FIRST INTERNATIONAL MEDICAL CONGRESS

Health Issues & Health Policies under Conditions of Economic Crisis

22-25 September 2010
Golden Sands, Bulgaria

Sofia, Bulgaria
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SOUTHEAST EUROPEAN MEDICAL FORUM

(SEEMF)

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HYPERTENSION AND RELATED DISORDERS

СИСТЕМЕН ЛУПУС ПРИ 44 ГОДИШЕН МЪЖ, СТАРТИРАЛ С БЕЛОДРОБЕН ТРОМБОЕМБОЛИЗЪМ, МЕДИАСТИНАЛНА ЛИМФАДЕНОМЕГАЛИЯ И ОСТЪР НЕФРИТЕН СИНДРОМ

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МБАЛ "Каспела", гр. Пловдив, България

Увод: СЛЕ е заболяване, което се среща предимно при жени – съотношение от 4:1 до 8:1. Сравнително рядко в клиничната картина се наблюдава пулмонална хипертония и белодробни хеморагии / под 5% /, както и лимфаденопатия /15%/.

Представя се 44 годишен мъж, който заболява остро със задух, фебрилитет до 39градуса, хемоптое, макроскопска хематурия, отоци по долните крайници. Започнато антибиотично лечение без ефект.

Методи: Изследвани са подробни хематологични и биохимични показатели, урина, коагулограма, имунологични изследвания, абдоминална ехография, ехокардиография, КАТ на гр.кош и абдомен. Проведена е пункционна бъбречна биопсия / имунофлуоресцентно и хистологично изследване /.

Резултати: Постави се диагноза Системен Еритематоден Лупус с Антифосфолипиден синдром и IV клас Лупус нефрит. Започнатата терапия с кортикостероиди, Циклофосфамид и антикоагуланти с добър ефект върху общото състояние и бъбречните прояви. След 2 месеца поради персистиране на дълбока тромбоза на тазовите вени и рецидивиращ белодробен микротромбоемболизъм пациентът се насочи към Сърдечно-съдова хирургия за поставяне на чадър в долна празна вена.

THE INFLUENCE OF HYPERTENSION, OBESITY AND DIABETES ON THE APPEARANCE OF ENDOMETRIAL CANCER IN THE MUNICIPALITY OF BITOLA, R. MACEDONIA-A CASE CONTROL STUDY

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Background: Hypertension, obesity and diabetes are important risk factors for the appearance of endometrial cancer. The aim of the study is to assess the influence of hypertension, obesity and diabetes in the appearance of endometrial cancer in the municipality of Bitola.

Methods: The research has been made as a case control study. The examined group consisted of 60 patients with pathohystologically verified endometrial cancer and an equal number of women without malignant diseases recruited as controls.

Results: The examined group of women is mostly at the age between 60-64 years (38.1%). Women at the age more than 50 years are presented in 93%. The extrimes were youngest as 47 years and oldest as 84 years old. The mean age was 60±7,9. The youngest women in the control group was 45 years old, and the oldest was 80 years of

age. The mean age of the control group is 60,2 ± 8,1. The examined group of women had higher procent of hypertension (65%). Diabetes was also present with a higher percentage (93,3%), as well as the obesity (93%) compared to controls. Diabetes and hypertension in the personal anamnesis were significant risk factors for appearance of endometrial cancer (diabetes: OR=154.0; 95%CI 34.34<OR<771.71 χ^2=83.36 p<0.05, hypertension: OR=2.27 95%; CI 1.02<OR<5.06 χ^2=4.07 p<0.05).

Conclusion: The obesity increases the risk significantly the risk of endometrial cancer up to 6 times (OR=6.49 95% CI 1.93<OR<27.79 χ^2=10.54 p<0.05). Health education of the women as well as control of the nutrition and the reproductive factors can be taken as precaution measures for prevention of endometrial cancer.

EXPERIENCE IN HEALING HYPERTENSION WITH ACE-INHIBITORS AT PATIENTS AFFECTED WITH DIABETES TYPE 2, HOSPITALIZED IN HOSPICE "SUE RYDER" BITOLA-R.MACEDONIA

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The aim of the work is to show the effect of angiotensin-converting enzyme inhibitors (ACE-i) as a monotherapy and combined therapy system along with other anti-hypertensive medicines at patients affected with diabetes mellitus type 2, which are hospitalized in Hospice "Sue Ryder-Bitola. Material and methods: There are used data from the hospitalized patients from the period of 01/01/2010 to 01/06/2010: measurement of blood pressure, EKG. The control and monitoring of blood pressure is done every day, in a period of 6 months. Results: In the Hospice "Sue Ryder" 19 patients with diabetes mellitus type 2, are cured from arterial hypertension with ACE- inhibitors in the given period.

From the research group 6 of affected patients are males (32%) and 13 of the remaining are female (68%). Also 5 (26%) of the affected patients are insulin-reliable, whereas non insulin reliable diabetics are 14 (74%). The middle age of the patients is 78.74± 9.50 (76.33± 8.50 for men, 79.84± 8.50 for women). Monotherapy with ACE-i has been given to 10 of the patients (52.6%). Double therapy (ACE-i + Thiazid diuretic) has been given to 7 of the patients (36.8%). Triple therapy has been given (ACE-i + Thiazid diuretic + Calcium antagonist) to 2 of the patients (10.6%). After the application of these therapies, the results show a significant decrease in the patients blood pressure in the controlled measurements.

Conclusion: Hypertension is frequently at the patients with diabetes mellitus type 2. The treatment with ACE-i shows efficiency in the curing of arterial hypertension and prolong the life span of the patients above 75 years of age.

CHANGES OF C-AMP LEVEL DURING OESTRUS CYCLE IN NORMOTENSIVE AND SPONATANEOUS HYPERTENSIVE RATS

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Background: The mammalian pineal gland is under adrenergic control; however, the physiological oscillations of gonadal steroids could strongly affect the melatonin synthesis and secretion by acting on the pre- and postsynaptic levels and by modulation of the target cells replay. The aim of our study was to determine the basal levels of cAMP in the pineal gland during the various phases of oestrus cycle in normothensive (NTR), Wistar rats and spontaneously hypertensive (SHR) Okamoto and Aoki rats and to describe the histological finding of the pineal gland tissues.

Methods: Two hundred female mature rats (100NTR and 100SHR) were investigated. They were divided in 4 groups according to the phases of the oestrus cycle (diestrus, proestrus, estrus and metaestrus). The phase of oestrus cycle has been determined by microscopic analysis of the vaginal smears. The level of cAMP (RIA) in the pineal gland was the parameter of its intracellular activity. The pineal gland tissues were stained on HaEo.

Results: In SHR there is a slight shortening of the oestrus cycle. In NTR there was an increase of the cAMP level from proestrus to metaestrus, in contrast to the dramatic decrease in SHR. Histological findings of pineal glands showed the presence of many changed pinealocytes with picnotic nucleuses, while the neuroepithelial cells, in the upper parts of the glands, were separated in gland-like islets. There was a normal pineal histology in NTR.

Conclusion: Our study indicated significant neurohormonal differences between NTR and SHR. The changed adrenal activity in SHR correlated with histological findings in the pineal gland.

THE ASSOCITION OF CORONARY ARTERY DISEASE AND AORTIC PULSE WAVE VELOCITY IN GENERAL POPULATION

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Background: Pulse wave velocity is a velocity at which a pulse travels through a medium, usually applied to arteries as measure of arterial stiffness. Arterial stiffness has been known as a major contributory factor to cardiovascular morbidity and mortality in patients with hypertension and coronary artery disease. Pulse wave velocity, a surrogate measurement of large artery damage, has not been ascertained as an independent risk factor of coronary artery disease. The **aim** of this study was to assess whether PWV is associated with coronary artery disease.

Methods: We measure pulse wave velocity with *Doppler ultrasound*. The electrocardiogram is used as a timing reference to determine the time delay or "transit time" between the upstroke of carotid and femoral pulse waveforms. Noninvasive diagnosis and functional evaluation of coronary artery disease should be accomplished

by a safe *myocardial perfusion imaging* method with a high accuracy to evaluate the patients with coronary artery disease. The study involved sixty (35 men, 25 women) consecutive patients aged 56.3 ± 7.9 years who had been referred to our clinical hospital for evaluation of chest pain. Exclusion criteria were previous myocardial infarction, cerebrovascular disease, valvular heart disease and congenital heart disease.

Results: Pulse wave velocity was higher in patients with coronary artery disease than those without (13.25 +/- 4.91 vs 11.26 +/- 2.95 m/s, $p < 0.001$). In multivariate logistic regression analysis, after entering for age, diabetes and other CV risk factors, pulse wave velocity remained the significant independent variable for coronary artery disease ($p = 0.050$). When the severity of coronary artery disease was expressed as one, two or three-vessel disease, pulse wave velocity was a significantly associated with the severity of coronary artery disease ($p < 0.001$).

Conclusion: We conclude that pulse wave velocity is an independent risk marker for coronary artery disease, as well as strongly associated with the severity of coronary artery disease.

APPROPRIATE MARKERS FOR OXIDATIVE STRESS LEVEL IN HEMODIALYSIS PATIENTS

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Background: Oxidative stress (OS) is common in hemodialysis (HD) patients that may lead to atherosclerosis, hypertension and other related disorders. The aim of the study was to examine the appropriate markers for oxidative stress determination.

Material and method: A number of 55 HD patients (20 female and 35 male, at mean age of 43±17 years) were examined. They were exposed on hemophane (n=21) and polusulphone (n=34) HD membranes. A control group of healthy subjects (n=38) was examined as a control one. For determination of antibodies against oxidazed LDL, an enzymatic immunoassay was used (Biomedica gruppe, Austria). Lipid peroxidation (LP) was used by Yagi fluorimetric method. Lipid profile was determined by determination of cholesterol and tryglycerids by enzymatic color test Vitros 250 (dry chemistry Ortho Diagnostic Johnson-Johnson, USA) and HDL and LDL determination by photometric method (Chod-pap Merck, Germany). For all the patients undergoing HD with average duration of 4 to 5 hours, bicarbonate buffer was used and none of them was given antioxidative agents.

Results: In HD patients, LDL-ox antibodies showed increased levels: 356±259 mU/ml on hemophane membrane ($p<0.01$) and 220±125 mU/ml on polysulphone membrane ($p<0.05$). Lipid peroxidation level has also showed increased values of 5.36±0.98 μmol/L for hemophane ($p<0.01$) and 4.52±0.22 μmol/L for polysulphone membrane ($p<0.05$). For tryglicerids, a significant increased level was found in all HD patients on both membranes: hemophane 2.37±0.7 mmol/L ($p<0.01$) and polysulphone 2.28±0.7 mmol/L ($p<0.01$) as well as decreased HDL level, 088±0.4 mmol/L for both

HD membranes ($p<0.01$). No significant difference was noticed for both markers, cholesterol and LDL in all HD patients.

Conclusion: Due to obtained results, increased values for LDL-ox antibodies and LP (for both used membranes) show that OS is present in HD patients compared to the control group, although no statistical difference for some lipid profile markers was found. According to this, more recommended OS markers would be the LDL-ox antibodies and LP for the examination of OS appearance and for its follow-up, respectively.

THE CARDIORENAL SYNDROMA IN THE ELDERLY HYPERTENSIVE PATIENTS

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Background: The cardiorenal syndrome (CRS)is a condition characterizated by kidney failure and heart failure .The primarily failing organ may be either the heart or the kidney, and it is often this failing organ that precipitates failure of the other.CRS is devided into 5 subtypes.One of the most common factor for heart failure and renal failure in hypertension which is unadeqate treated.

The goals of our work is to evaluate the prevalence of CRS(typ 2) in the elderly hypertensive patients with chronic heart failure,clinical feature,possibilities of prevention end treatment.

Methods: 350 patients ,aged between 62-78,have been obserced ,clinical feature,signs and simptomsECG,EHO,laboratory parameters.Kontrol examinations were done every 3 months. All the patients have been on antihypertensive therapy for years.

Results: Patients with NYHA 1- didnt manifest symptoms of kidney faiulure and their laboratory parameters were normal if hypertension have been controlled.. Patients with NYHA 2 somethimes –intermitently have had discrete higher level of creatinine besides sufficient regulation of hypertension..Patients with NYHA 3 have always had some higher level of creatinine ,which somethimes(infection,temperature) leaded to worsening of general health and indicated intensive care unit treatment.Patients with NYHA 4 (expetialy immobile ones)have been very careffuly observed because of critical medical condition which could appear immediately associated with higher blood pressure .

Conclusion: CRS is a syndrome in which therapy to relieve congestive symptoms of heart failure(ACE inhibitors,diuretics) is limited by further declining of renal function..Our current understanding of CRS is inadecvate to explain some of the clinical observations in heart failure or direct the therapy.The priority is very careffuly observation of the clinical feature (Symptoms end signs) in patients with chronic heart failure end control of kidney function and blood pressure at the same time .

SYMPATHO-VAGAL BALANCE DURING [CAV9]N/OFQ(1-13)NH2 APPLICATION IN SPONTANEOUSLY HYPERTENSIVE RATS

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The aim of the current study was to investigate the effects of the modified in nine position nociceptin analog [Cav^9]N/OFQ(1-13)NH_2 on the sympatho-vagal balance in spontaneously hypertensive rats (SHR). Experiments were carried out on conscious normotensive Wistar rats, used as control animals and on SHR, used as a animal model of human essential hypertension. One day before experiments under general anesthesia (Nembutal, 35 mg/kg, i.p.) catheters were inserted in femoral artery for blood pressure registration and in femoral vein for drug application. 24 hours after surgical manipulations, blood pressure wave registration was performed in conscious rats in control period and after [Cav^9]N/OFQ(1-13)NH_2 (100 nmol/kg) applications in the course of 90 min, within nine consecutive 10 min long intervals. The interpulse interval (IPI) was determined in terms of the time between two consecutive diastolic minimums of the blood pressure wave by AcqKnowledge 4.1 software. The sympatho-vagal balance was determined by the ratio between the spectral power in mid (P_{MF}) and high frequency (P_{HF}) band of interpulse interval spectrograms, derived by FFT algorithm in graphical programming environment Lab VIEW 3.1.1. The P_{MF}/P_{HF} ratio in SHR was lower in comparison to Wistar rats: 0.45 ±0.04 and 0.73±0.06 ms^2, ($p<0.05$). In Wistar rats application of [Cav^9]N/OFQ(1-13)NH_2 led to a decrease of P_{MF} in the intervals between 0-60 min by 42%, 39%, 46%, 42%, 47% and 46%, as well as of P_{HF} in the intervals between 30-90 min ($p<0.01$). In contrast to Wistar rats in SHR [Cav^9]N/OFQ(1-13)NH_2 increased P_{MF} in the 3rd investigated interval and this effect continued to the end of experiment, ($p<0.01$). In SHR the P_{HF} also increased in the 2nd investigated 10 min long interval from 0.98 ±0.03 to 1.33±0.06 ms^2 and keep this level till the end the experiment, ($p<0.01$). In Wistar rats the P_{MF}/P_{HF} ratio decreased between 0-30 min, but in SHR sympatho-vagal balance did not change because of simultaneously increase of both sympathetically (P_{MF}) and vagal (P_{HF}) mediated variations of interpulse interval.

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OBESITY AND HYPERTENSION – MAIN HEALTH RISK FACTORS IN THE POPULATION IN THE REGION OF GEVGELIJA

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Purpose: To present the results of the preventive health examinations of the adult population in the Health region of Gevgelija, and to show the representation of the main health risk factors.

Materials and methods of work: The data and material are derived from the individual evident sheet from the performed preventive health examination of the adult population in the Health region of Gevgelija in 2009. The method used is statistical-informative method of work.

Results: During the medical examination , a total of 991 persons were examinated which represents 2.82% of the population in this region. According to place of residence 456 (46,92%) are from the city, and 526 (53,08%) are from the surrounding villages. During the examinations, blood pressure over 140/95 mm Hg. Was found in 314 (31,91%) people. In the city population that percentage is 39.35%, and in the village population 25.19%.

According to BMI (body mass index) , only 34% of the examined people had normal nutrition. 38% of the examined are overweight, 18,8% are Obese Class I , 6,8% are Obese Class II , and 2.4% are Obese Class III.

7,31% of the examed have over 7 mmol/L blood sugar , and 33,63 have over 5.8 mmol/l cholesterol in blood.

Conclusion: It is necessary to create and implement a National Strategy for prevention and control of non-community diseases in R. Macedonia, and to implement that strategy on a local level aswell.

BILATERAL CAROTID DISEASE IN PATIENT WITH DIABETES TYPE II: CASE REPORT

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Color Doppler sonography is well-established method for detection of stenosis or occlusion of extracranial arteries. This procedure is reliable tool for diagnosis of hemodynamic disturbances evolving in extracranial circulation. Stenosis and occlusions of extracranial arteries are one of the most frequent complication of diabetic angiopathy and causes of stroke. A prompt and accurate diagnosis of stenosis/occlusion of carotid arteries is of great importance for therapy of stroke. We present a case of a 66-year-old man with diabetes type II with right common carotid artery occlusion and left internal carotid artery high-grade stenosis, that caused several TIAs and strokes in the vascular territories of left and right internal carotid arteries.

Keywords: occlusion; stenosis; carotid artery; diabetes ;

RISK FACTORS IN PATIENTS WITH ARTERIAL HYPERTENSION

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Introduction: Arterial hypertension is one of the major risk factors for the occurrence of ischemic heart disease , cerebral-vascular diseases, disease at the peripheral arteries and for sure the most important social-health problem. The etiology of arterial hypertension is mainly unknown , but for the occurrence, course and the diagnosis for this disease the existence of risk factors is extremely important. The early

diagnosis, discovering the factors and the control over the factors presents a vital significance for the patient.

Aim: To determine the risk factors , as well as the age and gender structure of the surveyed patients with hypertension .

Methods of work: Health cards and a questionnaire of 14 questions with 2-4 offered answers were used.

Results: 90 patients were interviewed of which 48 women and 42 men , all of them having hypertension. The age structure 4% to 30, 40% from 31-50, 43 % from 51 – 70 , and 13% more than 70 years old. Smokers 55% and 45 % non- smokers. Only 35 % consume alcohol in rare occasions , 10 % two glasses a day, 12 % want to drink more and 43 % do not consume alcohol. At 41% of the surveyed the food consists mainly from meat, meat products, at 30 % cheese , milk products and eggs, 29 % eat non-fat meat fish, fruit and vegetables. At 57 % there are parents with hypertension, 20 % have hypertension in the closer family (grandmother and grandfather) and 23 % do not have.23 % declare that are calm and reasonable, 40 % are sensitive and 37 % react violently. From physical activity 10 % do easy exercises , 33 % go walking , 36 % do not have time , 21 % avoid fatigue , 4 % go to a control once a week , 22 % once in a half an year , 51 % only when they do not feel good and 23 % go only to an appointed examination. 87 % are informed for their disease by their own doctor, 0, 5 % by the media and 0, 8 % by the medical literature.

Conclusion: A presence of risk factors is being proved in all patients with an exception in a great percent of heritage, age, and gender, the other risk factors are changeable by accepting the way of life and the professional work of the doctor.

ESTRADIOL LEVEL RELATED TO SOME HAEMOSTATIC FACTORS AS PREDICTOR OF ARTERIOSCLEROTIC AND THROMBOEMBOLIC DISORDERS IN WOMEN DURING MENOPAUSE

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Background: Diseases of the cardiovascular system, especially of the coronary blood vessels, as well as cerebrovascular diseases are among the leading causes of death in menopausal women. Numerous investigations have pointed out to the relation between estrogen status and the process of hemostasis.The mechanism through which estrogens exert their effect is still unclear. The aim of the study was to determine the relation between estradiol level, factor VII (proconvertin), and fibrinolityc enzymes (tissue type plasminogen activator antigen - TPA Ag and plasminogen activator inhibitor type 1 antigen - PAI 1 Ag) concentrations in women during menopause.

Methods: The total number of 68 women were divided into 3 groups according the following criteria: the regular (vs. irregular) menstrual cycle; the concentration of serum follicle stimulating hormone (FSH); the concentration of □□ □ estradiol (□□). The control group comprised healthy women (n= 20) with regular menstrual cycle. The second group comprised women in perimenopause (n = 22) with medical history of irregular menstrual cycle, the value of serum FSH being under 25 mIU/ml and the value

of E2 above 35 pg/ml. The third group consisted of postmenopausal women (n = 26), with anamnestic data for at least 12 months from the last menstruation, with values of serum FSH above 25 mIU/ml of E2 under 35 mIU/ml. Hormone concentration was determined with standardized tests based on the radioimmunological method. Factor VII concentration was determined by the method of deficiency plasma. T-PA Ag and PAI-1 Ag levels were determined by a sandwich technique known as enzyme-linked immunosorbent assay (ELISA). Data were entered into a data-base and were statistically analyzed, $p<0.05$ being considered as statistically significant difference. Correlation analysis (Pearson's coefficient) was used for assessing the relationships between the examined parameters.

Results: Statistical analysis has shown that there was a significant increase of PAI-1 Ag and factor VII in both peri- and post-menopausal examinees in comparison with the control group ($p<0,001$); and a significant decrease of TPA Ag ($p<0,001$) during perimenopause and postmenopause. There is a positive correlation between estradiol and TPA Ag ($r = 0.97$). It is also apparent that there was a negative correlation between estradiol level on one hand and concentration of PAI-1 Ag ($r = - 0.163$) and factor VII ($r = - 0.134$) on the other, in all 3 examined groups of women.

Conclusions: This study favors the view that decrease in estradiol level in perimenopausal and postmenopausal women may be responsible for the haemostatic and fibrinolytic disorders and increased risk of atherosclerotic and thromboembolic complications.

MID FREQENCY BLOOD PRESSURE OSCILATIONS IN SPONTANEOUSLY HYPERTENSIVE RATS DURING [CAV9]N/OFQ(1-13)NH2 APPLICATION

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This study investigate the effects of the modified in nine position nociceptin analog [Cav^9]N/OFQ(1-13)NH_2 on the blood pressure variability in spontaneously hypertensive rats (SHR). Experiments were carried out on conscious normotensive Wistar rats, used as control animals and on SHR, used as a animal model of human essential hypertension. One day before experiments under general anesthesia (Nembutal, 35 mg/kg, i.p.) catheters were inserted in femoral artery for blood pressure registration and in femoral vein for drug application. 24 hours after surgical manipulations, blood pressure wave registration was performed in conscious rats in control period and after [Cav^9]N/OFQ(1-13)NH_2 (100 nmol/kg) applications in the course of 90 min, within nine consecutive 10 min long intervals. The values of systolic (SAP), diastolic (DAP) and mean (MAP) arterial blood pressure was determined by AcqKnowledge 4.1 software from blood pressure wave in each heart beat. The spectrograms for SAP, DAP and MAP were derived from 512 successive values through virtual instrument developed in graphical programming environment Lab VIEW 3.1.1., by using Fast Fourier Transform algorithm. The spectral power (P) of mid frequency (MF:195-605 mHz) oscillations was studied. The power of sympathetically mediated oscillations (P_{MF}) in SAP, DAP and MAP spectrograms in SHR was lover in comparison

to normotensive Wistar rats: 1.1±0.1 vs. 2.17±0.2; 0.80 ±0.01 vs. 1.22±0.1; 0.86±0.09 vs. 1.25±0.1mmHg^2, ($p<0.01$). Application of [Cav^9]N/OFQ(1-13)NH_2 in Wistar rats led to a decrease of P_{MF} in the SAP, DAP and MAP spectrograms. The P_{MF} in the SAP decreased in first three 10 min long intervals to 1.01±0.20; 1.04±0.18; 1.55±0.16 mmHg^2, ($p<0.05$) but decrease of P_{MF} in the DAP in MAP spectrograms was displayed only in the first 10 min long interval, from 1.28±0.15 and 1.53±0.17 ms^2 to 0.81±0.09 and 1.03±0.14 mmHg^2 ($p<0.05$). In SHR [Cav^9]N/OFQ(1-13)NH_2 led to sustained increase of P_{MF} immediately after its application in SAP, DAP and MAP spectrograms, ($p<0.01$). The difference in response to [Cav^9]N/OFQ(1-13)NH_2 in normotensive and spontaneously hypertensive rats may be a result of increased sympathetic nerve activity in SHR.

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THE ROLE OF EDUCATION IN PATIENTS WITH HIGH BLOOD PRESSURE

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Introduction: High blood pressure is a common condition in which the force of the blood against the artery walls is high enough that it may eventually cause serious health problems, including heart attack and stroke. It affects millions of people and is the most common reason for adults to visit doctors. While strokes, heart failure, heart attacks, and kidney failure were common in people with elevated blood pressure years ago, treatment has had a dramatic impact on these problems. However , education ,in terms of teaching the patients of eating healthy food, decreasing the salt in their diet, maintaining a healthy weight, increasing physical activity, limiting alcohol and smoking and managing stress, seems to have an important role in keeping the blood pressure under control.

Method: We conducted a survey in our medical institution of patients with hypertension ,to examine their functional health literacy level and their knowledge of their chronic disease and treatment.

Results: 68 % of the patients had inadequate knowledge about their illness,4% marginal and only 28% adequate knowledge.

Conclusions: Inadequate f unctional health literacy poses a major barrier to educating patients with hypertension and current efforts to overcome this appear unsuccessful. One of the main reasons is alsso socioeconomic status of the patients. It's prooved that it is negativly associated with the outcome of this illnes and the quallity of life in these patients.

Because of this reasons,our medical institution PZU Prim.d-r Samardziski,has made a few intensive steaps in this field,by massive education of our patients through our free newspapers: Nie,vie i zdravjeto" and website "nvz.com.mk",only for one goal, to improve health and possibly save lives by generating and distributing information about hypertension and by promoting research and teaching in the field of hypertension.

HYPERTENSION: COMPLIANCE TO MEDICATION AMONG HYPERTENSIVE PATIENTS IN SKOPJE

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Background: Compliance in health care can be defined as the degree to which the patient conforms to medical advice about lifestyle and dietary changes as well as to keeping appointments for follow up and taking treatment as prescribed. Non-compliance to blood pressure-lowering medication is a major reason for poor control of Hypertension. The objective of this study was to determine the factors, which are associated with medication compliance among hypertensive patients registered in an outpatient clinic in Skopje.

Methods: Eighty-nine patients seen in the outpatient clinic of medicine were enrolled in the prospective study from March 2010 to May 2010. Simple structured questionnaire was elaborated and administered to patients who were taking antihypertensive drugs after obtaining an informed consent from the participants.

Results: The average age was 45 ± 12 years. The overall compliance rate was 47,3%; the rate was lower in those aged < 45 years than older patients (36,9% versus 46.7%;). It was also lower among educated than illiterate patients (32.7% and 48.1% respectively;). About 49,7% of patients thought that they should stop drug treatment once they achieved blood pressure control and 68% believed that emotional stress was the most important etiological factor in hypertension. The most common reasons for poor compliance were drug side effects, forgetfulness and economical cost.

Conclusion: These findings emphasize the important role of primary health care physicians(family doctor) in educating patients about hypertension. Prescribing an effective, inexpensive, one daily medication with minimal side effects will improve patient compliance considerably.

CONTROL OF ARTERIAL HYPERTENSION IN EASTERN EUROPEAN COUNTRIES

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Eastern European countries (EEC) are a geographic area characterized by high prevalence and mortality of cardiovascular diseases (CVD). Increased attention is being paid to the blood pressure (BP) control in the EEC, as they take first places in age-standardized mortality rate (among those 45-74 years) from cerebrovascular and ischemic heart diseases in Europe (year 2000).

The data for prevalence, treatment, and control of AH in EEC show great differences among countries. The control rate of AH in Russia is 8% for males and 16% for females. The data for Slovakia show control rate of the treated 8-10 %. The BP-Care Study established the control of hypertensive patients in 9 countries from Central and Eastern Europe: Albania, Belarus, Bosnia, Czech Republic, Latvia, Romania, Serbia, Slovakia and Ukraine. BP control (< 140/90 mm Hg) was achieved in only 27.1%. BP control was variable among countries, worse for systolic than for diastolic BP, better in

patients followed by specialists than by general practitioners, more unsatisfactory in high risk, diabetic, CHD and renal failure patients. Control rate in treated hypertensive population in the 5 biggest cities in Bulgaria established systolic blood pressure (SBP) <140 mm Hg in 15 to 32 % and diastolic BP < 90 mm Hg in 22.3-34.8%. The control rate of treated hypertensives is 25%, and for the patients with home blood pressure measurement - 37.4%.

The control rate of hypertension in Bulgaria has considerably improved in the last decade. The data from treated hypertensive railway workers published in1997 show 6% control rate. Ten years later, the same population shows 24.6% control rate.

The most frequently used drugs for monotherapy and for combination therapy (BP Care Study) were: ACE inhibitors (70%), Beta-blockers (57%), calcium channel blockers (51.2%), diuretics (45.8%), and ARB (13%). The drug choice improved; the data from Bulgaria comparing the drugs used in 2003 and in 2008 are as follow: ACE inhibitors 43% and 76%, diuretics 27% and 59%, calcium channel blockers 39% and 46%, beta blockers 58% and 41%, ARB 4% and 26%, and fixed-dose combination (FDC) 13% and 32% respectively.

The advantages of combination therapy and especially FDC for the improvement of BP control motivated development of a Consensus Statement for monotherapy and combination therapy in Bulgaria in 2005. Simple and clear recommendations are presented regarding how to choose the strategy for initial treatment - monotherapy or combination therapy

Conclusion: The control rate of BP in EEC is still low. Combination therapy and especially FDC is one of the priority strategies for improvement of BP control and prognosis of hypertensive patients. Great differences in BP control rate were observed among EEC, reflecting to a large extent the different levels of health education of the population and of the financial resources.

