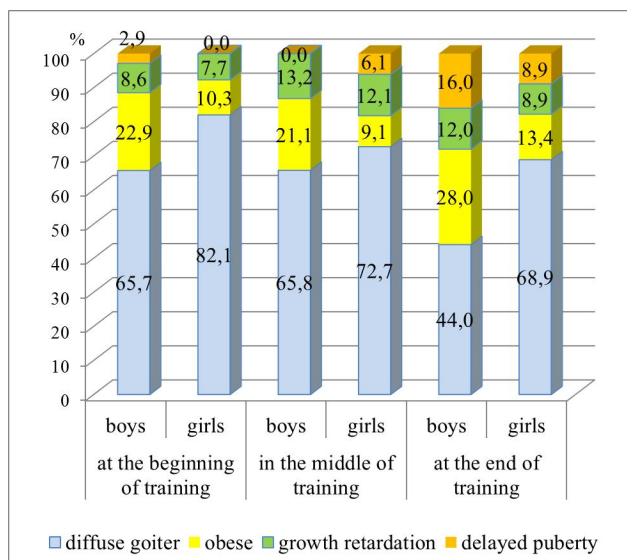
training, and 50% of girls in the middle of training had signs of hyperkinetic disorders.

The prevalence of diseases of the eye was probably higher among girls (p<0.05) during the entire study due to decreased visual acuity, which progressed in both sex groups from 272.0±35.4‰ to 430.4±39.4‰ (p<0.01). The prevalence of accommodation disorders increased during secondary school, but insignificant and amounted to 15% of all ophthalmic pathology.

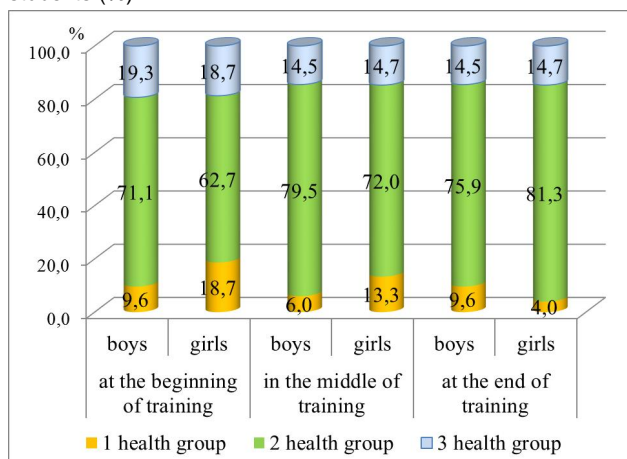
The distribution of students by health groups during secondary school is analyzed (Fig. 3).

It was found that, regardless of sex and stage of study,





**Fig. 2.** Structure of endocrine pathology of secondary school age students (%).



**Fig. 3.** Distribution of secondary school age students by health groups (%).

more than 80% of schoolchildren entered health groups 1 and 2. At the same time, among boys this distribution probably did not change, and the percentage of girls probably increased (by 9.3%). This percentage was included in group 2 due to 1 group of health ( $p < 0.05$ ). There is no significant difference between students of different sexes in terms of health groups.

## Discussion

An important role in the period of sexual development, which coincides with the middle school age, is played by thyroid hormones, which are involved in metabolic processes, bone and skeletal formation, growth process, development of sexual characteristics [16, 17].

In our study, we found that the most common diseases of

the endocrine system, and the first place in secondary school students of both sexes are diseases of the thyroid gland and account for 2/3 of all endocrine pathology. At the same time, growth retardation was registered in almost 10% of boys, sexual dysfunction in every sixth adolescent boy, which was twice as common as among girls of the same age group.

Previous studies have shown that oxidative stress caused by an imbalance of thyroid hormones in hypothyroidism affects testosterone levels and, consequently, the formation of hypoandrogenism in boys [1, 8, 16, 24]. There is a direct correlation between the content of thyroid hormones and nutritional status, fat content in the body [4]. The development of a child during early childhood and puberty is influenced by both the quality of nutrition and a number of neuroendocrine, genetic and environmental factors [14, 23, 31].

Attention should be paid to the almost doubling of the prevalence of ophthalmic pathology, where the leading place is occupied by myopia, which, according to world literature, is formed mainly in middle school age. Foreign researchers have found an increase in the prevalence of myopia during training and its direct correlation with age, sex, body mass index (BMI) and the type of educational institution, which coincides with our studies, which proved the predominance of visual pathology among girls and its likely increase during [2, 12, 13, 25].

Cohort studies have shown that the risk factors for the development of acquired myopia are the intensification of the educational process, educational achievements, low levels of natural and artificial lighting, the use of LED lamps when doing homework, reading disorders (distance less than 25 cm), insufficient night sleep and time spent outdoors, low level of physical activity, living in an urban environment [10, 11, 19, 20, 32]. Scientific confirmation of this fact was reflected in our previous research on the impact of risk factors from irrational regimes and lifestyles of secondary school students on the subjective and objective assessment of their health, including the formation of endocrine, ophthalmic, cardiorespiratory system, mental and behavioral disorders [27, 28].

A promising area of research is the further study of the structure of morbidity of students with different levels of academic success in the dynamics of general secondary education.

## Conclusions

1. The highest level of morbidity was found in diseases of the endocrine system, vision, circulatory and respiratory systems.

2. Sex features in the structure and dynamics of morbidity of secondary school students to a greater extent found for diseases of the endocrine system, eye with a general negative tendency to increase the prevalence of these groups of diseases.

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#### СТРУКТУРА ПАТОЛОГІЧНОЇ УРАЖЕНОСТІ ДІТЕЙ СЕРЕДНЬОГО ШКІЛЬНОГО ВІКУ

**Сотнікова-Мелешкіна Ж.В.**

Інтенсифікація навчального процесу є одним із чинників ризику збільшення розповсюдженості морфофункціональних відхилень, гострої та хронічної соматичної захворюваності, розладів психіки та поведінки, синдрому дезадаптації. Багатьма дослідниками встановлено негативну хронодинаміку стану здоров'я школярів та високий рівень захворюваності серед учнів середнього шкільного віку. Мета дослідження - порівняльний аналіз структури та динаміки патологічної ураженості дітей у період навчання у базовій школі. У дослідженні прийняли участь 266 учнів закладів загальної середньої освіти віком від 10 до 14 років. Стан здоров'я оцінювали за даними профілактичних медичних оглядів, проведених фахівцями ДУ "Інститут охорони здоров'я дітей та підлітків НАМН України" за наявності інформованої згоди батьків та згідно біоетичних норм Гельсінської декларації (у редакції 2013 р.). Статистичну обробку даних проведено за допомогою ліцензованого пакету SPSS Statistic v.20 з використанням критерію Стьюдента. Найвищий рівень патологічної ураженості був встановлений за хворобами ендокринної системи (468,4±39,7‰), органу зору та придаткового апарату (322,8±37,2‰), системи кровообігу (310,1±36,8‰) та дихання (303,8±36,6‰). Серед дівчат більш часто реєстрували ендокринну (520,7±57,7‰) та офтальмологічну патологію (386,7±56,2‰), а серед хлопців - розлади психіки та поведінки (168,7±39,9‰;  $p<0,05$ ). Протягом навчання визначена негативна динаміка щодо хвороб ендокринної системи (за рахунок вірогідного збільшення їх кількості серед хлопців, при  $p<0,05$ ), хвороб органів травлення, ока та придаткового апарату за рахунок зниження гостроти зору ( $p<0,01$ ). У структурі ендокринної патології 60% становили захворювання щитоподібної залози в обох статевих групах, а рівень розповсюдженості ожиріння 1 ступеня був вищим серед хлопців ( $p<0,05$ ). Розлади психіки та поведінки були представлені переважно порушеннями активності та уваги у хлопців-підлітків, розладами сну - у дівчат; гіперкінетичними розладами поведінки - в обох статевих групах. Встановлені статеві особливості у структурі та динаміці патологічної ураженості учнів середнього шкільного віку у більшому ступені за хворобами ендокринної системи, ока та придаткового апарату із загальною негативною тенденцією до зростання поширеності цих груп захворювань.

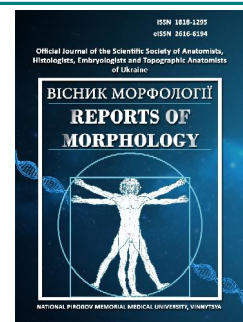
**Ключові слова:** патологічна ураженість, структура захворювань, учні, середній шкільний вік, хлопці-підлітки, дівчата.



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Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>



# Anatomo-functional characteristics of the pelvic organs in women with habitual miscarriage and chronic endometritis

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### ARTICLE INFO

Received: 1 September, 2020

Accepted: 5 October, 2020

UDC: 618.39-08-07:618.14-002

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*Chronic endometritis is a clinical and morphological syndrome, which under the influence of an infectious agent contributes to the violation of cyclic biotransformation and reciprocity of the endometrium. In the diagnosis of gynecological pathology, in particular chronic endometritis, or habitual miscarriage on the background of chronic endometritis, ultrasonography is a mandatory, non-invasive and highly specific method of research. The aim of the study was to assess the anatomical and functional condition of the pelvic organs in women with habitual miscarriage and chronic endometritis using ultrasound (ultrasound and Doppler) criteria. We examined 98 women of childbearing age who applied to the Inomed clinic in the city of Vinnytsya during 2019-2020. Patients were divided into two groups: the main group - 68 women with habitual miscarriage and chronic endometritis; control group - 30 re-pregnant women without previous pregnancy loss. Initially, ultrasound examination (ultrasound) of the pelvic organs was performed on day 5-7 of the menstrual cycle, and to monitor folliculogenesis, the study was repeated on day 13-17 of the cycle. One of the main signs of chronic endometritis is the heterogeneity of the structure of the endometrium, which was found in the vast majority of examined patients of the main group (80.88% at n=68). When determining the thickness of the endometrium, two diametrically opposite processes were established, namely: atrophy (39.71% at n=68) and atypical glandular hyperplasia (22.05% at n=68). In the second half of the menstrual cycle there was a significant thinning of the endometrial layer <0.6 cm. In the control group during the ultrasound examination revealed the following disorders: increased uterine peristalsis, dilation of the arcuate plexus, the heterogeneity of the subendometrial layer, and when re-ultrasound took into account the data of folliculogenesis. Follicular cysts were detected in 10.3% of cases in the main group and 3.3% in the control group of women. At the time of re-ultrasound in each ovary was observed 5-8 antral follicles (the size of which ranged from 6.8 mm to 11.5 mm) with the presence of one dominant, the size of which ranged from 18.2 to 23.4 mm. In order to increase the informativeness of ultrasound, Doppler was additionally performed. Thus, ultrasonography is a highly specific method for determining the anatomical and functional characteristics of the pelvic organs, in particular the pathology of the endometrium in women with habitual miscarriage. The main ultrasound characteristics of chronic endometritis, as one of the causes of reproductive losses, are changes in endometrium structure, thickness, the presence of additional structures (polyps) and fluid component. Informativeness of ultrasound examination of structural changes in the endometrium in chronic endometritis is complemented by Doppler characteristics of blood flow in the basal and spiral arteries of the uterus.*

**Keywords:** *chronic endometritis, habitual miscarriage, ultrasonography.*

### Introduction

Against the background of deteriorating demographic situation in Ukraine, one of the priority medical and social tasks is to preserve the reproductive health of women. Unfortunately, about 15-20% of normal pregnancies under the influence of certain factors go to the section "reproductive losses".

The complexity of diagnosis and treatment of habitual miscarriage for many years is due to a wide range of endogenous and exogenous etiological factors. Despite the fact that a clear determination has not yet been established, there are a number of background diseases that contribute

to abortion. Today, known causes of miscarriage are genetic (13%), anatomical (10-15%), endocrine, immune, infectious factors, "male factor", etc. [28].

Inflammatory diseases of the pelvic organs have a significant negative impact on the health of women of the most active reproductive age (due to the peculiarities of pathogenesis) [13, 22]. One such disease is chronic endometritis (CE).

The problem of chronic endometritis remains extremely relevant because this "uterine" factor often leads to menstrual and generative dysfunction: miscarriage, infertility [8, 14, 20, 26].

Chronic endometritis is a clinical and morphological syndrome in which due to persistent damage to the endometrium by infectious agents, multiple secondary morphofunctional changes occur, which disrupt the cyclic biotransformation and receptivity of the uterine mucosa [7, 19, 24]. Its course is often asymptomatic or coexists with mild nonspecific symptoms along with pelvic pain, abnormal uterine bleeding, vaginal discharge or pain during intercourse [9].

Given the lack of a pronounced clinical picture, modern diagnosis of CE is based on the integrated use of history, clinic, diagnostic methods and their evaluation [17, 23, 26]. Among the additional methods of examination, one of the mandatory is ultrasound, as a non-invasive and highly specific method of visualizing the condition of the reproductive system. The sensitivity of the method is 78.1%, and its specificity is 82.5% [2]. If we consider ultrasound only in the diagnosis of habitual miscarriage on the background of chronic endometritis, this study is not a highly specific method and belongs to the auxiliary. This judgment is shared by Groth, J.V. and co-authors, confirming this in their research [6, 16]. However, it should be noted the importance of ultrasound in detecting the synchrony of the transformation of the endometrium by phases of the menstrual cycle (MC) to diagnose CE and monitor the effectiveness of treatment and rehabilitation of fertility [21].

To increase the informativeness of ultrasound, it is recommended to use new technologies in Doppler: color U3D Doppler, three-dimensional imaging [21]. Impaired blood flow in the vessels of the uterus with a predominance of damage at the level of the basal and spiral arteries, as well as difficulties in visualizing the terminal artery indicate a strong violation of tissue perfusion due to chronic inflammation [12].

*The aim* of the study was to assess the anatomical and functional condition of the pelvic organs in women with habitual miscarriage and chronic endometritis using ultrasound (ultrasound and Doppler) criteria.

## Materials and methods

In order to study the main ultrasound features of the pelvic organs in women diagnosed with "habitual miscarriage on the background of endometritis" were examined 98 women of childbearing age who applied to the

clinic Innomed Vinnytsia during 2019-2020. All women applied to the clinic at the pre-pregnancy stage and continued their follow-up during pregnancy.

During the study, patients were divided into 2 clinical groups:

The main group - 68 women with a diagnosis of habitual miscarriage on the background of chronic endometritis. Criteria for inclusion of patients in the main group were the following: the presence of two or more reproductive losses in the anamnesis in the form of miscarriage, the absence of an embryo in the developing fetal egg or stillbirth; confirmed diagnosis of "chronic endometritis" by immunohistochemical determination of syndecan-1 (sampling of endometrium in the selection of patients was performed by hysteroscopy or pipette biopsy followed by immunohistochemical analysis of the material). The control group consisted of 30 re-pregnant women without a history of reproductive loss.

All patients underwent a typical general clinical and gynecological examination. Ultrasound examination of the pelvic organs to determine their anatomical and functional status and pathognomonic criteria of chronic endometritis was performed using the device Voluson E8 Expert. For a qualitative and most accurate assessment of the condition of the uterine cavity, this procedure was initially performed on day 5-7 of the menstrual cycle, and to monitor folliculogenesis, the study was repeated on day 13-17 of the cycle.

## Results

The age of patients ranged from 19 to 35 years (Table 1). The average age of the examined patients of the main group was  $27.25 \pm 0.29$  years, which probably did not differ from the age of women in the control group -  $26.74 \pm 0.18$  years. The indicator of the degree of probability ( $p$ ) between the two comparative values was considered reliable at  $p < 0.05$ .

Ultrasound of the main group of patients showed the following pathological changes, indicating chronic endometritis as the main etiological factor of habitual miscarriage: uneven endometrial contour, increased echogenicity in the first phase of the menstrual cycle and heterogeneous echostructure of the endometrium, diffuse focal changes of the myometrium and others. These pathological changes were observed only in isolated cases in re-pregnant women who formed a control group, which once again confirms the etiopathogenetic link of habitual

**Table 1.** The age structure of surveyed women.

Age	Main group (n=68)		Control group (n=30)	
	Absolute numbers	%	Absolute numbers	%
19-24	15	22.06**	6	20.0
25-29	36	52.94**	15	50.00
30-35	17	25.00**	9	30.00

**Notes:** \*\* - main group/control group  $p > 0.05$ .

**Table 2.** Ultrasound characteristics of the endometrium in the examined women.

Sign	Detection frequency				
	Main group (n=68)		Control group (n=30)		Total number
	Absolute numbers	%	Absolute numbers	%	
Heterogeneity of the endometrial structure	55	80.88*	2	6.7	57
Endometrial midline is blurred, uneven or not visualized	35	51.47	0	0	35
Fuzzy outer contour of the M-echo	29	42.65	0	0	29
Hyperechogenic outer contour of the M-echo	26	38.24	0	0	26
Endometrial atrophy	27	39.71	0	0	27
Increasing the echogenicity of the endometrium in the 1st phase of the cycle	23	33.82	0	0	23
Dilation of the uterine cavity due to fluid content	23	33.82	0	0	23
Endometrial micropolyps and polyps	22	32.35	0	0	22
Decreased echogenicity of the endometrium in the 2nd phase of the cycle	19	27.94	0	0	19
Hyperechoic endometrial midline	18	26,47	0	0	18
Expansion of the arcuate plexus	13	19.12*	3	10,0	16
Asymmetry of endometrial thickness	15	22.06*	2	6,7	17
Thickening of the endometrium more than 15 mm	15	22.06	0	0	15
Heterogeneity of the subendometrial layer	8	11.76	3	10,0	11
Gas bubbles in the endometrium or uterine cavity	7	10.29	0	0	7
Increased uterine motility	5	7.35	3	10,0	8
Synechia	2	2.94	0	0	2

**Notes:** \* - main group/control group  $p < 0,05$ .

miscarriage with chronic inflammation of the endometrium. A more detailed description of ultrasound changes and the frequency of their detection is presented in Table 2.

