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## Section 1. Clinical medicine

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### The difficulties of differential diagnosis of soft tissue Ewing's sarcoma

**Abstract:** the article presents a review of literature and observation of soft tissue Ewing's sarcoma. This tumor is interesting because it is rare and poorly studied and difficulties of preoperative and morphological diagnosis.

**Keywords:** Ewing sarcoma, soft tissue, morphology, diagnosis, histogenesis

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### Трудности дифференциальной диагностики мягкотканной саркомы Юинга

**Аннотация:** В статье приведены обзор литературы и наблюдение мягкотканной саркомы Юинга. Данная опухоль интересна редкостью и малой изученностью, а также трудностями дооперационной и морфологической диагностики.

**Ключевые слова:** саркома Юинга, мягкие ткани, морфология, диагностика, гистогенез.

Саркома Юинга — злокачественная опухоль, поражающая костную ткань. Заболевание названо в честь американского патолога и онколога Джеймса Юинга, открывшего и описавшего опухоль в 1921 году. В последнее время стали известны случаи внутримышечной локализации злокачественных новообразований, не отличающихся по строе-

нию от типичной внутрикостной саркомы Юинга [1, 58]. Такая опухоль была названа мягкотканной (внекостной, внескелетной, экстракелетной, экстраоссальной) саркомой Юинга. В настоящее время её относят к опухолям семейства саркомы Юинга, к злокачественным опухолям неясной дифференцировки. Чаще локализуется в мягких

тканях нижних и верхних конечностей (стопа, голень, область коленного сустава, бедро, ягодичная область, предплечье) и туловища (паравертебральная область, грудная стенка, заднее средостение, забрюшинное пространство). Среди опухолей мягких тканей (возраст до 21 года включительно) экстраоссальная саркома Юинга составляет 10% случаев [2, 5]. Может возникать в любом возрасте, но чаще возникает у детей и молодых людей 10–20 лет. Встречается одинаково часто у лиц обоего пола [3, 366]. Среди европейцев эта опухоль встречается в несколько раз чаще, чем среди выходцев из стран Азии и Африки [4]. Клинически ведёт себя как костная саркома Юинга [3, 366].

Собственное наблюдение.

В сентябре 2014 года в одну из клиник ВМедА поступил больной девятнадцати лет по поводу наличия опухолевидного образования в нижней трети левого предплечья, щадит левую кисть. Со слов пациента образование нижней трети левого предплечья заметил в мае 2013 года, за медицинской помощью обратился в поликлинику Республики Казахстан, где ему был поставлен диагноз: фиброма нижней трети левого предпле-

чья, рекомендовано выполнение МРТ. В августе 2014 года выполнено МРТ левого предплечья: признаки мягкотканного образования нижней трети левого предплечья больших размеров (9,0 см на 5,5 см), локального поражения диафиза локтевой кости на границе средней и нижней трети, без периостальной реакции.

Обследование и диагностика.

Status localis: по локтевой поверхности нижней трети левого предплечья определяется образование овоидной формы, размерами 11,0 на 5,0 см, расположенное подкожно. Кожные покровы в проекции образования не изменены. При пальпации: безболезненное, тугоэластическое, трудно-сдвигаемое, не ограничивающее движения пальцев левой кисти и движений в левом лучезапястном суставе. Амплитуда активных и пассивных движений в суставах левой кисти без ограничений. Мышечная сила одинакова в обеих кистях. Периферических нейро-сосудистых нарушений не выявлено.

Обще-клиническое исследование крови:  $E_r 4,43 \times 10^{12}/L$ ;  $H_b 132$  г/л;  $Le 3,7 \times 10^9/L$ ;  $T_r 303 \times 10^9/L$ ; СОЭ 6 мм.

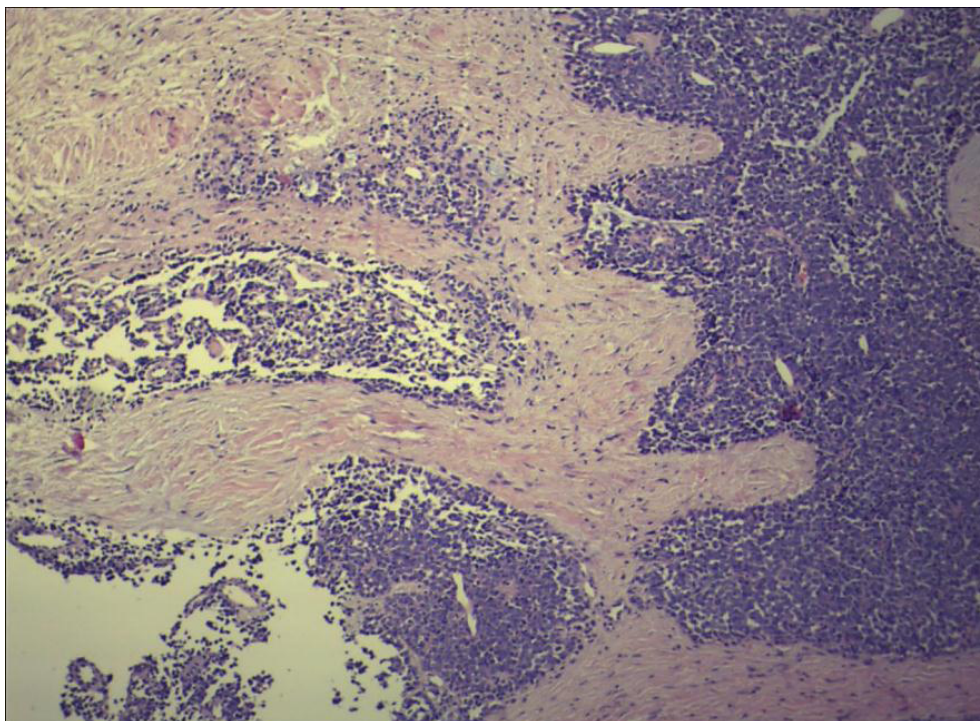


Рисунок 1. – Общий вид опухоли (окраска гематоксилин-эозином, увеличение  $\times 60$ )

Биохимическое исследование крови: АЛТ 8,3; АСТ 15,8; Общий билирубин 13,2; креатинин 90,3; глюкоза 4,28; белок 72,0; мочевина 4,8.

Электрокардиография: синусовая брадикардия; ЧСС 50 в 1 минуту; нормальная ЭОС.

УЗИ области левого лучезапястного сустава:



объёмное образование размерами 80×25×60 мм, образование имеет чёткую капсулу толщиной до 0,8 мм. Структура резко неоднородна: средней эхогенности с гипоэхогенными включениями. В образовании регистрируется кровоток, глубина от поверхности кожи около 5–6 мм. Заключение: объёмное образование в проекции левого лучезапястного сустава. Рентгенограммы левого предплечья в 2-х проекциях: костно-травматических изменений не выявлено.

Выполнена сцинтиграфия костей скелета: данных за изменения патологического характера

не получено. Данных за связь образования с костями левого предплечья не получено.

Под местной анестезией выполнена операция: открытая биопсия образования нижней трети левого предплечья. Тканевой материал взят на гистологическое исследование.

Гистологическое исследование: опухоль представлена солидными пластами однородных клеток с округлыми ядрами малого и среднего размера с диффузным хроматином, эозинофильным ядрышком и скудной цитоплазмой (рисунок 1, 2).

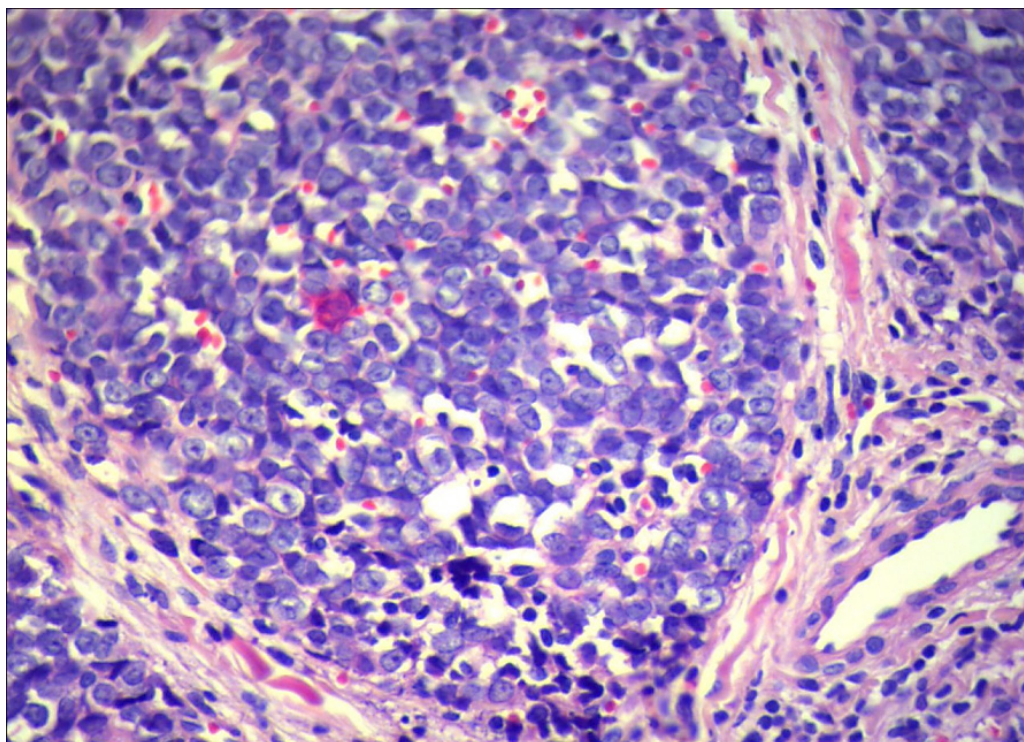


Рисунок 2. — Однородные клетки с округлыми ядрами малого и среднего размера с диффузным хроматином, эозинофильным ядрышком и скудной цитоплазмой (окраска гематоксилин-эозином, увеличение ×200)

Иммуногистохимическое исследование: МСК, виментин, CD99, Fli-1, СК18, СК19-положительные; ЕМА, десмин, SMA, MSA, CD34, CD31, СК — отрицательные.

CD99 — основной диагностический маркер для внекостной саркомы Юинга (позитивен в 90% случаев), Fli-1 — основной диагностический маркер для внекостной саркомы Юинга (позитивен в 85% случаев); виментин — используется в качестве маркера опухолей мягких тканей; МСК (мезенхимальные стволовые клетки) — согласно одним исследованиям стимулируют рост опухоли, согласно другим — угнетают опухоле-

вый рост; СК18 — используется для диагностики низкодифференцированных опухолей (аденокарцинома, нейроэндокринный рак); СК19 — определение концентрации данного маркера в крови обосновано при динамическом наблюдении пациентов перенесших хирургическую операцию по поводу удаления злокачественной опухоли; ЕМА — является отличительной чертой синовиальной саркомы от саркомы Юинга; десмин — чаще экспрессируется в рабдомиосаркоме, а также в лейомиосаркоме, ангиомиофибробластоме вульвы; CD34 — используется при определении низкодифференцированных ангиосарком, верете-

нообразных участков саркомы Капоши; CD31 — маркер ангиогенеза, определяет микрососудистую плотность опухоли, маркер эндотелия; CK — маркеры пролиферации опухоли у пациентов с эпителиально-клеточными карциномами; SMA — показатель аутоиммунного и хронических активных гепатитов; антитела к гладкой мускулатуре; MSA — маркер идиопатических миозитов.

Морфологическая картина и иммунофенотип опухолевых клеток соответствует внекостной саркоме Юинга. Данное наблюдение представляет интерес в связи с редкостью и малой изученностью мягкотканной саркомы Юинга, а также трудностями дооперационной и морфологической диагностики [7, 88].

Гистогенез данной опухоли, также как и саркомы Юинга кости, неясен. Ультраструктурные данные позволяют предполагать эндотелиальную природу или возникновение из примитивных мезенхимальных клеток [3, 366]. При световой микроскопии в саркоме Юинга иногда наблюдаются так называемые хомер-райтовские розетки (псевдорозетки) или подобные им структуры, которые обычно встречаются в нейрогенных опухолях. Электронно-микроскопически установлено наличие в клетках данной саркомы глыбок гликогена, нейроспецифической эналазы, изолированных дендритических отростков и синапсоподобных утолщений на них, обнаружены также промежуточные нейрофиламенты, нейротрубочки и нейросекреторные гранулы, что с большой долей вероятности позволяет относить эту опухоль к разряду новообразований нейрогенной природы [5, 5]. Известно, что внескелетная саркома Юинга тесно связана с периферическими примитивными нейроэктодермальными опухолями, которые, в отличие от мягкотканной саркомы Юинга, характеризуются наличием отчетливой нейроэктодермальной дифференцировки. Практически 95% клеток примитивной нейроэктодермальной опухоли и внекостной саркомы Юинга имеют характерные изменения хромосом в виде транслокаций [t (11; 22) (q24; q12)] между EWS-геном на хромосоме 22 и FLI-1-геном на хромосоме 11. Результат транслокации — общий FLI1/EWS ген. [6, 235]. Такие же хромосомные

нарушения обнаружены при опухоли Аскина. Хромосомные транслокации активируют транскрипцию, приводящую к синтезу химерной РНК и нарушению регулирования роста и дифференцировки клеток. Менее часто регистрируемыми цитогенетическими аномалиями у больных экстраклеточной саркомой Юинга и примитивной нейроэктодермальной опухолью являются трисомия хромосом 8 и 12, транслокация между хромосомами 1 и 16, а также делеция короткого плеча хромосомы 1. Частота и клиническая значимость этих повреждений генетического аппарата неизвестна. Результаты ряда молекулярно-генетических исследований позволяют предположить, что одним из ключевых моментов онкогенеза данных опухолей является повреждение гена, кодирующего синтез рецептора трансформирующего фактора роста-II типа (TGF-), который относится к белкам-супрессорам [6, 235]. Несмотря на различия в нейроэктодермальной дифференцировке, клетки экстраклеточной саркомы Юинга и примитивной нейроэктодермальной опухоли одинаково часто экспрессируют на своих мембранах продукт онкогена MIC-2, известный как гликопротеин p30/32 или CD99, который имеет диагностическое значение при дифференциальной диагностике внескелетной саркомы Юинга от низкодифференцированной нейробластомы; в последней, несмотря на морфологическое сходство с мягкотканной саркомой Юинга, реакция с CD99 не наблюдается [6, 235]. CD-экспрессия также обнаружена в опухолях из малых клеток голубого невуса, при острой лимфобластной Т-клеточной лимфоме, рабдомиосаркоме и других опухолях. Клетки низкодифференцированной синовиальной саркомы тоже могут слабо экспрессировать CD99, их отличительной чертой является наличие таких маркеров, как цитокератин и эпителиальный мембранный антиген. Кроме того, внекостную саркому Юинга необходимо отличать от нейроэпителиомы, низкодифференцированного рака, особенно от метастаза из бронха. Мягкотканная саркома Юинга характеризуется склонностью к рецидивам и метастазам, прежде всего в лёгкие и кости, нередко на ранних стадиях заболевания [3, 366].

Трудности диагностики экстраоссальной саркомы Юинга возникают из-за её сходства в строении с другими злокачественными новообразованиями мягких тканей (нейробластома, синовиальная саркома, злокачественная лимфома, рабдиосаркома, ангиоперицитомы, низкодифференцированный рак), которые, несмотря

на различный гистогенез, не имеют специфических морфологических признаков. Поэтому для постановки окончательного диагноза патоморфологическое исследование данной опухоли необходимо дополнять иммуногистохимическим и молекулярно-биологическим методами исследования.

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## Prospects for use of resorbable membrane made of polylactic acid in the treatment of mandibular fractures

**Abstract:** The method of intraoral polymer osteosynthesis with the use of resorbable polylactic acid membranes for fixation of bone fragments in treatment of the simple or complicated mandibular fractures is offered. Clinical and roentgenological researches confirmed its efficiency owing to atraumatic and reliable fixation during all period of treatment, that is promote the anatomic and physiologic rehabilitation in the optimum terms.

**Keywords:** fractures of the mandible, complication, polylactic acid membranes, polymer osteosynthesis.

The reduction in the frequency of complications in the treatment of mandibular fractures is the urgent task of modern maxillofacial surgery. It is necessary

to select imperfection of surgical treatment as reason causes development of complications. The most popular method of extraoral osteosynthesis has a



number of disadvantages, such as an undue increase of operation injury, a risk of trauma of tooth roots and *n. alveolaris inferior*, an unstable fixation [1, 32]. In accordance with majority opinion of authors, exactly imperfection of reposition and insufficiency of fixation stability are the basic local factors of origin of the secondary fragments displacements, a low consolidation of fractures, a formation of pseudoarthrosis, an adjunction of the secondary infection and development of posttraumatic osteomyelitis [2, 30–33].

It was set in numerous researches of biomechanics of lower jaw that after a break in the area of body or corner its anatomical features stipulate the area of functional tension and origin of fragments divergence at the level of alveolar bone, while at the lower border of mandible the compressive strain is dominate and bone fragments in this area do not branch off, but compress [3, 38–41]. In subsequent experimentally and clinical researches was evidently shown, that course of reparative osteogenesis is more optimized and has a close resemblance to the «primary type» if the fixators are located in the area of alveolar bone of lower jaw, than by the extraoral access of osteosynthesis with fixation in the area of the lower border of mandible [4, 124–125].

To date the advantages of the use of intraoral access of operation osteosynthesis with superior border plate at the patients with the mandibular fractures are obvious and out of question. Comparative analysis of results of mandibular osteosynthesis by miniplates shows that reduction of traumatic injury by intraoral access is provided the decline of the frequency of different complications development in 2 times, than by extraoral access [5, 25–26].

Traditionally intraoral osteosynthesis is realized by titanic miniplates, rarer by different wire. However, the question of the use of the metallic fixators remains disputable. The development of inflammatory processes as a result of response to a metal, corrosive destruction of fixing construction in consequence of the increase of electrochemical potentials are associated with this method. From positions of biomechanics, bone miniplates can not retain fragments in the correct position in horizontal,

vertical and sagittal planes at once. Ineffectiveness in the cases of comminuted fracture, possibility of reoperating for fixator removal is possible to subsume by the known lacks of miniplates [6, 603–607].

That's why the interest to the method of polymer osteosynthesis, which is based on the use of I-, T-, X-, Y- similar polyethylene or polylactic acid resorbable miniplates (1,5 mm thick) does not weaken the last years [7, 181–209; 8, 89–96]. Material has good biocompatibility, does not require the repeated operations for the remove of fixators. However, the development of method of polymer osteosynthesis passes while a way of research of optimum biomaterial and, in less degree, takes into account biomechanics of lower jaw at a trauma, especially in the cases of difficult comminuted mandibular fractures, at presence of bone defects.

Thus, our interest was attracted by the method of the directed regeneration of bone tissues, which deserved a wide popularity in dental surgical practice and provide for use of different barrier membranes. The resorbable membranes made of polylactic acid (Polylactic Acid Barrier) widely utilize in a clinic at the difficult bone defects of jaws. Such membranes possess sufficient inflexibility and, in also time, enables to keep under itself volume space, which correspond to topography and size of remodeling tissues and create a reliable barrier to migration of epithelium in the area of regeneration. They establish a reputation for using in combination with osteotropic materials at preimplantation preparation of cavity of mouth, at treatment of periimplantitis, however, it should be noted that in the clinic of maxillofacial traumatology such membranes did not find while application [9, 761–768].

A study of features of application of resorbable membranes from PLLA for fixing of bone fragments in the treatment of the uncomplicated and complicated or comminuted mandibular fractures with the different defects of bone tissues, and also for fixing of bone fragments at patients with posttraumatic osteomyelitis, low consolidation or pseudoarthrosis may be perspective.

**Purpose of research:** determination of clinical and roentgenological efficiency of membranes from PLLA using for fixing of bone fragments in the



treatment of the uncomplicated and complicated mandibular fractures.

**Materials and methods:** In this research 16 patients with the one-sided mandibular fractures in the area of dentition took part, average age was  $28,9 \pm 7,8$  years. All of patients appealed for a medical aid in the day of trauma. A voluntary consent to the participation in a research was obligatory. All of patients initially did not have serious concomitant somatic pathology influencing on the results of treatment.

The advanced clinical, laboratory and roentgenologic examination were carried out before treatment, on the next day after surgical treatment, in a month and 6 months after treatment. Computer tomography of mandible for identification of relation and degree of displacement of bone fragments and sizes of bone defects carried out at the all patients before operative treatment and in 1 month after it.

Mandibular fracture in area of incisors is diagnosed for 4 patients (25% cases), from them 3 patients had a lateral incisor in the line of break, plural small bone fragments were determined in area of frontal part of alveolar socket, for one patient was marked posttraumatic complete dislocation of central incisor and expressed defect of frontal wall of alveolar socket (to 3/4 its length). At 12 (75%) patients a mandibular fracture in area of lower third molar was determined with the expressed separation of bone fragments (to 6–7mm), which reposition

was hampered by a tooth in the line of fracture. Thus, all of patients selected to research, initially had a difficult clinical situation and the local risk factors of development of inflammatory and non-inflammatory complications of mandibular fractures.

For all of patients the operation of intraoral polymer osteosynthesis was conducted by the our method (Pat. Ukraine N 96510). An operation was executed after antiseptis by solution 0,02% chlorhexidine, surgical protocol was included the local anesthesia, intraoral access with the use of L-formed (in a retromolar area) or trapezoidal (in a frontal area) incision. After removing of mucoperiosteal flat and skeletization of buccal cortical bone and lingual surface of lower jaw in area of fracture, if it was necessary we extracted a tooth from the line of fracture, conducted curettage of bone wound, removed nonviable tissues, loose-lying bone fragments of alveolus collected and crushed by a mill to the chips (1,5 mm), the mobile, but intravital fragments of interradicular septa and frontal wall of alveolar socket remained in their places, carried out a hand reposition, filled the alveolar socket of remote tooth and line of fracture by osteoplastic material to renewal of anatomic form, conducted fixation of bone fragments — for this purpose covered the line of break by PLLA membrane, which was adapted to the surface of defect, recovering him from a vestibular side to the lingual, spread the edges of membrane for both sides from the line of fracture on ~15 mm.

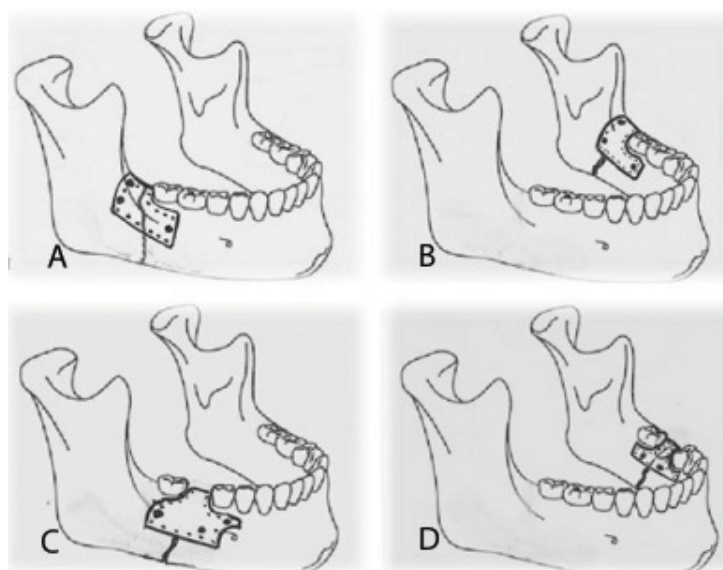


Fig. 1. Position of PLLA membrane relative to line of fracture and alveolar socket after teeth extraction in different clinical cases

After heating a membrane was laid on an alveolar bone of mandible, try for its dense contact with osteoplastic material. After cooling a membrane was fixed by 4–5 pins from PLLA (on the vestibular and lingual side of jaw), disposing them for both sides from the line of fracture opposite each other. Before wound closure we polished harden edges of membrane by a bone cutter. A mucoperiosteal flap was mobilized and laid over a membrane, fixed by U-shaped suture. For realization of such surgical protocol of mandibular fractures treatment we utilized Hypro-Oss/Alpha Bio's «GRAFT» (Israel) as osteoplastic material and resorbable plates-membranes made of PDLA «KLS Martin Group» (Germany) width 2,0–3,0 mm.

**Results and their discussion:** After the reposition of bone fragments of lower jaw and their fixation conducted according to the offered protocol with the use of PLLA membrane at all 16 patients a bite was restored completely, fragments mobility absented during clinical monitoring. The high-quality and stable fixation was provided due to accordance a construction to the biomechanics of lower jaw during a trauma: laying and fixing of dense membrane over the alveolar bone in the area of functional tension blocks horizontal divergence of fragments, and 4–5 pins from PLLA (on the vestibular and lingual side of mandible), located for both sides from the line of fracture opposite each other hinder deformation

of twisting and displacement of fragments in a lingual (cheek) side. A postoperative period passed without complications, for all of patients removal of sutures carry out on 7th day after an operation, recommend ambulatory treatment — after 8 days. The mouth opening was restored in full volume to 10th day after an operation.

At the clinical examinations in a month and in 6 months the patients did not have complaints, the union of bone fragments passed by contact osteogenesis without forming of expressed definitive callus. It was determined a full reposition and satisfactory fixation of bone fragments on control roentgenograms and CT. It was not set repeated displacement of fragments. In 6 months after an operation volume of bone tissues in the area of fracture, defects of alveolar bone and wall of socket after teeth extraction restored fully. Any cases did not required additional surgical procedure for the removing of fixators.