RAAS BLOCKADE IN HYPERTENSION AND CHRONIC KIDNEY DISEASE: IS IT BLOOD PRESSURE LOWERING ALONE THAT MAKES THE DIFFERENCE OR SPECIFIC MEDICATIONS?

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Chronic Kidney Disease (CKD) - The size of the problem in the general population. The number of patients with CKD is increasing and over the next decade, the number of patients treated by dialysis may double. The increase is being driven especially by the increase in patients entering end stage ren al disease (ESRD) without primary diagnosis of renal disease - more than half of the new ESRD cases (1). Societal and financial costs are an impossible burden for developing nations to meet. Developed countries appear to spend about 10% of their health care budgets on ESRD population and the cost is growing at 10% per year (2).

Hypertension and CKD. Hypertension increases CKD risk and the exact role as cause/consequence is still debated. Kidney has a role in hypertension development and modulation. Hypertension and renal parenchymal disease are closely interrelated. Hypertension accelerates renal disease and hastens the progression to ESRD. Recent

studies have firmly established the importance of blood pressure (BP) reduction as a means to slow the progression of different forms of renal parenchymal injury. For diabetic or non-diabetic nephropathy, the higher the BP the greater the renal risk. The beneficial impact from achieved control of mean arterial pressure (MAP) is clearly demonstrated in a meta-analysis of the 9 major clinical trials in diabetic and non-diabetic renal diseases. The GISEN Group, Klahr, and Moschio studies are those in non-diabetic subjects. The higher the MAP the faster the GFR declines; the better the control of MAP the slower the GFR declines. (3-7)

The Renal injury triad. The three major mechanisms of hypertension related CKD injury and progression are: 1). **Hypertension** causes vascular injury trough direct damage to the vessels, which in turn causes induction of angiotensin II pathways at the tissue level and increases the local angiotensin II production; 2). **Angiotensin II** increases intraglomerular pressure, changes vascular structure and function and induces vascular remodelling; 3). **Proteinuria:** Sustained intraglomerular pressure and/or increased oxidative stress damage the glomerular basal membrane and cause endothelial dysfunction which causes extravasation of protein. This activates inflammatory and vasoactive cytokines as well as intratubular complement, all of which results in interstitial scarring and progressive nephron loss.

Actions of the renin-angiotensin system (RAS). ***Circulating RAS*** is involved in the vasoconstriction of blood vessels, aldosterone and AVP release, stimulates thirst and sodium appetite, and controls renal sodium and water reabsorption. ***Tissue-based RAS*** is involved in processes of hypertrophy, hyperplasia, remodeling, cytokine activation and collagen deposition and fibrosis.

New aspects of RAS. A number of advances have been made in our understanding of RAS. ACE homologues include ACE2 (which shares ~42% of the catalytic domain of ACE) and a soluble form of ACE. In addition to angiotensin I and bradykinin, newly identified substrates for ACE include: the peptides angiotensin (1–7) and angiotensin (1–9), which may contribute to cardiovascular homeostasis; N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP), an inhibitor of hematopoietic stem cell proliferation; Amyloid β-protein, which has been implicated in Alzheimer's disease; A number of other peptidases have also been identified that catalyze the conversion of iotrenzin I to angiotensin II. Finally, there is evidence suggesting that ACE may act as a signal transduction molecule (8). ACE inhibitors (ACEi) mechanism of action leaves other pathways for angiotensin II production unaltered and this may lead to recovery of angiotensin II levels despite continuing ACEi therapy. Chymase-dependent angiotensin II formation predominates over ACE-dependent angiotensin II formation in some human tissues. ACEis increase levels of angiotensin I and would shunt this substrate to chymase preferentially (9). This finding has implications for the use of ACEis and ARBs. In an early trial (1982) of the ACEi MK 421, 19 hypertensive patients were treated with a range of doses. Although the iACE reduced BP, 24-hour control was far from satisfactory in all patients. While plasma ACE activity was markedly reduced within 4 hours of administration, plasma angiotensin II concentrations began to return to baseline levels after an initial fall at 4 hours post-dose. At 6 months, angiotensin II levels were no different from control when measured 12 to 16 hours following administration of MK 4211. ACEi therapy is known to increase plasma renin activity

and angiotensin I levels. These increases may overwhelm the capacity of iACE therapy to prevent angiotensin II formation, contributing to ACE escape (10).

Blockade of RAS and the evolution of benefits. From only BP reduction benefits, it was demonstrated that benefits also include cardioprotection, vascular protection, renal protection and recently improved glycemic control. Nowadays earlier and more aggressive BP control with RAS blockade is being the foundation for the antihypertensive therapy. ESH–ESC Guidelines 2007 list of conditions favouring the use of blockade of the RAAS**:** heart failure, left ventricular dysfunction, post-myocardial infarction, diabetic nephropathy, non-diabetic nephropathy, proteinuria / microalbuminuria, left ventricular hypertrophy, atrial fibrillation and metabolic syndrome (11)

Renoprotective benefits of blockade of the RAS are clearly demonstrated as hemodynamic and non-hemodynamic benefits. Hemodynamic benefits of RAS blockade with ACEis include decrese of systemic BP, intraglomerular pressure and of proteinuria, and non-hemodynamic include: stimulation of extracellular matrix degradaion and inhibiion of Mf/Mo infiltraion (12). AT1R blockade effectively reduces BP, improve heart failure symptoms, blunt progression of diabetic renal disease, and prevent stroke. However, trials of ARBs in high-risk patients have generally demonstrated a neutral effect on myocardial infarction.

Treatment approaches to retarding progression of CKD include good metabolic control (in diabetes), BP control, reduction of proteinuria, lipid control, anemia control, smoking secession and physical activity. Abundant evidence accumulated in the past decade justifying the wide use of agents that block the RAS and summaries of these studies are formulated in several **proven strategies for retarding progression of CKD.**

Strategy 1: Early detection - effective treatment of BP to target levels. It has been demonstrated that strict BP control with ACEis, aimed at reaching target values attenuates the deterioration of renal function. Number of studies **(**13-17) concluded that there is evident significant beneficial effect of the low BP goal on proteinuria, GFR decline, urine protein excretion in adults and children. Target BP is 110-130/75-80, if tolerated. BP of <130/85 mm Hg is recommended in all patients with renal disease, and BP < 130/80 mm Hg in those with urinary protein excretion of 1g/24 h. or less and BP <125/75 mm Hg in patients with proteinuric renal disease (>1 g/24 h.)

Strategy 2: ACEi provides greater renoprotection compared to other antihypertensive drugs in patients with diabetic and non-diabetic nephropathy. With respect to renoprotection, both diabetic and non-diabetic patients benefit when the actions of angiotensin II are inhibited. Numerous studies documenting the effectiveness of ACEis and ARBs in retarding the development and progression of diabetic complications (18-20) and the conclusion is that in patients with DM and >35% reduction of renal function ACEi reduced the risk of doubling of serum creatinine. ACEis, also reduce the risk combined endpoint of ESRD and death. Furthermore, it appears that drugs that inhibit the actions of angiotensin II yields superior outcomes compared to other drugs that act through calcium channel or through beta blockade. It appears that the effect of ACEi is independent of baseline BP, renal function and type of diabetes.

Strategy 3: ACEi for reduction of proteinuria. Proteinuria itself is pathogenic single best predictor of disease progression. Reducing urinary protein excretion slows the progressive decline in renal function in both diabetic and non-diabetic kidney disease. Target proteinuria is <500 mg/d. The beneficial effects of drugs that block the RAS are reflected in a parallel lowering of hypertension and proteinuria. There is also decreased progression of proteinuria from normoalbuminuria to microalbuminuria, and from microalbuminuria to macroalbuminuria. (21, 22). A Meta-analysis (11 RCT) showed that RAS blockade is more effective at comparable levels of BP than conventional antihypertensive agents (23). ACEi lowered BP and proteinuria, decreased the combined risk of progression of CKD to ESRD by 30%, independent of BP lowering effects. The conclusion of the studies on the benefits of RAS blockade is that the reduction of proteinuria over 30%, resulted in significant retardation of CKD progression.

Strategy 4: Double blockade of RAS with combination of ACEi and ARB. Complete RAS blockade was aimed for greater antihypertensive and antiproteinuric effect with reduced progression resulting from increased kinin production and possibly decreased aldosterone secretion. Additive effects in diabetic nephropathy and heart failure were expected. It was, also, proposed that angiotensin II escape with ACEis that may lead to AT2 receptor stimulation during combination therapy will be prevented. Blockade of the RAS beyond ACE inhibition decreases proteinuria and slows progression of renal disease in diabetics with overt nephropathy by suppressing aldosterone synthesis or blocking the aldosterone receptor. Effects of monotherapy and combination therapy on proteinuria and CKD were analysed in a meta-anlysis (24 of 49 controlled trials (from jan 1999 – Sept 2006) with 6181 patient with/out DM and with proteinuria randomized to ARBs vs. PLA, ACEI and CCB, combination ARBs+ACEI. Conclusion was that the reduction of proteinuria was similar with ACEI and ARBs, combinaion ARBs+ACEI was more efficient. The ONTARGET Study reported additional data (25) from 25,620 ≥55 years, high risk patients with established atherosclerotic vascular disease or diabetes with organ damage treated with telmisartan or ramipril dministered as monotherapy and in combination. The results showed that the reduction of albuminuria / proteinuria with the combination of drugs was superior to any agent given as monotherapy.

Strategy 5: Use of a triple blockade of the RAS with iACE + ARB +Spironolaktone. Triple blockade of RAS - ading of sprinolaktone when iAKE+ARB is no efficient, was shown to be efficient in reduction of proteinurie for 58% and colagen IV in the urine for 40% ($p<0.05$) (27)

Conclusion. Optimal vascular and renoprotection may be achieved by earlier and more aggressive BP control and RAS blockade as a foundation for antihypertensive therapy. Blockade of RAS yields additional renoprotection as monotherapy (ACEi or ARB) or in combination. Triple blockade of RAAS has beneficial effects only if double blockade was ineffective.

ONCOLOGY

ОНКОНЕВРОХИРУРГИЯ - НОВИ ТЕХНОЛОГИИ ПРИ НАРАСТВАЩА ЗАБОЛЕВАЕМОСТ И ЗАСТАРЯВАЩО НАСЕЛЕНИЕ

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Увод:Съвременното общество се характеризира с нарастваща невроонкозаболеваемост /първична и вторична/ поради застаряващото население, влиянието на множество онкогенни фактори, подобрената неврообразна диагностика и контрол върху първичния процес.

Цел и Методи: Анализ на съвременните възможности на диагностичния процес и лечебната стратегия при невротуморни процеси за последните 30 години.

Резултати: Въвеждането на нови технологии доведе до революционни постижения: микроневрохирургията повиши рязко оперативната активност и радикалност с намаление на периоперативната смъртност / 1-2 %/ и усложнения /около 5-10 %/. Другите технологични нововъведения като невронавигация, невроендоскопия, интраоперативна лъчетерапия, стереотаксична радиохирургия, ултразвукови и лазерни техники разшириха обема и възможностите на неврохирургичните интервенции при онкозаболявания. Анализират се резултатите при над 500 невроендоскопични , 800 невронавигационни и други интервенции с приложение на модерни технологии. Минимално-инвазивният характер на съвременните неврохирургични интервенции в съчетание с ранната прецизна диагноза на неврообразната апаратура / КТ, МР, ПЕТ и др./ позволяват разширяване на обема на операциите, както и на възрастовите граници, вкл. и над 85-90 г. като целта е съхраняване и подобряване качеството на живота с максимално удължаване на преживяемостта на оперираните пациенти.

Изводи: Модерните неврохирургични технологии в съчетание с прецизна ранна неврообразна диагностика, усъвършенствувана лъчетерапия и ефикасна химиотерапия дават реални надежди за многократно повишена преживяемост след невроонкологични интервенции при запазено или възстановено качество на живота при редица случаи, считани доскоро за иноперабилни или инкурабилни.

В ОЧАКВАНЕ НА ДЕЙСТВУВАЩА ПРОГРАМА ЗА ОПС/общ популационен скрининг/ ЗА РМШ

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Увод: Ракът на маточната шийка /РМШ/ е вторият най-често срещан карцином при жените и е на седмо място като причина за смърт при тях. За една година в Европа има 50 000 ново регистрирани заболели и 22 000 починали от РМШ. 175 000 жени живеят с РМШ –лекувани или по друг начин.

Метод: Практика в различни страни на ЕС и резултати от него-статистически данни. България се нарежда на челно място в заболеваемостта и диагностицирането в късен стадий в ЕС и на средно в света. До днес в България няма ОПС, дори плахите опити за такъв бяха спрени на 19.01.2009г.чрез промени в Нар.39 ва МЗ.

Резулати: Днес, ние можем да предотвратим 80% от случаите на РМШ чрез организиран скрининг, базиран предимно на цитологично изследване на намазки, взети при профилактичен преглед от ОПЛ или АГ-специалист. За целта е достатъчно всяка жена да посещава дори без оплаквания веднъж годишно гинеколога си. Възможностите за установяване на предракови и други промени чрез микроскопско изследване на клетките от вътрешната и външна част на маточната шийка с висок успех. При нужда се назначават допълнителни изследвания или лечение.През последните 20 години много проучвания показват, че персистирането на инфекция с високорискови типове човешки папиломен вирус, рискът от развитие на РМШ нараства, както и смъртността от напреднал карцином на шийката на матката.

РМШ е високоподатлив на скрининг, защото има продължителна предклинична фаза със сигнални промени, които могат да бъдат установени и лекувани лесно в ранен стадий. Методът е сигурен около 80%, с вариации от 30 до 87% в зависимост от компетентността на лекаря, извършващ микроскопското изследване в лаборатория.

Извод:Въпреки поредиците от всевъзможни политически срещи на високо равнище, препоръки от ЕС и водещи световни експерти все още сме на етап „предвижда се“. Обхванатите 20% жени, подлежащи на скриниг са причина за печалните резултати в България.

ВЪЗМОЖНОСТИ НА КЛИНИЧНАТА ХОМЕОПАТИЯ В ПАЛИАТИВНОТО ЛЕЧЕНИЕ НА ОНКОЛОГИЧНАТА БОЛКА

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Палиативната медицина е медицински подход на третиране поведение към болни с активно, прогресиращо и напреднало заболяване с лоша прогноза и изчерпани терапевтични възможности.Това са пациенти, при които потенциалният риск от конвенционално палиативно лечение превишава потенционалната полза.

Неефективността му и страничните явления съпоставени към страданието на пациента от трагедията и безсмислената болка изместват фокуса на лечението и грижите към качеството на живот в неговата последна фаза.

В генезата на понятието “ палиативен”- “pallium” – мантия / грижовна топлота/ и - palliare – облекчавам, авторът представя възможностите на клиничната хомеопатия.

Разгледани са основните патологични състояния водещи до необходимост от палиативни грижи в терминалния период, както и основните видове онкологична болка.

Локализацията, усещания и модалности на болковите симптоми – индивидуални за всеки пациент са основа за извеждане на индивидуално подбрани за всеки пациент хомеопатични медикаменти съобразно патогенезата им от Материя медика.

Презентацията разкрива богат набор от хомеопатични медикаменти съобразени с индивидуалната характеристика на болката и страданието на онкологичния пациент в терминалната фаза на заболяването.

Хомеопатичните средства могат да бъдат приложени заедно с различни специализирани и интердисциплинарни методи за лечение, на съпътстващата болестна или ятрогенната патология.Хомеопатията, може да бъде комплементарен метод към тях или алтернатива ,ако пациента пожелае това.

Приложеният клиничен случай е потвърждение на изложената теза.

ВЪЗМОЖНОСТИ НА ЛЪЧЕЛЕЧЕНИЕТО ПРИ БОЛНИ С НЕДРЕБНОКЛЕТЪЧЕН РАК НА БЕЛИЯ ДРОБ

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Увод: Карциномът на белия дроб е водеща причина за смърт от онкологични болести в Европа и България. Целта на настоящото проучване е да бъде направен анализ на терапевтичните резултати при дефинитивно лъчелечение (ЛЛ) с недребноклетъчен карцином на белия дроб, оценка на прогностичното значение на основни клинични и функционални параметри по отношение на общата преживяемост и сравнение на резултатите от схеми с различен обем и фракциониране на дозата.

Материали и методи: В проучването са включени 76 болни с недребноклетъчен рак на белия дроб, във II-III КС, на средна възраст 59,6 год. (33-83 год.), лекувани и проследени за периода 2005 – 2010 година в Клиниката по Лъчелечение на НСБАЛО и МБАЛ „Токуда Болница София". При всички болни е проведено дефинитивно перкутанно ЛЛ на линеен ускорител. Всички болни са планирани три-измерно (3D) при нехомогенност на дозата в облъчвания обем, не по-повече от 5% (conformal radiotherapy). При 46 болни е проведено ЛЛ по схема ДОД 3 Gy до ООД 51 Gy, в 4 фракции седмично, в обем обхващащ първичен тумор и позитивни лимфни възли, а при 30 болни - по схема ДОД 2 Gy до ООД 50-60 Gy, 5дни седмично, в обем обхващащ първичен тумор и медиастинум. Анализирани са биологични и клинични показатели по отношение на общата преживяемост (OS), като е използван методът на Kaplan-Meier.

Резултати: В края на проведеното ЛЛ при всички пациенти е постигнат пълен или частичен терапевтичен отговор. Пациентите са проследени средно 16 месеца (от 1,5 до 60) след проведеното ЛЛ. Двама пациенти са загубени от проследяване. Анализът на данните показва средна OS от 24,6 месеца, като на третата година кумулативният дял на преживелите е 19%, независимо от режима на ЛЛ. Изключение правят пациентите на възраст < 50 години, при които е приложена по-радикална схема (p=0,0006). Факторите пол, хистология, диференциация на тумора, стойност на хемоглобина и функционално изследване

на дишането в началото на лъчелечението не показват статистически значима корелация с общата преживяемост. Значимо по-продължителна преживяемост се постига при пациенти в I и II стадий (p=0,03), облъчван обем до 100 $см^3$ (p=0,007), без засягане на лимфни възли (p=0,03) и стойност 0 и 1 на ECOG (p=0,03).

Изводи: Получените при настоящото проучване терепевтични резултати са съпоставими с резултатите, получени от други международни проучвания. Потвърждава се прогностичното значение на стадия, ECOG статуса, туморния обем и свързания с това планиран обем. Ограничаването на планирания обем чрез прилагане на "conformal radiotherapy" до обема на първичния тумор и видимо ангажираните лимфни възли, не води до влошаване на общата преживяемост. При по-млади пациенти е уместно да се обсъжда по-радикална схема на ЛЛ.

ПРЕДОПЕРАТИВНО САМОСТОЯТЕЛНО И КОМБИНИРАНО (ЛЪЧЕ-ХИМИОЛЕЧЕНИЕ) ПРИ ЛОКАЛНО АВАНСИРАЛ РАК НА РЕКТУМА

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Увод: Цел на настоящото проучване е изясняване приноса на лъче-химиолечението, сравнено със самостоятелно лъчелечение, приложени в предоперативен план при локално авансирал рак на ректума, по отношение на лечебните резултати, локалната и обща токсичност.

Материали и методи: За периода 2006-2010 в клиниката по лъчелечение в СБАЛ по Онкология е проведено предоперативно лъчелечение при 83 болни с локално авансирал II-III стадий рак на ректума, на възраст от 40 до 75 години (средна възраст 57г.), от които 27 (33%) жени и 56 (67%) мъже. Стадирането е извършено чрез КАТ/МРТ на малък таз и ендоректална ехография. Болните са разпределени в две групи. В първата група (ЛЛ) от 50 болни е провеждано самостоятелно перкутанно лъчелечение за областта на малкия таз, чрез „бокс"техника на апарат „Терабалт" (Co_{60}) или на линеен ускорител до ООД 50Gy, при ДОД 2Gy пет пъти седмично. Във втората група (ЛХЛ) от 33 болни лъчелечението е комбинирано с Капецитабин – 825mg/m^2/d, в един прием вечер в дните на облъчването. Характеристиката на заболяването в двете групи е следното: в първата група cT3-20 болни (40%), cT4 – 30 болни (60%), cN0 -11 болни (22%), cN+ 39 болни (88%), във втората група cT3-18 болни (55%), cT4-15 болни (45%), cN0 - 5 (15%), cN+ 28 (85%). Разпределението на болните в първата спрямо втората група по степен на малигненост е както следва: G1-11:4 ,G2-28:19 ,G3-11:10; а според разстоянието на тумора от анокутанната линия, съответно: нисък ректум - 20:16, среден ректум - 25:10, и висок ректум - 5:7. Оценен е патоморфологично локалният контрол в четири степени и общата преживяемост в двете групи. Ранната токсичност е оценена по CTCAE v.3.

Резултати: Пълен контрол е постигнат при 1 болен от първа група ЛЛ и при 3 – от група ЛХЛ (съответно 2%:9%), частичен контрол с >50% редукция на тумора - съответно при 25:17 болни (50%:52%), частичен контрол с <50% редукция - при 22:13 болни (44%:39%), и прогресия - при 2 болни (4%) от група

ЛЛ. Болните са проследени средно 4,7 години. В първата група наблюдаваната обща преживяемост е 78,7%, а във втората с е 85%.
Гастронтестиналната токсичност съгласно CTCAE v.3 е отчетена, както следва: Grade 1 – при 25:19 болни (50%:57,5%), Grade 2 - 15:7 (30%:21%), Grade 3 – 10:7 (20%:21,2%), съответно в първата съпоставена с втората група. Наблюдавана е генитоуринарна токсичност само в лека степен: Grade 1 - при 20:7 болни (40%:21%) и Grade 2 - при 4:2 (8%:6%). Grade 3 и 4 не са наблюдавани.

Изводи: Комбинираното с Капецитабин ЛХЛ в предоперативен план предоставя възможност за подобряване на локалния контрол и общата преживяемост, при съпоставима ранна токсичност.

БРАХИТЕРАПИЯ С ВИСОКА МОЩНОСТ НА ДОЗАТА ПРИ БОЛНИ С ПРОСТАТЕН КАРЦИНОМ В ГРУПИ С УМЕРЕН И ВИСОК РИСК

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Увод: Изготвяне на лечебен протокол и първи клинични изпитвания у нас за брахитерапия с висока мощност на дозата (БтВМД) при болни с простатен карцином в групи с умерен и висок риск в съчетание с перкутанно лъчелечение за областта на малкия таз.

Метод: От януари 2009 г. до юли 2010 г. по договор ДО02-81/12.12.08 за безвъзмездна финансова помощ между СБАЛО-ЕАД и Фонд "Научни изследвания" с предмет на изпълнение на научно-изследователска програма на тема: „Рак на простатната жлеза - диагноза, прогноза, лечение и оценка на лечебните резултати" са лекувани болни с простатен карцином в група с висок и умерен риск с три месечно хормонално лечение, предхождащо лъчелечение. Предвидени са две рамена 1. Самостоятелно перкутанно лъчелечение на линеен ускорител в «малък» и «голям» обем и 2. Съчетано лъчелечение - Брахитерапия с ВМД в «малък» обем за простатната жлеза на апарат Микроселектрон и «голям» обем за малкия таз – перкутанно лъчелечение по подобие на първата група болни. При 30 болни за обема на простатната жлеза в „малък обем" са реализирани 9 x 2.75Gy и на втори план за областта на малкия таз 46Gy по 2Gy дневна доза до дефинитивна доза, еквивалентна на 76 Gy. За изпълнение на второ рамо от проучването - БтВМД бе въведена специализирана планираща система за клинично (анатомотопографско и дозиметрично) планиране в реално време. Това дава възможност за постигане на максимална точност при избор на вариант и корекция предлагани от системата в хода на лечебното планиране. Манипулацията е тип малка оперативна интервенция (трансперинеално пункционно поставяне на временни инпланти) в условия на обща или спинална (епидурална) анестезия.

Резултати: При всички болни провели дефинитивно перкутанно лъчелечение, месец след заавършването е установен биохимичен контрол със стойности на PSA < 1 ng/ml с трайна тенденция за намаляване, като на 3 месец след лъчелечението при 10% от болните, PSA е 0.00 ng/ml. При 5-10% от болните се е налагало прекъсване до 1 седмица в хода на лъчелечението поради остри

гастроинтестинална и урогенитална токсичност- II степен. По второ рамо на проучването през месец юли 2010 г. бе проведено обучение на лекари (лъчетерапевти, уролози и рентгенолози), медицински физици и ренгенови лаборанти за придобиване на умения, които през месец октомври 2010 г. с помощта на консултант лъчетерапевт от Щвеция, ще бъдат приложени при лечението на първите трима болни с оценка на диагностичния и лечебен метод и изграждане на окончателен протокол за изпълнение на методиката. До края на 2010 г. очакваме да приложим методиката със съчетано лъчелеление перкутанно и брахитерапия в 2 фракции през 20 дни по 8-9Gy при 15 болни., обсъждане поносимостта на лечебния метод, локална и обща токсичност и налагаща се корекция в лечебния протокол.

Изводи: С въвеждане на новата методика за страната – БтВМД при простатен карцином очакваме същите или по-високи лечебни резултати, при незначителна токсичност, което предполага брахитерапевтичния метод - максимално насищане на дозата в простатаната жлеза и минимално облъчване на предна ректална стена, в сравнение с облъчването на линеен ускорител.

ПРОБЛЕМЪТ ЗА КАРЦИНОМА ПРИ ХИРУРГИЧНИТЕ ЗАБОЛЯВАНИЯ НА ЩИТОВИДНАТА ЖЛЕЗА

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Извършен е ретроспективен анализ при 3420 болни с хирургични заболявания на щитовидната жлеза , на възраст 17-88 години , 1259 мъже =36.8 % и 2101 жени = 63.1 % оперирани в болници на Южна България / областите София – град, Смолян , Кюстендил , Стара Загора , Благоевград , Хасково , Кърджали , Ямбол през периода 2000-2009 г. Вкл. По вид заболяванията са били : нодозна струма-864 болни от общия брой 6 25.2 %, полинодозни еутиреоидни струми-1332= 38.9 %, тиреоидит на Хащимото -977 = 28.5 % , дифузна тиреотоксична струма , болест на Базедов – 246 болни = 7.1 % и 1 болен с ехинокок на щитовидната жлеза. Пълните хистологични изследвания са показали наличие на карцином , както следва : нодозна струма -92 болни = 10.6 % , полинодозна , еутиреоидна струма – 167 = 12.6 % , Базедова болест -29 болни = 11.7 % тиреоидит на Хищомото – 193 = 19.9 %. От болните с карцинома непластичен вариант е установен при 0.97 % , фоликуларен – в 14.6 % и при останалите папилиферен вариант на тиреоидния карцином .

Проучванията на водещия автор / Р. Петков / посочват , че при папилиферен карцином може в широки граници да се прилагат органосъхраняващи операции без риск от чести рецидивни и по- ниска преживяемост на болния след операцията . При останалите варианти се прилага тиреоидектомния с щалена шийна лимфна дисекция . Анализът посочва , че карциномът се наблюдава в по – старшите възрастови групи и при по продължително съществуване на струмата , при по –продължително лечение с

тиреостатици и е най – чест при тиреоидт на Хашимото , което предполага прецизно диспансерно наблюдение на болните.

GASTROINTESTINAL STROMAL TUMORS – MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY. NEED FOR STANDARDIZED GIST REPORTING

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Background: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in the gastrointestinal tract with majority arising in stomach and small intestine. In the past they were considered to be of smooth muscle origin, but many investigations showed a differentiation toward interstitial cells of Cajal (ICC) phenotype. Morphologic subtypes include spindle cell, epithelioid and mixed cell types. Generally GIST is a specific tumor type immunohistochemically KIT-positive which is driven by KIT or PDGFRA activating mutations. Evaluation on biologic behavior was according to Fletcher method of risk stratification, Miettinen's criteria while a new UICC TNM classification is been set for standardized GIST report.

Methods: We analyzed 32 cases diagnosed as GISTs in a period of 8 years (2002 to 2010). All slides were reviewed for tumour site, size, histological typing, immunohistochemical staining, and mitotic count along with their frequencies. The risk stratification was made by Fletcher method on 29 cases, and 3 cases (from 2010) were staged according the new TNM classification.

Results: Out of 32 patients 19 were females (59,4%) and 13 males (40,6%). Eleven (34,4%) patients were at age range 60-70 years, 9 patients (28,1%) at 50-60 years, 6 patients (18,7%) at age above 70 years, 4 patients (12,5%) at 40-50 years and 2 patients (6,3%) at 30-40 years. Determination of tumor site showed 14 cases (43,7%) in small intestine, 13 cases (40,6%) in the stomach, 2 cases (6,3%) in large intestine and 3 cases (9,4%) on other sites. Fourteen patients (43,7%) had a tumor size > 10 cm, 13 patients had size between 5 and 10 cm, and 5 patients had tumor size between 2 and 5 cm. The most frequent (75%) histological subtype was spindle cell type, mixed type we determined in 5 cases and epithelioid type in 3 cases. Immunohistochemical successful analyses were performed on 27 cases while on 5 cases were no conclusive. CD117(c-kit) was positive in 12 cases, CD34 in 10 cases, while 11cases were with neurologic differentiation and 5 cases were leiomyomatous. A total of 16 (50%) patients fall into high risk, 6 patients into intermediate risk, and 6 patients into low risk group. Two cases according to the new TNM classification were stage III and 1 case was stage IB.

Conclusion: According to morphology and immunophenotype GISTs can be diagnosed accurately and treated efficiently. Tumor site, size and mitotic rate are powerful criteria for staging and evaluation on biologic behavior. Great heterogeneity of GISTs has to be taken into consideration when proposing risk stratification and classification systems in order to have a standardized report.