Among women in the control group, the following ultrasound disorders were detected: increased uterine motility, dilation of the arcuate plexus, heterogeneity of the subendometrial layer. At the same time, in each patient of the main and comparison groups there were from 3 to 5 main above-mentioned ultrasound diagnostic criteria of chronic endometritis. It should be noted that the heterogeneity of the structure of the endometrium is one of the main signs of chronic endometritis, as it occurs in the vast majority of examined patients of the main group (80.88% at  $n=68$ ).

In order to increase the informativeness of the ultrasound examination, dopplerometry was additionally performed. Standard Doppler parameters were evaluated, namely the indices of pulsation and resistance, blood flow velocity in the uterine vessels. We found that in women of the main group, the indices of resistance and pulsation almost doubled, in contrast to the decrease in blood flow in the basal and spiral arteries of the uterus and varicose veins of the uterus, relative to the control group - the above pathological changes were not detected.

### Discussion

According to various authors, the sonographic signs of chronic endometritis are as follows: change in the thickness

of the endometrium, its thinning in the second half of the MC  $< 0.6$  cm; expansion of the uterine cavity to 0.4-0.7 cm after menstruation with asymmetry of the anterior and posterior walls of the uterus; uneven contours of the endometrium; heterogeneity of the echostructure of the endometrium; appearance of increased echogenicity of areas of different sizes and shapes in the proliferative phase, hyperechogenic inclusions in the basal layer of the endometrium; synechiae in the uterine cavity; diffuse focal and cystic changes in the subendometrial zone; appearance of gas bubbles [10, 14, 19, 24]. The above criteria were recorded in the course of our research.

The fact of heterogeneity of the endometrial structure as one of the main features of chronic endometritis (it was established by us in most of the examined patients of the main group) is repeatedly confirmed in the works of other authors [15, 18].

Regarding the thickness of the endometrium, the data are not so unambiguous, because there are two diametrically opposed processes, namely - atrophy (39.71% at  $n=68$ ) and atypical glandular hyperplasia (22.05% at  $n=68$ ). However, there is a clear advantage in the direction of thinning of the endometrial layer  $< 0.6$  cm in the second half of the menstrual cycle. Atrophic changes of the endometrium in more than a third of the surveyed women diagnosed with "Chronic endometritis" also notes S.M. Kornienko and fixes this criterion at 44.4% [11].

It is worth noting the following disappointing feature

(excluding the vector of change of the endometrial layer): in most women with habitual miscarriage on the background of chronic endometritis (61.76% at n=68) the thickness of the endometrium does not correspond to the phase of the cycle. In turn, this indicates a violation of the transformation of the endometrium, and, consequently, the difficulty of subsequent implantation. After all, the condition for successful implantation and further normal development of the fertilized egg is the morphofunctional fullness of the endometrium, which is characterized by adequate receptor activity that ensures interaction with the embryo, as well as an adequate immune response of the woman.

In addition, a third of the studied women have dilatation of the uterine cavity to 0.5-0.7 cm, fuzzy hyperechogenic outer contour of the M-echo, serosometer, as well as the presence of polyps in the uterine cavity, which is an important diagnostic sign. E. Cicinelli in his research repeatedly draws our attention to micropolyps as a reliable criterion for the diagnosis of "Chronic Endometritis". Although the rate of 11.7% detection of micropolyps in the studied women is not large, but 93.7% of these cases received histological confirmation of CE, which is statistically important [4, 5]. The presence of micropolyps - as predictors of the development of chronic endometritis - was confirmed in other scientific papers [3, 25, 27, 29]. Regarding our research, we recorded this figure in 32.35% of women in the main group.

During repeated ultrasound examination took into account the data of folliculogenesis, as one of the main functional characteristics of the pelvic organs. The analysis of the results showed that among the examined women 9 had follicular cysts - 7 (10.3%) cases in the main group and 1 (3.3%) - in the control group, in other women no pathology was detected. The size of the ovaries was within normal limits. At the time of repeated ultrasound, 5-8 antral follicles were observed in each ovary (their size ranged from 6.8 mm to 11.5 mm), with one dominant, the size of which ranged from 18.2 to 23.4 mm.

After Doppler, in women diagnosed with habitual miscarriage on the background of chronic endometritis found an increase of almost 2 times the indices of resistance and pulsation with a decrease in blood flow in the basal and spiral arteries of the uterus and varicose veins, as evidenced by most modern studies [1, 12], in

which the presence of hypovascularization of the uterus in all morphotypes of chronic endometritis, and an increase in the resistance index is most characteristic for hypoplastic type.

Although pelvic ultrasonography is not a highly specific method for diagnosing habitual miscarriage in chronic endometritis, monitoring endometrial transformation and monitoring the effectiveness of treatment and rehabilitation of fertility by ultrasound is a promising approach in the examination and treatment of this group of patients. For a clearer identification of chronic endometritis as the main etiological factor of gestational loss in the future requires endometrial biopsy in combination with immunohistochemical analysis.

### Conclusions

The results of the above studies indicate that ultrasonography is an indispensable method of diagnosis in obstetrics and gynecology in general and in the diagnosis of chronic endometritis in particular, but for a clearer diagnosis requires a comprehensive approach with analysis of clinical data and the results of several additional research methods.

1. The main ultrasound criteria for chronic endometritis in women diagnosed with habitual miscarriage are: inhomogeneous endometrial echostructure, uneven endometrial contour, increased echogenicity in the first phase of the menstrual cycle, endometrial thickness violation, enlargement of the uterine cavity, fuzzy hyperechogenic outer contour of the M-echo, serosometer, as well as the presence of polyps in the uterine cavity.

2. The thickness and structure of the endometrium is important for prognostic value as an indicator of successful implantation. In 61.76% of the examined women, the thickness of the endometrium did not correspond to the phase of the cycle, which indicated problems of cyclic transformation in the peri-implantation period.

3. In order to increase the informativeness of ultrasound examination, Doppler is performed. Doppler echo method indicates the following criteria for chronic endometritis: increase in pulsation index and resistance almost twice against the background of reduced blood flow in the basal and spiral arteries of the uterus and varicose of veins.

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#### АНАТОМО-ФУНКЦІОНАЛЬНА ХАРАКТЕРИСТИКА ОРГАНІВ МАЛОГО ТАЗА У ЖІНОК ЗІ ЗВИЧНИМ НЕВИНОШУВАННЯМ ВАГІТНОСТІ ТА ХРОНІЧНИМ ЕНДОМЕТРИТОМ

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Хронічний ендометрит - це клініко-морфологічний синдром, який під впливом інфекційного агента сприяє порушенню циклічної біотрансформації та рециптивності ендометрія. В діагностиці гінекологічної патології, зокрема хронічного ендометриу, або звичного викидня на тлі хронічного ендометриу, ультрасонографія являється обов'язковим, неінвазивним та високо специфічним методом дослідження. Мета роботи - оцінити анатомо-функціональний стан органів малого тазу у жінок зі



звичним невиношуванням вагітності та хронічним ендометритом за допомогою ультразвукових (ехографічних та доплерометричних) критеріїв. Ми обстежили 98 жінок дітородного віку, які звертались до клініки Інмед у місті Вінниця у період 2019-2020 років. Хворі були розділені на 2 групи: основна група - 68 жінок зі звичним викиднем та хронічним ендометритом; контрольна група - 30 повторно вагітних жінок без попередньої втрати вагітності. Спочатку ультразвукове дослідження (УЗД) органів малого таза проводили на 5-7 день менструального циклу, а для моніторингу фолікулогенеза дослідження повторювали на 13-17 день циклу. Одним з основних ознак хронічного ендометриту є неоднорідність будови ендометрію, котра була встановлена у переважній більшості обстежених пацієнтів основної групи (80,88% при  $n=68$ ). При визначенні товщини ендометрію були встановлені два діаметрально протилежні процеси, а саме: атрофія (39,71% при  $n=68$ ) та атипова залізиста гіперплазія (22,05% при  $n=68$ ). У другій половині менструального циклу відмічено значне витончення шару ендометрія  $<0,6$  см. У контрольній групі при проведенні ультразвукового дослідження були виявлені такі розлади: посилена перистальтика матки, розширення дугоподібного сплетення, неоднорідність субендометріального шару, а при повторному проведенні УЗД враховували дані фолікулогенезу. Фолікулярні кісти були виявлені в 10,3% випадках у основній групі та 3,3% у контрольній групі жінок. На момент повторного УЗД в кожному яєчнику спостерігалось 5-8 антральних фолікулів (розміри яких становили від 6,8 мм до 11,5 мм) з наявністю однієї домінанти, розмір якої становив від 18,2 до 23,4 мм. З метою підвищення інформативності УЗД додатково проводили доплер. Таким чином, ультрасонографія є високоспецифічним методом для визначення анатомо-функціональних характеристик органів малого таза, зокрема патології ендометрію у жінок зі звичним невиношуванням вагітності. Основними ультразвуковими характеристиками хронічного ендометриту, як одного з причин репродуктивних втрат, є зміни ендометрію, його структури, товщини, наявність додаткових структур (поліпів) та рідинного компоненту. Інформативність ультразвукового дослідження структурних змін з боку ендометрію при хронічному ендометриті доповнюють доплерометричні характеристики кровотоку в базальних та спіральних артеріях матки.

**Ключові слова:** хронічний ендометрит, звичне невиношування, УЗД.

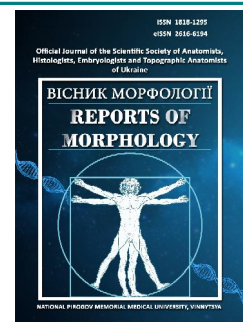
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## Morphometric characteristics of distal airways of guinea pigs sensitized with ovalbumin

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### ARTICLE INFO

Received: 31 August, 2020

Accepted: 07 October, 2020

**UDC:** 611.2.018:547.962.3]-092.9]:599.324.7

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*The reaction of the structural components of small bronchi and terminal bronchioles is the urgent issue of morphology and medicine in general, as well as one of the insufficiently studied issue in the study of morphological changes in the airways with allergic inflammation in the chronobiological aspect. The purpose of this work is to study the morphometric parameters of distal airways of guinea pigs sensitized with ovalbumin. We have studied the lung of 48 guinea pigs, using histological, morphometric and statistical methods under conditions of experimental ovalbumin-induced allergic inflammation, simulated by three times subcutaneous sensitization and subsequent 8-day intranasal inhalation of ovalbumin. The thickness of mucosa, muscular layer and adventitial layer was determined to assess morphometric parameters of bronchioles and terminal bronchioles. There are reactive changes in morphometric parameters of bronchioles on the 23rd and 30th days of observation, such as the thinning of mucosa and on the 36th day such as muscular-fibrous hyperplasia, accompanied by the narrowing of the bronchioles lumen. There are the most significant confirmed statistically changes in the terminal bronchioles on the 36th day of the experiment such as the thickening of mucosa and adventitial layer, accompanied by muscular hyperplasia and edema of the connective tissue stroma. Thus, sensitization and allergization with ovalbumin of experimental animals cause morpho-functional changes in the structural elements of the wall of bronchioles and terminal bronchioles, which have a staged, mainly multidirectional character and correspond to the main morphological manifestations of allergic inflammation with maximal changes in the late period of its development (the 36th day of the experiment).*

**Keywords:** airways, allergic inflammation, Ovalbumin, guinea pig.

### Introduction

There is a constant increase in the incidence of bronchial asthma (BA) in Ukraine and the world today, associated with environmental pollution, increased allergization of the population, deterioration of the gene pool of nations [7]. BA is considered today as a genetically determined disease with neuroendocrine and immune mechanisms of bronchial hypersensitivity development [4, 6, 10]. According to modern concepts, the development of bronchial hyperreactivity is the leading pathophysiological mechanism of the development of bronchial asthma, the degree of which correlates with the severity of the disease [8].

The morphological basis of bronchial hypersensitivity in bronchial asthma is allergic chronic inflammation of the airways, which is observed at all stages of the disease, regardless of its severity and course [11, 12]. Despite its importance, the problem of studying the morphogenesis of

allergic inflammation of the distal airways often remains outside the field of vision of scientists. The number of works, devoted to the study of bronchial morphogenesis in various pathological conditions [9, 13], including allergic inflammation in the chronobiological aspect, is insignificant. Considering the above, the study of morphological changes in the distal airways with allergic inflammation in the chronobiological aspect is the urgent issue in experimental medicine.

*The aim* of this work is to study the morphometric parameters of the distal airways of guinea pigs sensitized with ovalbumin.

### Materials and methods

This research is a part of the research work of Zaporizhzhia State Medical University "Immunomorphological

characteristics of internal organs under the influence of endo and exogenous factors on the body" state registration № 0118U004250.

The object of the experimental study was lung, removed from 48 sexually mature male guinea pigs weighing 450-600 g, which were kept in standard conditions of the vivarium of the Zaporizhzhya State Medical University. All manipulations were carried out in compliance with the basic principles of working with experimental animals in accordance with the provisions of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986), the General Ethical Principles for Animal Experiments adopted by the First National Congress on Bioethics (Kyiv, 2001), the Law of Ukraine "On the protection of animals from cruelty" (from 21.02.2006).

Allergic airway inflammation was induced by subcutaneous sensitization and followed challenging by intranasal inhalation with ovalbumin (OVA) (Sigma Aldrich, USA). Guinea pigs were actively sensitized by subcutaneous injections into the interscapular region of ovalbumin (0,5 mg/mL) with alum (10 mg/mL in saline) as an adjuvant (AlumVax Hydroxide vaccine adjuvant, OZ Biosciences France) on days 0, 7 and 14. From 21 to 28 days of the experiment, guinea pigs were challenged for 15 min with inhalation of either OVA (10 mg/mL in saline) via a nebulizer (Little Doctor International, Singapore, LD-211C) coupled to a plastic box. The animals were divided into 6 groups (8 animals in each group). The first four groups are animals sensitized and challenged OVA, withdrawn from the experiment, respectively, on the 23rd, 30th, 36th and 44th days after its start; 5 - control group, received injections and challenged with saline only; 6 - intact group. For the purpose of rational presentation of the obtained data and their interpretation, we conditionally distinguish the early (23rd, 30th days of the experiment) and late (36th and 44th days after the start of the experiment) periods of the development of allergic inflammatory process in lung.

The animals were withdrawn from the experiment by an overdose of thiopental anesthesia (50 mg/kg) according to the established terms (23rd, 30th, 36th and 44th days of the experiment). Histological sections were stained with hematoxylin-eosin. Masson staining was carried out to assess the organization of collagen fibers, alcian blue - to determine the dynamics of the distribution of glycosaminoglycans, the PAS reaction - to determine the dynamics of the distribution of glycoproteins.

The sections were viewed and photographed by a compound binocular light microscope (Primo Star, Zeiss, Germany). The thickness of mucosal layer, muscular layer and adventitial layer was determined to assess morphometric parameters of bronchioles and terminal bronchioles.

The research results were processed by modern statistical methods of analysis on a personal computer using the standard software package Microsoft Office 2010

(Microsoft Excel) and STATISTICA® for Windows 6.0 (StatSoft Inc., USA, license 46 No. AXXR712D833214FAN5). We use the Shapiro-Wilk test and the Kolmogorov-Smirnov test of consistency testing the hypothesis about the normal distribution of the studied parameters. We use the Kolmogorov-Smirnov homogeneity criterion testing the hypothesis that two independent samples belong to the same distribution law. The arithmetic means ( $M$ ) and standard errors of the mean ( $\pm m$ ) were calculated. The statistical significance of intergroup differences according to the data obtained was established using the parametric Student's t-test ( $p^*$ ) and the nonparametric U-Whitney-Mann test ( $p^{**}$ ). The obtained indicators were compared between the median and interquartile range  $Me$  ( $Q1$ ;  $Q3$ ). Differences between the compared values at the level of 95% ( $p < 0.05$ ) were considered statistically significant.