**Conclusions:** Offered method of intraoral polymer osteosynthesis with the use of PLLA membranes for fixing of bone fragments in the treatment of the uncomplicated and complicated mandibular fractures reduces traumatic injury of surgical procedure, provides the reliable fixation during all period of treatment, promotes anatomic and physiologic rehabilitation in the optimum terms.

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## **The place and the role of low invasive surgical technologies in the diagnosis and treatment of abdominal trauma with pancreatic injuries and pancreatitis**

**Abstract:** The article presents the results of applying low invasive surgical techniques in injuries of the pancreas in conditions of concomitant abdominal traumas. Minimally invasive techniques have advantages in improving the accuracy of diagnosis and improve the outcomes of surgical intervention, partially replacing open surgery and expand the technical capabilities of the surgeon.

**Keywords:** abdominal trauma, trauma of pancreas, diagnostics, treatment, low invasive methodic.

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## Место и роль малоинвазивных хирургических технологий в диагностике и лечении абдоминальных травм с повреждением поджелудочной железы и развитием панкреатита

**Аннотация:** В статье приведены результаты применения малоинвазивных хирургических методик при повреждениях поджелудочной железы в условиях сочетанной абдоминальной травмы. Малоинвазивные методики имеют свои преимущества в повышении точности диагностики и улучшении результатов хирургического вмешательства, частично заменяют открытые операции и расширяют технические возможности хирурга.

**Ключевые слова:** абдоминальная травма, травма поджелудочной железы, диагностика, лечение, малоинвазивные методики.

Малоинвазивные оперативные вмешательства постепенно становятся стандартом при целом ряде хирургических заболеваний, конкурируя с традиционными открытыми операциями [1; 2]. Они отличаются существенными лечебно-диагностическими преимуществами: детальной визуализацией, малой травматичностью, сокращением времени наркоза, операции и пребывания в стационаре [3; 4]. При абдоминальной травме повреждение поджелудочной железы (ПЖ) значительно усложняет диагностику и ухудшает прогноз лечения. В мировой хирургии накоплен достаточный опыт применения в этих случаях лапароскопических, эндоскопических, пункционных методик, которые признаны эффективными и безопасными в руках квалифицированных специалистов [4; 5]. Применение малоинвазивных методик способствует более быстрой регенерации тканей, уменьшению количества септических осложнений. На сегодняшний день еще не до конца выяснена эффективность малоинвазивных методик при тяжелых травмах, показания к их использованию и алгоритмы применения.

**Цель исследования** — изучить особенности применения малоинвазивных оперативных вмешательств в условиях неотложной хирургии у пациентов с закрытой травмой поджелудочной железы в составе абдоминальной травмы.

**Материалы и методы исследования.** В работе анализировались данные полученные у 32 па-

циентов (средний возраст —  $39,3 \pm 1,64$  лет), госпитализированных по поводу абдоминальные травмы с повреждением ПЖ различной степени. Результаты лечения сравнивали с данными 22 пострадавших с первичной лапаротомией. Степень повреждения железы определялась по международной шкале (AAST) [6]. Для диагностики и лечения применялись малоинвазивные методики: УЗИ контролируемые пункции и лапароскопические операции. Пункционные вмешательства проводили с помощью аппарата PIE MEDICAL SCANNER 150S с электронным линейным и конвексными датчиками частотой 3,5 и 5 МГц. Манипуляции осуществлялись с помощью игл типа Chiba калибра от 20 до 14 G. Видеолапароскопию проводили с помощью стойки фирмы „Storz” (Германия) с использованием лапароскопов с прямой и скошенной оптикой. Вмешательство осуществлялось под эндотрахеальным наркозом, через стандартные порты диаметром 5 и 10 мм. Полученные результаты обрабатывались статистически с использованием программы Statistica (StatSoft).

**Результаты исследования.** Пациенты с абдоминальными травмами госпитализировались преимущественно в течение первых суток (70%). По обстоятельствам получения травмы преобладали дорожно-транспортные происшествия, избиения, падения с высоты. Диагностические

и лечебные малоинвазивные манипуляции проводились при обнаружении с помощью УЗИ признаков травмы ПЖ с гематомой или ферментативным перитонитом, при выявлении жидкости в брюшной полости с целью санации последней и аспирации токсического выпота. Лечебно-диагностическая тактика исходила из травматичности вмешательства — вначале использовались пункции, затем лапароскопия и только потом, при необходимости, открытое вмешательство.

При выявлении жидкостных образований оценивали их размеры, количество, объем, форму, характер содержимого, наличие капсулы, определялись показания к манипуляции и возможность ее технического осуществления. При благоприятной для пункции локализации, определялось эхонегативное окно, через которое проводилась манипуляция по воображаемой прямой от точки проекции датчика на коже до объекта. При манипуляции избегали прохождения пункционной иглы через полые и паренхиматозные органы, через сосуды с целью предотвращения их ятрогенных повреждений. При успешном проведении манипуляции конец катетера визуализировался на мониторе в виде гиперэхогенной линии, в полости образования. Далее, с помощью шприца, аспирировали содержимое для общеклинических и специальных исследований. Катетер фиксировали к коже и подсоединяли к трубке, через которую остатки патологического содержимого вытекали пассивным путем в емкость для сбора жидкости.

Наряду с дренированием пункционная техника могла применяться для санации очага. При признаках инфицирования содержимого, проводилась санация антисептиками с частым фракционным или проточно-капельным их введением через катетер. Критериями эффективности методики были: уменьшение числа и размеров жидкостных образований при УЗИ контроле, снижение амилолитической активности экссудата полученного через дренажи, инволюция клинических и лабораторных показателей.

При недостаточной информативности УЗИ или подозрении на массивные разрывы органов проводили лапароскопию, с использованием стандартного набора инструментов. Лапаро-

скопия была первичной у 14 пациентов и у 8 пациентов после неудачи пункционного лечения. Показаниями к переходу было отсутствие положительной динамики от пункционного лечения в течение двух-трех дней, при сохранении интенсивного болевого и диспептического синдромов, стойком парезе кишечника, положительных перитонеальных симптомах и сохранении или нарастании количества жидкости в свободной брюшной полости по данным динамического УЗИ. Вначале проводилась тщательная обзорная лапароскопия с детальной оценкой органов верхнего и нижнего этажей брюшной полости, париетальной и висцеральной брюшины, гепато-билиарной и гастродуоденальной зон с прицельным выявлением прямых и косвенных лапароскопических признаков повреждения ПЖ или острого панкреатита. Особое внимание уделялось визуализации выпота в брюшной полости, его характеру, количеству, локализации. Оценивали также наличие другой ургентной хирургической патологии, возможности оперативного восстановления целостности органов и тактики вмешательства. В случае необходимости, для санации токсического экссудата, устанавливался дополнительный порт по срединной линии в области эпигастрия. Другие порты устанавливались в зависимости от локализации и характера поражения. Использовались манипуляторы для смещения внутренних органов с целью лучшей визуализации поврежденных зон, для дренирования и обеспечения адекватной санации брюшной полости, пункционные иглы для пункции и санации сальниковой сумки в случае выявления напряженного оментобурсита, или трубки аспиратора-ирригатора для промывания и отсасывания экссудата из брюшной полости. Дренажи в брюшной полости оставлялись на 3–6 дней, или же до прекращения выделения по ним экссудата. Это позволяло при сохранении адекватности дренирования предупредить вторичное инфицирование брюшной полости через дренажи.

Благодаря малоинвазивным методикам достигалась более точная диагностика, меньший объем операционной травмы, сокращение времени проведения операций ( $58,6 \pm 3,6$  мин. —  $85,3 \pm 8,2$  мин. при лапаротомиях). Эти показатели отражают

общее состояние больного и коррелируют с длительностью и травматичностью операции ( $r=0,56$ ,  $p<0,05$ ), а также величиной кровопотери ( $r=0,38$ ,  $p<0,05$ ).

Показаниями к конверсии в лапаротомию в нашей работе были: наличие жидкостного образования значительного объема, плохо дренируемых с густым гнойным или гнойно-некротическим содержимым, получение жидкости интенсивно геморрагического характера, указывающей на продолжительное кровотечение, отсутствие положительной динамики в общем состоянии больного и на УЗИ контроле. При обнаружении массивных повреждений паренхиматозных органов, проникающих повреждений полых органов, распространенных напряженных забрюшинных гематомах, некрозах и затеканиях в проекции ПЖ также осуществлялась конверсия. Любые сомнения по поводу продолжения малоинвазивного вмешательства решались в пользу лапаротомии.

Таким образом, в процессе лечения пострадавших с абдоминальными травмами с повреждением ПЖ малоинвазивные методики наряду с открытыми операциями выступали в качестве комплексного инструмента для достижения оптимального результата в рамках тактики многоэтапного хирургического контроля: от наименее до наиболее травматичного. Благодаря малоинвазивным методикам можно было минимизировать операционную травму и дополнять открытые операционные лечебных манипуляций.

**Выводы.** В большинстве случаев абдоминальной травмы с поражением ПЖ можно применить малоинвазивные методики, как с диагностической, так и с лечебной целью. Благодаря им повышается диагностическая информативность, расширяется технический диапазон оперативных вмешательств. Использование малоинвазивных методик ведет к уменьшению длительности операции, снижению травматизации тканей и кровопотери.

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## **Osteosynthesis unilateral plural shaft fractures of bones of a hip and a leg at associate to a trauma of a stomach and retroperitoneum**

**Abstract:** The purpose of research — the comparative analysis of methods of an osteosynthesis, time of carrying out at patients with plural unilateral shaft fracture of the hip and leg associated with the trauma of the stomach and retro peritoneum.

*Methods.* With 2006 on 2012 the author 93 patients with plural unilateral shaft fracture bones of the hip and leg associated with the trauma of the stomach and retro peritoneum were observed. Men — 79 (84,9%), women — 14 (15,1%). 76,3% of victims were able-bodied age (21–60 years). A principal cause of a trauma at 88 (94,6%) victims — road and transport incidents. Right-hand damage is marked at 51 (54,8%) victims, left-hand — at 42 (45,2%). The closed crises it is marked at 32 (34,4%) victims, crisis of a hip at 11 (11,8%), bones of a shin 21 (22,6%). Open crises it is marked at 61 (65,6%), from them a femur — at 19 (31,2%) victims, bones of a leg — at 42 (68,8%), were classified on scale Gustilo R. B., Anderson J. T. (1976). 36 patients were treated by a conservative method, 57 the operative osteosynthesis is made.

*Results.* 6 patients it is made relaporotomy, at 4 patients because of early loading — a floor of a DCP plate on a hip which were it are removed, made reosteosynthesis by intramedullar nail and the frame apparatus, pin an osteomyelitis — 8 (5 hip, 3 leg), the delayed union of bones of a leg — 9, mixed contracture a knee joint — 12 (7 — operative, 5 — non-operative) patients. The remote results are appreciated on scale Jonner R., Wruhs O. (1983). At patients treated a skeletal extension method: excellent — 19, good — 9, satisfactory — 8 (an average estimation — 4,3). An operative osteosynthesis: excellent — 31, good — 7, satisfactory — 11, unsatisfactory — 8 (an average estimation — 4,1).

*Conclusions.* Patients with plural unilateral shaft fracture bones of the of the bottom finitenesses, associated with the trauma of the stomach and retro peritoneum should be observed and treated in versatile hospitals or branches associated traumas, with the stipulated established posts. Where alongside with antishock treatment and surgical interventions, under vital indications, it is necessary to impose skeletal extension which is one of factors of antishock treatment and also an effective independent method of conservative treatment, and serves, necessarily, as preparation of the patient for the further operative osteosynthesis. From methods of an operative osteosynthesis a choice for metallic construction, allowing to receive a steady and stable osteosynthesis, early activity and development of movements in both segments from victims.

**Keywords:** a polytrauma, unilateral shaft fracture of the bottom finiteness, an osteosynthesis, damages of bodies of a stomach and retro peritoneum.

### **Introduction**

Associate the closed trauma of a stomach and various segments of the опорно-impellent device concerns to a category of the complex damages demanding rendering of the emergency help.

In the literature many works [1; 3; 5] are devoted to a question of treatment of unilateral crises of a femur and bones of a leg. However till now there is no common opinion be relative the most rational tactics of treatment of such crises. Tactics

treatment is even more various at associate traumas abdomen cavities and retro peritoneum spaces and unilateral crises of the bottom finiteness. One authors prefer conservative treatment, others at failure of conservative treatment resort to operative. The third — apply a combination of operative methods with conservative [2]. However the majority of authors [4; 5] count a method of a choice operative treatment.

Weight of a condition of patients is caused by a combination of damages of bones of various localization and internal bodies, and also a traumatic shock. Symptoms of a developing traumatic shock, frequently, veil a clinical picture of damage of bodies of a belly cavity that can serve as the reason of diagnostic mistakes. Quite often weight of damage of bodies of a abdomen cavity in a combination to damage of finitenesses both other bodies, and fabrics happens correct diagnostics and in time the carried out operative treatment is so great, what even, unfortunately, does not give desirable effect.

Diagnostics of damage of internal bodies at the closed trauma of a stomach combined to damage of the support-mowing apparatus, is rather difficult. The typical picture of an intrabelly bleeding is uneasy for differentiating with displays of a traumatic or spinal shock. Well-known clinical symptoms of a sharp stomach at patients with a polytrauma are characterized by extreme inconstancy. Radiological research, because of special weights of a condition of the victim, is not always feasible and cannot resolve all problem of diagnostics. Ultrasonic inspection not always, unfortunately, possible to reveal a pathology of bodies of a stomach of traumatic character. In such cases the emergency laparoscopy which has been lead{which has been carried out} with the diagnostic purpose which allows to refuse, sometimes,

to the surgeon from unnecessary laparotomy has crucial importance.

The purpose of research: the comparative analysis of methods of an osteosynthesis, time of carrying out at patients with plural unilateral shaft crises of bones of a hip and a leg associate with a trauma of a stomach and retro peritoneum spaces.

#### Materials and methods

For the period with 2006 for 2012 we observed 93 patients with plural unilateral shaft crises of bones of a hip and a leg, associate with a trauma of a stomach and retro peritoneum spaces, treated in versatile State Clinical Hospital № 3. Among them men was 79 (84,9%), women — 14 (15,1%). The majority (76,3%) victims were able-bodied age (21–60 years). A principal cause of a trauma at 88 (94,6%) victims were road and transport incidents.

Within the first hour from the moment of a trauma it is hospitalized 61 (65,6%) the victim, up to 12 ч — 16 (17,2%), up to 24 ч — 9 (9,7%). 7 (7,5%) patients are transferred from regional hospitals within one week from the moment of reception of a trauma.

Right-hand damage is marked at 51 (54,8%) victims, left-hand — at 42 (45,2%). The closed crises it is marked at 32 (34,4%) victims, crisis of a hip at 11 (11,8%), bones of a shin 21 (22,6%). Open crises it is marked at 61 (65,6%), from them a femur — at 19 (31,2%) victims, bones of a shin — at 42 (68,8%).

Open damages on classification Gustilo R. B., Anderson J. T. [7] were distributed as follows: type I — 26 (42,62% from the general number of open crises), type II — 19 (31,14%), type IIIa — 10 (16,39%), type IIIb — 6 (9,83%).

For definition of character of crises we used classification AO/ASIF (tab. 1).

Table 1. – Character and localization of crises (on classification of AO/ASIF)

Crises \ Segment	hip		leg		Total	
	Abs.	%	Abs.	%	Abs.	%
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
Type A2.1	15	16,1	18	19,4	33	17,7
A 2.2	12	12,9	8	8,6	20	10,8
A 2.3	9	9,7	10	10,7	19	10,2
Type B2.1	18	19,4	18	19,4	36	19,4
B 2.2	9	9,7	12	12,9	21	11,3

<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
B 2.3	10	10,7	7	7,5	17	9,1
Type C2.1	11	11,8	11	11,8	22	11,8
C 2.2	6	6,5	6	6,5	12	6,5
C 2.3	3	3,2	3	3,2	6	3,2
Total	93	100	93	100	186 segment	100

The admission acted patients were stacked in reanimation branch where the damage appeared necessary inspection and the corresponding help. Doctors of different structures (surgeons, traumatologists, neurosurgeons, urologists, oto-

laryngologists, ophthalmologists, etc.) were involved.

The carried out surgical interventions in abdomen cavities under vital indications at patients observable by us are resulted in table 2.

Table 2. – Dependence of weight of a trauma on localization of damage and the surgical operations which have been which have been carried out in abdomen of a cavity and retro peritoneum

Ball Points on RTS	Damages of bodies of a stomach and retro peritoneum spaces						
	Damage kidneys	Damage parenchima kidneys	Break of a bladder	Damage of a liver	Damage of a liver	Break mes- enterium	Break of intes- tines
7–8	3–3,22%	9–9,67%					27–29%
9–10			5–5,37%		19–20,4%		
11–12				18–19,35%			
13–14						12–12,9%	
Total	93–100%						

At carrying out by surgeons of operative interventions abdomen cavities and retro peritoneum spaces, traumatologists under indications and a condition of the patient, in parallel or consistently, were made a toilet of wounds (type I) or their primary surgical processing (type II and is higher).

In a question of a range of time of carrying out of an osteosynthesis damaged with associate a trauma of a stomach and the support-mowing apparat, according to the literature, do not have common opinion that is visible from table 3.

Table 3. – Range of time of carrying out of an osteosynthesis

The first 2 days (the period of primary indemnification)	Ohotskij V.P. et al. [6], Heuwinkel et al. [8].
Not earlier than 8 days after a trauma (the period of proof indemnification)	Ibrohimov G. I. et al. [3], Kapustin P. Φ. et al. [4], Krettek et al. [9]
Parameters objective choice of optimum time for an early osteosynthesis plural and associated crises does not exist	Sterk et al. [11]

At a choice of a method of an osteosynthesis the general condition of damaged, presence of an accompanying trauma and a shock, age of patients, character of crisis, extensiveness of damage of soft fabrics (tab. 4) was taken into account.

Patients observable by us have been subdivided into 2 groups, the group “A” — which has been applied a conservative method of treatment and group “B”- by which the operative osteosynthesis is applied.

From 93 patients with associated a trauma of a stomach and fracture of femurs and bones of a leg skeletal extension treated 36 damaged. The basic indications for conservative treatment counted: young age at a good or satisfactory parity of fragments, senile age on a background of cardiovascular insufficiency, and also heavy accompanying damages of internal bodies. From them double extension — for condylus a femur and for a calcaneal bone, treated



24 patients. 12-ru the system of skeletal extension has been imposed by the patient on a hip, and a leg, because of insignificant displacement of fragments, fixed by a plaster bandage. Skeletal extension carried out dempfer in [5] way on trunk Böler or the device of the author (the patent № İ 990161 « The Device for treatment of crises and

dislocations of bones of the bottom finiteness and development of movements in joints», 1999). The device enables to develop movements in knee and hip joints, not removing skeletal extension. Gips plaster fixing imposed through 1,5–2 months, after full healing abdomen wounds and occurrences clinical union, not removing extension.

Table 4. – Treatment of patients with plural unilateral shaft fracture of bones of a hip and a leg associate with a trauma of a stomach and retro peritoneum spaces

Methods treatments on togroups	Group "A" Conservative treatment		Group "B" Operative treatment									Total	
			A plate					Fram apparate				abs	%
	Skeleton extension	Gips plaster	DCS	DCP	Author	Clo-verle-af	T-standart	Iliza-rov	Screw-pin	Pin+ screw-pin (hybrid)	Nail+ Screw-pin		
Segment													
32 Hip													
A2.1	9	-	4	2	-	-	-	-	-	-	-	15	16,1
A2.2	8	-	-	-	2	-	-	-	-	-	2	12	12,9
A2.3	5	-	-	-	-	-	-	4	-	-	-	9	9,67
B2.1	9	-	-	-	-	-	-	7	-	1	1	18	19,3
B2.2	2	-	-	1	2	-	-	-	-	-	5	10	10,7
B2.3	3	-	-	1	-	-	-	2	-	-	3	9	9,67
C2.1	-	-	1	-	-	-	-	2	-	8	-	11	11,82
C2.2	-	-	-	-	-	-	-	-	-	2	4	6	6,45
C2.3	-	-	-	-	-	-	-	-	3	-	-	3	3,22
42 Leg													
A2.1	5	-	-	2	-	2	1	1	-	-	-	11	11,8
A2.2	2	1	-	-	1	-	1	2	-	-	-	7	7,52
A2.3	3	8	-	1	-	-	-	3	-	-	-	15	16,1
B2.1	9	-	-	-	-	2	1	6	-	-	-	18	19,3
B2.2	4	-	-	2	2	-	1	3	-	-	-	12	12,9
B2.3	1	3	-	1	1	-	1	3	-	-	-	10	10,7
C2.1	-	-	-	1	1	2	1	6	-	-	-	11	11,8
C2.2	-	-	-	1	2	-	1	2	-	-	-	6	6,45
C2.3	-	-	-	-	-	-	-	-	3	-	-	3	3,22
Total												93	100

At 57 patients operative intervention on an osteosynthesis of bones was carried out on deducing victims from a shock, after surgical interventions in abdomen cavities and retro peritoneum, and stabilization of the general condition. 3 (3,2%) the patient

with open shaft fracture of bones of a hip and a leg association with a separation of a kidney (1 patient), an intestines and a liver (2 patients), fixing of both segments is made by frame apparatus pain-screw in the emergency order. 54 patients (58,1%) have been

executed by the rest in the deferred order (later 10–14 day from the moment of a trauma). Indications to operative treatment were, basically, absence of contra-indications to him, and the consent of the patient to an operative osteosynthesis.

The osteosynthesis of bones of a hip and leg on bone plate, was carried out to patients with fracture of type A, B. With a fracture line of a break in m/3 shaft,

bones of a hip, were fixed intramedullar nail by entered retrograde, with the frame apparatus pain-screw. At open fracture, and also what because of a wound of a stomach, it was undesirable to impose a gips plaster bandage, an osteosynthesis was carried out frame apparatus Ilizarov or a frame apparatus pain-screw a hybrid (on the basis of frame apparatus Ilizarov), that is shown in table 5.

Table 5. – Kind of an osteosynthesis at patients with plural unilateral diafysis fracture a hip and leg associate with a trauma of a stomach and retro peritoneum spaces

№	Segment		Amount of patients	
	Hip	Leg	aбс	%
1	Plate	Screw — pin fram apparat	7	12,3
2	Plate	Plate	6	10,5
3	Nail + Screw — pin fram apparat	Plate	8	14,0
4	Nail + Screw — pin fram apparat	Screw — pin fram apparat Ilizarov	7	12,3
5	fram apparat Ilizarov	Plate	7	12,3
6	fram apparat Ilizarov	fram apparat Ilizarov	8	14,0
7	Screw — pin fram apparat Ilizarov	Plate	7	12,3
8	Screw — pin fram apparat Ilizarov	fram apparat Ilizarov	4	7
9	Screw — pin fram apparat	Screw — pin fram apparat	3	5,3
	Total		57	100

At fracture proximal and distal (h/3 and d/3) shaft hips at 5 patients are applied dynamic compression plates — screws — DCS, on bones of a leg — plates of the form of a maple sheet at 6 and “T”-standard at 7 operation, achieving the steady and stable osteosynthesis allowing in the postoperative period to do without of gips plaster fixing. With fracture m/3 diafysies hips at 4 patients the osteosynthesis is made dynamic compression plates DCP, and at 4 — a plate of the author (the patent № 980094 « The Device on bone fixings », 1998), on a leg plate DCP at 8 and a plate of the author at 7 operation.

#### Results:

It has been made 6 patients relaporotomy, 2 patients in 2,5 months, because of a breaking of a plate of AO system on a hip, it is made reosteosynthesis by intramedullar nail with the frame apparatus, pin an osteomyelitis has developed at 8 (5 hip, 3 leg) the delayed union of bones of a leg — 9, mixed contracture a knee joint — 12 (7 — operative, 5 — non-operative) patients. The remote results of treatment have been appreciated on classification Jonner R., Wruhs O. (1983 [8] (table 6).

Table 6. – The remote results of treatment of observable patients

	G	R O	U P	“A”	G R	O	U P	“B”
Criteria	Excel- lent	Good	Fair hip leg	Poor	Excel- lent	Good	Fair hip leg	Poor hip leg
1	2	3	4	5	6	7	8	9
1. Infection	none	none	none	none	none	none		3 3
2. Delayed union	none	none	none	none	none	none		none
3. Nonunion	none	none	none	none	none	notes	3 2	none
4. Reostheo- syntes	none	none	none	none	none	none		2

1	2	3	4	5	6	7	8	9
5. Neurovascular injury	none	none		none	none	minimal	none	none
6. Deformity Varus/valgus	0°–5°	6°	Varus to 15°	Varus to 10°	Varus to 5°	Varus to 8°	Varus 15°	Varus > 20°
7. Pro/recurvatum	0°–5°	none	none	>20°	none	none	none	none
8. Rotation	0°–5°	none	none	>20°	none	none	none	none
9. Shortening	0–5 MM	6 MM	18 MM	>20 MM	5 MM	9 MM	20 MM	> 20 MM
10. Mobility Knee Ankle Subtalar	90%	to >80%	to >75%	<75%	to 90%	to 80%	to 75%	75%
11. Pain	none	periodic	moderate	significant	none	periodic	moderate	significant
12. Gait	normal	normal	occasional lameness	lameness significant	normal	normal	occasional lameness	lameness significant
Results excellent (5)	19				31			
Good (4)		4 5				4 3		
Fair (3)			4 4				7 4	
Poor (2)				0				5 3
Average estimation		4,3				4,1		

### Conclusions

1. Patients with plural unilateral crises of bones of a hip and a leg associated with a trauma of a stomach and retro peritoneum spaces should be observed and treated in versatile hospitals or branch associated traumas with the stipulated established posts.