HIGH-RISK V-S LOW-RISK CUTANEOUS MELANOMA

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Clinical observations during surgery at our Clinic in Skopje, have led us to speculate that an anatomic basis may in fact exist for the poor prognosis associated with malignant melanoma arising in certain recognized "high-risk" areas. In our study we have treated and followed up 49 patients with primary malignant cutaneous melanoma for over 4 years. During the course of treatment, we identified variations in anatomic characteristics at the tumor sites. Criteria were established for high-risk and low-risk locations by the neurovascular structure encountered. We speculate that these sites that have neurovascular windows provide a readily accessible vascular pathway for the dissemination of malignant cells to deeper viscelar structures and may account for the poor prognosis associated with primary lesions in these locations.
Thirty two patients were clasiffied as being at high risk for developing metastasis, whereas 14 patients were classified as being at low risk; 3 patients were in a "special-risk" category.

To date, 13 of the 32 patients with "high-risk" melanoma have gone on to develop metastatic disease, which represents 40% of that group, whereas none of the patients classified as "low-risk" have developed metastasis during the dame period.

MOBILIZATION OF HLA IDENTICAL FAMILIAR HEALTHY STEM CELL DONOR IN ALLOGNEIC TRANSPLANT SETTING

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Background: Allogeneic hematopoetic stem cell transplantation is a procedure with the highest potential of curing patient with acute myeloid leukemia. Apart from the eradication of malignant cells by conditioning regimens, the main therapeutic benefit is ascribed to the immune mediated graft versus leukemia effect. Mobilized peripheral blood stem cells (PBSC) from healthy donors have become an increasingly used alternative to bone marrow for allogeneic transplantation. Granulocyte colony-stimulating factor (G-CSF) –primed peripheral stem cells harvesting may result in a graft with increased mononuclear cells collected, increased progenitor cell dose and potential for more rapid engraftment resulting in improved survival. Filgrastim is not only known to mobilize CD34+ progenitor cells but acts as a pleiotropic immune modulator. So, systematic donor follow-up in healthy donors is needed. The aim of our study was to evaluate safety and feasibility of G-CSF primed hematopoietic peripheral stem cells in familiar HLA-identical donors.

Methods: The follow-up focused on clinical and laboratory testing including reports of adverse event after the mobilization. Granulocyte colony-stimulating factor (G-CSF) was administrated in 51 healthy donors to reach sufficient mobilization in the period 2000-2010. The donors were characterized as follows: 43 years median; female

60% of the donors. G-CSF was administrated in the dose 10μg/kg of donor weight in five day and PBSC collections started on the fifth day using COBE Spectra cell separator. The aim was to collect mononuclear cells $2x10^8$/kg of recipient weight. Three donors were mobilized twice (for second transplant). Aphaeresis needed to reach target number of CD34+ cells were: 1 aphaeresis in 50%, more than two aphaeresis need in only 1 patient.

Results: The most frequent adverse event that was noted by patients was bone pain associated with increasing number of white blood cells. Better mobilization and higher PBSC yield correlated significantly with younger age. Four years after G-CSF – primed peripheral stem cells harvesting, a young female 48 years old was diagnosed with acute myeloblastic leukemia. Four years ago when she was 44 years old, she donated for her HLA identical sister with acute myeloblastic leukemia.

Conclusion: G-CSF is safe and very effective for PBSC mobilization in our group of healthy donors. This method allows certain collections of sufficient numbers of progenitors in virtually all healthy donors. We demonstrated that filgrastim mobilization for peripheral blood stem collection is effective and result with successful engraftment in all the recipients. Daily injection of 10μg/kg of G-CSF and first aphaeresis preformed at day 5 seems to be the best strategy to obtain the CD34+ cell count required for an allogeneic hematopoietic stem cell graft.

MODERN RADIOTHERAPY IN MULTIMODALITY TREATMENT OF CANCER

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The modern local cancer treatment strategy is an integration of different treatment modality into a more comprehensive approach to achieve both local tumour and micrometastatic disease control. Surgical therapy as a sole modality often fails because of micrometastatic disease already present at the time of surgery and availability of malignant cells beyond the surgical margins of the resection. Limitations of radiation therapy /RT/ are connected with different tumour radiosensitivity or radioresistance and dose restrictions to normal organ and tissue around the tumour. Radiotherapy alone fails to control large advanced bulky nonoperable lesions. There is a limited evidence that hyperfractionation, accelerated fractionation, intensive modulated radiotherapy and other sophisticated high- tech RT, applied as a single treatment has improved outcome.

Concomitant use of RT and chemotherapy /CH/ in solid tumour enhances tumour killing effect by several mechanisms: reoxigenation of hypoxic tumour cells; action on hypoxic tumour fraction and on S- phase /Mitomicin C/; tumour cells arest in radiosensitive parts of cell cycle - M и G1 phases /5-FU and Taxans /; impeding the repair process of sublethal radiation damage /Platinum, antimetabolites, antracyclines / ; manipulation of subclinical tumour dissemination and etc. / Fig 1/ The type of interaction between chemotherapy and radiotherapy within the radiation field could be

supra-additivity, additivity, or infra-additivity. Concomitant chemoradiation /RT-CH/ is one of the modern milestones in oncology, modeling the transition from removing the whole sick organ to a treatment that allow saving that organ and its function.

The author presents recent evidence based achievements in CT-RT as organ sparing modalities on the example of head and neck /H&N/and rectum cancer. All patients with T1-T2 laryngeal cancer should be treated, at least initially, with intent to preserve the larynx. Concurrent chemoradiotherapy therapy may be used for larynx preservation for selected patients with stage III, T2 N+ cancers. Meta-analysis of chemotherapy in H&N cancer as an update on 93 randomised trials with 17,346 patients confirmed that only RT-CH offers a considerable reduction of recurrence rate and 6,5% absolute difference in overall survival /OS/ at 5-th year, compared to other multimodality combinations. Perioperative treatment in rectal cancer offers preoperative or postoperative CH-RT in several aspects: reduction of recurrence rate, sphincter saving treatment and downstaging of border line operable cases. There are two strategies that have been proven to produce local recurrence reduction in the region of 5-10% in resectable rectal cancer. These are short course preoperative radiotherapy / 5 times 5 Gy/ followed by TME surgery (Dutch TME and CR07); or preoperative long course chemoradiotherapy followed by surgery (EORTC 22921; FFCD 9203; GAO/ARO/AIO-94).

It has been proved by several meta-analyses that preoperative CH-RT can provide definitive improvement in local recurrences, modest increase in proportion of patients undergoing curative surgery with a price of increased acute and late rectal toxicity. The evidence based medicine has not fully supported the expectation that preoperative radiotherapy in combination with chemotherapy is effective in improving the likelihood of accomplishing sphincter sparing surgery. If the objective is to increase the incidence of sphincter preservation, the use of endocavitary boost with / or brachytherapy shows promise. Nevertheless, the American experience shows a consistent drop in the abdomino-perineal resections rate with the increasing use of long-course preoperative radiation, from a high of 40% (1985–1986) to less than 30% by the mid-1990s.

Golden Standard in treatment for loco-regionally advanced cervical cancer /IB2-IVA/ is RT-CH with platinum. Considerable reduction of risk of death was proved by Cohraine date based systemic review on 4921 patients participated in 24 trails. It shows an improvement of overall survival and disease free survival with absolute benefit of 10% and 13% respectively . The effect was greater in trials including a high proportion of stage I and II patients. Chemoradiation appears to reduce both local and distant recurrence. In general, acute toxicity is increased, but the long-term side effects are still not clear.

Author also debates the progress of RT-CH with Temozolamide /TMZ/ in glioblastoma multiforme - one of the most aggressive human tumour. Three years OS with classical multimodality approach /radical ??? surgery , adjuvant RT and CH/ is not more than 5% . Improvement with a factor of 2,5 was reached when radiation si combined with TMZ , increasing 2-years OS to 31.7 %, compared to postoperative RT results - 10.4 %. TMZ causes DNA damage by methylation of the *O*-6 position of guanine and activates the p53-controlled DNA damage response pathway. The orally

administered drag also inhibits signaling of radiation-triggered cell migration and invasiveness and decreases tumor cell repopulation. It acts as radiosensitizer, increasing rate of DNA single brakes produced by RT to DNA double hits. Tumor with methylated promoter of DNA-methyltransferase (MGMT), a p53 DNA damage repair enzyme, is preferentially radiosensitized and the benefit of combined treatment is such a patient is greater.

Irradiation evokes a plethora of cell responses through several pathways, including those involved in cell proliferation, cell cycle regulation, apoptosis, angiogenesis, and inflammation /Fig 1/. The current preclinical and clinical availability of a number of newer products collectively termed "molecular targeted agents" has led to their study as new forms of radiosensitization. Comprehensive reviews on that are already being published. Molecular-targeted therapies are an attractive option combined with RT-CH because they are more specific for the target and can inhibit radioresistance pathways. Preclinical studies with the epidermal growth factor receptor /EGFR/ inhibitors cetuximab, gefitinib, and erlotinib show enhanced radiosensitivity leading to supra-additive efficacy both *in vitro* and *in vivo.* Proposed mechanisms for radiosensitization via EGFR inhibitors include inhibition of cell proliferation, impairment of DNA damage repair, attenuation of tumor neo-angiogenesis, inhibition of radiation-induced EGFR nuclear import and promotion of radiation-induced apoptosis. In particular, the antiproliferative effects of EGFR inhibition most likely prevent repopulation, a major mechanism implicated in radioresistance.

Angiogenesis is essential for sustained tumour growth. Many new cancer therapies are directed against modification of the tumor vasculature process of angiogenesis, mediated by multiple proangiogenic and antiangiogenic factors, with vascular growth factor receptor /VGFR/ having a central role.

Combination with different anti EGFR and anti VGFR / molecules with RT or CHRT are under investigation.

HEPATOCELLULAR CANCER IN PATIENTS WITH FOCAL LESIONS IN THE LIVER

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Background: The liver is the most common site of haematogenic metastases from different primary site of the tumor. Also, primary tumors of the liver represent one of the most common causes of death of malignant disease worldwide. The annual incidence of this disease is about 1 million cases. More than 80% patients are from developing countries. The aim of this study is to assess the frequency of primary hepatocellular cancer (HCC) in patients with unknown primary site of the tumor, and ECHO or CT detected focal lesions in the liver.

Methods: The study included 60 patients, hospitalisated in Clinic of Oncology Clinical Centre Banja Luka, with ECHO or CT detected focal lesions in the liver with malignant characteristics (primary tumor or secondary lesions). In all patients we have searched for the history of disease and performed oncological clinical examination, and further diagnostic processing.

Results: Cytological or pathohystological confirmation of malignant disease was found in 51 patients (85%). Fourthin patients (27%) had HCC, 13 M and 1 F, average age of 63 years (48 – 74 y), (χ^2= 9,40 p<0,01). HBsAg positive were 33,3% pts, HBV antibodies were found in 28,6% pts, and HCV antibodies were obtained in 14% pts. Four patients (28%) had previously cirrhosis. Data for frequently consummated alcohol gave 6 pts (43%).

Conclusions: Out of 14 patients confirmed as HBsAg positive, HCC was verified in 4 (28%). Extrahepatic primary process was found in 26 pts (51%). Colorectal cancer was found in 70% patients with proved extrahepatic primary site of tumor.

EARLY PROSTATE CANCER AND BENING PROSTATIC HYPERPLASIA DIAGNOSIS AND THERAPY

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Background: Prostate is a gland in man that surrounds the neck of the bladder and the proximal part of the urethra. Prostate produces a fluid that became part of semen. It is composed of glandular and muscular tissue and contracts during ejaculation of seminal fluid. The prostatic secretion contains alkaline phosphatase, citric acid, prostate specific antigen (PSA) and various proteolytic enzymes. The most commonly prostatic diseases are Benign Prostatic Hyperplasia (BPH) and Prostate Cancer (PC). Efforts have been made in order to establish the clinical criteria for early diagnosis and therapy of PC. Several medical therapies are also suggested for the treatment of BPH. The aim of this study was to evaluate the effect of 5ARI, α blocker and the combination of therapies for BPH on the quality of life and to see whether they provide symptom relief and reduce disease progression and the development of new morbidities. Evaluation of antiandrogen effects after orchiectomy or prostiectomy in patients with diagnosed PC was secondary aim of the study.

Methods: Since 2007, early BPH and PC diagnosis have been promoted by the department of Urology of the General City Hospital of Veles, Macedonia, using both digital rectal examination (DRE) and PSA diagnostic evaluation of asymptomatic and symptomatic men. The project was performed by medical examiners, urologists and medical laboratories. All men (n=2145) were between 40-90 years of age and all of them were advised and encouraged to undergo DRE and PSA testing. Furthermore, urologists performed the transrectal ultrasound (TRUS) guided biopsies for 98 men (n=98), who had a high level PSA (>4 ng/ml). Depending on the tumor level determined, watchful waiting, orchiectomy with following androgen deprivation therapy, radical prostatectomy, radiotherapy and chemotherapy were recommended.

The patients with BPH (n=2050) were treated either with α blocker (Tamlos) or 5ARI (Avodart) on the basis of its effects on symptoms and flow rates or with a combined therapies. On the other hand, antiandrogen (Androcur) was given as a subsequent oral therapy after the orchiectomy or prostatectomy, for patients with diagnosed PC.

Results: The highest incidence of PC (patients treated with Androcur) was obtained in 2007. It remained essentially constant until 2010, but it evidently changes the appearance in the age group. The incidence of BPH is rather high and it was diagnosed in more than 85% of the asymptomatic and/or symptomatic men above age of 40. Avodart (5ARI) was evaluated as efficient drug with reduction of BPH progression by reducing the prostate volume, improving the urinary outflow, decreasing the risk of acute urinary retention as well as the need of invasive surgery treatment. The best results we observed with combination therapy of Tamlos and Avodart.

Conclusions: This clinical evaluation is suggesting strategy for an early diagnosis of BPH and PC for all men above age of 40. If orchiectomy or prostatectomy is required, Androcur can be suggested as subsequent oral therapy. Several medical therapies can be suggested for the treatment of BPH. Since α-blockers provide only a symptom relief without reducing the prostate volume, for patient with higher risk of disease progression, combined therapy of both α-selective blocker and 5ARI is recommended.

CYTOGENETIC DAMAGE IN MINE WORKERS

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Background: Interaction between chemicals and genetic material results principally in two types of dezoxyribonucleic acid (DNA) alterations: first, changes in single genes at the molecular level and, second, chromosomal aberrations derived from breakage in the near coherence of chromosomes. Too little is known about the chromosomal effects of metal exposure. The aim of this study was to detect cytogenetic damage in mine workers working in a lead–zinc mine, which could be associated with a combined exposure to lead, zinc and cadmium like heavy metals and to determine risk factors for the frequencies of structural chromosomal aberrations (SCA) in peripheral blood lymphocytes of mine workers. The present article attempts to summarise current knowledge of the chromosomal effects caused by heavy metal exposure, pointing out the existing gaps in this knowledge and discuss future research needs.

Methods: Our study involved 120 mine workers from the lead–zinc mine in Macedonia, and a control group (30) - local people who had never worked in the mine. We used peripheral blood lymphocytes as the target material. The total share of structural chromosome aberration (SCA) are searched out over the 3 years of

monitoring. Also, we measured the blood level of lead, zinc and cadmium with ISP-AES.

Results: We found an increased blood lead level in exposed group (Mean=0,089) and in 20% of the control group (Mean=0,066); increased zinc blood level in exposed (Mean=1,391) and in control group (Mean=1,074); as well as an increased cadmium blood level in 62% of the exposed (Mean=0,007) and in 50% of the control group (Mean=0,006); Chromosomal aberrations (like dicentric and acentric chromosome) were found to be elevated in 7% of exposed individuals (mine workers) and in none of the control group. Individuals with chromosomal aberrations have worked above 20 years in the mine, and there is a positive correlation between the blood levels of heavy metals (lead, cadmium and zinc) and the chromosomal aberrations. Both chromosome type aberrations in the exposed group were accompanied with anemia, leucocitosis and anisocitosis.

Conclusions: We may conclude that the group of exposed persons showing increased levels of chromosome abnormalities has a higher risk of developing cancer compared to the group showing no increase in aberrations The earliest concern of the research work in the field of occupational diseases was intoxication with heavy metals. Eighty five percent of workers with long exposure were found to be suffering from various respiratory tract diseases like asthma and respiratory infections. Our research showed that nearly all workers complained of headache. The results of *in vivo* and *in vitro* studies with the same test system, human lymphocytes, sometimes disagree. This inconsistency may be due to differences in concentrations at target sites on one hand, or to the capacity of the body to eliminate heavy metals (lead, zinc and cadmium).

RAPID PROGRESSION OF MYELOMA WITH BULKY EXTRAMEDULARY TUMOR INVOLVEMENT UNDER TREATMENT WITH THALIDOMIDE IN A 67-YEARS OLD PATIENT - CASE REPORT AND REVIEW ON THE CONTROVERSIES IN THE MANAGEMENT OF ELDERLY MYELOMA PATIENTS

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Background: A rare case of myeloma with an aggressive clinical course and unusual manifestation of bulky extramedulary involvement under chemotherapy is described. Case report. A 67-years old man with recently developed paraparesis due to compressive fracture of the thoracic vertebraes has been diagnosed to have multiple myeloma of IgA type in stadium IIA. Radiotherapy and chemotherapy with melphalane and prednisolone (MP) resulted with improvement of the initial symptoms and complete clinical and hematological remission at six months disease evaluation. At relapse, one year later, unfortunately no control of the disease could have been achieved with thalidomide salvage therapy in a maximally tolerated dose of 200 mg daily: five months after start of thalidomide the IgA level further raised, hemoglobin decreased, even renal failure (not dialysis dependent) developed and again paraparesis appeared due to the compressive fracture this time of the lumbal vertebraes. Paliative radiotherapy and

chemotherapy with cyclophosphamide, vincristine, melphalane, prednisone (COMP) were no longer effective. Heavy backache developed further and big extramedulary tumor located paravertebraly in the cervical and thoracic region was found on CT scan, but the fine needle biopsy was unsuccessful. The patient performance progressively worsened making impossible any further treatment. He died soon therafter, at 9 months after the relapse.

Conclusion: Treatment of elderly myeloma patients is rather challenging: more than 60% of myeloma patients are aged over 65 and 75 years; different treatment strategies are now possible with the introduction of novel agents such as the immunomodulatory drugs and proteasome inhibitors. From the current data it could be concluded that the choice of treatment of elderly myeloma patients should consider the patients' biologic age, presence of comorbidities and the toxicity profile of the regimen. The optimal induction regimen, the feasibility of autologous transplant and the role of maintenance therapy in the elderly myeloma patients needs further evaluation.

A SMALL ULCER OVERTOOK A HALF OF THE HEAD – A CASE REPORT

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Introduction: Case report - a patient who was not compliant to take medical treatment to heal his small wound on his face which was growing slowly and took off a half of his head.

Methods and results: A 88-year-old man, appeared in 1992 with a small wound on his right temporal region. He didn't want to see a doctor and he was putting a bee populist on the wound. Crusts were forming on the wound and the patient thought that the wound is getting smaller. In 1995 the wound was raising at the size of a bean seed. The patient started to use black ointment and oil from a centariumflower. In 2006 a small wound appeared at the apex of his nose and was slowly spreading on his face. He was accepted in the geriatric department and was examinated by a team of dermatologists and surgeons and they couldn't agree about any further treatment. The wounds were spreading very fast and in august 2009 they joined to each other and pressed the right eye in the deep. The patient stopped seeing on his right eye. The tumorous tissue was continuously bleeding at its surface and compressive bandages were used. The CT scan reveals a heterodense tumorous lesion on the right side of the head with necrotic masses and calcifications in them and also completes destruction of the near bony structures. After application of the IV contrast, there was a pathological accumulation of the contrast.

On examination, the tumor obstructs the right half of the nose, covers his right eye and the orbit with spreading on the right frontal and parieto-temporal regions of the head completely deteriorating the right half of the face. The surface of the tumor was with irregular edges and cauliflower-like exophytic lesiones that bleed continuously and also places with calcifications into them. Over the right orbit, the tumor is in size of a two male fists.

On pathological examination, the tumor was classified as baso-cellular carcinoma.The tumorous tissue compromised a half of the head with a destruction of

the soft tissues and also the bony part of the skull with direct pressure onto the brain. The patient was still conscious and oriented in space, time and personality.

Conclusion: The patient was self-sacrificing since he was not willing to take a medical treatment at the time when the treatment was beneficial. If he had accepted the medical treatment at the very beginning, when the lesion was small, he would not developed this irreversible condition with a decreased quality of life and a poor prognosis.

LARGE LOWER EYELID CARCINOMAS –A CHALLANGE FOR TREATMENT

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Aim: To describe our treatment solutions after excision of malignancies in a series of patients with large lower eyelid carcinomas

Methods: This series included patients with BCC of the lower eyelid larger than 15mm in diameter respectively with postexcisional defects larger than 20mm in diameter. Most of the operations were performed under general anaesthesia. There was involvement of the medial canthus in 2/3 of the cases.

All postoperative defects were primarily closed using local skin flaps, combinations of local skin flaps and skin grafts and combination of two local skin flaps. We used buccal mucosa in order to solve the lack of conjunctiva, and for backing up flaps we used chondromucosal graft ear cartilage.

Results: The results of repair were satisfactory with respect to colour match, texture and functional properties. Considering that we are talking about large reconstructive procedures, we had complications in 20% of the cases including Lagophthalmos, epiphora, malposition of the eye and trichiasis. Patient follow up was 5 years.

Conclusion: Eyelid reconstruction encompasses a wide range of reconstructive options. While set algorithms have been proposed regarding eyelid reconstruction, the method of choice will ultimately depend on a combination of factors, including availability of tissues and a surgeon's experience with the available modes of reconstruction.

CHEEK PEDICLE TRANSPOSITIONAL FLAP IN RECONSTRUCTION OF EYELID POSTEXCISIONAL DEFECTS

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Aim: To describe a series of patients who have undergone lower eyelid reconstruction with cheek pedicle transpositional flaps.

Methods: A non-comparative retrospective case series of 20 patients with lower eyelid defect after excision of basal cell carcinomas of the lower eyelid who underwent reconstruction using a ckeek pedicle transpositional flap. The outcome

measures were closure of the defect, the cosmetic result, complications, and re-operations.

Results: Primary closure of the defect was achieved in all cases. The cosmetic result was highly satisfactory in all cases. There were no major complications or re-operations. Only two cases had minor webbing of the lateral part of the upper eyelid.

Conclusion. The cheek pedicle transpositional flap can be modified depending on the nature of the periorbital skin, localization, extent and depth of the defect. It is an efective, fast and simple technique used for reconstruction of the extramarginal and the marginal defects of the lower eyelid.

DETECTION OF THE JAK2V617F MUTATION IN THE EVALUATION OF THE BCR-ABL NEGATIVE CHRONIC MYELOPROLIFERATIVE DISORDERS (MPD): LONG TERM FOLLOW-UP STUDY

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Background: Recently, the activating V617F mutation in JAK2 has been identified as a marker of myeloproliferation, useful for proving clonality and securing diagnosis in a considerable proportion of patients with myloproliferative disorders (MPD). The prognostic significance of the mutation is still unknown and the results from the clinical correlations are inconclusive and require solid conformation.
The purpose of our study is to evaluate the incidence of the JAK2V617F mutation in the patients with MPD that had been followed for a median of 12,4 years at our institution and to investigate whether MPD patients that carry JAK2V617F mutation differ in clinical course and outcome with respect to MPD patients negative for JAK2V617F mutation.

Methods: The study group consisted of 74 living MPDs patients diagnosed at our Institution over the study period longer than 10 years. According to standard WHO criteria for diagnosis of MPD 29 patients were diagnosed as polycythemia rubra vera (PRV), 31 as thrombocythemia essentialis (ET), 6 as myelofibrosis primaria (MP) and 8 were classified as other myeloproliferative disorders (OMPD)

Results: We detected the V617F JAK2 mutation by the PCR-direct sequencing using DNA extracted from unfractionated blood samples in 87% of patients with PRV, in 43% with ET, 66% with myelofibrosis primaria (MP) and in 21% with OMPD.
The semi-quantification of the expression level of JAK2-V617F mRNA showed more than 50% higher level of JAK2-V617F mRNA compared with the wild type JAK2 mRNA in 80% of the PRV patients, 75% with MP and 12% with ET suggesting the presence of homozygosity for the JAK2-V617F allele.

Correlations between the two JAK2-V617F different MPDs groups were made using standard statistical tests. The two groups were comparable regarding the sex, age, intial hemoglobin, leukocyte and platelets level and overall survival. The JAK2-V617F

positive group has higher incidence of thrombotic complication (30%) compared with 14% in the other group.

We found the homozygosity for the JAK2-V617F allele in a substantial proportion of MPD cases. This observation was associated with long disease duration, data that support the hypothesis that homozygous mutations confer a longer survival time.

Conclusion: Our results confirmed the diagnostic significance of JAK2V617F mutation in MPDs but did not reveal any new information regarding the clinical characteristic and outcome of patients with MPD that carry this mutation.

LUNG CANCER AND SMOKING HABIT - CASE CONTROL STUDY

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Background: Lung cancer (LC) is the leading cause of cancer death in men and the second leading cause of cancer death in women. Smoking is the major cause of LC, accounting for about 80% of LC cases in men and 50% in women worldwide. The aim of the investigation is to determine the existence of an eventual causal association among the cigarette smoking and development and distribution of the lung cancer.

Methods: Our research was conducted as a case-control study. It includes 101 patients with lung cancer (investigated group-IG) and the same number of subjects without malignant disease (control group-CG). Both group members were interviewed within the period May 2008-May 2009. Risk analyses were done using unconditional logistic regression, which provides results in the form of crude odds ratio. The odds ratios and their 95% confidence intervals (CI) were computed.

Results: The habit of cigarette smoking was especially spread out among men diseased from lung cancer (68,8%), while in CG this percent were 40,3%. In IG, among the females, current smokers and nonsmokers were equally represented. Smokers and ex-smokers have 4,05 (95%CI 1,78<OR<9,19) times significantly higher risk to become ill compared to the non-smokers. The risk for becoming ill increases significantly in smokers who smoke >20 cigarettes per day (c/d) ($p<0.01$) and is 9,33 (95%CI 3,56<OR<24,48) compared to nonsmokers. The risk for developing lung cancer is 4,55 (95%CI 1,86<OR<11,12) times greater in persons smoking >15 years (y) >20 c/d, compared to those who smoke <15 y <20 c/d.

Conclusion: Our study supports the statement that cigarette smoking is by far the most important risk factor for lung cancer. Concerted control of smoking appears to be an urgent priority in lung cancer prevention, including efforts to prevent adolescents from start smoking.

BENIGN PROSTATIC HYPERPLASIA-IMPORTANCE OF THE ULTRASOUND DIAGNOSTICS IN PRIMARY HEALTH CARE

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Background: Every fifth 40-year-old and any other 70-year-old man has symptoms of enlarged prostate. More than 90% of men over 80 years have histological evidence of benign prostatic hyperplasia. Worldwide, more than 25 million older men have BPH II and III stages. The aim of our work is to emphasize the importance of ultrasound diagnostics in primary health care and the frequency of benign prostatic hyperplasia by age structure and representation of complications.

Methods: Data were obtained by analyzing the protocol ultrasound cabinet for a period 01.01.2009-31.12.2009 and results are shown in tables and graphs.

Results: In the reporting period, we reviewed 202 patients with symptoms of the urinary tract (aged 25-85 years). Out of that number, 82 men had an enlarged prostate. The average age of patients was 63 years. Thirty five percent of patients had more than 70 years, and complications were presented in 21 patient (25.6%).

Conclusion: Up to the age of 40 years, benign prostatic hyperplasia is a rare disease, and the increase of 9.7% at the age between 41-50 years of life is statistically significant. With the age, the percentage increases and reaches its maximum after 70 years of life.The primary health care should pay attention to this disease because of possible complications and disruption of quality of life of the individual and the environment.

THE BURDEN OF CANCER AND CHALLENGES OF CANCER CONTROL IN CENTRAL AND SOUTH–EASTERN EUROPE

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Background: Europe comprises only one eight of the total world population, but has around one quarter of the global cancer cases, about 3.2 million per year. Overall cancer incidence and mortality rates vary at least two-fold between European countries and the differences are often far greater for specific cancers. With some exceptions, the observed variation in incidence and mortality rates largely reflect varying prevalence and distribution of risk factors within and between European countries, as well as disparities in the delivery of cancer control measures. In most of these countries, the combined demographic effect of population ageing and population growth will result in a steady and continuing increase in the number of cancer patients, diagnosed each year over next 20 years, largely irrespective of changes in the incidence rates of the common cancers. Total cancer mortality remains a big problem within Europe; one in four deaths is attributed to cancer and about 1.3 million of deaths occurred in 2008. Despite better survival from some cancers, marked inequalities remain between European countries. This human burden must be borne by millions of European families, but also economies and health systems of the countries in which they live. But the implications for health systems go far beyond the financial. More than any other disease, cancer causes deep fears and anxiety in most people; many are unaware of what can be done to reduce the

risk of developing cancer and of successful treatment. An integrated strategy for cancer control is thus needed at all levels of the society, taking into account primary and secondary prevention, integrated care (treatment, rehabilitation and palliative care) and advances in research.

Data sources and methods: This presentation examines the geographic variations in cancer burden in 2008 and reviews the published evidence to explain the differences. Cancer incidence and mortality estimates for 2008 are from the GLOBOCAN database. In this database, countries or territories follow the geographical definition of the United Nations (World Population Prospects, the 2008 revision). According to this definition, Europe is divided in 4 regions: northern, western, central and eastern, and southern. For this review, a special emphasis will be on countries, belonging to central and eastern Europe (Belarus, Bulgaria, Czech Republic, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia, Ukraine), and southern Europe (Albania, Bosnia Herzegovina, Croatia, Cyprus, Greece, Italy, FYR Macedonia Slovenia, Montenegro, Malta, Portugal, Serbia, Slovenia and Spain). Basic incidence and mortality measures are used to present the cancer burden: absolute numbers, crude and age-standardised rates (per 100,000 population).