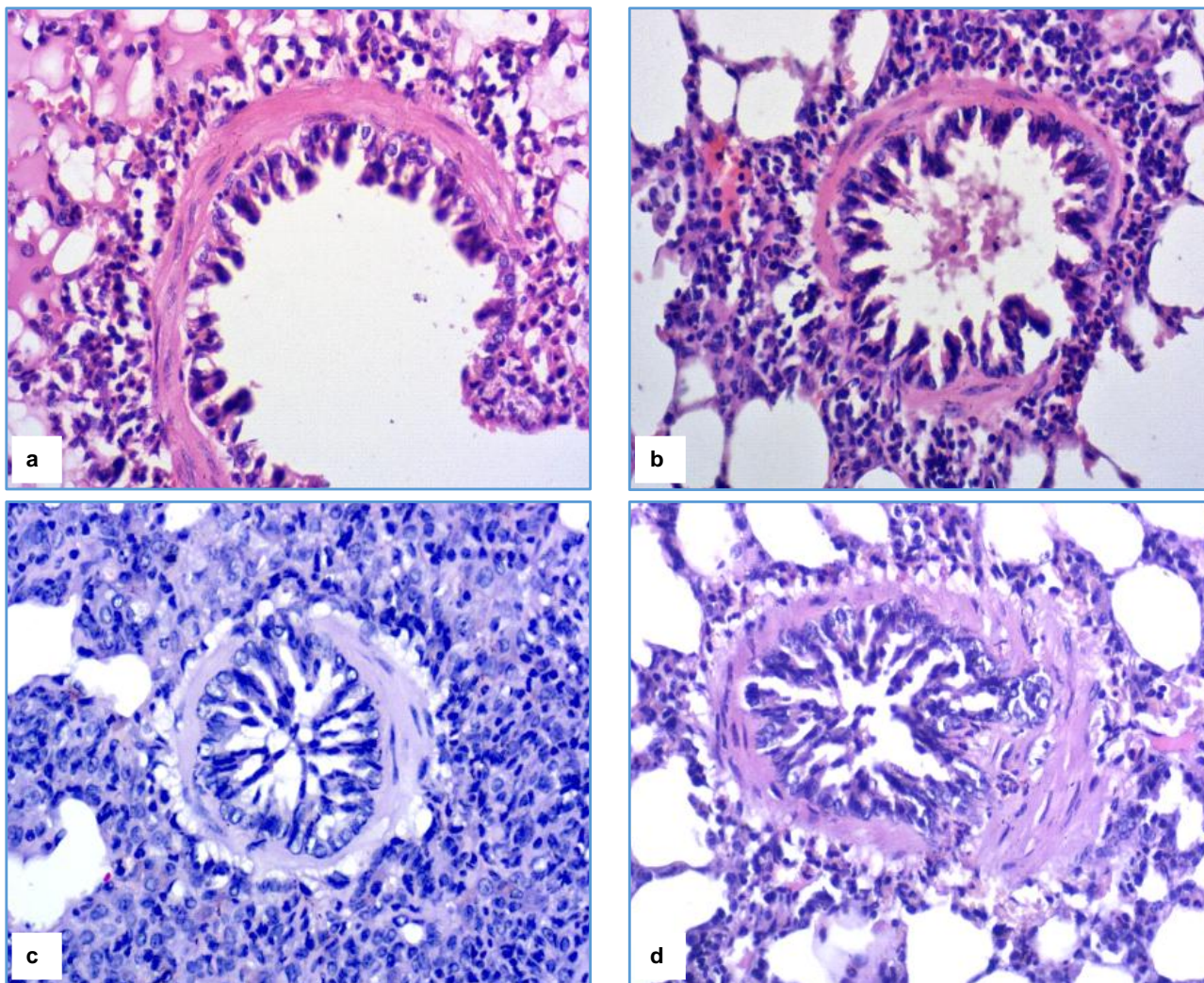
## Results

There are the thickening of the wall of bronchioles and terminal bronchioles of guinea pigs sensitized with ovalbumins, showed by histological analysis. There are also changes in the structure of alveoli, the increase in the number of peribronchial and perivascular lymphoid nodules, compared to the control group (Fig. 1). The degree of the manifestation of inflammatory changes increases with the decrease of the diameter of bronchi, reaching its maximum in the terminal bronchioles. We also observe the bronchiolar epithelium desquamation into the airways lumen, partial exposure of the basement membrane, eosinophilic peribronchial infiltration (Fig. 1b).

Noteworthy is the uneven thickening of the muscular layer of bronchioles due to muscular hyperplasia (Fig. 1a, 1b). The lumen of some bronchioles is narrowed (Fig. 1d) or even obstructed (Fig. 1c), which is a morphological confirmation of bronchospasm in animals after OVA-sensitization and challenge. There are disorganization of fibrous elements, accumulation of PAS + positive material and numerous of mast cells in the connective tissue stroma by the adventitial layer of bronchioles (see Fig. 1c).

Morphological changes in the structural elements of bronchioles and terminal bronchioles, appeared at the light-optical level, have their own regular morphometric display.

There was no statistically significant difference between the indices of the thickness of the mucosal layer of bronchioles in animals of the intact and control groups ( $p^{**} > 0.05$ ), which indicates that the experimental protocol does not itself affect the changes in the morphometric parameters of bronchioles. There is a tendency to the decrease in the thickness of the mucosal layer of bronchioles after OVA sensitization and challenge in the early period of development of experimental ovalbumin-induced allergic inflammation in lung. In animals of the first experimental group, the mucosal layer of bronchioles is  $40.46 \pm 0.44 \mu m$ , which is 1.3 times less than that in the control group. The statistically significant thinning of the mucosal layer of bronchioles is also manifested on the



**Fig. 1.** Microscopic changes in the wall of bronchioles and terminal bronchioles of guinea pigs after OVA-sensitization and challenge on the 23rd (1a, 1b), 36th (1c), 44th (1d) days after the start of the experiment. 1a - muscular hyperplasia of the bronchiole; 1b - the bronchiolar epithelium desquamation, lymphocyte - leukocyte infiltration of the wall of the bronchiole; 1c - obstruction of the lumen of the bronchiole; 1d - the uneven thickening of muscular layer and narrowing of the lumen of the bronchiole. Stain: 1a, 1b - G. and E.; 1c - alcian blue; 1d - PAS reaction. x400.

30th day of the observation in animals of the second experimental group -  $42.29 \pm 0.53 \mu\text{m}$ , which is 1.2 times less than the same indicator in the control group (Table 1).

There is a significant tendency towards the mucosal layer thinning of bronchioles in the late period of the development of allergic inflammation. A statistically significant decrease ( $p^{**} < 0.05$ ) in the mucosal layer thickness of bronchioles, compared to the control group, was observed in animals of the 3rd experimental group -  $43.38 \pm 0.55 \mu\text{m}$  (see Table 1). There is a tendency for the indicator of the mucosal layer thickness in bronchioles richers those in the control group on the 44th day of observation.

There are no statistically significant differences between the muscular layer thickness of bronchioles of animals in the intact and control groups ( $p^{**} > 0.05$ ). There is a tendency to the increase of the muscular layer thickness of

bronchioles in the early period of the development of experimental ovalbumin-induced allergic inflammation in lung. A statistically significant thickening of the muscular layer of bronchioles is manifested from the 30th day of the experiment in animals of the 2nd experimental group -  $25.59 \pm 0.23 \mu\text{m}$ , the increasing coefficient is 1.5 compared to the same indicator in the control group. In the late period of the development of allergic inflammation in guinea pigs' lung, a statistically significant muscular layer thickening by 1.7 times compared to the control appears in the third experimental group on the 36th day of observation -  $29.1 \pm 0.46 \mu\text{m}$  (see Table 1). The tendency to the muscular layer thickening in bronchioles persists to the 44th day of the experiment in the fourth experimental group and is  $24.73 \pm 0.12 \mu\text{m}$ , which is 1.5 times more than in the control group ( $p^{**} < 0.05$ ).

The adventitial layer thickness in bronchioles is

**Table 1.** Morphometric indicators of the wall of bronchioles of guinea pigs sensitized with ovalbumin.

Group	I	II	III
1	40.46±0.44*/**	20.57±0.29	26.12±0.18*/**
2	42.29±0.53*/**	25.59±0.23*/**	29.68±0.31*/**
3	43.38±0.55**	29.1±0.46*/**	30.01±0.32*/**
4	48.63±0.49	24.73±0.12*/**	25.93±0.18*/**
5	52.04±0.66	17.0±0.28	22.19±0.25
6	53.74±0.49	17.17±0.35	22.26±0.28

**Note:** \* - p<0.05 (Student's t-test); \*\* - p<0.05 (Whitney-Mann U-test) compared to the control group. M±m, (N=8); I - the mucosal layer thickness (µm); II - the muscular layer thickness (µm); III - the adventitial layer thickness (µm).

**Table 2.** Morphometric indicators of the wall of terminal bronchioles of guinea pigs sensitized with ovalbumin.

Group	I	II	III
1	21.23±0.2*/**	11.76±0.14	15.13±0.2
2	26.24±0.42	13.53±0.34**	14.02±0.09
3	32.17±0.39*/**	13.67±0.17*/**	18.76±0.1*/**
4	28.44±0.4	11.73±0.18	13.97±0.1
5	24.92±0.22	10.42±0.07	12.98±0.2
6	24.8±0.36	10.08±0.14	13.08±0.19

**Note:** \* - p<0.05 (Student's t-test); \*\* - p<0.05 (Whitney-Mann U-test) compared to the control group. M±m, (N=8); I - the mucosal layer thickness (µm); II - the muscular layer thickness (µm); III - the adventitial layer thickness (µm).

22.26±0.28 µm in the intact group. There is no statistically significant difference between these parameters in animals of the intact and control groups. There is a tendency to the increase of the adventitial layer thickness in bronchioles during all periods of observation after OVA sensitization and challenge (see Table 1). In animals of the 1st experimental group, the thickness of the adventitial layer in bronchioles is 26.12±0.18 µm, which is 1.2 times more than in the control group. A statistically significant thickening of the adventitial layer in bronchioles, compared to the control group, is also present in the animals of the 2nd experimental group - 29.68±0.31 µm, which is 1.3 times more than in the control group. The maximal thickening of the adventitial layer in bronchioles of guinea pigs reaches in the late period of the development of allergic inflammation on the 36th day of observation - 30.01±0.32 µm, the increasing coefficient is 1.4, compared to the same indicator in the control group.

There was no statistically significant difference between the mucosal layer thickness in terminal bronchioles in animals of the intact and control groups (p\*/\*\*>0.05). After OVA sensitization and challenge in the early period of the development of allergic inflammation in the lungs, there is a tendency to the decrease in the mucosal layer thickness in terminal bronchioles. In animals of the 1st experimental group the mucosal layer thickness in terminal bronchioles is 21.23±0.2 µm, which is 1.2 times less than that of the

control group (Table 2).

The gradual magnification in the thickness of the mucosal layer in terminal bronchioles is observed, starting from the 30th day of the experiment. A statistically significant thickening of the mucosal layer of terminal bronchioles appears on the 36th day of observation in animals of the 3rd experimental group - 32.17±0.39 µm, which is 1.3 times more than the same indicator in the control group.

There are no statistically significant differences between the parameters of the thickness of the muscular layer in terminal bronchioles in animals of the intact and control groups (p\*/\*\*>0.05). There is a tendency to the increase in the muscular layer thickness in terminal bronchioles in the early period of the development of experimental ovalbumin-induced allergic inflammation in lung of guinea pigs. A statistically significant thickening of the muscular layer in terminal bronchioles appears from the 30th day of the experiment in animals of the second experimental group - 13.53±0.34 µm, the increasing coefficient 1.3 compared to the same indicator in the control group. In the late period of the development of allergic inflammation in the guinea pig lungs, a statistically significant thickening of the muscular layer of terminal bronchioles, compared to the control group, appears in the 3rd experimental group on the 36th day of observation - 13.67±0.17 µm (see Table 2). On the 44th day of observation, there is a tendency for the thickness of the muscular layer in terminal bronchioles approaches those in the control group.

In the intact group, the adventitial layer thickness in terminal bronchioles is 13.08±0.19 µm. There is no statistically significant difference between these parameters in animals of the intact and control groups. There is a tendency to the increase in the adventitial layer thickness of terminal bronchioles during all periods of observation after OVA sensitization and challenge (see Table 2). The statistically significant thickening of the adventitial layer in terminal bronchioles, compared to the control group, in animals of the 3rd experimental group is 18.76±0.1 µm, which is 1.5 times more than in the control group.

## Discussion

Airways hyperresponsiveness develops as a result of bronchial allergic inflammation, caused by OVA sensitization and challenge [10]. The mechanism of inflammation is a cascade of processes involving neuroendocrine and immunocompetent cells, cytokines and mediators, the interaction of which forms the inflammatory process and the bronchial remodeling caused by it [14, 15].

Thus, this study determines the regularity of the dynamics of the structural elements of the wall of bronchioles and terminal bronchioles. The most significant and reactive changes in morphometric parameters of the wall of bronchioles were established on the 23rd and 30th days of observation - the thinning of the mucosal layer and on the 36th day - the thickening of the muscular layer and

the adventitial layer. In our opinion, the fact of the thinning of the mucosal layer in bronchioles is associated with alterative phenomenon in the early period of the development of airways allergic inflammation, namely the epithelial destruction and desquamation. Muscular hypertrophy in bronchioles is the morphological confirmation of the development of bronchial hyperreactivity as a result of OVA sensitization and challenge, which is also confirmed by the narrowing of the bronchial lumen, probably due to bronchospasm. The increase in the thickness of the adventitial layer of bronchioles is a confirmation of the development of the inflammatory process in the connective tissue, and, as a consequence, the development of stromal edema and disorganization of fibrous elements in the connective tissue of the bronchial wall. A similar trend of morphological changes in the bronchioles is observed in the studies of other scientists [1, 2, 3, 16]. The most significant changes in the terminal bronchioles, confirmed statistically, found on the 36th day of the experiment in the form of thickening of the mucosal and adventitial layers, is a consequence of muscular hypertrophy and edema of the connective tissue stroma in terminal bronchioles. It should also be noted the

multidirectional reaction of the mucosal layer in terminal bronchioles in the early and late periods of the development of allergic inflammation.

In the future, we aim to study ultramicroscopic changes of epithelial cells, basement membrane, connective tissue stroma of bronchioles and terminal bronchioles of guinea pigs with allergic inflammation.

### Conclusions

1. It has been established that OVA sensitization and challenge of experimental animals cause morphological and functional changes in the structural elements of the wall of bronchioles and terminal bronchioles, which have the staged, mainly multidirectional character and correspond to the main morphological manifestations of allergic inflammation.

2. Confirmation of the development of hyperreactivity of bronchioles and terminal bronchioles in experimental animals is muscular hypertrophy and narrowing of their lumen, which are most pronounced in the late period of development of allergic ovalbumin-induced inflammation (36th day of the experiment).

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tissues in rat asthma model. *Pharmaceutical Biology*, 55(1), 1561-1568. <https://doi.org/10.1080/13880209.2017.1310905>

**МОРФОМЕТРИЧНА ХАРАКТЕРИСТИКА ДИСТАЛЬНИХ ВІДДІЛІВ ДИХАЛЬНИХ ШЛЯХІВ МОРСЬКИХ СВИНОК, СЕНСИБІЛІЗОВАНИХ ОВАЛЬБУМІНОМ**

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Актуальною проблемою морфології та медицини в цілому, а також одним із недостатньо досліджених явищ у вивченні морфологічних змін дихальних шляхів при алергічному запаленні в хронобіологічному аспекті залишається реакція структурних компонентів малих бронхів та термінальних бронхіол. Мета роботи - дослідити морфометричні параметри дистальних відділів дихальних шляхів морських свинок, сенсibilізованих овальбуміном. За допомогою гістологічного, морфометричного та статистичного методів вивчили легені 48 самців морської свинки в умовах експериментального овальбумін-індукованого алергічного запалення, яке моделювали шляхом триразової підшкірної сенсibilізації та наступної 8-денної інтраназальної інгаляції овальбуміном. Для дослідження морфометричних показників структурних елементів малих бронхів і термінальних бронхіол визначали товщину їх слизової, м'язової, та адвентиційної оболонок. Встановлено реактивні зміни метричних показників стінки малих бронхів на 23 і 30 доби спостереження у вигляді потоншення слизової оболонки та на 36 добу у вигляді потовщення м'язової пластинки слизової та адвентиційної оболонок, що супроводжувалися зменшенням просвіту бронхів. Найбільш значимі зміни у термінальних бронхіолах, підтвержені статистично, виявлені на 36 добу експерименту у вигляді потовщення слизової та адвентиційної оболонок, що є наслідком гіпертрофії гладеньких міоцитів і набряку сполучнотканинної стромі термінальних бронхіол. Таким чином, сенсibilізація та алергізація овальбуміном експериментальних тварин викликають в структурних елементах стінки малих бронхів і термінальних бронхіол морфологічно-функціональні зміни, котрі мають стадійний, переважно різнонаправлений характер і відповідають основним морфологічним проявам алергічного запалення з максимальними змінами протягом пізнього періоду розвитку (36 доба експерименту).

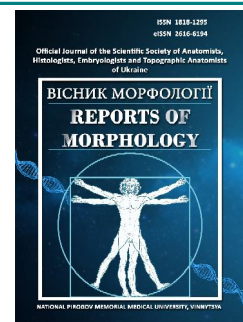
**Ключові слова:** дихальні шляхи, алергічне запалення, овальбумін, морська свинка.



## REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>



## Morphological condition of the pulp of intact and affected by caries third molars

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### ARTICLE INFO

Received: 3 September, 2020

Accepted: 12 October, 2020

UDC: 616. 314.18./8-002.4-091

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To date, there is a theory that increased resistance to caries is observed in the teeth, which for any reason underwent destructive changes in the pulp. That is why there is a need to study the impact of pulp vitality on the development of the carious process. The aim of the research was to study the microscopic structure of epoxy sections of intact and carious third molars. We studied 4 intact and 6 carious third molars. For this purpose, specimens were made taking into account the free penetration of the fixative solution into the pulp. To this end, immediately after the tooth was removed, we cut off its roots almost near the crown, preserving the integrity of the latter. The method relied on the impregnation of specimens with epoxy resin, according to the method of epoxy plastination of tooth specimens, developed at the Department of Human Anatomy of Ukrainian Medical Stomatological Academy. The epoxy blocks were cut with a disk into two halves until the hard tissues of the tooth crown were exposed together with the pulp. We found that the hard tissues (dentin and enamel coating) of intact third molars did not have any structural defects. However, their pulp chamber contained mainly an amorphous substance, devoid of any typical pulp tissue structures. That is, the pulp was in a state of complete devolution. Quite the opposite presentation was observed in specimens of carious teeth. We found that their pulp chamber contained quite noticeable tissue structures typical of the dental pulp. It is interesting that in the subodontoblastic layer, in front of the carious alteration of the enamel, there was compaction of the pulp, which may be due to infiltration of perivascular connective tissue by immunocompetent cells. It was found that on the border with carious destruction of enamel, there was a compacted spot of altered dentin, whose matrix was intensely pigmented in brown colour, due to the accumulation of melanin on the dentino-enamel junction. Its excessive formation is associated with the destruction of protein-carbohydrate complexes of organic matter in the deep layers of dentin. We found that the pulp compaction and the focus of carious alteration of the enamel are projectively connected by a radial cord of altered dentin, known in the literature as "dead tracts". Hence, there is reason to believe that the identified changes indicate a latent form of caries, with a pulpogenic mechanism of development. Thus, it can be argued that the teeth, which for any reason underwent degenerative changes in the pulp, are not prone to carious lesions, whereas in carious teeth, the pulp is active and involved in the pathogenesis of the carious process.

**Keywords:** caries, third molars, epoxy thin section, enamel, dentine, pulp.

### Introduction

Today, the existent theory of the exogenous nature of caries has not brought its correctness [6, 7, 8, 9, 10, 13, 18, 21, 23, 25, 28]. Thus, it is created a lot of contradictions, the main of them are the next facts that we find in the modern scientific literature [2, 5, 14, 21, 33]. They testify about the pulpogenic mechanism of the development of caries:

1. Discovery of subenamel caries and also retrograde (centered) its progress.

2. The hard tissues of the tooth which were left after carious necrosis of the pulp cannot be damaged by caries.

3. Cases of carious damage of the enamel-dentine area while the saving of integrity of the superficial enamel.

4. Caries has damaged the retained third molars.

More clear and principal new conception which opposite to the exogenic theory of caries, were proposed and substantiated theoretically Yu.P. Kostylenko and I.V. Boiko [21].



Authors noticed that organic structures of enamel, which are located in the border with dentine, have immunological properties and enamel is considered as "unbarrier" tissue which lets to consider the problem in the view of the theory about mechanisms of the damage of the immunological toleration. While, the source of the primaries sensitization can be both primary, natural and acquired, secondary autoantigens occur in the fissured areas of the teeth, under the influence of some physicochemical or infectious factors (theory of altered antigens) [15, 21]. In the works of many authors [5, 6, 9, 17, 26, 27, 29] were proved that damage of enamel occurs as a result of immune reaction in the tooth pulp. This conclusion was based that different affections of the dental system are related to any unfavorable condition of the organisms, are beginning of the pulp. Thus, degenerative changes in it during chronic rheumatic disease, endocrine disorders, infection disease, avitaminosis, toxicosis of pregnancy, etc. can be noticed when changes in the hard tissues had not been found yet.

That is enough for making a general conclusion: increasing of the stability to caries was observed in the teeth from various causes were took place destructive changes in the pulp while the teeth were isolated from the oral cavity and did not protect from carious damage of the hard tissues. Thus, we have reasons to consider the vital activity of the pulp as an indirect link in the development of carious process. But it should be taken into account, that this thesis has not proved yet, because the direct research in the literature is missing today. That is why we have tried to use opportunities which were received during the study of the individual diversity of third molars that may be got in the clinic during the extraction of the teeth in different clinical indication.

*The aim* of the research: the study of the microscopic structure of the epoxy sections of the intact and damaged by caries third molars.

### Material and methods

Connection of the study with planned scientific research works. This work is fragment of scientific research work "Age aspects of structural organization of immune system organs, glands of gastrointestinal tracts and urogenital system of human in norm and pathology", state registration № 0116U004192.

Four intact (crown without visible external damaged by caries) and six third molars with damage by caries, that were received from the Department of Oral and Maxillofacial Surgery with Plastic and Reconstructive Surgery of the Head and Neck of UMSA were studied.

In the view of methodical feature of our research, that includes the study of hard tissues of teeth with their pulps, we had to take measures for prevention of pulp` destroy in process of preparation of necessary prepares. For this, it was necessary to create ability for free penetration of fixative solution into the pulp. In this purpose, immediately after extraction and visual assessment of tooth, we cut its root

off on level of crown, care about saving of one's integrity. After this, it was washed for a short time by warm ( $t = 37^{\circ}\text{C}$ ) saline and plunged into bottle with 10% solution of neutral formalin.

After three-day fixation, received prepares washed from formalin away under running water, and they were dehydrated by spirit of incising concentration with the gradual transition to pure acetone according to our method [20, 22]. According to it, further procedure consisted in impregnation of epoxy resin. In this purpose, we used epoxy glue "Chimcontact-Epoxy". The final stage was moving prepares into appropriate for size ditches and filling them by freshly made epoxy resin.

After polymerization, received epoxy blocs were cut by disk for separation into two halves in necessary plane of intersection, which caused baring (on the end surfaces of the two halves) of hard tissues of tooth crown with pulp. It was found, that pulp of these teeth was impregnated by hardened epoxy resin.

The next stage in preparation of prepares for microscopic research was creation of polished epoxy sections that were carried out manually with sandpaper by alternatively changing it in decreasing order of the degree of abrasiveness. After this, these prepares can be studied by light microscope. However, excepting of Hunter-Schreger enamel strips, it was impossible to see any microscopic details. Besides, in this aspect tissue structure of the tooth on the section were unapproachable for reaction with according coloring because their organic components were hidden in the vast majority of minerals. Therefore, for get rid of them we subjected epoxy sections to superficial digestion (decalcification) in chelating agent - Trilon B. Necessity of fixation of hard tissues of tooth in epoxy resin becomes clear from it. It plays as a limiter for the directed action of the decalcifying solution in the section. It is possible only during the grinding of surface of hard tissues of tooth. After this procedure even uncolored sections permit to visualize their structure more clearly than those we used in some cases. However, full information we can receive only after coloring of epoxy section by 1% solution of methylene blue on 1% solution of borax.

Study and photo documentation of prepares were carried out by binocular magnifying glass MBS-9 equipped with camera at different magnifications.

Conducted research replies moral-ethical norms and basic principles of Council of Europe Convection on Human Rights and Biomedicine and relevant legislative documents of Ukraine. The Commission on Bioethics of VDNZU "Ukrainian Medical Stomatological Academy" (protocol №160 dated 14.12.2017 did not reveal any violations of moral and ethical norms during the research work.

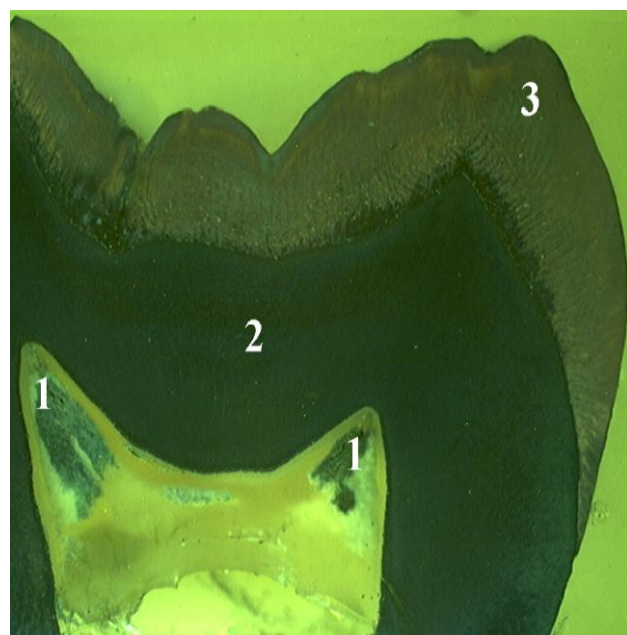
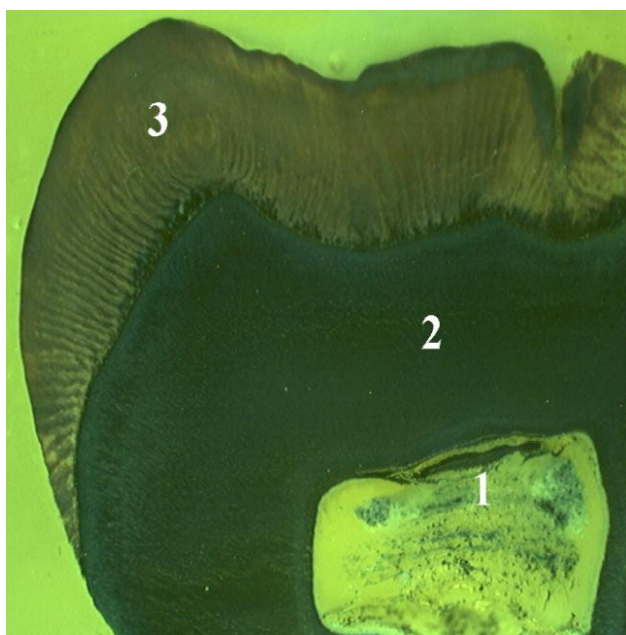
There was no special need for the application of parametric statistical analysis, because the changes in the microscopic structure of the third molars obtained by us did not differ significantly.

**Results**

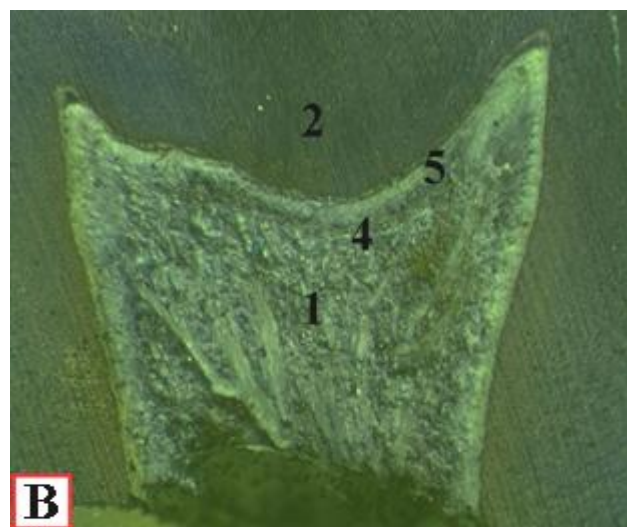
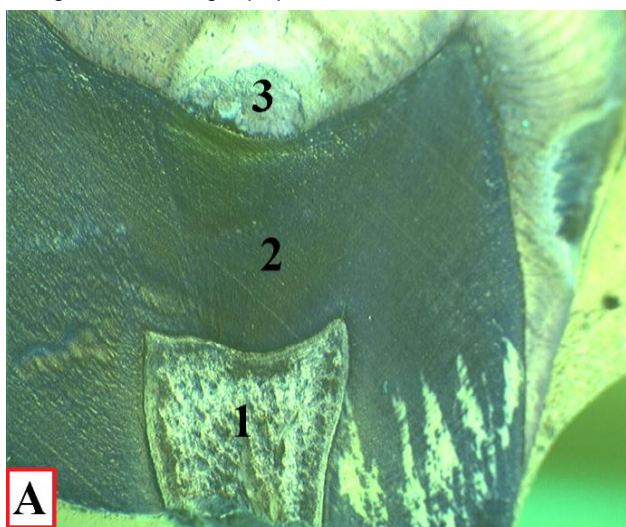
Figure 1 shows microphoto of crown department of two intact third molars on the same magnification. It attracts attention, that their enamel coating has no destructive defects. Due to surface decalcification and coloring by methylene blue, the Hunter-Schreger bands, which essentially nodal bundle0like chains of crystal fibers, became clearly visible. Dentine was without any visible alterative changes, in it the radial stripe was clearly visible due to typical orientation of dentinal tubules. Along with this, the content of the pulp chamber was mainly amorphous substance with no signs of the presence of such typical pulp tissues structures as: connective tissues elements,

blood microvessels, nerve fibers and odontoblasts. Only ones formations that were clearly manifested were pathological deposits in the form of denticles and various forms of petrification. Notable that most often they were in the area of the horns of the pulp chamber (Fig. 1).

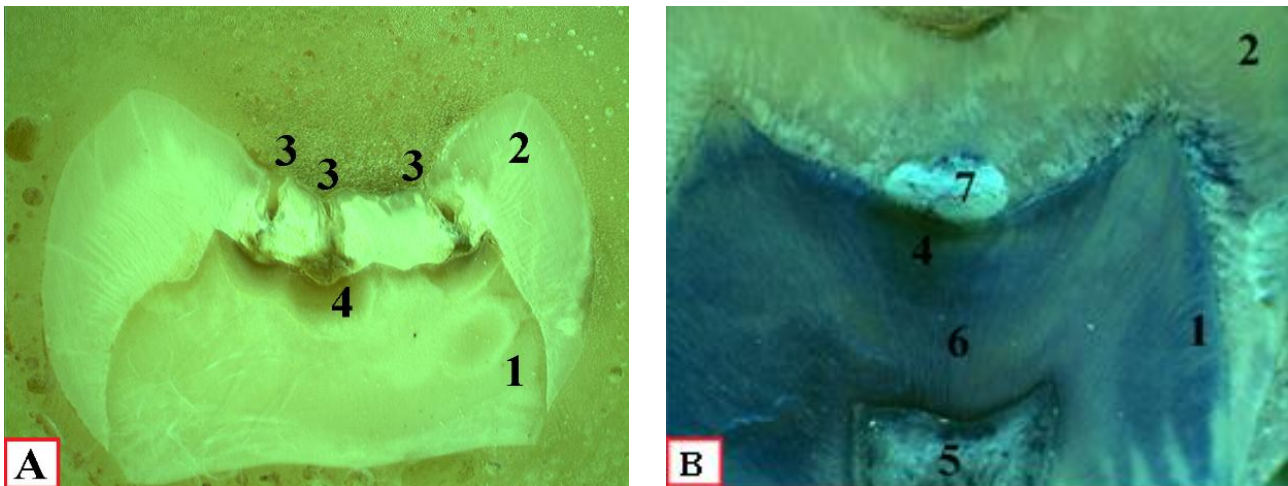
Quite the opposite picture is presented by prepares of carious third molars with stored pulp in them. Figure 2 convinces that pulp has peculiar to its tissue components. Presence of odontoblastic tissue component, collagen fibers and blood microvessels although they appear in somewhat coarser form indicates in this. It may be explained by inability to prevent completely of autolytic processes during preparation of prepares (Fig. 2).



**Fig. 1.** Crown departments of two undamaged by caries third molars. Epoxy sections. Coloring by methylene blue. Lens 4. 1 - petrificates in degenerative changed pulp; 2 - dentine; 3 - enamel.



**Fig. 2.** Crown department of damaged by caries third molar. Epoxy sections. Coloring by methylene blue. A - lens 4. Б - lens 7. 1 - pulp; 2 - radial alteration of dentine; 3 - the center of carious destruction of enamel; 4 - layer of odontoblasts; 5 - predentine.



**Fig. 3.** Crown departments of external damaged by caries third molars. Epoxy sections. A - uncolored prepare, lens 2. B - same prepare, colored by methylene blue. Lens 4. 1 - dentine, 2 - enamel, 3 - grooves, 4 - dark pigmented dentin spots in the area of carious alteration of the enamel, 5 - pulp, 6 - radial alteration of dentine, 7 - carious damage of basal enamel.

During more attentive study we paid attention, which on some prepares in odontoblastic layer just opposite the carious alteration of the enamel, there is a noticeable compaction of the pulp (Fig. 3).

According to location of pigmented spot clearly was manifested destruction of deep layers of enamel. It should be noted that focuses of its carious alteration were located not only in region of grooves, but quite often they were manifested on side of the masticatory tubercles and lateral surfaces of the crown.

### Discussion

Thus, in investigated by us intact teeth, pulp was manifested in condition of complete degeneration, reason of which unknown for us. But in this case we can refer to the literature, according to which development of pathological process in pulp should be considered from polyetiological positions [10, 12, 18, 21]. Herewith, the main link of its pathogenesis may be both external and internal factors, which cause loss of its caries-resistant properties, causing the pulpogenic mechanisms of caries development. This conception should be considered as important, because it force to pay attention on character of structural changes in tooth pulp in the beginning of the development of carious process, and it does not limit only with presence of external signs of damage of the enamel.

However, should be noticed that according to the thoughts of Yu.P. Kostylenko and I.V. Boiko [21] caries cannot damage enamel of teeth which for one reason or another it is non-available completely or it was prone to sclerosis, that is, no pulp - no caries. It also was confirmed by results of our research.

