2nd INTERNATIONAL CONFERENCE

NEURAL-HUMORAL AND CELLULAR REGULATORY MECHANISMS OF DIGESTION PROCESSES

OCTOBER 5-7, 2005, Kyiv, UKRAINE

ABSTRACT BOOK

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REGULATION OF FUNCTION OF GASTROINTESTINAL TRACT

R-1

CONTRIBUTION OF GLUCOCORTICOID HORMONES TO THE HEALING OF INJURED GASTRIC MUCOSA

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The lasting glucocorticoid therapy or glucocorticoids injected at pharmacological doses delay the natural healing of experimental gastric injury, however, the role of endogenous glucocorticoids in gastric mucosal healing processes remains unknown. Our studies were designed to elucidate the physiological role of glucocorticoids in the healing processes of injured gastric mucosa. We were interested in the contribution of glucocorticoids to the healing of both acute and chronic gastric mucosal lesions under both prostaglandin (PG) deficient and PG sufficient conditions. For these reasons, models of indomethacin-induced (35 mg/kg, i.p.) and cold-restraint-induced gastric erosions (at 8°C for 6 h) as well as acetic acid-induced ulcers were used. Chronic gastric ulcers were induced by both serosal and luminal application of acetic acid solution, 100% and 60% respectively. To investigate the role of glucocorticoid in the healing processes the action of glucocorticoid deficiency without or with corticosterone replacement on the healing of gastric erosions and chronic gastric ulcers were studied in male Sprague-Dawley rats. Glucocorticoid-deficient state was created by adrenalectomy (one week before the onset or immediately after the end of ulcerogenic stimulus) or by pharmacological blockade of hypothalamo-pituitary-adrenocortical axis (300 mg/kg, i.p., one week before the onset of ulcerogenic stimulus). All ulcerogenic stimuli used in our studies induced corticosterone rise. Glucocorticoid deficiency, created one week before the onset of ulcerogenic stimulus, promoted the formation of the gastric erosions and ulcers and delayed their healing. The areas of gastric erosions and ulcers in rats with glucocorticoid deficiency were significantly larger than that in control animals in all investigated time points. Replacing corticosterone reversed deleterious effect of adrenalectomy on healing of gastric lesion in rats with glucocorticoid deficiency. The results also showed that adrenalectomy delays the healing of pre-existing erosions and chronic ulcers, and this deleterious effect was also antagonized by corticosterone replacement. In conclusion, these results suggest that endogenous glucocorticoids contribute to the healing processes of injured gastric mucosa, particularly under PG deficient conditions.

The study was supported by grants from RFBR (04-04-48507), SPbNC-2005, Sci. School (1163.2003.4).

R-2

CONTRIBUTION OF GLUCOCORTICOID HORMONES TO GASTROPROTECTION DURING THE INHIBITION OF PROSTAGLANDINS AND NITRIC OXIDE PRODUCTION AND THE ABLATION OF CAPSAICIN-SENSITIVE SENSORY NEURONS

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Prostaglandings (PGs), nitric oxide (NO) and capsaicin-sensitive sensory neurons (CSN) play a pivotal role in modulation of the gastric mucosal defense of the stomach. We previously reported that glucocorticoids produced in response to ulcerogenic stimuli have a beneficial influence on various factors involved in the gastric mucosal defense. In the present study we tested the hypothesis that a contribution of glucocorticoids in gastroprotection becomes especially important during the deficiency of PGs, NO and desensitization of CSN. Male Sprague-Dawley rats were used after 24 fasting. The effects of the inhibition of PG and NO production or the ablation of CSN on the gastric mucosa were compared in the groups with different glucocorticoid supply: adrenalectomized rats without and with replacement of corticosterone (4 mg/kg sc) and sham-operated animals. Indomethacin (5 mg/kg ip) and L-NAME (50 mg/kg sc) were used to inhibit PG and NO production, respectively. Functional ablation of CSN was performed with neurotoxic doses of capsaicin (100 mg/kg sc, 3 days). Indomethacin at dose 35 mg/kg was given as ulcerogenic agent. Adrenalectomy by itself did not cause damage in the stomach. Neither inhibition of PGs and NO nor sensory desensitization alone provoked any damage in the gastric mucosa of sham-operated rats. However, each of these treatments provoked gastric damage in adrenalectomized rats, and these ulcerogenic responses were prevented by corticosterone replacement. Indomethacin-induced gastric erosions were aggravated to similar extension by either adrenalectomy, inhibition of NO or desensitization of CSN. Combination of adrenalectomy with inhibition of NO or desensitization of CSN profoundly potentiated the worsening effect of such treatments on indomethacin-induced gastric lesions, and the lesion score increased to 5 or to 10 times greater, respectively, when compared to that induced by each of these treatments alone. Corticosterone replacement totally prevented such worsening effects of adrenalectomy on the gastric ulcerogenic response induced by indomethacin under inhibition of NO production or desensitization of CNS. In conclusion, these results suggest a pivotal compensatory role of glucocorticoid hormones in the maintenance of gastric mucosal integrity in the case of impaired gastroprotective mechanisms provided by PGs, NO and capsaicin-sensitive sensory neurons.

The study was supported by grants from RFBR (04-04-48507), SPbNC-2005, Sci. School (1163.2003.4).

R-3

MORPHOFUNCTIONAL CHARACTERISTICS OF GASTRIC GLANDS AFTER PARASYMPATHETIC DECENTRALIZATION

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Aims: To investigate the reserve and adaptational possibilities of secretory gastric glands after selective proximal vagotomy (SPV).
Methods of the study: prolonged experiments were performed on dogs with gastric fistula by Basov before and after SPV. The functional state of gastric glands was estimated on empty stomach and on reaction to injections of Pentagastrin (PG) 6 times per day. The volume of juice and mucus, temp of H^+-ions secretion, pepsin (P) and glycoproteids (GP) were measured. The morphological structure of gastric mucosa was determined with gastroscopy and morphological methods.
Results: there were established that 6 months later after SPV investigated animals had less potency of stomach glands then intacted ones: gastric juice volume 1.3 times, temp of H-ions secretion 4 times, P 6 times and GP 1.2 times decreased, while the mucus production 3 times increased ($P<0.05$). Decrease of parietal cells dimension and of intracellular mucosal reserve was determined by morphology. More later after SPV (1.5 years) the mucus production surpassed control measures, and potency of gastric glands changed essentialier. So gastric juice volume 2 times and temp of H^+-ions secretion 15 times decreased, while mucus secretion 10 times increased ($P<0.001$). The morphological study of gastric mucosa revealed progressive enlargement of gastric foveae and decrease of parietal cells amount, while their dimension returned to initial one.
Conclusions: parasympathetic decentralization is accompanied by adaptional changes of activity and reactivity of regulative mechanisms, which changes sensibility of gastric secretory cells for PG. More later after SPV inconcordant activity of neurohumoral mechanisms is revealed, which cause inertness and exhaustion of acidoproductive potency of gastric cells, while their functional ability remains and even increases.

R-4

STUDIES ON CHEMICAL CONSTITUENTS FROM THE FENUGREEK (Trigonella foenum-graecum) AND THERAPEUTIC APPLICATIONS

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In recent times, several preclinical and clinical studies have confirmed the anti-diabetic action of ***Fenugreek seeds***, particularly, the fiber-rich, defatted portion of the seeds. The hypocholesterolemic activity of the defatted portions of the seeds has also been demonstrated. In addition, fenugreek seeds are assumed to have nutritive and restorative properties and they also stimulate the digestive process, great for breast feeding, inceases milk, stimulate the PMS syndrome, menopausal complaints. The differences between the physiological activity of these molecules occurs because the chemical groups attached to the basic steroid nucleus are slightly different. The British Herbal Pharmacopoeia reported its actions as demulcent and hypoglycemic (BHP, 1996). Hypoglycemic activity in healthy individuals has been reported for whole seed extracts. A significant reduction in serum-cholesterol concentrations in diabetic patients was also reported (Sharma, 1986). Fenugreek infusion has hypoglycemic effects in animals (Leung and Foster, 1996). The Merck Index reported its veterinary medicine therapeutic category as emollient (Budavari, 1996). The Commission E approved internal use of fenugreek seed for loss of appetite, reported secretolytic, hyperemic, and mild antiseptic activity. and external use as a poultice for local inflammation. Traditionally, fenugreek is used internally to treat anorexia, dyspepsia, gastritis, and convalescence, and topically for furunculosis, myalgia, lymphadenitis, gout, wounds, and leg ulcers. It is indicated for use externally as an emollient for treating furuncles, boils, inflamed indurations, and eczema, applied as a poultice (Duke, 1997; Newall et al., 1996; Wichtl and Bisset, 1994). **Screening** for antimicrobial properties the effects of aqueous, alcoholic, hexanic, and etheric extracts of fenugreek seeds on eight bacteria (*Bacillus subtilis* NCAIM B.01095, *Citrobacter freundii* B.01468, *Escherichia coli* HNCMB 35035, *Proteus vulgaris* B.00642, *Pseudomonas fluorescens* B.01469, *Sarcina lutea*, *Staphylococcus aureus* HNCMB 112002, *Xanthomonas campestris* pv. *campestris* NCAIM B.01071), one yeast (*Zygosaccharomyces bailii* NCAIM Y.00734), and five filamentous fungi (*Aspergillus wentii* NCAIM F.00167, *Botrytis cinerea* NCAIM F.00744, *Fusarium oxysporum* NCAIM F.00728, *Penicillium expansum* NCAIM F.00601, *Rhizopus stolonifer* NCAIM F.00654) were tested in this study. The in vitro bioassays were based on the agar diffusion method. The microorganisms screened were obtained from the National Collection of Agricultural and Industrial Microorganisms (NCAIM), Budapest, Hungary and the Hungarian National Collection of Medical Bacteria (HNCMB), Budapest, Hungary. From fenugreek seeds alcoholic extracts cshoved anti- E. coli activity, - *Sarcina lutea,- Pseudomonas fluorescens,-Fusarium oxysporum,-Penicillium expansum* antiactivity. The activity of fenugreek-extracts agains the E. coli strains opens new gates for future studies. Use of fenugreek in further evaluation as feed-additive for prevention or reduction of E. coli or some other bacterial infection, inflammation, and gastrointestinal ailments. Recommended treatments to ameliorate urinary symptoms.

R-5

DETECTION OF ORAL PART OF BRAIN-GUT AXIS

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In recent years, diffuse neuroendocrine system (DNES) attracted worldwide attention. Actual findings explain digestive physiology by newly recognized several groups of DNES hormones and transmitters that "cooperate" with the "brain-gut axis". Up till now, researches about gastro-intestinal DNES have been reported, but the data about oral DNES are scarce. Aim: 1) identification oral endocrinocytes (OE), 2) investigation OE features, that provides neuroendocrine acting mode.

Methodology: the electron-microscopic and imaging analysis (EMA) were used for study rat gingival bioptants.

Results: EMA recognized interaction gingival epithelial mucosa and connective tissues were observed OE. They characterized by small amount, localized in basal epithelial layer, surrounded by epitheliocytes and also existing the contacts with terminal endings of unmyelinated nerve fibres (UMNF). As the rule, these UMNF belong to oral cavity (OC) ANS. In the contact place of OE plasmatic membrane (PM) with terminal endings UMNF were observed unclear delimitation that gave basis to confirm close interpermeation. OE have been oblong shape with particularly elongated baso-apical orientation, increased nucleo-cytoplasmatic ratio, in cytoplasma was considerable amount of small electronic density granules, which connected with endoplasmatic reticulum tubular system. These ultrastructural peculiarities are basis for identification OE as D_1-cell type of DNES. Moreover, in cytoplasma located optimal developed mitochondries with more density matrix and good organized cristae. From carioteka draw off granular endoplasmatic reticulum channels, which wrap up mitochondries and gain signs of agranularity. PM which contacted with cytoplasmatic cortical layer was loosen and had direct contact with neighbouring cells and interstitial space. Described properties testify of releasing and penetrate peptide granules content into epithelium. Such findings indicate that structural contact may belong to OE with neuropeptide. Also OE cortical layer has less amount of granules, only single small unclear masses with different electrodensity and irregular configuration were evaluated. We suppose that peripheral difference in OE granule's electronic density correlated with findings of degranulation and depends from cell functional state. Accordingly, ability of peptide granules interacts with PM, and promotes carrying molecules to extracellular space and modulates releasing content.

Conclusion: OE shows morphological evidence of representation brain–gut axis in OC with a neuroendocrine mode of action.

R-6

BRAIN ACTIVATION PROCESSES UPON OLFACTIVE PERCEPTION OF IZOAMILACETATE

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It is know, that at all food flavor has been defined as a combination of olfactory (smell) and gustatory (taste) sensation. Key area in the brain involved in smell and taste is the orbitofrontal cortex, which contain neurons that are uni- and multimodal. Suggest that there are brain cells that appear to respond only to taste and smell and nearly cells that undertake an interactive, multisensory role. So, considering important role of olfactory information in the process of digestion the shifts in human brain electrical activity under odor stimulation with izoamilacetate were investigated. This substance is interesting firstly due to that it is exceptionally olfactive stimulus, secondly it is widely used as food flavour. 44 volunteers participated in EEG research. Subjective perception of the smell was estimated with special questioner. The results showed that within the whole group emotional estimation of the odorant was positively neutral. In the same time EEG shifts under the smell perception indicated quite prolonged brain activation. However, analysis of changes in relative spectral power of EEG in groups formed by criteria of the sign of subjective aroma estimation revealed that in individuals, who gave positive estimate to the smell, spectral power in teta-1, alpha-3 and beta-2 bands enhanced that indicates more emotional attitude of individuals towards investigated agent. In the meantime only changes in general brain activation were revealed in the alternative group. Thus, results of the investigation showed that subjective emotional estimation of izoamilacetate smell correlates with quite significant topographical reorganization of brain activation accompanying olfactory information processing. Certainly, such reorganization should influence the general neurohumoral regulatory mechanisms of digestion processes.

R-7

ANTIGENIC SUBSTANCE OF *STAPHYLOCOCCUS AUREUS* MODULATES ENDOGENOUS NEUROTRANSMITTERS RELEASE FROM NEURONS OF INTERAMURAL NERVOUS INTERLACEMENT IN SMOOTH MUSCLES

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Protein A (m.w. 42 kDa) and biopolymer peptidoglycan (m.w. 40-80 kDa) are main structural components of Staphylococcus aureus bacterial wall. Peptidoglycan mainly contributes to bacterial wall structure (400 monomers molecules **:** 1 protein molecule). Protein A covalent binds to peptidoglycan. Purified and cell-bound proteins A (CBPA) are obtained in laboratory environment and both of them are immuneactive. The goal of the research was to study CBPA action on non-adrenergic (purinergic, NO-ergic) inhibition in taenia coli smooth muscles (SM) of guinea pig using sucrose-gap technique. Cell-bound protein A (10^{-6}-10^{-4}mg/ml) depolarizes membrane, changes amplitude and frequency of spontaneous action potentials in smooth muscle strips. Exogenous adenosin-5'-triphosphat (ATP) (10^{-5}M/L) (agonist of P2X and P2Y purinoceptors) hyperpolarizes membrane, inhibits spontaneous action potentials in smooth muscle cells (SMC). When measured after few minutes, CBPA (10^{-4}mg/ml) enhanced purinergic inhibition. After prolonged CBPA action ATP did not hyperpolarize SM membrane, but inhibited spontaneous electric activity. CBPA had the same effect on uridine-3'-triphosphat (P2Y receptors activating agent) – induced inhibition in smooth muscles. Another inhibition transmitter – nitric oxide (sodium nitroprusside (SNP) as a source of exogenous NO (10^{-5}M/L)) also did not evoke membrane hyperpolarization. CBPA removed ATP inhibition action (or SNP) on histamine (10^{-5}M/L)-evoked SM contraction. When washed out, all these changes were reversible.