Results: In 2008, there were an estimated 3,213,522 incident cases of all forms of cancer (except non-melanoma skin cancer) diagnosed in Europe, 985,156 in central and eastern Europe and 713,858 in southern Europe. Of 1,721,828 cancer deaths, 634,819 were in central and eastern Europe and 380,536 in southern Europe. After adjusting for different age structure, the overall estimated incidence rates in males and females were higher in northern and western Europe than among central-eastern countries, while mortality was higher in males in central-eastern European countries.
High all cancer mortality rates for a number of central and eastern European countries despite lower incidence reflect the distribution of most frequent cancers and poor survival of these patients. While several published analyses of trends in cancer mortality in Europe over the past 30 years show, that in the majority of countries of the former EU-15, the age standardised mortality from most common cancer sites has fallen since late 1980s, in the majority of central and eastern European countries, the situation is less favourable. The most frequent cancer site in 2008 (except non-melanoma skin cancer) in males in north-western countries was prostate, followed by lung, colorectum and bladder, while in central-eastern Europe lung represented nearly a quarter of all cancer sites, followed by colorectum, prostate, stomach, and bladder. Among causes of death, lung cancer was the most important in all European regions. In females in northern and western countries breast cancer accounted for more than 30% of all new cancer cases (except non-melanoma skin cancer), followed by colorectal and lung, while in central and eastern part of Europe, breast and colorectal cancer are followed by uterine corpus and cervix cancer. While the proportion of deaths from breast and colorectal cancer are similar in both regions, cervical cancer accounts for 6% of all cancer deaths in females in central and eastern Europe.

Lung cancer is still the biggest public health problem in Europe, especially in its central and eastern part, where it accounts for nearly one third of all cancer deaths in males. As the most important risk factor for lung cancer is tobacco smoking, trends in lung cancer incidence and mortality reflect the stage of the smoking epidemics in different countries. While in some western European countries the mortality from lung

cancer, especially among younger men (age 30-64) started to decline, due to the modification in the smoking habit from generation to generation, there is an increasing trend in females. Decrease in mortality in males has been noted in some central and eastern European countries in the 1990s, such as Slovenia, in Hungary and Poland there was at least no further increase observed till the end of the nineties, while in Romania, Bulgaria and FYR Macedonia, mortality from lung cancer in males is still increasing. Unfortunately, there is still an increasing trend in mortality persisting among females in the whole Europe.

While lung is the most frequent cancer site in central, eastern and southern Europe, *prostate* leads in western and northern Europe. Apart from age and ethnic origin, a positive family history is probably the strongest known risk factor. The recorded incidence of prostate cancer has substantially increased in the past two decades, probably because of the uncontrolled introduction of screening with prostate-specific antigen, the use of improved biopsy techniques for diagnosis, and increased public awareness. Mortality changes are not of the same magnitude as the changes in incidence, and in some countries mortality has been stable or even decreased. The disparity between reported incidence and mortality rates leads to the probable conclusion that only a small proportion of diagnosed low-risk prostate cancers will progress to life-threatening disease during the lifetime of the patient.

Despite decreasing time trend in *stomach cancer* incidence, it is still the fifth most common cancer type in Europe, while its proportion is still highest in central and eastern Europe. The most important stomach cancer risk factors are: Helicobacter pylori infection, some dietary habits and smoking. In contrast to distal stomach cancers, those originated in stomach cardia are not caused by Helicobacter pylori infection. Diminishing the differences in socioeconomic status would decrease stomach cancer burden globally as well as locally.

While *primary prevention* by non-smoking or smoking cessation is the best measure to decrease the incidence of and mortality from lung cancer in both sexes, *secondary prevention by screening* is aimed to reduce mortality from colorectal, breast and cervical cancer.

Excess calorie intake and insufficient levels of physical activity leading to obesity clearly increase the risk of *colorectal cancer* and its constant rises in incidence have been observed within populations undergoing economic development. The incidence is high in many of western, but also central and eastern countries, e.g. Czech Republic, Hungary and Slovakia. While mortality trends tend to decrease in some of the north-western countries from 1990s onwards, they were still in the upward direction in many central and eastern European countries. Besides different lifestyles, these differences may be due also to earlier diagnosis, new treatment modalities and hence better survival in some western, but not to such extent in eastern countries. As screening for colorectal cancer has been shown to be effective, there is a need for organized programs throughout Europe.

Breast cancer was the leading cause of death from cancer in women in Europe. Genetic factors, including the major susceptibility genes (BRCA1, BRCA2), may account for up to 10% of breast cancer cases in developed countries, but their prevalence in the population is too low to explain much of the international variation in risk. The majority must therefore be a consequence of other risk factors. Besides age and sex, the

established breast cancer risk factors include previous breast cancer in one breast, family history of breast cancer, fibrocystic disease and ionizing radiation (the reported range of relative risk estimates of breast cancer 2.1 to more than 4). For others, the reported range of relative risk estimates is low, ranging from 1.1-2.0. These include hormonal and reproductive factors, such as early age at menarche, late age at menopause, late age at first birth, late age at any birth, nulliparity, current use of oral contraceptives and hormone replacement therapy. All these risk determinants are difficult to change, while life style related factors, such as body mass index, physical activity, diet and alcohol consumption should be the goal of primary prevention. Trends in the incidence of and mortality from breast cancer result from a variety of influences including screening programs (such as introduced in several European countries in the late 1980s), stage of disease at diagnosis and quality of treatment. A recent analysis of breast cancer mortality trends between 30 European countries in the period 1989–2006 has shown a reduction in breast cancer mortality of 19%, ranging from 45% reduction in Iceland to a 17% increase in Romania. The increasing mortality in some central European countries is correlated to low, usually non-organized screening activities, low numbers of mammography machines and their low quality, slow uptake of anticancer drugs, health expenditures below the European average and system inefficiency.

Mortality from *cervical cancer* is in Europe much lower than in developing world, where 80% of all deaths occur. There are great differences in its incidence and mortality between central and eastern European countries and other European countries, mostly due to different availability of organized screening programs. They reflect the fact that opportunistic screening, as currently present in the majority of these countries, is not effective. Sexually transmitted infection with some human papillomavirus (HPV) strains is fundamental to development of cervical cancer and HPV vaccine already available on the market is hoped to reduce incidence in the years to come, but screening programs will have to remain, as the vaccine does not protect against all HPV strains.

In Slovenia, organised, population-based, nationwide cervical cancer screening programme (NP ZORA) was implemented in 2003 with a three-year screening interval and call/recall system that insures the complete coverage of the target population (women aged 20–64). Before that time, opportunistic cervical cancer screening took place since 1960s'. It took several years to develop this programme, as the pilot started already in 1998, but the current results are encouraging. Coverage of the target population by smear tests in the last three-year screening interval (2007–2009) was 72.2 % and in the last five-year interval (2005 – 2009) the coverage was 82.6 %. In the first five years after the implementation of the screening programme, the cervical cancer incidence rate has decreased by about 40%. Crude incidence rate was 20.6 in 2003 and 12.6 per 100,000 in 2008, age-adjusted incidence rate (world population) were 12.8 and 8.8 per 100,000 accordingly. Stratification of cancer by stage shows important down-staging after the implementation of the screening programme in women who regularly attended the screening programme. The mortality rate has been decreasing since the mid-1990's, but it is still early to determine whether the introduction of ZORA in 2003 accelerated the existing downward trend.

Conclusions: Across Europe there are regional differences in cancer burden and time trends. They can be partially explained by differences in cancer risk factors, lifestyle-related and environmental, including tobacco, alcohol, dietary habits and

pollution. The results from the EUROCARE studies revealed great variations in cancer survival among European countries that are mostly due to differences in screening, timing of diagnosis and in quality of treatment. Many differences have their roots in social and economic inequalities as a consequence of political systems that existed among various geopolitical regions in Europe. It is hoped that the application of current knowledge on cancer prevention, early diagnosis and integrated care, will result in effective and efficient national cancer control programs, reducing the current disparities in cancer burden in many countries of central, eastern and southern of Europe.

A CASE OF ACTINIC RETICULOID ASSOCIATED WITH LUNG CANCER.

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Actinic retikuloid is a chronic cutaneous disease, connected with expressed photo sensibility to UVA, UVB as well as visible light. It could be associated with cutaneous lymphoms and with other neoplastic disorders.

We present a case of actinic reticuloid in a 65 years old man, who had a lung cancer.

The association between these two diseases, lead to exacerbation of actinic reticuloid.

LOCALIZED FORM OF LYMPHOMATOID PAPULOSIS, EVALUATING IN T-CELL LYMPHOM.

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Lymphomatoid papulosis is presented by spontaneously regressing cutaneous infiltrates, that microscopically resemble a lymphomas and may evolve into Hodgkin or non- Hodgkin malignant lymphoma.

We present a case of Lymphomatoid papulosis in a 64 years old male, who complains from reddish non painful papules, localized symmetrically on the back and lateral zone of the legs.

The patient was treated for 10 weeks with low dose of methotrexat (15 mg per week) with good clinical result.

One year after treatment interruption the same patient had a similar clinical changes and hystochemical signs for development of T-cell lymphoma.

LUNG CANCER IN PATIENTS DIAGNOSED AND TREATED IN THE HOSPITAL „JASENOVO„ - VELES: OUR 2,5 YEARS EXPERIENCE

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Background: The aim of our study was to evaluate Lung Cancer (LC) in patients of our Hospital and to compare these results with the European reports.

Methods: In a 2,5 years retrospective study 119 patients were bronchoscopically examined for diagnosis of LC. We followed up parameters of age, sex, smoking habit, type of cancer, localization, and a possibillity for operation.

Results: Out of 119 patients 18 (14%) were diagnosed with Lung Cancer. Older than 60 years were 61%, and in between 40-60 years were 39% of the patients (men 17 (94%) and only 1 woman (6%)). Excessive smokers with more than 1 box per day were 78%. From those malignancy was confirmed in 95%, and only 1 was histologically benign type - 5% (neurofibroma). According to the type differentiation plano cellular was found in 66%, followed by adenocarcinomas with 16%. According to the localization 89% were positioned in the main and segment bronchus. At the time of established diagnose 89% were inoperable.

Conclusion: Any comparison with the quality European studies shows similar results concerning the frequency. However, we do have extremely high (89%) inoperable cases at the moment of diagnosis. This may suggest either too late referral of our patients to the doctor or very long incorrect treatment mixed with other clinical conditions (exacerbation of COPD, asthma, pneumonia …) before the correct diagnosis was performed, or both alternatives.

DEVELOPMENT OF HOSPICE PALLIATIVE CARE IN THE REPUBLIC OF MACEDONIA

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Background: Republic of Macedonia is country in southeastern Europe with total population of 2 032 544 inhabitants. The life expectancy of the population is 71,15 years for male and 75,76 years for females. The number of patients older than 65 comprise 37,94% from the total morbidity. Five most common causes of death in Macedonia are (CDR on 100000 population): diseases of the circulatory system (599,4), malignant neoplasm (165,7), symptoms and undefined conditions (73,2), respiratory diseases (39,8), injuries and poisoning (37,9). Number of newly registered cases of cancer is around 6000 cases per year. Number of deaths from malignant diseases in Macedonia in year 2004 was 3194, from which 1908 were male and 1286 female. According to the place of death most of the people died at home (68%) and 32% died in health organizations. Because of these facts, the health system assumes liability for the care of the population, in order to reduce the sufferings and provide a longer, higher quality life.

Methods: Situation analysis and clinical researches for the palliative care in Macedonia in the past 11years.

Results: In 1998 the first plan for the development of palliative care was created; in the period 1998-2000 two specialized institutions for palliative care were built; in 2002 the Association for palliative care was formed; in 2003 palliative care was integrated into the Health Care System and national standards were defined; in 2004 the domiciliary palliative care program was developed; in continuity the health care services are financed by the Health Insurance Fund and opoids are free of charge.
Type of services offered in Macedonia:

Hospice Sue Ryder in Skopje for terminally ill cancer patients with capacity of 75 beds and provides care for 380 patients per year. The average time of treatment is 35 days. From the total number of patients 80% are with malignant diseases and 20% with chronic diseases. From the total number of hospice patients around 60 % died in the hospice and around 40% at home.

Hospice Sue Ryder in Bitola specialized institution for palliative care with capacity of 72 beds and provides care for 270 patients per year. The average time of treatment is 28 days. From the total number of patients 70% are with chronic progressive diseases and 30% with malignant diseases. From the total number of hospice patients 50% died at home and 50% in the hospice.

Domiciliary palliative care treats 100 patients per year with average time of treatment of 25 days. From the total mortality of the patients the malignant diseases participate with 64 % and chronic progressive diseases with 36%.

Conclusions: Next steps for the improvement of the palliative care in the R. of Macedonia: Dispersion of the domiciliary palliative care and creation of day-care hospitals for palliative care; strengthening of specialized units and services for palliative care; improvement of the standards for palliative care according to the Evidence Based Medicine; Introduction of palliative care in the educational programs of the Medical Faculty; and creation of a national council for hospice and specialist palliative care services.

USE OF STRONG OPOIDE ANALGETICS AT CANCER PATIENTS IN PALLIATIVE CARE IN THE REPUBLIC OF MACEDONIA

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Background: There are indicators in the Republic of Macedonia, which show that a great number of patients are still dying whit strong pain, without the use of strong opoid analgesics, such as morphine. This is due to the fact that there is still great number of doctors who are afraid use of morphine might make them morphine dependants from one side. From another side, there is also fear from the side effects of the strong opoid analgesics, which cause the cases where doctors prescribe non-appropriate, very low doses that causes unnecessary patient's suffering. There are not enough preparations for oral use at our market together without appropriate legislation for its use.

Objectives: Patients in the terminal stage of the malignant diseases, who are on palliative care in Sue Ryder Hospice in Skopje-capital of the Republic of Macedonia have been examined in the last five years. The Hospice was opened in 1998 and has

capacity of 75 beds which are intended for people with malignant diseases in their terminal stages.

Methods: There were total 748 patients with malignant diseases in terminal stage in Sue Ryder who were placed between the periods of 2002-2006. Most of them had breast cancer 250 (33,4%), lung cancer 156 (20,8%), colon cancer 88 (11,7%), digestive tract cancer 78(10,4%), brain cancer 55 (7,3%), prostatic cancer 49 (6,5%), maligned melanoma 11(1,4%) and other 61(8,1%). Before being placed in our institution most of the patients were treated with analgesics therapy/NSAIL, Tramadol, Codeine or tablets of Morphine Sulphate a 10 mg-short influence preparation of morphine, which is present on our market as the single oral preparation. During their stay in our Hospice they have been treated with strong opoid analgesics. 394 patients were given parenteral morphine Hydrochloride as sub coetaneous application, while others were treated with pills or ampoules Pentazocin, solution (drops) Methadone and Fentanyl (Durogesic) transdermal applications. Adjuvant preparations were used for the most of the patients(lactuloza as axant, antiemetic-Metoclopramid and Haloperidol)

Results: Sufficient analgesia was achieved at most of the patients. At 236 patients, as a result of the presence of neuropathic pain, sufficient analgesia was achieved with the addition of carbamazepin or amitryptillin. Expressed side effects were shown at small number of patients. In our country there is only short action form of oral preparation of morphine and still there are no preparations with long action and depo doses. As a result of this, the patients are forced to use paranteral form at early stage, which has an effect of their quality of life.

Conclusions: In the absence of proper legislative regulation for the use of strong opiod analgesics in home conditions, as well as non-existence of the possibility for the prescription by the family doctor in our country, there is a strong need for patients stationary treatment in hospice, which significantly increases the financial costs.

"IS THERE LIGHT IN THE FATALITY TUNNEL AFTER BRAIN METASTASES"

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Brain metastases are frequent (up to 40%) in the evolution of cancer patients. Classically, the occurrence of multiple brain metastases dramatically worsens the survival prognosis and results in shortened lifespan.

Here in this report we focus attention on a patient with desperate clinical onset of very symptomatic brain metastases of triple negative breast cancer disease. However, the patient was not subjected to systematic treatment previously. After a sequential radio/chemotherapy/RT/CT/ setting with 30 Gy WBRT and CT by an adapted CMF + BCNU protocol, the patient responded positively by achieving a long clinical stability with good quality of everyday functioning. The image analyses performed by serial CT scans showed partial response, confirming the observed clinical improvement of the patient.

Therefore an initial careful assessment of the clinical condition of patients presenting with aggressive brain metastasis disease is required for the best treatment outcome. Our mission is to strive even for patients in the most hopeless condition of their disease to achieve a satisfactory longevity.

AGGRESSIVE SURGICAL APPROACH TO BENIGN AND MALIGNANT LIVER TUMORS – IS IT CONSIDERED TO BE THE APPROPRIATE ONE

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Background: Benign liver tumors (BLT) consist of a broad spectrum of regenerative or true neoplastic processes. The most appropriate approach in theses cases is still disputable. Malignant liver tumors (MLT) are mainly secondary and less often primary. In patients with colorectal metastases surgical removal of a solitary of multiple metastases is the "gold standard". The other types of metastases and cholangiocellular cancer even being "radically removed" are connected with poor prognosis since the recurrence rate is very high. That's why different cases of BLT and MLT need an individual approach based on many characteristics.

Aim: Study on the clinical and diagnostic aspects of the cases of BLT and MLT that were operated at the authors' institution as well as analysis of the early and late postoperative results.

Material and methods: A total of 213 surgical procedures on the liver and portal venous system were performed at the First Surgical Clinic, Tokuda Hospital Sofia from 1st, Jan, 2007 till 31st, May, 2010. Liver tumors were the indication for surgery in 164 cases (76.99%). BLT were detected in 12 cases (7.31%) and 5 of them were "incidentalomas" while the other 7 were symptomatic. The ratio of secondary/primary MLT in our series was 7.44/1 (134 cases of metastatic liver disease and 18 hepato- and cholangiocellular carcinomas). All the 12 patients with BLT and 91 patients with malignancies (51.92%) received a radical procedure. Palliations, i.e. just tumor biopsies or citoreductive resections were done in the following cases: (a) palliative gastrectomy, colectomy or a by-pass operation in metastatic gastric or colorectal or pancreatic cancer where the indication for surgery was the primary tumor; (b) neuroendocrine tumors of the pancreas and GIST; (c) multiple small (less than 2mm) hepatic lesions were accidentally found at exploration. General statistical, clinical, laboratory and instrumental data as well as many surgical details and characteristic were analyzed retrospectively.

Results: Mortality rate was 1.82% (2 cases of acute liver failure and 1 case of hepato-renal syndrome). Morbidity rate included totally 12 specific early complications (7.32%). Massive bleeding necessitated re-operation in 3 patients, while bile leakage from the resection surface needed just 1 celiotomy out of 6 cases. The rest 5 ones received endoscopic papillotomy. The pathological specimen and staging contributed to precise the adjuvant therapy in cases where necessary. The 3-, 2- and 1-year follow-up included 23 (14.02%), 59 (35.97%) and 113 (68.90%) patients respectively. Thirty one patients (18.90%) received operation in the recent one year and 20 patients

(12.19%) were lost for follow-up. Survival rates varied a lot and depended on the essence of the disease and the type of the procedure.

Conclusions: Liver tumors are presented by a great variety of pathological identities and they require an individual approach. However surgical removal of the tumor when possible remains the "gold standard" in almost all the cases.

RISK FACTORS FOR MORBIDITY AND MORTALITY RATES IN PANCREATIC ONCOLOGICAL SURGERY

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Background: Pancreatic resectional surgery is still one of the most challenging fields in oncology. The "benefit to risk" balance doesn't always advocate an aggressive approach. Many factors contribute to this statement, namely: (a) advanced stage disease at the time of establishing the diagnosis which limits the percentage of radical surgery; (b) high rate of postoperative complications, some of them indicating re-operation and prolonged hospital stay; (c) poor long-term prognosis due to low survival rates.

Aim: To study some certain characteristics of cases of pancreatic resections and to analyze the role of possible risk factors which might be responsible for specific early postoperative morbidity.

Material and methods: A total of 159 consecutive pancreatic operations were performed at the authors' institution from Jan., 2007 till Aug., 2010. Benign and malignant tumors indicated surgery in 122 cases. Whipple's or modified procedures and left hemipancreatectomies were received by 32 and 23 patients respectively. The rest 67 of them received palliations. Recently we introduced in our practice a modified Whipple's duodenopancreatectomy with a triple derivation of pancreatic, biliary and gastric passage in order to avoid serous consequences of an eventual pancreatic leakage which is the most common specific complication. Data about (1) histopathology and stage of cancer; (2) type of procedure; (3) skin-to-skin operative time and (4) quantity of operative blood loss were collected. Patients were divided in 2 groups according to each of these criteria and the early postoperative results in different groups were compared. Statistical analysis was done and values of $p<0.05$ were considered significant.

Results: There were no fatal outcomes (mortality rate was 0%) while the early postoperative morbidity rate was relatively high - 40.16% (28 specific and 21 non-specific complications). Acute pancreatitis and pancreatic leakage were seen in 7 cases (12.73%). Two patients were re-operated. The median postoperative hospital stay was 10.2 days for radical procedures and 8.6 days for the palliative ones.

Conclusions: 1/ There was no significant difference concerning the early postoperative morbidity rate between patients with radical and palliative procedures. Patients with multiple organ resections and multiple anastomoses showed the same complication rate as patients with palliations. Most probably this is due to the fact that palliations were received by patients with an advanced cancer and/or with serious

concomitant diseases; 2/ The skin-to-skin operative time didn't influence the early postoperative morbidity rate; 3/ The intraoperative blood loss necessitating substitution with 2 or more units of blood proved to be associated with higher morbidity rate; 4/ The modified Whipple's duodenohemipancreatectomy with a triple derivation of pancreatic, biliary and gastric passage showed lower rate of pancreatic leakage than the standard procedure.

MEDICAL AND SOCIAL PROBLEMS IN TREATMENT AND DIAGNOSIS OF THE PROSTATE CARCINOMA

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Target: Presentation of diagnostic and treatment algorithm of prostate cancer

Materials: Diagnostic algorithm, Methods of conservative and radical treatment

Key words: prostate carcinoma, PSA, brachyterapy, radical prostatectomy

Discussion: The prostate carcinoma is the second common malignacy desease after pulmonary carcinoma among men. According to the diagnosis, the prostate gland carcinoma is unique, because it is the only neoplasy with organ-specific tumor mark – PSA.

Full diagnostic investigations – PSA, digital rectal examination, transrectal ultrasound, Tru-cut biopsy, CT pelvis scan, bone scan are imposible even at the begining because of the low funds provided.

1. Prostate gland carcinoma is probably the only one which, when found in early stage, could be treated radically. Clinically important are the brachyterapy and the radical prostatectomy.

The bulgarian society is suffering of the absense of brachyterapy. Radical prostatectomy is performed in a few medical centers in Bulgaria and remains suffering from insuficiant funding from the current healthcare system.

Conclusions: The absence of clearly set social and medical strategies regarding this social important disease and the following low-funding lead to an impact over the two main algorithms – diagnostic and treatment of the prostate gland carcinoma.

EXTRAMEDULLARY PRESENTATION OF MULTIPLE MYELOMA – CLINICAL COURSE, DIAGNOSIS, TREATMENT

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Introduction: Myeloma is a clonal plasma cell proliferation that can have different clinical manifestations. Presence of infiltrates in an extramedullary site can be a representation of multiple myeloma (MM) or solitary extramedullary plasmacytoma (EMP). The most frequent thoracic involvement by MM is bone involvement or

pulmonary infiltrate secondary to an infectious process. Primary plasmacytoma of the lung is exceedingly rare. Sometimes, the diagnosis of MM, which is a disorder of the aged population, is difficult because of its untypical clinical course and heterogeneous symptoms.

Method: We present an unusual case of multiple myeloma with extramedullary involvement of the bronchial mucosa as first evidence of the disease. A 68-year-old smoker male patient with bronchopulmonal symptoms was admitted for a clinical assessment. Routine laboratory exams showed anaemia, leukocytosis, thrombocytopenia, high creatinine level (284 umol/l), hypoproteinemia (51 g/l). Chest X-ray and CT revealed peribronchial infiltrates in the left lower lobe with atelectasis. Chest X-ray follow-up detected large bilateral-sided pleural effusions. An echocardiography showed pulmonal hypertension. The bronchoscopy revealed endobronchial lesions in the main right bronchus and in the left lower lobar bronchus. A transbronchial lung biopsy was done and the pathologic examination of the specimen demonstrated diffuse subepithelial plasmacytoid cell proliferation. A cytology examination of pleural fluid confirmed atypical plasma cells. According to the above findings the diagnosis of plasmacytoma was confirmed and additional prompt investigation to rule out multiple myeloma was undertaken. Bone marrow examination demonstrated 70% plasma cell infiltration. Some complex cytogenetic findings were detected. Serum and urine electrophoresis revealed M component and immunofixation found Bence-Jones kappa monoclonal protein (7,06 g/l). Bone survey revealed no abnormality. Beta-2 microglobulin was 38,51 mg/l. The patient was staged IIIB in the Durie-Salmon staging system and staged III in the International staging system (ISS).

Results: The patient was treated with VAD regimen which led to partly resolution of the pleural effusions but progression of the renal failure was observed. The advanced stage of the disease defined a bad prognosis. After three cycles VAD, patient was referred for treatment with Bortezomib.

Conclusions: Pulmonary involvement of MM is frequently associated with advanced, treatment-refractory disease or rapid progression and demonstrates the variability of X-ray manifestations. MM should be taken into consideration in the differential diagnosis of pulmonary infiltration in patients with systemic complaints. Differential diagnosis with other pulmonal cancers must be established to ensure the correct histological examination and proper therapy.

OBESITY, DIABETES MELLITUS TYPE 2, METABOLIC SYNDROME

КОРЕЛАЦИОННИ ПРОУЧВАНИЯ НА ПОСТПРАНДИАЛНИТЕ ГЛИКЕМИЧНИ ВЪРХОВЕ ПРЕДИ И СЛЕД ЛЕЧЕНИЕ С ROSAGLITAZONE

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Въведение: Постпрандиалната хипергликемия е едно от най-рано установимите нарушения при захарен диабет тип 2. Тя зависи от бързия прандиален инсулинов отговор, има решаващо участие в микро- и макроваскуларните увреждания и обуславя високия леталитет от сърдечно-съдови усложнения при това социално значимо заболяване.

Цел на проучването е да се проследи влиянието на Rosaglitazone върху постпрандиалната гликемия.

Пациенти и изследвания: При 32 болни от захарен диабет тип 2, на възраст 45 – 60 години, е проведено двуетапно лечение с Glipizide 3 пъти по 5mg и Rosaglitazone 2 пъти по 4 mg дневно. Изследвани показатели: кръвна захар на гладно и постпрандиално, гликиран хемоглобин (HbA_{1c}), серумни липиди, трансаминази, серумен креатинин, имунореактивен инсулин, артериално налягане, HOMA-индекс, индекс на телесна маса. Период на монотерапия с Glipizide – 45 дни, а в комбинация с Rosaglitazone – 95 дни.

Резултати: Средните стойности на показателите през първия период са следните: гликемия на гладно 7,9±1,2 mmol/l; постпрандиална гликемия 12,2±0,9 mmol/l; HbA_{1c} 8,7±0,6%. Високите стойности на последните два показателя са мотив за добавяне на Rosaglitazone към лечението. След тримесечен терапевтичен курс гликемията на гладно търпи несигнификантна промяна - 7,7±0,9 mmol/l. Статистически значимо се понижава постпрандиалната кръвна захар (до приемливите стойности 8,9±0,5 mmol/l), HbA_{1c} (7,6±0,1%; $p<0,001$) и HOMA-индекс ($p<0,05$).

Заключение: Rosaglitazone повлиява и двата ключови фактора, стоящи в основата на захарен диабет тип 2 – инсулинова резистентност и бета-клетъчна дисфункция. Повлиява се благоприятно постпрандиалната гликемия, което допринася за намаление на сърдечно-съдовия риск при това социално значимо заболяване.

ЛЕЧЕНИЕ НА ЗАХАРЕН ДИАБЕТ ТИП 2 С АЛФА-ГЛЮКОЗИДАЗНИЯ ИНХИБИТОР ACARBOSE

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Въведение: Захарен диабет тип 2 дълго време протича с повишена предимно постпрандиална гликемия поради нарушена ранна фаза на инсулиновата секреция. Тези отклонения са налице няколко години преди

диагностицирането на заболяването и са в тясна патогенетична връзка с васкуларните увреждания и високата сърдечно-съдова смъртност.

Целта на проучването е да се проследи терапевтичният ефект на алфа-глюкозидазния инхибитор Acarbose в изявата и развитието на втори тип захарен диабет.

Пациенти и изследвания: Обхванати са 67 болни, разпределени в 4 групи – нарушен глюкозен толеранс, новооткрит захарен диабет тип 2, комбинация на Acarbose със сулфанилуреен препарат и комбинация с инсулин. В продължение на 4 месеца пациентите приемат Acarbose 3x100 mg дневно. Проследени са следните показатели: кръвна захар на гладно и 2 часа след нахранване, гликиран хемоглобин (HbA_{1c}), имунореактивен инсулин, серумни липиди – общ холестерол, HDL-холестерол, триглицериди, кръвна картина, трансаминази, серумен креатинин, индекс на телесна маса.