2. At receipt of patients in a hospital with the above-stated damages, alongside with antishock treatment and surgical interventions, under vital indications, it is necessary to impose skeletal extension which is one of factors of antishock treatment, and serves as preparation of the patient for the further operative osteosynthesis.

3. At an emergency osteosynthesis the frame apparatus osteosynthesis is shown.

4. An operative osteosynthesis, with plural unilateral fracture of bones of hip and leg associated

with a trauma of a stomach and retro peritoneum spaces, on our supervision, it is necessary to carry out after surgical interventions and stabilization of the general condition of the patient.

5. The indication to an operative osteosynthesis is absence of contra-indications to it and the consent of the patient.

6. From methods of an operative osteosynthesis at patients with plural unilateral shaft fracture bones of a hip and a leg associated with a trauma of a stomach and retro peritoneum spaces a choice for metallic construction, allowing to receive a steady and stable osteosynthesis, early activity and early development of movements in both segments from damaged.

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## **Dietary sources of vitamin D and seasonal variations of 25 (OH) vitamin D serum levels in men over 45 years of age in Latvia**

**Abstract:** Introduction. Over 50% of population are found to suffer from vitamin D deficiency. Vitamin D deficiency in Europe, Northern Europe, especially in elderly people, was revealed by



many epidemiological studies. Insufficient vitamin D intake was detected in the population of the North America and Eastern Europe, comprising only 50% of vitamin D daily recommended dose.

**Materials and methods.** 134 males aged 45–80 were included in the research. None of the research participants were taking any vitamin D supplements or other supplements containing vitamin D. Serum vitamin D level ((25 hydroxyvitamin D: 25 (OH)D) was measured in all the participants and the amount of vitamin D taken with the diet was determined. The participants' height and weight were measured to calculate BMI and a survey on the amount of vitamin D consumed with food was conducted.

**Results.** Insufficient vitamin D intake was detected in 78,4%, vitamin D deficiency with consequent low vitamin D serum level — 94,1%. The mean data: vitamin D in food — 6,9 µg, 25 (OH) D — 16,9 ng/mL, BMI — 28,1 kg/m<sup>2</sup>, age — 59,4 years. The amount of vitamin D in food statistically reliably directly correlates with serum vitamin D level ( $r=0,961$ ;  $p=0,01$ ), there is also an inverse correlation with age ( $r=0,226$ ;  $p=0,009$ ). Vitamin D serum level correlates inversely with age ( $r=0,184$ ;  $p=0,033$ ). No statistical reliable correlation was found between serum 25 (OH) D levels and BMI. The major dietary sources of vitamin D are fat-rich sea fish, eggs, and dairy products.

**Conclusion.** Both insufficient intake of vitamin D with food and low serum level were marked in males of advancing age — 94.1%. Serum vitamin D level directly correlates with vitamin D intake. No statistically significant correlation among vitamin D levels, vitamin D in diet or BMI were found, although there was inverse correlation with age.

**Keywords:** 25-hydroxy-D3 vitamin, 7-dehydrocholesterol, dietary sources, body mass index (BMI).

### Introduction

Vitamin D deficiency rickets in children and osteomalacia due to Calcium malabsorption in adults were long thought to be the only manifestations of vitamin D deficiency [1, 1629–1637; 2]. However, nowadays vitamin D deficiency has been linked to the development of such chronic diseases as osteoporosis, multiple sclerosis [3, 2832–2838], cardiovascular diseases and cancer [4, 39–48]. Many types of human body tissue have vitamin D receptors, the ability to synthesize  $\alpha$ -hydroxylase, and, moreover, vitamin D itself. Nevertheless, the amount of vitamin D needed to provide the optimal health is still discussed by many researchers and clinicians. They consider both higher amounts and limits of normal 25 (OH)D serum level from 50 and over 75 nmol/mL necessary to prevent vitamin D deficiency and insufficiency [5, 542–550; 6, 53–58]. Healthy adult individuals get the most of their vitamin D from exposure to sunlight [1, 1629–1637]. With a diet vitamin D is obtained in limited amount [7, 1678–1688]. Therefore, seasonality [8, 860–868], latitude [9, 693–701], and life

style are the factors expected to affect vitamin D. In the Northern European countries vitamin D synthesis from the sun light is insufficient due to several factors. The population tend to stay indoors in the light period of the day. In the northern latitudes (57 °) cyclones taken away sea air masses from the Atlantic Ocean, in the warm seasons it results in foggy and rainy weather [10, 1287–1290]. For instance, in Scotland (the higher latitudes) the highest 25 (OH) D serum level is below 16 ng/mL compared with other UK population [8, 260–268; 11, 2461–2472].

Latvia is located in the northern latitudes 55°–58°, therefore, the sunlight waves of 260–320 nm needed for vitamin D synthesis in the skin can not reach the Earth between the end of November and the beginning of February [12, 14–18]. In the recent years vitamin D deficiency in adults has been recognized as a nutritional problem in the USA. The results from the National Health and Nutrition Examination Survey of 2000–2004 showed that over 10% males and 15% females suffer from moderate vitamin D insufficiency, that was defined as serum 25 (OH)D<sub>3</sub> < 15 ng/mL. [13, 1519–1527].

**The aim of the study.** To determine dietary sources of vitamin D, prevalence of vitamin D deficiency and insufficiency in male population over 45 years of age in Latvia. To determine whether there is any correlation between vitamin D intake, its serum level, BMI and age.

#### Materials and methods

The research was conducted between 26.10.2012 and 18.04.2014. The majority of the research participants included lived in the urban areas. Influence of UVB radiation was taken into consideration depending on the season.

Inclusion criteria:

- Male gender
- Between 45 and 80 years of age
- Absence of oncology in familial history
- Live at home, consume simple food

Exclusion criteria:

- Vitamin D supplement intake, as well as dietary supplements containing vitamin D
- Oncology diseases
- Chronic kidney disease
- Chronic liver disease
- Diarrhoea

Biomedical research. Quantitative research method was implemented. „Food Consumption Frequency Questionnaire” was used as a research instrument. This method has been used in many research works, to detect vitamin D insufficiency. Vitamin D in dietary sources ( $\mu\text{g}/100\text{g}$ ) was measured by means of the questionnaire. The German Nutrient Database BLS (Bundeslebensmittelschlüssel) of the Max Rubner-Institut was implemented in the research.” Food safety,

animal health and environmental research institute” (BIOR) program was used for the data processing of the dietary frequency questionnaire.

Vitamin D (25 hydroxylvitamin D 25 (OH)D) serum level was measured by the immunochemiluminescence method (Liaison). Mild vitamin D insufficiency was designated if 25 (OH)D serum level was  $< 30 \text{ ng/mL}$ , moderate vitamin D insufficiency between 20 and 29  $\text{ng/mL}$ , pronounced vitamin D insufficiency from 10 to 20  $\text{ng/mL}$ , and vitamin D deficiency, if 25 (OH)D serum level was  $< 10 \text{ ng/mL}$ . Vitamin D toxicity starts at 25 (OH) D serum level  $> 150 \text{ ng/mL}$ . The data were processed by „Food safety, animal health and environmental research institute” (BIOR) program, Excel 2010, IBM SPSS 21.0.

#### Results

158 males were included in the research, of whom 24 were excluded due to oncology diagnosis –prostate cancer. Vitamin D level was measured in 134 males.

The mean age of the males included in the research was  $59,4 \pm 8,4$  years. 31,3% were younger than 55 years. The mean BMI was  $28,1 \pm 3,9 \text{ kg/m}^2$  ( $20\text{--}41 \text{ kg/m}^2$ ). Obesity ( $\text{BMI} \geq 30$ ) was detected in 27,6% of males, increased weight was observed in 50,7% of cases.

The mean daily vitamin D amount consumed with the diet was  $6,9 \pm 5,2 \mu\text{g}$  ( $276 \pm 208 \text{ IU}$ ), the minimal amount of vitamin D —  $0,2 \mu\text{g}$  (8 IU), the maximal —  $30 \mu\text{g}$  (1200 IU). The demographic characteristics of the research participants are reflected in the Table 1.

Table 1. – Demographic characteristics of the respondents (levels of vitamin D serum and dietary vitamin D, BMI)

Characteristics of the research participants	n (%)
<i>1</i>	<i>2</i>
Number	134 (100)
Age, years	
45 –55	42 (31,3)
55–65	57 (42,5)
>65	35 (26,1)
BMI ( $\text{kg/m}^2$ )	
19–24,9	29 (21,6)
25–29,9	68 (50,7)
>30	37 (27,6)

<b>1</b>	<b>2</b>
25 (OH)D measured seasonally	
Autumn	85 (63,4)
Spring	49 (36,6)
25 (OH)D serum level (ng/mL)	
<10 (deficiency)	32 (23,9)
10–20 (pronounced insufficiency)	69 (51,5)
21–29 (moderate insufficiency)	25 (18,7)
≥ 30 (normal limit)	8 (6,0)
Vitamin D in diet $\mu\text{g}$ (IU)	
<5 (200 IU)	64 (47,8)
5–10 (200–400 IU)	41 (30,6)
10–15 (400–600 IU)	19 (14,2)
>15 (> 600 IU)	10 (7,5)

The mean vitamin D 25 (OH)D serum level was  $16,9 \pm 7,6$  ng/mL (2,2–43,2 ng/mL). Vitamin D deficiency was observed in 23,9% (n=32), pronounced insufficiency in 51,5% (n=69), moderate insufficiency — 18,7% (n=25) and only in 6% of males (n=8) vitamin D level was within normal limits.

Vitamin D serum level was measured from September to April. Depending on the season

two groups were made: the autumn (September, October, November) and spring (March, April, May). In 63,4% (n=85) vitamin D serum level was measured in the autumn and 36,6% (n=49) in spring. The mean vitamin D serum level measured in autumn was  $17,5 \pm 7,6$  ng/mL (4,8–43,2 ng/mL), and in spring —  $15,8 \pm 7,7$  ng/mL (2,2–39,3 ng/mL). Distribution of vitamin D serum level in the spring and autumn is reflected in the Fig 1.

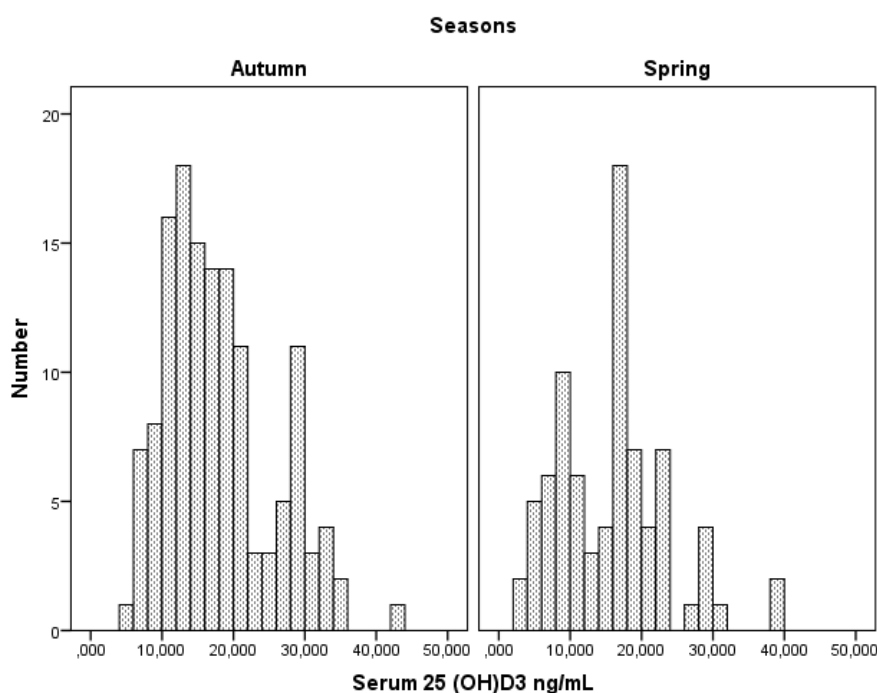


Fig. 1. Vitamin D level distribution histogram in the spring and autumn

The average amount of vitamin D consumed with herring —  $3,5 \mu\text{g}$  (140 IU) daily (0–20,7  $\mu\text{g}/\text{d}$ ), salmon —  $2,6 \mu\text{g}$  (104 IU) daily (0–30  $\mu\text{g}/\text{d}$ ), eggs —  $0,5 \mu\text{g}$  (20 IU) daily (0–5  $\mu\text{g}/\text{d}$ ), daily products:

butter  $0,2 \mu\text{g}$  (8 IU) daily, sweet cream  $0,12 \mu\text{g}$  (5 IU) daily, mackerel —  $0,14 \mu\text{g}$  (6 IU) daily (0–4,5  $\mu\text{g}/\text{d}$ ), that shown in the Table 2.

Table 2. – The average amount of vitamin D in various products ( $\mu\text{g}/100\text{g}$  product)

Vitamin D amount ( $\mu\text{g}$ ) in 100g of product	N	Minimal	Maximal	Average (SD)	IU	(%)
Salmon, raw	133	0	30,3	2,6 (1,4)	104	36,5
Herring, pickled	126	0	20,7	3,5 (2,8)	140	49,2
Mackerel, smoked	122	0	4,5	0,14 (0,09)	5,6	2,8
Egg, boiled	120	0	5,0	0,5 (0,3)	20	7
Butter	93	0	1,0	0,2 (0,08)	8	2,8
Sweet cream	18	0	0,8	0,12 (0,18)	4,8	1,7

SD — standard deviation, IU- international unit.

The average level of energy intake in the participants of the research was —  $3380,2 \text{ kcal} \pm 1084,9$  ( $1287,9\text{--}7175,0 \text{ kcal}$ ): in males over 45–55 of age —  $3341 \pm 119 \text{ kcal/daily}$  (95% CI), 55–65 years of age —  $3041 \pm 112 \text{ kcal/daily}$  (95% CI), and over 65 years —  $2546 \pm 154 \text{ kcal/daily}$  (95% CI). The daily intake of carbohydrates was  $345,0 \pm 131,6$ . The amount of carbohydrates consumed

( $102,2\text{--}760,5 \text{ g/d}$ ), proteins —  $154,8 \pm 62,3 \text{ g daily}$  ( $61,2\text{--}415,8 \text{ g/d}$ ), fats —  $148,3 \pm 56,7 \text{ g daily}$  ( $53,5\text{--}333,7 \text{ g/d}$ ), „ballast” substances —  $28,6 \pm 12 \text{ g daily}$  ( $2,6\text{--}56,9 \text{ g/d}$ ). The average intake of polyunsaturated fatty acids was —  $20,4 \pm 10,8 \text{ g/daily}$ , mono-unsaturated fatty acids —  $3,3 \pm 5,1 \text{ g/day}$ , saturated fatty acids —  $22,3 \pm 13,6 \text{ g/d}$ . All the data have been reflected in the Table 3.

Table 3. – Mean nutritional value (g.) and total energy (kcal)

	Min.	Max.	Mean (SD)	E%
Energy (kcal)	1287,9	7175,0	3380,2 (1084,9)	
carbohydrates (g)	102,2	760,5	345,0 (131,6)	53
proteins (g)	61,2	415,8	154,8 (62,3)	24
fats (g)	53,5	333,7	148,3 (56,7)	23
„ballast” substances (g)	2,6	56,9	28,6 (12,0)	
polyunsaturated acids	3,7	57,4	20,4 (10,8)	
monounsaturated acids	4,7	30,1	13,3 (5,1)	
saturated acids	2,5	73,7	22,3 (13,6)	

The working hypothesis about a correlation between vitamin D intake and 25 (OH)D serum level in males have been statistically verified. One-sample t-tests showed that the numbers obtained include in the confidence interval ( $p > 0,005$ ), as well as there also have been checked the data concerning the age of the respondents, BMI, and the mean value of the consumed vitamin D, standard deviation depending on the vitamin D.

Vitamin D serum level has been measured in subjects depending on their BMI. In the males with normal BMI ( $19\text{--}24,9 \text{ kg/m}^2$ ) the mean vitamin D serum level was  $17,3 \text{ ng/mL}$ ; with elevated BMI ( $25\text{--}29,9 \text{ kg/m}^2$ ) it was  $16,8 \text{ ng/mL}$ , and in obese males ( $> 30 \text{ kg/m}^2$ ) —  $16,3 \text{ ng/mL}$ .

Statistically significant correlation has been found between 25 (OH)D serum level and vitamin D level in food sources ( $r = 0,961$ ;  $p = 0,01$ ).

Indirect correlation has been found between 25 (OH)D serum level and age ( $r = 0,184$ ;  $p = 0,033$ ), as well as between vitamin D content in the diet and age ( $r = 0,047$ ;  $p = 0,009$ ), that is shown in the Fig. 2.

### Discussion

The age of the research participants between 45 and 80 years has been chosen since the risk of oncology, cardiovascular diseases, osteoporosis, osteomalacia, etc. increases in this age interval. The average life expectancy of Latvian males is 10 years shorter than that of females. The average life expectancy comprises 72,7 years: it is 67,3 years in males and 77,7 years in females. According to the Standardized mortality rate data, 48% of males in Latvia die before 65 years of age, while in the European Union (EU) only 29% of males die at this age [14, 9–10].

Data analysis confirmed the expected results on vitamin D deficiency in men with advancing age.



Vitamin D deficiency and insufficiency is common –94,1%. The research results from different countries vary, but, anyway, in almost all countries worldwide both vitamin D deficiency and insufficiency have been detected. 73% of the USA population are found to have vitamin D insufficiency, moreover, with figures almost reaching the upper limit < 30 ng/mL. [15, 1517–1524]. In Canada insufficient

25 (OH)D serum level was detected in almost 93% of population of the same age [16, 2066–2073].

In our research the lowest vitamin D serum concentration (< 10 ng/mL) was detected in 23,9% of males. It corresponds to the research data of the European countries — vitamin D serum level was lower than 10–12 ng/mL in 7–27% of population [17, 1079–1089].

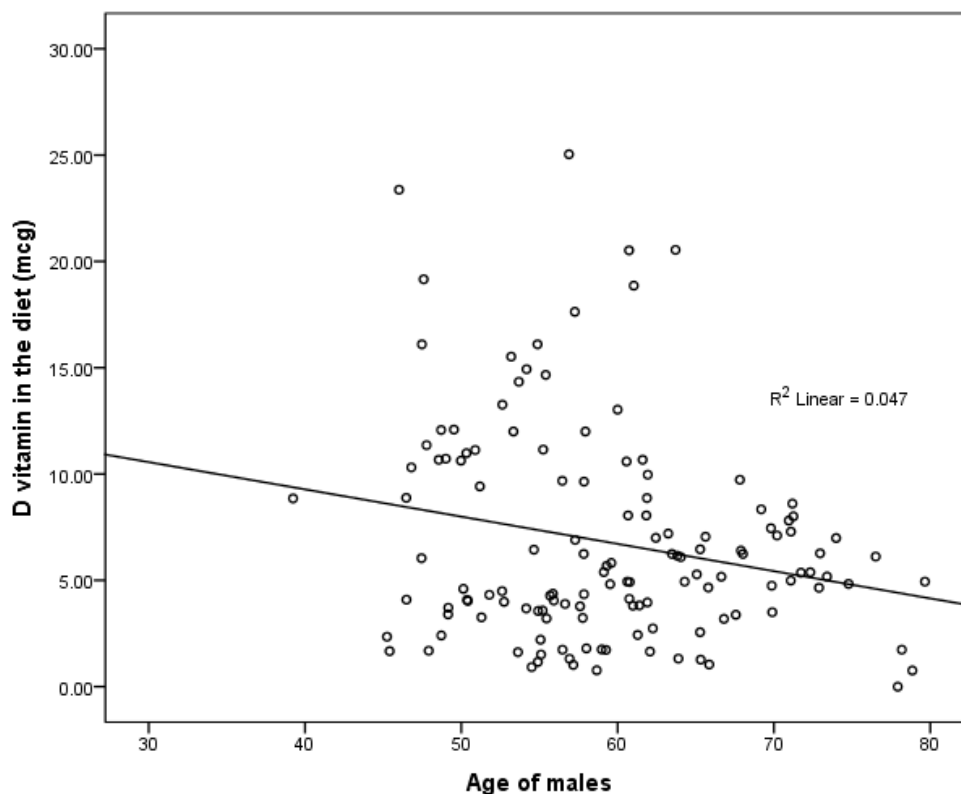


Fig 2. – Pearson correlation between vitamin D in the diet and age

In turn, the research data of the Northern countries show that in 8–17% of the population 25 (OH) D serum concentration is not higher 20 ng/mL [18, 62–83]. In our research vitamin D level was markedly insufficient in 51,5% of men (< 20 ng/mL). It is likely due to the higher average age of the participants compared to the analogous study. According to the research data from our neighboring country Lithuania, more than half of men had vitamin D deficiency in winter (12–30 ng/mL), 43% were found to have deficiency (< 12 ng/mL), and only 1,7% had vitamin D in sufficient concentration (> 30 ng/mL) [19, 558–588].

In our research only 6% of men (n=8) had vitamin D level within normal limits, moreover, it was close to the lowest limit. The highest vitamin D serum level was detected in 1 man (43,2 ng/mL), and that

was only slightly higher than the lower limit ( $\geq 30$ –70 ng/mL). However, the mean serum 25 (OH)D level was  $16,9 \pm 7,6$  ng/mL (2,2–43,2 ng/mL), that was lower compared to the research data from the USA. (23,9 ng/mL) [20, 76–83] and the Northern countries (18,7 ng/mL) [21, 207–210]. High vitamin D deficiency is related to the insufficient exposure to sunlight. None of the research participants were taking vitamin D supplements, that was one of the objective indicators. Vitamin D serum level was analyzed seasonally — in spring and fall. The research participants, whose blood test was made in summer were included into the fall group. Consequently, the men, whose vitamin D serum level was measured in winter comprised the spring group. It was very important to compare vitamin D level after winter, when sunlight exposure generally is low and 7-dehydro-

cholecalciferol absorption by the skin is minimal. The wavelength of UV should be 290–315 nanometers to provide for the natural vitamin D synthesis in the skin. In the Northern latitudes, as well as in Latvia, sunlight is not intensive enough to stimulate vitamin D production from October to March. Vitamin D<sub>3</sub> synthesis in the skin is triggered due to UVB radiation. In the course of absorption, the B ring of provitamin D<sub>3</sub> undergoes a photolysis reaction and is transformed into D<sub>3</sub> previtamin. Since this substance is thermodynamically unstable, the process of isomerization of 3 conjugated double bonds occurs extremely fast and D<sub>3</sub> vitamin is produced.

We received the expected results: vitamin D serum level in fall was higher  $17,5 \pm 7,6$  ng/mL (4,8–43,2 ng/mL) than in spring  $15,8 \pm 7,7$  ng/mL (2,2–39,3 ng/mL). We would like to mention one research conducted in England, that included 1766 participants over 65 years of age, who lived in both private houses and flats. 25 (OH) D serum concentration was lower in males (15,2 ng/mL) and females (14,7 ng/mL), who lived in flats, compared with those males (22,5 ng/mL) and females (19,4 ng/mL) living in private houses.

According to the literature data, vitamin D serum level is lower with age. It occurs due to the decreased vitamin D synthesis in the skin, as well as the impaired vitamin D absorption through the gastrointestinal tract and hydroxylation in the liver and kidneys. In our research we found a statistically significant indirect correlation between the age and vitamin D serum level. Many studies have been conducted in order to determine vitamin D level in elderly population in Europe. For example, we can name the famous SENECA research comprised 12 European countries. It was carried out to determine the relation between the dietary sources and health of persons of advancing age. It was concluded that in general 36% of males and 47% of females had insufficient 25 (OH)D serum concentration (< 12 ng/mL). Surprisingly enough, 50% of the Netherlands population were found to have 25 (OH) D serum concentration lower than 20 ng/mL [22, 2058–2065].

The analysis and comparison of the USA research data from two studies conducted between years

1988–1994 and 2001–2004 showed the extremely low 25 (OH) vitamin D serum concentration in all age groups [23, 26–32].

No statistically significant correlation between vitamin D serum level and BMI was found in our research. However, in the published literature there is data on the association between high BMI and low vitamin D serum level. [24, 796–804]. We did not find any correlation between the intake of vitamin D and BMI. It is likely due to the low number of obese subjects included. BMI in case of obesity is  $> 30$  kg/m<sup>2</sup>, while the average BMI of our research subjects was 28,1 kg/m<sup>2</sup>. Statistically significant correlation is found in case of BMI over 40 kg/m<sup>2</sup>. In our research there was only one subject with high BMI — 41,5 kg/m<sup>2</sup>, in other obese subjects (26,6%) BMI was close to the lower limit of obesity ( $> 30$  kg/m<sup>2</sup>).

Undoubtedly, vitamin D is essential to the human body. It is the main prophylactic factor for the muscle and bone health. Therefore, in the recent years the link between a diet and health is understood better – a promising prophylactic measure for the public health. Elimination of unhealthy eating habits and nutrient deficiencies is one of the priorities of the World Health Organization stated in the WHO Global Action Plan for 2008–2013 years. The high number of new interesting research papers shows the significance of vitamin D in prevention of many diseases, including cardiovascular, immune diseases, diabetes, asthma, multiple sclerosis and different forms of cancer.