Pulp of carious third molars looks more full-fledged in comparison of their intact analogs. Thus, we want to say that in teeth which are prone to carious process, the pulp is in an active state. It means, it has all necessary reactogenic

properties to change the antigenic composition of the hard tissues of the tooth, due to the influence of pathogenic microorganisms which occur in the grooves. Besides, this side of question about etiopathogenesis of caries is not as monosemantic as it seems at the first glance.

Due to the fact, that in the subodontoblastic layer of pulp, in opposite to the carious alteration of the enamel, locates exchange blood vessels, therefore it can be assumed that this consolidation occurred as result of infiltration of perivascular connective tissue, immunocompetent cells. The certainty of this assumption is proved by the fact that consolidation of the pulp and center of carious alteration projectively connect between each other with radial cord of alterative dentine known in literature as "dead tracts" [1, 10, 11, 12, 14, 19, 21, 31, 32]. According to thoughts of these authors which are based on the positions of modern immunology, in deep areas of the grooves under the influence of pathogenic microflora on organic components of basal enamel and superficial dentine occur creation of high active intermediate antigens (autoantigens) [9, 17, 21, 29, 33]. They are getting through the dentinal tubules into the pulp, cause activation of the local immune system, effector elements of which will cause the alteration of dental channels with the creation of "dead tracts" and further destruction of appropriate areas of enamel. Its damage may produce the new wave of antigen stimulation of immune reactions which cause the creation of antibodies that can react with antigen both damaged and intact enamel in connection with identity of separate specific determinant groups. This process accompanied by increasing of present damage, which cause new antigen galling. Thus, it is caused chain autoimmune (autoaggressive) process, which determines the pathogenesis of caries (carious disease).

In connection with this, it is impossible to leave without attention one very revealing morphological fact, which has

not been taken into account by researchers in the study of the pathogenesis of caries before [3, 21]. It means, that on the border with carious destruction, the consolidated spot of alterative dentine is located, a matrix of which has intensive brown pigmentation, which is very clearly visualized on unpainted epoxy sections (Fig. 3). It has the greatest intensity in the basal layer, where its compactness is decreasing and disappearing in the matrix of "dead tracts" of the dentine. Clearly pigmented spot on the border between dentine and enamel gives an opportunity to identify the hidden form of caries even on the simple sections of teeth without any coloration.

Results of our research don not give reasons to speak about exogenous nature of this pigmentation. However, today this phenomenon can be explained by that during caries, it occurs as the result of accumulation on the dentine-enamel border of melanin which was created by the way of some metabolic transformations of tyrosine which is a product of phenylalanine - one of the amino acids in the protein substance of dentine [4, 16, 21, 24, 30]. Thus, there is reason to believe that this pigmentation of superficial dentine, which is located under the defect of enamel, is a result of storing of melanin which was created in the process of dystrophic dissociation of protein-carbohydrate complexes of the organic substance of the deep layers of dentine. Products of the metabolic transformations of phenylalanine achieve the superficial layer of dentine due to the centrifugal movement of the "dental fluid" along the dentinal tubules.

Clearly expressed morphological signs of carious damage of hard tissues, which are characterized by destructive changes look as radial "dead tracts" with their location from the pulp chamber to the damaged enamel, in its deep layers and creation of dark pigmented spots on the border with enamel indicate a latent form of caries.

In our view, the primary reason of the dystrophic changes in dentine with caries needs to find in the pulp. Thus, we want to say that teeth, which are prone to carious process,

have the pulp in an active condition.

Thus, the above facts clearly indicate that hard tissues of third molars, which for one reason or another have degenerative changes in the pulp, are not prone to carious damage. Whereas, the pulp of carious teeth is in active condition, thus it has all need reactogenic properties for the changing of the antigen composition of the hard tooth tissues, so it has an influence on the development of the carious process.

There are reasons, to think that in the further development of the carious process, the pulp will be prone to complete necrosis, on which the destructive process of the hard tooth tissues will have stopped [11, 12, 21]. Practical conclusion: for the stopping of the carious process should be used depulping of the damaged tooth follows from it. But, it does not mean that it will stop a carious disease. It may include other teeth.

Pathomorphological connection between reactive changes in the pulp and carious damage of the enamel is alteration of the dentine which looks as radial "dead tracts". Thus, we pay attention to one important event which is characterized for carious damage, which consist in creation on the border with destructive enamel, dentine pigmented into brown color intensively. We think that destructive disintegration of protein-carbohydrates complexes of dentine with carious alteration which produces melanin lays at the base of this event. In our view, the study of this process can have determinant meaning in the knowledge of the etiopathogenesis of carious disease in which we see the further prospect of our research.

## Conclusions

1. In teeth that are prone to carious process, the pulp is in an active state.
2. Hard tissues of the third molars with degeneratively altered pulp are not prone to carious lesions.
3. In order to stop the carious process in the tooth, it must be depulped.

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#### МОРФОЛОГІЧНИЙ СТАН ПУЛЬПИ ІНТАКТНИХ ТА УРАЖЕНИХ КАРІЄСОМ ТРЕТІХ МОЛЯРІВ

Костиленко Ю.П., Талаш Р.В., Білаш С.М., Бойко І.В., Буханченко О.П., Іваницька О.С.

На сьогоднішній день існує теорія про те, що підвищення стійкості до карієсу спостерігається у тих зубів, у яких з тих чи інших причин відбулися деструктивні зміни в пульпі. Саме тому виникла необхідність вивчення впливу життєдіяльності пульпи на розвиток каріозного процесу. Мета роботи - вивчити мікроскопічну будову епоксидних шліфів інтактних і уражених карієсом третіх молярів. Були вивчені 4 інтактних і 6 уражених карієсом третіх молярів. Для цього виготовляли препарати з урахуванням вільного проникнення в пульпу розчину фіксатора. З цієї метою відразу ж після видалення зуба ми вдавалися до відсікання його коренів майже біля коронки, зберігаючи цілісність останньої. Методика полягала в просочуванні препаратів епоксидною смолою, згідно з методом епоксидної пластинації препаратів зубів, розробленим на кафедрі анатомії людини Української медичної стоматологічної академії. Епоксидні блоки розсікали диском навіпіл до оголення твердих тканин коронки зуба разом із пульпою. Встановлено, що тверді тканини (дентин і емалево покриття) інтактних третіх молярів не мали будь-яких структурних вад. Разом із тим, вміст їх пульпової камери представляв собою, в основному, аморфну речовину, позбавлену будь-яких типових для пульпи тканинних структур. Тобто, пульпа виявлялась в стані повного переродження. Зовсім протилежну картину представляли собою препарати каріозних зубів. Виявлено, що в їх пульповій камері містились цілком помітні, типові для зубної пульпи, тканинні структури. Примітно, що в субодонтобластичному

*шарі, навпроти каріозної альтерації емалі, має місце ущільнення пульпи, яке може бути обумовлено інфільтрацією периваскулярної сполучної тканини імунокомпетентними клітинами. Встановлено, що на межі з каріозною деструкцією емалі знаходиться ущільнена пляма альтерованого дентину, матрикс якого інтенсивно пігментований в коричневий колір, за рахунок накопичення на дентино-емалевій межі меланіну. Надмірне його утворення асоціюється з деструкцією білково-вуглеводних комплексів органічної речовини глибоких шарів дентину. Нами встановлено, що ущільнення пульпи і вогнище каріозної альтерації емалі проєктивно зв'язані між собою променеподібним тяжем альтерованого дентину, відомого в літературі під назвою "мертвих трактів". Отже, є підстави вважати, що виявлені зміни свідчать про приховану форму карієсу, з пульпогенним механізмом розвитку. Таким чином, можна стверджувати, що зуби, у яких з тих чи інших причин сталися дегенеративні зміни пульпи, не схильні до каріозного ураження, тоді як у каріозних зубах пульпа знаходиться в активному стані і залучена до патогенезу каріозного процесу.*

**Ключові слова:** карієс, треті моляри, епоксидний шліф, емаль, дентин, пульпа.

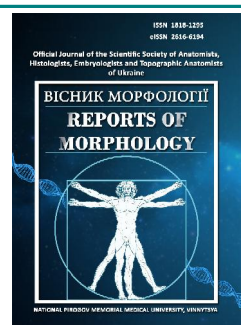
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# General craniometric characteristics of linear parameters of the middle cranial fossa of a mature person

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### ARTICLE INFO

Received: 7 September, 2020

Accepted: 15 October, 2020

UDC: 611.714.06-053.8:572.71

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*Given the rapid development of neurology, neurosurgery, otolaryngology and forensic medicine, there is a need for new, updated morphological data of internal base of the skull, in particular middle cranial fossa. This is due to the complex bone architecture of the middle cranial fossa and the location of important neurovascular structures in this area, which are important for surgeons not to damage during the operation. In this regard, it is necessary to detail the features of the structure, shape, position and size of the middle cranial fossa. The aim of the work is a detailed morphological and craniometric study of the linear parameters of the middle cranial fossa of a mature person depending on gender. The study was performed by studying 50 CT scans of the head and 50 bone preparations of the skulls of men and women of mature age. In our study, a detailed morphometry of longitudinal and latitudinal parameters at different levels of the middle cranial fossa, as well as determining its depth and area. Morphometry of linear parameters of the studied area of the skull showed the presence of a range of variability in length, width and depth depending on the sex of a mature person. The study showed an increase in the longitudinal size of the middle cranial fossa from the lateral to the medial; the transverse dimensions of the middle cranial fossa take on smaller values in its anterior parts and gradually increase to the posterior ones, which in our opinion is due to the characteristic shape of this part of the skull. The performed morphometry of longitudinal and latitudinal parameters, depth and area of the middle cranial fossa showed that these parameters are predominant in males in contrast to females, which is due to the slightly increased head size in this group of adult's people. Depth of the middle cranial fossa depth has the smallest range of variability depending on sex. It is established that right-handed asymmetry is more often observed in mature people of both sexes. Rarely, left-sided asymmetry is determined due to an increase in the length of the lateral sections in mature men. The data obtained make it possible to expand knowledge about the structure of the middle cranial fossa and can serve as a basis for further research.*

**Keywords:** craniometry, mature age, internal base of the skull, middle cranial fossa.

### Introduction

It is known that the middle cranial fossa (MCF) is one of the most complex parts of the inner base of the skull (IBS), which is limited in front by the posterior edge of the lesser wings of the sphenoid bone, behind - the back of the Sella turcica (ST) and petrous part of the temporal bone [6, 25].

In surgical practice, access to the MCF and the base of the skull is often performed in order to treat a large number of pathological processes [2, 4, 14, 15, 16, 18, 24]. Given the rapid development of neurology, neurosurgery, otolaryngology and forensic medicine, there is a need for new, updated morphological data of IBS, in particular MCF

[5, 10, 11, 17, 20, 22]. This is due to the complex bone architecture of the MCF and the location of important vascular and nervous structures in this area, which are extremely important for surgeons not to damage during surgery. In this regard, it is necessary to modern detail of the structure, shape, position and size of the MCF, which will reduce the number or avoid complications during and after surgery within this area of IBS [8, 9, 19, 21, 23, 26].

*The aim* of this work is a detailed morphological and craniometric study of linear parameters of the middle cranial fossa of a mature person depending on sex.

**Materials and methods**

The study was performed within the research work of the Department of Human Anatomy, Kharkiv National Medical University "Individual anatomical variability of craniotopographic features and spatial relationships of human head in the post-embryonic period of ontogenesis" № state registration 0118U000954.

The study was performed by examining 50 CT scans of the head and 50 bone preparations of the skulls of mature age men and women.

Craniometric examination of the MCF on craniotomograms of mature people was performed using the anatomical imaging system Anatomage table, with the installed program Launching Table 6.0 Application. Measurement of linear parameters of the MCF on bone preparations of the human skull was performed according to standard craniological methods, using a conventional set of measuring instruments. During the study, a detailed morphometry of longitudinal and transverse parameters of the MCF (Fig. 1), as well as determining its depth and area.

Variation statistics of the obtained data of complex measurements with calculation of arithmetic mean ( $\bar{x}$ ), standard deviation ( $\sigma$ ) and mean error (m) are carried out. Statistical analysis of the obtained quantitative data was performed using application packages "SPSS 7.0" and Excel from MS Office XP. The statistical significance of the obtained data was evaluated according to the Mann-Whitney test. The comparison results were considered plausible at  $p \leq 0.05$ .

**Results**

Given the rather complex form of MCF, it is important to study the basic craniometric linear parameters of MCF in mature men and women. Thus, we have established ranges of longitudinal and latitudinal parameters, depth and area dimensions in general and from both halves of the MCF depending on the sex.

It is determined that there is a certain range of longitudinal

parameters of the MCF in mature age (Table 1).

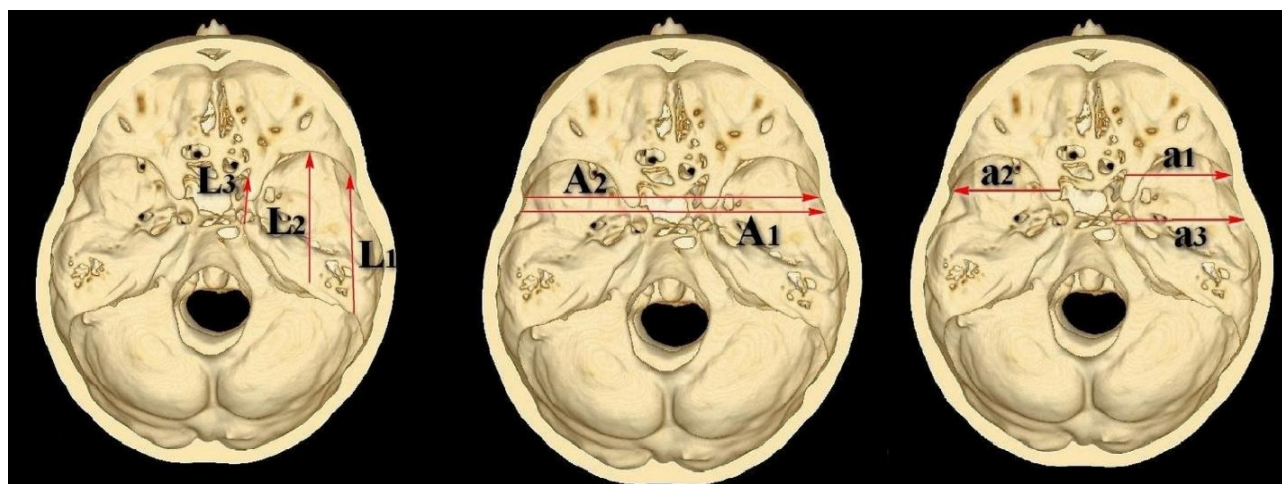
It is established that the length from the most protruding point of the lesser wings of the sphenoid bone to the opposite point of the stony part of the temporal bone ( $L_1$ ) in men of the left part of the MCF reaches  $\bar{x} \pm \sigma = 71.41 \pm 5.14$  mm and the right -  $\bar{x} \pm \sigma = 71.04 \pm 5.37$  mm. The length of the lateral sections of  $L_1$  in mature women from the left and right part of the studied area of IBS varies between  $\bar{x} \pm \sigma = 68.04 \pm 5.76$  mm and  $\bar{x} \pm \sigma = 68.59 \pm 5.25$  mm, respectively. It is known that this parameter is used in the calculation of the transverse-longitudinal index of the MCF.

In adult males and females, the total length ( $L_2$ ) of the left part of the left MCF is within  $\bar{x} \pm \sigma = 55.76 \pm 5.02$  mm and

**Table 1.** Variation and statistical indicators of longitudinal craniometric dimensions of the MCF in mature persons (mm).

Investigated signs	min	max	$\bar{x}$	$\sigma$	m	
Size $L_1$						
Left	Men	61.4	81.0	71.41	5.14	0.73
	Women	59.0	83.0	68.04*	5.76	0.81
Right	Men	61.7	82.0	71.04	5.37	0.77
	Women	59.7	81.0	68.59**	5.25	0.74
Size $L_2$						
Left	Men	44.8	65.0	55.76	5.02	0.72
	Women	42.9	64.0	53.34**	4.82	0.63
Right	Men	46.7	65.0	56.28	4.57	0.65
	Women	42.6	65.0	53.50*	4.48	0.63
Size $L_3$						
Left	Men	18.2	28.0	23.45	2.31	0.34
	Women	18.0	30.0	22.26**	2.64	0.39
Right	Men	17.9	28.0	23.77	2.51	0.37
	Women	17.7	33.0	22.33*	2.95	0.43

**Notes:** \* - a significant difference compared to men at  $p < 0.01$ ; \*\* - a significant difference compared to men at  $p < 0.05$ .



**Fig. 1.** Determination of MCF length distances in mature people on CT scans of the head:  $L_1$  - length of lateral departments,  $L_2$  - total length,  $L_3$  - length of the medial department,  $A_1$  - total width at the level of the sella turcica back,  $A_2$  - the total width at the level of the sella turcica tuber,  $a_1$  - front width,  $a_2$  - width at the level of the sella turcica tuber,  $a_3$  - rear width (mm).