Резултати: При всички пациенти се наблюдава статистически достоверно редуциране на постпрандиалната кръвна захар. В първите три групи е налице съществено понижаване и на кръвната захар на гладно, като това е най-изразено в групата с монотерапия и комбинация със сулфанилуреен препарат (респ. 12,4±1,8 / 7,7±0,8 mmol/l; 11,2±1,3 / 7,9±0,7 mmol/l). В резултат от проведеното лечение се наблюдава нормализиране на глюкозния толеранс при 9% от лицата в първата група. Статистически значимо е подобрен HbA_{1c} и в трите диабетни групи ($p<0,05$). Налице е съществено редуциране на инсулинемията в първа, втора и трета група. Пациентите на инсулиново лечение отбелязват по-леки и по-редки хипогликемии. Индексът на телесна маса също бележи тенденция към подобрение, но данните са статистически недостоверни.

Заключение: При нарушен глюкозен толеранс алфа-глюкозидазният инхибитор Acarbose забавя значително прогреса към изявен захарен диабет и намалява постпрандиалната хипергликемия. При комбинирана терапия със сулфанилуреен препарат Acarbose съхранява остатъчната инсулинова секреция и препятства неоправданото ранно стартиране на инсулиново лечение, а с това и последвалото хиперинсулинизиране на болните. Алфа-глюкозидазният инхибитор Acarbose е надеждна и оправдана алтернатива както в превенцията, така и в терапията на захарен диабет тип 2.

НАДНОРМЕНОТО ТЕГЛО И ЗАТЛЪСТЯВАНЕТО В УЧЕНИЧЕСКА ВЪЗРАСТ - РИСКОВ ФАКТОР ЗА АРТЕРИАЛНА ХИПЕРТОНИЯ

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Въведение: Честотата на наднорменото тегло и затлъстяването сред българските деца нараства през последните 20 години. Епидемиологични проучвания разкриват взаимовръзката между небалансираното хранене, наднорменото тегло у подрастващи и редица заболявания с висок

кардиоваскуларен риск – артериална хипертония, захарен диабет тип 2, метаболитен синдром.

Цел: Да проучим честотата на наднорменото телесно тегло и затлъстяването сред ученици и да анализираме риска от артериална хипертония при тях.

Пациенти и изследвания: Обхванати са 434 ученика (197 момчета и 237 момичета) на възраст 8 - 15 г, живеещи в градска зона и 406 ученика (188 момчета и 218 момичета) на същата възраст, живеещи в селски район. Определен е индекс на телесна маса, а за класификация на наднорменото тегло са използвани критериите на Cole и сътр. (2000г.). Артериалното налягане е измерено и съпоставено с референтните стойности за съответната възраст.

Реултати: 20,2% от децата в градски район и 17,4% от живеещите в селски район имат наднормено тегло и затлъстяване. Артериалното налягане е по-високо от референтните стойности в 10,2% от градската и в 8,5% от селската група. Установява се артериална хипертония в 41,2% от градските деца с наднормено тегло и затлъстяване [релативен риск 6,216 (95% CI 4,716-8,192), P<0,0001 със сигнификантна позитивна корелация (r= +0,52)] и в 28,4% от населяващите селска зона с наднормено тегло и затлъстяване [релативен риск 6,641 (95%CI 3,596-12,264), P<0,0001 с умерена позитивна корелация (r= +0,37)].

Заключение: Съществува голям сърдечно-съдов риск за децата с наднормено тегло и затлъстяване, живеещи както в градски така и в селски район. Този алармиращ факт налага стартиране на профилактични програми за рисковите групи. Необходимо е разработване и внедряване на адекватна и специфична обучителна програма за здравословни хранителни навици и физическа активност с оглед редуциране на здравния риск за учениците.

RENAL REPLACEMENT THERAPY IN DEVELOPING COUNTRIES IN ECONOMICAL CRISIS CONDITION - WHAT STRATEGY SHOULD BE ADOPTED?

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Background: It's essential to manage patients with End Stage Renal Disease (ESRD), especially those originating from hypertensive and diabetic nephropathy since they greatly contribute to an increased number of patients on Renal Replacement Therapy (RRT) and related cost of the treatment. Various measures could be undertaken in order to adopt the best available management strategy (different proportions of RRT, home hemodilaysis, everyday dialysis, increasing number of kidney transplantations, preventive fistulas creation and including as many as possible procedures on outpatient basis. Hence, ESRD patients starting HD should have matured AVF, being at no hospitalisation needs, and risk of infections and bleeding.

Methods: We reviewed the Medline reports on RRT in developing countries and those recently admitted in EU and NATO (Romania, Poland, Albania, Baltic countries), as well as a few developed countries (Canada, Australia and New Zeeland). We considered their strategies for health care organisation in 1990s comparing to ours

within the current economic crisis in our country. We also try to find possibilities for improvement of the health care system, in order to escape from the bad experience and detrimentally reduced possibilities for RRT treatment in 1990s.

Results: There are a lot of foreign experiences to help countries in poor economic and health-care condition as Macedonia is. In the last 2 decades RRT in our country is organised through 20 HD centers with approximately 1300 prevalent patients, PD 25 patients, and about 180 transplanted patients (mostly living related, 12-20 per year along with up to 10 paid commercial Tx patients/yearly). Based on the former bad experience (in 1990s) from Romania (only 1/3 of patients with a need for RRT were treated and the rest were put only on a supportive conservative treatment); Poland (diabetics and patients over 60-65 years of age were not put on RRT); Albania, 4 million patients country with only 14 patients on dialysis; we should seriously consider more appropriate treatment options in order to prevent the collapse of medicare system in this particular world economic crisis. In contrast, the proportion of RRT in Baltic countries [Hemodialysis (HD) 18%; Peritoneal dialysis (PD) 25% and Transplantation (Tx) 57%] may be an example for managing the RRT subjects in the Balkans. Additionally, we could follow a positive example of Canada and Australia-New Zeeland experience with 20, 30 and 50% of home HD sessions, respectively. Another option we should seriously consider is the cost-efficient everyday dialysis with a reduction in erythropoietin, antihypertensives and phosphate binders. Finally, it seems that the most important issue is to increase the Tx patient population, because of the reduced cost of treatment after the first year postransplant, and their family and Society resocialisation with an incomparable improved quality of life. Vascular accesses for dialysis should be prepared by nephrologists and golden standard should be arterio-venous fistula (AVF) in more than 90%. Thus, the number of patients with placed central catheters should not exceed 5-10%, meaning a reduced morbidity and hospitalisation costs as well as the mortality. A majority of procedures associated with RRT should be performed on an outpatient basis. A preventive AVF creation should be at least around 50% (a few months in advance of the beginning of HD program, and/or at glomerular filtration rate of 15-20 ml/min).

Conclusion: We should seriously consider more appropriate health care strategy for treatment of RRT patients in order to prevent the collapse of medicare system in this particular global economic crisis.

SYMPATHICOMIMETIC COMPOUNDS AND STIMULANTS IN FOOD SUPPLEMENTS – CLAIMS AND SAFETY ASSESSMENT

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Background: A large number of active compounds with different structure, origin and physiological activity determine the diversity in composition and the widespread use of food supplements in programs for weight reduction. Among them sympathicomimetics and stimulants are broadly included and used due to their effects on body composition, physical performance and psychological status.

Aims and Methods:. The aim of the present study is to assess the claims, the safety and interactions of proclaimed food supplements, containing sympathicomimetics and stimulants according to Bulgarian regulatory requirements on the basis of current scientific information and label's information of 46 food supplements, available in the Bulgarian market. In addition analysis possible interactions with drugs, foodstuffs and food supplements, rational ingredient combinations and the optimum conditions for the administration on the basis of described references were also within the scope of this study.

Results, Conclusion: 46 sympathicomimetics and stimulants-containing food supplements, available on Bulgarian market, are covered and assessment of claims and safety were evaluated. The reviewed food supplements are popular among users due to their potential to optimize body composition, to improve physical performance and psychostimulating activity. The present article confirms the statement that only after estimation of individual health status and needs the application of weight-loss food supplements could bring long-term health benefits. Besides their benefits, there is a serious risk for the health of users when the administration of food supplements is not controlled or correct especially for those containing sympathicomimetic compounds and stimulants. It is very necessarily that physicians and pharmacists obtain up-to-date information for permissible claims and safety of food supplements. Finally, the users should also inform their general practitioner or pharmacist in case they administer such supplements.

OBESITY IN CHILDHOOD AND ADOLESCENCE

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Introduction: Obesity is a pandemic problem. It is estimated that as many as 250 million people (7% of the estimated current world population) are obese. Two- to three-times more people than this are probably overweight. Some estimates suggest that the management of obesity in the USA costs approximately $100 billion yearly.
21-24% of American children and adolescents are overweight and another 16-18% are obese. The prevalence of obesity worldwide is increasing. The prevalence of overweight children and adolescents in the United States has increased by 50-60% in a single generation, the prevalence of obesity has doubled (1, 2, 3). The prevalence of obesity in American Indians, Hispanics, Hawaiians, Hispanics, and blacks is 10-40% higher than in whites. In addition, countries such as Japan, Australia, New Zealand, Malaysia, Middle Eastern countries of Bahrain, Saudi Arabia, Egypt, Tunisia, Jordan, and Lebanon and China report an epidemic of obesity in the past 2-3 decades (4). The prevalence of obesity is high in Macedonia, too. (5)

Criteria: World Health Organization (WHO) criteria for obesity in childhood and adolescence are based on BMI: BMIs greater than the 85th (overweight) or the 95th (obesity) percentile, for age-matched and sex-matched control subjects. Overweight, obese, and morbidly obese refer to children and adolescents whose weights exceed those expected for heights by 20%, 50%, and 80-100%, respectively.

In adults, grade 1 overweight (overweight) is a BMI of 25-29.9 kg/m^2. Grade 2 overweight (obesity) is a BMI of 30-39.9 kg/m^2 and grade 3 overweight (severe or morbid obesity) is a BMI greater than or equal to 40 kg/m^2. The surgical definitions describe BMI greater than 40 kg/m^2 as severe obesity, a BMI of 40-50 kg/m^2 is termed morbid obesity, and a BMI greater than 50 kg/m^2 is termed super obese.

Pathophysiology: Obesity is the result of energy imbalance which can result from excessive energy intake and/or reduced energy expenditure (sedentary lifestyle). Most overweight children have a familial form of obesity. Nevertheless, excess weight in obese children depends on both genetic and environmental factors. Concordance rates for obesity and type 2 diabetes mellitus are higher in monozygotic twins than in dizygotic twins.

Causes include *hormonal disorders* (growth hormone deficiency and growth hormone resistance, hypothyroidism, leptin deficiency or resistance to leptin action, glucocorticoid excess (Cushing syndrome), prolactin-secreting tumors), precocious puberty, polycystic ovary syndrome (PCOS); *medications* [glucocorticoids, sulfonylureas, tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs: e.g phenelzine), oral contraceptives, insulin, risperidone, thiazolidinediones, clozapine] and *genetic syndromes* (Bardet-Biedl syndrome, Prader-Willi syndrome, pseudohypoparathyroidism, Cohen syndrome, Down syndrome, Turner syndrome, POMC splicing mutation, prohormone convertase-1 Deficiency, melanocortin-3 receptor mutation (6), melanocortin-4 receptor mutation (7), SIM-1 mutation (SIM1- "single-minded").

Recent advances in the genetic causes. Leptin (from the Greek word *leptos,* meaning thin). Leptin is a 16-kD protein produced in white adipose tissue and, to a lesser extent, in the placenta, skeletal muscle, and stomach fundus in rats. Leptin has functions in carbohydrate, bone, reproductive metabolism and in body weight regulation. Leptin signals satiety to the hypothalamus. Most humans who are obese are not leptin deficient but rather leptin resistant, and have elevated circulating levels of leptin (8).

About 10 patients of Pakistani and Turkish consanguineous descent have been described with hyperphagia from birth, and early obesity (6 months)(9). The thyroid hormone levels are reduced, there was a lack of sympathetic tone, lack of pubertal progression. In addition the immunity was defective. Patients are short and lack the pubertal growth spurt. Impressively, treatment with recombinant leptin restores leptin signaling, and results in reduction of hyperphagia, resolution of obesity, induction of puberty, and restoration of immune regulation (10).

Leptin Receptor Deficiency patients are similar to those with leptin deficiency. However, they might have growth retardation, low IGF-1 and IGFBP-3 levels and low thyroid levels.

Proopiomelanocortin (POMC) and alpha–melanocyte-stimulating hormone (alpha-MSH) act centrally on the melanocortin receptor 4 (MC 4) to reduce dietary intake. Patients with POMC mutations tend to have red hair, and central adrenal insufficiency (11). Strikingly, as many as 5% of children who are obese have MC4 or POMC mutations.

In prohormone convertase deficiency, patients have clinically significant obesity, hypogonadotropic hypogonadism, and central adrenal insufficiency (12).

PPAR-gamma. Patients with mutations of the receptor (at band 3p25) described so far have severe obesity.

Melanocortin-4 Receptor Mutation. Mutations in the MC4R appear to account for up to 5% of morbid obesity in childhood. This mutation is transmitted as a co-dominant inheritance.

Melanocortin-3 Receptor Mutation. As in MC4R diagnosis can only be made by gene sequencing.

FTO ("fat mass and obesity associated" gene), *FTO* expression is high in regions of the hypothalamus involved in energy balance and its expression levels are regulated by variations in food intake (13). In humans, a genome-wide association study involving nearly 39,000 people found that people with 2 copies of an *FTO* variant weighed an average of 3 kg more than did people with no copies of that variant. Individuals with 2 copies of the variant were 67% more likely to be obese than people without the variant (14).

Nevertheless, individuals with these FTO variants can, with increased physical activity, "offset the genetic predisposition to obesity associated with the FTO polymorphism (15)."

Genome-wide linkage analyses and microarray technology have revealed a rapidly growing list of potential **susceptibility obesity genes**: chromosome arms 2p, 10p, 5p, 11q, and 20q.

Other causes. *It has also been suggested that inflammatory* and infective etiology may exist for obesity. Namely, adenovirus 36 infection is associated with obesity in chickens and mice. Humans who are not obese have a 5% prevalence of adenovirus 36 infection, while humans who are obese have a prevalence of 20-30%.

Co-morbidities and complications. Obesity has a considerable impact on quality of life, and some reduce life expectancy. Co-morbidities and complications are severe:

1. Cardiovascular: essential hypertension, coronary artery disease, left ventricular hypertrophy, cor pulmonale, cardiomyopathy, accelerated atherosclerosis, pulmonary hypertension.
2. CNS: stroke, idiopathic intracranial hypertension, meralgia paresthetica.
3. GI: cholecystitis, cholelithiasis, steatohepatitis, fatty liver infiltration, reflux esophagitis.
4. Respiratory: obstructive sleep apnea, Pickwickian syndrome), increased predisposition to respiratory infections, increased incidence of bronchial asthma.
5. Malignant: association with endometrial, prostate, gall bladder, breast, colon, lung cancer.
6. Psychologic: social isolation, peer problems, depression.
7. Orthopedic: osteoarthritis, coxa vera, slipped capital femoral epiphyses, Blount disease and Legg-Calvé-Perthes disease, lumbago.
8. Metabolic: insulin resistance, hyperinsulinemia, type 2 diabetes mellitus, dyslipidemia.
9. Reproductive: anovulation, early puberty, infertility, hyperandrogenism and polycystic ovaries in women, hypogonadotropic hypogonadism in men.

10. Obstetric and perinatal: pregnancy-related hypertension, fetal macrosomia, pelvic dystocia.
11. Surgical: increased surgical risk and postoperative complications.
12. Miscellaneous: reduced mobility, difficulty maintaining personal hygiene, Stress incontinence, Intertrigo (bacterial and/or fungal), acanthosis nigricans, hirsutism, increased risk for cellulitis and carbuncles, Venous varicosities, lower extremity venous and/or lymphatic edema

Treatment. Long-term diet, exercise, family support, team approach to therapy (nurse educators, nutritionists, exercise physiologists, and counselors) are the basis for treatment. Family therapy may be highly beneficial.

Exercise and physical activity: Controlled trials have demonstrated that lifestyle exercise programs, in association with dietary restrictions, provide long-term weight control in children and adolescents.

Nutritional counseling, especially the reduced fat diet: reductions in total and saturated fat may be particularly useful in adolescents who consume large quantities of high fat, snack, and packaged fast foods.

Very controlled–energy diets have high dropout rates and in adolescent growth and development, subsequent reproductive function, musculoskeletal development, and intermediary metabolism can be affected. The very controlled–energy diets cannot be recommended for the vast majority of children and adolescents with obesity.

Medication. Some medicaments have been also used as adjunct interventions. Sibutramine (Meridia),[9,10] a selective serotonin norepinephrine reuptake inhibitor, and orlistat (Alli, Xenical), a pancreatic lipase inhibitor are approved for use. Sibutramine may be classified as an anorectic drug, whereas orlistat's mechanism of action involves induction of lipid maldigestion. Benzphetamine (Didrex), diethylpropion, phendimetrazine (Bontril), and phentermine (Ionamin) have also been used.

The serotoninergic drugs fenfluramine and dexfenfluramine, were recently withdrawn because of their association with valvular heart disease and primary pulmonary hypertension.

Pediatric experience with the use of weight loss drugs has conflicting results (reduction and failure to reduce fat). Guidelines for the prevention and treatment of childhood obesity have been released.

Surgical Care. Various bariatric surgical procedures have been used in adults and some adolescents (in most centers, patients >15 y) with a BMI of more than 40 or weight exceeding 100% of ideal body weight (IBW).

In the vertical-banded gastroplasty (VBG), a pouch of 15-mL to 30-mL capacity is constructed, greatly reducing the amount of food that can be eaten at any time. In the gastric bypass, a larger pouch that empties into the jejunum is created. Laparoscopic placement of an adjustable gastric band (LAGB) has supplanted the VBG because of its relative safety and because of its reversibility. LAGB places a collar with an internal, saline-filled balloon around the upper stomach, 1-2 cm below the esophagogastric junction.

URINARY TRACT INFFECTIONS IN PATIENTS OVER 65 ASSOCIATED WITH DIABETES MELLITUS TYPE 2

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Background: The aim of our study was to confirm the involvement and the characteristics of the lower tract infections (LTI), in patients with Diabetes mellitus type 2 aged over 65 years.

Methods: Patients with clinical features of LTI (dysuria, alguria, suprapubic pain) and patients with asymptomatic bacteriuria were examined through microorganisms findings in the urinary sediment, and microbiological analysis (positive urine culture), i.e. significant bacteriuria.

Results: At distribution according to gender the female patients dominated (17 female, 3 male). According to the type of bacteriuria 12 patients were found with symptomatic bacteriuria and 8 with asymptomatic bacteriuria. A satisfactory glycoregulation was achieved in 13 patients, while it could not be controlled in 7 patients, 12 patients out of the total number were on oral hypoglycemic therapy, 5 were on a special dietary recommendation, and 3 on insulin therapy. The most frequent microorganism was E. Colli in 10 patiens, followed by Proteus mirabilis in 6 patiens. Enterobacter aerogenes was presend in 4 patiens.

Conclusion: Urinary infections are frequent finding in patiens with Diabetes mellitus. Those are more frequent in women (possibly associated with hormonal deficit). An excellent glucoregylation may be associated with a reduction of the infection rate, but it doesn't influence the effect of the therapy. The frequent testing of the urine and therapy according to the antibiogram were decisive in the treatment of the infections.

OUTCOME FROM THERAPY OF THE DIABETIC FOOT INFECTIONS

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Background: One of the most important chronic complications of diabetes is diabetic foot, which comprises a heterogeneous group of pathologic conditions such as somatic and autonomic neuropathy, diabetic micro and macroangiopathy, structural changes and bone lesions, plantar ulcerations and skin infections. The aim of our study was to evaluate the outcome from antibiotic, surgical and combined antibiotic and surgical therapy of the diabetic foot infections.

Methods: Examinations where performed in 90 patients with confirmed presence of diabetic foot infections. Patients were treated at the Clinic of endocrinology

and at the Surgery Clinic, Clinical Center in Skopje. According the type of infection, collection of specimens for microbiological analysis was performed as follows: dry or wet swab from infected tissue; aspiration of pus and biopsy of necrotic tissue. Microbiological analysis of specimens was performed at the Institute of Microbiology and Parasitology in Skopje, Macedonia. For isolation and identification of aerobic and anaerobic bacteria and fungi, standard microbiological methods were used. All isolated pathogen microorganisms were tested on 8 to 12 antimicrobial medicaments with disk diffusion method. All patients received therapy according to the antibiogram.

Results: Fifty two patients (57,7%) were treated with both antibiotic and surgical therapy and all patients were with improved outcome. From these 52 patients, 19 (36,6%) patients were treated with partial surgical interventions (debridman and wound treatment), while 33 (63,4%) patients were treated with total surgical intervention (amputation).From total of 90 patients, 38 (42,3%) patients were treated with antibiotic therapy only, from which 27 were with improved outcome, while 11 patients were with lethal outcome. After complete therapy of diabetic foot infections, a recidive of infection occurred in 11 (12,2%) patients, all with diabetes type 2.

Conclusions: A combined therapy (antibiotic and surgical) of diabetic foot infection is more reliable than single antibiotic therapy. When surgical treatment is indicated, total surgical intervention (amputation) could be a better choice than the partial surgical approach. The appearance of recidive of infection should be expected in about 10% patients, especially in patients with diabetes type 2.

OBESITY AND HYPERTENSION – MAIN HEALTH RISK FACTORS IN THE POPULATION IN THE GEVGELIJA REGION

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Background: The aim of our study was to present the results on the preventive health examinations of the adult population in the Gevgelija Health region showing the representation of the main health risk factors.

Methods: The data and material are derived from the individual evident sheet from the performed preventive health examination of the adult population in the Health region of Gevgelija in the year 2009. The method used is statistical-epidemiological method of work.

Results: During the medical examination, a total of 991 persons were examinated which represents 2.82% of the population in this region. According to the place of residence 456 (46,92%) are from the city, and 526 (53,08%) are from the surrounding villages. During the examinations, blood pressure above 140/95 mm Hg. Was found in 314 (31,91%) subjects. In the city population the percentage was 39.35%, while in the rural population 25.19%.

According to body mass index (BMI) , only 34% of the examined people had normal nutrition. Thirty eight percent of the examined subjects were overweighted, 18,8% were Obese Class I , 6,8% were Obese Class II, while 2.4% were Obese Class

III. In addition, 7,31% of the examined subjects had over 7 mmol/L blood sugar, and 33,63% had over 5.8 mmol/l cholesterol in blood.

Conclusion: It is necessary to create and implement a National Strategy for prevention and control of non-community diseases in R. Macedonia, and to implement that strategy on a local level as well.

"THINKING BIG "ON DIABETES WITHIN RECENT HEALTH SYSTEM REFORMS AND DIABETES HOUSE "AS CONCEPT

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Diabetes presents a major health and social problem in the world due to his unstoppable pandemic, increasing financial and social burden related to the late complications, disability and early death

Despite significant progress made during last decades in terms of reductions of diabetes harmful effects to individuals and to societies unfortunately globally speaking the diabetes management result to be almost a failure. Diabetes still in now days remains the leading cause of new blindness, leading cause of kidney failure, the most common cause of leg amputations, Diabetes is one of more frequent causes of Myocardial Infarction and Stroke which occur 2-4 time more often than in non diabetes populations. Diabetes is responsible for more than 10 % malformations and 3-5 % fetal mortality during pregnancy.

They are several causes why diabetes management results to be no as successful as expected. One of them is the way how is approached by health professionals, patients and society.

Unfortunately Diabetes often is used to be approached as an isolated health problem .Its management and control are focused on biochemical findings mainly on glycemic level. "In clinical practice diabetes management is considered usually a separate "box "not interlinked with management of other chronic diseases and not enough interconnected with the health system components

The WHO /Euro diabetes program based on the St Vincent declaration (1989) has created for the first time a multi partnership model toward quality development in diabetes care aiming to improve current situation within five years by reaching five common measurable targets: in terms of new Blindness reduction by 30% , the End stage kidney failure reduction by 30 % , Diabetes related leg amputations by 50 % , the major CVD accidents by 30 % and diabetes pregnancy outcomes equalized those of pregnant women without diabetes. This model was meant to be spread out and implemented afterward in others NCD quality development programs as well and hopefully as instrument to improve quality of health systems. in whole

In fact the St Vincent Diabetes program during ten years of implementation has proven that improvements in specific issues of diabetes care at the level of isolated clinics or individual "champions" have been possible. However the program failed to be successful and sustainable at the countries health system level. At countries national health care policies the St Vincent Diabetes Program failed to be disseminated and

implemented in other chronic disease programs nor to be interlinked as expected in the Health systems context.

Meanwhile Health systems are undergoing a very dynamic process of changes and intensive reforming aiming to adapt themselves with new increasing demands from patients and societies. Some of factors and directions of health system changes are the following: globalization, aging of population, need for more value for money, patients as smart as doctors, increasing importance of self care, new information technology, integrated care, team based care continues care, patient rights, and roles public accountability on outcomes of care, clinical guidelines of best practice more focused on evidence, Evidence based policies on financing , purchasing and clinical decisions ,quality standards of care , performance indicators ,of health organizations, their accreditation and ,new financing and payment systems. The relevant changes on Medical professionalism are ongoing in parallel also: by involving more actively doctors in management issues and by implementing new mechanisms for continues professional development as Licensing, and Certification .Management of diabetes care must follow these innovative processes by interconnecting and integrating within health systems reforms .

In this context , "Thinking Big "on diabetes become a necessity which means a System thinking approach in terms of recognition that we all work in complex systems and that we need to understand those systems and how to improve them in order to improve health care outcomes and patients experience in each specific field including diabetes care

Diabetes must be integrated within a comprehensive NCD management policy: shifting from interventions on specific patient group in health facilities to intervention on population level, shifting from vertical to horizontal vision, avoiding fragmentary care and sectorial strategies, integrating diabetes management with epidemiology, monitoring of processes and outcomes of diabetes care , and strengthening the health promotion and prevention vs. health Care.

"Diabetes House" presents one of models of such initiatives which are trying to adapt diabetes care to the current evolutions of health systems."Diabetes House": is an outpatient clinical practice which integrates the biomedical and psycho social educational approaches in care delivery. It is a place where patients find a warm and friendly environment to communicate and interact easily with diabetes care providers and ensuring a coordinated comprehensive long term clinical and psychological follow up. It's a target oriented model of care based on active patient and family members' partnership on common target setting and mutual consent on all diabetes care process. Albanian "Diabetes House" model functions with similar approach to a supermarket. It's meant to offer to patients within the same facility all medical consultations, services, lab tests, medical products, drugs, tools, ,foods technology needed for diabetes treatment or its self monitoring and all relevant information necessary for them. It's aim to save patient time and to respond and help them to solve diverse diabetes problems and to satisfy their disease related demands.. Its advantages are: best quality of care, higher clinical performance, better patients' compliance with treatment, more credibility, respect and trust between patients and health care providers

LIPID PROFILE RELATED TO VISCERAL OBESITY IN METABOLIC SYNDROME

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Background: Visceral obesity is related to the metabolic syndrome. The aim of our study was to determine the relationship of sagital diameter to hip circumference ratio (SHR) with anthropometric indexes of visceral obesity waist circumference (WC) and waist hip ratio (WHR) and their association with lipid profile levels.

Methods: Triglyceride (TG), cholesterol (C), HDLch, LDLch. levels, LDL/HDL, C/HDL as well as WC, WHR and SHR were determined. Examinees were 240 healthy women divided into 3 groups according to their body fat distribution by their WHR values: 1st group WHR<0,85; 2nd group WHR (0,85-1,0) and 3rd group WHR>1,0.

Results: WHR and SHR correlated significantly positively with TG ($p<0,0001$), LDL ($p<0,047$;$p<0,038$), LDL/HDL ($p<0,003$;$p<0,0001$), C/HDL ($p<0,0001$), also with WC and between themselves ($p<0,001$), and negatively with HDL ($p<0,001$). WC and SHR levels were significantly higher in the 3rd group (123,16±14,26cm; 0,27±0,03), compared to the 2nd group (108,87±13,93cm, 0,23±0,03) and the 1st group (87,27±16,59cm, 0,19±0,02) ($p<0,0001$). TG levels in the 3rd gr (1,86±0,75ng/ml) were significantly higher ($p<0,0001$) compared to the 1st group (1,02±0,43ng/ml) and 2nd group (1,74±0,93ng/ml). C/HDL in the 3rd group (6,4±1,96) was significantly higher compared to the 1st (4,11±1,01) ($p<0,0001$), and 2nd group (5,48±1,68) ($p<0,005$). HDL was (0,96±0,24ng/ml) significantly lower compared to the 1st group (1,22±0,28ng/ml) ($p<0,001$) and 2nd group (1,07±0,43ng/ml) ($p<0,028$). LDL, LDL/HDL and C levels were also significantly higher in the 3rd group.

Conclusions: Dyslipidemic profile and visceral obesity are the main characteristics of the metabolic syndrome. It was confirmed that visceral obesity is characterized with increased values of WHR, WC and SHR, which are positively related with dyslipidemic profile. Positive relation of SHR with atherogenic lipids, atherogenic indexes, WHR and WC, and negative relation with HDL, confirmed it as an important diagnostic parameter of visceral obesity in metabolic syndrome.

ADIPOSE TISSUE

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In humans, adipose tissue is located beneath the skin – subcutaneous fat and around the internal organs – abdominal fat or visceral fat. White adipose tissue is subdivided into incomplete lobules, by means of loose connective tissue containing a nerve network and rich vascular bed.

The main cell type of the fat tissue are the adipocytes, but other cell types – fibroblasts, stromal cells, monocytes, macrophages, immune cells and endothelial capillary cells represent about half the total number of the cell population in the tissue. The human organism possesses a limited capacity to store proteins and carbohydrates. Therefore, energy reserves are accumulated in the lipid droplets in fat cells in the form of triglycerides. These chemical compounds are more efficient form of energy storage. The adipose tissue is also an important place for sex hormone metabolism.

