MAKING SENSE FOR STRESS: FROM HANS SELYE'S ANIMAL STUDY TO THE MOLECULAR PHYSIOLOGY OF STRESS AND ITS PHYSIOLOGICAL CONSEQUENCES ON HEALTH AND WELL-BEING (TO 110-ANNIVERSARY FROM BIRTH OF H.SELYE)

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Key words: stress, stress-related conditions, Hans Selye, brain-gut interactions

Professor Hans Selye (1907, Vienna – 1982, Montreal) is one of the greatest scientists of the 20th century who stood at the cradle of studies of the manifestation of the stress and stress-related conditions. He is often named as father of "biologic stress" concept but he is still unknowing in XXI century to a wide audience. Selye's fate was closely tied to the history of region of former Austro-Hungarian empire where he was born and grow up. He graduated German Medical School in Prague, and later moved to New World where performed his influential investigations at the Université de Montréal (Canada) and where during 35 years he was a scientific mentor of more than 60 MSc and PhD students, including the Nobel Laureate Roger Guillemin (1977) as well as hundreds of visiting scientists from all over the world. H. Selye was author of about 1700 original and review articles, as well as 39 books. The first monograph with the short title "Stress" was published in 1950 in Montreal (Canada) and author supposed "stress" to be a non-specific neuroendocrine reaction of the body on two and more stressors (agents which cause stress) of different nature (physical, chemical, biologic and psychologic). Selye also distinguished three stages of stress response: alarm reaction, resistance and exhaustion and introduce term 'eustress" and "distress". It is important to note that the research of Selye was not limited to stress, but he also worked in the field pharmacology and was first who introduced term "glucocorticoids". However, Selye's groundbreaking work and ideas were done in the time when tools for investigation molecular mechanisms were unknown. His PhD students Yvette Tache and Sandor Szabo followed stress-related research and now they are recognized leading experts in neurobiology of stress and gastroenterology, as well as brain-gut interactions, the role of peptides and growth factors in the underlying mechanisms of stress-related gut dysfunction. These data provided the preclinical groundwork showing potential benefit of blocking corticotropin releasing (CRF) or angiogenesis signaling pathways in experimental models of irritable bowel syndrome. 2017 is the 110th anniversary of his birth which is internationally celebrated and it is good reason to reminder historical lessons of life story and work H.Selye on modern physiology, psychology, and medicine.

THE ROLE OF STRESS IN GERD – WHAT DO WE KNOW?

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Key words: stress, GERD, gastric acid, acid reflux

Various studies evaluated the effect of stress on the gastrointestinal tract. More recent studies have focused on the relationship between stress and reported symptoms of GERD. However, when evaluating these studies, one should consider the stressors used, if the stress is acute or chronic, if the complaints are subjective or objective and, most importantly, the subjects being evaluated. There are a variety of stressors that have been used in these

studies, including white noise, exposure to cold temperature, loud noises and anticipation of stressful situations such as giving a speech. Overall, these stressors result in acute stressful situations. Other studies screened for subjects who experience a prolonged stressful situation such as being primary caregiver to a terminal loved one.

It has been shown that subjects who have been exposed to prolonged life stressors are more likely to complain of symptoms of GERD. One study demonstrated a correlation between discussion of emotionally charged topics and nonpropulsive activity in the esophagus. Another study assessed gastric acid output in relation to personality traits. It was found that subjects who were considered to have a higher level of impulsivity and expressed emotions more freely were more likely to react with an increase in gastric acid output when subjected to stress simulated by a problem-solving session than patients with low level of impulsivity. In fact, subjects with low level of impulsivity reacted to this stress with a decrease in gastric acid secretion. Increased gastric acid secretion has been seen in subjects with a higher tendency towards emotional lability. One study evaluated the relationship among stress, psychological traits associated with chronic anxiety, acid reflux parameters and perceptions of reflux symptoms. The researchers found that stress tasks did not influence objective measurements of acid reflux (total acid exposure, number of acid reflux events and duration of longest acid reflux event). Another significant finding was that reflux patients who were chronically anxious and exposed to prolonged stressful stimuli may be more likely to perceive low-intensity esophageal stimuli as painful reflux symptoms. Therefore, even normal esophageal acid exposure could trigger complaints of GERD symptoms. Also, it is not a specific psychiatric disorder that may be responsible for gastrointestinal distress but the presence of psychological distress that predisposed a patient to have clinical manifestations of GERD.

A study by Naliboff et al. found that 'vital exhaustion', which is a measure of sustained stress symptoms, was most closely correlated with symptoms of heartburn. Fass et al. have shown that acute auditory stress can exacerbate heartburn symptoms in GERD patients by enhancing perceptive response to intra-oesophageal acid exposure. This greater perceptual response is associated with greater emotional responses to the stressor.

EFFECTS OF STRESS ON BEHAVIOUR AND SLEEP

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Key words: stress, glucocorticoid receptor, cortisol, memory, cognition

Psychologists Yerkes and Dodson described already in 1908 the inverted-U shaped relationship between arousal and performance. When the level of arousal heightens, behavioural performance increases but only to a certain point. When the level of arousal, produced by stress, becomes too high, adequacy of behaviour decreases while sleep is affected. Physical and mental performance generally follows the level of circulating stress hormones, in particular the glucocorticoid hormone cortisol. The secretion of cortisol in response to a stressful event triggers a chain of events, ultimately leading to energy for fight-or-flight behaviour. Under non-stressed basal conditions, the level of cortisol follows a circadian pattern: a maximum in the morning, necessary for daily activities, with slowly declining levels during the day, and a trough during sleep. Cortisol binds to two glucocorticoid receptor subtypes: Type I with a high affinity and Type II with a lower affinity for cortisol. There are also differences in brain location between the types. The differences between the two subtypes results in a discrepancy of receptor occupation. During the nocturnal sleep trough all Type I receptors are occupied by the endogenous hormone, while during the morning wake peak Type 1 receptors are fully saturated and Type 2 receptors come into action. The mix of Type I and Type II occupation is also the situation by stressful events. The differential qualities

of both receptors have created a new hypothesis about the cortisol effects on behaviour and sleep (De Kloet et al, 1999; Lupien et al, 2007). Elevated levels of cortisol due to stress have commonly detrimental effects on performance, such as on memory, but it is more than once reported that cortisol could have positive effects on cognition. The Type I/Type II ratio hypothesis suggests that performance by cortisol can be enhanced when Type I receptors are activated. However, when both Type I and Type II receptors are saturated, shifting the ratio towards Type II occupancy, performance and sleep are affected. It is in this way that the double function of cortisol as a sleep/wake–hormone as well as a stress-hormone, can be understood. The hypothesis is now that the inverted-U shaped relationship between arousal and stress at one side and behavioural and cognitive performance at the other, might be explained by the presence of two different types of glucocorticoid receptors.

THE NEUROSCIENTIFIC BASIS OF EVIDENCE-BASED TREATMENTS FOR PTSD – A SELECTIVE REVIEW

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Key words: posttraumatic Stress Disorder , selective serotonin reuptake inhibitors, memory, cognitive behavioral therapies

Posttraumatic Stress Disorder (PTSD) includes a) exposure to a significant traumatic event, b) intrusive recollections, c) avoidant symptoms d) increased physiological arousal or amnesia for the traumatic event). While up to 90% of the US adult civilian population has a lifetime exposure to at least one significant traumatic event, only 8-10% develop PTSD. While PTSD can result in significant morbidity and dysfunction, evidence-based treatments can now be matched with an emerging understanding of underlying neurobiology.

Meta-analysis demonstrates that certain selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) are superior to placebo in attenuating PTSD symptoms. Unfortunately, the effect size is small (0.23), side-effects are common and these drugs may be less efficacious when PTSD results from combat trauma rather than from civilian trauma.

Recurring nightmares of the triggering event contribute to the sleep disturbances that affect some 70% of patients with PTSD. Although available data unequivocally support the efficacy (effect size ~ 1.0) of prazosin, an α1-adrenergic receptor antagonist, it remains underutilized in most clinical settings.

Patients with PTSD are more sensitive to the anxiogenic effects of an intravenously administered 5HT2C agonist or an adrenergic α2 receptor antagonist. This suggests that SSRIs and SNRIs may act by downregulation hypersensitive 5HT2C receptors. Analogously, since presynaptic α2 receptors are inhibitory to efflux of noradrenaline, symptoms of PTSD could be mediated by excessive stimulation of postsynaptic α1 receptors. Prazosin may act to attenuate this stimulation.

Brain regions involved in modulation of emotion, such as the dorsal and rostral anterior cingulate cortices, as well as the ventromedial prefrontal cortex show decreased activity in PTSD, resulting in excessive input from the amygdala, an evolutionarily older brain region dominant in threat responses. Thus, PTSD can be conceptualized as a dysregulation of brain circuits that integrate historical information of a traumatic event (memory) and autonomic responses.

Fortunately, memory storage is not a onetime event but a process repeated with each use of that memory. Retrieval of a memory renders it temporarily available for modification at the cellular and systems level. This principle is thought to underlie several independently developed psychotherapeutic approaches. The observation that recurring, disturbing thoughts of PTSD could be permanently abolished, if the subject's eyes were automatically moving in a multi-saccadic manner while the disturbing thought was

being held in consciousness, catalyzed the development of Eye movement desensitization and reprocessing therapy (EMDR). Analogous neurobiological mechanisms are likely operative in other trauma focused cognitive behavioral therapies (TFCBTs). Indeed, the favorable side effect profile and relatively large effect sizes (~ 1.0) of EMDR and TFCBTs have led to their designation as first line treatments for PTSD, ahead of pharmacological approaches. Available studies show that EMDR and TFCBTs affect memory-driven activation of cortical regions implicated in emotional processing, including the amygdala.

Neuroscience provides a mechanistic explanation for current, evidence-based treatments for PTSD and promises to facilitate developments of additional treatment approaches. Such somatic and psychotherapeutic modalities should be considered part of a balanced, biopsychosocial approach to recovery and rehabilitation for individuals with PTSD.

HOW PATHOGENIC BACTERIA PROFIT FROM YOUR STRESS

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Key words: Crohn's disease, inflammation, Escherichia coli, oligomannose glycans

Crohn's disease (CD) is a life-long chronic disorder characterized by intestinal inflammation. Current treatments for CD are directed towards abnormal immune responses rather than the intestinal bacteria that trigger intestinal inflammation.

Disease-molecular aspects: Adherent-Invasive Escherichia coli (AIEC) bacteria abnormally colonize the ileal mucosa in a subgroup of CD patients. Here we elucidate mechanisms by which clinical isolates of adherent-invasive *Escherichia coli* (AIEC) initially penetrate into the epithelial cell layer, replicate, and establish biofilms in Crohn's disease. AIEC utilises the type-1 fimbrial fimbrial FimH adhesin to bind to oligomannose glycans on the surface of host cells. Oligomannose glycans, exposed on early apoptotic cells, are the preferred binding targets of AIEC, so apoptotic cells serve as entry points for bacteria into the epithelial cell layer. Thereafter, the bacteria propagate laterally in the intercellular epithelial spaces. We demonstrate oligomannosylation at 2 distinct sites of a glycoprotein receptor for AIEC, the carcinoembryonic cell adhesion molecule 6 (CEACAM6 or CD66c) on human intestinal epithelia. The presence of the highest-affinity binding target of FimH (oligomannose-5 glycan) on CEACAM6 is demonstrated using LC-MS/MS. FimH interacts with CEACAM6, which then clusters. As mannose-dependence is omnipresent in microbial infections, this mechanism of colonization could also apply to other adherent-invasive pathogens.