Presynaptic CBPA action was investigated with stimulation of endogenous transmitter release from intramural interlacement neurons in smooth muscles, using nicotine receptors agonist – nicotine (NC). At the action beginning bacterial substance increased, and later decreased fast component of NC (10^{-5} M/L)-evoked inhibition of histamine contraction in SMC. CBPA action on nicotinic relaxation was removed with nitric oxide synthase blocker N^{ω}-nitro-L-arginine (10^{-5}M/L). Obtained data revealed CBPA property to modulate purinergic inhibition in SM in a way of action on smooth muscle cells and on endogenous transmitter release from intramural interlacement neurons.

R-8

Ca^{2+} DYNAMICS IN SALIVARY ACINAR CELLS: DISTINCT MORPHOLOGY OF THE ACINAR LUMEN UNDERLIES NEAR-SYNCHRONOUS GLOBAL Ca^{2+} RESPONSES

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The Ca^{2+}response of polarized secretory epithelial cells is due to Ca^{2+} release from intracellular stores and shows complex variations in time and space. In pancreatic acinar cells (PACs) apical-to-basal Ca^{2+} waves are widely observed. However in salivary acinar cells, some reports show waves [1], others show a near-simultaneous Ca^{2+} response across the cell [2]. We have studied Ca^{2+} signalling in mouse submandibular acinar cells (SMACs) to try to resolve these differences.

We use large fragments of freshly isolated mouse exocrine glands which preserve the structure of the intact tissue. We use 2-photon microscopy to measure single-cell Ca^{2+} responses with Fura-2 (AM loaded) and visualise the acinar lumen by simultaneously imaging an extracellular dye sulforhodamine (SRB;500μM). For immunohistochemistry we fixed tissue in -20^{o}C methanol , and immunostained using standard techniques, imaging with a confocal microscope (LSM-510).

The Ca^{2+}response to ACh, measured with Fura-2, showed near-synchronous Ca^{2+} signals in SMACs, with an apparent apical to basal wave velocity of 31.4 $\mu m.s^{-1}$ (n=39) compared to an apparent velocity of 9.5 $\mu m.s^{-1}$ in PACs (n=30). Immunostaining experiments show differences in the extent of the acinar lumen, as defined with the tight junction protein zona ocludens (ZO-1), between the two exocrine glands. In SM tissue fragments the lumen encircled individual acinar cells but in the pancreas it ended abruptly at the secretory pole of acinar cells. Inositol-trisphosphate receptors (type 3 and type 2) and aquaporin (AQP5) both followed the acinar lumen in the two cell types.

We conclude that the more extensive luminal/ductal network in SM tissue leads to an encircling of SMACs with IP_3Rs generating near-simultaneous Ca^{2+} responses across the cell.

(1) Giovannucci et al (2002) J.Physiol. 540, 469-484
(2) Lee et al (1997) J.Biol.Chem. 272, 15765-15770

R-9

Co^{2+} INFLUENCE ON MEMBRANE BONDED Ca^{2+} LEVEL OF SECRETORY CELLS OF *CHIRONOMUS PLUMOSUS* SALIVARY GLAND

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Cations of heavy metals are known to blocking Ca^{2+} transporting systems of different types of cells, including secretory cells. Calmodulin as Ca^{2+} binding protein is effective modulator of functional activity of the Ca^{2+} transporting systems. We suggested that heavy metals cations effect may be mediated with its action on calmodulin. So we decided to find out the influence of Co^{2+} to typical heavy metal.

We judged about the functional activity of Ca^{2+} transporting systems on the basis of membrane bound Ca^{2+} changes. The method of membrane bound Ca^{2+} measuring is based on property of chlortetracycline to fluorescence after binding Ca^{2+} in hydrophobic environment. Because fluorescence changes of chlortetracycline-Ca^{2+} complex inside the membrane reflect shifts of ionized Ca^{2+} level close to cell membranes. Fluorescence of chlortetracycline-Ca^{2+} complex was measured at λ_f=480-530 nm and λ_{exc}=380 nm.

We established that adding Co^{2+} to normal external medium for intact cells with pH 7,2 in concentrations 0,01, 0,1 and 1 mM caused decreasing of membrane bonded Ca^{2+} in all cases. Such, after adding of 0,01 mM Co^{2+} decreasing of membrane bonded Ca^{2+} was 8,10 % (P=0,177, n=6); 0,1 mM Co^{2+} evoked change of membrane bonded Ca^{2+} was 15,48 % (P=0,023, n=6) and 1 mM Co^{2+} lead to reduce of membrane bonded Ca^{2+} to 22,68 % (P=0,006, n=6) according to the control. Co^{2+} may be suggested to concur with Ca^{2+} for binding with functional groups, forming fixed superficial charges of plasma membrane.

At the next stage we make external solution acidation to pH 4,0, under these conditions fixed superficial charges have to bind protons. Such acidation caused non significant membrane bonded Ca^{2+} changes: decreasing of membrane bonded Ca^{2+} level to 4,11 %, rising to 0,71 % and 10,90 % according to the control after application of 0,01, 0,1 and 1 mM Co^{2+} respectively. The absence of decreasing effect can confirm our assumption about Co^{2+} to concur with Ca^{2+} for binding with functional groups forming fixed superficial charges of plasma membrane.

After salivary glands treated with saponine 0,1 mM Co^{2+} lead to membrane bonded Ca^{2+} level reducing to 35,50 % according to the control (P<0,0001, n=6). Adding to incubatory medium Co^{2+} and chlorpromazine simultaneously caused membrane bonded Ca^{2+} level diminishing to 18,10 % (P=0,018, n=6). As to our opinion chlorpromazine reduces an inhibitory effect of Co^{2+} to Ca^{2+} pump of endoplasmic reticulum membrane.

R-10

THE "SHIFTED PHASES" PRINCIPLE IN REGULATION OF CELLULAR Ca^{2+} TRANSPORTING SYSTEMS

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Until now in cellular physiology static approach in estimating different processes has been predominant. Especially it concerns the flowing of Ca^{2+} dependant processes. Intuitively, while estimating functional activity of a certain Ca^{2+} transporting system under particular conditions we take into account only increasing or decreasing of cytosolic Ca^{2+} concentration and pay no attention to temporal parameters of the process. Modern cell paradigm is based on ideas about the ***same direction*** functioning of corresponding Ca^{2+} transporting systems of ***plasma membrane*** and ***endoplasmic reticulum*** (e.g. pumps), this paradigm is generated by the static approach. At the same time the paradigm does not take into account the fact that different Ca^{2+} transporting systems of the same ***cell domain*** have different kinetics, i.e. in the simplest case transporting velocity by Ca^{2+} pump is less than by channel. Therefore, as a result of even simultaneous activation of these systems, local increase of Ca^{2+} concentration enough for appropriate physiological answer will be observed in cytosol. This is even more relevant to sensitivity of transporting systems to physiological active substances. Simultaneous stimulation (depression) of active and passive Ca^{2+} transporting systems of the cell domain will lead to ***changes of frequency*** (!) of Ca^{2+} signal and, thus, to better cell adaptation to the physiological needs. According to the static approach, in order to coordinate functioning of Ca^{2+} transporting systems of the cell domain physiologically active substances must have manifold effect on these systems. But such a scheme is not energy efficient; therefore there is no point in activating Ca^{2+} pump when channels are blocked. More efficient solution is to use the ***"shifted phases" principle***, i.e. the maximum activity of one system is only dislocated as to another one. As it appears, the cell prepares itself to the local Ca^{2+} concentration increase, therefore, while the probability of corresponding cell domain Ca^{2+} channels activation increases, Ca^{2+} pump stimulation of the same domain takes place. It happens simultaneously or (according to the general scheme) with some delay. Only under such conditions the activation of local Ca^{2+} wave is possible. This activation would be optimal to the cell physiological needs, and, at the same time, it would be energy efficient. Accordingly cell productivity and plasticity is better.

R-11

THE INFLUENCE OF THE THIOPERAMIDE ON THE MOTOR ACTIVITY OF THE STOMACH AND DUODENUM IN DOGS.

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It is well known that histamine takes part in the regulation of gastrointestinal motility. At least investigated question in action of histamine on food and fast motility is the role of H_3 histamine receptors. Most of experiments connected with the investigation of H_3 histamine receptors' role in the regulation of gastrointestinal motility were done in vitro. So it is important to investigate the role of H_3 histamine receptors in the action of histamine on food and fast motility in vivo.

The aim of the study was to investigate the action of antagonist of H_3-receptors on fast and food motility of stomach and duodenum in dogs.

The methods: the investigations were carried out in chronic experiments on dogs with fistulas of fundal part of stomach and duodenum. By ballonographyc method we recorded the periodical and food motility (100 g of bread) of stomach and duodenum. Antagonist of H_3 –receptors thioperamide (Sigma Chemical Co, USA) was injected intravenously in dose 0,07 mg/kg on the background of the phase of rest and on 15 min after feeding. During each 15 min period of experiment we calculated motor index.

The results: in control experiments it was established that the phase of rest in stomach lasted 61.8 ± 3.36 min and in duodenum 35.16 ± 3.45 min. The phase of work in stomach and in duodenum lasted 27.4 ± 1.49 and 51.06 ± 2.97 min consequently. Antagonist of H_3–receptors thioperamide evoked the lengthening the phase of work of periodical motility in the stomach on 64.85 min (236.6%, $p<0,001$) and in duodenum - on 62.94 min (123%, $p<0,001$). The phase of rest in the stomach slightly decrease on 8.3 min (13.4%, $p>0,05$) and in duodenum on 2.91 (8.27%, $p>0,05$) min. Motor index did not change during the fast motility. It was shown that thioperamide did not influence on the character and motor index of food motility in dogs.

Conclusion: endogenous histamine through the H_3 histamine receptors determines the duration of the phases of rest and work of fast motility. But it did not influence on food motility.

R-12

THE ROLE OF ENDOGENOUS NITRIC OXIDE IN PERIPHERAL REGULATION OF GASTRIC ACID SECRETION

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Nitric oxide (NO) donors have a potent influence on gastric acid secretion (GAS). In dependence of dose, this influence is stimulatory or inhibitory. However, role and character of influence of endogenous NO remains insufficient examined. Using non-selective NOS inhibitor N^G-nitro-L-arginin-methyl-ester (L-NAME) it has been shown that NO mediates central inhibitory action on GAS of endotoxin [Barrachina, 1995], oxitocin [Espluges, 1996], bombesin [Beltran,1999], glutamate [Garcia-Zaragoza, 2000]. We assumed that NO is involved in peripheral mechanisms of GAS regulation.

The aim of the study was to investigate the influence of blockade of endogenous NO on basal and stimulated GAS in rats.

Investigations were carried out in acute experiments on rats under urethane anesthesia (110mg/100g). Gastric acid secretion was studied by the method of continuously perfused isolated stomach described by Ghosh and Shild [1958]. We examined the effect of L-NAME in doses 5, 10 and 20 mg/kg (i.v.) on basal and stimulated GAS by pentagastrin, carbachol and histamine.

It has been shown that L-NAME in doses 5 and 10 mg/kg decreased the basal GAS by 52,7% ($p<0,01$) and 65,3% ($p<0,01$) respectively, but in dose 20 mg/kg it didn't influence basal GAS. L-NAME evoked dose-dependent increase of GAS stimulated by pentagastrin (16μg/kg, i.p.) and carbachol (10 μg/kg, i.p.). Opposite L-NAME in doses 5 and 20 mg/kg diminished histamine (3 mg/kg, i.p.) GAS. Since NO may have different effects on GAS depending on secretory stimuli were used.

Thus the present findings confirm inhibitory role of NO in the pentagastrin GAS and show that endogenous NO oppressed GAS stimulated by carbachol. Further studies should be done to determine the participation of NO in the mechanisms of basal and histamine GAS.

R-13

NO AS A MEDIATOR OF SOMATOSTATIN INHIBITORY ACTION AT GASTRIC ACID SECRETION, STIMULATED BY PENTAGASTRIN.

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Somatostatin is a well-known physiological inhibitor of gastric acid secretion. Results of some experiments demonstrate somatostatin"s ability to regulate nitric oxide (NO) production. For example, somatostatin in vitro dilates preconstricted cat superior mesenteric artery segments via the endothelial release of NO [Dezsi, 1997]; somatostatin modulate the release of NO by Kupffer cells in rat"s cirrhotic liver [Chao, 1999] and in human and rat retinal pigment epithelium cell cultures [Vasilaki, 2002]; somatostatin-induced gastroprotection and restoration of gastric blood flow during ethanol exposure involve mechanisms which are dependent on NO generation [Ancha, 2003]. It is known that NO inhibits gastric acid secretion [Berg, 2001]. We assumed that NO is involved in somatostatin"s inhibitory action of gastric acid production.

The aim of this study was to determine the role of nitric oxide in inhibitory action of somatostatin on gastric acid secretion stimulated by pentagastrin.

Investigations were carried out in rats in conditions of acute experiment under urethane anesthesia (110mg/100g). Gastric acid secretion was studied by the method of perfusion of isolated stomach described by Ghosh and Shild [1958].

It was established that sandostatin, synthetic analogue of somatostatin (10 μg/kg/h) inhibited gastric acid secretion stimulated by pentagastrin (26 μg/kg/h) by 61%. This effect was sensitive to the action of L-NAME (10 mg/kg, i.v.). However, L-NAME only decreased but not fully removed inhibitory action of sandostatin on pentagastrin acid secretion. In this experiments sandostatin concurrently increased NO_2^- content in the blood. L-NAME decreased augmentation of NO_2^- content in the blood evoked by sandostatin.

These results suggest that NO partially mediates inhibitory action of somatostatin on pentagastrin-stimulated acid secretion in the rat stomach.

R-14

THE NEW FINDINGS ABOUT ROLE OF PERIFERAL GLUTAMATE NMDA-RECEPTORS IN THE REGULATION OF GASTRIC ACID SECRETION

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In spite of the substantial progress in the investigation of regulatory mechanisms of acid secretion, the mechanism of hypersecretion are still poorly understood. It is known that excitability of central glutamate receptors stimulate gastric acid secretion. The role of peripheral glutamate receptors in the secretory processes in stomach unknown.

The aim of present study was: to investigate the influence of activation of peripheral ionotropic NMDA receptors on basal, carbachol and histamine gastric acid secretion in the rats.

Methods: The investigations were carried out in acute experiments in rats by method of stomach perfusion by Ghosh and Shild. Agonist NMDA receptors N-methyl-D-aspartate which don't pass blood-brain barrier (Gmyro et al., 2000; Shinozaki et al., 1990) was used.

Results: Administration of N-methyl-D-aspartate (3 mg/kg, i.v.) had no significant effect on basal and stimulated by histamine gastric acid secretion and increased carbachol gastric acid secretion by 40%.

Conclusion: peripheral ionotropic NMDA receptors take part in the regulation of carbachol stimulated gastric acid secretion and don't influence on basal and histamine gastric acid secretion in rats.

R-15

EFFECTS OF CHOLECYSTOKININ UPON ELECTRIC AND MECHANIC ACTIVITY IN TAENIA COLI SMOOTH MUSCLES

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The effects of cholecystokinin upon electric and contractile activity in guinea pig taenia coli smooth muscles, using sucrose-gap technique and 6MX1C transductor, was investigated. It was shown that cholecystokinin in $1 \cdot 10^{-4} – 1 \cdot 10^{-15}$ M concentrations increase the amplitude and time of action potentials contraction in longitudinal muscles in dose-dependent manner, while the membrane's potential decreased.

Cholecystokinin in all concentrations $1 \cdot 10^{-4} – 1 \cdot 10^{-15}$ M induced the increase of amplitude and time of contraction in smooth muscles in normal Krebs solution (PSS), which contained 5 mM TEA or ouabain in $1 \cdot 10^{-5} – 1 \cdot 10^{-7}$ M concentrations.

Cholecystokinin induced the increase of amplitude and time of action potentials in visceral longitudinal muscles in both normal (37^0 C) and low temperature extracellular PSS.

In calcium-free PSS this biologically active substance after 5-7 min was ineffective.

Cholecystokinin didn't induce the increase of amplitude and frequency of muscle contraction in normal PSS, which contained $LaCl_3$ or D-600.

Thus we can suggest that extracellular Ca^{2+} ions play central role in mechanisms of cholecystokinin action upon taenia coli smooth muscles of guinea pig.