Now, it is well known that tha fat tissue takes part in energy metabolism, neuroendocrine function and immune function. The fat cells secrete in two ways: autocrine or paracrine and endocrine. The visceral fat is located inside abdominal cavity – between internal organs and torso. According the physiological properties intra-abdominal fat is different if compared to hypodermis, and intramuscular fat. The visceral fat cells are larger in men and lipolytic rate is greater than in abdominal subcutaneous fat. The adipocytes in the visceral fat are associated with hepatic and peripheral insulin resistance. The increase in abdominal fat is important for pathogenesis of insulin resistance but also for glucose intolerance, dyslipidemia, hypercoagulable state, hypertension, and cardiovascular risk.

The adipose tissue was accepted as an endocrine organ, while proteins with endocrine and immune functions are derived from the adipocytes – leptin, TNFα, IL-6, PAI-1, adipsin, adiponectin, apolipoprotein E, cytochrome P450 dependent aromatase, angiotensinogen and others. The adipocytes possess numerous membrane receptors for hormones – insulin receptor, glucagons receptor, TSH receptor, GH receptor and others, receptors for catecholamine and cytokine receptors as well as nuclear or cytoplasmic receptors – glucocorticoid receptors, thyroid hormone receptors, estrogen receptors, pogesteron receptors, androgen receptors and vitamin D receptors. The amount body adipose tissue is regulated by two physiological systems. The first is connected with short-term weight regulation and second with long-term weight regulation. With the first are connected with two gastrointestinal peptide hormone – grelin – an appetite stimulant and peptide YY – an appetite suppressant.

The long-term regulation of body weight is linked with two hormones: leptin and insulin. The secretion of leptin by the fat cells is increased by insulin, glicocrticoids and estrogens and decreased by androgens, growth hormone and free fatty acids. In most obese individuals levels of leptin mRNA in fat tissue and serum levels are elevated. The insulin enhances the conversion of glucose into triglycerides in the lipid droplets in the adipocytes.

The leptin and insulin regulate body weight by acting on some hypothalamus areas. The stimulation of the adipose tissue by neural and endocrine or hormonal mechanisms leads to break down of triglycerides into fatty acids and glycerol – a process called mobilization. The norepinephrin liberated from the postganglionic sympathetic axons, stimulates a series of metabolic stepsq that activate the lipase, which splits truglycerides.Hormonal mobilization involves a complex system of hormones and enzymes that controls fatty acid release from fat cells.

HEPARIN INDUCED EXTRACORPORAL LDL-PRECIPITATION (H.E.L.P.-AFFERESIS) IN TREATMENT OF PATIENTS WITH METABOLIC SYNDROME AND TERMINAL KIDNEY INSUFFICIENCY

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Introduction: Metabolic syndrome includes a number of risk factors for atherosclerosis development such as hypercholesterolemia, hypertension hyperglycemia, hyperfibrinogenemia, low levels of HDL, obesity and hypodynamism. With the increase of cholesterol levels the acute coronary death risk increases uninterruptedly on dose-response basis.

Objectives: The physicochemical fundament of H.E.L.P. therapy is based on the fact that lipoproteins and fibrinogen can precipitate selectively through heparin and low levels of pH. The precipitate then can be removed through simple filtration. The experience shared is of this kind of treatment with patents who have developed kidney insufficiency and who are at haemodialysis treatment.

Material & Methods:: Six patients at chronic dialysis treatment and with metabolic syndrome are treated for the period of 4 years. Three of them were with evidence of magisterial arteries engagement by an atherosclerotic process. We performed H.E.L.P. therapy with Plasmat " Futura"system while the volume of the plasma treated per procedure varied between 2000 ml to 3 500 ml.

Results: We observed excellent hypercholesterolemia affect as the output values of triglycerides and LDL averagely decreased with 55% and these of fibrinogen with 36%.

Conclusion: H.E.L.P. therapy is applied for the first time in Bulgaria in the complex treatment of this highly risk group of patients and it confirms high effectiveness of the procedure. It creates preconditions for more gentle diet for the patients. It reduces medicinal treatment with Simvastatin and other HMG- CoA reductive inhibitors.

OBESITY AS A RESULT OF THE MODERN WAYS OF DIETING AND RISK FACTOR TO CHILD HEALTH

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Background: Obesity is a positive energy intake with reference to the energy expenditure. It presents a risk factor to all systems of the organism from earliest age as a result of the modern ways of dieting and lifestyle. It has an epidemic character and presents personal, family and social problem. Our aim is to show the direct link between the obesity and morbidity in the early childhood as a result of the modern lifestyle.

Methods: Observation of 100 children born in 2003 – their obesity and morbidity in the first and seventh year. We used the comparative method.

Results: In the first year, 40 children (40%) have body weight over 10 kilos; 18 of them (45%) were female and 22 (55%) were male. During the time of observation,

22 children (55%) usually suffered from lower respiratory tract infections (bronchitis, bronchiolitis, and pneumonia). In the seventh year, 60 children (60%) were obese with body weight over 22 kilos – 38 (64%) female and 22 (53.6%) male. According to the morbidity, 36 (60%) had lower respiratory tract infections, 21 (35%) had defects of the locomotor apparatus, 10 (6%) had psychiatric disorders, and 3 (5%) had diabetes.

Conclusion: Obesity is a risk factor to child health and threat to the health of adults as well. It may turns into epidemic becoming a problem of the society. The doctors shold be leaders in their environment and public advocates for the health of the children and adults. We can fight obesity by: preparing prevention programs; promoting healthy diets; abandoning the sedentary lifestyle and increasing the physical activity; giving up vices (smoking, alcohol and narcotics). Finally, we could say that the prevention of the children's health is the biggest investment into the future.

EVALUATION OF MACROVASCULAR COMPLICATIONS IN DIABETES MELLITUS

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Background: Patiens with type 2 Diabetes mellitus(DM) are with greater risk for macrovascular complications. Establishing the incidence and prevalence of macrovascular complicatios in patients with DM as a base for prevention programs.

Methods: The study involved 1320 patiens with DM from Dispensary for diabetes from Negotino, of wich 16 patiens were DM type 1 and 1304 type 2 (331 patients on insulin therapy).

Patients were on age from 12 to 89 years and duration of diabetes 8.6+-7.6 years. Retrospective study on 1304 patiens with DM type 2 was performed. Included investigatios: laboratory tests, ECG, coronary stress test, doppler sonograhy, coronarography, CTM.

Results: With high blood pressure (over 130/85 mmHg) were 404 (31%), coronary artery disease 339 (26%), peripheral artery disease 210 (16,1%), and cerebrovascular disease 143 (11%).

Conclusions: The results indicated high prevalence and incidence of macrovascular complications in patiens with DM type 2. There is a need for more agressive preventive care of DM patiens,early detection, education and insulinisation, as a preconditon for lowering the incidence of diabetic complication and better quality of life.

COMPARATIVE STUDY ON CHILDHOOD OBESITY IN VILLAGES AND TOWN

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Background: Levels of childhood obesity are increasing at alarming rates in many countries, including Macedonia. This rise in the number of overweight children is disturbing because it causes health problems and can lead to social problems. The most common causes are genetic factors, lack of physical activity, unhealthy eating patterns, or a combination of these factors.

Methods: Study involves more than 400 school-aged children (two generation with 7 and 10 years) in Stip (Macedonia), and 100 children (the same generation) in surrounding villages of Stip. Overweight children are measured (BMI) in primary care during the past 3 years (2007-2010).

Results: During the past three years there has been a increase in childhood obesity in children who live in Stip. Like illustration, in 2008, prevalence of obesity (to children with 7 years) in Stip had a less than 10%. In the same year, on the same generation, the villages had a prevalence of obesity equal to 3%. The obesitas is more estimated in boys than in girls (equal in the town and the villages).

Conclusion: The last indicates that children who lives in the town (Stip) are more likely to be obese compared to children in the villages. Most probably, the changes in the environment are playing the key role. Environmental and social factors are the prime cause of modern obesity. Environmental and behavioural factors have a greater influence - consuming excess calories from high-fat foods and doing little or no daily physical activity over the long run will lead to weight gain. Regular monitoring of physical parameters, psychological, behaviour, diet and exercise should be part of the treatment package. Childhood obesity represents one of our greatest health challenges.

OBESITY IN SCHOOL'S PREPUBERTAL CHILDREN IN SKOPJE, HEALTH AND SOCIAL PROBLEM

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Background: Obesity,(result of genetic, biological, psychological, social, cultural etc.factors interaction) is one of the most important actual public health challenges for the people's health condition with alarming increase in epidemiological world trend. In Europe, last 2-3 decades obesity has threshold more increased, especially in children and adolescents (annual rate rise trend is: 10 X (ten times) more/ than in 1970 year) Above 60% of obese school children, become obese adults, liable and susceptible on early arteriosclerosis, hypertension, diabetes-2, malignancy, osteoporosis, carries, psychosomatic disturbances etc. Obesity is one of frequently causes for non-contagious morbidities and second of causes of mortality that is

preventable in early ages. Early notifying the risk of obesity in children is imperative, for undertake professional, multidiscipline, complex measuresteps for these children as early as it is possible!

Aim: Pilot study in order to analyze of obesity frequency in school prepubertal urban children from Skopje.

Material and Methods: We analyzed 233 children,114-boys and 119-girls; A-group=115 in IInd class(mean age-7,39yr.) and
B-group=18 in Vth class (of primary schools from Skopje) (with mean age–10,78yr.) Body weight /for the age, height /for the age, BMI/for the age, skin wrinkles:-(skinfold-triceps/for the age, skinfold-subscapularis/for the age), were measured and countered.

Results: From investigated children, in A-group=16(13,91%)were with overweight of Ist^{o} and IInd^{o}(degree), and 5(4,35%)were obese, In B-group=14(11,86%)were with overweight of Ist^{o} and IInd^{o}(degree), and 4(3,38%)were obese, (from both sex.).

Conclusion: Such kind of obesity increasing degree is alarming in school age children! It is necessary to undertake urgent strategic measuresteps for prevention and treatment of obesity with professional and well planed multidisciplinary and complex national program. It is necessary to be included: the low-support on health, school and other education, and wide public community and mediums too. It is important to support great and necessary changes in number of inactive and actual domains and changes of many cultural and social valuables and standards, also.

THE PREVALENCE OF OVERWEIGHT/OBESITY AND UNDERWEIGHT CHILDREN IN A SUBURBAN AND RURAL "M.A.CENTO" AREA IN SKOPJE, R.MACEDONIA

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BACKGROUND: Overweight/obesity are defined as abnormal or excessive fat accumulation and are major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases, musculoskeletal disorders and cancer. Once considered a problem only in high income countries, overweight/obesity are now dramatically on the rise in low- and middle-income countries, particularly in urban settings. In the USA (1980 to 2004) the percentage of obese tripled from 7% to 19% in children and 5% to 17% in adolescent.

METHODS: We determined the BMI in school children aged 7-14 years, from 6 primary schools (4 in a suburban, and 2 in a rural area). There were 628 children at the age of 7 years (420 Macedonians and 208 Albanians), 641 children aged 9 years (430 Macedonians and 211 Albanians), 642 children aged 11 years (436 Macedonians and 206 Albanians), and 619 subjects aged 13 years (423 Macedonians and 196 Albanians). The weight-for-height status of this target group identifies the percentage of students who are overweight/obesity/ underweight. The WHO defines "overweight" as a BMI $\geq$ 25, "obesity" as a BMI $\geq$ 30 and "underweight" as a BMI < 5.

RESULTS: The prevalence of overweight/obesity/underweight found are as follows: I. Children aged 7 years: overweight 19% (24% Macedonians and 9% Albanians), obesity 9% (11% Macedonians and 5% Albanians) and underweight 9% (7% Macedonians and 13% Albanians), II. Children aged 9 years: overweight 23% (29% Macedonians and 12% Albanians), obesity 12% (16% Macedonians and 6%Albanians) and underweight 5% (4% Macedonians and 8% Albanians), III. Children aged 11 years: overweight 22% (28% Macedonians and 9%Albanians), obesity 10% (13% Macedonians and 4% Albanians) and underweight 10% (6% Macedonians and 17% Albanians), IV. Subjects aged 13 years: overweight 23% (27% Macedonians and 15% Albanians), obesity 10% (11% Macedonians and 8% Albanians) and underweight 6% (4% Macedonians and 10% Albanians).

CONCLUSION: The prevalence of overweight/obesity is high, particularly at suburban area. Interestingly there is a significant difference when nationality is taken into account: Macedonians have 2-3 times higher rate of overweight/obesity, when compared to their Albanian classmates. Interestingly, the prevalence of underweight is 2 times higher in Albanian subjects, when compared with Macedonians. Overweight/obesity/underweight, as well as their related chronic diseases, is largely preventable. This urges a concentrated society programme for their prevention.

ALLERGY AND AUTOIMMUNE DISEASES

ДИАГНОСТИКА НА АВТОИМУННИТЕ БОЛЕСТИ- ПРАКТИКА И ПРЕДИЗВИКАТЕЛСТВО

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Доказано е постоянно наличие на различни автоантитела и авто-реактивни клетки, които не причиняват болестни увреждания. Този имунологичен толеранс към собствените анигени се осигурява от различни нива на регулация на съзряването и персистирането на имунните клетки, както и от постоянно действащата идиотип-антиидиотипна регулаторна мрежа на организма.

Автоимунитетът е патологичен феномен, при който дисрегулация на имунната система стартира образуването на извънредни автоантитела или клетки, насочени срещу собствени на организма антигени, които могат евентуално да увредят организма. Автоимунни отговори има непрекъснато, но само около 5 % водят до клинична болест. Досега има дефинирани над 80 автоимунни болести.

Автоимунните увреждания се причиняват от: автоантитела и имунни комплекси, клетъчни фактори и цитокини и различни дефекти в имунната регулация. Разглежда се ролята на автоантителата, начините за изследването им и интерпретация на резултатите, както и някои основни групи автоантитела, имащи утвърдено диагностично значение. Представени са примери за диагностичното използване на имунологичните показатели при най-честите автоимунни болести. Очертани са и някои предизвикателства на съвременната автоимунна диагностика.

БРОНХО-ОБСТРУКТИВЕН СИНДРОМ В ДЕТСКА ВЪЗРАСТ И ВЪЗМОЖНОСТИ НА ХОМЕОПАТИЯТА В ТЕРАПЕВТИЧНОТО МУ ПОВЛИЯВАНЕ

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Увод: Бронхо-обструктивният синдром в детска възраст и неговите усложнения са честа причина за посещение при лекар в ежедневната практика. **Цел** на настоящата разработка е установяване терапевтичната ефективност на хомеопатията при деца с бронхо-обструктивни състояния – суха кашлица, свиркащо дишане, задух и експираторна диспнея.

Материал и методи: Осъществено рандомизирано, ретроспективно проучване върху хомеопатичните досиета на 51 деца с бронхо-обструктивен синдром, проследявани минимум 6 месеца от практиките на четирима лекари хомеопати. Лечението е провеждано строго индивидуално, в зависимост от тежестта

и причините за появата на бронхиалната обструкция. Направен е анализ на терапевтичния подход, който включва лечебни, профилактични и организационни мерки. Анализирани са 337 прескрипции с хомеопатични средства. Данните за всички пациенти са въведени в специално подготвена анкетна карта и обработени статистически с програмата SPSS.11.

Резултати: На 40% от децата е изписвана комбинирана хомеопатична и алопатична терапия. Най-често употребявани симптоматични медикаменти са Poumon histamine, Blatta orientalis и Antimonium tartaricum. За терен най-често е изписван Natrum muriaticum (13%), Calcarea carbonica (12%) и Sulfur iodatum (8%). При голяма част от пациентите ефектът от симптоматичното хомеопатично лечение настъпва бързо - при 43% до 24-тия, а при 57% - до 72-рия час от започването на терапията, а в дългосрочен план на края на третия месец 80% от тях отчитат подобрение на основното страдание и качеството на живот.

Заключение: Резултатите разкриват възможностите и ефикасността на хомеопатията при лечение на бронхо-обструктивните състояния в детската възраст. Те биха могли да послужат за основа на комплексен терапевтичен алгоритъм.

ПСОРИАЗИС – СИСТЕМНИ ПРОЯВИ ПРИ КОЖНОТО ЗАБОЛЯВАНЕ

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Псориазисът е кожно заболяване, което се характеризира с формирането на еритемопапулосквамозми плаки. Веднъж появила се болестта съпътства целия живот на пациента като риск от рецидив винаги съществува. Кожната болест влошава значително качеството на живот на пациентите. Проучвания го сравняват с това на онкоболни или болни с тежки сърдечносъдови заболявания.

Псориазисът е значително асоцииран с метаболитен синдром, като в резултат рискът за развитие на сърдечно-съдови, мозъчно-съдови заболявания при тези пациенти е значително повишен. Едно от най-вероятните обяснения е системното възпаление, на което са изложени тези болни. Връзка се търси и в сходството в патогенезата на атеросклероза и псориазис.

SKIN PRICK TEST - SPT ON CHILDREN WITH ASTHMA

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Introduction: Asthma is chronical inflammatory disease of respiratory system where many cells play great part and is characterised by seizures of reversible bronco obstruction which is clinically manifested with expiratory dispnea, wheezing, stab in chest and cough.

Aim:of our study is to prove the applicability of skin prick test on the children with asthma.

Material and methods:10 children from 5 to 12 years old in which was evident bronco obstructive crises with difficult persistent asthma. At half of the children for complete confirmation of the diagnosis and further treatment, except the above mentioned tests, the following additional tests were performed: eosinophily in swab from nose mucus membrane and in sputum, UniCAP total IgE and UniCAP specific IgE, lung functional tests, additionally performed in the Clinical center in Skopje.

Results: the test was negative for 2 children, for other 4 children the test was positive for pollen of grass and home dust, and the rest 4 children were allergic to pollen from trees and weed and Dermatophagoidinae.

Discussion: Recently it was proven that atopy as genetic predisposition for development of IgE response to repeatable aero-allergens is the strongest predisponirant factor for asthma development. Specific allergens can provoke early asthmatic response by IgE which provoke release of mediators from mast cells and late response (LAR) which shows 6-10 hours starting from allergic exposition and this is as a result of infiltration of inflamatory cells - eosinofiles and Th2 cells.

Conclusion: Skin tests are necessary tests in diagnosis and treatment of difficult and persistent asthma.

NOVEL IMMUNE MODULATING THERAPY: TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO BASIC THERAPY

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Background: Modern progress in pharmaceutical development as well as in understanding of the immunopathogenesis of rheumatoid arthritis (RA) have allowed the introduction of new immune modulating therapies for this disease. This has spurred the development of biologic agents targeting components of the aberrant immune response in respect to the occurrence and sustenance of the immune driven systemic inflammation characteristics typical for RA. One of the cytokines with effects on numerous cell types including those involved in the pathogenesis of RA is IL-6. Numerous studies on the effects of inhibitors of IL-6 were conducted in animals and subsequently in humans, which showed that IL-6 appears to be a viable target for autoimmune disease. Our experience is with tocilizumab, a humanized monoclonal antibody specific for the IL-6 receptor (IL-6R). It has been shown to be of significant efficiency in patients with RA. The objectives of the present article are to report the efficacy and safety of tocilizumab in patients with active RA in clinical practice.

Methods: In total, 8 patients (all women), with severe disease activity, were treated with tocilizumab. Any prior infections, as well as other comorbidities, were treated before the drug was administered. Guidance on disease control and prevention was adviced. During treatment, one patient was diagnosed with pneumonia and

therefore application of tocilizumab was terminated. Mean age of the patients was 49,5±8,28, while their mean disease duration was 8,42±8,75 years. Before the application of tocilizumab the patients were treated with basic therapy including different combinations of metotrexate, resochine, steroids, and two with rituximab, but without satisfactory effects. Patients remained on metotrexate, steroids and nonsteroid anti-inflammatory drugs during the treatment with tocilizumab.

Results: Mean DAS28 score was 6,59±0,79 initially, and decreased to 4,86±1,04 after three doses (n=7). After three doses all patients were significantly improved, the remission rate was 28,57% (2 patients) and all of them had achieved moderate disease activity. With the notable exception of one patient who developed pneumonia because of which application of tocilizumab was terminated, all others responded well to the therapy and there was no decrease of efficiency of tocilizumab during the treatment.

Conclusion: Tocilizumab has been shown to have significant efficiency in patients with RA. Treatment with this agent can rapidly induce remission in RA in a high proportion of patients and is generally well tolerated. Tocilizumab would seem to be a promising treatment option, even as a possible first-line choice in the management of RA. Studies, on a large scale, analyzing its effects in varied populations of RA patients, as well as further detaila concerning its long-term efficiency and safety of tocilizumab are needed to more precisely define its role in the treatment of RA.

ALLERGIC RHINITIS – TREATMENT AND COMPLIANCE IN CHILDHOOD

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Allergic manifestations on the upper airways tract in children are more often presented in the last decade. Consequently, it is very necessary to have special approach in diagnosis, therapy and management for these patients.

Our aim was to perceive appearance of the symptoms, their representation and frequency and seasons' manifestation, also. In addition, following of the other clinical entities presentation, therapy and its difficulties during utilization was noticed.

Material and Methods: In this study we analyzed data from 105 patients at the age of 5-18 years. Patients were ambulatory followed at the Institute in the period of the last 5 years. Gender distribution was: 57 (54, 28%) male and 48 (47, 72%) female. In all patients were realized ENT, laboratory and allergy investigations.

Results: Pollens and Dermatophagoides pteronyssinus were dominant triggers. In all patients we realized forehead rhinoscopy. Ashy livid slime was detected in 102 (97, 14%). Rhinorea was presented in all children and for 52 (49, 52%) data for manifesting cough was given.

Therapy was realized with local corticosteroid in 50 patients (47, 62%), antihistamine -42 (40%) and in the same time application of asthma prevention with topic corticosteroid -38(36, 19%). Local treatment was discontinue realized, but in 11(10, 47%) patients we had no good response on the local treatment. It has to be notice that with those children and their parents we had not very good compliance.

Conclusion: Because of the good health benefit in relation with used therapy it is necessary to have very good compliance between physician form the one side and parents/child, from the other side. In that case, possibility for patients dissatisfaction and because of that treatment withdraw will be minimal.

ASTHMA IN CHILDHOOD (CASE PRESENTATION)

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Background: Asthma in childhood is usually a misdiagnosed condition by the doctors or because of the parents' behavior that can't accept their child has asthma. A typical case of uncontrolled asthma in a five years old girl is presented in the abstract.

Method: The girl was from a lower social class living in poor conditions. She has had bronchitis frequently since the age of two and she has been on medications (antibiotic + Salbutamol syrup) once or twice monthly because of the severe symptoms. When she was brought to the ward she didn't have fever, but she had tachydyspnea, tachycardia, chest indrawing, air hunger, slow and almost unhearable vesicular breathing on both lung sides. The oxygen saturation was 75%. A basic blood test and an x-ray image of her lungs were made. The results from the blood tests were: WBC - 10.2 x 10^9/l; RBC - 4.68 x 10^{12}/l; Hgb - 121g/l, HCT - 45.4% and the erythrocyte sedimentation rate was 8. The x-ray image of the lungs showed emphasized hiluses, increased and potentiated bronchovascular image and hyperinflation.

Results: A short-acting β2-adrenergic receptor agonist-Salbutamol (Ventolin sol.) was immediately administered to the girl via nebulizer in dosage of 0.025ml/kg, twice in a time period of 20 minutes. The girl was put on an oxygen support. The asthmatic symptoms were very severe and therefore a systemic corticosteroid was given to her and also a single dose of Aminophylline amp. i.v. in dosage of 5mg/kg. The condition of the patient drastically improved in two hours and the oxygen saturation increased to 92%. As a result of the poor social conditions, the parents rejected further investigations in a specialized institution. The girl was put on an inhalational corticosteroid - Flixotide 50μg (Fluticasone propionate). She was taught to inhale it by volumatic. In the next five months she had just one mild obstruction.

Conclusions: The good anamnesis, the typical clinical manifestations and the appropriate answer to the therapy completely confirmed the diagnosis of bronchial asthma.

MACEDONIAN NATIONAL CONSENSUS FOR DIAGNOSIS AND TREATMENT OF ASTHMA, REALITY AND PERSPECTIVE

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Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role (mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells). These mediators act on cells in the airway, leading to

contraction of smooth muscle, oedema due to plasma leakage and mucus plugging. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.

There are many things that can cause asthma symptoms and everyone's asthma triggers are unique. Allergic triggers are dust mites, mould, certain foods, animal dander and pollen. Non-Allergic triggers are exercise, infections like colds and flu, cold or humid air, intense emotions, medications like aspirin and beta-blockers, hormones, air pollution and occupational irritants such as paint or chemicals.

Asthma is a worldwide problem and also is one of the most common chronic diseases worldwide —300 millions or 7.2% patients suffered from asthma. Prevalence increasing in many countries, especially in children — 6% and in adult 10%. There are 180,000 deaths annually. In the Republic of Macedonia 100,000 or 5% of the population suffer from asthma.

Morbidity and mortality from asthma and is in constant growth that imposes the necessity of unifying the diagnostic and therapeutic approach to asthma through detailed protocols which specify the exact location, the role and significance of each diagnostic and therapeutic procedure, and any entity connected in any way with this enigmatic disease.

The Global Initiative for Asthma (GINA) works with health care professionals and public health officials around the world to reduce asthma prevalence, morbidity, and mortality. Through resources such as evidence-based guidelines for asthma management.

GINA was launched in 1993 in collaboration with the National Heart, Lung, and Blood Institute, National Institutes of Health, USA, and the World Health Organization. Only two years later in Macedonia was open the first Center for Asthma at the Clinic of Pulmonology and Allergy. In 1996 was published the first Macedonian National Program for Diagnosis and Management of bronchial asthma who wants to uniform diagnostic and therapeutic modalities or single doctrine. In 1999 was published the first Macedonian National Consensus on the Diagnosis and Treatment of asthma and chronic obstructive pulmonary disease. In 2007 were open another 12-Regional Centers for asthma in Macedonia.

Greatest benefit of specific immunotherapy using allergen extracts has been obtained in the treatment of allergic rhinitis. The role of specific immunotherapy in asthma is limited. Specific immunotherapy should be considered only after strict environmental avoidance and pharmacologic intervention, including inhaled glucocorticosteroids, have failed to control asthma. Perform only by trained physician.

Approach in pharmacological therapy in patients with asthma is described as step approach, which means an increase or decrease the number of medications and frequency of application depending on the severity of asthma.

PROFESSIONAL ALLERGY BRONCHIAL ASTHMA FOUND IN A WORKER IN LEATHER INDUSTRY

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Introduction: Professional bronchial asthma (PBA) is caused by specific agens from the working enviroment, it is reversable obstruction of the respiratory system which is caused by dust, gas, steam and smoke from the working enviroment.

Descripton: 45 years old patient, has been observed, taylor in a leather industry with 10 years working experience. The patient has suffered from dry cough for 5 years, hard breathing, missing air, expectorate white glued secretion, lungs sound, tightening and repression.

Directed examinations has been done, including clinical auscultatorn diagnosis of the lungs, alergicy skin tests with standard inhalation and specific professional alergens following prick method, total IgE, laboratory and hematological analyzes and functional lungs monitoring. Special place in the evaluation of PBA exsisting has the positive working anamnesis, exposition and elimination test, spirometry, non-specific bronchoprovocative test with Metaholin, functional lungs monitoring before and after the work with spirometry, as wen as PEF monitoring (the largest expiratory flow), with pursuance of the FEV_1 value, before and after bronchoconstriction and after the bronchodilatation. After inhalation of 5000gama Metaholin, auskultator and spyrografic diagnosis changed inasence of bronchoconstriction. FEV_1 value lowered for more than 20% hyperactivity wag registered in the breathing chanel. With bronchodilatator inhalation, FEV_1 value increased for more than 15% therefore positive bronchodilatatoren test with Ventolin was confirmed.

Conclusion: It is necessary to have prevention on time with a control of the enviroment (ecological monitoring), early detection of the symptoms and signs of the disease, timely halt of the exposion and prevention of the development of the disease as wen as appropriate therapy and rehabilitation of the diseased with PBA.

POLENIC ALLERGY AT CHILDREN

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Introduction: Polenic allergy as others allergies has an explosive trend of increase. About one ot third of the mankind have this problem esspecially the children are more often expose on different air allergens.

Methods: In 310 children in age of 2-11 years with rhinitis are made blood examinations as the number of leukocytes, eosinophils in blood and in nose secret. The examination is made with hematology analysator, leukocytes formula and eosinophils are examinated in smears which are coloured by May Grinwald- Gimza's and the absolut number of eosinophils are determinated in counting chamber to Neubauer and coloured with eosin by Dunger.

Results: The number of leukocytes is 8,9+/-2,1 H 10^9 /L and in 93 of the children (30%) there are increased number of eosinophils- in blood smears 0,06+/-0,02 and by Dunger with chamber method- 0,425+/-0,125 H 10^9/L. In 14 of children (15% of the immunosensibilitation children) are detected eosinophils in nose secret.

Conclusions: Polenic allergy represent a global helth problem. Affecting at least 15% of the children population induced after allergen exposure, air contamination, artificially materials, by an immune response of the body. Polenic allergy opposite in relation to ordinary rhinitis has increased absolute number of eosinophils in blood and nose secret. The prevention and protection at children by allergic rhinitis is very important, to avoid the late complications of long continued sensibilitation on allergen- allergic bronchitis and asthma, by using the management of allergic rhinitis- avoid the pollen, using medications in prevention at least 2-3 weeks before the seasons with allergens or specific immunotherapy and education.

DETERMINING OF SPECIFIC IMUNOGLOBULIN E IN SERUM OF CHILDREN WITH ALLERGIC DISEASES

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Background: To determine the serum levels of specific IgE in serum of children with allergenic diseases.