Healing from the disease: AIEC can promote or perpetuate chronic inflammation and are therefore an interesting therapeutic target. Various strategies that target these *E. coli* strains have been developed to promote their intestinal clearance. Here, we review current AIEC-targeted strategies, especially anti-adhesive strategies that are based on the development of FimH antagonists. We discuss their potential as personalized microbiota-targeted treatments for CD patients abnormally colonized by AIEC.A large panel of mannose-derived FimH antagonists has been tested for their ability to inhibit E. coli adhesion to host cells. Documented reports suggest that monovalent mannosides are promising candidates

that could represent a complementary therapeutic strategy to prevent intestinal inflammation in the E. coli-colonized CD patient subgroup. Ongoing research continues to improve the pharmacokinetic properties of mannosides, and hopefully, clinical trials will be performed in CD patients in the near future.

THE PATIENT-PHYSICIAN RELATIONSHIP: IT'S HOW MEDICINE SHOULD BE

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Key words: patient-physician relationship, Medical ethics, healing

The patient-physician relationship underpins the essence of what transpires between patient and physician. It has evolved over the centuries from a totally paternalistic one to one of autonomy in the last half of the 20th century and finally to one of shared decision making in the 21st century. Medical ethics requires that both patient and physician share the knowledge available about the patient's illness, treatment and prognosis and then allow decisions for future care to be determined by mutual consideration and respect by both parties.

Clinical medical ethics in the US has been evolving and approaches to multiple patient care problems have taken on great significance as we as physicians comprehend the need for incorporating the elements of ethics into daily medical practice. These elements include: beneficence to the patient, avoidance of maleficence, respect for the autonomy of the parent and fairness and justice. The incorporation of these ethical principles begins with the physician himself manifesting traits of empathy and compassion.

The American Medical Association published in 1847 the "Code of Medical Ethics". It was the first national code of ethics written for its members. In 2017 the AMA has updated and expanded the information needed for all members of the medical profession to follow in their relationship with patients and society. This code of ethics is universal and should be followed by all practitioners of the healing arts.

THE LEVEL OF TUMOUR NECROSIS FACTOR ALPHA IN ACUTE CHOLECYSTITIS, ACUTE APPENDICITIS AND ABDOMINAL TUBERCULOSIS DEPENDING ON THE TYPE OF ADAPTATION REACTION

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Key words: stress, orientation reaction, TNFa, inflammation

It was investigated by Garcavi L. (1987) that stress reaction (SR) is a breakdown of adaptation reactions witch is accompanied by lymphopenia (in blood there are less than 20% of lymphocytes). Another type of nonspecific adaptation reaction is orientation reaction (OR), which has antistressour potential. The OR is characterized by lymphocyte window in blood of 21-27%. Otherwise, tumour necrosis factor alpha (TNFa) is one of the most important immune mediators of inflammation.

To investigate the peculiarities of TNFa blood level depending on the type of adaptation re-

action at the condition of acute abdominal pathology and abdominal tuberculosis.

Peripheral blood serum were analyzed with ELISA for concentration of TNFa preoperatively in the patients with acute cholecystitis (AC) (n=50), acute phlegmonous appendicitis (APA) (n=41), abdominal tuberculosis (AT) (n=30) and in 35 healthy people. The types of adaptation reaction were determined by the lymphocyte count in blood formula: les than 20% - SR: 21-27% - OR.

It was shown by the investigation, that in AC level of TNFa in SR was 15,51 ±1,1 pg/ml, that is 3 times higher ($p<0,05$) than in healthy people (4,97±0,18 pg/ml). In AC whit the OR the level of TNFa was 7,65±0,5 pg/ml, that was 2 times lower than in SR and 1,5 times higher than in healthy people ($p<0,05$). In patients with APA in SR TNFa level was 21,82±1,2 pg/ml and in OR - 11,83±1.1 pg/ml that was 1,8 times lower than in SR ($p<0,05$). In chronic inflammatory process (AT) in SR TNFa level was 12,82±1,0 pg/ml and in OR - 6,31 ±0.4 pg/ml that was also 2 times lower than in SR ($p<0,05$).

Stress reaction is associated with 2 times higher level of TNFa than in orientation reaction. It has been shown that when orientation reaction an immune response is implemented without sings of systemic inflammation.

IMPACT OF PRENATAL PROGRAMMING ON BROWN ADIPOSE STRESS-RELATED CHANGES IN ADULTHOOD

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Key words: Brown adipose tissue, stress, GRO/CINC-1, IL-1β

Brown adipose tissue (BAT) is most obvious in small mammals and infant humans, but was often believed to be lost postnatally within the first few years of the human life. Recent studies using positron emission tomography have demonstrated that healthy adult humans do possess significant depots of metabolically active BAT. Regarding to its significant capacity to control chemical energy, triglyceride and glucose metabolism, BAT could be a potential target for treatment obesity and metabolic syndrome.

Aim: to study the influence of stress and different kinds of high-calorific diet during the prenatal period on adult offspring BAT formation and cytokine activity in experimental animals.

Histomorphological researches of interscapular BAT were estimated in nonlinear rats: control group (intact) and offsprings of mothers which during pregnancy were induced social stress by Pratt N.C., 1989 and following kinds of high-calorific feeding: 1 group - high-calorific diet with chronic introduction of 30% saccharose (by Kozar, 2009); 2 group - high-calorific diet with prevailing of fats (by A. Lintermans, 2009); 3 group - a binary influence of those factors. Serum cytokines was measured using a GRO/CINC-1 (rat) ELISA kit) and IL-1β (rat), ELISA kit («Enzo Life Sciences», UK).

BAT of the animals from control had an ordinary histological structure and serum cytokines level: GRO/CINC-1 - 321±2,85 pg/ml, IL-1β – 28,29±2,06 pg/ml. In the 1 group plural macrovesicle adipocytes among the multilocus cells of brown fat were revealed; GRO/CINC-1 was greater on 56 %, IL-1β – 100 % *vs* to control. In the 2 group appeared separate macrovesicle adipocytes; GRO/CINC-1 – greater on 46 %, IL-1β – on 57 % by comparison to control group. In the 3 group appeared areas of macrovesicular cells and leukocytes perivascular infiltration; GRO/CINC-1 – greater on 99 % l, IL-1β – on 217 % *vs* to control.

Brown fat forming is prenatally programmed. Prenatal stress modulates BAT differentiation and causes pro-inflammatory changes that is the foundation for metabolic disbalance in post-natal period. These findings advanced our understanding on brown fat functioning and provided insight to the role of BAT in metabolic regulation of physiological and pathological conditions.

STRESSFULL FACTORS OF MODERN UKRAINIAN REALITIES IN THE CONTEXT OF DEFICITS OF CHILDREN AND ADOLESCENTS OF THE SCHOOL POPULATION

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Key words: children and adolescents of the population of school age, chronic diseases and mental deficits, permanent neuroemotional tension, stress, mental health.

Health care for children and adolescents, ensuring their proper development, should be one of the key priorities of the development of any society. Unfortunately, at present, Ukrainian children and teens are limited to the basics of healthy childhood. The following stress-related factors are particularly relevant in our society: a significant shortage of communication with parents; parents are destabilized by the present, having little and chaotic boundaries, and therefore do not contribute to a sense of security; inadequate intensification of the educational process with inflexible outdated pedagogical technologies; unbalanced diet and insufficient sleep; hypodynamia; excessive stimulation, technological amusements, which lead to a sense of instant pleasure and produce the need for it; the effect of a military injury (at the national level). Thus, children and adolescents of the population of school age are in a state of permanent neuroemotional tension, stress. This reduces the overall resistance. It is accompanied by an increase in functional deviations, chronic diseases and mental deficits.

Explore the current context of health problems in children and adolescents in a school population that is in constant neuroemotional tension and stress. To analyze features to Ukrainian realities and generalize the system of factors that lead to violations of health and mental deficits.

Scientific materials used in the process of writing theses, scientific publications domestic and foreign authors, personal observation results, clinical studies (inspected 257 children and adolescents of the population of school age during last year), news media reports. The methods by which the materials were processed, compared, scientific generalizations, heuristics, observation.

To achieve real success we should develop those skills that are not available for robots: creativity, imagination, initiative and leadership. By our work, we sought to put our modest footprint into the process of raising the level of mental health of Ukrainian children and adolescents. In consultation with school address family problems should be, above all, to deploy the strategy, «you can do for your child?»

TRANSLATIONAL ASPECTS OF PLACE OF HYDROGEN SULFIDE-RELEASING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON THE TOMORROW'S LANDSCAPE FOR STRESS-ASSOCIATED DISORDERS

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Key words: cytoprotection, stress, non-steroidal anti-inflammatory drugs, VCAM-1, IL-6

Non-steroidal anti-inflammatory drugs (NSAID) are ones of the most widely prescribed drugs in medicine and up-to-date data have expanded their therapeutic role into complex biological processes such as oncogenesis, tissue repair, and different disorders related to aging, despite of dangerous adverse effects which can be fatal (gastrointestinal (GI) bleeding etc). Latest extensive research of multifunctional activities of hydrogen sulfide (H_2S) has proven its potent cytoprotective and vasoprotective, as well as anti-inflammatory effects and developed background of introduction novel NSAID-H_2S-releasing moiety compounds (NSAID-H_2S). Different NSAID-H_2S were created and tested in multicentral investigations (Wallace, 2007-2017) recently.

According to modern views and 11th Revision of International Statistical Classification of Diseases and Related Health Problems (ICD 11), stress is a major pathophysiological factors in several visceral pathologies, including stress-associated GI diseases (SAGID), as stress-associated gastritis, duodenitis, stress-induced ulcer of gastric or duodenal mucosa, therefore, development of effective and safe anti-stress therapies remains an urgent priority. Since histologically stress-associated damage in SAGID look similar, we also predicted that the GI mucosal defence might be also improved by stimulating anti-inflammatory and vasotropic activities. angiogenesis.

In our sets of experiments we tested our hypothesis that NSAID-H_2S: hydrogen sulfide-releasing derivative of naproxen (H_2S-naproxen, ATB-346) and hydrogen sulfide-releasing derivative of aspirin (H_2S-aspirin, ATB-340) vs classical NSAID may results on GI cytoprotective activity. Pre-treatment of NSAID-H_2S in both (single and 2 weeks) administration against stress-related injury inducted by water immersion restricted stress model (Takagi, 1964) results in potent cytoprotective and anti-inflammatory effects which were estimated by histomorphological analysis on esophageal, gastric, intestinal mucosa in the animal models of SACID and serological level of VCAM-1, IL-6 by ELISA. We reviewed here similar and differential age-depended actions of ATB-340 on gastric mucosal defence too. Our recent data also indicate that expression of stress-associated damage was decreased in mesenterium during administration of ATB-340. Hence, NSAID-H_2S are potent, based on endogenously derived agents (stimulation H_2S and elimination cyclooxygenase activities), which are directly associated with mucosal defence against stress injury, in which inflammation seems to be the most important process, they are promised drugs in short future for SAGID treatment after clinical trials.

THE CONDITION OF C-FOS GENE IN THE NEUROSECRETORY NUCLEI OF THE HYPOTHALAMUS IN RATS STRESSED BY LIGHT AND THE EFFECTS OF MELATONIN AND EPITHALON

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Key words: melatonin, epthalon, gene – protein c-Fos, epiphysial hypofunction

The aim was to study the effect of melatonin and a synthetic bioregulator – epthalon for the purpose of correction stress-induced changes of the activity of the gene of "ultraearly response" c-fos in the lateral large cell subnuclei of the paraventricular nucleus (lIPVN) of the rat hypothalamus at different intervals of 24-hour period (in the daytime and at night). The expression of the product of this gene – protein c-Fos – in animals kept under normal conditions of alternating illumination and darkness demonstrated a clear-cut circadian pattern (with a higher level by day). The diurnal index of the c-Fos content in the animal's lIPVN is lower by 33,0%, under conditions of light stress, whereas the nocturnal one approximated to the control values. An injection of melatonin (0,5 mg/kg) to light-stressed animals reflected at 02.00 p.m. hundred by exceeding the index of the c-Fos protein in the animal's lIPVN almost twofold compared to the experimental findings on stressed animals without hormone introduction, as well as by a normalization of the circadian dynamics of the expression of the gene under study. An augmentation of the index of the c-Fos protein concentration was disclosed in the structure upon using tetrapeptide epithalon (0,5 μg/kg) at night in relation to individuals with epiphysial hypofunction without undergoing experimental therapy with epithalon. No such effect was fixed at night.