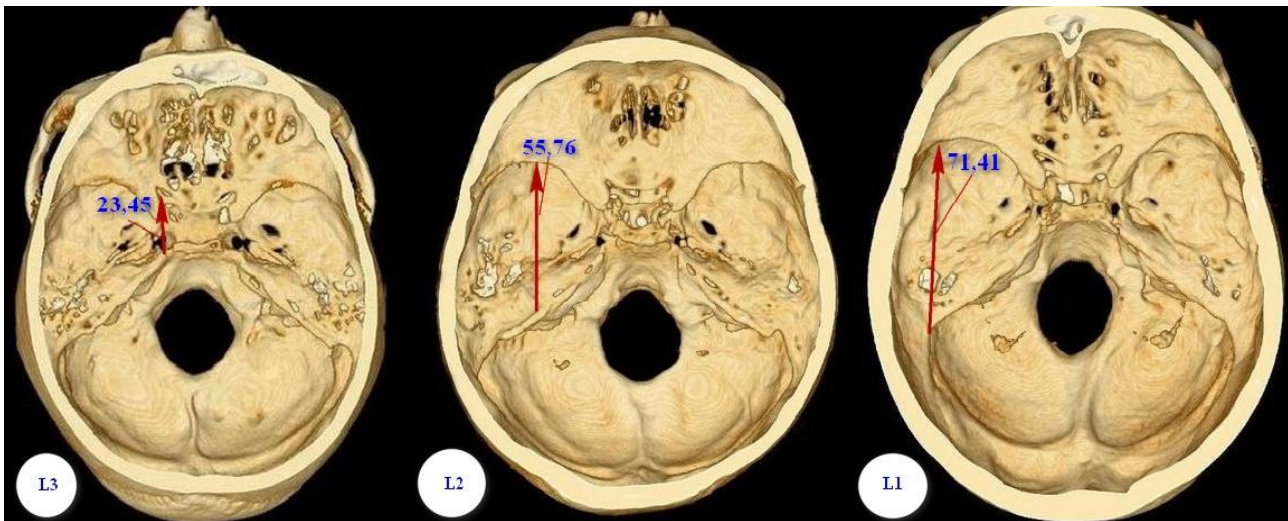


Fig. 2. The mean values of the longitudinal linear dimensions of the MCF on CT scans of the head in mature men (mm).

$\bar{x} \pm \sigma = 56.28 \pm 4.57$  mm, respectively. At the same time, in the right parts of the studied area of the skull of the same age period, the size of  $L_2$  decreases slightly:  $\bar{x} \pm \sigma = 53.34 \pm 4.82$  mm in men and  $\bar{x} \pm \sigma = 53.50 \pm 4.48$  mm in women.

According to the obtained data, the length of the medial parts of the left and right halves of the MCF in males reaches  $\bar{x} \pm \sigma = 23.45 \pm 2.31$  mm and  $\bar{x} \pm \sigma = 23.77 \pm 2.51$  mm, respectively. While in females this size is characterized by slightly smaller values, namely:  $\bar{x} \pm \sigma = 22.26 \pm 2.64$  mm on the left and  $\bar{x} \pm \sigma = 22.33 \pm 2.95$  mm on the right.

From the above data, an increase in the longitudinal dimensions of the MCF from the lateral to the medial (Fig. 2), which in our opinion is associated with the characteristic shape of this part of the skull.

The performed morphometry of the longitudinal parameters of the MCF showed that in women of mature age there is a decrease in all sizes in contrast to men (Fig. 3).

According to our data, it was found that left-sided asymmetry is observed in the study of the lateral length of the MCF in males. When determining the parameters of the length of both sexes of mature age, in addition to the above, we found the predominance of the size of the right half over the left. This suggests a right-sided asymmetry of the MCF of mature persons. These values are confirmed by statistical indicators.

In parallel, to detail the craniometric characteristics of the MCF, a number of transverse parameters at different levels in adults of both sexes were studied (Table 2).

The total width of the MCF through the center of the ST ( $A_1$ ) in male and female of mature age is  $\bar{x} \pm \sigma = 121.42 \pm 5.34$  mm and  $\bar{x} \pm \sigma = 116.69 \pm 5.48$  mm. In mature males, the transverse total size at the level of the ST tubercle is  $\bar{x} \pm \sigma = 119.55 \pm 7.12$  mm and in women -  $\bar{x} \pm \sigma = 114.41 \pm 7.06$  mm.

According to our data, the anterior width ( $a_1$ ) of the left and right halves of the MCF has a certain range of variability depending on sex: in males it is  $\bar{x} \pm \sigma = 40.97 \pm 3.33$  mm

and  $\bar{x} \pm \sigma = 41.71 \pm 3.21$  mm, respectively; in mature women it reaches  $\bar{x} \pm \sigma = 39.71 \pm 2.74$  mm from the left side and  $\bar{x} \pm \sigma = 40.29 \pm 3.47$  mm from the right part of the study area.

According to the obtained data, the transverse size  $a_2$  in mature males ranges from  $\bar{x} \pm \sigma = 47.81 \pm 3.59$  mm from the left and  $\bar{x} \pm \sigma = 48.94 \pm 3.15$  mm from the right parts of the MCF, while in women the same size takes slightly smaller values:  $\bar{x} \pm \sigma = 45.70 \pm 3.53$  mm (left) and  $\bar{x} \pm \sigma = 46.48 \pm 3.53$  mm (right).

It was found that the width of the posterior part of the MCF, as in the previous transverse parameters, tends to increase in values in males and decrease in females. Thus, from the left half of the MCF, the size from the back of the ST to the opposite point of the lateral wall of the skull reaches  $\bar{x} \pm \sigma = 52.13 \pm 4.02$  mm in men and  $\bar{x} \pm \sigma = 50.48 \pm 3.86$  mm

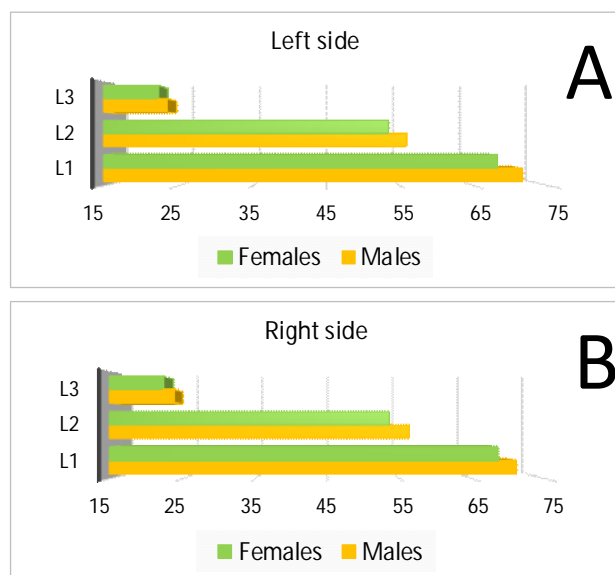


Fig. 3. The range of longitudinal MCF sizes of the skull of a mature human depending on sex (mm): A - left half of the MCF; B - right half of the MCF.

**Table 2.** Variation and statistical indicators of the transverse dimensions of the MCF in mature persons (mm).

Investigated signs	min	max	$\bar{x}$	$\sigma$	m	
Width A <sub>1</sub>						
Men	112.0	134.0	121.42	5.34	0.77	
Women	105.0	127.0	116.69*	5.48	0.77	
Width A <sub>2</sub>						
Men	106.1	133.9	119.55	7.12	1.42	
Women	102.4	124.2	114.41**	7.06	1.41	
Width a <sub>1</sub>						
Left	Men	34.0	49.3	40.97	3.33	0.49
	Women	34.7	46.0	39.71**	2.74	0.40
Right	Men	35.0	49.0	41.71	3.21	0.48
	Women	35.0	51.3	40.29**	3.47	0.50
Width a <sub>2</sub>						
Left	Men	42.0	54.8	47.81	3.59	0.72
	Women	39.2	52.2	45.70**	3.53	0.71
Right	Men	42.1	54.6	48.94	3.15	0.63
	Women	39.1	51.1	46.48**	3.53	0.71
Width a <sub>3</sub>						
Left	Men	44.0	59.0	52.13	4.02	0.57
	Women	42.0	58.0	50.48**	3.86	0.54
Right	Men	46.0	59.2	53.29	2.91	0.42
	Women	43.0	62.0	51.40*	3.68	0.52

**Notes:** \* - a significant difference compared to men at  $p < 0,01$ ; \*\* - a significant difference compared to men at  $p < 0,05$ .

in women; on the right,  $\bar{x} \pm \sigma = 53.29 \pm 2.91$  mm and  $\bar{x} \pm \sigma = 51.40 \pm 3.68$  mm, respectively. For modern craniology, the transverse size of a3 is of great importance in determining the transverse-longitudinal and depth-transverse indices of the studied area of the skull.

According to the obtained data, the transverse dimensions of the MCF take smaller values in its anterior

parts and gradually increase to the posterior ones (Fig. 4).

It should be noted that these parameters are predominant in males in contrast to females, which is due to the slightly increased head size in this group of adults (Fig. 5).

During the morphometric analysis of the transverse linear dimensions of individual sections of the MCF, it was determined that there is a slight difference between its left and right divisions. Thus, it was found that the anterior width, the width from the tubercle of the ST to the side wall of the skull and the posterior width of the right part of the specified area of IBS take greater values than the left in both sexes.

Depth parameters, which are used in the calculations of the depth-transverse index of the MCF, acquire a certain value (Table 3).

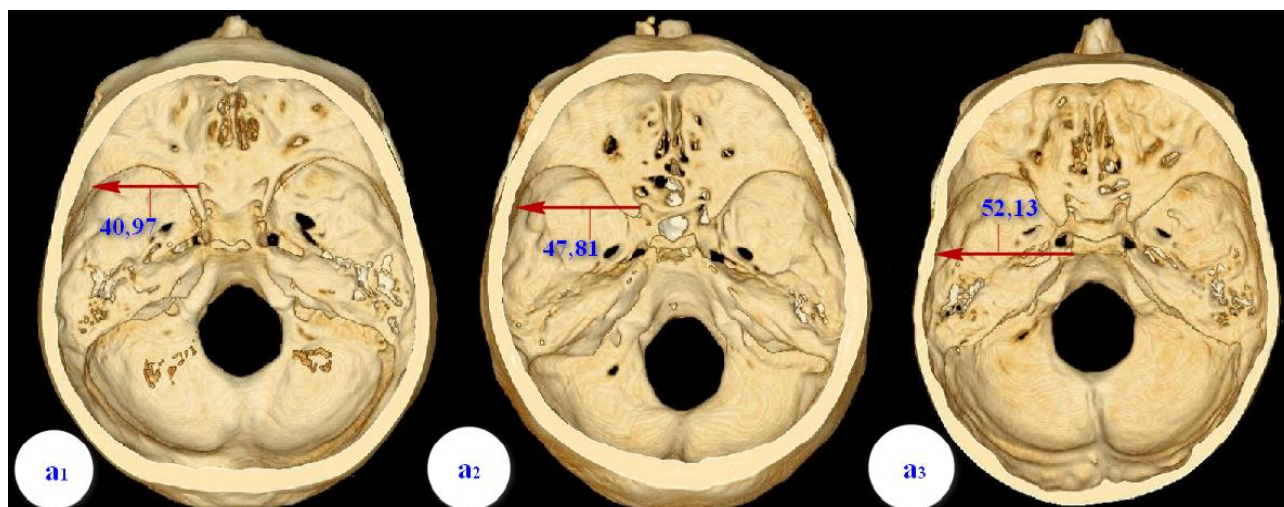
From the data in Table 3 it is clear that the depth in the male from the left half of the MCF does not exceed  $\bar{x} \pm \sigma = 21.23 \pm 3.44$  mm and from the right half reaches  $\bar{x} \pm \sigma = 21.69 \pm 3.01$  mm. Women of the same age period are characterized by slightly smaller values of  $\bar{x} \pm \sigma = 19.99 \pm 2.66$  mm (left) and  $\bar{x} \pm \sigma = 20.49 \pm 2.89$  mm (right).

According to the above, the size of the depth of the MCF has the smallest range of variability depending on sex (Fig. 6).

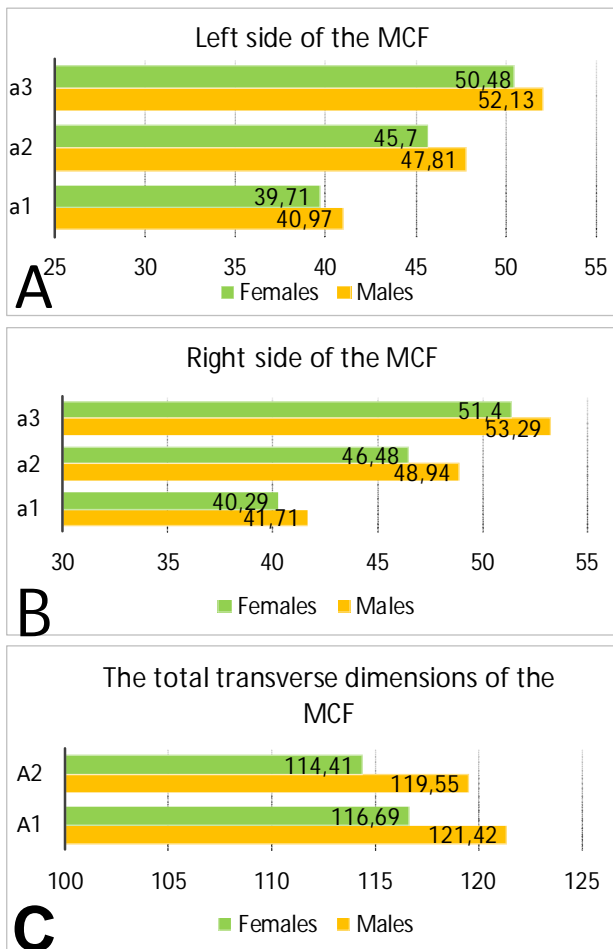
In parallel, there is a right-sided asymmetry of this parameter of the studied area of IBS in both sexes of mature age.

Additionally, measurements of the total area of the MCF and the area of both its departments were performed (Table 4).

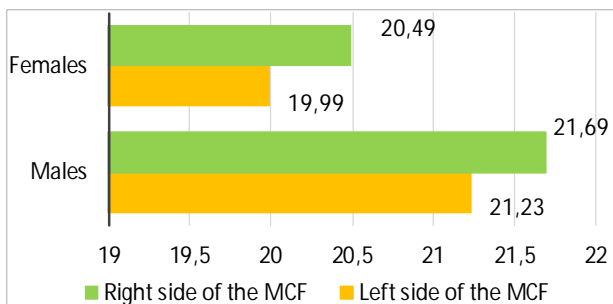
Thus, in adults the total area of the entire MCF in men is  $\bar{x} \pm \sigma = 57.40 \pm 6.13$  cm<sup>2</sup> and in women -  $\bar{x} \pm \sigma = 51.49 \pm 4.95$  cm<sup>2</sup>. In this case, the area of the left part of the left ventricle in males and females is equal to  $\bar{x} \pm \sigma = 27.53 \pm 3.31$  cm<sup>2</sup> and  $\bar{x} \pm \sigma = 24.49 \pm 2.58$  cm<sup>2</sup>, respectively. The right part of the studied area of the skull is characterized by slightly smaller values of this parameter  $\bar{x} \pm \sigma = 27.69 \pm$



**Fig. 4.** The average values of the transverse dimensions of the MCF on CT scans of the head in mature men (mm).



**Fig. 5.** Graphical display of transverse craniometric parameters of MCF depending on sex: A - transverse parameters from the left half of the MCF; B - transverse parameters from the right half of the MCF; C - general width parameters.



**Fig. 6.** Graphical display of depth on both sides of the MCF depending on sex.

2.89 cm<sup>2</sup> (men) and  $\bar{x} \pm \sigma = 25.06 \pm 2.75$  cm<sup>2</sup> (women).

According to our data, the total area and the area of the left and right parts of the MCF are characterized by a gradual increase from female to male of mature age, which is quite similar to the previously similar values of variability of linear parameters of the MCF depending on sex. Similarly to most of the determined linear parameters of the study of the inner base of the skull, when determining the area of both

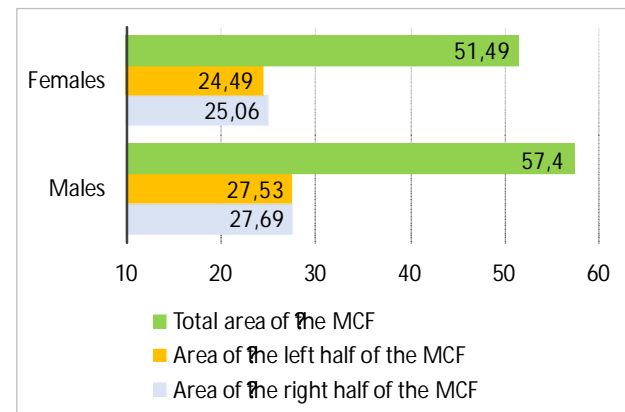
**Table 3.** Variation and statistical indicators of size and depth of MCF in mature persons (mm).