Methods: Analyzed population were 69 children below 10 years of age 42 (60,8%) male and 27 (39,2 %) female patients from our institute. A retrospective evaluation was performed on material from 3 months period (April - June) 2005, with measurements of the level of specific IgE in serum. We used the method of "ELFA" from the company "Bio Merieux".

Results: The results that we got showed that distribution of children based on their age was: 30 children between 1 month and 1 year, 27 children between 1 and 3 years, 3 children from 3 to 5 years and 9 children from 5 to 10 years. From all analyzed samples in 36 (52,2%) cases there were increased values of some of the specific IgE in serum. From inhalation allergens: Dermato. pt. 58.3% x 0.70 KIU/L class 2, Dog 33.3% h 0.81 KIU/L class 2, Cat 33.3% h 0.87 KIU/L class 2, Alternaria 25.0% x 0.45 KIU/L class. From nutrient allergens: Wheat 87.5% h 3.73 KIU/L class 3, White of egg 73.7% x 2.56 KIU/L class 2, Soya 61.5% x2.09 KIU/L class 2, Milk 20.0% x 2.09 KIU/L class 3.

Conclusion: The ELFA test is highly applicative method, simple and quick for accomplishment, economic tests and calibration in time of 14 days. It is good for determining the circulatory antibodies among children below 3 years, when it is not possible to use the skin tests and it is independent from the used therapy. It can be accomplished regardless the medical condition of the patient, and avoiding systemic reactions, such as anaphylactic shock.

EFFECT OF INHALED CORTICOSTEROIDS-BUDESENIDE ON THE OUTCOME OF ASTHMA BRONCHIALAE

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Background: Airway inflammation, hyperreactivity and mucous hyperproduction are the main characteristics of asthma. The study aims to assess the effect of inhaled corticosteroid (ICS) - budesonide in the treatment of asthma.

Methods: The study group consisted of 40 outpatients with mild to moderate asthma with forced expiratory volume in one second (FEV1)75 ±5%, and vital capacity (VC) 3,02. At recruitment into the study treatment period, they discontinued their regular therapy and started the therapy provided for the study purposes. Twenty three patients were on ICS- Budesonide 800µg/day and 17 received B2 agonist–inhaled Salbutamol 300 µg /day. All of them received theophylline 700 µg /day. Six weeks later, the subjects were assessed by spirometric measurement of lung volumes (FEV1,VC). In a 6 mouth follow-up study we observed the presence or absence of respiratory symptoms, the frequency of exacerbation episodes and hospital admissions to reflect an ongoing airway inflammation and its association with the blood eosinophillia.

Results: The first group showed a 20± 3% greater improvement in FEV1 and Vc rates when compared to the Salbutamol group - 16±2%. Respiratory symptoms, number of exacerbations and the need for hospital admission were significantly higher in the second group which correlated well with the increased eosinophil activation.

Conclusions: Inhaled corticosteroids as potent anti-inflammatory agents can effectively improve the clinical expression of bronchial asthma.

NERVOUS AND IMMUNE SYSTEM INTERACTION

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The main communication systems – immune, endocrine, and cardiovascular are influenced by the nervous system trough direct supply and by means of circulating hormones. In turn, these systems feedback signals to the nervous system – completing the circle.

The nervous system and immune systems are interconnected. The lymphoid tissue receives postganglionic sympathetic supply. The lymphocytes possess receptors for number of hormones, neurotrasmitters and neuromodulators. The corticoids, endorphins and enkephalins, which released during stressful conditions possess immunosuppressive effects. The corticosteroids are the most powerful endogenous suppressors, especially for the innate immune response. The hypothalmo-Pituitary-

Adrenal axis is the central integrative system, that rules the stress homeostasis. This system controls the synthesis and release of the peptide and steroid hormones. There is connection between behavior and immune functions. Between psychosocial factors, including stress there is link with susceptibility and progression of immunological mechanisms. Chronic stress is associated with increased incident and

severity of the common cold and decreased survival in patients with breast cancer and melanoma. In such cases was established lower level of NK cell.

CNS controls the immune system in two ways. Most lymphoid structures received direct sympathetic supply for the blood vessels in the lymphoid tissue and directly to the lymphocytes. CNS directly and indirectly controls the secretion of different hormones, and especially corticoids, growth hormone, prolactin, α-melanocyte stimulating hormone, thyroxin and epinephrine. Of all biological systems, the most complex are the human brain and human immune system. Each in its distinctive way has evolved the capacity to remember experience, learn, and communication. The memory mechanisms and communications in both systems are essential different. The immunological memory is at present better understand. The brai memory processes are much more complex and flexible. The receptors on T cells bind neurotransmitters such as norepinephrine and endogenous opiates and norepinephrine – the immune cells are equipped to received messages from the brain. There is traffic in the other direction – immune chemical messengers, called cytokines, could affect the brain. The neurotrophins, including NGF mediate neuronal survival, also affect survival of immune cells. The pathogenesis of neuroimmunological disorders is still poorly understood.

Demyelinating autoimmune diseases involved damage to the myelin in the nervous system. In some cases the attack starts from "defective" immune cells, but in other cases the defect is in myelin. For nearly a century, an autoimmune basis for schizophrenia onset and progression has been proposed.

ALLERGY AT CHILDREN'S AGE

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Allergy means a situation of changed reactivity that occurs after continuous exposure at unknown substance, in fact, antigen and this kind of situation is harmful for people. The allergy is a negative consequence of immunological process in the body, essentially, it is a consequence of the negative reaction antigen-antibody.

According to statistics, the occurrence of allergy diseases at children's age varies between 5 and 10%. In this study, we examined 45 children, at the age 0-14. 69% or 31 of them were boys and 31% or 14 were girls. According to the place of living, 20% or 9 children were living in villages and 80% or 36 in the city. According to their age, 56% or 25 children were younger than 3 years, 22% or 10 children were at age 4-6, and 22% or 10 children were at age 7-14. 53% or 24 children manifested allergy in the first year of life, 25% or 11 children in the period of 1 to 6 years old and 22% or 10 children after they were 7 years old. In the case of 23 children (51%), the manifestation of the allergy was the atopic dermatitis, in 14 cases (31%) – bronchial asthma and in 8

cases (18%) – with symptoms of allergic rhinitis. From the 23 cases with first diagnose atopic dermatitis; later on 48% or 11 of them manifested symptoms of bronchial asthma.

From the cases with bronchial asthma, later on 21% or 3 children manifested allergic rhinitis, also. 91% or 41 children had a positive family anamnesis: in the cases of 22 children (54%) both parents manifested allergy, in the cases of 9 children (22%) only one of the parents manifested allergy, in the cases of 10 children (24%) the allergy symptoms were manifested in the family (grandparents, also). 20% or 45 children were relatives.

We may conclude that the allergy is manifested in the early ages, till the first year of life, it is more usual for male children and the children that live in the cities. The most common way of manifestation is the atopic dermatitis, later on, part of them start to manifest the symptoms of respiratory allergy, although it can start with symptoms in the respiratory system.

Most of the examined children had positive family anamnesis, and part of them were relatives.

ALLERGIC CONSTITUTION IN CHILDHOOD AND RECIDIVE LARYNIGITIS EPISODES

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Aetiology of laryngitis episodes, especially those repeated is unclear, yet. The acute onsets of attack, without signs and symptoms of acute infection, short duration, and early response on symptomatic therapy lead to conclusion that there is important role of allergic constitution in childhood.

The aim of this professional work is to determine the degree of correlation between repeated laryngitis episodes and allergic component.

Material and methods. There were 60 children included in this work. They had anamnesis data about repeated laryngitis episodes and performed skin prick tests about allergy predisposition. Personal and familiar evidence about allergy was assessed, too.

Results. Positive results from allergy skin prick tests were confirmed in 31 child. From them, in correlation with this basic disease, allergic constitution (asthma, allergic dermatitis, and allergic rhinitis) was determined in 19 patients. The most positive allergen causes were: pollen-21, Dermatophagoides ptt.-16 patients … From those 29 patients with negative results on allergic skin prick tests, 16 had positive anamnesis of personal/familiar allergy, allergic dermatitis in 6, asthma in 4, recidivate broncho-obstructive episodes -4, positive asthma anamnesis – 3. Only in 13 patients allergy was not evidenced.

Conclusion. There is high degree of significant correlation between repeated laryngitis episodes and allergic constitution in childhood. Allergy is appeared as very important factor in etiology of repeated laryngitis episodes.

FOLLOWING OF GROWTH IN ASTHMATIC CHILDREN - OUR EXPERIENCES

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Background: Some authors published temporary suppression of growth in children who received high doses of inhaled corticosteroids(ICS),but still definitive childrens growth was reached and it depends mainly from reached asthma control. Using low doses of inhaled corticosteroids (ICS)(≤400mcgBDP or≤200 FP),most of the authors,did not show eventual suppression of the definitive child's growth.

Aim: To show our experience in follow up of the growth in asthmatic children, that used or didn't use ICS.

Material and methods:We followed height growth in 360 children, mean age:10,34yr. male:219(60,83%) female:141(39,16%). Constitutionally low growth was excluded with parent's exam. Puberty signs were noted, low feedings and bad social condition were anamnestical detected and excluded. Children were divided in three groups: I gr.: those who received ≤400mcg of BDP,or≤200 FP > 6 monthes, II gr.those who received Ketotifen or Chromoline, III gr: those who didn't receive anything.Measurements were performed with standard antropometric procedures (with stadiometar).

Results and discussions: There were no statistic significant differences between these three groups. In fact even in III group were measured minimal growth reterdance although not statistical enough significant which probably owes to the fact that notprevented B.A.and not enough controlled is more dangerous for childrens growth than low doses of ICS.

Conclusion: Low doses of ICS (≤400 mcg BDP,or ≤200 FP.)did not produced anu suppression on childrens growth and they are first line choise for threating allergic inflamation in respiratory system.

PATIENT SAFETY

БЕЗОПАСНОСТ НА ПАЦИЕНТИТЕ В „АКТА МЕДИКА”

Елена Узунова – Заместник Изпълнителен директор
Д-р Христина Костадинова - Медицински директор
Д-р Иван Ненков – Началник „Оперативен сектор”
Снежана Михайлова – Главна медицинска сестра

Качеството на лечение, здравни грижи и безопасността на пациентите са наш основен приоритет. По проблемите за безопасност на пациентите организацията ни работи още от стартирането на дейността на многопрофилната болница за активно лечение през 2007 година.

2007 г – 2010 г. – Програма за борба с вътреболничните инфекции

Реализирани обучения:

1. Почистване и дезинфекция на под и повърхности – болнична стая и санитарен възел.
2. Почистване и дезинфекция на операционен блок.
3. Почистване и дезинфекция на кухня – разливочна.
4. Дезинфекция на ръце.
5. Ръчна работа с тежести
6. Дезинфекция на хирургичен инструментариум.
7. Управление на болничните отпадъци.
8. Събиране, деконтаминация, дезинфекция и опаковане на инструменти за стерилизация.
9. Поведение на хората в условия на пожар
10. Защита на медицинският персонал от причинители на инфекции предавани по кръвен път – хепатит В, хепатит С и СПИН. Преекспозиционна и постекспозиционна профилактика
11. Хигиена на ръце
12. ВБИ. Индикаторни инфекции – постоперативни раневи инфекции. Проблемни рани в хирургията. Антисептика.

2009 г – стартиране на процеса по акредитация на стандартите на Joint Commission International

I етап – Превод на международните стандарти на JCI

II етап – Сформиране на групата по качество, която се грижи за разписване на политиките в организацията съгласно стандартите на JCI, внедряването и контрола по спазването

III етап – Внедряване на международните цели за безопасност на пациентите

Дейност 1. Разписване и одобряване на политиките по шесте цели за безопасност на пациентите

Дейност 2. Одобрение на план за действие по внедряването на целите за безопасност – пилотен проект «Оперативни отделения»*

Дейност 3. Подготовка и реализация на обучения съвместно с експертите по човешки ресурси за всяка конкретна политика.

Дейност 4. Сформиране на комисия за вътрешен одит по спазването на целите за безопасност.

Пилотното внедряване на международните стандарти за болници на Joint Commission International в АКТА МЕДИКА ще бъде в оперативен сектор, обхващащ

- Гинекологично отделение
- Хирургично отделение
- Ортопедично отделение
- Операционен блок

Внедряването на стандартите за качество е част от един по-голям вътрешно организационен проект касаещ оперативните ни отделения, а именно „Повишаване на качеството, безопасността и ефективността на работата в операционен блок чрез фокус върху пациента"

Обхват на проекта

Оперативни отделения и Операционен блок

Период на реализация

Септември 2010 – Март 2010

ОСИГУРЯВАНЕ НА БЕЗОПАСНОСТ ЗА ПАЦИЕНТА И ОЦЕНКА НА РИСКА ВЪВ ФАРМАЦЕВТИЧНАТА ПРАКТИКА

Доц. И. Гетов, д-р Н. Радева-Дафинова

Медицински университет София, Фармацевтичен факултет

Интересът към безопасността на пациента и нежеланите събития и нежелани лекарствени реакции не е нов. Още бащата на медицината – Хипократ е отбелязал, че медицината преди всичко трябва да не вреди на пациента, принцип по-късно изказан от Галенус в известната латинска сентенция "Primum non nocere".

Безопасността за пациента е значим и до скоро, в повечето случаи, скрит проблем в системите на здравеопазване. Докладът "To Err is Human" (1999) на Institute of Medicine на САЩ е първият, който не само разкрива неизвестни факти за грешките и нежеланите събития, но и се отнася към въпроса с конструктивен, образователен и мобилизиращ подход.

Според Техническия доклад „Подобряване на безопасността на пациентите в ЕС", изготвен за Европейската комисия и публикуван през 2008 г., в държавите-членки между 8-12% от приетите в болница пациенти стават обект на нежелани събития в процеса на получаване на здравни грижи.

Много държави насочват вниманието си към изследване на проблема и възможностите за изграждане на системи за безопасност за пациента и отчитане на грешките. Подобни системи обикновено са част от системата за оценка и осигуряване на качество.

Качеството придобива все по-голямо значение през последните две десетилетия, т.к. става фокус, както на медицинските специалисти, така и на обществото, като важен аспект на здравните грижи. Безопасността е основа на качеството и ето защо практика с високо качество не може да се достигне при липса на безопасност, т.е. адекватен контрол на риска. Безопасността и рискът са тясно свързани, тъй като безопасността не може да се измери директно, но може

да се определи количествено, ако се разгледа като "степен, в която риска е намален", с нарастване на риска за допускане на нежелано събитие, нивото на безопасност намалява.

Оценката и управлението на риска в контекста на подобряване на безопасността за пациента би могла да се представи схематично, като се набележат основните етапи в една цялостна схема на процеса, в основата на който стои комуникацията. Анализът и оценката на риска са ключови етапи в един цялостен процес. Това може да се осъществи чрез два различни подхода: проактивен и реактивен.

При реактивния подход както рискът, така и нежеланото събитие са вече факт, докато при проактивния подход се търсят потенциалните рискове, като целта му е предотвратяването или намаляването на ефекта на тези рискове преди появата им. Трябва да се подчертае, че управлението на риска ще е ефективно, ако едновременно се използват техниките и на двата анализа.

Основен инструмент на реактивния подход е т. нар. „Анализ на Основната Причина" (АОП) или Root Cause Analysis.

Реактивният подход използва различни инструменти, като най-разпространените са:

1. Анализ на слабостите и на техните ефекти върху процесите – Failure Mode and Effects Analysis (FMEA) – Инструмент за оценка и превенция на влиянието на потенциалните слабости/рискове в структурата и дейността на дадена организация, позволяващ количествена оценка на ефекта от потенциални пропуски и приоритизиане на превантивните действия за намаляването и отстраняването им.
2. Матрица на риска – Risk Matrix – Този инструмент класифицира рисковете в групи в зависимост от тяхната връзка (приложимост) на базата на вероятността за появата им и потенциалното им влияние, в случай на възникване.

Безопасността на пациента и висококачествената практика са неразривно свързани. Взаимоотношенията между отделните участници и звена са ключов елемент в процеса на качествена грижа, особено когато грижата е комплексна и включва различни специалисти и подизпълнители в една сложна ситуация, каквато е съвременната фармакотерапия. Необходимо е да се направи фокус върху нуждите на пациента за да се разбират, планират и вземат правилни решения. Пациентите често поставят комуникацията като един от най-важните компоненти при оценката на качеството на здравните грижи, докато за медицинските специалисти са водещи административните, икономически, технически и регулаторни аспекти при осигуряването на безопасност.

INTERNATIONAL PATIENT SAFETY GOALS AND INTERNATIONAL HOSPITAL ACCREDITATION: THE JCI PERSPECTIVE

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In October 2004, WHO launched the World Alliance for Patient Safety in

response to a World Health Assembly Resolution (2002) urging WHO and MemberStates to pay the closest possible attention to the problem of patient safety. The Alliance raises awareness and political commitment to improve the safety of care and facilitates the development of patient safety policy and practice in all WHO Member States.

In 2005 the World Health Organization (WHO) launched the World Alliance for Patient Safety and identified six action areas. One of these action areas is the development of "Solutions for Patient Safety". In the same year, The World Health Organization (WHO) designated the Joint Commission and Joint Commission International (JCI) as the world's first WHO Collaborating Centre dedicated solely to patient safety. Main objective was identification of affordable solutions to the most important and spread patient safety issues. JCI has introduced in all its accreditation programs, 6 specific patient safety related goals, called International Patient Safety Goals, which have become integral components of the requirements for getting the accreditation status.

Those goals are:

IPSG.1 Identify Patients Correctly
IPSG.2 Improve Effective Communication
IPSG.3 Improve the Safety of High-Alert Medications
IPSG.4 Ensure Correct-Site, Correct-Procedure, Correct-Patient Surgery
IPSG.5 Reduce the Risk of Health Care–Associated Infections
IPSG.6 Reduce the Risk of Patient Harm Resulting from Falls

The purpose of the IPSG is to promote specific improvements in patient safety. The goals highlight problematic areas in health care and describe evidence- and expert-based consensus solutions to these problems. Recognizing that sound system design is intrinsic to the delivery of safe, high-quality health care, the goals generally focus on system wide solutions, wherever possible.

Just as an example, rationale and background of the first IPSG -Identify patients correctly- it is quoted from the Manual of International Standard Accreditation for Hospitals: Wrong-patient errors occur in virtually all aspects of diagnosis and treatment. Patients may be sedated, disoriented, or not fully alert; may change beds, rooms, or locations within the hospital; may have sensory disabilities; or may be subject to other situations that may lead to errors in correct identification. The intent of this goal is twofold: first, to reliably identify the individual as the person for whom the service or treatment is intended; second, to match the service or treatment to that individual.

Policies and/or procedures are collaboratively developed to improve identification processes, in particular, the processes used to identify a patient when giving medications, blood, or blood products; taking blood and other specimens for clinical testing; or providing any other treatments or procedures. The policies and/or procedures require at least two ways to identify a patient, such as the patient's name, identification number, birth date, a bar-coded wristband, or other ways. The patient's room number or location cannot be used for identification. The policies and/or procedures clarify the use of two different identifiers in different locations within the organization, such as in ambulatory care or other outpatient services, the emergency department, or operating theatre. Identification of the comatose patient with no identification is also included. A

collaborative process is used to develop the policies and/or procedures to ensure they address all possible identification situations.

Working on IPSG can be a good starting point but, not sufficient to guarantee high quality and high reliability to hospital performance. Many more other aspects need to be considered; hospital is a highly complex system where interactions between subsystems represent a major source of potential risks. Addressing those risks means looking at the hospital as a unit, a "whole" where differences (medical specialties, professional cultures, patient and families values, different stakeholders, available technologies) must be considered and appropriate integration tools must be developed and implemented to make sure that the process of care is as safe as required and highly responsive to patients demands and stakeholders expectations.

This is basically the main reason why JCI – the international arm of The Joint Commission USA- has adopted a systemic approach to evaluate and eventually reward with accreditation recognition, hospitals or other healthcare facilities, around the world.

Meaning of Accreditation

Accreditation is a process in which an entity, separate and distinct from the health care organization, usually nongovernmental, assesses the health care organization to determine if it meets a set of requirements (standards) designed to improve the safety and quality of care. Accreditation is usually *voluntary*. Accreditation standards are usually regarded as optimal and achievable. Accreditation provides a visible commitment by an organization to improve the safety and quality of patient care, ensure a safe care environment, and continually work to reduce risks to patients and staff. Accreditation has gained worldwide attention as an effective quality evaluation and management tool.

Accreditation Programs Characteristics

JCI accreditation programs are based on an international framework of standards adaptable to local needs. The programs are characterized by:

- International consensus standards, developed and maintained by an international task force, and approved by an international Board, are the basis of the accreditation program.
- The underlying philosophy of the standards is based on principles of quality management and continuous quality improvement.
- The accreditation process is designed to accommodate the legal, religious, and/or cultural factors within a country. Although the standards set uniform, high expectations for the safety and quality of patient care, country-specific considerations related to compliance with those expectations are part of the accreditation process.
- The on-site survey team and agenda will vary depending on the organization's size and type of services provided. For example, a large multi-specialty hospital organization may require a 5-day survey by a physician, 2 nurses, and 2 administrator, while a smaller dental center or diagnostic center may only require a two- day survey by a smaller team.
- JCI accreditation is designed to be valid, reliable and objective. Based on the analysis of the survey findings, final accreditation decisions are made by an international accreditation committee

Fundamental of JCI accreditation programs is the standard concept as:A statement that defines the performance expectations, structures, or processes that must be in place for an organization to provide safe and high-quality care, treatment, and service.For hospitals accreditation program, standards are grouped in different functions, divided into two main sections, named I) Patient-centered standards and II) Organization-centered standards

Section I: Patient-Centered Standards

- International Patient Safety Goals (IPSG)
- Access to Care and Continuity of Care (ACC)
- Patient and Family Rights (PFR)
- Assessment of Patients (AOP)
- Care of Patients (COP)
- Anesthesia and Surgical Care (ASC)
- Medication Management and Use (MMU)
- Patient and Family Education (PFE)

Section II: Health Care Organization Management Standards

- Quality Improvement and Patient Safety (QPS)
- Prevention and Control of Infections (PCI)
- Governance, Leadership, and Direction (GLD)
- Facility Management and Safety (FMS)
- Staff Qualifications and Education (SQE)
- Management of Communication and Information (MCI)

Each of the mentioned functions contains a different number of standard adding up to a total number of 315.

Tracer methodology as the foundation for accurate evaluation

The tracer methodology is the foundation of the JCI on-site survey. Tracer is a process that JCI surveyors use during the on-site survey to analyze an organization's systems by following individual patients through the organization's health care process in the sequence experienced by the patients. Depending on the health care setting, this may require surveyors to visit multiple care units, departments, or areas within an organization or a single care unit to "trace" the care rendered to a patient. There are two different kind of tracer observations

Patient tracer: the process used by JCI to evaluate an individual patient's total care experience within a health care organization.

System tracer: a session during the on-site survey devoted to evaluating high-priority safety and quality-of-care issues on a system wide basis throughout the organization. Examples of such issues may include infection prevention and control, medication management, staffing effectiveness, and the use of data.

Value of Accreditation

The accreditation process is designed to create a culture of safety and quality within an organization that strives to continually improve patient care processes and results. In doing so, organizations

- improve public trust that the organization is concerned for patient safety and the quality of care;

- provide a safe and efficient work environment that contributes to worker satisfaction;
- negotiate with sources of payment for care with data on the quality of care;
- listen to patients and their families, respect their rights, and involve them in the care process as partners;
- create a culture that is open to learning from the timely reporting of adverse events and safety concerns; and
- establish collaborative leadership that sets priorities for and continuous leadership for quality and patient safety at all levels.
- Grants recognition from third payers internationally and allows improvement of competitive strategies.

From a strategic point of view accreditation process is to be considered a powerful risk prevention tool.

WHO WORLD CAMPAIGN SAFE SURGERY SAVES LIVES

Jovan Tofoski, MD PhD President of Macedonian Medical Association and Vice-President of SEEMF

Macedonian Medical Association, Republic of Macedonia

An estimated 234 million major operations are performed around the world each year, corresponding to one operation for every 25 people alive. Yet surgical services are unevenly distributed within 30% of world population receiving 25% of major operations. Very often surgery is the only therapy that can alleviate disabilities and reduce the risk of death of common conditions. Each year an estimated 63 million people undergo surgical treatment due to traumatic injuries, and 31 million more are undertaken to treat malignances and 10 million operations are performed for pregnancy related complications.

While surgical procedures are intended to save lives, unsafe surgical care can cause substantial harm. In the developed industrialized countries a number of studies suggest that major complications are reported to occur in 3 – 16 % of inpatient surgical procedures with permanent disability or death rates of approximately of 0.4 – 0.8%, while in developing countries studies suggest a death rate 5 – 10 % during major surgeries.

At a minimum 7 million surgical patients could be harmed by surgical complications each year including at least 1 million patients who could die during or immediately following the procedure. WHO underline 5 facts about surgical safety: 1. Complications after inpatient operation occur up to 25% of patients; 2. He reported crude mortality rate after major surgery is 0.5 – 5%; 3. In industrialized countries nearly half of all adverse events in hospitalized patients are related to surgical care, 4. At least half of the cases in which surgery led to harm are considered to be preventable; 5. Known principles of surgical safety are inconsistently applied even in the most sophisticated settings.

The problem of surgical safety in developing and transitional countries is additionally burdened because of poor state of infrastructure and equipment, unreliable

supplies and quality of medications, shortcomings in organizational and management and infection control, inadequate capacity and training of personnel and severe under-financing. Therefore WHO and World Alliance for Patients Safety (WAPS) initiated a global movement to promote a system-wide approach to safer surgical care could save lives of millions of people worldwide.

There is no single remedy that will improve surgical safety. It requires reliable completion of a sequence of necessary steps in care, not just by the surgeon, but by a team of health-care professionals working together within a supportive health system for the benefit of patients. Special working groups of international experts of WHO and WAPS reviewed the literature and the experiences of clinicians around the world. They reached consensus on four areas in which dramatic improvements could be made in the safety of surgical care. These are: surgical site infection prevention, safe anesthesia, safe surgical teams and measurement of surgical services.

There were identified 10 essential objectives for safe surgery: 1. The team will operate on the correct patient at the correct site, 2. The team will use methods known to prevent harm from anesthetic administration, while protecting the patient from pain, 3. The team will recognize and effectively prepare for risk of high blood loss, 5. The team will avoid inducing an allergic or adverse reaction known to be a significant risk to the patient, 6. The team will consistently use methods known to minimize risk of surgical site infection, 7. The team will prevent inadvertent retention of sponges or instruments in surgical wounds, 8. The team will secure and accurately identify all surgical specimens, 9. The team will effectively communicate and exchange critical patient information for the safe conduct of the operation, 10. Hospitals and public health system will establish routine surveillance of surgical capacity, volume and results.

WHO established the WHO Guidelines for Safe Surgery which includes a review of the evidence for interventions that can improve surgical safety in wide range settings and contexts. After evaluating the evidence of number of safety standards that could be used to improve surgical patient care they were included in the WHO Surgical Safety Checklist. While the guidelines provide evidence based, the checklist is a simple practical tool that any surgical team in the world can use to ensure the preoperative, intra-operative and postoperative steps that have been shown to benefit patients are undertaken in a timely and efficient way. By implementing WHO Surgical Safe Checklist or similar safety checks to ensure that the steps to promote safe surgery are accomplished in a systematic timely fashion, every country can improve the safety of surgical care in hospitals. Also the implementation of the checklist can enable every country to establish routine surveillance of surgical capacity, volume and results.

WHO Surgical Safety Checklist among others has three very important additional qualities: simplicity, wide applicability and what is very important measurability. The checklist will help ensure that teams consistently follow critical safety steps and thereby minimize the commonest avoidable risks that endanger life and wellbeing of surgical patients.

For significant improvement of the surgical safety it is important that each surgical team implement 10 essential objectives for safe surgery, 5 surgical “vital statistics” to measure progress and 1 Surgical Safety Checklist for each surgical procedure. It is essential that safe practices be integrated into surgical care in a

systematic way. So far around 4000 hospitals are in WHO network of this program for safe surgery from more than 120 countries.

Unfortunately, in the Southeastern Europe region still there is very small number of surgical hospitals implementing the checklist. This essential WHO Surgical Safe Checklist can be extended according to specific needs of each hospital. Presentation of this topic on The First International Medical Congress of South Eastern Europe (SEEMF) is intended to boost adoption and implementation of this simple, but very valuable tool for improving surgical safety.

Erare humanum est. Only God does not make errors, but humans can elaborate a system to decrease the errors as much as possible.

HEALTH ISSUES AND HEALTH POLICIES UNDER CONDITIONS OF ECONOMIC CRISIS – EUROPEAN AND INTERNATIONAL PRACTICE

ВТОРИЯТ СТЪЛБ НА ЗДРАВНОТО ОСИГУРЯВАНЕ – КЛЮЧОВ ЕЛЕМЕНТ НА РЕФОРМАТА В БЪЛГАРСКОТО ЗДРАВЕОПАЗВАНЕ

проф. д-р Ц. Воденичаров, дмн, Б. Борисов

Съвременните европейски системи на здравеопазване и здравно осигуряване са социално ориентирани и гарантиращи солидарност, свободен достъп, свободен избор на изпълнител, високо качество на предоставяните здравни услуги и стоки чрез активна координация на системите за социална сигурност. Характерен белег е разширяването на предприемачеството като субект на здравното осигуряване и свеждане на държавното участие до контрол върху функционирането на здравноосигурителната система за реализиране на договорените параметри.