HELICOBACTER PYLORI SEROPOSITIVITY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Key words: chronic obstructive pulmonary disease, ulcer, stool-test, urease test

Introduction. In recent years serious attention has been paid to the study of extrapulmonary manifestations in patients with chronic obstructive pulmonary disease (COPD), of which combined defects of the gastrointestinal tract are of great concern.

The aim of the investigation was put to the role of COPD in the development of the erosive and ulceral defects of the gastroduodenal area.

Materials and methods. 79 patients were examined. Among them 25 patients without COPD belong to the control group. 26 patients without COPD but with high level IgG Hp consist the second group. And the third group include 28 patients with COPD and erosive and ulcerous defects of gastroduodenal area.

Patients' age fell into the range between 30 and 72.

Patients were diagnosed using PC-based spirometry, fibrogastroduodenoscopy, intragastric pH, Stool-test and rapid urease test of biopsy.

Results . In patients of the 1-st and the 2-nd group we observed the normal range of the spirometry indicators, but the same indicators were reduced in patients of the 3-rd group .

The level of IgG H.pylori in the control group was 0,54±0,05 U/ml, and an esophagogastroduodenoscopy shows only the hyperemia and bulbit.

The level of IgG H.pylori in patients of the 2-nd group was 4,5±0,51 U/ml, at the same time the esophagogastroduodenoscopy also shows the hyperemia and bulbit.

But in the 3-rd group the level of IgG Hp was 4,46±0,43 U/ml, at the same time the esophagogastroduodenoscopy shows the erosive and ulceral defects of the gastroduodenal area in 57,1 cases.

Conclusions. The results of experiment show that chronic obstructive pulmonary disease plays the main role in the development of erosive and ulcerous defects and peptic ulceration.

LECTIN RECEPTORS IN STRUCTURAL COMPONENTS OF PARATHYROID GLANDS DURING THE HYPERPLASIA AND NEOPLASTIC CHANGES

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Key words: lectins, glycoconjugates, parathyroid gland, hyperplasia, tumor processes.

Different origin stress factors lead to the adaptation, compensation or development of the disease depending on their activity. Plasma membrane glycoconjugates play an important role in the reflection of intracellular transformation processes and intercellular cooperation on the development of benign and malignant changes. Its specificity and level of expression reflects the peculiarities of division and maintenance of lectin receptors, which bind with different carbohydrate determinants. The aim of the work was the study of lectin receptors' cytotopography in structural components of parathyroid glands (PTG) on the development of tumor processes. Research was conducted on the bioptatic material of humans aged from 25 to 76 years with hyperplasia (7), adenomas (3) and cancer (1) of PTG, which has been taken during operative treatment on a thyroid gland (TG) or PTG, and on autopsy material of PTG (20) in a norm, which has been taken during the current pathomorphological section according to the basic principles and standards of bioethics in medical research and publishing. The paraplast histological sections with the thickness of 6-7 μm was stained by hematoxylin-eosin for general morphological characteristics. For the detection of glycoconjugates in order to conduct lectinohistochemical reactions the set of lectins was used: Wheat germ lectin (WGA), Peanut lectin (PNA), Ricinus communis agglutinin (RCA), Concanavalin A (Con A), Laburnum anagyroides lectin (LABA), Sambucus nigra lectin (SNA). The WGA, LABA, RCA lectins showed the homogeneous binding with PTG parenchyma in norm and at the pathology. The expression of PNA and Con A lectin receptors increase in the perinuclear zone and on the surface of plasmalemma of parenchymal cells during the development of PTG hyperplasia. The similar expression was manifested with PNA lectin in the parenchymal cells in separate parathyroid lobules that may be evidence of the tumor progression of adenomas. The detected peculiarity – was the formation of large masses of colloid in parenchyma with intense accumulation of WGA lectin receptors (NAcDGlc-specific) and reduction SNA-related sialospecific receptors in structural components of parenchymal cells. Process of malignization is accompanied by the redistribution of PNA lectin receptors from the surface of plasmalemma inside the cells which concentrated in a perinuclear area and subsequent tumor progression correlates with reduction of receptors of this lectin in tumor cells. High expression of lectin PNA is observed in the vascular wall, while it can't be observed in a norm. In the process of malignization the carbohydrate type of tunica intima of blood vessels changes with accumulation of βDGal-specific receptors. It predetermines the loss of intercellular contacts of tumors cells, their invasion in a vascular bed with subsequent possibility of spreading in other organs and tissues.

METHODS TO DETECT STRESS RESPONSE IN BLOOD PHAGOCYTES

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Key words: myeloid blood cells, phagocytosis, stress, autoimmune disorders

The ability of myeloid blood cells, particularly neutrophils and monocyte, to engulf and digest objects constitute the important stress-defense mechanism of the body. These object are both pathogens – bacteria or viruses, virus-infected cells, dying cells and debris. Besides, blood samples can be readily obtained and used to evaluate individual response to stress of particular person and under specific treatments. Both engulfment (phagocytosis) and subsequent digestion of harmful material is needed to accommodate the stress action. The latter process is usually accompanied by activation of ROS-producing machinery aimed to kill potentially harmful pathogens (bacteria).

It is known that inappropriate clearance of apoptotic cells is a primary cause of autoimmune disorders. This defective clearance of apoptotic cells causes secondary necrosis with a release of intracellular content and inflammatory mediators. Rapid cold stress decrease phagocytic activity. Reduced phagocytosis observe in patients with recurrent bacterial skin, wound infections from burns, AIDS etc. Also reduced phagocytic activity of neutrophils was found as a negative predictor for survival of patients with sepsis. At the same time, failure of ROS-producing machinery results in efficient phagocytosis without destruction of pathogens, in organism level resulting in Chronic granulomatous disease (CGD) and related pathologies. ROS-production is critical component of neutrophil activation, followed by production of neutrophil extracellular traps (NETs).

Currently available tests for phagocytosis and activation (often referred as "phagoburst" to reflect respiratory burst of phagocytes) of blood phagocytes usually have drawbacks due to different activity of monocytes and neutrophils to be tested in one tube. The aim of current work was to develop the method for evaluation of the phagocytosis of bacteria by whole blood cells (neutrophils and monocytes) and to access their ability to produce ROS species.

The *Escherichia coli* bacteria that used in the test was opsonized with immunoglobulin and complement of pooled sera. And it showed very good results with neutrophils activation but not with monocytes. Thus, different bacteria strains were tested for their capacity to activate neutrophils and monocytes. It was found that adherent-invasive *E. coli* (AIEC) bind and penetrate into human monocytes-derived macrophages better compared to non-pathogenic bacteria (strain K12) and strain UTI89 causing urinary tract infection. Specific labeling of monocytes allowed to discriminate monocyte response in hyper- and hypoactive conditions. The utilization of the developed approach to test ROS production in neutrophils and monocytes allowed us to test the potential drug candidates aimed to enhance diminished phagoburst activity of blood phagocytes.

This work allowed to develop and optimize an effective method for detecting the phagocytic ability of whole blood monocytes and neutrophils.

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«PROSTIR RADITY» CAMP AS AN EXAMPLE OF THE TREATMENT CONCEPT OF SECURE TRANSITIONAL HOLDING SPACE AND DIGRESSION IN CASE OF PTSD AND GAD

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Key words: anxiety, postraumatic stress disorders, rehabilitation, psychotherapy

Our experience shows that neither clinical nor psychodynamic concepts are sufficient quiet enough for explanation clinical manifestation both of generalized anxiety (GAD) andpostraumatic stress disorders (PTSD).

Existing concepts are not sufficient for planning of integrative treatment too.

This was the reason for the work of own conception.

Because of the lack of satisfactory psychoanalytic understanding and theoretical explanation for clinical and therapeutical experience gained by us in the treatment of PTSD condition, we tried to develop a special kind of psychodynamic setting , named "the SECURE TRANSITIONAL HOLDING SPACE".

Psychotherapeutic project – clinical and psychodynamic oriented – was conducted in 2014-2017 and used as a basis our concept. The purpose of our Project is psychological, physical, and emotional rehabilitation with emphasis on psychotherapy. The basis of psychotherapy is the psychodynamic approach.

"PROSTIR- RaDity": the title has two parallel meanings: one of them literally means "the SPACE of joyful children – the Enlightened Space". The second, metaphoric one – "the SPACE of the RaChildren".

The Psychotherapeutic camp (the Enlightened Space) is located in the Carpathian village of NEDILNA in the Lviv region of Ukraine.

Children aged 6 to 16 come here in groups (min. of 12, max. of 20) – for 12 days.

In total, during 2 years the camp was visited by more than 300 children from different regions of Ukraine.

Prostir RaDity believes in three basic principles for forming of the general setting: RESPECT, SAFETY and TRUST.

Two main results fixed in our Project:

- Traumatic experience becomes less isolated and better integrated into the Ego structures.
- Within our Space, the children learn to better use available resources of the Ego.

A two-year follow-up feedback from children who participated in our project shows that they can well enough "transfer' the obtained experience of our "TRANSITIONAL SECURE SPACE" into everyday life.

ACTION OF HYDROGEN SULFIDE RELEASING 2-MERCAPTOACRYLIC ACID-BASED DERIVATIVE ON NITRIC OXIDE METABOLISM AND OXIDATIVE STRESS IN SMALL INTESTINE OF RATS WITH MEDICATION-INDUCED ENTEROPATHY

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Key words: NSAIDs, sulfur-containing compounds, COX/LOX, H_2S

Small intestinal injury is one of the most commonly appeared pathologies resulting in use of medications such as: nonsteroidal anti-inflammatory drugs (NSAIDs), anti-tumor drugs and inhibitors of angiotensin-converting enzyme (ACE). Taking into consideration the fact that these drugs are widely used for the treatment of various serious diseases, the search of new drugs without any side effects is an important medical and pharmaceutical problem. A new approach in this sphere may be demonstrated by novel sulfur-containing compounds based on mercaptoacrylic acids and thiazolidinones as their synthetic precursors which possessing a dual COX/lipoxygenase (LOX) inhibitory action. The purpose of this study is to evaluate the action of a novel 2-mercaptoacrylic acid-based, possessing dual COX/LOX inhibitory action and able to release H_2S on parameters of NO-synthase system and oxidative stress at the background of drug-induced enteropathy.

The structure of this study and the experimental procedures performed on the animals were approved by the Ethical Committee of Lviv National Medical University. Three types of medications were used to induce enteropathy: indomethacin, a NSAID (35 mg/kg); metothrexate, an anti-tumor drug (10 mg/kg); enalaprile, an ACE inhibitor (2 mg/kg/day). 2-[(4-chlor-phenyl-carbamoyl)-methyl]-3-(3,5-Di-tert-butyl-4-hydroxyphenyl)-acrylic acid (2C3DHTA) was introduced on the background of medication-induced entepopathy (10 mg/kg/day). In the mucosa of small intestine were determined: malonic dialdehyde (MDA) concentration, activity of mieloperoxydase (MPO), superoxide dismutase (SOD), catalase, NO-synthases (NOS).

Administration of indomethacin induced the development of ulcerative lesion of small intestine manifested by erosions and haemorrhages, localised mainly in its distal part. Neither metothrexate nor enalapril caused any visual changes of small intestine surface. It should be pointed out that metothrexate-treated animals were suffering from severe enterotoxicosis manifested by diarrhoea and vomiting. In spite of different mechanisms of their action upon metabolic processes in small intestine, all used medications (indomethacin, metothrexate and enelaprile) caused serious changes of NO-synthase system parameters. Administration of indomethacin and metothrexate caused a rise in iNOS activity. ACE-inhibitor decreased cNOS activity. 2C3DHTA demonstrated a cytoprotective effect: it returned iNOS activity to its control level and increased cNOS activity. Enterotoxic action of studied medication was accompanied by the development of oxidative stress manifested by rise of MDA concentration, activity of MPO was increased. 2C3DHTA reduced MPO activity and manifestations of oxidative stress.