R-16

THE INFLUENCE OF L-ARGININE ON WATER AND ELECTROLYTE TRANSPORT IN PERFUSED RAT COLON IN VIVO

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It is well known that nitric oxide (NO) stimulates electrogenic chloride secretion in inflamed colon, a mechanism responsible for secretory diarrhea. In organism NO is generated from L-arginine by NO synthases rate of which increasing during bowel inflammation. *The aim of our study* was to investigate the influence of L-arginine on water and electrolyte transport in normal colonic epithelium of rats. *Methods*: water and electrolyte transport were evaluated by in vivo perfusion technique with the colon of anesthetized rats. Test solution containing (in mM/l): NaCl – 100; $NaHCO_3$ – 20; KCl – 4.7; $CaCl_2$ –1.3; $MgCl_2$-1.2; Na_2HPO_4-16.8; NaH_2PO_4-3.2; glucose-5, pH=7.4 was perfused through colonic loop for 140 min. at perfusion rates of 0.25 ml/min. The nonabsorbable marker, phenol red, we added to each test solution at a concentration of 20 mg/l in order to determine net water absorption. The concentration of phenol red, Na^+, K^+, Cl^- was measured to calculate net water and electrolytes absorption. Absorption or secretion rates we determinated spectrophotometrically and used to calculate net water absorption The concentration of Na^+, K^+, Cl^- in the test solutions and their perfusates we determinated by ion-selective electrodes. The rates of net water (μL/min per g dry weight) and electrolyte (μmol/min per g dry weight) absorption we calculated as described in Schedl (1966). *Results*: After equilibration period (60 min), the basal net water flux was 42,03+/-4,29 μL/min per g dry weight, net Na^+ flux was 33,14+/-33.9 μmol/min per g dry weight, net K^+ flux was -0.44+/-0.21 μmol/min per g dry weight, net Cl^- flux was 7.64+/-6.96 μmol/min per g dry weight. L-arginine administration (500 mg/kg, i.p.) didn't change level of basal net water and electrolyte flux. Conclusions: In normal physiological conditions administration of L-arginine had no significant effects on the net water and electrolyte flux.

R-17

THE INFLUENCE OF MACROLIDES ON SECRETORY FUNCTION OF STOMACH.

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Motilin (M) is a slow excitation mimetic of particular interest because it is implicated as a messenger substance in the initiation of the migrating motor complex in the interdigestive period. Editional interest emerges from findings that macrolide antibiotics (eg, erythromycin, roxythromycin - motilides) act on M receptors to facilite gastric emptying in disoders such as diabetic gastroparesis. There has been only three reports regarding the effect of erythromycin on gastric secretion (GS) [Fiorucci et al., 1993; Narchi et al., 1993; Asai et al., 2000].The aim of the study was to investigate the mechanism of action of agonists of M receptors on GS.

The investigations were carried out in chronic experiments on 11 dogs with fistulas of stomach and duodenum and on 40 white rats. GS in rats we investigated by method of perfusion of isolated stomach by Ghosh and Shild.

In dogs with intact nervous system erythromycyn and roxythromycin diminished GS stimulated by carbachol, histamine and pentagastrin and didn't influence on GS evoked by insulin. Vagotomy didn't influence on inhibitory action of macrolides on GS. It was concluded that M receptors in central nervous system don't paticipate in regulation of GS in dogs. Nonselective antagonist of nitric oxide synthetase L-NAME removed the inhibitory influence of roxythromycin on GS stimulated by histamine and didn't influence on its inhibitory action on GS stimulated by carbachol in dogs. In rats nonselective antagonist of vasoactive intestinal polypeptide [Lys^{1},$Pro^{2,5}$,$Arg^{3,4}$,Tyr^{6}] removed the diminishing action of roxythromycin on GS stimulated by carbachol. We concluded that macrolides oppress the GS through the excitation of M receptors on interneurons of enteral nervous system that leads to release of acetylcholine from axons of these neurons. In its turn acetylcholine stimulate inhibitory motoneurons from endings of which nitric oxide and vasoactive intestinal polypeptide are released.

MECHANISM OF INJURIES AND CYTOPROTECTION OF GASTROINTESTINAL TRACT

M-1

PROTEIN TYROSINE PHOSPHATASE ACTIVITY IN LYMPHOID CELLS UNDER CONDITIONS OF ETANOL- ASPIRIN- AND STRESS-INDUCED STOMACH ULCER DEVELOPMENT COMBINED WITH CYCLOFERONE TREATMENT

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It is known that one of factors involved in pathogenesis of stomach ulcer desease is an immunusupression leading to decreasing of functional activity of lymphoid cells of spleen and thymus. Widespread enzymes regulating cell proliferation, differentiation and immune reaction forming in lympoid cells are protein tyrosine phosphatases (PTP). The levels of protein tyrosine phosphatase activities in membrane and cytosol of rat spleen and thymus lymphocytes under conditions of different models of stomach ulcer development. Also it was evaluated a cycloferone administration effect on these parameters. Three models of stomach ulcer disease were used – aspirin-, stress- and ethanol- induced. Stomach ulcer initiation was performed using 80% ethanol *per os* administration (once), 150 mg/kg aspirin *per os* administration (every 12 hours) or immobilization stress. It was shown, that ethanol-induced stomach ulcer was accompanied by stimulation of PTP activity in membrane fractions of spleen and thymus lymphoid cells. The significant increasing of cytosol PTP activity in thymocytes and decreasing of this parameter in spleenocytes were observed. Development of stress- induced ulcer leads to the thymocyte cytosol PTP activity stimulation and spleenocyte cytosol PTP activity inhibition. There were found no changes in activity of membrane PTP. It was shown inhibition of PTP activity in most of studied origins, except thymus membrane-associated fractions under conditions of aspirin-induced stomach ulcer development. These data confirm that different processes were involved in ulcer-accompanied immune disbalanses under conditions of various type of ulcer. Cycloferone is sintetic molecule posesses potent immunomodulating effect connected with increasing of interferone synthesis. The effect of injections of cycloferone (twice a day in dose 62 mg/kg during 5 days) was an increase of intracellular PTP activity and decrease of membrane-associated one in Control. The combination of cyclopherone treatment and aspirin-induced ulcer development on rats leads to increasing and normalisation of PTP activity levels in thymus lymphoid cells, but not in the spleen ones.

M-2

LONG-TIME EXPOSION OF INTESTINAL EPITHELIAL CELLS TO PRO-INFLAMMATORY MEDIATOR LTD_4 CAUSE NEOPLASTIC TRANSFORMATION VIA STABILIZATION OF β-CATENIN AND ITS ASSOCIATION WITH BCL-2.

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The inflammatory mediator leukotriene D_4 (LTD_4) is present at high levels in many inflammatory conditions, and areas of chronic inflammation have an increased risk for subsequent cancer development. We have previously shown that LTD_4 induces up-regulation of β-catenin, as well as other proteins, which can influence survival and proliferation in intestinal epithelial cells. We demonstrate here that following LTD_4 stimulation, β-catenin is translocated to the nuclei triggering the transcriptional activity of the T-cell and lymphoid enchanced factor (TCF/LEF) family of transcription factors. The nucleic translocation was confirmed with both cell fractionation and confocal microscopy. These events were dependent on phosphoinositide-3-kinase (PI-3 kinase) activation and GSK-3β inhibition. We also report that free β-catenin can translocate to mitochondria upon LTD_4 stimulation and associate with the cell survival protein Bcl-2. Effects of the interaction between these two proteins could also be demonstrated, (1) Bcl-2 over-expression leads to enhanced TCF/LEF promoter activity and, (2) high β-catenin levels counteract mitochondrial apoptosis. Our data suggest that, similar to Wnt signaling, LTD_4 increases free β-catenin via inactivation of GSK-3β, followed by the initiation of TCF/LEF transcriptional activity. Also, this Wnt-like signaling affects cell survival in a positive, previously unknown, manner by permitting the association of Bcl-2 and β-catenin at the mitochondria. Together with previous findings this work further delineates the crossing point between inflammation and carcinogenesis.

M-3

INVOLVING SECOND MEDIATORS ON HISTAMINE H3 RECEPTORS SIGNAL TRANSDUCTION IN RAT PARIETAL STOMACH MUCOSAL CELLS UNDER THE STRESS ULCER FORMATION

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H3 receptors are located in the gastrointestinal tract in cholinergic and NANC neurons of the myenteric plexus, in endocrine and/or paracrine cells of the gastric mucosa. The role of histamine H3 receptors in regulation of parietal cells function remains not enough trained. As the endocellular calcium and cyclic nucleotides are the basic second mediators in the transmission of signals in cells the study of contents of these compounds became the purpose of our research.

The object of experiments was white Wistar rats by mass 180-220 g. A stress ulcer was caused by means the immobilization stress. The parietal cells were isolated. R-alpha-methylhistamine and thioperamide (H3 receptor agonist and antagonist correspondingly) were injected intraperitoneal in 0,5 and 1,0 mg/cg doses accordingly on the second day of experimental ulcer formation. The contents of cyclic nucleotides was determined in cells cytosol using Cyclic AMP [^{3}H] Assay System and Cyclic GMP [3H] Assay System, code TRK500. The contents of endocellular calcium was determined loading the cells fluorescent sound Indo-1.

Intraperitoneal injection of histamine H3-receptor agonist (R)-alpha-methylhistamine caused decrease of $[Ca]_i^{2+}$ contents on 20% , increase of the cGMP content on 42% and enhancement of the cAMP production on 26% in cytosol of rat gastric parietal cells under the experimental stress. H3-receptor antagonist thioperamide led to attenuation of the cAMP production on 47% and enhancement of the cGMP on 105% and enhance of $[Ca]_i^{2+}$ contents on 10% in isolated parietal cells. Also our research demonstrated dependence between changes of $[Ca]_{i2+}$ contents and conforming Ca^{2+}, Mg^{2+}-ATPase activation.

It was shown that H3 receptor demonstrated different effects on the contents of endocellular calcium and cyclic nucleotides under the experimental stress ulcer formation.

M-4

2′,5′-OLIGOADENYLATE-SYNTHETASE ACTIVITY IN RAT LYMPHOID CELLS UNDER EXPERIMENTAL STOMACH ULCER

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The aim of the work was to study 2′,5′-oligoadenylate-synthetase activity in rat spleen and thymus lymphoid cells under the development of aspirin, alcohol and stress experimental model of stomach ulcer and also to investigate the immunomodulatory antiulcer drug squalene influence on this parameter.

It was shown that 2′,5′-oligoadenylate-synthetase activity increased under the aspirin and stress stomach ulcer model regarding to control. Perhaps its rise is a result of interferon system activation. And observed effect may be related with immunocompetent cells protective mechanisms activation. On the other hand investigated parameter decreased noticeably comparatively with control under the alcohol model of stomach ulcer. This may be evidence of the interferon-dependent regulatory cascade functioning depression because of present stomach ulcer aetiology peculiarities.

Peroral introduction of biological active substance squalene possessing antioxidant and wound healing activities to the animals with aspirin stomach ulcer caused an additional rise of 2′,5′-oligoadenylate-synthetase activity in lymphoid cells 1.5 times and twice as much after its administration during 1 and 3 days accordingly. Thus squalene intensified the effect of investigated enzyme activation in rat immunocompetent cells against a background of aspirin stomach ulcer development that could be related with intensification of immune cells compensatory mechanisms under the conditions of pathology development. Besides squalene action was more effective after its durable introduction to the animals.

M-5

EARLY GROWTH RESPONSE FACTOR – 1: A KEY GENE & TRANSCRIPTION FACTOR IN EXPERIMENTAL DUODENAL ULCERATION.

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Previously we demonstrated that cysteamine releases endothelin-1 in the rat duodenal mucosa, followed by increased expression of the early growth response factor – 1 (egr-1). We hypothesized that egr-1 is a key mediator gene in the multifactorial mechanisms of cytoprotection and healing in duodenal ulcerogenesis because its transcription factor product Egr-1 regulates the expression of angiogenic growth factors. Methods: Non-fasted female Sprague-Dawley rats (200g) rats were treated with saline or cysteamine-HCl (25mg/100g) and killed 0.5-48 hr later; certain animals were pretreated with scrambled control or Egr-1 antisense phosphothioate oligonucleotides: a) Egr-1, HIF-1α/DNA binding and Egr-1 or HIF-1α transcriptional interactions with redox-sensitive transcription factors were determined in duodenal mucosal samples. b) DNA microarray, real-time RT-PCR and Western blotting were used to assess the expression of egr-1 mRNA, Egr-1 protein as well as ERK, bFGF, PDGF and VEGF. c) Duodenal mucosal oxygenation and redox status were also measured by using oxygen and redox electrodes in other group of rats. Results: Cysteamine increased the expression and nuclear translocation of Egr-1, Ref-1 and Trx, and activated binding of Egr-1 to DNA. Moreover, Egr-1 forms a complex with other redox-sensitive transcription factors (e.g., AP-1, AP-2, NFATc, Sp1, MTF-1, c-Myb and CREB) in rat duodenal mucosa and cysteamine enhanced the formation of these complexes. Cysteamine only slightly increased the binding of HIF-1α to DNA, however, it markedly increased (45-50%) the HIF-1α interactions with other transcriptional factors e.g., Egr-1, AP-1, AP-2, CREB, NFkB, STAT4 and MTF-1 and their binding to DNA in duodenal mucosa 0.5 and 12 hr after cysteamine. Cysteamine induced the phosphorylation of both ERK1/2, enhanced the synthesis of bFGF, PDGF and VEGF in the pre-ulcerogenic stages of duodenal ulceration while the egr-1 antisense inhibited the expression of egr-1 mRNA and Egr-1 protein, markedly decreased the synthesis of bFGF, PDGF and VEGF in the duodenal mucosa. The antisense egr-1 dramatically increased the duodenal ulcer from 8.1±1.8 in controls to 20.7±4.0 mm^2 ($p<0.01$). Cysteamine treatment reduced by 18-22% duodenal mucosal pO2 (vs. baseline) and significantly increased the redox status in the proximal duodenal mucosa. Conclusions: Thus, Egr-1 seems to play a critical role in cysteamine-induced duodenal ulceration because Egr-1 downregulation aggravates the experimental duodenal ulcers, most likely through the transcriptional inhibition of bFGF, PDGF and VEGF synthesis.

M-6

THE EFFECT OF ALCOHOL ON STOMACH SECRETION AND MUCOSAL DEFENCE UNDER M_1-CHOLINERGIC RECEPTORS AND L-CA^{2+} CHANNELS INHIBITION

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Alcohol is very important cause of morbidity in the gastrointestinal tract. The changes in gastric secretion, motility and adaptive cytoprotection in the upper tract are likely to be associated with alcohol (ethanol, vine spirits) ingestion. Alcohol active pathways are connected with concentration of intracellular Ca^{2+} in parietal cells, by histamine release from ECL cells and by acetylcholine-dependent mechanisms, etc. The aim of recent investigation was to analyse role of M_1-cholinergic receptors and L-Ca^{2+} channels in gastric secretion and mucosal defence in rats with ethanol-induced gastric mucosal lesions.

The experiments were carried out on the urethane anaesthetised rats. The stomach was perfused with physiologic saline and pH, debit of H^+ ions and pepsin concentration were determined. Gastric mucosal lesions were developed immediately after 2 minutes of 50% ethanol perfusion. Gastrocepine (6 mg/kg i.v.), is known to be agonist M_1-cholinergic receptors, was used alone and with and L-Ca^{2+} channels blocker verapamile (1.25 mg/kg i.v.).

Perfusion of gastric lumen with 50 % ethanol inhibited debit H^+ ions by 30 % ($p<0.05$) compared with base level. Decrease of pepsin concentration was not so significant (16 %, $p<0.05$). The 50 % ethanol exposure resulted both the gross mucosal injury (erosions, haemorrhagic) and hyperemia on 17 % and 61 % areas of rat glandular mucosa accordingly.

Significant inhibition of gastric secretion by 18 % ($p<0.05$) on 30 min. and by 30 % ($p<0.01$) on 60 min was associated with prior i.v. administration of L-Ca^{2+} channels blocker verapamile. There were not changes in pepsin level during the hour after ethanol administration. L-Ca^{2+} channels inhibition enhanced the development of gross haemorrhagic erosions caused by ethanol up to 34 % ($p<0.05$).