The research conducted in Tartu, Estonia in 2006 included 367 subjects (200 females, 167 males) with the average age  $48,9 \pm 12,2$  years (ranging from 25 and 70 years). The mean vitamin D serum level in winter was found to be  $17,5 \pm 6$  ng/mL, and —  $24,2 \pm 7,4$  ng/mL in summer. Vitamin D insufficiency in winter was detected in 73% of subjects, deficiency was found in 8% of males, while in summer only 29% had vitamin D insufficiency and deficiency in 1%, consequently. The data of our research have been similar. Only 1/3 of the Estonian population had a sufficient vitamin D serum level, and merely in 3% it was found to be over the optimal norm  $> 30$  ng/mL. Even though the average vitamin D

concentration is summer reached 24 ng/mL, in almost 2/3 of the population it was still suboptimal (30 ng/mL). [25, 9–22; 16, 2066–2073]. If a person is obese or suffers from some kidney or liver disorders, the effect of vitamin D is impaired, thus the intake of vitamin D could be increased. However, vitamin D overdose is not desirable either. In case of vitamin D hypervitaminosis muscle pain, weakness, headache, fatigue, increased Calcium serum level, constipation, and kidney stones are observed, as well as Calcium deposits on the heart valves, in the heart, blood-vessels and kidneys. Therefore, vitamin D serum level should be measured prior to taking vitamin D itself or its supplements.

It has been recommended by many studies to take vitamin D containing supplements, dietary supplements and vitamin D containing products. One of the most effective, and pleasant to some individuals, ways to get vitamin D is sunbathing. One should bear in mind that sunscreens applied on the skin decrease vitamin D synthesis, therefore, prolonged exposure to sunlight may lead to sunburns. Optimal vitamin D dose can be produced after 20–30 minutes of sun exposure to the face, arms and legs. In our research we have found a statistically significant correlation between vitamin D serum level and vitamin D amount in diet. Sun exposure, undoubtedly, is very important to increase vitamin D level, but dietary sources also influence vitamin D level.

A dietary questionnaire was used to detect the frequency of certain product consumption by the research subjects within last six months. By this method we received information on the amount of the consumed food, trade mark of the products, methods of cooking, and terms of consumption. The method is relatively inaccurate, very subjective, but anyway, can provide with an overall impression. Some subjects had morbid obesity ( $BMI \geq 41 \text{ kg/m}^2$ ), therefore, the energy intake exceeded normal limits significantly. According to the Latvian comprehension food consumption research in 2007–2009 the mean result of the total daily energy intake from the diet in men was 2234 kcal/d. The amount of energy taken by adult men relatively lowers with age, that was also confirmed by our research.

The data of our research show that the most of vitamin D men consumed with herring (140 IU/d) and salmon (104 IU/d). According to the literature sources, fatty sea fish is the richest in vitamin D, it was also confirmed by our results. In turn, only 6 IU/d was consumed with mackerel, since it was eaten very seldom (once a month or even less).

Dairy products — milk, kefir, sour cream did not provide any significant amount of vitamin D. One liter of milk is required daily to provide for 20 IU of vitamin D, besides, it is only 5% of daily recommended dose (400 IU/d). Fatty dairy products such as butter, is considered to be a good source of vitamin D. Our research subjects received 8 IU of vitamin D with 20 g of butter. 69,4% of subjects consumed butter, that, undoubtedly, was not the main vitamin D source. Due to high fat content (80%) excessive butter intake may lead to increase of serum cholesterol level. 5 IU daily was consumed with sweet cream, that was insufficient, too. With eggs were consumed 20 IU of vitamin D daily. Consumption of eggs is common and frequent in men.

Vitamin D fortified products are widespread in the United States. The wide range of the products is available: dairy products (yogurt, milk, and cheese), juice (orange), grain products (bread, cereals, biscuits, crackers). In Latvia there are the products that are enriched with vitamin D (drinking yogurts, canola oil, butter, margarine, cheese), but the vitamin D level in these is insignificant ( $\approx 0,8 \mu\text{g}/100 \text{ ml}$ ).

Since fish oil and fatty fish are very rich in vitamin D, their regular consumption (2–3 times a week) allows to retain vitamin D serum level within normal limits. In lower concentrations vitamin D is also found in egg yolk, caviar, liver, grains, grain shoots and parsley. Furthermore, some types of fish, for example mackerel, herring, salmon and trout contain the recommended daily amount of vitamin D in 1 portion (120 g.). In case of low vitamin D serum level ( $< 30 \text{ ng/mL}$ ), it is required to take 800–1000 IU of vitamin D supplement daily [26, 66–81].

### Conclusion

1. Vitamin D deficiency and insufficiency are common in the Latvian males of advancing age — 94,1%.



2. Vitamin D serum level directly correlates with the amount of the consumed food. No statistically reliable correlation has been found between vitamin D level, vitamin D in diet, and BMI, but it indirectly correlated with age.

3. It is essential for males over 45 years of age to take vitamin D supplement 800–1000 IU/daily, with

prior detection 25 (OH)D serum level (<30 ng/mL). It is strongly recommended for the Latvian population to be sufficiently exposed to the direct sunlight from March to November.

4. Further research with a larger number of participants is required to prove and confirm the significance of the diet in case of vitamin D deficiency.

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## **The quality of life of patients with postoperative and ventral hernias and abdominal obesity before and after surgery**

**Abstract:** Treatment treatment of postoperative and ventral hernias in patients with obesity affects not only surgical but also a number of social problems. The quality of life of patients in the late period after the removal of the ventral hernia is different from the average population indicators and does not depend on the chosen method.

**Keywords:** postoperative and ventral hernias, quality of life, anterior abdominal wall, abdominoplasty.

Relevance. The social significance of the problem and surgical treatment of postoperative and ventral hernias (POVH) exacerbates the fact that the largest number of patients with age ranging from 40 to 60 years, i. e., working age [3, 55–56]. 46% of patients operated on for POVH engaged in physical labor, and are in need of total rehabilitation [4, 138]. Among patients women prevail — 67.8% [5, 62–63]. The most common hernias occur in individuals

with a cone-shaped [6, 3–7] and spherical shape of the abdomen, mostly located in the cut hypogastric region [8, 14–15].

Contributing factors of recurrence POVH is obesity [8, 14]. Patients with obesity POVH varying degrees ranging from 50 to 70% [7, 37–39]. Of all patients with postoperative and ventral hernias and in 34% of patients had morbid obesity in 23% of cases had recurrent hernia [14, 199–201]. With

obesity comes an atrophy of muscles of the anterior abdominal wall and hyperextension aponeurotic and fascial layers [15, 1869–1873]. Obesity, on the one hand, predispose to the formation of a hernia, other — it progresses in its appearance [16, 6–7]. That is, obesity — an etiological factor in the occurrence or recurrence of hernias [10, 240]. Some authors believe that the skin and fat “apron” in patients with obesity stand out as an independent cause of the formation of primary hernias, because it creates a constant static load on the fascia [11, 26].

Treatment POVH in patients with obesity affects not only surgical but also a number of social problems. [1, 39–40]. The quality of life of patients in the late period after the removal of the ventral hernia is different from the average population indicators and does not depend on the chosen method of plastics [12, 415]. Application of mesh explant has no advantages over other methods of plastics in terms of quality of life [2, 476]. Based on this study the quality of life of patients operated on after various methods hernia abdominoplasty we consider unsatisfactory [13, 44–47].

An analysis of the current literature shows that not identified the best way to hernia repair with abdominoplasty. On the other hand, related to the need to remove the pendulous abdomen surgeons controversial: some consider abdominoplasty hernia repair with justifiable, others on the contrary, believe that it is only prolongs the operation, increases the wound surface and increases the risk of local complications [9, 69–74]. Therefore, we studied retrospectively the results of hernia repair without abdominoplasty and hernia repair in patients with obesity. We studied the complications, relapse, quality of life parameters in patients with obesity POVH after hernia repair with abdominoplasty and without abdominoplasty.

**Objective:** To evaluate the parameters of the quality of life of patients with postoperative ventral hernias with obesity after hernia repair with and without abdominoplasty.

**Material and Methods:** From January 2007 to 2014. in surgical department of city hospital № 1 of Tashkent there were operated 237 patients with POVH anterior abdominal wall, in the age of 19–82 years. In 174 (73.4%) patients were accompanied

by varying degrees of obesity (BMI 28 to 60.9). The inclusion criterion was the presence of abdominal obesity and POVH varying degrees, exclusion criterion — recurrent inguinal and femoral hernia.

Patients were divided into two groups. The control group (90 patients), operated from 2007 to 2009, who underwent hernia repair with plastic prosthetic materials. The main group (84 patients) who underwent complete surgical treatment of hernia repair with prosthetic material abdominoplasty between 2009 and 2014. Long-term results of abdominoplasty hernia repair without POVH studied in 42 (46.6%) patients out of 90 operated patients. Term monitoring of patients ranged from 3 months to 4 years. Long-term results with abdominoplasty hernia repair POVH studied in 46 (54.7%) of 84 patients were operated. Term monitoring of patients ranged from 3 months to 3 years. Patients were called in for a check-up by telephone, on which were 27 (32.1%) patients who underwent hernia repair with abdominoplasty, and 20 (22.2%) patients undergoing surgery without abdominoplasty. The remaining 19 (22.6%) patients of the main group and 22 (24.4%) patients in the control group completed questionnaires (containing specific questions) during a conversation on the phone.

One measure of the effectiveness of the treatment is to improve the quality of life. The study baseline efficacy in patients of the control group and the main based on completing a special questionnaire «SF-36 Health Status Survey», which shows a significant reduction in physical and mental health component. The general health of patients is very low and only 32.6% of the patients indicated a satisfactory state of health. 25% of respondents pointed to the preservation of mental health, role functioning due to emotional state, was even lower, and 14% of irrigated patients indicated it satisfactorily. It is associated with low activity of social functioning and vitality, so the majority of patients were quite passive way of life, dominated by physical inactivity. Only 40% of the patients to live a normal career, and ¼ of the respondents pointed to the safety of the patients vitality. This quality of life of patients is in direct relation with the size of the hernia defect, the degree of ptosis and obesity.

Quality of life was assessed immediately before surgery and within the period of 3 months to 3 years after hernia repair with abdominoplasty. To do this, patients filled special questionnaire — «SF-36

Health Status Survey» (Ware JE, 1993) relating to the non-specific questionnaires to assess quality of life, these data are given in Table 1.

Table 1. – The quality of life study group before and after gernoabdominoplasty (n = 84)

General index	The overall scale	Preserving the function (%)	
		Before surgery	After surgery
The physical health component (Physical health — PH)	Physical functioning	37,56±6,56	80,23±10,45
	Role functioning due to physical state	16,78±8,56	84,34±21,34
	Pain intensity	42,17±5,54	64,56±11,76
	General health	30,09±6,26	61,62±10,23
Психологический компонент здоровья (Mental Health — MH)	The psychological component of health	31,70±6,06	80,11±9,10
	Role functioning due to emotional state	20,86±7,45	88,45±7,42
	Social functioning	41,54±9,39	61,67±6,32
	Vital activity	23,94±8,63	79,34±8,39

As the table shows, the physical health component was characterized by a significant decrease in physical functioning, role, due to a physical condition before treatment. In addition, each patient complained of pain so intense pain were assessed as moderate. The general health of patients is very low and only 32,55 ± 14,34% of patients indicated a satisfactory state of health.

The psychological component of health in patients with POVH was also rated as very low in the preoperative period. Thus, only ¼ of patients indicated the safety of mental health. Role functioning due to emotional state, was even lower with only 14% of respondents pointed to his patients is satisfactory. This is due to low activity of social life of patients, with the majority of the patients were relatively passive way of life, dominated by physical inactivity. Only 40% of the patients to live a normal career, and ¼ of the respondents indicated only for the safety of vital activity. Consequently, the initial quality of life of patients was quite low as a result of low physical and mental components of health. The quality of life of patients is directly related to the magnitude of the hernia defect, the degree of ptosis and obesity. Given these facts, we estimated the quality of life of patients with POVH late after hernia repair with abdominoplasty. It was found a significant improvement in the quality of life of operated patients. For example, physical activity in the study group increased 9.06 times. In this case, 2 times reduced the number of patients

complaining of pain in the hernia protrusion, discomfort in the area and not least the appearance of most patients satisfied.

The same positive trend was noted in the psychological component of health. For example, 80% of patients in the postoperative period pointed to a good mental state of the operated patients, in 3.04 times higher relative to the performance of treatment. To improve the psycho-emotional background, indicated 88% of operated patients that 3.36 times the original value. On the preservation of social functioning and vitality indicated 62 and 79% of the patients, in 1.55 and 3.25 times more than those who for some reason refused the proposed surgery (tab. 2).

Thus, the quality of life of patients after hernia repair surgery with abdominoplasty is greatly improved. At the same time increase physical activity of patients, the possibility of self-service, the basic pathology did not significantly affect the performance of certain physical activities. In addition, the improvement of the general health, absence of cosmetic defects and reducing pain improved the emotional state of patients, contact with others, significantly decreased the number of patients with depression, isolation and others.

Analyzing the physical and mental status in both the test data, the proposed method of treatment indicated in 1.43 and 1.26 the best indicator of the physical status of patients who underwent abdominoplasty.



Table 2. – The quality of life of patients after surgery abdominoplasty hernia repair with or without

General index	The overall scale	Preserving the function (%)	
		hernia re- pair without abdomino- plasty	hernia repair with abdomi- no-plasty
The physical health component (Physical health — PH)	Physical functioning	56,23±4,76	80,23±10,45
	Role functioning due to physical state	66,76±6,65	84,34±21,34
	Pain intensity	52,15±3,37	64,56±11,76
	General health	50,87±8,23	61,62±10,23
The psychological component of health (Mental Health — MH)	The psychological component of health	33,54±8,36	80,11±9,10
	Role functioning due to emotional state	31,44±9,78	88,45±7,42
	Social functioning	46,43±7,63	61,67±6,32
	Vital activity	27,76±6,86	79,34±8,39

Therefore, if 56% of patients operated without abdominoplasty basic health does not interfere with their daily work, when combined with abdominoplasty this figure increased to 80%. The intensity of pain in both groups was similar. The number of patients is indicative of good health, were 1.21 times more than with conventional operations.

The mental health component was also higher in patients undergoing hernia repair with abdominoplasty. Thus, the number of patients with normal mental health were 2.4 times higher than in patients without abdominoplasty, ie if the number of patients with depression, anxiety and mental ill feelings in the group without abdominoplasty was 66.5%, whereas in the proposed treatment, this figure has increased significantly. And only in 31.5% of operated without abdominoplasty emotional state does not interfere with daily operations, while in the group of patients undergoing hernia repair with abdominoplasty, the figure was 1.81 times higher, amounting to 88.5%.

More than 50% of patients with traditional hernia repair remained significant limitations of social contacts, reduce the level of communication in connection with the deterioration of the physical and emotional state, whereas in patients with abdominoplasty, it decreased by 38% of patients in the late postoperative period, which is 1.4 times became less common.

In the group of patients with hernia repair without abdominoplasty only 27.8% of patients in the remote periods after surgery feel themselves full

of vigor and energy, 72.8% complained of fatigue, decreased vitality. At the same time in the group of patients operated with abdominoplasty, the number of patients with high vital activity was 2.86 times higher. Consequently, abdominoplasty hernia repair with significantly improved quality of life of patients. An increasing number of patients with preservation of physical and mental components of health, most of them returned to active work, there are signs of emotional satisfaction.

Quality of life of patients after hernia repair surgery have improved, increased physical activity of patients, the possibility of self-service, the basic pathology did not significantly affect the performance of certain physical activities. In addition, the improvement of the general health, absence of cosmetic defects and reducing pain improved the emotional state of patients, contact with others, significantly decreased the number of patients with depression, isolation and others. However, despite these positive developments, full recovery was not observed.

Quality of life study group was significantly higher than the control. Thus, the preservation of the physical component of health, including physical functioning and role functioning due to physical condition, with the proposed method of treatment indicated in 1.43 and 1.26 are more likely than those without abdominoplasty. If 56% of patients operated without abdominoplasty basic health does not interfere with their daily work, when combined with abdominoplasty this figure increased



to 80%. The intensity of pain in both groups was similar. The number of patients is indicative of good health, were 1.21 times more than the control.

The mental health component was also higher in patients undergoing hernia repair with abdominoplasty. If the number of patients with depression, anxiety and mental ill feelings in the group without abdominoplasty was 66.5%, whereas the proposed treatment — only 20%. More than 50% of patients in the control group remained significant limitations of social contacts, reduction of communication due to the deterioration of physical and emotional state, whereas in the group with abdominoplasty, it was detected in 38% of patients. In the group of patients with hernia repair without abdominoplasty 72.8% of respondents complained of fatigue, decreased vitality. At the same time in the group of patients operated with abdominoplasty hernia repair in patients with high numbers of vital activity was 2.86 times higher.

Summarizing the findings it can be said that, with the hernia repair in patients with abdominoplasty POVH by obesity significantly improves outcomes, reduces the frequency of general and local early and late postoperative complications and mortality. This is confirmed by the increasing number of patients with preservation of physical and mental components of health and return them to the active work, reduce depression and suggestions about the incurability of the underlying pathology. All of the above testifies to high efficiency of the proposed method of treatment POVH on the background of obesity and calls for its widespread introduction into clinical practice.

### Clinical Example № 3.

*Patient P, 52 years old, and/W 6753 received 26.04.2014, with the diagnosis of postoperative ventral*

*hernia, ptosis of 2 degrees. Height 156 cm, weight 81 kg, BMI 33.2 kg/m<sup>2</sup>. Type of obesity — genoidnoe reason — alimentary. Concomitant diseases: hypertension 1 tablespoon and chronic bronchitis. Received appropriate treatment.*

*From history 15 years ago was made laparotomy. The patient then was thin, slender. After that, the patient recovered. After 5 years after surgery appeared hernia in postoperative scar. The patient connects the appearance of a hernia with obesity. Gradually I began to increase in hernia volume. During these years, she added weight. The last 2 years was accompanied by a hernia pain became often bother to interfere with walking. By all measures, the quality of life has deteriorated.*

*When you receive a general state of moderate severity.*

Locally: In midline abdominal wall there are n/a scar the size 18x2.0 sm giant hernia the size of 20x20 sm.

In order to prepare a thorough preoperative examination:

Complete blood count: HB — 128 g/l, er. — 3.5., Layk — 7.4., NT — 37%, T-t — 4st., fib. A — 3.95 g/l.

Biochemical tests: ALT — 0.68 mmol/l, total protein — 72.4 g/l.

ECG — heart rate, 78 min., Sinus rhythm, moderate left ventricular hypertrophy.

TSMW-without features.

ERF (External respiration function) — chronic bronchitis for obstructive type.

Diagnosis: Postoperative ventral hernia. M. W4. R1. Obesity I st. (BMI 33.2). ptosis. (Mean ptosis).

Concomitant Hypertension.: 1 tbsp. Chronic bronchitis.

The patient was examined by a physician, pulmonologist and the anesthesiologist.

#### ERF Indicators

Parameters	Norms	Before operation	Post operation
VC (L)	2.41	1.70	2.12
FVC (L)	2.31	1.78	2.08
FEV (L)	1.92	0.89	1.12
Power exhalation	5.50	2.87	3.90
The flow-volume 75%	4.98	2.32	3.56
The flow-volume 50%	3.35	1.29	2.56
The flow-volume 25%	1.13	0.90	1.08
MVL (l)	83.1	66	—

Operation: 28.04.2014.

Hernia repair. Reconstruction of the abdominal wall (Method Ramirez) with the surgical mesh.

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## Section 2. Biomedical science

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### **Influence of thiol antioxidants on state of neurons antioxidant system in conditions of glutathione system deprivation**

**Abstract:** A decrease of thiols level in antioxidant system of neurons is the reason of early neurodestructive mechanisms development and non-coordination in transport system of nitrogen oxide. Glutathione synthesis deprivation by means of buthionine sulfoximine (BSO) introduction caused a formation of pathobiochemical reactions of oxidative and nitrosative stresses in cerebral tissues. Introduction of thiol containing drugs which are donors of thiol groups restricts negative influence on active forms of oxygen and nitrogen by means of cellular thiol redox state regeneration.

**Keywords:** glutathione, buthionine sulfoximine, thiol-disulfide balance, oxidative stress.

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### **Влияние тиоловых антиоксидантов на состояние антиоксидантной системы нейронов в условиях депривации глутатионовой системы**

**Аннотация:** Депривация синтеза глутатиона путем введения бутионинсульфоксимиона (BSO) вызывала формирование в тканях головного мозга патобиохимических реакций оксидативного и нитрозативного стресса. Снижение уровня тиолов в антиоксидантной системе нейронов является причиной развития ранних нейродеструктивных механизмов и несогласованности в транспортной системе оксида азота. Введение тиол-содержащих препаратов, являющихся донорами тиоловых групп, ограничивает негативное воздействие на нейроны активных форм кислорода и азота путем восстановления тиолового редокс-статуса клетки.

**Ключевые слова:** глутатион, бутионинсульфоксимин, тиол-дисульфидное равновесие, оксидативный стресс.

Наиболее важную при развитии различных патологий в биологическом плане роль играют окислительно-восстановительные реакции, в ходе которых тиоловые группы легко окисляются с образованием дисульфидных группировок, и вновь регенерируют при их восстанови-

тельном расщеплении. Возникающая на основе этих превращений обратимая тиол-дисульфидная система (ТДС) имеет очень большое значение в регуляции окислительно-восстановительного равновесия в клетках и тканях организма [1, 178–180]. Система глутатиона представленная

восстановленным (GSH) и окисленным (GSSG) глутатионом, а также ферментами его метаболизма: глутатионпероксидазой (GPO), глутатионтрансферазой (GST) и глутатионредуктазой (GR). Она является одной из ведущих антиоксидантных систем в организме и играет ключевую роль при всех физиологических процессах клеток [2, 3–5]. В частности глутатион непосредственно, либо посредством ферментативных реакций, эффективно защищает клетки от свободных радикалов и других реактивных разновидностей кислорода, например, гидроксильного радикала, липид-пероксильного радикала, пероксинитрита и перекиси водорода. Помимо этого глутатион принимает участие в функционировании глутаредоксин-зависимой системы, играющей важную роль в поддержании внутриклеточного редокс-гомеостаза [3, 255–260].

Восстановленный глутатион, из всех тиол-содержащих компонентов клетки, является наиболее важным в поддержании внутриклеточного редокс-потенциала. Его значение определяется участием в регуляции редокс-зависимого сигналинга и активности транскрипционных факторов, а также тем фактом, что он является внутриклеточным антиоксидантом, играя роль «ловушки» свободных радикалов, косубстратом в реакциях детоксикации пероксидов, катализируемых GPO и GST, и выступает в качестве агента, восстанавливающего окисленный глутаредоксин. Сохранение оптимального для клетки соотношения восстановленного глутатиона к окисленному — GSH/GSSG является важным условием для поддержания жизнеспособности клетки [4, 300–301].

Нашими предыдущими исследованиями на моделях *in vitro* и *in vivo* было показано значительное смещение тиолового статуса в сторону окисленных форм в поддержании механизмов антиоксидантной защиты и выживания нейронов [5, 124–129; 6, 31–35].

Целью настоящего исследования явилось изучение состояния антиоксидантной системы в тканях головного мозга крыс с депривацией системы глутатиона и возможность модуляции возникающих нарушений препаратами, которые являются

донорами SH-групп — тиоцетама, тиотриазолина, ангиолина и  $\alpha$ -липоевой кислоты.

#### Методы исследования

Исследования проводились на белых крысах линии Вистар массой 180–210 г, содержащихся в стандартных условиях вивария. Все экспериментальные процедуры и оперативные вмешательства осуществляли в соответствии с «Положением об использовании лабораторных животных в биомедицинских исследованиях». Депривацию глутатионовой системы моделировали путем введения бутионинсульфоксимида (BSO) — селективного ингибитора  $\gamma$ -глутамилцистеин-синтазы ( $\gamma$ -GCS) в дозе 4 ммоль/кг.

Все животные были распределены на следующие экспериментальные группы: I — интактные,  $n=7$ ; II — животные с введением BSO,  $n=7$ ; III — животные с введением BSO и тиотриазолина (50 мг/кг),  $n=7$ ; IV — животные с введением BSO и тиоцетама (125 мг/кг),  $n=7$ ; V — животные с введением BSO и ангиолина (50 мг/кг),  $n=7$ ; VI — животные с введением BSO и  $\alpha$ -липоевой кислоты (50 мг/кг),  $n=7$ .

Для иммуноферментных и биохимических исследований использованы фрагменты, находящиеся в области сенсо-моторной зоны коры головного мозга и гомогенизированные в жидком азоте. Цитозольную фракцию выделяли методом дифференциального центрифугирования (15 000 g) при температуре +4 °C на 0,15 М фосфатном буфере pH 7,8. Содержание нитротирозина определяли с помощью твердофазного иммуноферментного анализа с использованием стандартного тест-набора «Nitrotyrosine ELISA Kit» («HyCult biotechnology») в соответствии с прилагаемой к набору инструкции. Уровень SH-групп, активность глутатионпероксидазы и глутатионредуктазы определяли спектрофотометрически [7; 355, 422–424]. Содержание окисленного и восстановленного глутатиона определяли флуорометрически [8, 45]. Состояние антиоксидантной системы оценивали по активности СОД, каталазы, показателям окислительной модификации белка. Определение активности СОД проводили по методике, описанной С. Чевари с соавторами [9, 679–680]. Активность каталазы



определяли спектрофотометрически по методу М. А. Королук [10, 17–19]. Показатели окислительной модификации белка в тканях головного мозга по методу В. Halliwell [11, 264]. Результаты исследования обработаны с использованием статистического пакета лицензионной программы «STATISTICA® for Windows 6.0» (StatSoft Inc., № AXXR712D833214FAN5), а также «Microsoft Excel 2010». Статистическую обработку проводили с применением t-критерия Стьюдента и U-критерия Манна-Уитни. Для всех видов анализа статистически значимыми считали различия с уровнем значимости менее 0,05 (95%) [12, 287].