Effects of 2C3DHTA on one hand can be explained by action of H_2S, released from this compound in gastrointestinal system, on the other hand by the dual inhibition of pro-inflammatory enzymes COX and LOX. Thus in our study we showed, that H_2S released from compound 2C3DHTA was involved in mechanisms cytoprotection in small intestine.

LIMIT PHYSICAL ACTIVITY AND STRESS: CORRECTION MECHANISM

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Key words: stress, coagulation, thromboplastin, thrombin-plazmin system

INTRODUCTION

Known that under conditions of stress, including limiting physical activity (like stress model) is activated coagulation system. With this is associated cases of sudden death in athletes. We also know that under the conditions of formation of a large amount of thromboplastin observed damage not only the heart, but all parenchymal organs. According to a new understanding of the role of thrombin-plazmin system (TPS) that the damage is the result of thrombin. TPS operates not only in blood but also in the intermediate connective tissue and cells and regulates the functional and metabolic homeostasis: the significant formation of thrombin it is broken, and with considerable formation of plasmin – restored (Monastyrskyj, 2002). To test this theory, the effect of heparin and fibrinolysin homeopathic (HF) athletes during exercise «to failure».

METHODS

Investigated two experimental group (EG) and control group (CG) runners qualified men 18-20 years in terms of physical activity (PhA). Against placebo control athletes EG 1 before PhA injected dose prophylactic heparin and athletes EG 2 - taking HF. It studied: heart rate variability; indices of central hemodynamics; free radical and metabolic homeostasis parameters; concentration of D-dimer - markers of coagulation and fibrinolysis. Also analyzed the duration and power of physical work «to failure». Results processed statistically.

RESULTS

Is noted positive effects of heparin on duration and load power; circulatory parameters: significant economization, which is manifested in the reduction and chronotropic and inotropic cardiac function ($P < 0.05$), shows the optimization of parameters of metabolic processes to decrease the depth changes homeostasis. Athletes EG single dose HF has led to an increase in total HRV in terms of the total variability (TP) to 33.6% ($P < 0.01$) and decreased stress index (SI, $P < 0.05$), creating a more powerful functional metabolic reserve in athletes EG and reduced the concentration of D-dimers.

DISCUSSION

Effect of heparin due to its anticoagulant effect, because heparin with FN did not lead to verifiable changes in homeostasis, but only if PhA «to failure» accompanied by severe hypercoagulation, and thus form a significant amount of thrombin (Cooper, 2004). Thrombin can cleave other proteins of cells (Morel, 2005), as well as affect other cell processes, including the work of Na+, K+- pump and pH (Kolodzeyskaya, 2004), which is the basis for changes in the structure and function of cells.

CONCLUSION

Thus, heparin leveled the complex enzymatic TPS body equilibrium shift toward the predominance subsystem thrombin caused by excessive physical and emotional stress, a reception HF led to the activation of plasmin and recovery subsystem changes the body's homeostasis and increase its reserves.

INFLUENCE OF HIGH-ENERGY DIET ON ENZYME ACTIVITY OF MAIN COMPLEXES OF MITOCHONDRIAL RESPIRATORY CHAIN AND ACTIVITY OF H^+– ATPASE OF MITOCHONDRIAL INNER MEMBRANE OF RAT HEPATOCYTES

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Key words: mitochondrial functions, metabolic syndrome, non-alcoholic steatohepatosis.

Previously, it has been demonstrated on rats that 20 week high-energy diet (HED) leads to non-alcoholic fatty liver disease development, which was closely correlated with visceral adiposopathy and insulin resistance. Taking into consideration a known fact that hepatocytes contain a large amount of mitochondria (each hepatocyte contains 800 mitochondria which makes approximately 18% of a hepatocyte), researchers have assumed that mitochondrial function is one of the main regulators of lipid in liver [10], and mitochondrial dysfunction contributes to hepatic steatosis development [4,8]. It is repeatedly emphasized in literature, that changes in liver which precede steatosis development as well as attend it, are still unanalyzed. For instance, findings concerning the change of enzyme activity of a respiratory chain and energy-dependent processes in hepatocytes mitochondria are inconsistent. This is the basis for formulation of the research objective [2,5,9].

The objective of this research is to study the enzyme activity of a respiratory chain of mitochondria and activity of H+ATpase of mitochondrial inner membrane of rats hepatocytes under the conditions of a long-term high-energy diet.

The research was conducted on 100 white non-pedigree rats with initial weight of 200-215 g. During a week they received standard food and afterwards were randomly divided into two groups. The rats of the first (control) group received standard food while the rats of the second group were put on a high-energy diet (HED) which consisted of standard forage (47%), sweet concentrated milk (44%), maize oil (8%), and amylum (1%) (diet No. C11024, Research Dietes, New Brunswick, NJ). In 3, 9, and 20 weeks after the beginning of the research, 10 rats were taken from each group for receiving biological material (liver homogenate). Mitochondria, namely their inner membranes, were separated out of hepatocyte fraction and using spectrometric method the activity of NADH-coenzyme Q oxidoreductase, succinate-coenzyme Q oxidoreductase, coenzyme Q-cytochrom C oxidoreductase, cytochrome oxidase, and H+ATpase was determined.

As a result of the research, it was ascertained, that 20 week high-energy diet did not cause significant changes in body weight index in comparison with the group of rats on standard nutrition. However, the mass of visceral lipid of rats on HED increased by 92.3% ($p<0.01$). The activity of main enzymes of respiratory chain of hepatocytes mitochondria was increasing during the research proportionally to the duration of HED. In 20 weeks of HED, the activity of NADH-coenzyme Q oxidoreductase, coenzyme Q-cytochrom C oxidoreductase, cytochrome oxidase increased by 26% ($p<0.05$), 12% ($p<0.05$), and 21% ($p<0.05$) compared to the relative results of the control group. During the experiment, the activity of succinate-coenzyme Q oxidoreductase of rats on HED did not significantly change. At the same time, a gradual suppression of the activity of H+ATpase was determined. In 20 weeks of HED the activity of H+ATpase of mitochondrial inner membrane of rats hepatocytes decreased by 43% ($p<0.05$) in comparison to the relative results of the control group.

Ascertained increase of the activity of NADH-coenzyme Q oxidoreductase, succinate-coenzyme Q oxidoreductase, coenzyme Q-cytochrom C oxidoreductase, and cytochrome oxidase at hepatocytes mitochondria may indicate the increase of electron motion at respiratory chain and increase of hydrogen gradient. The activity of succinate-coenzyme Q oxidore-

ductase was within normal limits, therefore, we may assume that the catabolism processes related to Krebs cycle remained unchanged.

It is known that during the destruction of mitochondrial membrane, the membrane-bound H+ATpase may change its conformational structure and lose its activity. At the same time, the formation of lipidic hyperoxides, which appear during inflammation of mitochondria and are potential isolators, may lead to isolation of the process of coupling of oxidation and phosphorylation. One of the reasons of functional failure of H+ATpase may be oxidation of thiol groups and transformation of lipid microenvironment of enzyme.

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EFFECT OF WHOLE-BODY VIBRATION ON BONE REMODELING

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Key words: vibrations, bone, mineral density, osteoporosis

Chronic mechanical vibrations combined with the physical attributes of the human body can amplify the incoming energy and present the potential for negative health effects. The aim of our study was to determine the effect of vibration oscillations of various frequencies upon the process of bone tissue remodeling.

Experimental research was conducted on 30 pubescent male rats of the weight of 180-220 g. The animals were distributed into 5 groups, 6 rats in each. Experimental animals of four study groups were exposed to heave vibration oscillations of the frequencies of 15, 25, 50 and 75 Hz correspondingly twice a day for 20 minutes, during 28 days. Then we conducted CT scanning of lumbar spine and blood sampling.

Mineral density of lumbar vertebrae of the control group was from 311,90±5,44 to

334,00±8,08 mg/cm^3. Maximum loss of bone mass of vertebral trabecular layer was observed in the III-rd and the IV-th groups of experimental rats, which was decreasing to 12% ($p<0,05$) and 14% ($p<0,05$) correspondingly in comparison with the control group. In the first and the second groups the parameter decreased to the values of ≤ 4% ($p > 0,05$) and 8% ($p<0,05$) correspondingly comparing to control group. Level of osteocalcin in the control group constituted 39,52 ± 0,78 ng/ml. In the first experimental group the rate amounted to 48,55 ± 1,31 ng/ml, in the II-nd and III-rd – rates showed 59,60 ± 1,21 ng/ml and 70,80 ± 1,79 ng/ml correspondingly. In the IV-th group the rate increased twice and constituted 85,75 ± 1,92 ng/ml ($p<0,05$).

Thus, the results obtained by us suggest that with the increase in vibration acceleration >0,51 g (50 Hz, amplitude 2 mm) the velocity of bone tissue metabolism grows. It is accompanied by acceleration of the process of collagen catabolism and loss of bone mineral mass, which further lead to osteoporosis.

FEATURES OF STRESS INDICATORS IN REPRESENTATIVES OF ABNORMAL POLITICAL PARTICIPATION

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Key words: political behavior, stress, mental well-being, young people

The results of preliminary surveys indicated that level of knowledge and understanding of citizens and young people how to engage with authorities and have the opportunity to defend their own interests is insufficient. This leads to using of protest, aggressive forms of political behavior that are not desirable in society.

Heß-Meininger, Barnes, Steinbrecher speak about the existence of types of political participation: electoral; instutionalized activities; non-tradition and abnormal kind of participation, including protests, demonstrations, mitings visiting, which presume a violent nature.

Relying on my research, where I highlighted the emotional, affective component for participants of different types of political activity, the highest rates were found in representatives of abnormal political participation in comparison with other types of political participation.

Decision of participants of abnormal political participation corresponds to high rates of irrationality, instability and affectivity. The dominance of the emotional sphere over all other components of political competence. This indicates that the accepted decision will not necessarily be translated into practical activity. External conditions have a significant impact on it's change.

The dominance of the emotional sphere leads to exhaustion, increases level of stress and vulnerability of the participants psyche.

To avoid unproductive interactions with the authorities and to increase the level of mental well-being of citizens it is necessary to raise the level of cognitive, rational component through civic education and political competence.

EMOTIONAL STRESS IN PATIENTS WITH ACUTE PANCREATITIS

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Key words: stress, anxiety, acute pancreatitis, cortisol

Modern medical science evaluates emotional stress as one of the most serious diseases of our time, which can become the basis of other physical or psychological ailments. A certain level of anxiety is characteristic of a person in general and depends directly on external stimuli, health and many other factors. At the same time, the level of anxiety for each person is individual and is determined by the degree of personal adaptation.

In case of an acute illness, the deterioration of the health status associated with somatic illness, the level of situational anxiety and emotional stress is significantly increased. At the time of hospitalization of such patients on inpatient treatment, psycho-emotional stress and anxiety increase significantly. The maximum critical emotional stresses is found in surgical patients, in particular with acute pancreatitis.

The purpose of the study: to study of the state of the psychoemotional sphere and signs of emotional stress in patients with acute pancreatitis (AP).

The level of situational anxiety in 17 patients with AP, who were treated in the Lviv City Hospital of Emergency Medical Care in 2017 was analyzed. According Atlanta classification (2012) the mild stage of the AP was noted in 6 (35.3%), moderate - in 11 (64.7%) patients. The age of the patients varied from 22 to 62 years.