Investigated signs		min	max	$\bar{x}$	$\sigma$	m
Depth of the left half of the MCF	Men	14.0	27.5	21.23	3.44	0.49
	Women	13.0	27.5	19.99	2.66	0.37
Depth of the right half of the MCF	Men	16.0	27.3	21.69	3.01	0.43
	Women	12.0	25.0	20.49	2.89	0.41

**Table 4.** Statistical indicators of MCF area in men and women (cm<sup>2</sup>).

Investigated signs		min	max	$\bar{x}$	$\sigma$	m
The area of the left half of the MCF	Men	19.99	33.22	27.53	3.31	0.66
	Women	19.82	29.15	24.49*	2.58	0.52
The area of the right half of the MCF	Men	20.81	62.67	27.69	2.89	0.58
	Women	19.46	28.99	25.06*	2.75	0.55
The area of the entire MCF	Men	42.85	68.71	57.40	6.13	1.23
	Women	41.16	58.53	51.49*	4.95	0.99

**Notes:** \* - a significant difference compared to men at  $p < 0.01$ .



**Fig. 7.** The range of variability of the MCF plane as a whole and its individual parts depending on sex.

parts of the MCF, their asymmetry was revealed with the predominance of the values of this parameter in the right departments (Fig. 7).

### Discussion

A small number of works are devoted to the general characteristics of the structure, shape and size of the central part of the IBS, in which different methods of determining the length, width, depth and area of the MCF are used [1, 3, 7, 12, 13].

For the first time we conducted research not only on bone preparations of the skull of a mature person, but also on CT images of the head. Given the rather complex shape of the skull, which was studied, linear parameters were measured at different levels of the MCF and from both its departments in men and women of mature age.

The study of sexual differences in longitudinal, transverse parameters and depth dimensions showed that these dimensions in males predominate over females,

which coincides with the data of other authors who found that men have larger linear MCF dimensions than women [3, 12].

According to the results of our study, the presence of right-sided asymmetry of the studied parameters of the MCF of both sexes mature persons was determined. J. Lang (1982) in his study also noted the predominance of the size of the lateral parts of this area of the IBS on the right rather than on the left [13]. V.G. Koveshnikov (1959), on the contrary, noted that there is no significant difference between the sizes of the left and right halves of the MCF [12].

At the same time, we determined that the posterior parts of the MCF predominate over the anterior and lateral over the medial ones, which, in our opinion, is due to the characteristic shape of this part of the IBS.

The results of the study can further contribute to a better interpretation of craniotomograms, which will improve the diagnosis of pathological conditions within this area of the skull. Based on this study, it becomes possible to improve existing and develop new methods of surgical interventions.

The obtained data allow to expand the knowledge about the structure of MCF and can serve as a basis for further development.

### Conclusions

1. The performed morphometric analysis showed the presence of a wide range of longitudinal, transverse and depth parameters of the MCF with their characteristic predominance in males.

2. The study found that the morphometric parameters of the length of the study area gradually increase from its medial to lateral, as well as from anterior to posterior departments.

3. The maximum values have the length of the lateral sections, the width of each half at the level of the back of the ST.

4. At mature people of both sexes the right asymmetry is more often noted. Rarely, left-sided asymmetry is determined by increasing the length of the lateral part in mature men.

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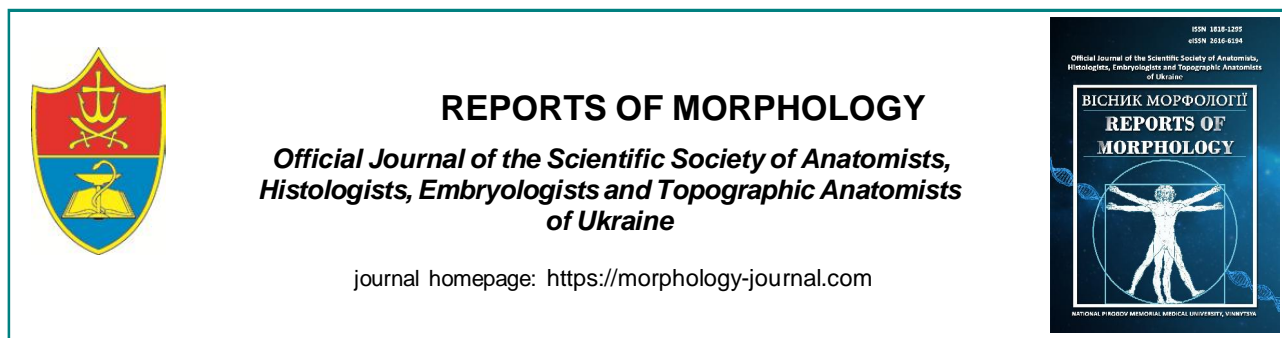
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#### ЗАГАЛЬНА КРАНІОМЕТРИЧНА ХАРАКТЕРИСТИКА ЛІНІЙНИХ ПАРАМЕТРІВ СЕРЕДНЬОЇ ЧЕРЕПНОЇ ЯМКИ ЛЮДИНИ ЗРІЛОГО ВІКУ

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З огляду на стрімкий розвиток неврології, нейрохірургії, отоларингології та судової медицини виникає потреба нових, уточнених морфологічних даних внутрішньої основи черепа, зокрема середньої черепної ямки (СЧЯ). Це обумовлено складною кістковою архітектурою СЧЯ та розташуванням у цій ділянці важливих судинно-нервових структур, які важливо хірургам під час операції не пошкодити. У зв'язку з цим, необхідна сучасна деталізація особливостей будови, форми, положення та розмірів СЧЯ. Метою роботи є детальне морфологічне та краніометричне дослідження лінійних параметрів СЧЯ людини зрілого віку в залежності від статі. Дослідження виконано за допомогою вивчення 50 КТ знімків голови та 50 кісткових препаратів черепів чоловіків та жінок зрілого віку. В нашому дослідженні проведена детальна морфометрія поздовжніх та поперечних параметрів на різних рівнях СЧЯ, а також визначення її глибини та площі. Морфометрія лінійних параметрів досліджуваної ділянки черепа показала наявність діапазону мінливості розмірів довжини, ширини та глибини в залежності від статі людини зрілого віку. Проведене дослідження показало збільшення поздовжніх розмірів СЧЯ від латеральних відділів до медіальних; поперечні розміри СЧЯ приймають менші значення у передніх її відділах та поступово збільшуються до задніх. За нашою думкою, це пов'язано з характерною формою цієї ділянки черепа. Проведена морфометрія поздовжніх та поперечних параметрів, глибини та площі СЧЯ показала, що зазначені параметри переважають у чоловіків порівняно з жінками, що пов'язано з дещо збільшеним розміром голови у цієї групи людей зрілого віку. Глибина СЧЯ має найменший діапазон мінливості в залежності від статі. Встановлено, що у зрілих людей обох статей частіше відмічається правобічна асиметрія. Досить рідко визначається лівобічна асиметрія за рахунок збільшення довжини латерального відділу у чоловіків зрілого віку. Отримані дані дозволяють розширити знання щодо будови СЧЯ та можуть слугувати основою до подальших досліджень.

**Ключові слова:** краніометрія, зрілий вік, внутрішня основа черепа, середня черепна ямка.



## REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists,  
Histologists, Embryologists and Topographic Anatomists  
of Ukraine

journal homepage: <https://morphology-journal.com>

### Peculiarities of girth body sizes in men with mild and severe psoriasis course

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#### ARTICLE INFO

Received: 21 September, 2020

Accepted: 26 October, 2020

UDC: 616.517.8

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Given the most frequent manifestation of psoriasis at a young working age and in some cases severe, continuously recurrent course, the presence of many treatments, none of which is a guarantee of complete recovery and no recurrence - now there is an urgent need to find prognostic signs therapy and prevention of relapses. In the absence of ideal biomarkers, the study of constitutional markers becomes crucial. The aim of the study was to examine the differences in girth body sizes between healthy and/or psoriatic men depending on the severity of the disease. Anthropometric examination according to V.V. Bunak was performed for 32 men of the first mature age patients with mild and 68 with severe psoriasis course. The PASI index was used to clinically assess the severity and area of psoriatic lesions. The control group, according to anthropometric parameters, consisted of 82 practically healthy men of the same age, selected from the database of the research center of National Pirogov Memorial Medical University, Vinnytsya. Statistical data processing was performed in the license package "Statistica 5.5" using non-parametric methods of evaluation of the obtained results. In patients with psoriasis of mild and severe course, compared with healthy, we found: greater values for - the girth of the shoulder in a tense state by 8.9% and 6.8%; shoulder girth in the unstressed state by 14.2% and 12.3%; forearm girth in the upper part by 8.0% and 7.1%; forearm girth in the lower part by 4.2% and 4.5%; hand girth by 5.1% and 5.8%; hip girth by 11.4% and 9.3%; hips circumference by 8.7% and 6.5%; crus girth in the upper part by 10.2% and 7.9%; crus girth in the lower part by 8.7% and 5.9%; neck girth by 6.9% and 7.8%; waist circumference by 17.1% and 18.2%; chest girth on inspiration by 7.8% and 7.2%; chest girth on exhalation by 10.6% and 10.3%; chest circumference at rest by 10.0% and 9.6%. Thus, there are pronounced differences in the girth sizes between healthy and patients with mild and severe psoriasis Ukrainian men of the first mature age. Between patients with varying degrees of severity of dermatosis, differences are established only for the girth of the crus in the lower part.

**Keywords:** psoriasis, girth body sizes, men.

#### Introduction

More than 200 years have passed since the first detailed description of psoriasis by Robert Willan, the "father" and founder of modern dermatovenereology, but humanity still has no effective treatment for this disease, which causes a deterioration in the quality of life of patients [6].

The prevalence of psoriasis is heterogeneous in different parts of the world and within the same country and different age groups. Thus, in northern India, psoriasis affects between 0.44 and 2.8% of the adult population. The peak of the disease occurs at the age of 6-10 years in boys and 11-15 years in girls [6].

Scientists estimate that psoriasis affects approximately 125 million people worldwide. Taiwan and the United States

are considered to be the countries with the low prevalence of psoriasis, where the prevalence of this disease among the adult population is 0% and 0.91%, respectively; examples of countries with a high prevalence of psoriasis are Italy and Norway, where the figure is about 2.1% and 8.5%, respectively [10, 18]. The prevalence of psoriasis among children in the United States is 40.8 per 100 thousand people/year, among adults - 78.9 per 100 thousand people/year, while in Italy the figure is 230 per 100 thousand people/year [18].

Given these facts, in the last decade there has been an increase in the number of works on the search for markers that would help determine the risk and severity of psoriasis, and in this aspect, special attention should be paid to the

relationship between these phenomena and such markers as body size of human [2, 4, 11, 26, 27].

Ferguson L. D. and co-authors [8] conducted an anthropometric survey of more than 500 thousand people aged 40-70 years, of which 5074 people suffered from psoriasis. In order to identify the relationship between certain anthropometric indicators and the chance of psoriasis, a statistical analysis of the data was performed. The adjusted odds ratios (OR) for psoriasis were according to the standard deviation (13.5 cm): the highest waist circumference was 1.20 (95% CI 1.16, 1.23) ( $p < 0.001$ ). This OR remained significant after further adjustment according to body mass index in patients with psoriasis (OR 1.19 (95% CI 1.12, 1.27)) ( $p < 0.001$ ).

An anthropometric study was performed on 135 children with psoriasis of varying severity and 73 healthy children (control group). Significantly higher prevalence of weight-to-height ratio (WHR) of 0.5 and more in children with psoriasis compared with the control group ( $p = 0.002$ ). OR with WHR more than 0.5 in children with psoriasis compared with the control group was 3.30 (95% CI 1.45-7.52). However, researchers have not found a significant difference in the rate of WHR in different forms of psoriasis. Only in children with moderate and severe forms of psoriasis, the average rate of WHR was higher than in children with mild psoriasis (0.48 vs. 0.46,  $p = 0.04$ ) [13]. Plasma adiponectin levels, insulin resistance, waist circumference, and psoriasis have been found to be related [14].

The authors' analysis of 1259 literature sources, 17 of which were selected for meta-analysis, revealed that there is a statistically significant relationship between the occurrence of psoriasis in childhood and WHR, if it is more than 0.5 [19].

A group of Norwegian scientists conducted two examinations of 34,996 people, without psoriasis in 1995-1997 and 2006-2008, in order to identify the risks of this disease. Between examinations, in 374 people developed psoriasis. Statistical analysis of the data revealed that there is a relationship between body mass index (BMI) and waist circumference and the risk of psoriasis [21]. One standard deviation, such as higher body mass index, waist circumference, and waist-to-hip ratio, gave a relative risk of 1.22 (95% confidence interval (CI) = 1.11-1.34), 1.26 (95% CI = 1.15-1.39), and 1.18 (95% CI = 1.07-1.31) respectively [22].

Similar results were obtained in another study. The examined children with psoriasis had higher BMI (?85th percentile; OR 4.4; 95% CI 1.2-15.6), waist circumference (>75th percentile; OR 7.4; 95% CI 2.0-27.7) and waist-to-height ratio (>0.490; OR 4.6; 95% CI 1.3-17.0) [24].

The aim of the study was to found the differences in girth body sizes between healthy and/or psoriatic men depending on the severity of the disease.

### Materials and methods

Men aged 22 to 35 years, patients with psoriasis ( $n = 100$ , including 32 with mild and 68 with severe course) at the Department of Skin and Venereal Diseases with a course of postgraduate education at National Pirogov Memorial

Medical University, Vinnytsya and the Military Medical Clinical Center of the Central region, an anthropometric examination was conducted according to V.V. Bunak [3].

The PASI (Psoriasis Area and Severity Index) was used to clinically assess the severity and area of psoriatic lesions [9]. According to the scoring system, the intensity of erythema, infiltration and peeling was determined: 0 points - no symptom, 1 - mild, 2 - moderate, 3 - severe, 4 - very severe. The following formula was used to calculate the PASI index for each body area: the anatomical area of the body (for the head - 0.1, the upper extremities - 0.2, the torso - 0.3, the lower extremities - 0.4) x (severity of erythema + severity of infiltration + severity of peeling) x area of skin lesions of the corresponding anatomical region of the body. Assessment of the severity of psoriasis was performed on the total PASI index (the sum of the obtained indices for each body area): mild -  $PASI < 10$ ; medium degree - PASI values from 10 to 20; severe -  $PASI > 20$  [1].

The control group consisted of anthropometric data of 82 practically healthy men of the same age group from the data bank of the research center of National Pirogov Memorial Medical University, Vinnytsya.

In this study, an assessment of the circumferential size of the body (cm) done. Statistical processing was performed in the license package "Statistica 5.5" using non-parametric evaluation methods. The reliability of the difference between the values between the independent quantitative values was determined using the Mann-Whitney U-test.

### Results

In healthy men, compared with patients, lower values were found for:

*shoulder girth in a tense state* ( $33.23 \pm 2.84$ ) compared

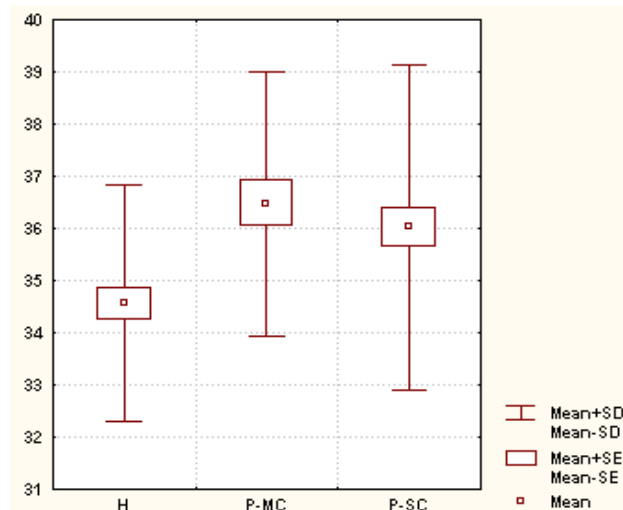
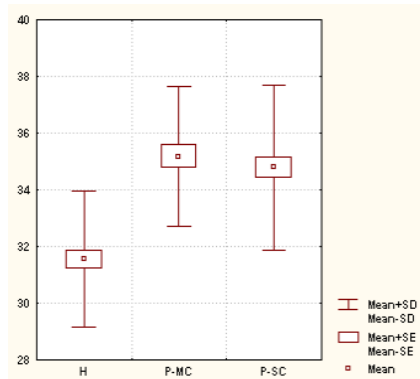
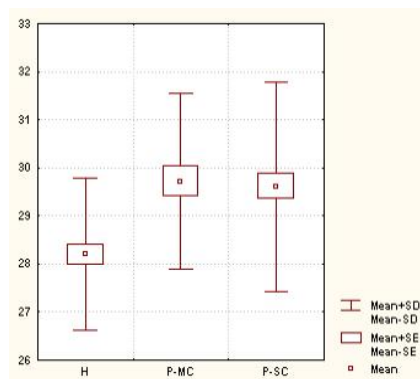


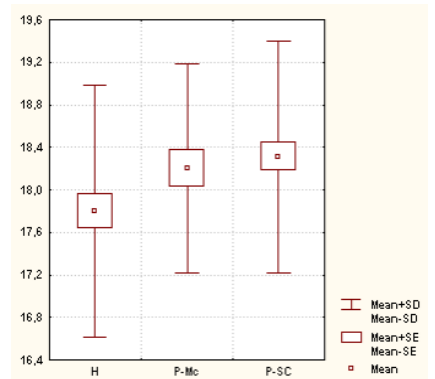
Fig. 1. Shoulder girth in stressed state in healthy and psoriatic men without taking into account somatotype (cm). In this and similar figures in this section: H - healthy men; P-MC - men with mild course of psoriasis; P-SC - men with severe course of psoriasis; Mean - average value; Mean ± SE - average value ± error average; Mean ± SD - average value ± standard deviation.