### Результаты исследования

Результаты проведенных исследований указывают на то, что депривация глутатионового звена тиол-дисульфидной системы путем введения BSO вызывает нарушение синтеза глутатиона и разворачивание реакций оксидативного стресса. Торможение синтеза глутатиона в клетке проявлялось снижением уровня его восстановленной формы на 56,6% с параллельным повышением содержания дисульфида и нарушением соотношения GSH/GSSG (табл. 1), что выражалось и в снижении уровня общих SH-групп на 43,6%.

Смещение тиол-дисульфидного равновесия в сторону окисленных интермедиатов обуславливало нарушение функционирования антиоксидантных ферментов и накопление окислено модифицированных макромолекул, в первую очередь, белков. Так, активность СОД снижалась на 57,5%, каталазы — на 37,7%, что обуславливало повышение ранних (АФГ) и поздних (КФГ) маркеров повреждения белковых молекул на 52,8% и 2,4 раза соответственно (табл. 2). Окислительной модификации подвергались и ферменты, участвующие в метаболизме глутатиона. Так, активность GPO в тканях мозга животных с введением BSO была ниже на 17,1%, а GR — на 20,4% относительно показателей интактной группы. Введение изучаемых препаратов вызывало положительные эффекты в отношении как реактивации антиоксидантных ферментов, так и восстановления тиол-дисульфидного равновесия. Модуляция системы глутатиона, а также связанных с его обменом антиоксидантных ферментов — GPO и GR защищает мозг от активных форм  $O_2$ , продуктов пероксидации и в определенной степени позволяет восстановить равновесие и улучшить редокс-регуляцию [13, 146–147].

Таблица 1. – Состояние системы глутатиона в головном мозге животных на 4 сутки введения BSO

Группа животных	GSH, мкмоль/г белка	GSSG, мкмоль/г белка	SH-группы, ммоль/г белка	GPO, мкмоль/(мг белка*мин)	GR, мкмоль/(мг белка*мин)
Интактные животные	3,85 ± 0,05	0,15 ± 0,03	18,8 ± 1,22	72,5 ± 3,1	14,2 ± 1,3
Животные с введением BSO	1,67 ± 0,07	0,84 ± 0,04	10,6 ± 1,04	60,1 ± 2,8	11,3 ± 1,4
Животные с введением BSO + ангиолин	3,12 ± 0,03*	0,22 ± 0,03*	16,5 ± 1,13*	69,6 ± 2,4*	14,0 ± 1,1*
Животные с введением BSO + тиотриазолин	2,84 ± 0,06*	0,36 ± 0,05*	14,2 ± 0,96*	66,2 ± 2,6	13,6 ± 1,2
Животные с введением BSO + тиоцетам	2,89 ± 0,07*	0,45 ± 0,07*	14,8 ± 1,02*	65,7 ± 2,9	12,2 ± 1,2
Животные с введением BSO + α-липоевая кислота	2,33 ± 0,08*	0,77 ± 0,06*	13,2 ± 1,1*	65,1 ± 3,2	12,5 ± 1,5

Примечание: \* —  $p < 0,05$  по отношению к группе с введением BSO

Повышение уровня окисленных низкомолекулярных тиолов приводит к нарушению транспортных функций оксида азота и усиливает

образование его цитотоксических дериватов — нитрозония, нитроксила и пероксинитрита, накопление которых дополнительно усиливают

окисление тиоловых групп [13, 38–39]. Подтверждением этих процессов является отмеченное нами повышение активности NO-синтазы

(на 80,3%) и накопление нитротирозина — главного маркера образования пероксинитрита и развития нитрозативного стресса на 93,0% (табл. 2).

Таблица 2. – Состояние антиоксидантной системы и синтазы оксида азота в головном мозге животных на 4 сутки введения BSO

Группа животных	СОД, у. е./ (мг белка*мин)	Каталаза, мкат/(мг белка*мин)	Продукты ОМБ, у. е./г белка		Нитротирозин нмоль/г белка	NO- синтаза, нмоль/г белка*мин
			АФГ (270 нм)	КФГ (363 нм)		
Интактные животные	285,7 ± 12,3	7,7 ± 0,98	8,9 ± 0,74	6,7 ± 0,68	8,6 ± 0,73	14,2 ± 1,07
Животные с введением BSO	121,3 ± 10,3	4,8 ± 0,46	13,6 ± 1,4	16,4 ± 1,76	16,6 ± 1,32	25,6 ± 0,96
Животные с введением BSO + ангиолин	227,5 ± 9,8*	6,6 ± 0,55*	9,6 ± 0,85*	9,1 ± 0,84	10,2 ± 0,95*	16,1 ± 1,05*
Животные с введением BSO + тиотриазолин	211,1 ± 11,1*	5,8 ± 0,63*	10,1 ± 1,1*	10,6 ± 0,93*	12,4 ± 1,03*	18,3 ± 0,84*
Животные с введением BSO + тиоцетам	217,3 ± 10,7*	6,0 ± 0,72*	10,8 ± 1,24*	10,4 ± 0,75*	12,7 ± 0,82*	18,7 ± 0,95*
Животные с введением BSO + α-липоевая кислота	194,6 ± 9,4*	5,2 ± 0,89	11,8 ± 1,51	13,6 ± 1,17*	13,3 ± 0,9*	20,5 ± 1,11

Примечание: \* —  $p < 0,05$  по отношению к группе с введением BSO

Введение исследуемых препаратов оказывало однонаправленный, но не равнозначный по силе модулирующий эффект. Наиболее активными в этом отношении были ангиолин, тиоцетам и тиотриазолин, применение которых статистически достоверно ( $p < 0,05$ ) приводило к нормализации функционирования СОД и каталазы, и как следствие, ограничивало окислительную модификацию белковых молекул. Отмеченные эффекты обусловлены тем фактом, что указанные препараты относятся к группе антиоксидантов, которые являются «ловушками» свободных радикалов и переводят их в неактивное состояние, способствуя реактивированию антиоксидантных ферментов и более эффективному расходованию неферментативного антиоксиданта токоферола [13, 338–340]. α-Липоевая кислота оказывала менее выраженный эффект, не оказывая существенного влияния на активность NO-синтазы, каталазы и накопления АФГ (табл. 2). Однако,

следует отметить, что этот препарат, наравне с более активными в этом плане, статистически достоверно ( $p < 0,05$ ) препятствовал накоплению пероксинитрита и КФГ, как наиболее токсичных соединений для ткани мозга. Полученные данные свидетельствуют о важной роли этого естественного метаболита в функционировании системы глутатиона и механизмах депонирования оксида азота, повышая, таким образом, его биодоступность и препятствуя образованию цитотоксических дериватов.

Таким образом, при проведении фармакотерапии тиол-содержащими препаратами устанавливается наиболее оптимальное соотношение между уровнями восстановленных и окисленных тиольных групп, а также глутатиона, что свидетельствует об активной мобилизации тиол-дисульфидной системы в нейтрализации продуктов свободно-радикального окисления. Кроме того, увеличение функциональности ТДС в условиях

введения BSO способствует повышению биодоступности оксида азота, а также уменьшает цитотоксичность его активных дериватов, что проявлялось в виде нормализации активности NO-синтазы, на фоне выраженного снижения

уровня нитротирозина. Вероятно, что в условиях нитрозирующего и оксидативного стресса, благодаря указанным механизмам, изученные средства увеличивают устойчивость нервной ткани к явлениям ишемии [13, 150–152].

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## **Neutrophilic granulocytes reactive response in candida vulvovaginitis patients with intracellular microorganism persistence complications**

**Abstract:** Polymorphic neutrophilic granulocytes reactive response and body immune reactivity in general considerably decrease in patients suffering from candida vaginitis on the basis of intracellular microorganisms persistence.

**Keywords:** candida vaginitis, neutrophilic granulocytes reactive response.

Among frequently occurring infections candida vulvovaginal takes a considerable place affecting 70–75% of women of child-bearing age at least once a lifetime. Primary episodes of VVC with subsequently recurrent infection (RVVC) are experienced by 5%-10% of women while RVVC is defined as at least three-four episodes of the disease within one year. There is a primary RVVC identified with unknown predisposing factors and secondary RVVC that has an acute form due to the certain predisposing factors [1, 1–2].

Despite the existence of acquired cell-mediated candida-specific immunity, the studies of vaginal candidiasis in women show the lack of the local and systemic adaptive immunity protection. These data provide few clues to the protective mechanisms against the infection and the high rate of asymptomatic vaginal fungal persistence in adolescents has considerably limited the insights into the immunopathogenesis of vaginal candidiasis [2, 2939].

**Objective of the research** is to establish reactive response of polymorph nuclear neutrophilic granulocytes of periphery blood in women suffering from candida vaginitis at the presence of chronic persistent intracellular infection.

**Resources and methods.** Clinic laboratory and special examination was conducted in 107 women suffering from candida vaginitis. Clinic diagnosis

was confirmed by yeast-fungi secretion of Candida genus and content from vaginas of all women in population level  $5.69 \pm 0.37$  lg CFU/ml in monoculture and in association with non-pathogenic bacteria or trichomonas.

Calculation and analysis of periphery blood elements were conducted according to the recommendations listed in “User’s manual” of analyzing device [3, 58].

### **Investigation results and their discussion.**

Viruses and other intracellular microorganisms add their contribution to the weakening resistance of a human body. The presence of persistent viral infection was identified by the increase of IgM and IgG concentration in the periphery blood. The investigation of the IgM and IgG concentration was held in 57 patients suffering from candida vaginitis. The persistent viruses and other intracellular infections investigation results according to the ELISA data are given in the table 1.

For uncovering the persistence mechanisms of intracellular non-pathogenic microorganisms in women suffering from candida vaginitis, the ecological method was used. It allowed to investigate the co-existence characteristics of ecosystem representatives “microorganism-microbiota” and trace the ecosystem changing direction. Dominant typology was completed on the basis of the constant index iden-



tification, Simson's domination indexes and Berger-Parker's indexes of generic abundance. Cytomega-

lovirus and viruses of Herpes Simplex type 1, 2 are considered to be dominant species.

Table 1. – The generic content of persistent intracellular microorganisms in women suffering from candida vaginitis

Intracellular microorganisms with identified IgG	The amount of examined patients	The amount of identified IgG to microorganisms	Index of constancy	Frequency	Margaleph's generic abundance index	Simson's generic domination index	Berger-Parker's generic abundance index
Cytomegalo virus	57	17	31,48	0,31	0,30	0,10	0,321
Herpes Simplex virus type 1, 2	57	15	27,78	0,28	0,26	0,08	0,283
Rubella virus	57	5	9,26	0,09	0,08	0,01	0,094
C. trachomatis	57	5	9,26	0,09	0,08	0,01	0,094
M. hominis	57	3	5,56	0,06	0,04	<0,01	0,057
T. gondii	57	8	14,81	0,15	0,13	0,02	0,151
Hepatitis C virus	57	1	1,75	0,02	0,01	<0,01	0,019

Rubella virus, Chlamydia, Mycoplasma and Toxoplasma are additional intracellular microorganisms that persist in a human body.

Margaleph's generic abundance index was calculated for persistent microbiota abundance characteristics. This index is believed to be rating to characterize spatial cellular resources and environmental conditions for providing the existence of intracellular microorganisms. The highest indexes of the persistent intracellular biota were identified in Herpes viruses (Herpes Simplex viruses type 1,

2 and Cytomegalovirus). Viral and other intracellular microorganisms persistence always leads to the development of the secondary immunodeficiency state established during the study of the neutrophilic granulocytes reactive response level. An approximate level of the intracellular viral and other microorganism concentration was identified according to the IgG concentration level in the serum of the patients. IgG concentration study results in the serum of the women suffering from candida vaginitis are given in table 2.

Table 2. – Ig G concentration in the serum of women suffering from candida vaginitis

Intracellular microorganisms	Units of measure	IgG concentration in the patients' serum	IgM concentration in the patients' serum
Cytomegalovirus	m.o/ml	6,42±0,37	negative
Herpes viruses type 1,2	Optical units	9,88±0,49	negative
Rubella virus	m.o/ml	92,40±0,87	negative
Chlamydia	Optical units	3,73±0,31	negative
Mycoplasma	Optical units	1,56±0,14	negative
Toxoplasma	m.o/ml	130,31±1,19	negative
Hepatitis C virus	Optical units	0,497	negative

Given IgG concentration depends on the antigen (virus or other microorganisms). The absence of IgM increase suggests that there is no acute inflammatory state, stipulated by persistent intracellular microorganisms, and the Ig 5G titre increase justifies the chronic inflammatory

process, at which the secondary immunodeficiency state is formed. Candida vaginitis persists on the basis of this state.

It is known that candida of any localization refers to the opportunistic mycosis. The fungi of Candida genus are widespread. A carrier has got 46–52% of

these fungi on his mouth mucous membrane, 80% in faeces, 12% on vagina mucous membrane and this amount may considerably increase to 30–35% in the last trimester of pregnancy. However, this result must not exceed Ig 3–4 CFU/ml. Vaginitis development persists on the immunodeficiency state background, and particularly on the basis of granulopenia. Neutrophilic granulocytes possess the functions of hemotoxicity, phagocytosis and secretion.

They are the first to penetrate the inflammation foci that is connected with hyper susceptibility to hemoattractant substances that provide the direct cell penetration into inflammation foci. The importance of neutrophilic granulocytes in anti-infective unspecific protection became the basis for the establishment of neutrophilic granulocytes reactive response in the periphery blood in patients suffering from candida vaginitis (table 3).

Table 3. – Polymorphic neutrophilic granulocytes reactive response in the periphery blood of patients suffering from candida vaginitis

Immuno-hematologic indexes	Measure units	Patients suffering from candida vaginitis (n=30) M±m	Healthy people (n=30) M±m	Level of immune disturbance	P
Neutrophilic granulocytes reactive response index	equivalent units	2,67±0,26	2,97±0,29	–I	>0,05
Neutrophilic lymphocytic coefficient	equivalent units	1,71±0,17	2,50±0,22	–I	<0,05
Neutrophils shift index	equivalent units	0,110±0,011	0,033±0,009	+III	<0,01
Leucocytes shift index	equivalent units	1,52±0,16	2,15±0,19	–I	<0,05
Lymphocyte-granulocyte index	equivalent units	0,57±0,05	0,40±0,04	+II	<0,05
Neutrophils and monocytes ratio index	equivalent units	9,43±0,17	16,50±0,19	–II	<0,001
Leucocytes and ESR ratio index	equivalent units	0,63±0,05	0,43±0,4	+I	<0,05
Leukocytic index	equivalent units	1,57±0,13	0,85±0,10	+III	<0,05
Unspecific body reactivity index	equivalent units	0,40±0,03	0,64±0,06	–II	<0,05
Immunologic reactivity index	equivalent units	5,80±0,45	6,90±0,55	–I	>0,05
Body resistance index	equivalent units	310,15±3,11	802,12±5,40	–II	<0,001

For identification of informational index changes in neutrophilic granulocytes reactive response of the periphery blood, as probable prognostic meaning of candida vaginitis development, complicated by intracellular infection, the immunologic disturbance level of each immunohematologic index was established. At the presence of reactive response insufficiency there was a negative number and the index with “+” indicated the hyper function of the immune system. Neutrophilic granulocytes reactive re-

sponse index in the periphery blood of patients suffering from candida vaginitis has a decreasing tendency by 11,24%. Neutrophilic-lymphocytic coefficient falls by 46,20%, leucocytes shift — by 41,45%, but at the same point it increases in 3,33 times that serves as an evidence of appearance of new forms (rod-nuclear) of neutrophilic granulocytes in large amount that cannot substitute the function of mature forms. Decrease of neutrophils and monocytes ratio index certifies the weakened function of neutrophilic granulocytes in

comparison with monocytes/macrophages function which activity prevails over neutrophilic function. Increase of leucocytes and ESR ratio index by 46,51% proves the development of autoimmune process, leading to cell destruction infected by intracellular microorganisms, and the leucocytes index increase to 85,88% justifies the immune response humoral component prevalence over the cell chain.

**Conclusions:**

1. The development and persistence of candida vaginitis is accompanied by a considerable (by 35,38%) decrease of factor activity and mechanisms of unspecific protection against the infection, and also the specific immune reactivity by 62,41% that causes body resistance decline in patients by 29,78%.

2. Body resistance decline in patients suffering from candida vaginitis is conditioned by Herpes viruses persistence in the body (Cytomegalovirus and Herpes simplex virus), Rubella virus and other intracellular viruses — Chlamydia, Toxoplasma, Mycoplasma.

3. Candida vulvovaginitis persistence, associated with intracellular infection (Herpes viruses, Rubella virus, Chlamydia, Toxoplasma etc.), is accompanied by the decline of polymorph nuclear neutrophilic granulocytes reactive response that leads to unspecific reactivity decrease (inherent immunity) by 60,0%, immunologic body reactivity by 18,97% that is conditioned by general body resistance decline in 2,59 times.

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## Section 3. Preventive medicine

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### Choice of earphones and influence of their use on organs of hearing

**Abstract:** In article the questions connected with deterioration of hearing when using earphones are considered, and also the questions connected with prevention of violations of negative impact when using different types of earphones in the professional sphere.

**Keywords:** otolaryngology, hearing disorder, decrease in acoustical sensitivity, influence of earphones.

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### Выбор наушников и влияние их использования на органы слуха

**Аннотация:** В статье рассматриваются вопросы, связанные с ухудшением слуха, при использовании наушников, а также аспекты связанные с профилактикой нарушений негативного воздействия при использовании разных типов наушников в профессиональной сфере.

**Ключевые слова:** отоларингология, нарушения слуха, снижение слуховой чувствительности, влияние наушников.

Звуковые сигналы, окружающие человека, представляют собой колебания воздуха с разной частотой и силой, они возбуждают слуховые рецепторы, находящиеся в улитке внутреннего уха. Рецепторы активируют первые слуховые нейроны, после чего сенсорная информация передается в слуховую область коры большого мозга через

ряд последовательных отделов, которых особенно много в слуховой системе.

Слуховая система — одна из важнейших дистантных сенсорных систем человека в связи с возникновением у него речи как средства межличностного общения. Слуховая система человека — чрезвычайно сложный аппарат, приспособ-



бленный в основном для восприятия не громких звуков. Несмотря на то, что слуховая система человека представляет собой уникальный и совершенный механизм, возможности ее ограничены при восприятии таких параметров, как звуковое давление, частота, временные интервалы и др.

Сегодня уже более 10% всего населения земного шара по разным причинам страдает нарушениями слуха разной степени тяжести — от тугоухости до полной глухоты. Большую долю занимают внешние воздействия, особенно громкие или усиленные звуки, так как при воздействии на слуховой аппарат громких звуков в течение длительного времени приводит к необратимым потерям слуха (называемым нейросенсорной глухотой), вызванным повреждениями волосковых клеток внутреннего уха. Медицинскими исследованиями установлено, что допустимое время нахождения в зоне повышенного звукового давления различно: для 90 дБ — до 8 часов, для 95 дБ — до 4 часов, для 100 дБ — до 2 часов, для 105 дБ — до 1 часа, 110 дБ — до 30 минут, 115 дБ — до 15 минут, 120 дБ — недопустимое звуковое давление, при котором может произойти повреждение слуха.

Появившиеся мощные системы звукоусиления, которые используются для различных мероприятий (концерты рок, металл и других групп), неизбежно привели к постепенному ухудшению слуха, особенно у молодого поколения, как у слушателей, так и у профессионалов-музыкантов, звукорежиссеров, о чем свидетельствуют многочисленные исследования. На современных концертах, если находиться рядом с звуковым оборудованием, можно получить уровни звука 120–130 дБ.

Последние исследования показывают, что музыка любого рода может приводить к ухудшению слуха, если в течение длительного времени на малом расстоянии от уха создаются звуки с уровнями, приносящими вред слуху. По данным Университета Флориды США, у 14 из 56 студентов, считающих, что их слух нормальный, на самом деле имелось снижение слуха на 15 и более дБ. Исследования показали, что у студентов, которые регулярно слушают музыку в плеере, снизилась способность различать звуки высокой частоты.

Негативное влияние на слуховые органы обнаруживается по сдвигу порога слышимости после того, как они подверглись акустическому возбуждению. Обычно вначале возникает временный сдвиг порога, который исчезает после периода восстановления (период этот может достигать 16 часов). Если ухо подвергается очень длительным или очень высоким и частым акустическим возбуждающим воздействиям, может возникнуть постоянный сдвиг порога слышимости, указывающий на действительное ухудшение слуха.

Слух, являясь одним из значимых органов чувств, очень важен в жизнедеятельности человека. Слух помогает общаться с окружающим миром, качественно обучаться, полноценно развивать интеллект и психику.

В последнее время в России значительно возросло количество людей, которые ежедневно пользуются наушниками, особенно учащиеся образовательных школ и студенты. Частое использование наушников при высоком уровне громкости на улице, в спортзале, в транспорте, неизбежно приводит к ухудшению слуха, о чём свидетельствуют многочисленные научно-медицинские исследования. К сожалению, на электронных устройствах отсутствуют предупреждения о возможных неблагоприятных последствиях для здоровья, в лучшем случае о вреде упоминается в инструкциях. Статистика о прогрессировании снижения слуха неутешительна. При проведении медицинских осмотров врачи констатируют нарушения слуха у детей и подростков. С возрастом эти люди, вероятнее всего, будут вынуждены пользоваться слуховыми аппаратами, поэтому так важно внимательнее изучить эту проблему.

Для обоснования непосредственного влияния использования наушников на слух кратко рассмотрим механизм проведения и восприятия звуковых сигналов.

Звуковая волна проходит в слуховой проход, вызывая колебания барабанной перепонки, которая, в свою очередь, проводит колебания на цепь трех косточек: молоточек, наковальню и стремечко. Механическое колебание передается в улитку, где перелимфа воздействует на волосковые клетки и уже в улитковом ганглие колебания превра-

щаются в электрический импульс. Этот импульс, поступая в центры слуха височной доли коры головного мозга, обеспечивает восприятие звуков. Чем больше сила звуковых сигналов, тем сильнее колеблется перепонка. Ухудшение слуха может возникать при возникновении нарушения одного из этапов проведения звука.

Причин нарушения слуха много, они могут быть как врождённые, так и приобретённые. Но так как в современном обществе возрастает процент ухудшения слуха у современного населения, использующего наушники.

В процессе прослушивания музыки в наушниках при высоком уровне громкости, многие не раз замечали снижение слуха, но не уделяли данной проблеме должного внимания. Безусловно, с возрастом начинается возрастная деградация органов слуха у каждого индивидуально. Однако неутешительные тенденции ухудшения слуховых способностей у молодых лиц не может не вызывать беспокойство.

При постоянном использовании наушников передача звуковых сигналов становится значительно хуже, люди начинают испытывать дискомфорт: шум и звон в ушах, головокружения, нарушение пространственной ориентации, при этом звуки умеренной громкости воспринимаются глухими, сливающимися, сконцентрироваться на отдельном звуке сложно. Поврежденные сенсорные элементы внутреннего уха постоянно посылают нервные импульсы в головной мозг вне зависимости от того, поступает ли на самом деле звук. В результате и возникают ощущения звона и шума в ушах. Этот звук может достигать уровня в 90 дБ. При этом у человека возникают проблемы во взаимодействии с окружающим миром.

Вред от наушников напрямую связан с их функцией по передаче звука, особенно очень громкого. В норме человеческое ухо воспринимает звуки от 10–15 дБ. Если громкость прослушиваемой музыки превышает 60 дБ — возникает дискомфорт. Критичный уровень 80–100 дБ достигать нежелательно. Громкость 130–140 дБ (дискотека или рок-концерт) может привести к появлению боли в ушах или даже к травме. Здоровые барабанные перепонки без ущерба могут

переносить громкость плеера в 110 дБ максимум в течение 1,5 мин. Качество звука также очень важно, поэтому при необходимости использования наушников нужно обращать внимание на качество устройства.

Под воздействием резких ударов звуковых волн барабанная перепонка колеблется с большой амплитудой. Из-за этого она постепенно теряет свою эластичность, и у человека притупляется слух.

Высокий уровень громкости влияет и на другие системы организма. Нарастание звукового сигнала провоцирует стресс. Когда звук нарастает, организм производит много гормонов стресса, например, адреналин. При этом сужаются кровеносные сосуды, замедляется работа кишечника. В дальнейшем всё это может привести к нарушениям работы сердца и кровообращения.

Сегодня ассортимент наушников очень разнообразен, но любые виды музыкальных наушников со временем приводят к ухудшению слуха, однако проведённые исследования свидетельствуют, что наименее опасными для слуха являются накладные полноразмерные наушники. Это достигается наименьшей нагрузкой на барабанную перепонку.