Two basic questionnaires were used to assess the severity of the symptoms of situational anxiety and stress: the Spielberger-Hanin situational and personal anxiety scale (STAI; State - Trait Anxiety Invertory), which includes a three-step grading of symptoms and the Hamilton scale (NARS). Comparison of the results of the questionnaire data with the level of "stress" hormone cortisol (norm 171.0 - 536.0 nmol/L) were performed.

Manifestations of emotional stress and situational anxiety have been confirmed in 92 % of patients. The following symptoms of anxiety dominated: feelings and excitement (13; 76,5 %); feeling of danger (14; 82,4 %); irritability (16; 94,1 %); sleep disturbance (13; 76,5 %). According to the results of the questionnaire it was stated that the degree of situational anxiety in women was 45 ± 3,2 points, in men 37 ± 4,1 points. Cortisol level correlated with the results of questionnaire: for women - 543.12 ± 154.00 nmol / L, for men - 645.88 ± 323.24. It should also be noted that levels of cortisol were significantly higher in patients with moderate AP due to the severity of the clinical course and severe pain syndrome.

In most of inpatients with AP the problem of emotional stress is important in shaping the general condition of the patient. Correction of the psycho-emotional status of the patient and the treatment of vegetative-somatic manifestations is an obligatory and expedient components in the treatment of this contingent of patients.

LEUKOTRIENE B4 AND PROSTAGLANDIN E2 LEVELS IN PATIENTS WITH NSAID-GASTROPATHY AFTER PANTOPRAZOLE TREATMENT

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Key words: NSAIDs, PPIs, PgE2, LTB4, NSAID-gastropathy

Inroduction. NSAIDs (nonsteroidal anti-inflammatory drugs) are widely used for the prevention of cardiovascular diseases. However, depending on the dose and NSAIDs duration, there may be development of the stomach and duodenum mucosa lesions in the erosions form and ulceration even. Proton pump inhibitors (PPIs) are used to play the main role in preventing adverse effects of NSAIDs, which is called "gastrocytoprotection". Leukotriene B4 and prostaglandin E2 are the most important factors involved in processes of the aggression and protection the stomach and duodenum mucous membrane. In physiological conditions, there is a balance between the production of its arachidonic acid derivatives. NSAIDs appointment in patients with cardiovascular disorders for the thrombosis and embolism prevention leads to cyclooxygenase inhibition by changing the balance between PgE2 and LTB4, in favor of the latter, with further NSAID-gastropathy development.

Aim. The aim of this study was to investigate the impact of pantoprazole on NSAIDs gastropathies healing in patients with coronary heart disease, who took aspirin for a long time.

Materials and Methods. The study involved 70 patients with coronary heart disease, who were hospitalized to the department of Therapy of Lviv Municipal City Clinical Emergency Hospital. There were 41 male patients (58,6%), 29 female patients (41.4%). The average age was 63,5 ± 2,06 years. General clinical examination included the data of past medical history, laboratory tests, FGDS (fibrogastroduodenoscopy), stool-test to determine H. pylori. The endogenous PGE2 serum level have been determed, using ELISA reagent set PGE2 Immunoassay R&D.

According to the study design, there were 2 groups of patients. First group included 37 patients, who have been taking ASA in a dose of 75 mg per day for a long time. The second group included 33 patients which therapy included ASA in a dose 75 mg and pantoprazole 40 mg per day as additional admission. To verify the endoscopic degree evaluation of gastric mucosa destruction with NSAID gastropathies, Lanza score (2009) was used.

Results. Clinical features of erosive and ulcerative lesions in the majority of patients with NSAID-gastropaties were asymptomatic 46 (66%). However, endoscopic examination revealed changes in the stomach and duodenum mucosa. The LTB4 level in patients taking pantoprazole combined aspirin was lower (20 ng/ml) in comparing the patients treated aspirin only (50 ng/ml), $p < 0,001$. After comparing the PGE2 level in both groups, no significant difference in PGE2 level was noted ($p > 0,05$). Hence, the pantoprazole course assignment in patients with NSAIDs gastropathies occurred a significant reduction of LTB4 ($p < 0,01$), without no significant changes in PgE2 content.

Also, it was investigated that the degree of lesions on the Lanza score, was lower in patients taking pantoprazole ($p < 0,01$). The positive correlation between LTB4 level and Lanza score was marked. It means, that increasing of area of gastroduodenal mucosal lesion could significantly correlate with the LTB4 level raising. Thus, could be an important marker for the NSAIDs gastropathy diagnosis. On the other hand, correlation between PGE2 and Lanza score wasn't found.

Conclusion. The pantoprazole action mechanism in patients with NSAIDs gastropathy is associated with LTB4 inhibition, which reduce the erosive ulcerous defects progress.

METHOD OF DIAGNOSIS NONALCOHOLIC FATTY LIVER IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Key words: NAFLD, 13C-MBT, steatosis, steatohepatitis, portal vein.

Introduction. Usually for the determination of nonalcoholic fatty liver disease (NAFLD) there are instrumental and laboratory techniques, including ultrasound, transaminases level, fibrotest etc. These methods in the diagnosis of NAFLD clinical forms is not specific and do not allow make difference between steatosis and steatohepatitis. However, more attention is paid to early diagnosis of NAFLD by using a special set of design formulas biochemical parameters, data Fibroscan or respiratory test with 13C-methacethine (C13-MBT). The determination of NAFLD clinical form is a priority in the prediction of further disease and choice of treatment. Steatohepatitis isan active form of NAFLD and often progresses to fibrosis with subsequent liver parenchyma degeneration into cirrhosis. Simultaneously, steatosis could be possibly treated in the early stages of disease.

Methods. The study involved 65 patients with type 2 diabetes and coronary heart disease with metabolic syndrome, aged 37 to 82 years (mean age 55,82 ± 3,46), 29 men, 36 women. According to the ultrasound, the level of fatty infiltration were differentiated by such criteria as diffuse liver parenchyma echogenicity intensification against the background of a slight increase in its size (liver echogenicity was significantly higher than normal kidney or lumbar muscle echogenicity) for steatosis; hyperechogenicity of liver parenchyma and expansion of portal vein (13 mm or more in diameter) - for steatohepatitis.

Results. For steatosis and steatohepatitis determination the ALT monitoring was used, where the level exceeding 0.68 mmol/l signed to steatohepatitis, and below 0.68 mmol/l - to steatosis. Portal vein diameter size above 13 mm subscribed steatohepatitis, and below 13 - steatosis. 13C-MBT data, which showed the level of liver antitoxic function, was used. 13CO2 range on 120 minute from 15% till 10% was classificated as decreased detoxification liver function means steatohepatitis, range from 20% till 15% - steatosis. The present study found that ALT and portal vein diameter negatively correlated with cumulative dose 13CO2 on 120 minute in patients with steatohepatitis.

Conclusion. Cumulative dose 13CO2 on 120 minute range from 15% to 10% with simultaneously ALT level increasing (more than 0.68 mmol/l) and portal vein diameter enlargement (over 13 mm) are criteria of steatohepatitis.

THE SCREENING OF ADAPTATIONAL POTENTIAL IN PATIENTS WITH SURGICAL STRESS

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Key words: stress, electromyography, pain perception, autonomic nervous system

The degree of stress expressiveness in surgical patients depends on the adaptation reserve of their organisms. That is why we aimed to make a screening of the adaptational potential in stomatological patients with different individually-typological peculiarities under condition of surgical stress.

The objects of clinical observation were 95 surgical stomatological patients. Their individual psychological characteristics were assessed by special questionnaire (S.Novikova, 2007) allowing defining the preference of either sthenic or asthenic manifestations in both emotions and behavior of the pa-

tients. Neurofunctional research was done by electromyography M-TEST. Stress in patients was induced by electrical stimulation of mental nerve till the appearance of pain reaction that was measured by method of exteroceptive suppression of arbitrary activity of masticatory muscles. It was determined: the threshold of pain, its range and tolerance to pain. According to the results of algometry all the patients were classified into 4 pain perception types (PPT). Adaptational vegetative cardiovascular reactions (AVCR) to stress were assessed by the Bayevsky index of functional changes (IFC) = 0,011*pulse rate + 0,014*systolic blood pressure + 0,008*diastolic blood pressure + 0,014*age + 0,009*body weight - 0,009*growth - 0,27.

26 patients with asthenic psychotype in which the threshold of pain and pain tolerance were not high (9,62 ± 2,07 mA and 25,41 ± 1,47 mA respectively) belong to the 1st PPT. In these patients AVCR were unsatisfactory (IFC = 3,35 ± 0,49 points). In patients with 2nd PPT threshold of pain sensitivity was similar to those of the 1st type, but the range proved to be much longer because of the high threshold of pain tolerance – 35,61 ± 0,95 mA ($p < 0,01$). In this group we noticed functional manifestations of stress-induced analgesia accompanied by exertion of adaptation mechanisms – IFC = 2,86 ± 0,14 points. Such PPT was diagnosed in 35 patients with a great prevalence of sthenic features (5,8 ± 1,2 points). High pain thresholds (25,91 ± 2,49 mA) were diagnosed in patients with 3rd and 4th PPT, however, owing to the insufficient activity of endogenous antinociceptive system in the 3rd group the range of pain sensitivity was short – 6,9 ± 1,73 mA ($p > 0,05$). Such PPT was found in 15 patients. They manifested both sthenic and asthenic features during psychological testing, Bayevsky stress index (IFC = 3,48 ± 1,12 points) showed unsatisfactory adaptation of cardiovascular system to stress in these patients. High indicators of antinociceptive system activity were found in patients with 4th PPT including personalities having considerable sthenic characteristics. They showed to have tolerable adaptation of cardiovascular system to stress (IFC - 2,35 ± 0,89 points).

Adaptational potential of patients under stressogenic influence depends on their individually-typological peculiarities, level of antinociceptive system activation and autonomic nervous system condition that should be considered in perioperative medication management.

EMOTIONAL INTELLIGENCE AS RESOURCE OF STRESS-RESISTANCE OF PERSONALITY

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Key words: emotional intelligence, psychology, ielf-motivation, adaptation

Introduction. The concept of emotional intelligence is relatively new in psychology. There are different models of understanding emotional intelligence. In particular, D.Goleman includes into this term ability to self-motivation, resistance to frustration, control over emotional outbreaks, ability to abandonment of pleasure, mood regulation and the ability to think on the background of strong emotions, empathize, and trust. Model of J.Meyer and M.Salovey include mental skills that determine the psychological health of the individual, including his stress-resistance, sustainability and adequacy of self-esteem, activity, ability to effectively plan life steps and, accordingly, manage his own behavior. The above features reduce the potential of victimity and contribute to the growth of personality stress-resistance.

Methods. We conducted a psychological study that examined the level of emotional intelligence of respondents and the presence of different forms of victimal behavior in them. We used the "Questionnaire for emotional intelligence EMIN" D.V.Lucin and the "Test for the determination of propensity to victim behavior" O.O.Andronikova, we aclculated the Pearson correlation coefficient is calculated for the obtained results. The

study was attended by 35 girls aged 17-21 who received a pedagogical education in one of the universities in the city of Lviv.

Results. Statistically significant inverse correlation exists between the level of interpersonal emotional intelligence and the tendency to depend and helpless behavior; between the level of inner personal emotional intelligence and the tendency toward victim aggression, dependent and helpless behavior, uncritical behavior, and the level of victimization implemented; between the indicator of understanding of emotions and the tendency to depend and helpless behavior, uncritical behavior and the level of implemented victimity; between the ability to manage emotions and the level of victim aggression and the tendency toward dependent and uncritical behavior; as well as between the level of general emotional intelligence and the tendency to depend and helpless behavior. The above-mentioned features can be briefly summarized as follows: the higher the indicators are different under the scales of emotional intelligence, the less pronounced is the tendency towards victim behavior that constitutes a threat to the individual and affects their stress-resistance.