Pretreatment with M_1-cholinergic receptor antagonist gastrocepine did not prevent the ethanol-induced injury. Gross mucosal haemorrhagic lesions were not attenuated by prior i.v. administration of gastrocepine, but hyperemia area was reduced insignificant. In this case gastrocepine was found to depress H^+ ions output in great manner (50 %, $p<0.05$) and did not changed pepsin level.

Simultaneous action of gastrocepine and verapamile attenuated the gastric mucosal lesions up to 10 % ($p<0.05$) comparably with the verapamile action alone. Acid secretion was inhibited by 23 % ($p<0.05$) and pepsin concentration by 12 %.

M-7

GHRELIN ATTENUATES THE GASTRIC MUCOSAL DAMAGE INDUCED BY ISCHEMIA/REPERFUSION

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Background and Aims: Previous studies demonstrated that ghrelin exhibits protective effects on gastric mucosa. However, the exact mechanisms responsible for this phenomenon are still poorly understood. The aim of the present study was: 1) to assess the effect of exogenous ghrelin on acute gastric mucosal damage induced by ischemia-reperfusion (I/R); 2) to analyze the role of prostaglandins and sensory nerves in this phenomenon and 3) to study the effect of ghrelin treatment on the gastric mucosal gene and protein expression of constitutive NO synthase (cNOS) and calcitonin gene related protein (CGRP) **Methods:** Gastric ischemia was induced for 30 min by applying a small vascular clamp to the celiac artery and reperfusion was produced by removal of the clamp for 60 min. Several series of rats were used to assess the effect of ghrelin on the acute gastric lesions induced by I/R; 1) I/R applied alone; 2) rats exposed to I/R and pretreated with ghrelin (5, 10 or 20μg/kg i.p.); 3) rats exposed to I/R and pretreated with ghrelin in combination with rofecoxib (5 mg/kg i.g.) or methylated prostaglandin E2 (5 μg/kg i.g.), 4) rats with inactivated sensory nerves by capsaicin exposed to I/R and pretreated with ghrelin in combination with CGRP (10 μg/kg s.c.), 4) control group without exposure to I/R. Gastric erosions were counted and mucosal blood flow (GBF) was assessed by H_2 gas clearance method. **Results:** I/R of the stomach produced numerous small gastric erosions, decrease of GBF and expression of cNOS. Ghrelin dose dependently attenuated the number of lesions induced by I/R and the protective effect was accompanied by the increase of GBF and increase in expression of cNOS and CGRP. The protective effect of ghrelin was attenuated by the treatment with selective COX-2 inhibitor and inactivation of sensory nerves by capsaicin and this was reversed by the treatment with prostaglandin E_2 or CGRP, respectively. **Conclusions**: Ghrelin exerts a potent gastroprotective activity against I/R-induced erosions and this protection involves the gastric hyperemia and increase in NO generation due to increased cNOS expression.

M-8

SEROTONIN AND NITRIC OXIDE IN INJURY AND HEALING OF GASTRIC MUCOSA

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The aim of the presented work was to study the influence of nitric oxide (NO) on damages in gastric mucosa (GM) evoked by serotonin.

Male white rats weighting 180-200 g were used. These animals were starved for 24 h prior to experiments, but were allowed free access to water. Gastric injury was induced in rats by i.p. injection of serotonin creatinine sulfate complex (10 mg/kg) (Sigma Chemical). We investigated the influence of NO donor sodium nitroprusside (SNP) (Sigma Chemical) on gastric injury induced by serotonine. Since injected serotonin is completely metabolized by monoaminooxidase in about 100-120 minutes, two hours later the animals were killed and their stomachs were removed. We evaluated the length of erosions, area of ulcers and massive hemorrhages. Simultaneously the content of NO_2^- in the blood was estimated with Griess reactive. Products of painting were spectrophotometrised on waves of λ=540-550 nm. Results of spectrophotometry were sorted and medium data were counted and taken to estimate the concentration of NO_2^- by calibration curve. NO synthase (NOS) activity was measured in homogenate of GM by method described by Hevel et al. (1991).

Serotonin evoked the formation in GM of erosions (5,18$\pm$0,95 mm), ulcers (8,48$\pm$3,10 mm^2) and hemorrhages (3,68$\pm$1,02 mm^2). Serotonin enhanced the NOS activity by 43% ($p<0,05$). In results the content of NO_2^- in the blood was increased by 23% ($p<0,05$). SNP in doses 1-4 mg/kg markedly protected the rat GM from damages induced by serotonin. SNP had dose-dependent action.

We concluded that in reply to vasoconstriction in GM evoked by serotonin occurs compensatory the generation of NO (vasodilating agent) via the action of the NOS. However this level of NO isn't insufficient to protection of GM from damages. That's why treatment of NO donor SNP protected GM from injury induced by serotonine.

M-9

INFLUENCE OF PGP ON THE CNS STRUCTURE CAN BE ONE OF THE MECHANISMS OF IT'S ANTIULCER EFFECT REALIZATION

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It was shown in our previous investigations that short prolinecontaining peptides (PGP, GP, PG), belonging to the glyprolines family, show pronounced protective antiulcer effect. Preliminary peptides administration considerably reduced degree of the gastric mucosal damages in different experimental models, including stress model where central regulatory mechanisms disfunction is the main cause of ulcerogenesis. At the same time possibility and effectiveness of glyprolines influence at the level of CNS structures is poorly studied. We've shown earlier that PGP and GP have pronounced preventive effect: their preliminary administration (before stressor application) leaded to much lesser expressed stress-caused changes in behavior. The goal of this work was studying therapeutic effects of PGP. The experiments were carried on outbred white male rats weighing 200-250 grammes. The stressor used was 10-minutes forced-swimming. Orientation-exploratory activity and level of anxiety was estimated in the test of hole board and elevated plus-maze test. Peptide was administrated intranasally in the dose of 3,7 mkmolkg in the volume jf 0,5 milliliter /200g of the body weight in 5 min, 15 min, and 3 hours after the end of the stressor influence. The animals of the control group got the equal volume of physiological solution. The stress caused significant increase of anxiety and decrease of orientation-exploratory activity level. PGP practically completely eliminated stress-caused changes in behavior. In 3 hours after PGP administration the effect fully remained in force. So PGP not only prevents stress-caused changes in behavior but also eliminates already existing ones thus possessing not only preventive but also curative action. The observed results point at the possibility of PGP influence on the CNS structures participating in the organism stress factor action response forming. Gastric mucosal homeostasis supporting central regulatory mechanisms normalization may appear to be one of the important factors in glyprolines antiulcer effect realization.

This work was support by the Russian Foundation for Dasic Research № 48664

M-10

PHARMACOKINETICS OF PEPTIDE ANXIOLYTIC SELANK *IN VIVO* AND *IN VITRO*.

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The study deals with the distribution of peptide anxiolytic Selank (TKPRPGP), and its fragments, in rat brain and blood after introperitoneal administration, as well as with the degradation pathways of this peptide's in blood plasma (*in vitro*). Solid state catalytic isotope exchange was used for production [G-^{3}H]Selank (110 Ci/mmol) with the isotope label in all its amino acid residues. [G-^{3}H]Selank was administrated into the rat or incubated with rat blood plasma *in vitro*. After that HPLC of brain tissues and blood extracts, enriched with nonlabeled Selank and its fragments in UV-detectable concentration, was performed. The concentration of [G-^{3}H]Selank and its fragments was evaluated by measuring radioactivity of appropriate chromatographic fractions. At the first minute after intranasal administration Selank was detected in bulbus olfactorius, in brain cortex and in brainstem. At the third minute the peptide concentration in above-mentioned brain regions was several times higher, than in blood. Selank biodegradation in blood plasma was mainly due to c-end dipeptides restriction (90%) leading, in series, to the formation of TKPRP and finally to the long-living TKP and RP fragments. Contribution of dipeptidylaminopeptidases to Selank biodegradation in blood plasma was about 10%, while amino- and carboxypeptidases did not take part in Selank hydrolysis at all. It was also shown that the sets of Selank biodegradation products formed in the blood plasma of rat and man are similar, although the rate of hydrolysis in rat blood plasma is three times as rapid as that in human blood plasma. Selank biodegradation in blood *in vivo* was similar to that in blood plasma *in vitro*; however, some products of amino- (4%) and carboxypeptidase (0,4%) activities were detected in the blood. In conclusion, we demonstrate that after intraperitoneal administration, Selank quickly enters the brain and the blood. The main biodegradation pathway of Selank in rat blood is hydrolysis by dipeptidylcarboxypeptidases.

This work was suppoted by Russian Foundation for Basic Research № 03-04 48664

M-11

THE PROTECTIVE EFFECT OF KETCHENEROVSKAYA MINERAL WATER (REPABLIK OF KALMYKIA) ON ETHANOL ULCER-INDUCED ALBINO RATS

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The stomach ulcer is a widespread disease. The search for preventive and therapeutic medicines is very actually. S ome medicinal mud and mineral waters are of anti-ulcer effect. We have previously proved that medicinal mud and rapa of Lake Manych (Republic of Kalmykia) have a marked anti-ulcer effect (2002,2003). In 2004 our group together with Test Centre of Natural Recources of the Russian Scientific Centre of Recovering Medicine and Balneology made a chemical analysis of Ketchenerovskaya mineral water (Republic of Kalmykia).

According to its chemical composition the tested water is sodium chloride mineral water (Cl 90, $Na^+ + K^+$ 96 mg-ekv%, M=9,6 g/dm^3) with weak alkaline reaction of the medium. A conditioned content of boron(H_3BO_3-76 mg/dm^3) and increased content of bromine (Br –16 mg/dm^3) were discovered in the water.

The formula of the chemical composition is the following:

$$M_{9,6}\ \frac{Cl\ 90}{(Na+K)\ 96}$$ Sp: H_3BO_3 –76 mg/dm^3

The analysis of the tested mineral water shoved that it might be effective at disfunctions of alimentary canal. In this connection we decided to check up anti-ulcer effect of the water on ethanol-induced experimental model.

Ulcer was caused by injecting ethanol 96^0 C into the stomach of albino rats 200-250 gr. by weight. A week before inducing ulcer animals of the tested group(n=12) were given mineral water as potable water, which they drank readily. The control group of animals (n=11) had usual drinking water.

The weight of ethanol affection was assessed by a degree of the ethanol injury area reduction in the tested group in comparison with the control one. The total area of stomach mucous membrane injury decreased in the tested group to 72% in relation to the control one (117±4,7 mm^2 - control, 32±4 mm^2 - test, $p<0,05$).

Thus, it has been experimentally proved that Ketchenerovskaya mineral water has a maked protective antiulcer effect on ethanol-induced ulcer and can be recommended for correction of alimentary canal disfunctions.

M-12

ROLE OF COLLAGEN FRAGMENTS IN GASTRIC HOMEOSTASIS

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The new glyproline family was distinguished from other regulatory peptides recently (Ashmarin et al., 1998). It includes the simplest proline-and glycine-containing peptides: Pro-Gly, Gly-Pro, Pro-Gly-Pro, cyclo-Pro-Gly and respective peptides with hydroxylated proline residues. Glyproline's bioactivity covers many important systems of the body including suppression platelet aggregation and gastric mucosal maintenance It was shown that Pro-Gly-Pro, Pro-Gly и Gly-Pro have a wide spectrum of antiulcer activity with respect to gastric mucosal damages of various aetiology. Gly-Hyp and Hyp-Gly-Pro show also antiulcer action.**.** In vivo glyprolines may be generated during synthesis and catabolism of collagen. It is well known that approximately 10-60% of newly synthesized collagen degrade intracellularly with succeeding secretion of small peptides composed of less than 5 aminoacid residues out of cells. Different simplest proline and hydroxyproline fragments of glyprolines are revealed in various type of collagen: Gly-Pro, Gly-Hyp, Pro-Gly, Pro-Pro-Gly, Pro-Gly-Pro, Pro-Hyp-Gly, Gly-Pro-Hyp, Gly-Pro-Pro, Gly-Pro-Gly, Gly-Hyp-Pro, Hyp-Gly-Pro. It is possible that these fragments may be secreted out of cells during the stage of degradation of newly synthesized collagen. We showed that the intragastric (per oral) introduction of gelatin hydrolyzate, having 40 small peptide fragments, including Pro-Gly-Pro and Hyp-Gly-Pro, also increase gastric stability showing antiulcer effect. The corresponding receptors for glyprolines are not completely identified yet but it may be supposed that Pro-Gly-Pro, Gly-Pro and other glyprolines interact with the same receptors to which the III type collagen is binding platelets. Characteristics of parameters of inhibition with intact octapeptide and glyproline, as well as the receptor's structure - that's our concern for the nearest future. This work was supported by the Russian Foundation for Basic Research №03-04-48664.

M-13

PECULIARITIES OF THE STOMACH AND DUODENAL MYOELECTRICAL ACTIVITY IN DIFFERENT GASTRO-DUODENAL INJURIES

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Aims: to investigate stomach (S) and duodenal (D) motor activity in disturbances of gastroduodenohepatobiliary system. Methods: 35 white rats in mass of 200-280 g were used. Mucosal damage was produced by daily administration of bile solution on an empty stomach (per os) in a combination with cold-stress (12 days). A cholestasis (C) was modelled in a separate run by applying of two ligatures on the common bile duct. S and D myoelectrical activity (MEA) was recorded with the help of bipolar electrodes (accordingly at 5 mm more proximally and more distally from pylorus). Results: it was fixed that S and D MEA had a phase character in intact state, thus the resting phase (40-50 min), a phase of irregular spike activity (50-60 min) and a phase of regular spike activity (5-9 min) was distinguished. Under modelling of damages of gastroduodenal zone (GDZ) the phasal nature of S and D MEA became broken with dominance of the II phase that was especially expressed on the 12 day of experiment. The period (P) of basic electrical rhythm (BER) on a 6 day was found unstable as against parameters of the 12 day. At the same time, arrhythmia of D BER wasn't observed, but irregular spike activity and more "provoked" state were typical for electroduodenomyogramm (EDMG) than for electrogastromyogramm (EGMG) and general picture of EDMG corresponded to the II phase of MEA. Besides the tendency to diffusion of D rhythm on S was appreciable, last testifies to infringement of a local neuroendocrinal system (NES) activity and an opportunity of antiperistaltic locomotions. It's necessary to note there were observed periodic highamplitude fluctuations (waves) on the EGMG with the P (83,07±0,289) sec and the voltage (10,56±0,064) μV in the I phase of MEA in many experiments just as fluctuations with voltage (11,76±0,171) μV arose on EDMG. With the beginning of the II phase the voltage of this rhythm on EGMG increased on 45,0 %, and on 57,7 % on EDMG respectively ($p < 0,05$). Modelling of C, as against erosion-ulcerative injuries (EUI), was accompanied by infringement of periodic activity of GDZ on the first minutes of experiment. Ascending of D BER voltage in 1,7 times and insignificant decrease of its P was observed. In the course of time D BER wasn't changing, however arrhythmic fluctuations of various voltage and duration appeared on its background. Conclusions: both EUI of GDZ and acute disturbanses of biliary outflow were accompanied by changes of S and D MEA with infringement of the phasal nature of waves. Last fact can be caused by a mismatch of activity of NES, and the last, in turn, assists changes of cortico-visceral interrelations.

M-14

INFLUENCE OF ANTIOXIDANTS ON CONTENT OF ADENINENUCLEOTIDES IN CELLS OF THE MUCOSA OF THE STOMACH AT THE ETHANOL ULCER

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The peptic ulcer of stomach is one of the most wide-spread diseases of organs of digestion. For today treatment of this pathology remains an actual problem as use of existing means of treatment does not yield desirable results and the illness gets chronic flow with relapses. Normalization of the power status of a cell is the necessary condition for regeneration of stomach mucosa at the given pathology. Therefore studying of properties of drugs influencing these processes will allow to find new ways of treatment of peptic ulcer.