При использовании вставных наушников, максимально приближающих источник звука к внутреннему уху, значительно увеличивается нагрузка на перепонку. В хрящевой части прохода кожа раздражается, что способствует повышенному выделению железами серы. Использование таких наушников не должно превышать 2–3 часа с громкостью до 60% от возможного уровня.

Наличие достаточного количества ушной серы говорит о хорошей работе эндокринных желёз. Ушная сера является защитным барьером слухового прохода и барабанной перепонки. В её функции входит бактерицидная активность, удаление из слухового прохода слущивающегося эпителия, а также предупреждение проникновения внутрь уха из окружающей среды инородных веществ и микроорганизмов. Сера постепенно выделяется из уха во время жевания или разговора, а также выносится наружу вместе с ростом кожи.

Наиболее опасными считаются внутриканальные наушники. При их использовании звуковой

сигнал, минуя ушную раковину, непосредственно попадает в слуховой проход. Вследствие этого, ушная раковина не может способствовать усилению звука, и человек вынужден увеличивать громкость поступающего сигнала сверх нормы. В дополнение происходит обтурация наружного слухового прохода, что препятствует эвакуации серы с микрофлорой из наружного слухового прохода, сера уплотняется, может развиться воспаление. В результате образуется серная пробка. «Меломаны» предпочитают продолжительное время слушать громкую музыку. Звук свыше 90 дБ приводит к поражению и атрофии чувствительных волосковых клеток в улитке, в результате развивается неврит, возможны кровоизлияния в органы слуха. Звуковая волна идет непосредственно на среднее ухо, что приводит к появлению болевых ощущений от любого шума. Вначале погибают волосковые клетки, воспринимающие высокие ноты, поэтому человек не замечает прогрессирующую глухоту.

На сегодняшний день слух снижен примерно у каждого четвертого человека. Поэтому люди, пользующиеся по много часов полноразмерными наушниками в силу своих профессиональных обязанностей (радисты, звукорежиссеры, диспетчеры), в меньшей степени подвергаются радикальному ухудшению слуха, в отличие от поклонников плееров с внутриканальными наушниками. Существует несколько типов наушников:

1. открытого типа частично пропускают внешние звуки, достигая более естественного, «прозрачного» звучания. Несмотря на отсутствие звукоизоляции здесь отсутствует превалирующий бас, «резонансные» призвуки, а само звучание более объёмное, и можно услышать детали, которые не будут слышны в наушниках закрытого типа.

Открытое акустическое оформление оставляет аудиальную связь с окружающим миром. При этом высокий уровень внешнего шума в таких наушниках отрицательно отразится на слышимости звука. К тому же открытые наушники, работающие на большой громкости, могут мешать окружающим.

2. полуоткрытого типа обладают большинством свойств открытых, обеспечивая приличную звукоизоляцию.

3. закрытого типа не пропускают внешний шум и обеспечивают максимальную звукоизоляцию, что позволяет использовать их в шумных средах, а также при необходимости полностью сосредоточиться на прослушивании. Наушники такого типа оказывают наибольшее давление на среднее ухо. В них больше баса, чем в самой записи.

Универсальные критерии выбора наушников — качество звучания и эргономические свойства наушников, которые характеризуют удобство и комфорт эксплуатации изделия в системах «человек — среда — изделие».

У наушников есть еще одно неприятное качество. Человеческое ухо вынуждено постоянно адаптироваться к громким звукам, поэтому со временем приходится постепенно увеличивать уровень громкости, чтобы получить тот же эффект, что и раньше. Кроме того, наушники заставляют слуховой анализатор работать в условиях акустической изоляции, искажая звуковое восприятие внешней среды. Изоляция также усиливает эффект глухоты.

Непосредственный вред наушников не доказан, но есть данные о влиянии на слух громкости, длительности прослушивания музыки, качества её звучания и правильного подбора наушников. Нарушение правил провоцирует возникновение осложнений и даже таких заболеваний как наружный отит. Кроме того, снижение слуховой чувствительности сказывается на психологическом состоянии человека. Привычка постоянно прослушивания музыки рано или поздно ведёт к стойкому мнению, что музыка — всего лишь ненавязчивый фон. В результате падает её значимость в жизни человека. Утрачивается смысл, идея, образы, призыв. Появляется раздражительность, беспокойство, бессонница. При игнорировании подобных симптомов возможно развитие неблагоприятных изменений внутреннего уха.

Важным моментом является выживания человека в наушниках на улицах большого города. Исследованиями доказано, что наушники сужают поле зрения. Это значит, что у человека, идущего в наушниках, боковое зрение почти не используется. Можно сказать, что такие люди нахо-



дятся «в разных измерениях»: тело — в реальном мире, а один из важнейших органов чувств, слух, — в виртуальном, созданном усилиями звукорежиссеров. Эти миры не имеют общих точек приложения, и поэтому мозг не может адекватно оценивать окружающую обстановку. В итоге подобно «раздвоению» можно получить травмы.

Конечно, наушники предназначены не только для развлечения. Многие слушают аудиокниги, занимаясь домашними делами, однообразной работой, в общественном транспорте. А слабослышащим людям наушники просто помогают услышать окружающие звуки. Но не стоит забывать о правилах их использования.

В творческой сфере даже профессиональные музыканты, в зрелом возрасте столкнувшиеся с ухудшением слуха, но при этом владеющие своим инструментом на интуитивном уровне, всё

равно вынуждены ограничить или даже полностью прекратить выступления и занятие музыкой. Например, Фил Коллинз, завивший о завершении своей концертной деятельности из-за прогрессирующего снижения слуха.

Обратимся к одному из авторитетных музыкальных журналов «Rolling Stone», в котором открыто обсуждается проблема глухоты от прослушивания музыки. Специалист-сурдолог сообщает, что без вреда для здоровья можно лишь в течение часа в день использовать обычные наушники с громкостью чуть выше половины от максимальной. Для минимизации неблагоприятных воздействий на слух, поведение и настроение человека необходимо внимательно отнестись к выбору наушников, следовать правилам их использования и обращаться к ним только по крайней необходимости.

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## **Assessing the impact of workplace stress on total cholesterol and low density lipoprotein levels: the example of the application of log-linear analysis in medical studies with small samples**

### **Abstract.**

**Objective:** assess the impact of workplace stress on the lipid profile by using two-dimensional and log-linear analysis.

**Methods:** 118 patients on the basis of inclusion criteria selected from the PROFILE I registry's database. They were divided into two groups, depending on the availability of nervous tension in the workplace: 1 — the presence of stress 2 — no stress.

**Results:** Significant differences in the level of total cholesterol (TC) and LDL-cholesterol (LDL-C) were observed between the two groups (5.1 [4.3, 5.9] vs. 4.5 [3.8, 5.1],  $p=0.01$ ; [2.3; 3.9] vs. 2.5 [2.1, 3.1],  $p=0.04$ ). It is worth noting the absence of statistically significant differences in the groups in statin intake ( $\chi^2=2.48$ ,  $p=0.1$ ). Additional data analysis was done by using the log-linear analysis. The model which was created for the analysis included 5 signs (entrance signs: A-stress, B-physical activity, C-diet, D-statin therapy, and a sign-response: E-achievement of target lipid levels). If the effects of the interaction of pairs of signs regarded as equivalent to the effect of, the hierarchy of these factors contribute to the formation of this model is as follows: 1) sign B (physical



activity) has a major influence on the formation of the model and its contribution averaged 41.65% (40.2–43.1); 2) sign C (diet) was second in importance in the formation of this model and its contribution averaged 30.85% (29.0–32.7); 3) sign D (statins intake) was the third of its importance in the formation of this model and its contribution averaged 19.85% (12.9–21.3); 4) the contribution of the sign A (workplace stress) on the formation of the model averaged 7.55% (5.7–9.4).

**Conclusions:** Stress is a known risk factor for CVD, both directly and indirectly through other factors. The impact of workplace stress on lipid factors was confirmed in this study. But the contribution of stress in the development of a common model was less important than other factors, and its influence revealed through sign's interaction. Conducting a specially-designed randomized clinical trials is expedient to assess the role of stress on lipid factors. Log-linear analysis may be used to decision of tasks in medical studies with a small samples.

**Keywords:** workplace stress, lipid profile, registry, log-linear analysis.

### Introduction

All of us in everyday life are often faced with stressful situations. And as is known, stress is a risk factor for cardiovascular and other chronic non-communicable diseases. The impact of stress factors on the development of the disease is probably related to the time duration and regularity of residence under stress — that is, “exposure time”.

Previous studies have shown that psychosocial factors account for 32.5% of the total contribution of the main factors in the risk of myocardial infarction (MI) in all regions of the world, regardless of age and sex of the patients studied [1]. Daily emotional stress increases the risk of MI more than 2.5 times (OR, 2.81; 95% CI, 2.07 to 3.82,  $p < 0.0001$ ) [2].

Czech scientist F. Blaga studied deceased prisoners of the Nazi camp of Dachau during World War II and studied the role of stress in the development of atherosclerosis. They showed signs of extreme exhaustion that many authors have classified as the term «alimentary dystrophy». At the same time they had a marked development of atherosclerosis with fresh cholesterol deposits in the vessel wall [3; 4].

The opposite results were obtained in the work of Volkova VG et al. Study of the dead residents of besieged Leningrad, were in a state of «alimentary dystrophy», found that they had evidence of resorption of cholesterol deposits and reducing the phenomena of hyalinosis of small arteries [5]. The appearance of differences in the data on the state of the vascular wall in patients in a state of «alimentary dystrophy» can presumably be attributed to the role of heavy painful stress tension.

Thus, the study of the effect of stress on lipid factors has particular interest.

### Objective

The aim of this study was to assess the impact of workplace stress on the lipid profile by using two-dimensional and log-linear analysis.

### Methods

Database of Profile I registry was used for this analysis. PROFILE registry is a registry of patients of one of the divisions of the National Research Center of Preventive Medicine (NRCPM MoH) — department of preventive pharmacotherapy. All patients who applied to the Department for the purpose of consultation or participating in observational clinical trials sequentially turned to the PROFILE registry. The methodology of creating a registry has been described previously, and it can be found in previous publications [6; 7].

Patients who appealed to the department of preventive pharmacotherapy during the period from May 1 to December 31, 2011 were included in this study. Everyone who appealed during this period has been granted a specially designed questionnaire, which allows us to estimate the presence of nervous tension in the workplace, qualifying by patient as everyday stress. The questionnaire also provided an opportunity to evaluate the use of cholesterol-lowering drugs — statins (regularly, no, irregularly). Registration card filled in for each patient applied for this period by the results of inspection and survey. Registration card included clinico-anamnestic and anthropometric data, the results of clinical, laboratory and instrumental studies, as well as data from a survey of patients.

Inclusion criteria were as follows: the employment at the time of the study, the availability of data of presence of stress in the workplace, the availability of data of statin intake, the availability of data of investigation on lipid profile in the registration card.

Criteria for target lipid levels in this study were adopted for people with moderate cardiovascular risk (SCORE scale < 5%): — total cholesterol <5 mmol/L (<190 mg/dL) — LDL cholesterol <3 mmol/l (<115 mg/dL) [8].

All patients signed informed consent to participate in the study and the questionnaire was approved by the Independent Ethics Committee of NRCPM. Blood tests for cholesterol and its fractions were carried out in the laboratory of NRCPM in the day of patient's appeal.

#### Statistical analysis

Statistical data processing was performed using software package Statistica 6.0 (Statsoft). Data are presented as median and interquartile range or the true number and% of total patients.  $\chi^2$  criterion was used to compare the groups on the basis of quality. U-Mann-Whitney test was used to compare two independent groups by quantity.

Differences were considered statistically significant at  $p < 0,05$ . Log-linear analysis was applied for additional data analysis. Log-linear analysis allows to determine value of the impact of analyzed signs to sign-response (which was adopted for the achievement of target lipid levels).

#### Results

Data of 118 patients were valid for the final analysis. The scheme of selection of the patients is shown in Figure 1.

Patients were divided into two main groups based on the presence of nervous tension in the workplace, qualified by the patient as an everyday stress: 1 — presence of stress, 2 — absence of stress.

Main clinical, anamnestic and nosological characteristics of these groups are shown in Table 1. Comparison of these groups carried out on lipid profile (see Table 2).

Differences in the level of total cholesterol (TC), LDL- cholesterol (LDL-C) and triglycerides (TG) were marked between the two groups: all indicators of lipid profile in patients who had daily nervous strain in the workplace were higher than in patients who didn't have it (see Table. 2).

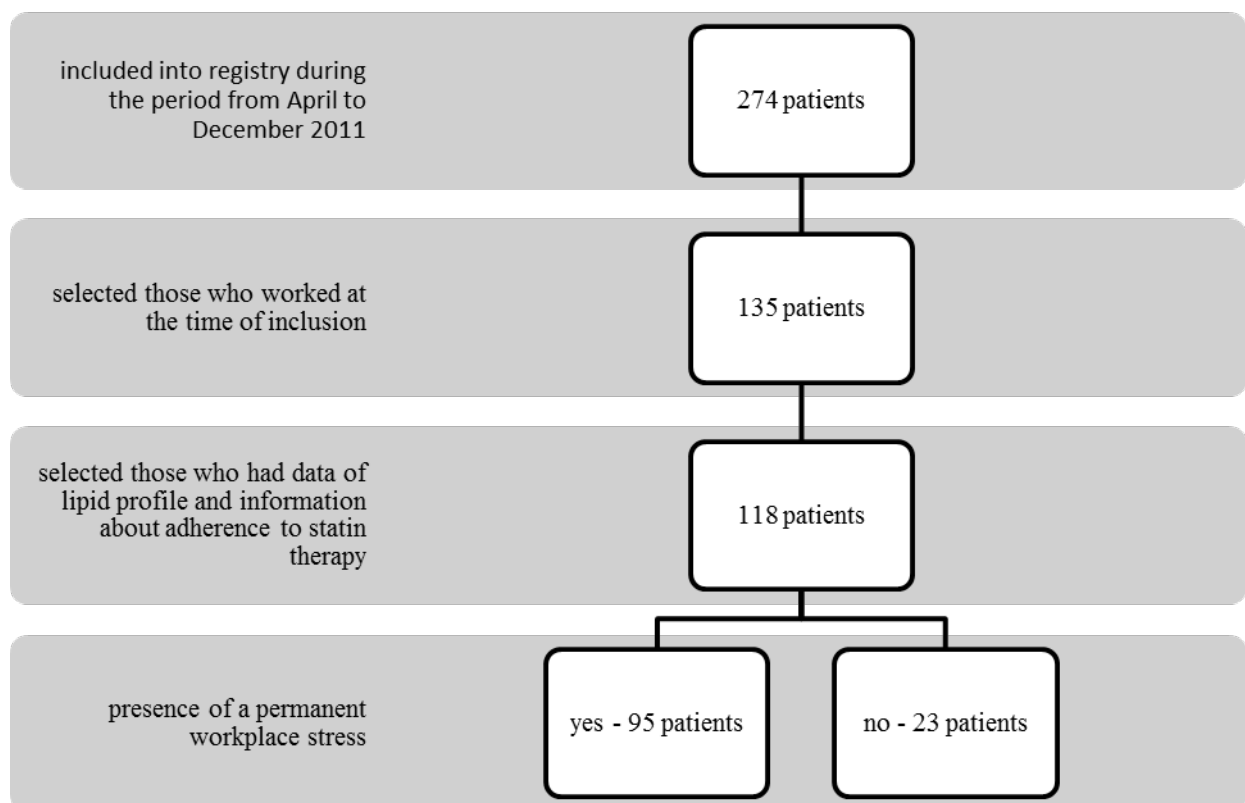


Fig.1. Scheme of patient's selection

Table 1. – The main characteristics of groups

Sign	Group 1: presence of stress (n=95)	Group 2: absence of stress (n=23)	p-level
Age	60,0 [53,5; 66,0]	66,0 [59,0; 70,0]	0,04
Male	53 (55,8%)	16 (69,5%)	0,14
High education	84 (88,4%)	21 (91,3%)	0,98
Smoking	13 (13,7%)	2 (8,7%)	0,76
Body mass index	27,9 [24,8; 30,5]	27,5 [25,2; 30,0]	0,87
Arterial hypertension	73 (83,1%)	18 (78,2%)	0,89
Diabetes mellitus	12 (12,6%)	2 (8,7%)	0,86
Coronary artery disease	19 (20,0%)	12 (52,2%)	0,01
Atrial fibrillation	15 (15,8%)	6 (26,1%)	0,39
Regular intake of statins	42 (44,2%)	15 (65,2%)	0,12

When using the statistical analysis the reliable differences were registered only for the TC and LDL-C levels (see Table 2, Figure 1 and 2). It is

worth noting the lack of statistically significant differences in groups on the fact of statins intake ( $\chi^2 = 2,485$ ,  $df = 1$ ,  $p = 0,12$ ).

Table 2. – Comparative characteristics of groups by lipid profile

Sign*	Group 1: presence of stress (n=95)		Group 2: absence of stress (n=23)		p-level
	Mean (St. D.)	Median [Lower; Upper]	Mean (St. D.)	Median [Lower; Upper]	
TCH	5,17 (1,19)	5,10 [4,30; 5,90]	4,45 (0,90)	4,48 [3,80; 5,10]	0,01
LDL	3,20 (1,01)	3,06 [2,31; 3,92]	2,72 (0,82)	2,53 [2,13; 3,16]	0,04
VLDL	0,70 (0,38)	0,62 [0,46; 0,81]	0,63 (0,28)	0,62 [0,40; 0,78]	0,68
HDL	1,21 (0,31)	1,17 [1,01; 1,36]	1,21 (0,27)	1,22 [1,01; 1,39]	0,89
TG	1,44 (0,73)	1,31 [0,90; 1,69]	1,31 (0,63)	1,12 [0,84; 1,69]	0,42

\* TCH — total cholesterol; LDL — low density lipoproteins cholesterol; VLDL — very low density lipoproteins cholesterol; HDL — high density lipoproteins cholesterol; TG — triglycerides

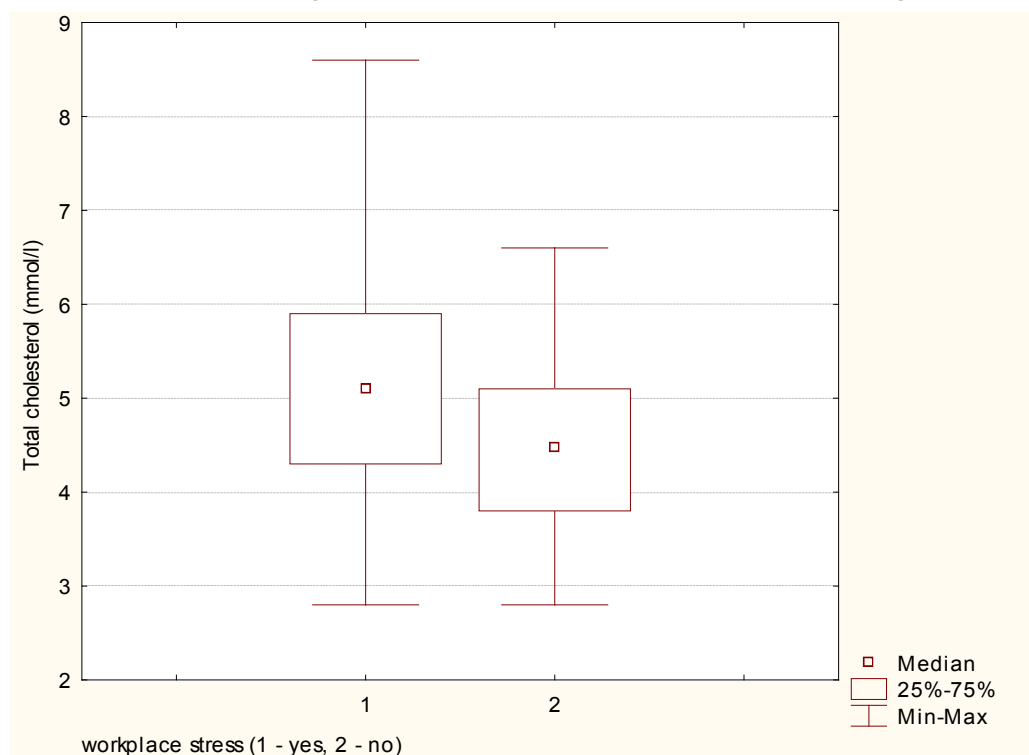


Fig. 2. Differences in groups by level of TC on the presence of nervous tension in the workplace, qualifying as stress

Log-linear analysis was applied for additional data analysis. Log-linear analysis allows to determine value of the impact of analyzed signs

to sign-response (which was adopted for the achievement of target lipid levels).

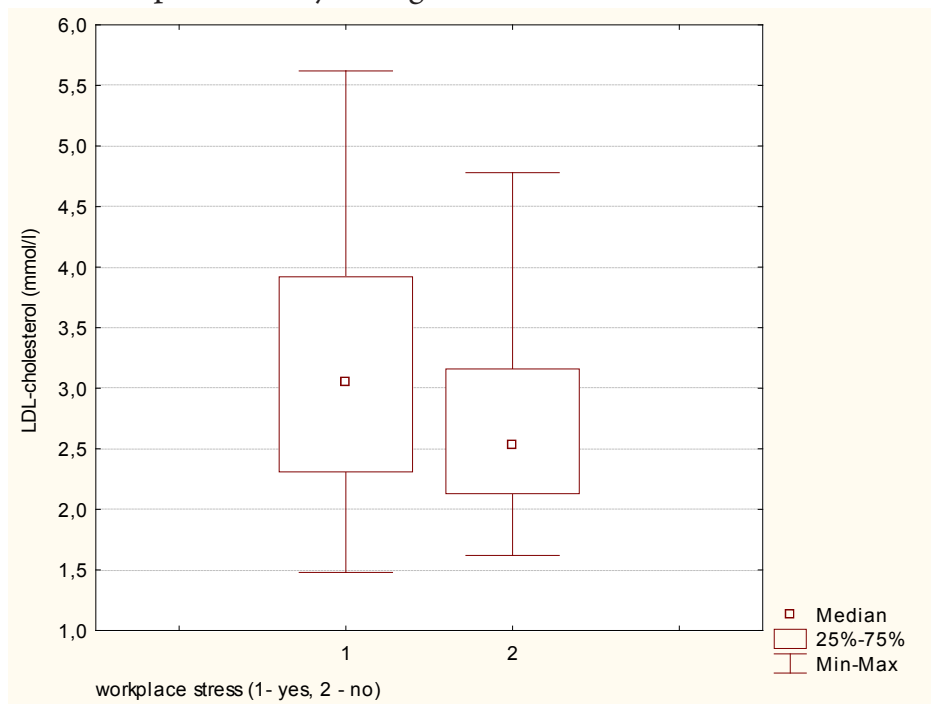


Fig. 3. Differences in groups by level of LDL- C depending on the presence of nervous tension in the workplace, qualifying as stress

The model which was created for the analysis included 5 signs (entrance signs: A-stress, B-physical activity, C-diet, D-statin therapy, and a sign-response: E-achievement of target lipid levels).

Results of log-linear analysis to verify the significance order effects are shown in Table 3. The table shows that the effects of the first and second order are significant, i. e. the effects of all the factors separately and their pairwise interactions.

Table 3. – The results of log-linear analysis: testing the significance of effects of the K-th order

Number of interacting signs	Max.Lik.	Pearson	Probab.
1	129,2276	239,5696	0,000000
2	24,2621	24,3319	0,006767
3	6,5373	5,5579	0,850942
4	2,5424	2,4861	0,778586
5	0,2808	0,2822	0,595253

Optimal model explaining the signs interaction in this study was automatically selected by the program. It was a model including the interaction of AC, BD and DE signs. When analyzing the Test of marginal and partial associations 7 effects were found out significant

and reliable. The effects listed in Prt.Ass. column of Table 4, and based on degree Km effect on the frequency of observation and calculated as  $\Sigma\chi^2 = 146,1$  to all effects. Significant effects of the interaction of factors explain the observed frequency in this study their complex influence.

Table 4. – The results of log-linear analysis: Tests of Marginal and Partial Association

Factor's effect*	Prt.Ass.	$K_m, \%$	Mrg.Ass.
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
A	8,44505	5,7	0,003660
B	58,72299	40,2	0,000000



<b>I</b>	<b>2</b>	<b>3</b>	<b>4</b>
C	42,35201	29,0	0,000000
D	18,90443	12,9	0,000014
AC	5,55800	3,7	0,027543
BD	4,29919	2,9	0,015789
DE	7,99022	5,5	0,002549

\*A — work stress, B — activity, C — diet, D — statin intake, E — target level

If the effects of the interaction of pairs of signs regarded as equivalent to the effect of, the hierarchy of these factors contribute to the formation of this model is as follows: 1) sign B (physical activity) has a major influence on the formation of the model and its contribution averaged 41.65% (40.2–43.1); 2) sign C (diet) was second in importance in the formation of this model and its contribution averaged 30.85% (29.0–32.7); 3) sign D (statins intake) was the third of its importance in the formation of this model and its contribution averaged 19.85% (12.9–21.3); 4) the contribution of the sign A (workplace stress) on the formation of the model averaged 7.55% (5.7–9.4).

### Discussion

Standard statistical analysis of the data based on the  $\chi^2$  test and Mann-Whitney test gave an affirmative answer to the question posed in the study. When carrying out of log-linear analysis were obtained the expected results, but they were ambiguous. One would expect that the D-sign (statins intake) will have a greater impact on the sign-response E.