Conclusion. The level of emotional intelligence determines the ability to objectively recognize the threat in different situations and increases the potential for confronting various kinds of dangers, in other words, a high level of emotional intelligence reduces the level of victimhood and promotes a constructive socio-psychological adaptation, and thus increases stress tolerance.

THE EFFECT OF TRIPEPTIDE T-34 ON NITRIC OXIDE SYSTEM AND LIPID PEROXIDATION PROCESSES IN STOMACH MUCOSA UNDER CONDITIONS OF WATER-RESTRAINT STRESS IN RATS

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Key words: stress, nitric oxide, NO-synthases, gastric mucosa

Stress was shown to involve multiple systems of human body and the search for safe and effective stress-protective compounds is an actual interdisciplinary task of the uptodate science. Literary data provides increasing evidence on the stress-protective features of the certain regulatory oligopeptides, in particular the tripeptide T-34 (H-Glu-Asp-Gly-OH), although its effect on mucous membranes of gastrointestinal tract is poorly elucidated.

Aim of the study was to evaluate the effect of T-34 on nitric oxide system and lipid peroxidation processes in mucous membranes of the digestive organs under conditions of water immersion-restraint stress (WRS) in rats.

The studies were conducted on white male rats, devided into 3 groups (n=6 per group): 1) control animals; 2) rats, exposed to WRS (5h); 3) rats, intragastrically pretreated with T-34 (10μg) 30 min before WRS exposure. Afterwards the rats were sacrificed under urethane anesthesia. Gross inspection of the mucous membranes of stomach, small and large intestine was performed and in homogenates of the mentioned above organs nitrite anion and thiobarbituric acid (TBA) products content was determined as well as the activity of NO-synthases (NOS). In blood plasma L-arginine concentration was measured.

WRS resulted in the formation of gastric lesions (14.1 ± 1.7 mm^2), accompanied by acute rise of NO-synthase activity ($p<0.05$), in particular its inducible isoform – iNOS ($p<0.01$), increased production of NO and TBA products content ($p<0.05$) in gastric mucosa (GM) compared to control rats. No macroscopically visible changes of the mucous membranes of small and large intestine were noted under conditions of WRS although in small and large intestine mucous membranes homogenates the parameters indicative of nitrosooxidative stress were

also elevated compared to control rats. WRS decreased the concentration of L-arginine, NO precursor, in blood plasma ($p<0.05$). Pretreatment with T-34 caused 27% ($p<0.05$) decrease of GM ulceration area, at that NOS activity decreased for 45% ($p<0.05$), iNOS activity diminished for 60% ($p<0.01$) compared to the effect of WRS. Decrease of NO ($p<0.05$) and tendency to decrease of TBA products content in GM were also noted in T-34-pretreated rats on the background of WRS, whereas L-arginine concentration in plasma increased ($p<0.05$). In mucous membranes homogenates of the small and large intestine of T-34-pretreated rats on the background of WRS the tendency to decrease of NOS activity was found, whereas TBA products content did not change significantly.

WRS induced an acute rise of nitrosooxidative stress parameters in mucous membranes of the stomach, small and large intestine. Tripeptide T-34 exerted cytoprotective effect towards mucous membranes of the examined digestive organs, mediated mainly by the decrease of inducible NOS activity. The effect of T-34 on GM was superior to its action on small and large intestine.

NARCOTIC ANALGESICS: ANGIOPATHIC EYE CHANGES IN RATS

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Key words: eyeball, narcotic analgesics, vascular tunic, experiment

Pain constitutes up to 90% of all patient complaints in primary health care, so effective pain control and proper drug therapy are relevant problems. However, besides the appropriate use of analgesics for pain control, the gross misuse of analgesics a growing epidemic recent years. The prevalence rate of opioid use (at least once a year) is 61.0/ per 1000 adults in the USA and up to 27.0/ per 1000 adults in Europe (RecoveryBrands, 2013). According to the data of UNODC (United Nations Office on Drugs and Crime) total number of individuals using opioids attained 33 million people in 2014.

Modeling of the long-term effect of narcotic analgesics was performed by using a semi-synthetic opioid analgesic Nalbuphine. The study was carried out on 48 mature white male rats aged 3.0-3.1 months and with the body weight 160-180 g. All experimental procedures were approved by the University Animal Care and Use Bioethical Committee. The studies were conducted with application of morphological, in particular, histological, electron microscopy and morphometric methods of investigation; mathematical; modeling the prolonged effect of the opioid. The research material was presented by the specimens of the eyeball vascular tunic, consist of the iris, ciliary body and choroid.

After 2 weeks of injecting Nalbuphine to the rats choroid, ciliary body and iris are clearly differentiated both, in the eyeball vascular tunic of the experimental animal such in the control animal The administration of Nalbuphine to white rats over a 4 week period of time causes the following lesions in the eyes of the rat: in the endothelial and basement membrane of the microcirculation, in the epithelium of the ciliary processes, in the cellular and non-cellular elements of the iris and in the choroid. After 6 weeks of injecting Nalbuphine to the rats there are observed deep destructive changes in the eyeball vascular tunic. Arterioles' walls are thickened due to sclerosis. Thin-walled, elongated venules prevail. Choriocapillar layer is destroyed. Layers of the iris are not clearly differentiated. Ciliary processes are fragmented, epithelium that covers them is disorganized, the processes are thickened, shortened.We have demonstrated changes of restructuring angioarchitectonics of the eyeball vascular tunic which indicates the development of angiopathy, potentially contributing to circulatory disorders of the organ of vision.

As a result of these angiopathic changes we expect a deterioration of visual function in conditions of long-term use of narcotic analgesics. The first signs of impairment of the vascular tunic ultrastructure are noticeable already after two weeks of the experiment. 6-weeks long injection of the opioid causes irreversible destructive changes in the rat's eyeball vascular tunic.

THREE FACTOR MODEL OF ADOLESCENT RISKY BEHAVIOR

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Key words: mental health, risky behavior, adolescents

Adolescent risky behaviors have lately become a reason for considerable concern of mental health professionals as the grounds for why a teenager would consciously and willingly compromise their health and, in some cases, life still remain unclear. Results of multiple researches run in different cultures indicate various reasons for risky behavior and suggest it be a biopsychosocial phenomenon.

Three groups of schoolchildren aged 12-18 y.o. – adolescents that do not practice risky behaviors, adolescents that get engaged into risk from time to time, and adolescents who reported active engagement into multiple risky behaviors – were interviewed for studying their psychological features. The differences between the three groups were so significant that it allowed to conclude that regular engagement into any type risky behavior leads to major emotional, cognitive, psychological, personality, and social levels.

We found out that a wide array of psychological features associated with engagement into risky behaviors falls into three-factor model. The first factor (32,8% variation share) we called 'Negative evaluation' as it comprises features like life unsatisfaction (χ^2 = 0,7409), lost of interest to the environment (χ^2 = 0,6710), irritability (χ^2 = 0,6506), sadness (χ^2 = 0,6471), loneliness (χ^2 = 0,6117), difficulty in making decisions (χ^2 = 0,5980), helplessness (χ^2 = 0,5955), anxiety (χ^2 = 0,5796), perceived stress (χ^2 = 0,5480), self-criticism (χ^2 = 9,5129), feeling a looser (χ^2 = 0,5027). The heightened levels of negative feelings have high correlations with risky adolescents' levels of depression and anxiety.

The second factor (10,4% variation share) – 'Difficulties perception' – is made up of such features as emotional reactions to difficulties (χ^2 = 0,8918), admitting having difficulties (χ^2 = 0,8752), durability of difficulties (χ^2 = 0,8311), believing that difficulties influence relations with others (χ^2 = 0,6996). We suggest that negative emotional states that dominate in the first factor predispose teenagers to experience emotional, psychological and social difficulties. Probably, perception of difficulties as long-standing followed up with negative feelings leads to formation of steady idea that these difficulties are impossible to overcome. Such attitude affects the feeling of helplessness, which in its turn can provoke tunnel thinking and cognitive rigidity that are associated with suicide activity.

The 'Problems with behavior' factor (6,8% variation share) includes hyperactivity (χ^2 = 0,7594), feeling punished (χ^2 = 0,5545), behavioral problems (χ^2 = 0,5475). We believe that most behavior problems that a risky teen experiences affect their social connections. Due to that, a risky teen has a little chance to get integrated with the community.

We presume that when starting risky behavior adolescent can consider it as a way to grow their personal experience. However, regular engagement into such behavior inevitably leads to increase in the number and frequency of its types and results in significant personality transformations. Being involved into risky behavior intensifies negative feelings, increases depression and anxiety, weakens stress-resilience. All these can provoke suicidal ideation that could later take practical turn.

CIRCADIAN DISFUNCTION, AS NOVEL FACTOR FOR STRESS-RELATED FUNCTIONAL GASTROINTESTINAL DISEASES OF LIFESTYLE

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Key words: circadian rhythms; physical inactivity; functional gastrointestinal diseases, medical students.

Melatonin is major regulator of circadian rhythmicity (CR). Our previous pre-clinical data has shown that melatonin is potent cytoprotective agent for gastrointestinal tract. Last data suggests disorders of CR is key factor of life style diseases (LSDs) and for prevention the LSDs, it is important to understand how an imbalance of key factors (sedentary life style, diet and environment) and para-mechanisms (including genetic, metabolic, the gut-brain axis, gut microbiota, immune response and so on) results in the development of LSD, related to functional gastrointestinal diseases (fGID).

Aim: to investigate the role of CR on health and well-being in medical students (MS).

A cross sectional study using a sleep diary and sleep/health-related questionnaire data were collected at in 70 MS of LNMU (females 37, males 33, aged 18-21), focusing on body weight index (BWI, normal 18.5-24.9), sleep pattern (timing, duration per day, week), manifestations of fGID, included in Rome III Consensus, physical activity (graded to 3 groups: 1-low, 2-regular, 3-intensive), learning performance (graded to A, B, C class), incidences of acute respiratory infections (ARI) per year divided to: low <4 or high >4 times/year.

Physical activity of 1 group was in 42.8%, II-50%, and III-7.2% of total MS. The daily duration of computer work (DCW) > 6 hrs was in 68%; < 6 hrs - 32%. The daily lack of sleep (6 hrs and less) was in 42.85%; sleep for 6-7 hrs - 41.42%, > 7 hrs - 15.73%. The studying performance: A was in 26%, B-56%, C-18% of total population. The incidence of ARI > 4 were in 25.71%; < 4 times/year - 74.29% of MS. Self-estimation of stress confirmed 87% of MS but in male MS - 60.6%. The incidence of ARI >4 times/year was highest in 1 group (53.3%). MS with moderate and intensive physical activity were sick 3-4 times/year. C academic level had MS, who sleep less than 6 hrs/day (15.71%), all of them had ARI >4 times/year and highest incidence of fGID.

Our data has shown that physical inactivity which resulted in abnormal sleep pattern recognized in 51.4% MS (in female-28.5%, in male 22.9%) are the key factors for fGID.

The results also show the influence of physical inactivity on learning performance of MD. The results support the hypothesis that LSDs affect MS health by fGID.

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Our study was approved by Bioethical Committee of LNMU (2015/7).

POST-TRAUMATIC STRESS DISORDER IN SOLDIERS ATO

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Key words: post-traumatic stress disorder, cognitive functions, psychopathological manifestations

Until 2014, the military service in Ukraine looked rather unattractive. In the ranks of the Ukrainian military forces in most cases were drafted individuals who did not have any possibilities to escape from service in the army. It is clear that the specific conditions of the army service such military courtesy, hazing, the impossibility of staying alone, increased responsibility, regulated daily routine, and the other were quite different from life in the family.

Today, the fighting in the East of Ukraine, the so-called ATO, has a massive psycho-traumatic impact on the personality of the soldiers, which inevitably leads to post-traumatic stress disorder (PTSD). All participants in military engagements inevitably, to varying degrees, manifest changes in mental state. The emotional load, under which they constantly stay, does not allow to objectively determine the severity of their psychological state when receiving traumatic injuries. In such patients, the number of complaints is minimal, typical of the avoidance, isolation and linguistic behavior, which must necessarily be taken into account not only when diagnosis and differential diagnosis are performed, but also in treatment.