Researches in studying the content of adeninenucleotides in cells mucous of stomach of rats were led in pilot model of ulcer with action of natural antioxidants (ammivit and squalene) on these parameters. Experiences were carried out on rats of Vistar line with mass of 180 - 230 g. The experimental stomach ulcer was invoked by peroral introduction of 80% of ethyl alcohol by standard method. Separation and quantitative definition of the content of adeninenucleotides in cells was carried out by method of thin-layer chromatography and direct densitometry of silufol plates in UV-light.

It was shown, that for 5 day at ethanol ulcer in cells mucous of stomach the content of ATP and AMP decreased on 31% and 19% accordingly and the level of ADP increased by 27% in relation to the control that testified to predominance over cells of catabolic processes. Regeneration of balance of adeninenucleotides in cells mucous of stomach was fixed at 5-th day of introduction of ammivit to rats with ethanol ulcer. At combined use of ammivit and squalene the content of ADP returned to control values, ATP level increased on 14% and content of AMP remained reduced on 20%.

Thus, received results testified that natural antioxidants - ammivit and squalene - normalized the content of adeninenucleotides in cells mucous of stomach and consequently could be recommended for application in complex treatment of peptic ulcer of stomach.

M-15

SUBSTANCES OF LEUKOCYTES ON THE EFFECTS OF BRAKE AND EXCITED NEUROTRANSMITTERS IN THE INTESTINAL SMOOTH MUSCLES

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It is known that the Transfer Factor (TF) Staphylococcus aureus is oligoribonukleopeptid. This substance is a product of the sensibilized lymphocyte-helpers (specifically sensitive donors) in the presence of antigen.
The TF of delayed type hypersensitivity to the Staphylococcus aureus antigens was used in experiments. The TF influence on the contraction-relaxation of the smooth-muscle (SM) preparations of guinea pig taenia coli was investigated using the tensometric method in the isometric regime. It is established that this substance dose - dependency increases the amplitude and duration of single spontaneous contractions, and also the contraction, caused by the depolarization of plasmatic membrane of the smooth-muscle cells (SMC). It was shown that the intensification of the excited synaptic transmission and oppression of the brake synaptic transmission (such as the adrenergic, ATP-, NO- and VlP-ergic) in the SM can be one of reason for the described above effects. It is established that this substance in the normal Krebs solution always causes a fast increase in both the phasic and the tonic components of the acetylcholine - induced contraction, and also oppresses the Ca^{2+} release from the inositol-1,4,5-phosphate-sensitive depot of sarcoplasmatic reticulum. The study of TF influence on the contractions of SM taenia coli under the ATP (10 μM) action showed that the ATP induces the contraction instead of relaxation. Analogous effect was also observed, when ATP was added to the Krebs solution during the tonic component of the acetylcholine -caused contraction took place. It was found that substance decreases the amplitude of the brake postsynaptic potentials of taenia coli SM. All effects of TF appeared with the latent period, which indicate on the TF metabotropic action. Further experiments showed that this substance somewhat oppresses the relaxing action of exogenous NO. It was also established that the noradrenaline (10 μM) and isoproterenol (10 μ/M*)* actions remain permanent in the TF presence. Thus, the iritracellular processes, connected with the a-and P-adrenoreceptors activation are not modulated by this substance.
The results obtained testify that the TF, as the natural substance, can transfer the ATP brake action into the excited one in SMC of taenia coli, and also activate the mechanisms of cholienergic activation in theirs.

M-16

EXPRESSION OF PROTEIN TYROSINE KINASES OF SRC AND SYK FAMILIES IN THE COLON OF AGED RATS

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Tyrosine kinases of the Src family are involved in the wide spectrum of intracellular signalling pathways. The corresponding genes participate in such vital processes as cell growth, motility, differentiation, adhesion, mRNA transcription, etc. Specific structural changes confer oncogenic properties to the Src protein (viral form, v-Src). The c-Src non-receptor tyrosine kinase is overexpressed and activated in a large number of human malignancies and has been linked to the development of cancer and progression to distant metastases. However, the concentration of research activity around the role of Src in differentiation and growth was neglect importance of Src in aging processes. Moreover, the investigation of Src expression profiles is a problem of high importance considering that the cancer disproportionately affects older persons. One of age-related types of cancer is colorectal cancer. The aim of the present study was to compare Src and Syk kinase expression in the colon mucosa of different age rats. Two groups of intact male rats were used. In the first group we use of 2-3 weeks old rats and for the second group 3-6 years old rats. Proteins expression was estimated in total colon mucosa extract by specific antibodies in immunoblotting procedure. Semi-Quantitative immunoblotting experiments revealed that the level of proteins phosphorylated on tyrosine changed in old rats up to 30% of level in control rats. At the same time we did not detect significant differences in Src expression in old rats, but the decreased level of tyrosine kinases Syk and Fyn was observed in older rats comparatively to young rats on 20% and 80% respectively. Lower level of phosphorylated tyrosine in old rats gives an evidence about decreased intensivity of colon cells metabolism, of their proliferation rate and probably lower specialization. Effect of down-regulation of colon Syk and Fyn expression leads to decreasing tyrosine phosphorylation. The same phenomenon will be result in weak tyrosine kinase activity and this can be linked to increased risk of colorectal cancer in aged persons. It will be of great interest to determine the mechanisms of kinase disregulation during aging.

M-17

CYTOCHEMICAL ZINC INVESTIGATION IN SUBMAXILLARY GLANDS, PANCREAS AND INTESTINE UNDER VARIOUS EXPERIMENTAL INFLUENCES

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Mice, rats and rabbits were used in experiments. The animals were injected with adrenaline, prednisolone, atropine, pylocarpine, alloxan, streptozotocin, dithizone, were subjected to physical load, immobilization, starvation, alcoholization, cooling. In acute experiments the animals were exposed to single action of indicated factors but in chronic ones – to repeated action of these factors. The pieces of organs were fixed during 6 - 12 h in a cooled 70 % alcohol saturated with H_2S and were embedded in paraffin. Deparaffinized sections were stained with dithizone and 8 – (p – toluenesulfonilamino) – quinoline (8 – TSQ). On the preparations stained with dithizone zinc was revealed in the cell cytoplasm as red granules. While investigating with the aid of fluorescent microscopy (light filters V-1 and Y-18) of the preparations stained with 8 – TSQ a yellow – green granulation was detected in the cytoplasm. In the submaxillary glands zinc was revealed in duct epithelium and acinar cells. In the pancreas positive cytochemical zinc reaction was noticed in islet cells. This metal was also detected in the cells of basal departments of intestinal crypts. For secretory material determination the pieces of pancreas were fixed in Bouin's fluid and the pieces of other organs – in neutral formaline. Deparaffinized sections were stained with aldehyde fuchsine or phloxine. A conformity of zinc and secretory material localization was observed in the cells. The amount of zinc and secretory material in the cells of investigated organs increased after the injection of adrenaline, prednisolone, atropine, acute stress influences. On the contrary, after the injection of pylocarpine, diabetogenic drugs (alloxan, streptozotocin, dithizone) and during chronic stress influences zinc and secretory material content was decreased. Similar changes of zinc and secretory material content in various cells kinds permits attribute these changes to cellular – molecular mechanisms of nonspecific adaptative syndrome and indicate the possible functional connection this metal and material in the cells.

M-18

INFLUENCE OF XENOBIOTICS OF A DIFFERENT NATURE ON SPECIFIC FUNCTIONS OF RAT HEPATOCYTES AND STOMACH MYOCYTES

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The damage of a liver is most typical parameter of toxic effect of many pesticides. The membrane dysfunctions occur under different pathological processes in a liver, including change of activity membrane binding enzymes.

We have studied the influence of agrochemicals (herbicide 2,4-dichlorophenoxyacetic acid (2,4-D), plant growth regulators - ivin, poteitin) and heteropolynuclear compounds of the Cu (II) and Co (III) with diethanolamine on Mg^{2+},Ca^{2+}-ATPase activity of the rat hepatocytes and bile secretion.

The parabolic concentration dependence of Mg^{2+},Ca^{2+}-ATPase activity under the influence of 2,4-D is observed. Reliable inhibition of Mg^{2+},Ca^{2+}-ATPase activity (60%) is observed under the concentration of 2,4-D 10^{-9} M and 10^{-4} M while micromolar concentration leads to the increasing of enzymatic activity (to 25%). Therefore ATPase activity changes under the influence of different concentration of 2,4-D may be rated as display of "paradoxical toxicity". Ivin and their molecular complex with succinate – poteitin are much less toxic substances and don't change significantly Mg^{2+},Ca^{2+}-ATPase activity.

Under the same conditions the reduction of membrane binding enzyme activity is shown under the influence of compound $[Cu_2Co_2\ (H_2Dea)_2(Dea)_4]Cl_2 \cdot 2H_2O$ (C-1). The maximal effect (55%) is observed under the action of 10^{-4}M of C-1. Compound $[Cu_2Co_2(H_2Dea)_2(Dea)_4](NCS)_2 \cdot 2CH_3OH$ (C-2) raises enzyme activity in 2,4 times. The maximal effect is registered under the concentration of 10^{-9} and 10^{-5} M. By our preliminary researches that were carried out on artificial lipid membranes, also it was determined that the intensity of interaction of such compounds with membranes depends on a type anion.

On tissue and organ levels (liver, smooth muscles, the stomach of rat) is determined that 2,4-D and heteropolynuclear compound C-1 inhibit bile secretion and spontaneous contractive activity of myocytes. Since these processes are calcium-dependent, it can be supposed that investigated xenobiotics work doubly: reduce Ca^{2+}-conductivity of membranes and inhibit Mg^{2+},Ca^{2+}-ATPase activity. As inhibition Mg^{2+},Ca^{2+}-ATPase activity is less effective in comparison with Ca^{2+}-conductivity plasma membrane, the concentration of intracellular calcium is not enough for the performance of specific functions by hepatocytes and myocytes.

M-19

VASOCONSTRICTION-EVOKED ANOXIA MOBILIZES HISTAMINE BUT NOT PANCREASTATIN FROM RAT STOMACH ECL CELLS.

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The ECL cells in the oxyntic mucosa control gastric acid secretion by releasing histamine, activating adjacent parietal cells. Histamine in the rat stomach occurs in ECL cells and mast cells. ECL cells are rich in chromogranin A-derived peptides, such as pancreastatin (PST) which are released together with histamine in response to gastrin. Mucosal mast cells are few; they lack chromogranin A and do not known to respond to gastrin.

We studied histamine and PST mobilization in response to clamping of the celiac artery (for 30 min) and microinfusion of endothelin, adrenaline, vasopressin. These treatments were found to mobilize large amounts of histamine during a short period of time. Microinfusion of gastrin was used for comparison. Submucosal concentrations of ECL-cell secretory products (histamine and PST) as well as the lactate/pyruvate ratio in the submucosa (an index of hypoxia) were monitored by gastric submucosal microdialysis. Samples of the stomach wall were collected for immunocytochemistry (histamine and PST), and the histamine and PST concentrations in the oxyntic mucosa were determined.

The lactate/pyruvate ratio in the submucosa was raised by arterial clamping and by microinfusion of endothelin, vasopressin or adrenaline. These treatments induced spectacular mucosal damage. Experiments on isolated rat gastric arteries showed endothelin, vasopressin and adrenaline to be powerful vasoconstrictors.

Gastrin induced a sustained release of both histamine and PST, while arterial clamping and microinfusion of the vasoconstrictors mobilized histamine but not PST. Immunocytochemical and chemical analysis of the gastric mucosa revealed that the ECL cells were virtually devoid of histamine but had unchanged PST content. The mucosal mast cells seemed unaffected. The histamine concentration remained reduced for a few days but was normalized 1 week after clamping, indicating that the ECL cells are able to recover from the ischemia.

In conclusion: Gastrin mobilizes both histamine and PST from the ECL cells. Arterial clamping and microinfusion of vasoconstrictors induce gastric ischemia, accompanied by mobilization of histamine but not PST. Thus the mechanism of histamine release during hypoxia differs from that induced by gastrin.

M-20

EXOGENOUS HISTAMINE STIMULATES GROWTH OF COLORECTAL CANCER VIA IMMUNOSUPPRESSION IN MICE

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Recent data suggest the possible role of endogenous histamine in regulating immunocompetent cells to modulate tumor growth. As the matter of fact, our previous study clearly showed that both roxatidine and cimetidine are capable to exert suppressive effects on the growth of colon cancer implanted in mice, most probably by inhibiting angiogenesis via reducing VEGF expression. This study was done to demonstrate the effects of exogenous histamine on colorectal cancer growth and immune response against tumor in mice. [Methods] Histamine 2HCl was delivered for 21 days to Colon 38 mouse colon adenocarcinoma-implanted syngeneic mice and the volume of tumor was measured throughout the experiments. At the end of histamine treatment, the interferon (IFN)-γ/interleukin (IL)-4 ratio in peripheral lymphocytes, histamine contents and cytokine expressions in tumor implants were determined. Histamine caused a significant increase in the growth of tumor implants compared with the vehicle. Interestingly, histamine levels in tumor implants did not change by histamine treatment. Tumor implantation significantly augmented the IFN-γ/IL-4 ratio in contrast to no tumor-bearing mice, however the increased IFN-γ/IL-4 ratio was markedly inhibited by histamine treatment in contrast to the vehicle. In addition, histamine treatment significantly decreased IFN-γ and IL-12 mRNA expressions, yet increased IL-10 mRNA expression in tumor implants. We conclude that exogenous histamine dysregulates the balance between Th1 and Th2, then attenuates anti-tumor cytokine expressions in tumor site, resulting in the stimulation of colorectal cancer growth.

M-21

NITRIC OXIDE AS MEDIATOR OF MELANIN CYTOPROTECTIVE ACTION ON GASTRIC MUCOSA

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It is established that melanin has cytoprotective action on injuries of gastric mucosa evoked by stress, serotonine and aspirine. But mechanism of its action is unknown. As why as ischemia is included in mechanism of injuries of gastric mucosa we supposed that melanin influence on production of nitric oxide (NO) which in some conditions participate in mucosa healing.

The aim of the study was to investigate the influence of melanin on NO production in rats.

The researches were done on 15 white male rats. We investigated the influence of melanin on injuries of gastric mucosa evoked by immobilization stress. Melanin was obtained from Nadsoniella nigra var. hesuelica sown from vertical rocks (Ukrainian antarctic station by akademik Vernadskyiy). Melanin was injected per os in dose 5 mg/kg during 3 days before stress (5 times with interval of 12 hours). We estimated also the content of NO_2^- in blood with Griess reactive. Products of painting were spectrometrised on waves of λ=540-550 nm.

It was shown, that melanin markedly protected gastric mucosa from injuries evoked by immobilization stress. Stress didn't influence on the level of NO_2^- in the blood but melanin enhanced it by 111,9%. It was concluded that nitric oxide mediate one of the mechanisms of cytoprotective action of melanin via improvement of gastric mucosa blood flow.

M-22

THE INFLUENCE OF LEAD ACETATE ON THE METABOLIC FUNCTION OF THE LIVER

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The problem of spreading of exochemical pathology from time to time has catastrophic character and leads to increasing of general disease incidence. In general balance of drugs which dirty the atmosphere compounds of heavy metals occupies substantial volume and rate as global pollutants. The development of industry evoked widespread using of lead. As why as lead has long-term action it belongs to the most dangerous pollutants of biosphere. Key role in disintoxication of organism belongs to the liver. But our knowledge about influence of long-term action of lead acetate on metabolic function of liver are limited. The aim of study was to investigate the influence of long-term introduction of lead acetate on metabolic function of liver. The investigations were done in chronic experiments on 24 white male rats. The rats were divided into 4 groups. The rats of the first group were control. The rats of second, third and forth groups during 10 days were received lead acetate in dose 3,45, 34,5 and 345 mg/kg accordingly. These doses amounted accordingly 1/2000, 1/200 and 1/20 from LD_{50} (LD_{50}=6900 mg/kg). In 10 days in the blood of the rats we measured the content of bilirubin, kreatine, urea nitrogen, blood urea, cholesterol and triglycerides. It was established that in dose 3,45 mg/kg lead acetate decreased the content of bilirubin by 42,7%, in dose 34,5 mg/kg – by 20,3%. But in dose 345 mg/kg it didn't influence on the content of bilirubin. On the content of kreatine lead acetate had effect only in dose 3,45 mg/kg. It decreased the content of kreatine by 11,1%. In all doses lead acetate didn't influence on urea nitrogen. In dose 3,45 mg/kg lead acetate decreased the content of blood urea by 19,3%, in dose 34,5 mg/kg – by 21,6%. But in dose 345 mg/kg it didn't influence on the content of blood urea. On the content of cholesterol lead acetate had effect only in dose 3,45 mg/kg. It decreased the content of cholesterol by 26,1%. In doses 34,5 and 345 mg/kg lead acetate increased the content of triglycerides by 20% and 30% accordingly. We concluded that lead acetate evoke toxic effect in organism and on subject to doses impair the metabolic function of liver. First of all it has concern with bilirubin formation and metabolism of lipids.