Basic role in control over achievement of target lipid levels based on the results of this study in these patients belonged to the non-drug influencing factors, namely, regular physical activity and diet. Their joint contribution to achieving the goal was more than 70%. Despite the fact that doctors and patients often believe that statins play a major role in achieving target lipid levels, the contribution of statins therapy was more modest, but it was significant and amounted to a total of about 20%. The contribution of stress in the formation of a common model was even less essential (average about 7.55%) and its influence revealed through sign's interaction.

The obtained interactions of signs AC (stress-diet) and BD (physical activity- statins intake) have also been logically explainable. Interaction of factors of stress and eating behavior is well known in

the medical communities. It has been studying for a long time and described in a number of recent publications [9–12]. This interaction appears reactive eating behavior — anorexia nervosa (typical for sympathicotonic) and bulimia nervosa (typical for vagotonic) are extreme manifestations of it.

The motivation of the patient to lead a healthy lifestyle is the explanation of the of sign's interaction of physical activity and statin's intake. If a person motivated to lead a healthy lifestyle, thus he more strictly observes the guidelines for treatment, including statin therapy [13–16].

Thus, if relations between signs in the model will be changed, they can redistribute a significant impact and have a totally different contribution to the final picture. This probable can be explained such a multidirectional process of atherosclerosis for the residents of besieged Leningrad and prisoners of Nazi camps.

At the same time it is worth noting limitations of this study: the small sample size and selectivity of the surveyed group. But it was devoted to the study of contemporary issues — the effects of stress on ordinary patients from real clinical practice.

If mainly males (especially the military and extreme professions) have been studied in previous studies associated with the effects of stress and the risk of CVD, but recently more and more attention paid to the presence of gender differences in the impact of stress in daily life.

Sloven N et al. showed in their study, that cardiovascular events during 10-year follow-up of almost 40% more likely to be registered in women experiencing a lot of stress at work than their colleagues who noted the minimum level of stress in the workplace [17].

An interesting fact was obtained in this study: that more than 70% contribution to the existence of the relationship between stress in the workplace and the

risk of cardiovascular events could not be explained by the presence of traditional risk factors for CVD.

This study was a part of a ten-year Women's Health Study. In this study were included more than 22,000 women who were health care workers. They were interviewed for the presence of stress at work, including in relation to the intensity and workload requirements, skills and control over decision-making. 170 cases of myocardial infarction, 163 cases of ischemic stroke, 440 cases of coronary revascularization and 52 cases of death from cardiovascular disease have been reported in over 10 years of observation.

The following data were obtained from Cox proportional hazards models: women with high level of stress tension at workplace 38% more likely to have the chance of developing cardiovascular events than their colleagues who reported low level of stress tension at workplace (rate ratio 1.38; 95% CI 1.08 – 1.77).

Similar data are available regarding the influence of nervous tension in the workplace and the risk of hypertension and coronary heart disease in women. The aim of a recent meta-analysis of observational studies on hypertension has been explore whether the effect of emotional stress at work in the formation of arterial hypertension in the future.

The combined relative risk of developing of arterial hypertension, resulting from the analysis of data from all nine studies included in the analysis, was 1.3 (95% CI 1.14 to 1.48;  $p < 0.001$ ), from "case-control" studies — 3.17 (95% CI 1.79 to 5.60;  $p < 0.001$ ), from cohort studies — 1.24 (95% CI, 1.09 1.41;  $p < 0.001$ ) [18].

Preliminary results of the study carried out by Samad Z et al. have shown that there are psychological and physiological differences in how men and women with stable coronary artery disease respond to the impact of stress. The women had mental stress-induced myocardial ischemia symptoms more often than men (57% vs. 41%,  $p < 0.04$ ), but this was not observed no significant differences by gender in the identification of signs of myocardial ischemia after exercise test [19].

In this regard, it is worth noting the presence of another limitation of our study — in this study, we did not put the question of whether there are gender differences in the effects of stress in everyday life at risk for developing of cardiovascular disease. The study was not statistically significant differences between groups studied in relation to nervous tension in the workplace by gender.

### Conclusion

Stress is a known risk factor for CVD, both directly and indirectly through others, in particular lipid factors. The impact of workplace stress on lipid factors was confirmed in this study. But the contribution of stress in the development of a common model was less important than other factors, and its influence revealed through sign's interaction. Conducting a specially-designed randomized clinical trials is expedient to assess the role of stress on lipid factors. Log-linear analysis may be used to decision of tasks in medical studies with a small samples.

Conflict of interests: author declare no conflicts of interest.

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## **Use of stabilized stannous fluoride in the dental diseases prevention in young people**

**Abstract:** The author investigated and presented the literature deals with the use of stabilized stannous fluoride which includes oral care products, their effectiveness of prevention and treatment of common dental diseases.

**Keywords:** stabilized stannous fluoride, dentifrice, dental caries, periodontal disease, dentine hypersensitivity, prevention.

**Introduction.** Nowadays one of the current problem is to preserve dental health of young people, namely keeping children and youth`s teeth healthy, which determines their status in the following age periods [1, 285–287; 2, 52–53]. At present, the degree of prevalence of dental caries and periodontal diseases take the top spot among all dental diseases, they affect about 92–98% of the population of Ukraine [3].

The WHO has available data on the incidence of dental epidemiology and organization of dental services in most countries of the world. It has also highlighted the key ages [3; 6; 12; 15, 35–44, 65–74 years old], at which the survey for the dental status is conducted under special program in different countries. According to the UNO definition, youth is the age group of 16–25. This category also includes students. The WHO states it is not attributed to groups of key epidemiological survey. According to the data of Kytsul Y. S. (2006) and Casas M. J. (2003), maximum morbidity and loss of dental health is still developed at the age of 15–35. Therefore, data on the prevalence and intensity of caries should be included into a group of important parameters for designing methods of prevention and assessment of oral health. It is the prevention which remains a priority and cost-effective way to maintain dental health in terms of economic reforms. The most appropriate option in this case can be a rational oral hygiene with the use of directed action agents that is one of the effective methods of mass and individual prevention of dental caries.

**The aim of the research** was to study the literature, to search and analyze the sources regarding clinical efficiency of treatment and prevention of major dental diseases with agents of oral care, such as toothpastes containing stabilized stannous fluoride.

**Materials and methods.** Literature search has been conducted among the library sources, searching systems PubMed, Google Scholar, Cyber Leninka, as well as electronic archives of domestic and foreign medical publications.

**The results of the study.** Caries and periodontal disease are the most common dental diseases of our time. Studying the causes of high prevalence of dental diseases is a subject of a number of local and foreign scientists` researches [4, 109–117]. The main etiological factors are: oral microflora, nutrition, fluoride contents in water, quantitative and qualitative composition of saliva, overall health, and extreme effects on the body [5, 25–26].

Taking into account that the main cause of dental caries and periodontal tissues disease is a soft plaque — the product of oral microflora, the most effective are preventive methods affecting the cause of the disease. Therefore, the focus of prevention should be directed to individual oral hygiene, aimed at eliminating the causes of oral diseases [6, 2–32; 7, 7–808; 8, 27–30].

Regular individual hygiene provides oral health by 85–90% and is an important component in the prevention of dental diseases [9, 66–69]. After investigation and determining the index of hygiene, it`s necessary to amend it, to manage



an additional training, to recommend specific toothbrushes and to hold the control.

Today toothpaste is the most common means of oral care. Particularly noteworthy are fluoride toothpastes, which usage in 2000 increased by 29.7% throughout the world. In the USA fluoride toothpastes use is 95% [12, 1–9]. In some countries (the Netherlands) to sell toothpaste containing no fluoride is even forbidden.

According to the data, with regular using fluoride toothpastes caries reduction growth is 25–40%. Fluoride in a toothpaste composition shows its effect not only through direct contact with the surface of the tooth — it also accumulates in dental plaque, where *Str. mutans* is known to accumulate, thus compensating the insufficient cleaning the tooth surface.

Both from scientific and practical point of view, tin fluoride is of greatest interest of all fluoride compounds. Tin fluoride is a source of fluoride, endorsed by the US Food and Drug Administration, FDA.  $\text{SnF}_2$  is a single fluoride product with anti-caries, antibacterial and hyposensitive properties able to fight plaque, periodontal disease and caries of tooth enamel [14, 742–748]. The forms of the first products containing  $\text{SnF}_2$  in its composition had several disadvantages: they caused astringent sensation in the patients' mouth and stained teeth enamel into brown or even black, as tin fluoride has a low stability and is easily hydrolyzed. These drawbacks limited the widespread use of fluoride tin for decades. With the advent of new technologies and systems based on dry hydrolysis, the ability to stabilize the divalent tin fluoride (II) in the composition of oral care agents by preventing its hydrolysis, oxidation and avoiding loss of bioavailability, by adding ether of organic acid, appeared. In 2004 Procter & Gamble Company received a licence for stabilizing tin fluoride in the tooth paste by adding sodium hexametaphosphate. In 2005 tin fluoride sodium hexametaphosphate (SFSH) was introduced into the composition of the toothpaste as a separate ingredient to combat surface staining and reduced formation of bacterial plaque [15, 1–4]. By stabilizing tin fluoride with polypyrophosphates, pronounced clinical effect and

antibacterial properties are evident. In this regard, in recent years broad opportunities for the introduction of this compound into clinical practice have been offered [16, 24–28].

It is a combination of physic, chemical and antimicrobial effects of  $\text{SnF}_2$  which is a basis of anti-caries action [17, 122–128]. Stannous fluoride (II) in conjunction with enamel hydroxyapatite  $\text{Ca}_5(\text{PO}_4)_3\text{OH}$  forms more resistant to acidic environment fluorapatite by rapid forming deposits of tin enamel  $\text{Sn}_2(\text{PO}_4)_2\text{OH}$ , which inhibits the superficial demineralization and promotes remineralization of damaged enamel structures. In addition, tin fluoride has an ability to inhibit the activity of cariogenic microorganism *Streptococcus Mutans*. Before the introduction of tin fluoride sodium hexametaphosphate (SFSH) into the toothpaste composition a lot of clinical studies were made confirming the high efficiency of tin fluoride to fight tooth decay. Stookey G. K. with co-authors (2004) conducted a large clinical trial of 955 people to study anti-caries effect compared with early prototype of divalent SFSH toothpaste with positive control of standard feed sodium fluoride with high fluoride content (2800 ppm F) and its low content (500 ppm F). Using clinical and radiographic methods of investigation at the beginning, after 12 and 24 months of use reduction of caries using toothpaste with SFSH by 17% and 25% respectively, and toothpaste with high fluoride content — by 13% and 23%, compared with the control group with low fluoride, was found out.

In the research of mineralization and demineralization *in situ* Wheel J. S. (2002) determines that the bivalent tin fluoride/sodium hexametaphosphate in the toothpaste has an excellent anti-caries action, while hexametaphosphate sodium does not reduce an anti-caries action of tin fluoride.

A series of studies of Pfarrer I. M. (2005) *in vitro* claims on anti-caries potential of tin fluoride due to its absorption and accumulation in the demineralized enamel. In experimental and clinical study of pH-cycle components of tin fluoride/sodium hexametaphosphate toothpastes have a strong protective effect against comprehensive primary demineralized enamel lesions and their subsequent

progression [18, 41–46].

Goriacheva V.V. (2013), in the study of the toothpaste containing stabilized sodium hexametaphosphate stannous fluoride (0.454%) in children older than 12, established the remineralization of demineralized areas of enamel, after a month average index of demineralization lesions, stained with a solution of methylene blue, reached 20 points, DMF index decreased from  $0.9 \pm 0.28$  to  $0.1 \pm 0.05$  ( $p = 0.004$ ).

Foreign researches by Archilla L. (2005), Mankodi S. (2005), Makin [19] show antimicrobial properties of stannous fluoride and its ability to inhibit the metabolism of plaque microorganisms either related to cariogenic or parodontopathogenic oral microflora [19, 3–9]. The antibacterial effect of fluoride compounds is realized due to reducing the amount of organic acids formation by microorganisms, by hindering the regulation of intracellular metabolism and membrane transport impair and the adhesion of microorganisms on the surface of teeth.

The antimicrobial effectiveness of tin fluoride toothpaste has been investigated for its effect on the activity of microorganisms using confocal scanning laser microscopy (CSLM). According to Busscher (2008), the total number of non-vital plaque after using toothpaste with  $\text{SnF}_2$  (0,454%) has become 71%.

Bellamy (2008, 2014) investigated comparative study of antibacterial action of the toothpaste with  $\text{SnF}_2$  and the toothpaste with chlorhexidine. Due to modern method of the digital analysis of the dental deposit (DPIA), which is used for quantitative evaluation of deposit formation in vivo, it has been proved the decrease of dental plaque was in 25,6% by using toothpaste with  $\text{SnF}_2$ , than with chlorhexidine one. It has been known antimicrobial action of chlorhexidine in the toothpaste was decreased or absent that contains sodium lauryl ether sulfate [20, 117–123].

Also Gunsolley J.C. (2006) defined the intensity of stannous fluoride on bacteria metabolism [21, 1649–1657]. Bellamy P.J. with co-author (2014) in randomized clinical research of comparative evaluation of an effectiveness of inhibition of dental

plaque by using toothpaste with fluoride sodium or potassium and toothpaste with stabilized stannous fluoride sodium hexametaphosphate manifested that to use a toothpaste with  $\text{SnF}_2$ /SHMP enamel covering of dental plaque is smaller in 23,0%, than with with  $\text{NaF}/\text{KNO}_3$ .

Eversole S.L. with co-author (2014) compared modern means for teeth cleaning and brushing with stabilized stannous fluoride, sodium, and sodium monofluorophosphate in order to prevent erosions on the surface of enamel, produced in lab conditions at 1% acidic etching by citric acid, potentially dangerous acid that contains in products and drinks. Authors defined that means with stabilized stannous fluoride have increased enamel protection in comparison with other toothpastes [22, 22–28].

Petersson L. G. (2013) determined high activity of toothpaste with stannous fluoride to inhibit the demineralization of the tooth root. Besides,  $\text{SnF}_2$  prevents wedge-shaped defects of the enamel of the tooth neck, during cleaning demineralized surfaces of dentin [23, 1505–1514].

Archilla L. (2005), Boyd R.L. (1994), Beiswanger B.B. (1995), Ciancio S.G. (1992), Chitke U.M. (1991), Mallat M. (2007), Mankodi S. (2005), Perlich M.A. (1995), Tinanoff N. (1989), Williams C. (1997) manifested the influence 0,454% of stannous fluoride on the reduction of dental plaque, gingivitis and gum bleeding and they demonstrated that during three, six, twelve and eighteen months the reduction of gingivitis contains from 20,5% to 54%, dental plaque from 3% to 55%, bleeding gums from 27,4% to 57% (according to author's researches).

Papas A. (2007) in researches manifested high level of an effectiveness of the stannous fluoride in the prevention main dental diseases among 330 people, that suffer from xerostomia or have increased dryness from different reasons (drug-induced xerostomia), and also its ability to remineralize the caries of the root.

Results demonstrated means with stabilized stannous fluoride (sodium hexametaphosphate) which are used daily twice per day, demonstrate the advantages in the reduction of the depth of periodontal pockets, recession, bleeding gums,

and also better indices of caries remineralization in comparison with 3 fluoride triclosan toothpaste. So, saliva content changes due to the increase of acidity in the oral cavity, it causes the risk of caries and leads to candidiasis in patients who suffer from xerostomia [24]. Villa A. and Abati S. (2011) defined xerostomia in 19,6% (117 people) among 601 examined people, that it is manifested by dryness of the mucous membrane of the oral cavity, lips, skin and eyes. It has been established that these symptoms appear with the age and during the intake of drugs and the usage of removable dentures [25, 811–816].

Researches of scanning electronic microscope demonstrated there are dental plaques in dentinal tubules in the result SnF2 reaction with the dentine surface.

White D.J. (2007) confirms SnF2 has the ability to protect open dentinal tubules by chemical precipitation, which prevents its opening at acidic etching in the research in vitro [26, 55–9]. So the mechanism of analgesic action of SnF2 is connected with the obturation of dentinal tubules that excludes the ability to irritate mechanoreceptors that cause the pain during the hyperesthesia. SnF2 toothpaste prevents the uncovering of dentinal tubules in the dentin layer and its softening at acidic factor. Schiff T. (2006), noted in order to achieve clinical improvement of teeth hypersensitivity it is necessary and enough to use toothpaste with SnF2 during several weeks. He T. (2011) in randomized research which was done in China determined and proved the effectiveness of hyposensitized action of toothpaste with fluoride after three days. [27, 46–50]. Such scientists as Qaqish J. and Sharma N. (2014) determined the next factors: according to the tactile sensitivity (Yeaple Probe) and the temperature sensitivity of dentine (Schiff Air Index), during two and eight months toothpaste use with 0,454% SnF2 and 0,32%

NaF/triclosan, in 97 people. Means with 0,454% SnF2 demonstrated high clinical effectiveness of tactile (184%) and temperature sensitivity of dentine decrease (68%) according to the statistic data ( $p < 0,0001$ ), in comparison with NaF/triclosan [28, 13–18].

SnF2 helps to reduce bacteria in the oral cavity that causes bad breath. Halitosis is caused by gram-negative anaerobic bacteria of oral cavity, which are located on the tongue. In the process of decomposition by bacteria of food amino acid, there are different volatile compounds of sulfur. Van den Broek A.M (2007), Farrell S. (2007), Zhang Y (2008), He T. (2010), Nachnani S. (2008) manifested the inhibition of these bacteria by stabilized stannous fluoride causes minimal formation of volatile compounds of sulfur that leads to the breath freshness. [29].

Nowadays there is the market demand to teeth bleaching means and SFSH. It has advantages not only as main dental disease fighter and also it is an effective means in the bleaching of superficial spots at external enamel staining and continued inhibition of new chromogenic adsorption [30, 309–314]. The effectiveness of stained spots on the enamel surface contains 96,6% in researches of vestibular and oral surfaces of the twelfth frontal teeth after two-week SnF2 usage due to clinical evaluation in the modification Loben. In general it is necessary to indicate stannous fluoride sodium hexametaphosphate for oral hygiene has not only advantages to save oral health and also responds to cosmetic needs of patients.

**Conclusion:** Considering peculiarities of ethiopathogenetic and the influence of toothpastes with stabilized stannous fluoride on the development main dental diseases and marked clinical effect there are wide aspects of their usage for caries and periodontal diseases prevention among young people.

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## **Description of the prison social deprivation syndrome: clinical aspects**

**Abstract:** Research prison health correlates of stress lead to the statistically valid conclusion: in a prison social isolation, along with deep mental disorder of convicted person also observed global changes in basic physiological regulatory systems. Changes to such a specific, have been described as independent syndrome, called by us the syndrome of prison social deprivation.

**Keywords:** prisoners, prison social deprivation, penitentiary stress, maladjustment.

As you know, the conditions of detention of prisoners in the penal system are characterized by strict regulation of behavior, coupled with the continuous influence of criminal society, restriction of freedom — social deprivation, isolation from family and convict the usual social environment of existence.

Influenced by significant strength and duration of internal and external stimuli, or more precisely, under chronic stress are consistently condemned in all its development stage adaptation syndrome. And if in the life around us influence of external stimuli on the body are often short and ends, mostly, his functional rehabilitation on some new level

when adaptive resources of the organism again as balanced, the conditions of prolonged stress reaction reserve of protective forces gradually depleted with followed by disruption of compensatory possibilities and alteration of target organs. If short-term stress response is a protective adaptive, or eustress, mobilizing the body to overcome the obstacles to achieving the vital biosocial goals, in a brief but heavy or, on the contrary, a long and continuing influence, called distress, it is transformed into its opposite — pathogen factor leading to the breakdown of the compensation and the formation of psychosomatic diseases.

The human body is dynamically balanced on the basis of neurohormonal mechanisms for self-regulation, functional system, becomes labile phase of short-term exposure to external stress factors, achieving homeostasis through change adaptation strategies of interaction of the subject with the external environment. In this primary response to an external stimulus Biosystems first nonspecific ultimately always specific and is a multistage reaction system for complex external environmental influences, the nonspecific and specific adaptation units are a single functional mechanism of defining typology response in accordance with external exposure. According to R. M. Baevsky [1], these changes are the result of an adequate response of the autonomic nervous system — a multi-level and self-regulatory system homeostasis, where each level has a self-regulating ability to influence downstream or upstream segments of the downlink (forward) or upward (reciprocity) type.

Long and continuous stress, first transiently then stably affects the mechanisms of self-regulation of the autonomic nervous system, leading to a breach of her jet lag, disintegration nejrógumoralnoj, hormonal system, somatic dysfunction in the central nervous, cardiovascular, respiratory, and other life-support systems, breaking mechanism permeability various tissue barriers disorganization of connective tissue, secondary immunodeficiency. According to K. V. Sudakov [2], against the background of distress observed summation of pathological changes, it becomes a prerequisite for the formation of irreversible consequences, and somatic disorders. These are

generally the basic pathophysiological mechanisms that accompany the psychological stress penitentiary in prison.

The penitentiary science topic of social deprivation and stress penitentiary devoted quite a lot of research. It should be noted that the number of these materials is growing from year to year and reveals new aspects of the problem.

Research carried out previously allow us to make a statistically valid conclusion: in conditions of social isolation prison along with deep psychopathy of the convicted person for the first time are also observed and global changes of basic physiological regulatory systems. Changes to such a specific, have been described independent syndrome, called by us the syndrome of prison social deprivation.

Developed using the methods of correlation, variance and regression analysis algorithm, during which analyzes heart rate variability and the immune status of the body of a teenager, allows a high degree of certainty to diagnose the presence of this syndrome.

In this context it is very difficult problem of the formation on the basis of expressed maladjustment syndrome so-called diseases of adaptation — of pathological conditions that develop as a consequence of chronic stress.

We know that social isolation as punishment is triune beginning, viewed from three perspectives, each of which is inseparable from the other two. On the one hand, the violent prison social deprivation — a punitive measure — society response to illegal actions of one of its members. In this incarnation of the punishment of imprisonment it has two functions — deterrence and retribution. However, the problem lies in society to rehabilitate the criminal resocialise it. This is the second component of the prison. Finally, the third objective of punishment — is prevention, prevention of possible new socially dangerous acts.

Those mental suffering experienced by convicted for the first time the teenager in an artificial situation, deprivation, fit into the concept of social retribution, retribution for the crime. But whether they promote re-socialization of the young citizen of Russia, if they help prevent further conflict with the law?

As has been shown in studies, the psychological prison (penitentiary) prolonged stress causes significant dysfunction of the immune, endocrine, nervous and cardio-respiratory systems of preclinical level. Thus, the inmates increase the risk of many diseases in the future: cancer, cardiovascular disease, autoimmune diseases, neuropsychiatric disorders, infectious lesions [3].

As the results of our research, the majority of the surveyed convicts were observed such phenomena characteristic of the syndrome of prison social deprivation as pronounced immunodeficiency, permanent catecholamine “storm”, “burnout” adaptation reserves of the body, desynchronization of biorhythms.

In such circumstances, in a situation of prolonged, chronic distress of juvenile offenders, the preservation of their health — it is a truly titanic and often an impossible task for prison doctors. The best solution here would be an elimination of deprivation situation as a cause of the disease state of the young man. But it is just impossible to do.

Carrying out earlier in one educational colony comprehensive research that addresses psychological, physiological, immunological, hormonal, and other characteristics of the pupil allowed to make one more important step to understanding the essence of psycho-physiological state in which the person under artificial prison deprivation [3].

The fundamental difference between our proposed methodology for assessing the stress of prison is that it is based on objective data (heart rate variability, immunological characteristics, etc.), giving less importance to subjective factors — in particular, the complaints of patients [18; 19; 20]. This is not least due to the fact that in the penal system, in most cases doctors have to deal with antisocial personalities are often prone to simulation, aggravation and lies. Recall that, for example, specified in the ICD-10 Chronic Fatigue Syndrome is placed on the basis of complaints of the patient, in the event that a person, in addition to debilitating fatigue, there are at least four of the following symptoms: 1) muscle pain; 2) pain in multiple joints; 3) unrefreshing sleep; 4) discomfort after physical or nervous and mental load of more than 24 hours; 5) violation of short-term memory or concentration; 6) signs of inflammation

of the mucous membrane of the throat; 7) neck pain or axillary lymph nodes. As seen from the above, the proposed criteria are highly subjective (anyway — the first five), and offer ample opportunity for cheating the doctor stating the purpose of the false diagnosis of “chronic fatigue syndrome”.

The application of criteria based on the measurement of parameters of heart rate variability and data immunograms, can completely eliminate the subjective factor. However, to rely only on these criteria — would be to neglect the classical canons of propedeutics, principles of differential diagnosis. Therefore, in each case it is important to determine — whether the changes in the regulatory systems are a direct consequence of the psychological experiences associated with the presence of a person in a prison or what they are due to, or other factors (severe organic damage, infection, disease of the cardiovascular system, tuberculosis, HIV, drug addiction, etc.).

It should be emphasized that intervalokardiography — an inexpensive, highly sensitive and simple in execution of a method that is widely used at present in various fields of medicine: from monitoring the health of astronauts in orbit, to forecasting life-threatening conditions of patients in the intensive care unit. The new application of the method under the penal system will undoubtedly be interesting for prison doctors and pediatric therapeutic and prison psychologists.

A role in the diagnosis of prison stress also plays an analysis of the immune system. While currently holding immunograms is still very expensive and very time-consuming diagnostic procedure, it is possible to objectively estimate the premorbid background and make informed choices about the health of the first convicts held in detention.