In current research we examined 218 ATO soldiers with a traumatic brain injury of mild to moderate degree who were treated at a Military Medical Clinical Center of the Western Region in Lviv.

In the study of psychopathological manifestations in ATO fighters in comparison with ordinary patients, the results were follows: the period of oscillation of mood of ATO fighters was 26,6 ± 3,1% and in ordinary patients was 8,5 ± 1,1%, respectively; nightmares: 15.5 ± 2.1% and 4.2 ± 0.6%; Feeling of uncertainty: 17.7 ± 2.3% and 6.4 ± 0.8%; Fatigue: 48.8 ± 4.6% and 19.1 ± 1.6%; The social alienation was: 22,2 ± 2,6% and 10,6 ± 1,2%. According to the presented data it was observed the violations of cognitive functions, where the frequency of detection of psychopathological manifestations is significantly higher in ATO fighters as compared to ordinary patients with similar indicators ($p < 0,05$), which makes it possible to consider the study of cognitive functions in this category of patients as part of the clinic that requires a mandatory correction.

Conclusion: All patients who participated in military engagements in the East part of Ukraine have one of the form of a psychological trauma with new qualitative and quantitative characteristics during of a long period of life and requires frequent psychotherapeutic and medical correction.

COMBINED EFFECT OF STRESS WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND IRRADIATION ON NITROSO-OXIDATIVE PROCESSES IN DIGESTIVE ORGANS

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Key words: stress, anti-inflammatory drugs, irradiation, NO-synthase, naproxen

Introduction. Digestive organs may simultaneously be affected by different factors, such as stress, xenobiotics and other cytotoxic and ulcerogenic agents. Significant role among them belongs to nonsteroidal anti-inflammatory drugs and irradiation. Simultaneous combined effect of stress and ulcerogenic factors, different due to their pathogenetic mechanism, requires deeper elucidation.

The studies were conducted on white outbreed rats weighing 200-240 g. Rats were devided into 6 groups: the first – control group animals (n=10), the second – animals (n=8), which during 20 days were irradiated in daily dose 1sGy (total dose 20 sGy); the third group – animals (n=8), who were exposed to the effect of water-immobilisation stress (WIS) during 5h; the 4th group - animals (n=8), exposed to the action of WIS after the end of the effect of low intensity X-ray irradiation (total dose 20 sGy); the fifth group – animals (n=8), administered COX blocker naproxen (10 mg/kg); the 6th group – animals (n=8), administered naproxen on the background of WIS. In homogenates of the mucous membranes of stomach (MMS), small intestine (MMSI) and large intestine (MMLI) activity of NO-synthase, arginase, myeloperoxidase (MPO), superoxide dismutase (SOD), catalase, content of TBA-active products and nitrite-anion were determined, in blood plasma – content of H2S, nitrite-anion and L-arginine. Statistical procession of the results was performed using the methods of variation statistics with the help of ANOVA "Statistica" package.

Independent effect of WIS, blocker of COX/COX-2 (naproxen) and irradiation in total dose of 20 sGy resulted in the increase of the content of TBA-active products, nitrite-anion, activity of inducible NO-synthase (iNOS) and MPO in MMS, MMSI and MMLI homogenates; in blood plasma the content of nitrite-anion increased, whereas H2S and L-arginine concentration decreased. At that destructive macroscopic lesions of the mucous membranes, predominantly MMS, were noted under the effect of WIS and naproxen and absent under the conditions of irradiation. The combined effect of WIS with naproxen increased the area of destructive damage in MMS, at that TBA-active products content increased in the digestive organs mucous membranes, however iNOS activity decreased. Under the conditions of WIS effect on the background of irradiation the increase of TBA-active products content, activity of catalase and cNOS and decrease of iNOS activity compared to the indices of the independent effect of WIS were noted.

The combined effect of stress and COX-1/COX-2 blocker naproxen showed the cytoprotective role of prostaglandins and interrelationship between NOS and COX. The effect of stress on the background of the low intensity irradiation showed the cytoprotective effect of radiation, the key role in which belongs to the decrease of iNOS activity. The changes of the level of lipid peroxidation processes and iNOS activity under the conditions of the combined effect of stress with different ulcerogenic factors do not change simultaneously, mediating specific morphologic changes of the mucous membranes of the digestive organs.

HOW THE MULTIFUNCTIONAL NANOCARRIER MAKES THE MEDICINE «SMART»?

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Key words: nanoscale platform, anti-cancer drugs, nanocarrier, on Fullerene C60

The principal problems in pharmacology are non-addressed action of medicines causing negative side effects in the organism and rapid development of drug resistance in treated patients. Here we present examples how drug encapsulation in the polymeric or mineral nanoscale platform can enhance its treatment effect, improve its targeting in the organism, as well as provide the drug with ability to circumvent drug-resistance mechanisms. Thus, such encapsulation makes the drug "smarter" during its action.

Different anti-cancer drugs (Doxorubicin, Cisplatin, Ruthenium-containing drug KP-1019, Landomycin A, novel 4-tiazolodininone derivatives) were conjugated with either poly (VEP-GMA)-graft-PEG additionally functionalized with phospholipid or conjugated with Fulleren C60. The drugs were applied in native and nanocarrier-immobilized forms for treatment of mammalian tumor cells of various tissue origin and with different mechanisms of resistance to anticancer drugs.

Immobilization of Doxorubicin and KP-1019 on a new polymeric-phospholipidic hybrid delivery system distinctly enhanced the accumulation and activity of these drugs in all tested tumor cell lines including several drug-resistant lines. The resistance levels against Doxorubicin were reduced 6- to 22-fold. The new nanocarriers were shown to rapidly (within 10 min) and effectively transport Doxorubicin into drug-resistant as well as drug-sensitive tumor cells. The treatment with new Doxorubicin-containing nanocarriers resulted in effective cell cycle arrest in G2/M phase and ROS-induced cell death. In both *in vivo* tumor models – murine NK/Ly lymphoma and murine L1210 leukemia – Doxorubicin delivery by the new nanoformulation resulted in 100% cured animals already at low concentrations (0.1 mg/kg), while the native Dox solely extended a survival time. Thus, polymeric nanocarriers functionalized with phospholipids and PEG enhance the efficacy and reduce the toxicity of Doxorubicin.

In another set of experiments, Doxorubicin or Cisplatin (CDDP) were immobilized on Fullerene C60 that enhanced an ability of these anticancer drugs to circumvent resistance of tumor cells to chemotherapy *in vitro.* Cytotoxic activity of CDDP-C60 nano-complex towards different lines of drug-resistant tumor cells was 1.5-2.0 times higher than that of native CDDP. In parallel, an enhanced uptake of this drug and double induction of apoptosis in target tumor cells were observed. The anticancer effect of CDDP-C60 nano-complex was confirmed in tumor-bearing mice.

We also functionalized the developed polymeric nanocarriers with specific antibody or lectin in order to improve their cell targeting properties.

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SLEEP QUALITY AND ANXIETY LEVEL IN STUDENTS WITH HIGH ARTERIAL BLOOD PRESSURE

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Key words: adaptation, functional reserves, sleep quality, anxiety

Introduction. It is known that the process of adaptation of students to new learning conditions is a long-term and complicated process that is demanding for the plasticity of the psyche and the functional reserves of the body of young people (Agadjanyan N.A., 2006 p.). The initial sign of the violation of adaptation is the development of a «burnout syndrome» (Oliynyk O.V., 2013p.). Further development of psychosomatic disorders are a markers of functional disorders of the cardiovascular system, because these changes could further lead to persistent disorder of the body (Monakhova L.Y., 2002 p).

Materials and methods: To determine the quality of sleep, was used the Ukrainian version of Pittsburgh sleep quality index (Buysse, Daniel J., et al, 1989). We interviewed 228 people (students of TSMU), of which 85 males and 143 females, aged 18 to 20 years. Among the questioned students, a group of 40 students of 2 years aged 18-20 years who had a low level of sleep quality was selected. In this group of students, anxiety levels were determined using the Spielberger-Hanin questionnaire (Spielberger, Ch.D., and Y.L.Khanin, 2000). Blood pressure was measured using the Korotkov method. Statistical processing of the results was carried out using nonparametric methods (Man-Whitney U-criterion).

Results: A large number of respondents (25.88%) had various sleep problems three or more times a week. In 41.23% of the polled, such problems occurred once or twice a week. More than 7 hours slept during the month only 29.82% of people, less than 7 hours - 67.17%. Subjectively, their own quality of sleep was estimated as satisfactory by 68.86% of students, as low as 31.14%. An increase in the level of situational anxiety was found in 14 (35%) of the examined students. An increase in personal anxiety was found in 18 (45%) of the surveyed. The average BP of students with normal level of satisfactory quality of sleep and situational anxiety was 125/80 mm Hg. The average level of blood pressure in students with low quality of sleep and high situational anxiety was 140/90 mm Hg. A significant difference ($p < 0.05$) was found between the level of BP in students with normal and high situational anxiety.

Conclusions: Subjectively, the majority (68.86%) rate the quality of their sleep quality, 31.14% consider it low. 67,11% of the students, there were problems with sleep at least once a week, which causes them the risks of further complications in the process of sleep and disorders of the functioning of the nervous system and other systems of the body. 67,17% of students sleep less than physiological norm in 7-8 hours. Blood pressure increased in students with poor sleep quality and increased situational anxiety.

THE PECULIARITIES OF THERAPY FOR POSTTRAUMATIC STRESS DISORDER OF VETERANS OF ANTI-TERRORIST OPERATION IN UKRAINE

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Key words: veterans, neuropsychological study, guilt, secular meditations

Veterans can resocialize, provided the model of their peaceful future has been formed. It turned out that all the parts of this model malfunctioned for the veterans of anti-terrorist operation: social time rejection, lost time perspective and psychophysiological time malfunctions. It is know that the time perspective is closely linked to a self-image and belongs to the cognitive component of personal time.

It was found that veterans tend to use language without sense of time and their personal biography was divided into two parts: "before the war" and "after the war". Veterans stay in the "after the war" time interval, its structure they describe as slowly and linearly flowing boundless and shapeless space with no future. It is difficult to say whether the veterans overestimate or underestimate the time retrospective of the war since they consciously try to forget the very war period.

Lack of understanding their problems by other people, who have not been on the front line, make the veterans withdraw into themselves. They can find comfort in communication with animals and in different deviant activities. The other characteristic features of veterans are: depressive mood, suicidal behavior, fundamental attribution error and belief that it is impossible to regain the lost feeling of happiness and the structure of self-image they used to have before the war.

The neuropsychological peculiarities of the veterans of the antiterrorist operation are: timing mechanism malfunctions; short-term memory weakening; decreased ability to plan activity with regard to time; attention span reduction; slightly poorer vocabulary. At the same time, though it may look as paradox, the veterans reproduce well short time intervals, have good orientation and lasting attention. They are also characterized by good critical thinking, pro-social orientation, empathy and good neuroplasticity.

The analysis of neuropsychological study results made the author assume that hyperactivity of the right hemisphere inhibits frontal association areas of the left hemisphere of the veterans. It is also likely that weakness of hippocampus and hyperactivity of amygdala hinder time perspective formation and cause disappearance of common time sensation.

The program of neuropsychological treatment of disorders has been created. A deep sense of guilt the veterans had for what they did placed a big obstacle in the way of the therapy. Sense of guilt was based on the religious worldviews (Abrahamic religions). Only after the veterans dropped their religious views as a result of broadening their knowledge about the World, other worldviews of humanity and cognitive distortions they were able to them start the therapy.