M-23

A REVIEW: ROLE OF VAGUS COMPONENTS IN GASTRIC SECRETION AND CYTOPROTECTION MECHANISMS IN STOMACH

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The key role in activator or inhibitory processes of gastric secretion and adaptation the rhythm of secretion to peculiarities of food, motor function and cytoprotection belongs to nerve vagus.

Afferent part of vagus is represented by sensitive C-afferents with vaniloid receptors. They are localized in mucosa and smooth muscles, around blood vessels in submucosal layer. The activation of afferents terminals deals to neuropeptides secretion (somatostatin, substantion P, calcitonin gen-related peptide, neurokinins A and B, etc.), which are involved in gastric mucosal blood flow and cytoprotection reinforcement and modulation of noncholinergic nonadrenergic neurons activity also.

The impulses transmission in central part of vagus way (neurons of solitarius and dorsal nucleuses) is intermediated by more than 20 neurotransmitters. Neurons of dorsal nucleus are in great dependence with gastroenteropancreatic hormones secretion (pancreatic polypeptide, peptide YY), cytokines, bacterial endotoxins, NO-syntase blockers.

Preganglion neurons regulate secretion and cytoprotection by the inhibitory and exciter fibers, which could demonstrate controversial action sometimes. They are intimately involved in contact with noncholinergic nonadrenergic neurons. Inhibition of M_1-cholinergic receptors of methasympathic neurons by gastrocepine did not reveal inhibitory effect on acid secretion, but depressed pepsin production in great manner. These findings were accompanied by decreasing of MDA content and NO concentration, while increasing of SOD activity and no significant changes in catalase activity. The acid production and pepsin concentration under combined action of gastrocepine with L-Ca^{2+} channels blocker verapamile was significantly lower, than in case of gastrocepine and verapamil action alone. Simultaneous inhibition of M_1-cholinergic receptors and L-Ca^{2+} channels revealed to intensify the cytoprotection in gastric mucosa by means of oppressing lipid peroxidation and activation of SOD.

Postganglion neurons provide regulation of secretor glands, endocrinology cells function and mucosal blood flow level. Two or more mediators can simultaneously enter intercellular specie from one neuronal terminal with others active biomolecules (NO) and hormones. This “cocktail” act to complicated relations between efferent neurons, target cells, leucocytes, blood vessels that are ensure gastric secretion and cytoprotection processes.

CLINICAL

GASTROENTEROLOGY

C-1

HELICOBACTER PYLORI INFECTION AMONG RURAL AND URBAN POPULATION WITH DYSPEPSIA.

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Introduction: Geographic variations in the prevalence of *Helicobacter pylori* (Hp) infection suggest that similar differences may occur between rural and urban populations.

Aims and methods: The aim of the study was to compare the occurrence of Hp infection among rural and urban inhabitants who underwent endoscopy due to dyspeptic disorders. Gastroscopy was performed in 526 patients with dyspeptic disorders: 403 (77%) rural inhabitants - 45% of males and 55% of females, aged 16-87, mean age 57, and 123 (23%) urban inhabitants - 41% of males and 59% of females, aged 18-87, mean age 53. During the endoscopic examination biopsy specimens were taken for histopathological and urease tests.

Results: Hp infection was observed in 61% of rural patients with dyspepsia examined and in 72% of urban inhabitants ($p<0.05$, Ch^2 Pearson test). No differences were noted in the incidence of Hp infection among rural and urban patients diagnosed with gastritis (77% of rural inhabitants and 72% of urban inhabitants).

Conclusions: Hp infection is more frequent among urban than rural patients with dyspeptic disorders, however, no differences in the incidence of Hp infection are observed between rural and urban patients with dyspepsia and gastritis.

C-2

HISTOPATHOLOGICAL CHANGES IN THE STOMACH OF PATIENTS WITH TYPE-2 DIABETES AND CHRONICALLY DIALYSED PATIENTS.

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INTRODUCTION: Diabetes and uraemia are chronic diseases which in their course lead to pathological changes in the alimentary tract. Among many factors responsible for the occurrence of these changes are metabolic disorders associated with diabetes and uraemia, as well as secondary bacterial and mycotic infections. AIMS & METHODS: The aim of the study was the analysis of histopathological changes in the stomach in association with *Helicobacter pylori* (Hp) infection in patients with type-2 diabetes (DMt2) and those receiving chronic dialysis (CHD). The study covered 30 patients with DMt2 aged 40-72, mean age 57.2 + -9.8, 15 of them were males - who had been treated for a period of 3 - 28 years, mean treatment time 9.5 years, and a group of 25 patients receiving CHD, aged 26-62, mean age 45+-11.8, 18 of them male, who had been treated by hemodialyses for a period of 7 months to 17 years, mean duration of therapy 8 years. Endoscopic examination was performed and biopsy specimens taken for histopathological tests according to Sydney System principles. The material obtained was dyed by haemotoxylin and eosin, with mucicarmine according to Mayer, and by the Giemsy method modified by Romanowski. A quick urease test was performed and Hp antibodies were determined in the blood serum.

RESULTS: The table below presents the results of the study:

Table. Compilation of the results of histopathological examinations of gastric mucosa in patients with type -2–diabetes (30) and chronically hemodialysed patients (25).

Histopathological features	Chronically dialysed patients (A)		Patients with type-2 diabetes (B)		Test results Chi^2 A-B
	No	%	No	%	
Chronic active gastritis	6	24,0	11	36,7	1,03
Chronic inactive gastritis	19	76,0	19	63,3	1,03
Lymphoplasia	1	4,0	4	13,3	1,43
Intestinal methaplasia	1	4,0	6	20,0	3,14
Dysplasia	-	-	2	6,7	-

* $p < 0,05$

Gastritis was histologically confirmed in all patients in the study. Considerably advanced gastric changes were noted in 67% of patients with DMt2 and 64% of those who received CHD - IV^{o} and III^{o} according to Sydney System classification, and II^{o} in the remaining patients. All cases of chronic active gastritis, both in patients with DMt2 (11) and receiving CHD (6), were connected with Hp infection. The majority of patients with advanced inflammatory changes in the stomach (IV^{o} and III^{o}) were also infected with Hp. CONCLUSIONS: 1. Type 2 diabetes and uraemia are conducive for the occurrence of chronic gastritis. 2 In patients with diabetes and uraemia chronic gastric seems to be associated also with *Helicobacter pylori.*

C-3

THE NATURE OF CYTOPROTECTIONAL MECHANISMS IN STOMACH UNDER CONDITIONS OF DALARGINE, GASTROCEPINE AND L-ARGININE ACTION

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In the regulation of cytoprotectional mechanisms of gastric mucosa different substances of endogenous origin take part (prostaglandines, nitric oxide, opioid peptides, substance P, calcitonine gen-related peptide, neurokinines A and B, somatostatine), as well predecessor NO — L-arginine. Except them, there are pharmaceutical preparations, which are widely used, such as gastrocepine that is the blocker of M_1-cholinergic receptors (M_1-ChR), dalargine – the blocker of δ-opioid receptors, etc. In this connection, the task of recent research was to study the lipid peroxidation process, the activity of antioxidative enzymes and the content of tumor necrosis factor (TNF) in rats with ulcerogenic damage of gastric mucosa by adrenalin, and to define the modeling action of gastrocepine and L-arginine in case of dalargine influence.

The experiments where carried out on Wistar rats. Ulcerogenic damage of gastric mucosa was modeled by adrenalin administration. The following factors were examined in gastric mucosa: the changes of lipid peroxidation processes by the content of MDA and NO, the activity of antioxidative enzymes - SOD and catalase, the content of TNF under action of δ-opioid receptors antagonist – dalargine (0.1 mg/kg) in conditions of M_1-ChR blockade by gastrocepine (6 mg/kg) or L-argignine (500 mg/kg) influence and the triple action of this drugs.

The influence of dalargine with M_1-ChR inhibition under adrenalin action decreases the MDA content and NO level and slowdown SOD and catalase activity; TNF content increased by 38 % in comparison with adrenalin action alone. Synchronous action of L-argnine and dalargine led to a slight increase in MDA content (by 11 %), while the NO level and activity of antioxidative enzymes were reducing. The influence of L-arginine and dalargine in conditions of M_1-ChR blockade resulted in a slight decrease in MDA content, slowdown in the activity of SOD and catalase in comparison with L-arginine and dalargine influence, while the content of TNF decreased by 13 % comparing to dalargine influence in case of M_1-ChR inhibition.

Cytoprotectional action of dalargine is modeled by the presence of L-arginine that was resulted in activation of lipid peroxidation and decreasing of TFN content. In case of M_1-ChR blockade, the influence of dalargine leads to the slowdown in lipid peroxidation processes and activity of antioxidative enzymes, reduction of NO content and increase in the content of TNF. Under the triple action of δ-opioid receptors antagonist, M_1-ChR blocker and L-arginine the specific effects of both L-arginine and gastrocepine can be noticed.

C-4

EFFECT OF AMARANTH OIL ON POL PROCESSES AND ACTIVITY OF ANTIOXIDANT PROTECTION ENZYMES IN ULCEROGENIC LESIONS OF THE MUCOSA OF LARGE INTESTINE

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Development of structure-hemorrhagic lesions in the mucosa of large intestine is accompanied by the changes of a great number of biochemical processes, the POL processes playing the key role among those. Ulcerogenic lesions of the mucosa of large intestine induce a sharp activation of the local protection mechanisms. It is essential to seek for the means of cytoprotection, focusing on the oils of plant origin and, in particular, the oil of amaranth. Materials and methods. Investigations were conducted on 19 white male rats of Wistar line. Experimental colitis was modeled by means of rectal injection of 4 % acetic acid. For the investigation of the amaranth oil cytoprotective effect, it was introduced for 3 days by the stomach tube in the amount of 0.2 ml per 100 g of the animal body weight. Content of thiobarbituric acid products was determined by the generally accepted methods (Timirbulatova R.A., Seleznyova E.I., 1981), activity of SOD (Kostyuk, Potapovich, Kovalyova, 1990), catalase activity(Korolyuk V.B., 1991), and NO content – by means of Grease's reagent (Lyall F. et al., 1995). Obtained findings were processed by the variation statistics method and Student's *t*-criterium determined. Results. Experimental ulcerative colitis was accompanied by the structure-hemorrhagic lesions in the form of petechiae, erosions, ulcers, and necrotic changes, extending approximately 1.5-2 cm on the intestinal mucosa. At that the content of thiobarbituric acid products in the mucosa of large intestine increased by 49 % and no significant changes were revealed in SOD and catalase activity, while the NO content increased by 44 %. Modeled ulcerogenic lesions of the large intestine at the background of the amaranth oil introduced preliminary to the rats resulted in a considerable cytoprotective effect – no necrotic changes, ulcers, and erosions were present on the surface of mucosa; only solitary petechiae were found at the background of hyperemic mucosa and visible signs of colitis were completely undetectable. Content of thiobarbituric acid products decreased by 13 %, activity of SOD – by 40 % and catalase activity – by 38 %, and nitric oxide content decreased by 76 % as compared to the indexes in animals with experimental colitis. Thus, the manifested cytoprotective properties of the amaranth oil are proved by the absence of morphological lesions in the mucosa of large intestine, by the decrease of lipoperoxidation processes, SOD activity and NO content. The amaranth oil may be recommended for application in practical gastroenterology to improve cytopropective processes.

C-5

PROCESSES OF LIPOPEROXIDATION IN THE DIGESTIVE SYSTEM ORGANS UNDER EXPERIMENTAL ULCERATIVE COLITIS

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Changes in the functional status or development of pathological processes in any of the digestive organs are associated with the changes in metabolic processes in other organs of the digestive system. These changes are characterized by certain organospecific peculiarities. On this account we investigated changes of the lipoperoxidation process, activity of antioxidant protection enzymes (SOD, catalase), and nitric oxide content in the mucosa of large intestine under experimental ulcerative colitis. *Materials and methods*. Investigations were conducted on 19 white male rats of Wistar line. Experimental colitis was modeled by means of rectal injection of 4 % acetic acid. Content of thiobarbituric acid products was determined by the generally accepted methods (Timirbulatova R.A., Seleznyova E.I., 1981), activity of SOD (Kostyuk, Potapovich, Kovalyova, 1990), catalase activity (Korolyuk V.B., 1991), and NO content – by means of Grease's reagent (Lyall F. et al., 1995). Obtained findings were processed by the variation statistics method and Student's *t*-criterium determined. *Results.* In the lesions of a distal part of large intestine, structure-hemorrhagic impairments were noticed to appear in the form of petechiae, erosions, ulcers, and necrotic changes, extending approximately 1.5-2 cm the surface of intestinal mucosa. Content of thiobarbituric acid products was observed to increase by 49 % in the mucosa of large intestine, by 68 % - in gastric mucosa, by 22 % - in blood serum, and changes in the hepatic tissue were insignificant. In the impairments of large intestine mucosa, SOD and catalase activity remained almost unaltered, NO content increased by 44 %, SOD and catalase activity in gastric mucosa - by 82 %, catalase activity and NO content slightly rose. In the hepatic tissue, SOD activity reduced by 22 % and catalase activity and NO content displayed an insignificant increase. Any considerable changes in the activity of antioxidant protection enzymes were not observed whereas contents of thiobarbituric products and NO increased by 22 % and 15 %, respectively. Consequently, ulcerative lesions of the large intestine cause not only the changes of lipoperoxidation processes and activity of antioxidant protection enzymes in the mucosa of large intestine itself, but also in the gastric mucosa, hepatic tissue and blood. Detected unidirectional changes in the content of thiobarbiturate acid products, NO content and catalase activity in the mucosa of large intestine and stomach are primarily associated with the presence of reflex correlations between the organs of digestive system, whereas local changes in the mucosa of large intestines are associated with the increase of lipoperoxidation processes on the account of both oxygen metabolites and increase of NO level and NOS activity.

C-6

PROPHYLAXIS OF POSTOPERATIVE COMPLICATIONS OF IMPLANTATION OF GENERAL BILIOUS DUCT AND DUCT OF PANCREAS DURING OPERATION OF DOUODENECTOMY IN EXPERIMENT

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Experiments are conducted on 11 not thoroughbred dogs (6 females, 5 males). Weight of dogs was 18-20 kg. Animals were distributed on two groups. 6 dogs to which douodenectomy (DE) is executed after a method Tanaca and Sarr entered in the first group, in the second group – 5 dogs to which this operation is executed on a modified by us method.

Operation of isolated DE in the first group was erected to that after chopping of pyloric part of stomach from antral part, mobilization of proximal and distal part of duodenum (D) separate its areas round the bee-entrances of general bilious duct (GBD) and pancreatitic duct (PD), which were implanted separately in an jejunum below than formed before it gastroenteroanastomosis, were cut out. A lavsan was stitch material. Two animals with 6 were perished from the intraabdominal bleeding, 4 – from acute pancreatitis, peritonitis. In the second group of animals mobilization and deleting D was executed, applying longitudinal DE, subserouse hydropreparation and thrifty separation D from a pancreas (P). Visual location the inflow GBD and PD in D by pressure on a gall-bladder and the P, catheterisation GBD and PD separate by thin catheters. Implantation GBD and PD in an jejunum was executed by one nearductal part of wall D, using stitch material „Ethibond" (USA). Catheters were deleted before stringing of the last stitch of implantation. Three dogs survived from five animals of the second group. Two animals perished at nearest time after the operation at non-determine reasons. Therefore, by the surgical methods, that promote of warning of postoperative complications and survival of animals were: thrifty separation D from P, complete visual location the inflow GBD and PD in D by longitudinal DE belonging prejudicedly DE and confidence in their integrity, presence of catheter in gap of duct at all time of implantations, adaptation of implantation „Ethibond" by one nearductal circumference of jejunum.