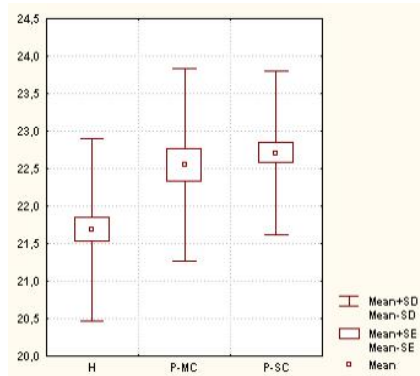
**Fig. 2.** Shoulder girth in non-stressed state in healthy and psoriatic men without taking into account somatotype (cm).



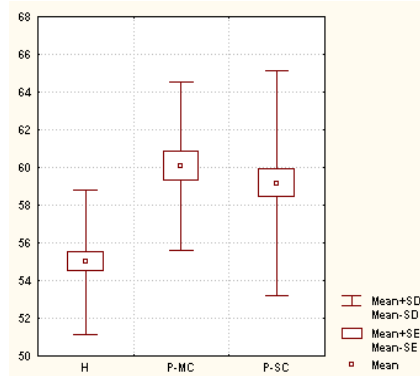
**Fig. 3.** Forearm girth in the upper part in healthy and psoriatic men without taking into account somatotype (cm).



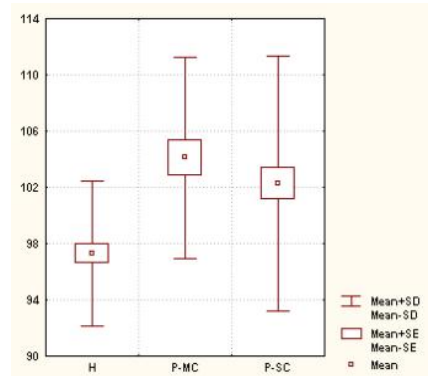
**Fig. 4.** Forearm girth in the lower part in healthy and psoriatic men without taking into account somatotype (cm).



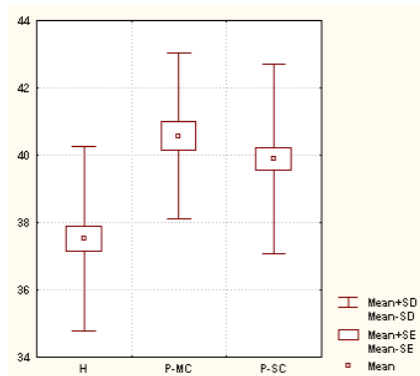
**Fig. 5.** Wrist girth in healthy and psoriatic men without taking into account somatotype (cm).



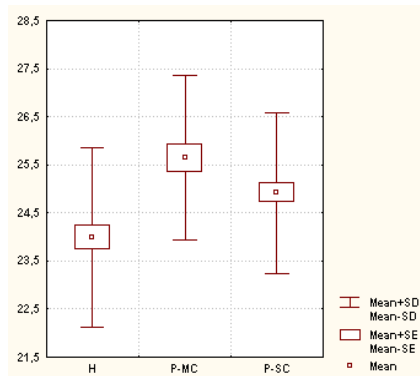
**Fig. 6.** Hip girth in healthy and psoriatic men without taking into account somatotype (cm).



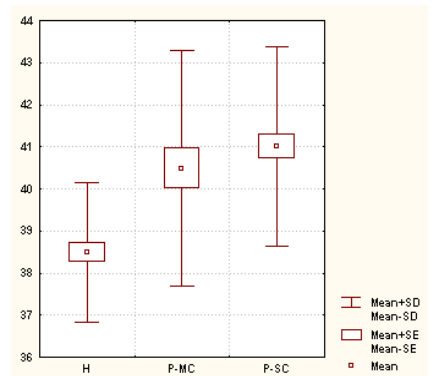
**Fig. 7.** Hips girth in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 8.** Crus circumference in the upper part in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 9.** Crus circumference in the lower part in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 10.** Neck girth in healthy and psoriatic men without taking into account somatotype (cm).

with men with mild psoriasis ( $36.47 \pm 2.54$ ;  $p < 0.001$ ) and severe psoriasis ( $35.67 \pm 3.34$ ;  $p < 0.001$ ) (Fig. 1);

*shoulder girth in a relaxed state* ( $30.17 \pm 2.94$ ) compared with men with psoriasis of mild ( $35.17 \pm 2.47$ ;  $p < 0.001$ ) and severe course ( $34.41 \pm 3.19$ ;  $p < 0.001$ ) (Fig. 2);

*forearm girth in the upper part* ( $27.33 \pm 2.01$ ) compared with men with mild psoriasis ( $29.72 \pm 1.84$ ;  $p < 0.001$ ) and severe psoriasis ( $29.41 \pm 2.26$ ;  $p < 0.001$ ) (Fig. 3);

*forearm girth in the lower part* ( $17.44 \pm 1.24$ ) compared

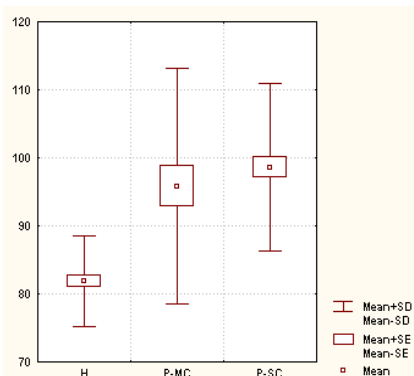
with men with mild psoriasis ( $18.20 \pm 0.98$ ;  $p < 0.01$ ) and severe psoriasis ( $18.27 \pm 1.10$ ;  $p < 0.001$ ) (Fig. 4);

*wrist circumference* ( $21.39 \pm 1.22$ ) compared with men with mild psoriasis ( $22.55 \pm 1.28$ ;  $p < 0.001$ ) and severe psoriasis ( $22.70 \pm 1.09$ ;  $p < 0.001$ ) (Fig. 5);

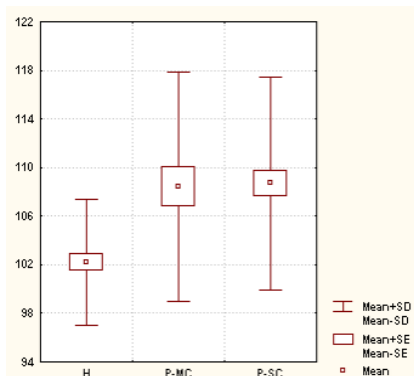
*hip circumference* ( $53.25 \pm 4.49$ ) compared with men with mild psoriasis ( $60.08 \pm 4.45$ ;  $p < 0.001$ ) and severe ( $58.70 \pm 6.09$ ;  $p < 0.001$ ) (Fig. 6);

*hips circumference* ( $95.04 \pm 6.39$ ) compared with men

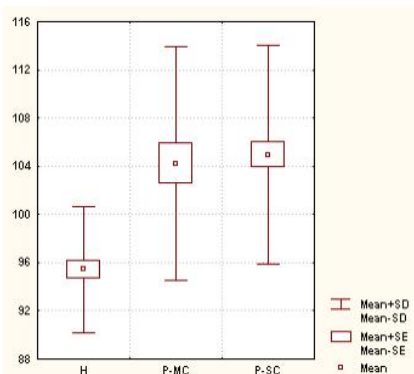




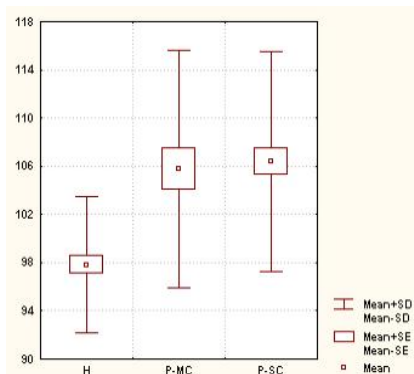
**Fig. 11.** Waist circumference in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 12.** Chest girth on inspiration and in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 13.** Chest girth on exhalation in healthy and psoriatic men without taking into account somatotype (cm).



**Fig. 14.** Chest girth at rest in healthy and psoriatic men without taking into account somatotype (cm).

with mild psoriasis ( $104.1 \pm 7.1$ ;  $p < 0.001$ ) and severe psoriasis ( $101.6 \pm 9.2$ ;  $p < 0.001$ ) (Fig. 7);

*crus girth in the upper part* ( $36.43 \pm 2.91$ ) compared with men with mild psoriasis ( $40.56 \pm 2.47$ ;  $p < 0.001$ ) and severe psoriasis ( $39.55 \pm 3.05$ ;  $p < 0.001$ ) (Fig. 8);

*crus girth in the lower part* ( $23.41 \pm 1.87$ ) compared with men with mild psoriasis ( $25.64 \pm 1.71$ ;  $p < 0.001$ ) and severe psoriasis ( $24.88 \pm 1.65$ ;  $p < 0.001$ ) (Fig. 9);

*neck circumference* ( $37.67 \pm 1.92$ ) compared with men with mild psoriasis ( $40.48 \pm 2.80$ ;  $p < 0.001$ ) and severe ( $40.85 \pm 2.38$ ;  $p < 0.001$ ) (Fig. 10);

*waist circumference* ( $79.48 \pm 7.32$ ) compared with men with mild psoriasis ( $95.83 \pm 17.27$ ;  $p < 0.001$ ) and severe psoriasis ( $97.18 \pm 13.31$ ;  $p < 0.001$ ) (Fig. 11);

*chest girth on inspiration* ( $100.0 \pm 6.0$ ) compared with men with psoriasis of mild ( $108.4 \pm 9.4$ ;  $p < 0.001$ ) and severe ( $107.8 \pm 9.4$ ;  $p < 0.001$ ) (Fig. 12);

*chest girth on exhalation* ( $93.18 \pm 6.39$ ) compared with men with mild psoriasis ( $104.2 \pm 9.7$ ;  $p < 0.001$ ) and severe psoriasis ( $103.9 \pm 9.8$ ;  $p < 0.001$ ) (Fig. 13);

*chest girth at rest* ( $95.20 \pm 6.57$ ) compared with men with mild psoriasis ( $105.8 \pm 9.9$ ;  $p < 0.001$ ) and severe psoriasis ( $105.3 \pm 9.8$ ;  $p < 0.001$ ) (Fig. 14).

In patients men with mild psoriasis compared with

patients with severe psoriasis found greater values only of the girth of the crus in lower part ( $25.64 \pm 1.71$ ;  $24.88 \pm 1.65$ ;  $p < 0.05$ ) (see Fig. 9).

## Discussion

Given the most frequent manifestation of psoriasis at a young working age and in some cases severe, continuously recurrent course, the presence of many treatments, none of which is a guarantee of complete recovery and no recurrence - now there is an urgent need to find prognostic signs therapy and prevention of relapses [16].

In the absence of ideal biomarkers, the study of constitutional markers becomes crucial. Currently, there is a growing interest in comparing the somatypological features of the organism in terms of normal and pathology. In this direction both anthropometric characteristics of a human body as a whole, and their separate features are investigated. The use of this area in the practical work of the doctor allows for a holistic and personalized approach in the process of diagnosis and treatment [17, 23].

In patients with psoriasis, a significant multiplicative interaction was found between BMI, waist circumference

and two SNPs in the IL12B (rs3212227) and IL23R (rs7530511) genes [15]. It has been established that increased body mass index and increased waist circumference are risk factors for psoriasis. The association has been documented consistently in both case studies and cohort studies. Larger waist circumference, hip circumference, and waist-hip ratio were associated with a higher risk of psoriasis [7].

Recent studies have shown a positive and strong, compared to body mass index, correlation between abdominal girth and disease severity [1]. Sandeep Kumar et al. [12] found a direct stepwise correlation between body mass index, waist and hip circumference, and the risk of psoriasis in 67,300 women over a 12-year period.

A team of researchers led by E. Toussiot [25] and A.R. Setty [20] determined that the waist and hip circumference was higher in patients with psoriasis compared with the control group. S.V. Dmitrenko [5] in men with widespread psoriasis on the background of a decrease in the girth of the extremities found multidirectional changes in the girth sizes of the body.

The data obtained by us confirm the information provided by the authors about the predominance of the girth size of the limbs and torso in patients studied in comparison with

the control group. The data were checked by the authors in the analysis of different age and ethnic groups.

In sick men in comparison with healthy we found higher values for - shoulder girth in a tense state by 8.9% and 6.8%; shoulder girth in the unstressed state by 14.2% and 12.3%; forearm girth in the upper part by 8.0% and 7.1%; forearm girth in the lower part by 4.2% and 4.5%; hand girth by 5.1% and 5.8%; hip circumference by 11.4% and 9.3%; hips circumference by 8.7% and 6.5%; crus girth in the upper part by 10.2% and 7.9%; crus girth in the lower part by 8.7% and 5.9%; neck girth by 6.9% and 7.8%; waist circumference by 17.1% and 18.2%; chest girth on inspiration by 7.8% and 7.2%; chest girth on exhalation by 10.6% and 10.3%; chest girth at rest by 10.0% and 9.6% compared with men with psoriasis of mild and severe course.

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### ОСОБЛИВОСТІ ОБХВАТНИХ РОЗМІРІВ ТІЛА У ЧОЛОВІКІВ ХВОРИХ НА ПСОРИАЗ ЛЕГКОГО ТА ТЯЖКОГО ПЕРЕБІГУ

Обадех Бассам Абдель-Рахман Аль-Каралех, Дмитренко С.В., Шаюк А.В., Гунас І.В., Прокопенко С.В.

З огляду на найбільш часту маніфестацію псоріазу в молодому працездатному віці та в ряді випадків важкий, безперервно рецидивуючий перебіг, наявність безлічі методів лікування, жоден з яких не є гарантією повного одужання і відсутності рецидивування, наразі виникла нагальна необхідність пошуку прогностичних ознак, необхідних для корекції терапії та профілактики рецидивів. За відсутності ідеальних біомаркерів, дослідження конституціональних маркерів стає вирішальним. Мета дослідження - вивчити відмінності обхватних розмірів тіла між здоровими та/або хворими на псоріаз чоловіками в залежності від тяжкості перебігу захворювання. 32 чоловікам першого зрілого віку, хворим із легким перебігом і 68 із тяжким перебігом псоріазу проведено антропометричне обстеження за Бунаком. Для клінічної оцінки важкості перебігу і площі псоріатичних уражень використали індекс PASI. Контрольну, за антропометричними параметрами, групу склали 82 практично здорових чоловіки аналогічного віку, відібрані з банку даних науково-дослідного центру Вінницького національного медичного університету ім. М. І. Пирогова. Статистичну обробку даних проведено в ліцензійному пакеті "Statistica 5.5" із використанням непараметричних методів оцінки отриманих результатів. У хворих на псоріаз легкого та тяжкого перебігу чоловіків, порівняно зі здоровими, нами встановлено: більші значення - обхвату плеча у напруженому стані на 8,9% і 6,8%; обхвату плеча у ненапруженому стані на 14,2% і 12,3%; обхвату передпліччя у верхній частині на 8,0% і 7,1%; обхвату передпліччя у нижній частині на 4,2% і 4,5%; обхвату кисті на 5,1% і 5,8%; обхвату стегна на 11,4% і 9,3%; обхвату стегон на 8,7% і 6,5%; обхвату гомілки у верхній частині на 10,2% і 7,9%; обхвату гомілки у нижній частині на 8,7% і 5,9%; обхвату шиї на 6,9% і 7,8%; обхвату талії на 17,1% і 18,2%; обхвату грудної клітки на вдиху на 7,8% і 7,2%; обхвату грудної клітки на видиху на 10,6% і 10,3%; обхвату грудної клітки у спокійному стані на 10,0% і 9,6%. Таким чином, виявлені виражені відмінності обхватних розмірів між здоровими і хворими на псоріаз легкого та тяжкого перебігу українськими чоловіками першого зрілого віку. Між хворими з різними ступенями важкості дерматозу відмінності встановлені лише для обхвату гомілки у нижній частині.

**Ключові слова:** псоріаз, обхватні розміри тіла, чоловіки.

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For publication, scientific articles are accepted only in English only with translation on Ukrainian, which contain the following necessary elements: UDC code; title of the article (in English and Ukrainian); surname, name and patronymic of the authors (in English and Ukrainian); the official name of the organization (institution) (in English and Ukrainian); city, country (in English and Ukrainian); structured annotations (in English and Ukrainian); keywords (in English and Ukrainian); introduction; purpose; materials and methods of research; research results; discussion; conclusions; bibliographic references.

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The introduction reflects the state of research and the relevance of the problem according to the world scientific literature (at least 15 references to English articles in international journals over the past 5 years). At the end of the entry, the purpose of the article is formulated (contains no more than 2-3 sentences, in which the problem or hypothesis is addressed, which is solved by the author).

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In the discussion, it is necessary to summarize and analyze the results, as possible, compare them with the data of other researchers. It is necessary to highlight the novelty and possible theoretical or practical significance of the results of the research. You should not repeat the information already listed in the "Introduction" section. At the end of the discussion, a separate paragraph should reflect the prospects for using the results obtained by the author.

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Signed for print 28.12.2020

Format 60x84/8. Printing offset. Order № 1820. Circulation 100.

Vinnitsia. Printing house "Tvory", Keleckaya St., 51a

PO Box 8825, 600-Richchya Str., 21, Vinnitsya, 21007

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