Good spatial orientation allowed the formation of the time perspective on the basis of spatial gnosis. It was possible to regain sense of time in the language they use and to cope with cognitive distortions thanks to the ability to understand complex logical and grammatical constructions. The lowered ability to plan time was of secondary importance and was increased by a workshop on time management. Secular meditations within cognitive behavioral psychotherapy helped to relocate activity from the right to the left hemisphere and to decrease anxiety.

OVERCOMING PSYCOLOGICAL BARRIERS IN PATIENTS WITH RARE GENETIC DISORDERS

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Key words: orphan disorders, stress, depression, helthcare

Nowadays there are lots of rare (orphan) genetic disorders caused by different types of mutations. Obviously, defect genes encode dysfunctional proteins which modify general biochemical pathways, but also it's worth mentioning about a great number of patients with rare diseases who have psychological problems, such as high levels of stress, depressions and problems with social adaptation. Moreover physicians face difficulties in sharing experience of treatment of these diseases.

The research aims to assemble all types of knowledge concerning treatment, diagnosis of orphan genetic disorders, prevention of mental issues and to make statistical assessment of Ukrainian progress in this field of medicine. Several tasks were set:

- detailed review of online blogs, groups, sites, where patients and doctors from different parts of the world can fluently communicate with each other;
- searching for Ukrainian patient communities;
- analysis of the statistics of diagnostics and treatment of rare genetic disorders in Ukraine;
- assessment of the level of psychological assistance to people with rare genetic syndromes.

To complete the tasks of the research online clinical bioinformatics and genomic resources (Undiagnosed Diseases Network), medical databases (OMIM, Genetics Home References, NCBI,PHG Foundation), medical organizations' sites (Genetic Alliance), patients' personal blogs (written by parents of the child with NGLY1 deficiency, by family with rare mitochondrial disease) and patient communities (RareConnect) have been used. In order to find out real information about diagnostics and treatment of unique illnesses in Ukraine, some sites of patient organizations were reviewed (Debra Ukraine, Orphan Ukraine).

Surprisingly many Ukrainian patients with orphan genetic disorders have depression. These people always live in stress, because actually they are not treated or even consulted by specialists. The main cause of mental problems is the lack of adequate financial government support. According to the statistics given by Ukrainian healthcare committee, financing has increased by 4.45 times (2011-2015 y.), but that is not enough for providing a good healthcare. It was estimated that this financial support is only 10-30% of the required sum. We also have people with undiagnosed pathologies. Only 5% of Ukrainian patients with rare ailments know their true diagnosis.Surely, some international organizations help our patients. In fact, people with such disorders should find assistant communities by themselves. In foreign countries (UK as an example), scientists use next generation sequencing that provides better diagnostics of rare diseases and helps in treatment, also physicians collaborate with patients by using blogs, healthcare sites.

There is an extremely critical situation with financial support for patients with orphan genetic syndromes in Ukraine, but international organizations are ready to help. People don't know about their possibilities, and that is the key problem. Ukrainian physicians should integrate their knowledge with colleagues from other countries, pay attention to the patients' psychological problems. International cooperation will help patients with undiagnosed pathologies, which are mostly caused by mutations in genes, and have polysymptomatic presentation pattern.

SALIVA MICROCRYSTALISATION AS A PREDICTOR OF STRESS RESISTIBILITY AND AN APPROXIMATE OVULATION TIME

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Key words: stress-spectrum diseases, menstruation phase, saliva microcrystalisation

WHO developing the International Classification of Diseases, version 11 (ICD-11) is included *stress-spectrum diseases* in it. Moreover, acute and chronic changes and adaptation during stressful life events may trigger accelerated aging, as well as psychological disorders and oncogenesis. Determining personal stress level in real time could be of special interest in health monitoring and early prediction of stress-associated disorders. Recent data of saliva secretome has shown a growing body of evidences for its using, as easy and early diagnostic tool.

Aim: The aim of the study was to reveal the relationship between stress resistibility levels and saliva microcrystallization and to investigate whether menstruation phase has influence on the saliva microcrystalisation.

Methods:30 people aged 19-30 were involved in the study, 26 female and 4 male.

Facies of saliva were investigated by dehydration of drops of mixed saliva. For estimation of stress resistibility levels questionnaire created by ISMA (International stress management association) was used.

To reveal the influence of menstrual phase on the microcrystalisation saliva facies were collected from women every three days during the menstrual cycle.

Results:It was discovered that the absence of microcrystalisation (4th type) was most often seen among people with low stress resistibility (44,4%), while there were 35,3% of 4th type among people with medium resistibility and no this type among people with high resistibility.

What about relationship between saliva microcrystalisation and menstrual cycle, all types of crystalisation were seen with the equal incidence with the trend of high incidence of 1st and 2nd types during the ovulation.

Conclusions:Saliva investigation can be used as an additional method of estimation of stress and as a method of the approximate detection of the ovulation and can be used for planning pregnancy. This method is very simple, cheap and noinvasive, so it can be used widely.

LIVER FUNCTION IN PATIENTS WITH CORONARY ARTERY DISEASE AND NONALCOHOLIC FATTY LIVER DISEASE ASSOCIATED WITH OBESITY

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Key words: obesity, coronary artery disease, statins, comorbide pathology

Introduction: Obesity is a global epidemic. It is associated with numerous comorbidities such as cardiovascular diseases, nonalcoholic fatty liver disease (NAFLD), type 2 diabetes, cancers and others. Cardiovascular disease is one of the most important causes of morbidity

and mortality of patients with NAFLD and in the general population. Statins are considered as first-line drugs for treatment coronary artery disease (CAD).

Aims and Methods: The aim of this study is to investigate liver function during statin therapy of patients with CAD and NAFLD, associated with obesity, depending on percutaneous coronary intervention (PCI). The study included 59 patients with documented CAD and NAFLD aged 45-72 years. Patients were divided into groups: 1st group includes patients treated with PCI , 2nd group - with optimal medical therapy for 1 year. Patients with PCI were receiving higher doses of statins. Standard tests were carried out for all patients including tests for lipids, transaminases, alkaline phosphatase, gamma-glutamyltranspeptidase, glucose, uric acid, urea, creatinine.

Results: The lipid levels were nearly identical in both groups, but we noted that patients who had been treated with PCI had abnormal level of ALT (p=0,01) and AST (p=0,04). ALT and AST are elevated but are less than 3 times the upper limit of normal and did not require discontinuation of statin.

Conclusion: Patients with PCI had higher compliance with drug therapy. During the treatment of patients with CAD, NAFLD and obesity it is important to take into account the individual peculiarities of comorbide pathology to achieve high efficiency and safety of treatment. Medication adherence should be followed carefully by CAD patients treated with and without PCI.

Disclosure of Interest: All authors have declared no conflicts of interest.

METFORMIN THERAPY FOR PATIENTS WITH METABOLIC SYNDROM ASSOCIATED WITH CHRONIC PANCREATITIS

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Key words: metabolic syndrome, pancreatic steatosis

Introduction: Nowadays the problem of average increasing number of cases of peoplesuffering from inveterate non communicable diseases is discussed much. Metabolic syndrome (MS) has already reached proportions of non communicable epidemic, "epidemic of XXI c." MS represents a combination of cardiovascular risk determinants such as obesity, insulin resistance and lipid abnormalities such as hypertriglyceridemia, increased free fatty acids, low high-density-cholesterol and hypertensionWe can definitely call it a "civilization disease". Metabolic conditions giving rise to pancreatitis account for 5%-10% of cases. The causes include hypertriglyceridemia, diabetes mellitus, porphyria. In cases of metabolic pancreatitis, apart from the standard routine management of pancreatitis, careful management of the underlying metabolic abnormalities is of paramount importance. Evaluation of pancreatic steatosis should be considered for patients with pancreatitis associated with metabolic syndrome. Metformin is the drug of choice to relieve from the main symptoms of MS.

Aims and Methods: To determine the effects of metformin on the risk factors of metabolic syndrome associated with chronic pancreatitis. The study included 33 patients (10 men and 23 women) aged 38-78 years with MS, who had a concomitant diagnosis of chronic pancreatitis. Patients were divided into 2 groups:the first group (n=20) took metformin at a dose of 500 mg thrice a day for 6 months, the second group (n=13) didn't takemetformin. All patients underwent astandard therapy of chronic pancreatitis. Both groups were given recommendations as to modification of their lifestyle: healthy food, physical activity, bad habits break. All patients performed ambulatory blood pressure monitoring, measured blood glucose, HbA1c, insulin resistance indices, lipid profile and anthropometric parameters (body mass index , waist circumference , the circumference of the hips and their ratio) before treatment and 6 months after.

Results: Patients with MS associated with chronic pancreatitis, who were treated with the

drug metformin, had more evident positive results of indices of insulin resistance, glycemia, glycosylated hemoglobin, decreased blood pressure. We noted a downward trend in total cholesterol, low-density lipoprotein cholesterol and triglycerides. Metformin had a positive effect on carbohydrate and lipid metabolism. Those patients had a more significantly decreased body mass index, OT, waist circumference , the circumference of the hips and their ratio,lose weight.

Conclusion: Group with chronic pancreatitis on the background of metabolic syndrome, treated with the drug metformin, had more evident positive dynamics indices of insulin resistance, glycemia, glycosylated hemoglobin, decreased dyspeptic syndromes. It is reasonable to include metformin in the complex therapy of patients with MS associated with chronic pancreatitis .Use of metformin for patients with metabolic syndromin combination with chronic pancreatitis can reduce symptoms of disease and improve quality of life.

Disclosure of Interest: All authors have declared no conflicts of interest.

CYTOPROTECTIVE EFFECT OF NOVEL 4-THIAZOLIDINONE DERIVATIVES AGAINST STRESS CONDITIONS IN SMALL INTESTINE OF RATS

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Key words: Stress, H_2S, 4-thiazolidinone-based derivatives, small intestinal mucosa

Introduction. Stress affects the integrity of the intestinal barrier and increases it permeability, reduces mucosal blood flow due to catecholamines driven vasoconstriction, leading to hypoxia and nitroso-oxidative processes. The experimental data demonstrates that H_2S can exert protective actions against injury induced by various factors. The purpose of this investigation was to explore the role of 4-thiazolidinone-based derivatives as a novel donors of H_2S in promoting the resolution of inflammation in small intestine.

Methods. The experiment was performed on 40 white rats. Water-immobilization stress (WIS) during 5 h was used to induce GI damage. A series of 4-thiazolidinones (Les-5054 and Les-5055) were administered at a single dose 10 mg/kg per os 30 minutes before modeling WIS. The activity of NO-synthases, arginase, myeloperoxidase, the content of nitrite anion (NO^{2-}), L-arginine and MDA were determined in homogenates of small intestinal mucosa (SMI). The study was approved by local bioethics committee 16/03/2015 № 3.

Results. The activity of iNOS in WIS increased about 3 times ($p<0,01$), as well as the content of MDA for 44 % ($p<0,01$) and NO_2^- more than 2 folds ($p<0,01$) as compared to the indices of the control group. Les-5054 on the background of WIS effect decrease activity of iNOS for 21 % ($p<0,01$) as well as content of MDA and NO^{2-} ($p<0,01$), 23 % and 27 % respectively) and increase the activity of cNOS for 48 % ($p<0,01$) compared with indeces of stress group. Parameters of NO-synthase system in Les-5055-treated group showed the same tendency as under the effect of Les-5054.

Conclusion. In the present study, we investigated the effect of novel 4-thiazolidinone derivatives (compounds Les-5054 and Les-5055) on various intestinal events occurring in association with stress-induced intestinal damage. It was observed an intensification of lipid peroxidation, myeloperoxidase activity, accompanied by increase of iNOS activity, NO production and decrease of H_2S content in rats with WIS group. In animals treated with compounds Les-5054 and Les-5055 the reduction of the activity of iNOS, myeloperoxidase, intensity of lipid peroxidation and increased generation of H_2S were revealed.