C-7

EFFECT OF INTERMITTENT HYPOXIC TRAINING ON OXYGEN-DEPENDENT PROCESSES IN RAT BRAIN TISSUES UNDER CHRONIC ETHANOL INTOXICATION

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It is generally assummed, that intermittent hypoxic training (IHT) increases the activity of antioxidant defense enzymes, stimulates the growth of capillaries and functions as a nonspecific stimulator of plastic processes in the nervous tissue.

Aim: to study the influence of iht on the free radicals oxygen-dependent processes in brain tissue of animals with chronic ethanol intoxication (15% ethanol solution as a single source of drinking during 30 days).

Methods: the lipid peroxidation (LPO) processes and antioxidant activity, nitrite-ions (NO) concentration in rat brain tissues on the initial stages of ethanol intoxication as well as application of IHT in these conditions were investigated. IHT was performed in the altitude chamber in the following mode: five 10-min "elevations" to a height of 6km at a rate of 20m/s, intervals between the elevations being 15min.

Results: It can be seen from our biochemical studies that alcohol intoxication was accompanied by a decreased activity of enzymes of antioxidant defense system, catalase (by 48.2) as well as superoxide dismutase (SOD) and glutathione peroxidase (GPO) in rats brain. The content of the intermediate LPO product, malone dialdehyde (MDA) increased by 50%. A significant increase in the level of diene conjugates in rats brain was observed. Results obtained are in accordance with literature, where mechanism of action of alcohol intoxication in brain is connected with peroxidation syndrome. Application of the hypoxic therapy in the group of animals with chronic alcohol intoxication was accompanied by a decrease in brain MDA in comparison with the alcoholized animals, and the level of diene conjugates normalized. In this case, a significant increase SOD and GPO activities in brain were noticed in comparison with the alcoholized animals not subjected to hypoxic training. In our study, nitrite-ions levels were significantly higher in the ‘ethanol+IHT’ group than in the control group. The evidence indicates that NO can have either a prooxidant or an antioxidant effect on lipid peroxidation. At relatively high concentrations, NO can attenuate and exacerbate membrane dysfunction and tissue injury, while acting as a reactive oxygene metabolite. On the other hand, NO can be converted into a range of potent antioxidants which can have the inhibitory effects on the formation of malone dialdehyde (D’Ischia M. et al., 2000).

Conclusion: The results of our study suggest that the training to intermittent hypoxia in the mode used by us can be an efficient means of increase in the adaptive potential of brain, consequently, of the whole organism.

C-8

NITROGEN OXIDE, ACID AND MUCOUS-ELECTROLYTE SECRETION IN PATIENTS WITH DUODENAL AND GASTRIC LOCALIZATION OF ULCEROUS DEFECT.

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The aim of this research was to study acid and mucous-electrolyte secretion and nitrogen oxide(NO) in patients with duodenal and gastric localization of ulcerous defect.

30 patients with ulcer disease were examined. There were 10 young volunteers examined, considered to have no pathology. Patients aged 18 - 44 years old. The duration of disease was from 1 to 10 years.

Probable reasons of disease were: Helicobacter pylori (100%), smoking (47%), constitutional and inheritable factors (33%), and alcohol abuse (20%).

Methods for diagnosis approval were: fibrogastoduodenoscopy, Helicobacter pylori verification, fractional gastric juice examination. Gastric acidity, pepsin and NO concentration, Na^+ and N-acetylneuraminic acid(NANA) level in gastric juice and adherence mucus were determined.

It was found what in healthy people basal NO concentration is corresponding 10-12Mkm/L and was 2-4 times lower in case of increased acidity.

The same pattern in NO level change observed in cases of duodenal ulcerous defect localization. Gastric localization of the ulcer lead to 1,5 - 2 times increase of NO levels in comparison to healthy group and duodenal ulcer.

It was discovered what there no correlation is between NO and concentration of pepsin, Na+ions and NANA.

Results: NO concentration correlates to H-ions concentration in gastric juice. It probably plays no defense role in gastro protection, considering severity of ulcer disease.

C-10

NEW APPROACHES TO PREVENTING OF GASTROINTESTINAL MALIGNANCIES

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Gastric acid hyposecretion leads to dysregulation of negative feedback control of gastrin release via somatostatin, excess gastrin biosynthesis and ultimately results in hypergastrinemia which stimulates the proliferation of gastrointestinal malignancies. Today pharmacological means for increasing of gastric acid secretion are absent. Perspective drug for it is Betaserc® (Solvay Pharmaceuticals B.V., Weesp, Holand), which has considerable H_3-histamine receptors (HR) antagonistic and weak H_1-HR agonistic properties and uses for healing of Meniere's Syndrome. Because of inhibition of H_3-HR induced both effects: increasing of somatostatin secretion and stimulation of gastric acid secretion. **The aim of study:** to investigate the effects of Betaserc® on gastric acid secretion in dogs. **Methods:** the investigation was carried out in chronical experiments on intact conscious dogs with Basov-Pavlov gastric and duodenal fistulas in accordance of the European Union Council Directive. **Results:** based on answer to injection of histamine (0,05 mg/kg, i.v) dogs were divided on 2 groups: I (n=5) - with weak secretory answer 39,4$\pm$3,16 ml and II (n=5) - with strong secretory answer 111,8$\pm$6,63 ml. From aim of our study effects of Betaserc® have been investigated on group with weak secretory answer. Injection of Betaserc® (1,2 mg/kg, i.d.) caused significant increasing of histamine (0,05mg/kg, i.v.) gastric acid secretion (n=10). The volume of gastric juice was increased by 57,1% ($p<0,01$), output of acid - by 77,8% ($p<0,01$). Comparative investigation between effect of Betaserc® and effect of thioperamide (0,07 mg/kg, i.v.) (n=10), classical antagonist of H_3-histamine receptors, on histamine gastric secretion hasn't shown significant differences. **Conclusion:** Betaserc® is perspective pharmacological means for increasing of gastric acid secretion and preventing of gastrointestinal malignancies.

C-11

Ca^{2+} TRANSPORT AND TIGHLY COUPLED WITH IT O_2 ABSORPTION IN MITOCHONDRIA OF HEPAR OF RATS WITH TETRACYCLINE FAT HEPATOSIS

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Investigation of fat hepatosis molecular mechanisms remains one of the actual tasks of the modern science in connection with the wide incidence of this pathology in the whole world. The aim of this work was to investigate Ca–flow intensity in mitochondria (Mch) of hepar of rats with tetracycline hepatosis in condition of usage of different oxidation substrates. Fat hepatosis was provoked by intraperitoneal injection of tetracycline hydrochloride in dosage of 125 mg/kg of weight. Control animals received normal saline solution in the same conditions. Investigations took place in 24 hours after drug injection. Mitochondrial fraction was taken by differential centrifugation (J.E.Hogeboom et al. 1948). Detection of Ca-flows (E.J.Carafoli 1988) was made with the help of ion-selective Ca-electrode made by "Niko". Media of incubation contained $CaCl_2$ (100 mkM), succinate (5 mM) or glutamate+malate (4 mM+1mM), Mch (2-3 mg of protein/ml). In rats with tetracycline damage a tendency of decreasing of summarized Ca^{2+} absorption (nM/mg of Mch protein) was discovered. In succinate oxidation it decreased from 93.44±19.01 in control group to 63.21±16.2 in hepatosis, in glutamate+malate – from 139±38.2 to 41.03±15.11. The speed of Ca^{2+} absorption (nM/sec·mg of Mch protein) changed in the same way. In succinate oxidation it was 8.11±1.32 in control group and 5.62±1.03 in tetracycline hepatosis, whereas in glutamate+malate oxidation – 9.43±1.81 and 2.13±0.64 respectively. Molar ratio Ca^{2+}: O_2 in succinate oxidation was 3.91 in control and 3.39 in hepatosis, whereas in glutamate+malate oxidation - 6.5 i 1.37 respectively. Therefore, in rats with tetracycline fat hepatosis Ca^{2+}-accumulating ability of mitochondria was decreased in comparison with the control group. During this energy-dependent Ca^{2+} absorption and tightly coupled with it cellular respiration decreased, and especially Ca^{2+} output from mitochondria, connected with the work of electroneutral Na/Ca transferor. The changes were more significant in NAD-dependant substrates oxidation.

C-12

THE INFLUENCE OF TRANSECTION OF PYLORUS ON EVACUATION FROM STOMACH OF FAT FOOD IN THE DOGS

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There are a lot of data about influence of different types of vagotomy on gastric emptying. But for today our knowledges about the role of branch of nerve vagus (ramus pyloricus nervi vagi (RPNV)) which innervates pylorus in regulation of gastric emptying are limited.

The aim of the study was to investigate the influence of transection of RPNV on gastric emptying in the dogs.

The investigation were carried out in chronic experiments on 2 groups (5 dogs) of dogs with fistulas of fundus and duodenum. The dogs of first groups (3 dogs) were with intact nervous system (control). The dogs of second groups(2 dogs) were after operation of cutting of RPNV. The study began immediately after finishing the test meal. 600 rubber corpuscles plus 25 gram of the oil were added into the 100 gram bread and mixed. The volume of each of corpuscles was not more $1mm^3$. In every 25 minutes we drained the duodenal fistula and during 5 minutes collected the chyme. In every sample of chyme we established its volume and amount of rubber corpuscles in it. As why as rubber corpuscles leave the stomach regularly with chyme, amount of corpuscles shows what part of food left the stomach for 5 minutes. Obtained data were extrapolated on total 30 minute period. Also we determine the absolute and relative rate of evacuation.

It was established that the time of emptying of 100 gram of bread with 25 gram of oil from stomach in dogs in control group amounted 379±14,3 min. In dogs after transection of RPNV the time of emptying of fat food was diminished by 28,8 % ($p<0,001$) and it amounted 270±5,15 min. On dynamics of gastric emptying the transection of RPNV did not influence. We concluded that transection of RPNV disturbs the functioning of duodeno-gastric reflex that leads to relaxation of pylorus and acceleration of gastric emptying of the fat food from the stomach.

C-13

INVESTIGATION OF ALAT AND ASAT ACTIVITY IN RATS BLOOD DURING THE OMEPRAZOLE AND OSID ACTION

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Omeprazole is one of the most effective gastric secretory inhibitors available at present with potential use in the therapy. A great deal of evidence to support the hypothesis that gastric ECL cell carcinoids develops as a result of life-long administration of omeprazole. After 24 weeks of omeprazole administration in rats the hypergastrinaemia is developed. Humans and rats react differently to the drugs therapy because the distinctions of the gastric carcinogenesis mechanisms in this two species. The mechanisms of the drug-induced gastric carcinogenesis in rats has not been defined and consequently it is not even possible to attempt to guess the risk to man.

In this connection the tolerability doses of omeprazole (omez) and osid has been investigated in rats treated for up to 3 weeks.

It has been shown that activity of Alaninaminotransferase (AlaT) is decreased after the osid and omez treatment. The maximum effect is run up after drugs administration for up 14 days in both cases.

The activity of Aspartataminotransferase (AsaT) is increased after osid but is decreased after omez for up 7 and 14 days of treatment.

The dates that we obtain may be the result of stress status (injuries and necrosis of muscles) or toxicological damage of liver after specific drugs using.

C-15

RESEARCH OF PARAMETERS FREE-RADICAL OXIDATION IN PATIENTS WITH AN ONCOLOGIC PATHOLOGY

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The introduction In etiology and pathogeny of oncological disease the key role belongs to perturbation of oxidation, particularly to increasing of the active forms of oxygen (AFO). The basic radicals, that are produced in cells are oxygen radicals (superoxide (O_2^-), hydroxide) and NO radical. As a result in 5-7% of tissue breathing forms hydrogen peroxide. The certain part of oxygen is restored by cells of our organism to superoxide radical. In norm and in case of absence of metal ions with removable valency superoxide radicals turn into H_2O_2 (this reaction is catalyzed by superoxide dismutase (SOD)). Glutationperoxidase and catalase (CAT) removes the surplus of H_2O_2.

Hemoglobin is strong catalyst of free-radical oxidation. Damage of oxygen transporting by erythrocytes, owing to their abnormality and destruction under the influence of oxygen stress, serves as the reason of hypoxia which, in turn, activates free-radical oxidation. Besides O_2^- is an intermediate product in reactions with an oxygenation of metabolites and xenobiotics, that are catalyzed by dioxygenise. Rising of concentration of free radicals and peroxides is accompanied by series of metabolic negative consequences: damage of structure and integrity of biological membranes, structure functional disturbance of fermental systems of respiration, dicreasing in biosynthesis of macroergic compounds. Enlarged forming of free radicals in organism, connected with intensifying processes of lipids peroxidation ("oxidation stress") is accompanied, in particular, by oxidation of thiolical compounds, damaging of transport ATP. Oxidation of SH-groups of membranous proteins results in occurrence of defects in a lipid layer of cells membrane, mitochondrion's and nucleus. Under action of electric potentials on membranes through these pores Na^+ enter cells and K^+ – mitochondrion's. As a result there is an augmentation of osmotic pressure inside mitochondrion's, their swelling and destruction. The intensification of lipoperoxidation assists in leucocytes to their adhesion between themselves and to walls of vessels which results in their destruction. Therefore intensity of the immune answer in an organism is reduced. It results in impossibility of recognition of cancer cells by immune system of an organism. Function of protection against AFO and of some other toxiferous metabolites realizes antioxidant system (AOS), which render harmless of AFO and neutralizes radicals at subcellular level. The purpose. Research of changes in metabolite oxidation processes, their parameters are: level of neutral bases of oxidizing updating of proteins (nOUP) and a level of nitrites (NO_2), and condition of AOS.

Parameters of activity of AOS in given work are SOD, CAT, glutationreductase (GlR) and the active form of vitamin E (Vit.E). Materials and methods. There were surveyed 22 patients on a cancer of a rectum (CR) in age of 57-78 years. Control group is practically healthy and consists of 14 persons of the same age. nOUP we define by Dubininas method, and expresse in unit of optical density (UOD) to 1 ml serum (UOD/ml). SOD activity – by a degree of inhibition of reduced blue nitrotetrazolium and expresse in absorption percent; CAT activity – by Korolyk's method and expresse in nmol[H_2O_2]/ml·h; GlR activity – by Jusupovas method and expresse in mmol[NADP·H]/ml·min; nitrite anion – by reaction with Hisses reagent and expresse in mmol/l. Concentration of vitamin E in serum we define by extractiofluorometric method and expresse in mmol/l.

Results of research

Parametres	**Control**	**CR**
nOUP, UOD/ml	3,42±0,09	5,54±0,14
SOD, %	9,83±0,9	16,98±1,45
CAT, nmol[H_2O_2]/ml·h	84,35±3,99	77,94±3,4
GlR, mmol[NADP·H]/ml·min	$1,59±0,12·10^{-6}$	$2,84±0,15·10^{-6}$
Vit.E, mmol/l	6,25±0,19	1,87±0,08
NO_2, mmol/l	4,71±0,11	7,53±0,9

In patients on CR parameters of nOUP grow on 61,9 %, SOD activity – on 72,7 %, GlR – on 78,6 %, CAT activity is reduced on 7,6 %, Vit.E contents – on 70 %, NO_2 concentration grows to 59,9 %. Summary. In patients on the given kind of oncologic pathology is observed activation of OUP processes and intensification of forming NO, owing to oxidative stress. It is observed imbalance in structure of AOS, raising of SOD and GlR activity, but decreasing of CAT activity and contents of Vit.E. Under conditions of tumoral process these changes show system influence of the tumour on an organism, which complicates metabolism in it.