In general, the main features of the syndrome of social deprivation in prison contingent subordinated MIS can be reduced to the following key points:

- the basis of formation of the syndrome is an artificial social deprivation, implemented in the form of imprisonment; the primary role in the development of the syndrome have psychological stressors;
- pathophysiological basis of a significant increase in serum cortisol, and as a result, improved

metabolism with prevalence of catabolic component intensification energy expenditure, chronic energy crisis, which can be determined by indirect methods of investigation [4];

— for the test condition characterized by specific immunologic changes — the development of immunodeficiency with reactions to the first indicators of nonspecific immunity, T-helper cells, suppressor and natural killer cells [5];

— The condition is characterized as specific changes in the autonomic nervous system — the development of complex physiological rhythms of DS, which is manifested, in particular, a decrease in the relative power of fast and slow waves and a significant increase in the overall proportion of the spectrum is very slow waves in the analysis of heart rate variability [4];

— the inmates found a high proportion of asymptomatic detection of arrhythmias and conduction with a predominance among them combined arrhythmias (atrial and ventricular premature beats) [5];

— there is a high proportion of detection of the virus Epstein-Barr, isotropic to lymphoid tissue [5];

— the probability of developing this syndrome can be calculated using the prognostic indices;

method showed highly informative when testing on the materials independent groups.

However, despite the positive results of the research, it should be emphasized that identified the inmates of the prison of social deprivation syndrome needs further study and comprehensive analysis. This is great interest in issues of its prevalence, the possible ways of treatment and refinement of diagnostic criteria.

As practical recommendations that can be formulated based on the results of the research, we propose the following:

— It is necessary to improve the competence of prison doctors and health workers in recognition of symptoms of stress penitentiary in order to carry out the correction of these conditions with medications, or with the assistance of the prison psychologist and psychiatrist.

— As a measure of prevention is necessary to conduct diagnostic prison stress using non-invasive methods of screening, what, for example, a heart rate variability. The techniques demonstrated highly informative when testing materials for independent groups.

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## Section 4. Physico-chemical biology

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### **Evaluation of the organoleptic characteristics of the dry lactulose and its properties**

**Abstract:** conducting organoleptic characteristics of lactulose. The main distinguishing feature of sensory research is the lack of objective registration results using measuring instruments or means of fixing the results, which however does not exclude the use of technical means improving perceptions or increase the sensitivity or resolution for support functions.

**Keywords:** lactulose, organoleptic characteristics, microorganisms, mass fraction.

Lactulose is a highly hydrophilic material capable of exchanging moisture with the environment. It has energetically unsaturated areas called active sorption sites and are capable of binding one or more water molecules. This substance is actively reacting with water in any conjugation conditions. The structural form of the water molecule itself defines the high reactivity through hydrogen bond formation. The hydrogen bond is characterized by high mobility, so even with a slight change in the parameters of the material interaction with water, noticeable transformation of its properties occurs. In other words, a change in temperature, in atmospheric moisture saturation or in pressure the reciprocal changes occur in the structure and properties of the storage or processing.

Organoleptic evaluation of the goods is the the generalized result of its quality assessment, made

using the human senses. In some cases, organoleptic assessment can draw the conclusion about such parameters as the freshness of raw materials, production process violations is much faster than the instrumental techniques.

When assessing the product the appearance, shape, color, gloss, transparency and other properties are determined first [2].

Among the organoleptic characteristics the quality parameters are those that define consumer properties, i.e. the properties that directly affect the human senses (smell, touch, sight). The most significant of these parameters are taste and odor do not amenable to formal measuring, so their determination is done by experts. When conducting the organoleptic quality analysis it is necessary to comply with certain requirements, including: a

room, devices and materials, and those skilled in the organoleptic analysis.

Under laboratory conditions, organoleptic test should be carried out in a specially equipped room, which should provide the optimal conditions for the analysis. The average size of the room should be 13–20 m<sup>2</sup> (depending on the number of concurrent appraisers). The room should have a constant temperature of + 18–20 °C and relative humidity of 70–75% because the susceptibility of flavor at a temperature above 36 °C is reduced in relation to sour and bitter tastes, and at a temperature below 15 °C against salty taste [1]. The room must be isolated from

extraneous odors that can enter from adjacent rooms and outside, as well as noise and other distractions appraiser during the organoleptic analysis.

For a more detailed study of the production process of dry lactulose solution the organoleptic characteristics of the finished product were evaluated. The research results of organoleptic characteristics of lactulose powder are presented in Table 1.

From an organoleptic analysis (Table 1) it follows that the finished product is a fine powder having high water absorbency. Taste and odor of the product is a sweet and clean, without extraneous tastes and odors. The powder color is from white to light yellow.

Table 1. – Organoleptic characteristics of lactulose powders

Indicator	Characteristics
Appearance and consistency	The homogeneous fine powder.
Taste and odor	Sweet, clean, without extraneous tastes and odors.
Color	White, with a faint yellow shade..

The next stage of research was to study the physical and chemical characteristics of lactulose powders. Physical and chemical methods are characterized by high sensitivity and selectivity, require a small amount of analytes. In many cases, there is no longer need for analytes from the test material, and the whole course of analysis sometimes takes only

a few minutes. [1] Therefore, physical and chemical control can quickly gather the necessary information to evaluate the quality of various products. It enables to determine the level of purity, the presence and type of impurities.

Study results of the physical and chemical indicators of dry lactulose are presented in Table 2.

Table 2. – Physical and chemical properties of dry lactulose

Indicator	The norm	Actual value
Mass fraction of lactulose, %, not less than	75.2±0.2	75.2±0.2
Mass fraction of the rest carbohydrates, %, not more:	25.0±0.2	24.8±0.1
– lactose:		13.1±0.1
– α- lactose;		7.8±0.1
– β- lactose;		5.3±0.1
– galactose		11.7±0.1

Based on research findings the mass fraction of lactulose in the final product was 75.2%, which meets the norm of 75%. Mass fraction of the rest of carbohydrates is 24,8%, which is below the rated value is equal to 25%. The accompanying carbohydrates include lactose, which accounts 13.1% of the mass. Lactose in syrup is presented by α- and β- isomers. Galactose with a mass fraction of 11.7% from the total weight of the carbohydrates in the sample also presents in the solution.

Based on the physical and chemical parameters of dry lactulose, we can conclude that the finished

product meets the quality requirements for dry powders of lactulose [4].

Microbiological indicators can control the process and hygienic conditions of the production. The results of microbiological examination of the final product are shown in Table 3.

According to the results of microbiological tests after the development of dry powders of lactulose it can be concluded that the developed technology allows to produce a finished product that meets the microbiological criteria set out in SanPiN 2.3.2.1078-01.

Table 3. – Microbiological indicators of dry lactulose

Indicator	The norm	Actual value
Number of mesophilic aerobic and facultative anaerobic bacteria in 1 g of the product, CFU, no more than	5000	not revealed
Escherichia coli bacteria in 1 g of the product	not allowed	not revealed
Number mold fungi in 1 g of the product, CFU, no more than	100	not revealed
The amount of yeast in 1 g of the product, CFU no more than	50	not revealed
Pathogenic microorganisms, including Salmonella, in 50 g of product	not allowed	not revealed
S. aureus in 1 g	not allowed	not revealed

In addition to the microbiological studies the research on the content of toxic elements in the products after production was also conducted. The data obtained are presented in Table 4.

The results indicate that the migration of toxic elements in the product is not marked, potentially hazardous controlled chemicals are contained in the product at the concentrations for more than an order of magnitude does not exceed the established norms [3].

Table 4. – Content of toxic elements in the dry lactulose

Indicator	Valid value	Actual value
Lead, mg/kg, no more than	0.5	0.10±0.001
Arsenic, mg/kg, no more than	0.5	0.20±0.001
Cadmium, mg/kg, no more than	0.1	0.04±0.001
Mercury, mg/kg, no more than	0.02	0.01±0.001
Pesticides		
Hexachlorocyclohexane, no more than	0.5	not detected
DDT and its metabolites, no more than	0.05	not detected
Radionuclides		
Caesium-137, Bq/kg, no more than	400	not detected
Strontium-90, Bq/kg, no more than	100	not detected

During the research on the basis of MUK 4.2.1847-04 «Sanitary and Epidemiological evaluation of the shelf life and storage conditions of food» under normal storage conditions (temperature no higher than 24 °C, humidity less than 75%) the expiration date of powders of lactulose, obtained by spray-drying were determined.

Analysis of the obtained results showed that the content of sanitary and indicative and pathogens

test samples are highly reliable because the desired microorganisms (Coliform bacteria, Staphylococcus aureus, Salmonella) in standardized mass product are not found.

Based on these studies we can conclude that the storage in a packed form at a temperature no higher than  $25 \pm 1$  °C and humidity not more than 75%, lactulose in dry form can be stored for up to two years without significant loss of its qualities.

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## Section 5. Physiology

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### **Apoptose der Leukozyten der Kälber bei den Adaptations- und Pathologieprozessen**

**Abstrakt:** Der Artikel enthält die Angaben, die nachweisen, dass die Kennziffer der Apoptose der Leukozyten der Kälber aus den großen Tierhaltungsbetrieben diejenigen der Kälber anderer klinisch-physiologischen Gruppen übersteigen. Die höhere apoptische Aktivität der Blutzellen der neugeborenen Kälber zeugt vom adaptativen Umbau der Homöostase des Organismus verursacht durch den Übergang aus einem Lebensmilieu (Mutterorganismus) in ein anderes (Umwelt). Die Dynamik der apoptischen Aktivität der Neutrophile und Leukozyten der an Misch-Infektionen erkrankten Kälber beweist die scharf ausgeprägte Herabsetzung der Zahl der immunkompetenten Zellen und die Entwicklung des Immundefizits.

**Schlüsselwörter:** apoptose, leukozyten, adaptation

#### **1. Einleitung**

Adaptation ist ein komplizierter und vielseitiger Prozess. Ihre Effektivität hängt von mehreren Faktoren ab, vor allem von der Reaktion der Systeme des Organismus auf die Umwelteinflüsse. Man spricht von drei integrierten Systemen des Organismus und zwar vom Nerven-, Endokrin- und Immunsystem, die Reaktionen des Organismus auf externe Einflüsse kontrollieren und korrigieren.

Das Immunsystem ist für die genetische Unveränderlichkeit des Innenmediums des Organismus verantwortlich. Die vollwertige Aktivität des Systems der Immunabwehr ist durch die Funktionsfähigkeiten der immunkompetenten Zellen einerseits und durch die Intensität ihrer Bildung und des Untergangs andererseits bestimmt.

Gegenwärtig mehren sich Einzelbefunde auf dem Gebiet der Forschung der zentralen Ereignisse im Leben dieser Effektorzellen (Proliferation, Selektion, Migration, Produktion der aktiven Substanzen, Apoptose), so dass bisher noch kein einheitliches Bild für ihren Zusammenhang existiert.

Das erklärt auch die Schwierigkeiten bei der Bestimmung der Rolle der Neutrophile und Lymphozyten für verschiedene physiologische und pathologische Prozesse [1].

Deswegen erscheint die Frage über die Signifikanz der Apoptose der immunkompetenten Zellen des peripherischen Blutes als Kriterium für die Einschätzung des Adaptationsstatus der Kälber in Abhängigkeit vom klinisch-physiologischen Status aktuell.

Die Apoptose oder der programmierte Zelltod ist ein genetisch vorausbestimmter, aber gleichzeitig von verschiedenen Faktoren abhängiger Mechanismus der Aufrechterhaltung der optimalen Zellzahl des mehrzelligen Organismus sowohl in der Embryonal-, als auch Postembryonalperiode bei der Ausführung der Funktionen diverser Spezifika.

Die Mechanismen der Apoptoseauflösung sind kompliziert und ihr vielseitiges Studium dauert an [2]. Aber die Apoptose interessiert die Forscher nicht nur als ein Mechanismus der Aufrechterhaltung der optimalen Zellzahl im Organismus, son-



den auch als ein potenzielles Kriterium für die Einschätzung des Adaptationsstatus bei Menschen und Tieren [3].

Unterschiedene Umweltfaktoren können die Apoptose sowohl induzieren, als auch inhibieren [4]. Unter Berücksichtigung der Tatsache, dass die Äußerung der Krankheiten des Verdauungsapparates und zwar der gemischten Infektionen in bedeutendem Grade von Umwelteinflüssen abhängt, kann man die Beteiligung apoptischer Prozesse bei zahlreichen Krankheiten erkennen. Dabei zeugen diese Prozesse von Umwelteinflüssen auf das Immunsystem und die Wechselwirkung der einzelnen Komponenten innerhalb des Immunsystems und des Immunsystems und anderer Gewebe oder der Mikroorganismen.

Aber die Anwendbarkeit des Apoptoseindex für die Überwachung des Adaptationsstatus der Kälber soll bestätigt werden.

## 2. Das Ziel der Forschung

Das Ziel der Forschung ist es die Signifikanz der Apoptoseindices der Zellen des peripherischen Blutes der Kälber abhängig vom klinisch-pathologischen Status auch bei den gemischten Infektionen des Magendarmtraktes zu bestimmen.

## 3. Material und Methode

In die Untersuchung des Apoptosestatus der neutrophilen Granulozyten und der Leukozyten des peripherischen Blutes wurden Kälber verschiedenen klinisch-physiologischen Status eingeteilt in 5 Gruppen einbezogen.

Die 1. Gruppe (n=48) bildeten klinisch gesunde Kälber im Alter von 3 bis 13 Tagen von Bauerngehöften, bei denen infolge der Laboruntersuchungen und auf Grund der Analyse der epizootologischen Situation latente und persistierende Infektionen ausgeschlossen wurden.

Der 2. Gruppe (n=48) wurden klinisch gesunde Kälber im Alter vom 1 bis 2 Tagen aus Rinderanlagen zugeteilt.

Die 3. Gruppe bestand (n=48) aus klinisch gesunden Kälbern im Alter von 3 bis 12 Tagen aus Rinderanlagen.

Zur 4. Gruppe (n=48) gehörten klinisch kranke Kälber aus Rinderanlagen mit gemischter Infektion des Verdauungsapparates, bei denen die Rotavirus-

und E.coli Infektion mittels Laboruntersuchungen festgestellt wurde.

Die 5. Gruppe (n=48) bestand aus klinisch kranken Kälbern mit gemischter Infektion des Verdauungsapparates aus Rinderanlagen, bei denen die BVD-, Rotavirus und E.coli Infektion nachgewiesen wurde.

Für die Untersuchung der Apoptose wurde die Methode der Einschätzung der strukturellen Veränderungen der Leukozytenpopulationen (Neutrophile und Leukozyten) mittels Lichtmikroskopie verwendet [5].

## 4. Ergebnisse und Diskussion

In Tabelle sind einige Indices der spontanen und mitogen-induzierten Apoptose der neutrophilen Granulozyten und Lymphozyten des peripherischen Blutes der Kälber verschiedener klinisch-physiologischen Gruppen erhalten.

Die Indices der Apoptose der Leukozyten des Blutes der neugeborenen Kälber aus Rinderanlagen (2.Gruppe) waren erheblich höher gegenüber den Kälbern anderer klinisch-physiologischen Gruppen. So liegen die Indices der spontanen Apoptose der Neutrophile der Kälber bei  $559,5 \pm 2,1 \times 10^6$  Zellen/Liter und der Leukozyten  $-310,5 \pm 1,8 \times 10^6$  Zellen/Liter; die Indices der mitogeninduzierten Apoptose der Neutrophile betragen  $1289,64 \pm 19,2 \times 10^6$  Zellen/Liter, der Lymphozyten  $-606,12 \pm 13,3 \times 10^6$  Zellen/Liter. Diese Indices waren um 73,7%, 86,8%, 64,6% und 57,6% höher als entsprechende Indices der klinisch gesunden Kälber im Alter von 3 bis 12 Tagen aus den Rinderanlagen (3.Gruppe). Wir führen das auf die Charakteristika der Neugeborenenperiode, die für die Tiere kritisch ist, zurück. Anders gesagt ist die hohe apoptische Aktivität der Blutzellen der neugeborenen Kälber nichts anderes als die Adaptationsumstellung der Homöostase des Organismus verursacht durch den Übergang aus einem (Mutterorganismus) in ein anderes Milieu (Umwelt). In anderen Lebensbedingungen wirken auf den Organismus des neugeborenen Kalbes neue Antigene ein, was die entsprechende Adaptation erfordert, die die Regulierung der Rezeptoren der immunkompetenten Zellen bedeutet. Die Erneuerung des Rezeptorenrepertoires der immunkompetenten Zellen hat die Eliminierung auf dem Wege der Apo-

ptose der „alten“ immunkompetenten Zellen, auf deren Oberfläche die Expression der in den veränderten Lebensbedingungen unnötigen Rezeptoren nachgewiesen ist, und die Ergänzung ihres Pools durch die Proliferation und Selektion der neuen Zellen zur Folge hat.

Aus dem oben Gesagten kann geschlossen werden, dass in den ersten Lebenstagen die Effektivität der Adaptation des Kalbes als der wichtigsten Bedingung der Lebenserhaltung im neuen Antigenmilieu direkt von der Balance zwischen Apoptose alter und Proliferation und Selektion neuer für die Entwicklung der Abwehrreaktionen verantwortlicher Zellen abhängt.

Wenn aus irgendwelchen Gründen die Proliferation und Selektion der immunkompetenten Zellen unmöglich sein oder im ungenügenden für die volle Adaptation und die Abwehr des Organismus Umfang verlaufen werden, können sich die Kälberkrank-

heiten mit möglichem Letalausgang entwickeln. Aus der Mangelhaftigkeit der Prozesse der Apoptose können die Autoimmunprozesse resultieren. Das wird darauf zurückgeführt, dass erstens eine große Zahl der aktiven Zellen vorhanden ist und zweitens die Apoptosekörperchen nicht phagozytiert werden. Dabei sollte die Phagozytose nach dem Prinzip Feedback eine mäßige Immunsuppression sichern. Geschieht das nicht, greift das Immunsystem die eigenen Gewebe an, was die massive Beschädigung und den Tod des Organismus nach sich zieht.

Der Vergleich der Indices des Apoptosestatus der Leukozyten des Blutes der gesunden gleichaltrigen Kälber, die in unterschiedlichen Umweltbedingungen und bei verschiedenen Tierhaltungstechnologien aufgezogen werden, zeugt von hoher Adaptationsaktivität der Neutrophile und Granulozyten des Blutes der Kälber aus Rinderanlagen gegenüber den Kälbern von Bauerngehöften.

Tabelle. Leukozytenzahl und Indices der Apoptose der Zellen des peripherischen Blutes der gesunden und kranken Kälber (gemischte Infektionen)

Kennwerte	1. Gruppe (n=48)	2. Gruppe (n=48)	3. Gruppe (n=48)	4. Gruppe (n=48)	5. Gruppe (n=48)
1	2	3	4	5	6
Leukozyten, $10^9/\Lambda$	6,62±0,4	9,32±0,7	7,68±0,03	11,85±0,6	10,26±0,7
Neutrophile,%	32,5±1,1	30,0±1,2	28,04±0,6	32,33±1,3	28,0±1,29
Neutrophile, abs.	2,15±0,3	2,79±0,3	2,15±0,02	3,83±0,22	2,87±0,06
Lymphozyten,%	61,0±1,2	56,91±1,3	58,32±0,8	53,33±1,4	51,4±0,78
Lymphozyten, abs..	4,04±0,5	5,5±0,44	4,48±0,44	6,31±0,36	5,27±0,8
SPONTANE APOPTOSE					
Anteil der Neutrophile mit Apoptosemerkmalen,%	0,83±0,01	6,0±0,72	1,93±0,05	1,50±0,04	3,40±0,4
Absolute Zahl der Neutrophile mit Apoptosemerkmalen, $10^6$ Zellen/Liter	55,18±2,1	559,5±2,1	146,97±0,9	177,75±2,3	348,84±1,65
Anteil der Lymphozyten mit fragmentiertem Kern,%	0,44±0,04	3,33±0,81	0,53±0,01	0,50±0,01	0,60±0,02
Absolute Zahl der Lymphozyten mit fragmentiertem Kern, $10^6$ Zellen/Liter	29,44±5,2	10,5±1,8	41,02±0,74	59,25±1,3	61,56±3,6
MITOGENINDUZIERTE APOPTOSE					
Anteil der Neutrophile mit Apoptosemerkmalen,%	2,19±0,11	13,83±1,4	5,95±0,06	7,0±0,55	12,0±0,5
Absolute Zahl der Neutrophile mit Apoptosemerkmalen, $10^6$ Zellen/Liter	145,35±6,3	1289,64±19,2	457,13±1,0	829,5±2,2	1231,2±20,3

<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>
Anteil der Lymphozyten mit fragmentiertem Kern,%	1,38±0,09	6,5±0,77	3,34±0,01	2,66±0,2	2,80±0,90
Absolute Zahl der Lymphozyten mit fragmentiertem Kern, 10 <sup>6</sup> Zellen/Liter	91,95±2,2	606,12±13,3	257,22±2,0	315,21±1,3	287,28±3,34

So liegen die Indices des Apoptosestatus bei Kälbern im Alter von 3 bis 12 Tagen aus Rinderanlagen bei  $146,97 \pm 0,98 \times 10^6$  Zellen/Liter (spontane Apoptose der neutrophilen Granulozyten),  $41,02 \pm 0,74 \times 10^6$  Zellen/Liter (spontane Apoptose der Lymphozyten),  $457,13 \pm 1,0 \times 10^6$  Zellen/Liter (mitogeninduzierte Apoptose der neutrophilen Granulozyten) und  $257,22 \pm 2,08 \times 10^6$  Zellen/Liter (mitogeninduzierte Apoptose der Leukozyten). Diese Werte sind in 10,1, 10,5, 8,8 und 6,5mal höher als die entsprechenden Werte bei Kälbern im Alter von 3 bis 13 Tagen von Bauerngehöften (1. Gruppe).

So liegen die Indices des Apoptosestatus bei Kälbern im Alter von 3 bis 12 Tagen aus Rinderanlagen bei  $146,97 \pm 0,98 \times 10^6$  Zellen/Liter (spontane Apoptose der neutrophilen Granulozyten),  $41,02 \pm 0,74 \times 10^6$  Zellen/Liter (spontane Apoptose der Lymphozyten),  $457,13 \pm 1,0 \times 10^6$  Zellen/Liter (mitogeninduzierte Apoptose der neutrophilen Granulozyten) und  $257,22 \pm 2,08 \times 10^6$  Zellen/Liter (mitogeninduzierte Apoptose der Leukozyten). Diese Werte sind in 10,1, 10,5, 8,8 und 6,5mal höher als die entsprechenden Werte bei Kälbern im Alter von 3 bis 13 Tagen von Bauerngehöften (1. Gruppe).

Der festgestellte Unterschied in den Indices des Apoptosestatus der Leukozyten des Blutes der gleichalterigen Kälber gehalten in unterschiedenen Umweltbedingungen weist darauf hin, dass die Umweltfaktoren die Realisierung des Apoptosepotenzials der Zellen beeinflussen.

Die Apoptose als ein wichtiges Element des Komplexes der Adaptationsmechanismen ändert ihre Dynamik nicht nur im Rahmen der Schwankungen der physiologischen Norm, sondern auch bei der Pathologie.

Die Vergleichsanalyse der Indices der Apoptose der Leukozyten des Blutes der gesunden Kälber im Alter von 3 bis 12 Tagen aus den Rinderanlagen

(3. Gruppe) und der kranken Kälber mit gemischter Infektion verursacht sowohl durch Rotavirus und E.coli, als auch BVD-, Rotaviren und E.coli zeigt, dass bei den kranken Tieren diese Werte erheblich höher sind.

So liegen die Apoptoseindices bei den Tieren der 4. Gruppe bei  $177,75 \pm 2,3 \times 10^6$  Zellen/Liter (spontane Apoptose der Leukozyten),  $59,25 \pm 1,3 \times 10^6$  Zellen/Liter und  $315,21 \pm 1,3 \times 10^6$  Zellen/Liter (mitogeninduzierte Apoptose der Neutrophile und Lymphozyten) um 20,9%, 44,44%, 81,45% und 22,54% höher gegenüber gesunden Kälbern.

Die Werte der spontanen Apoptose der Neutrophile und Leukozyten, der mitogeninduzierten Apoptose der Neutrophile des Blutes der Kälber bei gemischter Infektion verursacht durch BVD-, Rotaviren und E.coli sind in 2,3, 1,5 und 2,7 mal höher als die entsprechenden Werte der gesunden Kälber. Zwischen den Gruppen 5 und 3 bestehen hinsichtlich der mitogeninduzierten Apoptose der Leukozyten keine signifikanten Unterschiede.

Vorliegende Angaben über die Dynamik der Apoptoseaktivität der Neutrophile und Lymphozyten bei Kälbern mit gemischten Infektionen zeugen von der ausgeprägten Abnahme der Zahl der immunkompetenten Zellen.

### **5. Zusammenfassung**

Die Apoptose als eine wichtige Komponente der Aufrechterhaltung von Homöostase des Organismus der Tiere ist bei ihrer Adaptation in den sich veränderten Umweltbedingungen unentbehrlich. Die Realisierung des Apoptosepotenzials der Zellen wird nicht nur von internen (physiologischen Aktivatoren), sondern auch externen (Umweltfaktoren) Faktoren beeinflusst. Die Apoptose tritt als ein physiologischer Prozess auf. Am Beispiel gemischter Infektionen des Magendarmtraktes der Kälber wird gezeigt, dass die Apoptose zugleich eine Komponente der Krankheitspathogenese ist.

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