C-16

CHANGES OF LIPOPEROXIDATION PROCESSES IN GASTRIC AND LARGE INTESTINE MUCOSA UNDER CONDITIONS OF ULCEROGENIC LESIONS IN THE STOMACH AND THEIR CORRECTION WITH VERAPAMIL

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Development of ulcerogenic lesions in gastric mucosa (GM) is accompanied by the changes in metabolic processes, bloodstream, and immune processes in other digestive organs. One of the cytoprotective mechanisms against the action of various ulcerogenic factors is an adequate level of blood supply. The reported work is dedicated to the parallel research of changes in the processes of peroxidation of lipids (POL), activity of enzymes, antioxidant protection, and nitric oxide (NO) content in the stomach and distal portion of large intestine in the ulcerogenic lesions of GM caused by ethanol, since this problem has not been studied sufficiently well. **Materials and methods**. Investigation was conducted in 26 white rats under the condition of an acute experiment. Ulcerogenic lesions were modeled by means of 50% ethanol solution perfused for 2 min. (Katsuharu B., 2002, Yoshimura T., 2002). Contents of malonic dealdehyde (MDA) and NO, activity of antioxidant protection enzymes, superoxidismutase (SOD) and catalase, in gastric mucosa and mucous membrane of the distal portion of large intestine were determined. Correction of the cytoprotective processes was performed by blocking of L-calcium channels with verapamil in the dose of 1.25 mg/kg. **Results.** Action of ethanol resulted in development of characteristic structure-hemorrhagic lesions of gastric mucosa accompanied by the activation of POL processes, increase in SOD activity and NO level, and reduction of catalase activity. Similar changes were observed in the mucosa of the distal portion of large intestine where MDA content increased by 20 %, NO – by 29 %, catalase activity reduced by 43 % and SOD – by 45 %. Blockage of L-calcium channels with verapamil was accompanied by the decrease of MDA and NO contents in gastric mucosa and mucous membrane of the distal portion of large intestine, and increase in SOD and catalase activity, peculiarities of these changes being of organospecific character. **Conclusions.** Thus ulcerogenic action of ethanol is accompanied not only by the changes of lipoperoxidation processes in GM but also by the increase of POL processes in the mucous membrane of the distal portion of large intestine that is likely to be one of the factors causing development of ulcerative colitis. Verapamil injected at the background of ethanol action displays a cytoprotective effect manifested by the decrease in POL activity, increase in the level of antioxidant protection of enzymes, and decrease in NO content. Protective effect of verapamil realized thereby can be attributed not only to its vasodilative action but also to the changes of iNOS activity.

C-17

THE INFLUENCE OF AZITHROMYCIN ON MOTOR ACTIVITY OF DUODENUM AND PROPULSION RATE IN JEJUNUM

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Azithromycin (zytromax) is first and exclusive representative of new 15-nomial sub-group of macrolide antibiotics which have got name azalides. It is well known the prokinetic properties of 14-nomial macrolides. In relation to prokinetic properties of azithromycin our knowledge are very limited.

With connection with this the aim of the study was to investigate the influence of azithromycin on periodical motility of duodenum and rate propulsion in jejunum.

The investigations were carried out in chronic experiments on dogs with fistulas of duodenum. By ballonographyc method we recorded the periodical motility of duodenum. Azithromycin was injected intraduodenal in dose 0,05 mg/kg on the background of the phase of rest. During each 15 min period of experiment we calculated motor index. Next we investigated the influence of azithromycin on rate propulsion in jejunum by method of measuring of bolus rate in cm/min during food motility.

It was established that latency time of azithromycin action was 6,20$\pm$4,08 min. Action time of azithromycin on motility was 24,5$\pm$3,54 min. During this time motor index was increased from 818,75$\pm$13,50 to 925,01$\pm$16,90, or by 13% ($p<0,001$). Bread with a touch of azithromycin evoked considerable acceleration of bolus rate in jejunum. Latency time of azithromycin action was 30 min. Action time of azithromycin on of bolus rate was 120 min. The most greatest acceleration of bolus rate was during 60-90 minutes of experiment and was on 149,7% more than in control.

Thus azithromycin has prokinetic properties and may be useful for stimulation of duodenal motility in patients with acute pancreatitis for prevention of bacteria migration from distal part of intestines in pancreas and development of purulent pancreatitis.

C-18

THE NEW METHOD OF CORRECTION OF FUNCTIONAL STATE OF ORGANISM

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It is well known that different organs and systems of organism are connected with well-defined region of body skin – representational points (RP) which at once react to least functional changes in systems of organism long before organic modifications. Thus we have possibility to determine voltage-current characteristic of RP or the temperature in it and to reveal the changes in organism.

We developed the method of differential diagnostics and correction of functional state of organism (KOFUSO). Technique KOFUSO is based on Nakatani Test. It is a program for processing electropunkture results and thermal diagnostics of a state of health of the person, automated analysis of the received results and development of references on correction of a functional condition of an organism. Technique KOFUSO is developed on a basis electropunkture and thermal diagnostic functional condition of meridians and back roots of a spinal cord, according to gauging volt - ampere characteristic and temperature in 24 representative points of an acupuncture (THAT) and 12 steam (on 12 at the left and on the right, only 24) segments of a thoracic department of a spinal cord, with the subsequent selection of a way of correction of a functional condition of an organism. Gauging of temperature speaks about a condition parasympathetic nervous system, electrophysiological gaugings - about a condition of sympathetic nervous system. From the medical point of view the technique is intended for: carrying out electropukture and thermo diagnostics ; corrections of a functional condition of an organism by an original technique under given references; selection of points and variants of influences; studying a method of a reflex therapy. On the functionalities technique KOFUSO is universal as for doctors of family medicine, and local doctors.

C-19

THE INFLUENCE OF DEXAMETAZONE ON DEVELOPMENT OF ACUTE MESENTERIC ISCHEMIA

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Acute mesenteric ischemia (AMI) is associated with a high mortality rate. Pre-operative death in patients with AMI is usually due to peritonitis, multiple-organ failure. It is well known that nitric oxide (NO) participate in the development of pathology of gastrointestinal tract. It was established that NO make negative contribution in development of septic shock: its hyperproduction leads to system hypotension, induce apoptosis. It is believed that AMI is one of the variant of septic shock. We didn't find data about role of NO in development of AMI but it is known that glucocorticoids oppress synthesis of NO.

The aim of this study was to investigate the role of nitric oxide in the pathogenesis of AMI in rats and the influence of dexametazone on development of AMI.

The investigations were carried out in acute experiments on rats, which superior mesenteric artery (SMA) was ligated after laparotomy. The rats were divided into 2 groups. The first group (24 rats) was the control one. The second group (24 rats) has got dexametazone immediately after ligation. Content of NO_2^- in central vein blood in both groups were estimated with Griess reactive. Products of painting were spectrometrised on waves of λ=540-550 nm. Also we determine the lifetime of rats.

One hour after ligation of SMA in control rats the length of staggering intestine was 10,13$\pm$0,36 sm and the content of NO_2^- in the blood was increased by 12 % ($p<0,05$). In 4 hours the content of NO_2^- was increased by 39 % ($p<0,01$) in comparison to its level before ligation of SMA. The lifetime of rats in this group was 8 hours. In comparison with rats of first group dexametazone in rats of the second group in 4 hours decreased the length of staggering intestine by 15% ($p<0,01$) and the content of NO_2^- by 31% ($p<0,01$), improved the status of intestinal wall and increased the lifetime of rats to 12 hours.

C-20

PROPHYLAXIS OF POSTOPERATIVE COMPLICTION IN PATIENTS WITH PATHOLOGY OF PANCREAS

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The aim of this study to analyse of origin of postoperative complications and their prophylaxis in patients with pathology of pancreas which were treated in Department of Surgery of Khmelnitsk Regional Hospital. There were observed the consequences of surgery treating of 56 patients with chronic pancreatitis (cystes and intraductal hypertension) and cancer of pancreas (different localisation) during 2003-2004. 44 male and 12 female, aged 17-80 years (83.9% capable of working subjects), participated in the study. All patients were operated according to plan (9 patients- gastropancretoduodenal resection, 7 patients - distal resection of pancreas, 4 Frey's operation, 1 patient - Beger's operation, 15 patients - longitudinal pancreatostomia with elimination of ileum loop using Ru's method. Sparing anatomical operation, careful intraoperation hemostasis and precision technique of development of pancreatoenteroanastamosis guaranteed noncomplicated postoperative period. Pancreatoenteroanastamosis formed in most cases with elimination of ileum loop using Ru's method. In the case of complication during forming of pancreatoenteroanastamosis the distal enterostomy was complited with operation. Pancreatoenteroanastamosis decompression and its irrigation of antibiotic solution, aminocapronic acid were made via enterostomy. Sandostatin (0.05-0.1 s.c.) injected during operation, after pancreas action (duct transection or delatation) for prevention of development of chronic pancreatitis and impossibility of pancreatoenteroanastamosis. Injection of sandostatin was continued in postoperative period during 3-5 days (2-3 time/per day) depending on level of increasig of amylase or elastase. After sandostatin withdrawal patients were treated for inhibition of pancreas function by blocators of nociceptive impulses in CNS (dalargin - 4mg/ 3 time per day), proton pump, H2-receptors, M-acetylcholine receptors. All patients were carried out by intensive infusion (stabisol, refortan, reosorbilakt, nelofusin) and protein substituent (albumine, native one-group blood , amino acid solution) therapy, early enteral feeding. Prophylaxis of recurrent thromboembolism in postoperative period was carried out by bandage of lower extremities, active region, control of hemodilution, prescription of low-molecular heparin (klexan, phraksiparin) or acelyzyn. Patients were in hospital 15+/-3,2 days. All patients were discharged from hospital. Inconsistency of pancreatoenteroanastamosis and effect of postoperative chronic pancreatitis were not observed. Used complex of procedures during operative intervention on pancreas allowed to escape serious postoperative complications and mortality.

C-21

THE OMEPRAZOLE-INDUCED HYPERGASTRINEMIA AND THE COLONIC EPITHELIUM TRANSPORT

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The aim of our study was to investigate the influence of hypergastrinemia on water electrolyte transport in colonic epithelium.

We investigated the effects of omeprazole-induced hypergastrinemia (Watson S.A., Smith A.M., 2001) on electrolyte and water transport in colon of male rats using an in vivo perfusion technique. Test solution containing (in mM/l): NaCl – 118; $NaHCO_3$ – 20; KCl – 5,63 was perfused through colonic loop for 3 hours at perfusion rates of 2 ml/min. The nonabsorbable marker, phenol red, we added to each test solution at a concentration of 20 mg/l in order to determine net water absorption. The concentration of phenol red, sodium, potassium was measured to calculate net water and electrolytes absorption. Absorption or secretion rates we determinated spectrophotometrically and used to calculate net water absorption (ml/min per g dry weight). The concentration of sodium, potassium and chloride in the test solutions and their perfusates we determinated by ion-selective electrodes. The rates of absorption (mmol/min per g dry weight) we calculated as described in Schedl (1966). Animals were divided into groups: control (received vehicle – 0,2 ml intraperitonial soline) and omeprazole-treated (1,38 g/100g injections for 14 days).

After omeprazole-induced hypergastrinemia an increased water secretion (-295 mkl/min*g) occured, the rate of water absorption in control was 69,98 mkl/min*g ($p<0,05$; $\alpha=0,057$). The absorption of Na^+ ions in colon of hypergastrinemic animals was decreased at 64,6% compared with control ($p<0,05$; $\alpha=0,057$). The absorption of K^+ was increased at 58,6% compared with control ($p<0,05$; $\alpha=0,057$). There weren't significant differences in Cl^- absorption between the control and omeprazole-treated animals.

We concluded that omeprazole-induced hypergastrinemia causes significant water secretion in colon epithelia. This fact could be explain by inflammation processes in colon caused by hypergastrinemia.

C-22

GASTRIC ACIDITY IN PATIENTS WITH RECTAL POLYPS

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Ninety-five percent of colorectal cancers are predominantly epithelial-derived adenocarcinomas and arise from benign adenomas through the gain of mutations in key genes such as *APC*, *K*-ras and *TP53*. Longitudinal studies in which patients with adenomas are followed up for 20 years, have revealed that the risk of developing colorectal cancer at the adenoma site is approximately 25%, higher than that expected for the normal population (Winawer et al., 2000). In further confirmation, removal of adenomatous polyps is associated with a reduction in colorectal cancer incidence. It is well known that gastrins are trophic for gastrointestinal mucosal cells and play an important role in the renewal of colonic mucosa (Majumdar, 1990). In mouse with increased serum levels of Gly gastrin a significant increase in polyp number in colon was observed.

As why as hypoacidity of gastric juice cause gastrin secretion the aim of the study was to establish the gastric acidy in patients with anal and rectal polyps.

It was examined 20 patients. Ten patients were healthy volunteers. In another ten patients were diagnose the anal and rectal polyps. The gastric acidy was determined by method of intragastric pH-metry.

It was established that in healthy volunteers pH of gastric juice on an empty stomach was from 1,8 to 2,4. In all patients with anal and rectal polyps pH of gastric juice on an empty stomach was $5,9 \pm 0,6$.

It is well known when luminal pH overtops 3 it cause gastrin secretion. May be the anal and rectal polyps are the results of hypergastrinemia which evoked by hypoacidity of gastric juice. Also we recommend the patients with high pH in stomach to be included in group of risk of polyps formation and routinely check up.

C-23

INFLUENCE OF LIPIN ON GASTRIC MUCOSA LIPIDS AND MUCUS GLICOPROTEINS AT GASTRIC ULCERS IN RATS

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Significant difficulties in the treatment of acute gastric ulcer lesions require searches of effective methods on the basis of our knowledges about mechanisms of injury development and purposeful influence on the individual sites of pathogenesis. Cellular membranes disturbance in gastric ulcer desease is one of the main pathogenic link in ulcerogenesis. Modern therapy not always achieves membranereconstructing effects. Clinical researches of the ukrainian preparation lipin, which was created on the basis of phosphatidylcholine (PC) liposomes, have been confirmed it's antioxidant, membraneprotective, immunomodulatory, and antimicrobic action in some diseases. Thus, the aim of this study was to investigate the lipin influence on the lipids composition in gastric mucosa and to study the glicoproteins content in the mucus gel layer in acute ethanol gastric ulcer lesions in rats. Investigations were carried out in acute experiments on male rats. Animals were divided into 3 groups: 1) control group, 2) animals with gastric ulcers induced by ethanol, 3) ethanol ulcer animals which lipin was administrated by intraperitoneally in dose 15 mg/kg within 7 days twice per day. Results of researches have been shown, that in acute ethanol ulcer animals reveals the reduction of phospholipids (PL) total content in a 1,9 fold; in particular individual PL: PC – in a 2 fold, phosphatidylethanolamine and sphingomyellin in a 1,6 fold, phosphatidylinositol – 1,4 fold. The cholesterol (Ch) content was increased in a 2,4 fold. The ratio Ch/PL was increased to 2,5. Received changes provide the evidence about disturbances of physical, chemical and dynamic properties of cell's membranes of gastric mucosa in conditions ethanol gastric ulcer. Lipin administration of animals with ethanol gastric ulcer lesions promoted to restorate the content of PL up to initial level and decreased the Ch content. Thus, lipin improved the restoration of morphofunctional properties of gastric mucosa cell's membranes injured by ethanol. At the action of ethanol it was observed essential changes in mucus gel layer glycoproteins content. Reliable decrease of amount monosaccharides in comparison with the control was observed: gexozamines - by 25%, galactozamines - by 45%, fucoza - by 50%, sialic acids - by 60 %. Decreased monosaccharides content in the stomach with erosive-ulcerous injures suggests about the depolymerization of glycoprotein layer. Application of lipin promoted restoration of the gastric glycoproteins content that testifies about increase of mucus gel layer resistance in part and about resistance of gastric mucosa, in general. The received results can be used for development of methodical recommendations for application in complex therapy of the ukrainian drag lipin as one of effective medicinal means in preventive maintenance and treatment of patients with erosive-ulcerous defects of the mucosa of the gastroenteric path.

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МАТЕРІАЛИ

ІІ МІЖНАРОДНОЇ КОНФЕРЕНЦІЇ

НЕЙРОГУМОРАЛЬНІ І КЛІТИННІ МЕХАНІЗМИ РЕГУЛЯЦІЇ ФУНКЦІЙ ТРАВНОГО ТРАКТУ

ЖОВТЕНЬ 5-7, 2005, Київ, УКРАЇНА