Здравното осигуряване в Р. България е в процес на реформиране по пътя към внедряване на високите европейски принципи, директиви, стандарти и правила за професионално поведение. На фона на потребността от основно реформиране на здравната система, на народопсихологичната специфика и здравни нагласи на населението, на значителните финансови ограничения в условията на глобална икономическа криза при ниска база на БВП развитието на националната система на здравно осигуряване закономерно следва да премине през преходния тристълбов модел за достигане до стабилния двустълбов модел на задължително и доброволно здравно осигуряване.

Авторът развива своята идея за втория стълб на здравното осигуряване в България, като синтетично представя неговите основни компоненти: определение, основна цел, основни принципи, субекти на здравното осигуряване, основни дейности, общи и специални условия и изисквания за оказване на здравното осигуряване, формиране на здравноосигурителната вноска, финансово устройство, права и задължения на здравноосигурените лица, пряко договаряне на здравно осигуряване, информационно осигуряване, други параметри.
Формулират се изводи и препоръки за внедряване на преходния втори стълб на здравно осигуряване в Р. България.

ФИНАНСИРАНЕ НА БЪЛГАРСКОТО ЗДРАВЕОПАЗВАНЕ И РОЛЯ НА ИНСТИТУЦИИТЕ

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В съответствие с решенията на Европейския парламент и Европейския съвет Република България считано от 1 януари 2007 г. е редовен член на Европейския съюз. Това налага задачи от количествено и качествено естество, които българското общество и българската икономика следва да постигнат, за да се осъществи успешно догонващо развитие на България с цел достигане на средното ниво за Европейския съюз.

Както е известно, мисията на здравеопазването, изразяваща се в профилактика на болестите, диагностика, лечение и рехабилитация на болните

граждани, промоция на здравето, оценка и предотвратяване на рисковете за здравето свързани с околната и работната среда и по-нататъшното укрепване на здравето и трудоспособността на населението има водещо значение за развитието на човешкия потенциал.

Отнесени към здравеопазването на Република България тези съображения показват, че догонващото развитие на здравната система до 2020 г. следва да отчита както високото ниво на икономиката в Европейския съюз, така и динамичното развитие на икономиката в страните - членки.

Постигането на успешно догонващо развитие на здравеопазването у нас за периода до 2020 г. изисква изграждането на адекватен за горепосочените условия работен капацитет на здравната система.

Осигуреността с болнични легла на 10 000 население през 2006 г. у нас (56,8) е на нивото на средната осигуреност за страните от Европейския съюз – 58,5.

Страни близки до България по население и територия като Австрия, Белгия, Чехия, Унгария, имат значително по-висока осигуреност с болнични легла от България.

Средният престой на пациент на болнично легло е по-голям от този в развитите страни на Европейския съюз. Нивото на заболеваемостта и смъртността у нас е значително по-високо от аналогичните показатели за развитите страни от Европейския съюз. Тези данни показват, че по-нататъшното снижение на броя на болничните легла у нас е неуместно даже вредно.

Необходимо е преструктуриране на легловия фонд, като се увеличат леглата за долекуване и продължително лечение за сметка леглата за активно лечение.

Анализът на данните от Националната статистика показват, че през последните 16 години числеността на персонала в здравеопазването е намаляла с около 90 000.

Сред основните причини за това намаление следва да отбележим:

- Обстоятелството, че основните съставни части на капацитета на здравеопазването (болнични легла, лекари, стоматолози, фармацевти, медицини сестри, акушерки и други) през етапа на централното планиране се съобразяваха с разчетите за потребност на населението от медицинска помощ, което доведе до висока осигуреност с болнични легла и медицински персонал. Това наложи след въвеждането на пазарни елементи в здравеопазването след 1998 г. да се пристъпи към значително редуциране на броя на болничните легла, както и към кореспондиращото с това намаление на щатовете на персонала в здравеопазването.
- Обстоятелството, че клиничните пътеки покриват до 60 – 70 % от реалната стойност на лечението и че 40 % от цената на клиничните пътеки следва да се използва за заплащане на труда води до редица дейности, съкращаващи щатовете на персонала: наемане на фирми за охрана, почистване, изпиране, кетъринг и други обслужващи дейности. След тези съкращения посочените 40 % от цената на клиничните пътеки се разпределят между по-малък брой персонал.

- Ниските трудови възнаграждения и свободния трудов пазар на Европейския съюз създават условия за обезлюдяване на амбулаториите и болниците в България, като първи си тръгват младите лекари и медицински сестри.

Отчетите на НСИ за 2006 г. показват достигнато ниво на БВП - 49090,6 млн. лева, което отнесено на глава от населението възлиза както следва:
6376,2 лева или 4088,4 щатски долара или3260,1 евро.
Разчетените на тази икономическа основа публични разходи за здравеопазването през 2007 г. възлизат на 2216 млн. лева. Това прави около 4,4 % от очаквания БВП на страната за 2007 г. На човек от населението тези разходи възлизат както следва: 244 лева или 189 щатски долара или 125 евро.

Макар и увеличена с около 200 млн. лева спрямо 2006 г., посочената сума на публични разходи за здравеопазването го обрече на хронично недофинасиране. Чрез осъществяването на национални програми в областта на здравеопазването държавата е в състояние да провежда ефективна политика, насочена към важни за етапа национални здравни приоритети. Тези национални програми следва да се одобряват от правителството и да се финансират основно със средства от държавния бюджет.

В изпълнение на отделни инициативи на СЗО или Европейския съюз могат да бъдат приети за изпълнение и регионални програми с международно значение.

Проучено бе мнението на 431 здравни мениджъри от цялата страна по въпроси, отнасящи се до реформата, капацитета на здравеопазването, основните проблеми и националните здравни приоритети:

Отношението на анкетираните здравни мениджъри:

към модела на ПМП в (70 %) е положително и удовлетворително;

към модела на специализираната доболнична медицинска помощ е в (69,1 %) положително и удовлетворително;

към модела на болничната помощ отношението е в (47,2 %) негативно.

По отношение на финансирането най-голямо недоволство показват здравните мениджъри към финансирането на болниците от НЗОК (33,9 %). Известно е, че клиничните пътеки покриват около (60 – 70 %) от реалните разходи за стационарно лечение.

Анкетираните препоръчват приемането на следните нови закони:

Закон за защита правата на потребителите на здравни услуги.
Закон за майчиното и детско здравеопазване.
Закон за допълнителното здравно осигуряване.

Беше разработен модел, предвиждащ плавно нарастване на относителния дял на публичните разходи за здравеопазване от държавния бюджет и от НЗОК средно с 0,1 – 0,2 % годишно за целия период;

С оглед осигуряване изпълнението на редица национални програми, целящи решаването на приоритетни за държавата здравни проблеми, моделът предвижда също плавно нарастване на средствата, заделени от държавния бюджет за Министерствата и ведомствата.

Запазва се относителният дял от 1,9 % на разходите на домакинствата за здравеопазване до 2015 г., а от 2015 до 2020 г. този дял се завишава на 2 %.

Тенденцията, заложена с този показател на модела, е задържане на нивото на разходите на домакинствата за здравеопазване.

Моделът предвижда постепенно завишаване участието на ДЗОФ във финансиране на здравеопазването, като през 2015 г. – този дял достига 1,4 % от БВП, а през 2020 г. – 2,0 %.

Като краен резултат по финансовия модел се достига относителен дял на разходите за здравеопазване при оптимален сценарий за 2015 г. – 9,1 %, а за 2020 г. – 10,5 %. Ако това бъде постигнато по този показател се изравняваме с нивото на останалите страни в Европейския съюз.

Разходите на глава от населението за здравеопазване даже и при оптималния сценарий достигат едва 715 щ.д. през 2015 г. и 1161 щ.д. през 2020 г. Тези данни показват, че поради сравнително ниския БВП и при оптималния сценарий по показателя разходи на глава от населението за здравеопазване през 2020 г. ще достигнем ниво под средното за Обединена Европа. Този прогнозен показател, съпоставен с препоръчаните от анкетираните здравни мениджъри разходи на глава от населението, показват определено сходство.

Посочените по-горе резултати показват, че даже и през 2020 г. Българското здравеопазване ще работи в условия на недостатъчно финансиране.
Анализът на данните, получени от гореизложената разработка, показват необходимостта от:

- ефективно използване на наличните ресурси;
- промяна на модела на финансиране в посока към неговото либерализиране;
- въвеждане на система от данъчни облекчения за работодатели и отделни граждани в процеса на доброволното здравно осигуряване.

Изграждането на капацитета като съвременен системен подход за постоянно изучаване как да бъдат подобрени способността и потенциала на институцията, за да могат да бъдат използвани най-ефективно и най-пълноценно нейните човешки, материални и финансови ресурси е придобил през последните години широко разпространение в икономиката на развитите страни.
Във връзка с това могат да се отправят следните препоръки към Министерството на здравеопазването:

- Разработване на предложение за промяна на финансирането на здравеопазването чрез надграждане.
- Внедряване на актуализирана Национална здравна карта и преструктуриране на болничната здравна мрежа.
- Регламентиране на приватизацията в болничното здравеопазване и въвеждане на адекватно за настоящия етап публично / частно партньорство.
- Ограничаване на монопола на НЗОК и запазване на всички принципи, въведени чрез осигурителния модел.
- Запазване на финансирането от бюджета на следните дейности: хемодиализата, спешната медицинска помощ, психиатричната помощ, онкологичната помощ, диспансерите, ражданията, инфекциозната заболеваемост, ТЕЛК, РИОКОЗ.

SOCIAL MARKETING AS AN INSTRUMENT OF VOLUNTARY HEALTH INSURANCE

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The mission of marketing is to balance between the three types of interests: the consumer, the company and society to ensure a more desirable, better, more sufficient and more efficient goods or services. The problems of marketing in health care require a broader approach than the standard market close vision. According to some experts in health pure pursuit of market efficiency can work against justice (Delcheva E. E. Callahan, etc.). There may be so called market failures in health care such as "moral hazard" (moral gambling), selection of risk (risk aversion), "adverse selection" (selection of wealthier patients), etc. This can lead to an increase in the percentage of dissatisfied health needs.

On this basis, a trend emerged for social (or socio-ethical) marketing. Socio-ethical marketing is directed primarily to the realization of social control on the market in terms of long-term benefit to society, adequate law and morality (Ph.Kotler).
In voluntary health insurance this trend makes the need for reliable information to customers-patients. Difficulty of implementation of socio-ethical marketing is poor or unfair competition between health insurance funds.

Reorientation of traditional commercial marketing to a new style of social-ethical marketing leads to increased importance of information on health needs as a criterion to assess the overall marketing culture in a hospital. In this aspect very important challenge to health insurance management is the realization of marketing, based on knowledge of the specific health needs and social assessments.

Patients perceive the different health insurance funds and doctors are not always specific. We need a health insurance fund to show their clients how patients differ from others and to show how consistent expectations and claims of patients with the quality of health services. Health insurance fund should provide the necessary support, information and orientation of the patient to take the right decisions about their health, diagnostic and therapeutic procedures.

This inter alia may reduce interference in the relationship between patients and medical personnel, and conflicting situations with them.

THE CONCEPT OF SUSTAINABLE HEALTH SYSTEM

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Disturbing conclusions and recommendations in the famous report "Our Common Future» was conceptual basis for the preparation of the UN Conference on

Environment and Development in Rio de Janeiro in 1992, there was formulated the concept of sustainable development in the XXI century forthcoming.

The concept of sustainable development defines as a sustainable society that meets the needs of today's generation without depriving future generations the opportunity to meet their needs. So you can ensure human progress through development, which does not destroy resources for future generations.

In Bulgaria's transition to a market economy and the process of integration requires the uninitiated to develop an integrated and comprehensive national strategy for sustainable development in the XXI century. It is imperative to overcome the inertia of highly specialized and limited only bring problems to environmental pollution to endangered species and so on. The fundamental nature of sustainable development requires an integrated approach in solving problems. This is the point to update all aspects of policy and primarily social and health policy with its exceptional, vital importance to achieve a sustainable society.

New challenges in the areas of social and health equity, cultural diversity, economic stability, environmental protection and optimal use of scarce resources.

Concepts and strategies for sustainable development is a new style of thinking and action not only globally but also the level of individual nations and their regions, and the level of individual sectors and institutions.

In healthcare, the concept of sustainable development has not yet found its full and adequate development and administration. In publications on health reforms rarely focuses on the sustainability of health systems. Therefore, strategies and health policy concepts of these reforms suffer from insufficient integrity, unclear priorities and occasional risks in their practical realization.

Such situation obstacles the sustainable development of the health system, leading to its destabilization and low medical-social and economic efficiency.

This trend is demonstrated very vividly in our process of health reform that started after 2000. According to experts in healthcare management one of the main negative effects of this reform is the destabilization of the national health system. The main factor of this instability is the lack of consistently occurring long-term vision and strategy.

Contributions were also defective health laws that are adopted without fractional correlation between them. Hence the necessity of accurately developed a comprehensive long-term vision for sustainable health development in Bulgaria in its systemic integrity. We think this is a general challenge to the strategic health management in Bulgaria now and in coming years.

STRATEGIC MANAGEMENT - BASIC DEFICIT OF HEALTH REFORM

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Cardinal change in our health system breeds acute need for a new style of management thinking and action. The new generation of healthcare leaders in Bulgaria

must have a clear strategic vision in the difficult transition from rigid administration to a modern, creative management style.

Observations indicate that in the current health reform dominated the enclosed short-term operational thinking in almost complete absence of large-scale and long-term strategic forecasts. Change "blind" or "as time" is not uncommon. This type of change is expressed mainly by power reforms under the dictates of urgency, fashions, recipes, and learned models, revolutionary enthusiasm, political situation etc. Examples in this direction are: shock unprepared introduction of Commercial Law, GPs, irresponsible eradication of clinics, school health and many others.

New organizational culture in health care involves primarily sound strategic vision, overcoming administrative approach to problems. Competent vision for fundamentally changing the health organization is essentially a global vision and should therefore be developed as a consensus among top managers, ie higher political and strategic level of management. Responsibility for such a vision can not be delegated to lower management levels.

Basic principles, respectively. criteria of strategic thinking in health managers are contained in the so-called. triad of the three "P":

• Priority - requires global vision summary and systematic thinking.
• Prognosis - requires long-term vision and thinking.
• Pluralizm - requires alternative (variant) vision and thinking.

Strategic management is a new philosophy and style of management in healthcare, which overcomes the shortcomings of the daily operational (internal, closed) thinking of managers.

Strategic management is the specific management of change. It sets long-term objectives of the health system through comprehensive analysis of the situation. He looks for ways to deal mainly with the unexpected, not only for improving the status quo.

Strategic management focuses on risk and uncertainty in order to ensure long-term adaptability of the health organization to the changing environment (political, economic, cultural, social).

Intentions for imminent change in health is a serious challenge to strategic thinking and action of the leaders of the national health system. In light of the concept "Evidence based medicine» is imperative that any new managerial decision for change to be clearly justified and proven concerning its strategic effectiveness.

PROFESSIONAL CAREER OF YOUNG DOCTORS - DIFFICULTIES AND PROSPECTS

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In general issue of human resources management in health care become increasingly important issues for young doctors. These problems have their quantitative and qualitative aspects. Qualitative aspects related to the quality of training and qualification level of young doctors in their professional start and route, with real prospects and difficulties of their professional career.

The problem of young doctors is particularly acute in the public hospital sector and should be considered and decided as a priority management problems for medical institutions.

More relevant decisions of hospital management in district hospitals on the stabilization of the staff and doctors in particular, establishing conditions for the realization and development of physicians with the least seniority.

A problem for the professional satisfaction of young doctors is of great importance. Our data show that it is unsatisfactory.

Directly related to this problem is turnover of young doctors. There are two types of turnover – real and potentially implemented. According to the author's tendency for potential turnover is high and it must be specifically analyzed by hospital managers in order to stabilize the young doctors and their whole career. The report justifies specific approaches to reduce turnover of young doctors in hospitals.

INADEQUACY THE HEALTH SYSTEM IN SERBIA AND CORRUPT INSTITUTIONS

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Rapid changes in the health system require a new trained professionals who fully understand the processes of health and organizational problems and have the knowledge and skills that enable them to manage health care services. Health services to their largely rests on a system of solidarity and "socialism", and only partly on market principle, and more than in other sectors of the economy requires individuals who are able to bridge that gap. Realize savings in the system that one side is not profitable, on the other hand is able to swallow a huge media arts is that simply needs to learn - just relying on common sense and intuition that no longer helps. The increase in costs.

Advances in medicine and technology, and discovery of new drugs, namely, the almost daily increase the costs of diagnosis and treatment. Advances in medicine prolongs life expectancy by increasing the number of patients, especially those with chronic diseases, the biggest consumer of drugs and frequent guests hospital. The development of civilization and way of life associated with it - poor diet, lack of physical movement, stress - creating more and more patients and more disease. The need for trained personnel are higher in countries whose health is a significant part of the market and management, "which has a business - where revenue has increased accountability for its allocation and spending.

TIME MANAGEMENT IN MODERN HOSPITAL

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The role of time as a complete resource of health is still underestimated by healthcare managers. When looking for hidden untapped resources to increase efficiency are not talking about the weather. Effective management of the resource at the forefront the issue of time-budget - it must have its logical structure. Responsibility of the hospital manager is to identify the basic elements of this structure and the amount of each element in hours, minutes and rates.

According to some observations useful ratio of real time is very low and the need for proactive management of time in hospital is particularly acute. Data of different authors for spending time in hospital are varied. Most aggregate time for direct contact with patients (history, examination, visiting) varies between 40 and 60%, for indirect production time (working meetings, written work) - 35 to 40%, unloaded time (holidays, breaks, etc. .) - 5 to 15%. There are large variations between individual doctors, thereby hindering the establishment of norms and standards at the time cost of medical staff.

According to our records the expenditure of time by surgeons for direct contact with the patient (without medical intervention) moving average of 91 to 95 minutes per shift, and the costs of intern from 103 to 107 minutes (approximately 25-30% of working time)..

Key to effective time management is the ability to set priorities. The problem is what percentage of the structure of time is spent for high priority tasks. Initial tests show that a particular chief divisions and clinics spend no more than 40 percent for high priority tasks.

Kingcraft art of time management is the art to manage our own priorities. We can not manage time itself as a natural phenomenon, we can manage ourself in time. So the problem "Time Management" is essentially a problem of "selfmanagement" of the hospital staff.

The structure of time-cost is not an constant value. It varies depending on the organization of work that reflects managerial skills of hospital manager, and especially line managers of fixed points - Head Boards and senior nurses.

Time is a crucial resource and its skillful management and utilization should be the primary concern of every hospital manager.

ON THE NECESSITY OF COMPARATIVE ANALYSIS OF HEALTH REFORMS

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The object of the presented article is to discus the importance of the comparative analyses in the process of comparative healthcare reforms. These analyses requires a reliable information about different aspects of the organizational change in the national health systems. There are some types of comparative analyses of healthcare reforms – international, regional, public and professional analyses. With a view to good analyses it is necessary to cumulate broad comparative information on standard indicators concerning the process of healthcare reforms in different countries.

Since each health reform necessarily affect the relationship between health professionals and patients (population), then special attention should be paid to information and monitoring of public opinion, public attitudes, expectations and evaluations of the progress of change in healthcare.

WHO concept of New public health issues rise to some discussion on the principles and implementation of health reforms. This aspect is an interesting comparative analysis of health trends in the European Union and the Balkan region. In the former socialist countries in the Balkans a major driving force of health reforms were not deep scanning and analysis of problems, but rather a momentary political pressures and external models.

Against this background, the need for increased research partnership is especially evident in countries of the Balkan region.

The comparative analysis should be compliance with corrective solutions to optimize the process of health reform. It is appropriate to regulate the systematic monitoring and evaluation processes of organizational change in healthcare system. For this purpose, we need to periodically collect data on various indicators of the progress of health reform.

Is an urgent need for a comprehensive comparative analysis between public satisfaction with health care reform and professional assessment and satisfaction.

MISCELLANEOUS

ПСОРИАЗИС – СИСТЕМНИ ПРОЯВИ ПРИ КОЖНОТО ЗАБОЛЯВАНЕ

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Псориазисът е кожно заболяване, което се характеризира с формирането на еритемопапулосквамозми плаки. Веднъж появила се болестта съпътства целия живот на пациента като риск от рецидив винаги съществува. Кожната болест влошава значително качеството на живот на пациентите. Проучвания го сравняват с това на онкоболни или болни с тежки сърдечносъдови заболявания.

Псориазисът е значително асоцииран с метаболитен синдром, като в резултат рискът за развитие на сърдечно-съдови, мозъчно-съдови заболявания при тези пациенти е значително повишен. Едно от най-вероятните обяснения е системното възпаление, на което са изложени тези болни. Връзка се търси и в сходството в патогенезата на атеросклероза и псориазис.

МЕДИАТОРИ НА ВЪЗПАЛЕНИЕТО ПРИ ГРИП А/ H1N1/ - АСОЦИИРАНИ ПНЕВМОПАТИИ

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Авторът анализира клиничните резултати при 20 пациенти със свински грип А/ H1N1/ в област Шумен м.XI.2009 год. в „МБАЛ Шумен”- АД постъпили с картина на ОДН за интензивно лечение в ОАРИЛ.Групата включва 12 жени и 8 мъже. Средна възраст 48 год. ± 3. Основната група пациенти обхваща възрастта 31-60 год. – 14 случая 70%. От тях 8 пациента с утежнена придружаваща патология.- наднормено тегло – 75% - 6 случая / вкл. и дете на 9 год. /60кг/.- Захарен диабет . 38% / 3 случая/

Поради ниската честота на изолиране на патогенна флора - 25% необясняваща тежкото клинично протичан е проведеното имунологично изследване на:- плазмени цитокини (TNFα, IL-1, IL-6, IL-10) - антифосфолипидни автоантитела (ACA , B2GP1, APA)

Въз основа на клиничните наблюдения и резултатите от лабораторни изследвания, авторът мотивира хипотезата, че тежкото и фатално протичане на вирусната инфекция AH1N1 е свързана с масивното освобождаване на цитокини - цитокинова „буря” прерастваща в унищожителен „смерч”за клетките на алвеоларния апарат.Разгледана е патогенезата на цитокиновата буря и възможността за преодоляването й.

КАТАСТРОФАЛЕН АНТИФОСФОЛИПИДЕН СИНДРОМ

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Авторът разглежда участието на антифосфолипидните антитела в патогенезата на антифосфолипидния синдром /APS/ - сложен патогенетичен механизъм, отключен от инхибиращия ефект върху различните антикоагулационни системи, директното активиране на тромбоцитите, левкоцитите и потенциране на клетъчната апоптоза. Разгледани са основните клинични прояви на APS в различните клинични специалности, като особено внимание е отделено на пациентите, станали обект на интензивно лечение в ОАИЛ.

Материал и метод: Анализирани са пациенти на интензивно лечение с клинични белези на APS. Проследени са резултатите от имунологичните изследвания и нивата на антифосфолипидните антитела, тежестта на клиничното протичане и резултатите от интензивното лечение.

Резултати и обсъждане: Съпоставя се констелацията между клиничното протичане и имунологичните маркери. Обсъжда се възможността за своевременна диагностика на APS със съответното поведение и лечение.

Изводи: Високата честота на наблюдаваните патологични промени при пациенти на интензивно лечение и опасността от CAPS налага целенасочено търсене и верифициране на този синдром в практиката на интензивните отделения.

REVIEW OF IMMUNIZATION PROCESS FOR YEAR 2009 ON THE TERRITORY OF SKOPJE AND LOCAL DISTRIC AREAS

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Prevention, disease prevention is the key of the preventive public health. It is always better to prevent a diseass than to treat it.The most effective way to reduce disease and death from infections disease is to vaccinate suspectible population.

Aim: Review of realized vaccination for year 2009 on the territory of Skopje and local distric areas.The aim of preventive teams was to achive high level,more than 90% of the vaccinated plan,with results for high collective immunity. That will guarantee good epidemiological status on the territory of skopje and around.

Material and methods: In year 2009 vaccination was realised by 42 preventive teams, from which 23 for children 0-6 years old.

Conclussion: In year 2009 procent of realization of the primovaccination was 96,1,recruitment in the city area was better than in the distric areas. Suppliment with the vaccines was regular by the central store of Ministry of Health, taking care for the cold way of transport. Perspective ideas for more quality realization of the children vaccination

ROLE OF BIOACTIVE PEPTIDES IN PAIN

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Bioactive peptides are important starting structures for the development of potential therapeutic agents. They bind to different receptors (opioid, non-opioid or both) and are involved in a wide spectrum of physiological functions – cardiovascular, respiratory, gastrointestinal, renal, behavioral, analgesic and etc. In addition to pain inhibitory pathways, which include endogenous opioid systems, several lines of evidence suggest that there are "anti-opioid" neuronal peptide systems which act in an opposite manner by blocking pain inhibition. Besides reducing the acute effects of opioids, the triggering of anti-opioid systems by opioids themselves could explain, at least partly, the development of tolerance and dependence to opioids.

Currently available data showed that the most studied anti-opioid peptides (cholecystokinin (CCK), nociceptin (OFQ/N) neuropeptide FF (NPFF) and Tyr-MIF-1 family of peptides) in fact have complex properties: they can act as opioid as well as anti-opioid peptides (AOP). This suggest that "opioid modulating peptides" would be a better term to designate these peptides, and that the systems of multiple feed-back loops they actually form with the opioid systems take place within the framework of the classical and general concept of homeostasis. Generally, they have been shown to act through the activation of opioid and their own receptors.

The knowledge of their mechanisms of action has potential therapeutic interest in the control of opioid functions, notably for alleviating pain and/or for the treatment of opioid abuse.

INFLUNCE OF NEWLY SYNTHESIZED TYR-MIF-1'S ANALOGUES ON TYROSINE HYDROXYLASE

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All living organisms respond to stress changes in environment in various ways. The stress system has to major divisions: central and peripheral. The central division is represented by the medullary and hypothalamic nuclei whose neurons release corticotrophin releasing factor (CRF), catecholamines and arginine-vasopresin.

Regulation of the stress system is extremely complicated and occurs at multiple levels. Activation of the stress system leads to behavioral and peripheral

changes to improve the ability of the organism to adjust homeostasis and increase its chances for survival.

Many stress models have been reported to affect the levels of catecholamines and stimulate the gene expression of enzymes (tyrosine hydroxylase, TH) engaged in their synthesis.

Literature data showed that periaqueductal gray (PAG) is a major module in the circuitry mediating stress-induced analgesia. Also, many stress models have been reported to affect the opioid receptors within the PAG and expression of tyrosine hydroxylase (TH) which activate descending opioid and noradrenaline inhibitory pathways and suppress nociception. On the other hand, Tyr-MIF-1 is neuropeptide/ neuromodulator, which is able to inhibit the expression of some forms of stress.

Knowing that stress affect the level of opioids, catecholamines, neuropeptides, our aim was to investigate the effects of newly synthesized Tyr-MIF-1 analogues containing citrulline (Tyr-Cit-MIF-1) and canavanine (Tyr-Cav-MIF-1) on NOS and TH expression in PAG after immobilization stress in rats.

The obtained results revealed that investigated peptides mentioned above decreased expression of TH in PAG in immobilized rats.

TRACHEO-BRONCHIAL FOREIGN BODY IN CHILDREN

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From January 2005 to December 2007 in 49 patients aged 7 months to 14 years inhaled foreign bodies (FB) were extracted from the tracheobronchial system. Eighty percent of the children were younger than 3 years. 61.2 % were in the second year of life. There were four as many boys as girls. Eighty percent of the FB were nuts, of these more than 48% were peanuts. Fifty-nine percent of inhaled FB was localized in the right bronchial system, 36.7 % in the left and 4.01% in the trachea. All FB could be removed by endoscopy. There were no complications, no postoperative tracheotomy was necessary, no cardiac arrest and no death occurred.

The interval between inhalation and intervention was longer than 3 weeks in one-fifth of the cases; in four cases it was longer than 3 months with the consequence of chronic damage on the bronchial system. The possibilities of prevention appear to be limited; thus it is necessary to diminish the frequency of prolonged lodging of FB in the respiratory tract by considering inhalation early in the differential diagnosis of airway symptoms.

NOVEL IMMUNE MODULATING THERAPY: TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO BASIC THERAPY

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Background: Modern progress in pharmaceutical development as well as in the understanding of the immunopathogenesis of rheumatoid arthritis (RA) have allowed the introduction of new immune modulating therapies for this disease. This has spurred the development of biologic agents targeting components of the aberrant immune response in respect to the occurrence and sustenance of the immune driven systemic inflammation characteristics typical for RA. One of the cytokines with effects on numerous cell types including those involved in the pathogenesis of RA is IL-6. Numerous studies on the effects of inhibitors of IL-6 were conducted on animals and subsequently on humans, which showed that IL-6 appears to be a viable target for autoimmune disease. Our experience is with tocilizumab, a humanized monoclonal antibody specific for the IL-6 receptor (IL-6R). It has been shown to be of significant efficiency in patients with RA. The objectives of the present article are to report the efficacy and safety of tocilizumab in patients with active RA in clinical practice.

Methods: In total, 8 patients (all women), with severe disease activity, were treated with tocilizumab. Any prior infections, as well as other comorbidities, were treated before they had been given the drug. Guidance on disease control and prevention was given. During treatment, one patient was diagnosed with pneumonia and therefore application of tocilizumab was ended. Mean age of the patients was 49,5±8,28, while their mean disease duration was 8,42±8,75 years. Before the application of tocilizumab the patients were treated with basic therapy including different combinations of metotrexate, resochine, steroids, and two with rituximab, but without satisfactory effects. Patients remained on metotrexate, steroids and nonsteroid anti-inflammatory drugs during the treatment with tocilizumab.

Results: Mean DAS28 score was 6,59±0,79 initially, and fell to 4,86±1,04 after three doses (n=7). After three doses all patients were significantly improved, the remission rate was 28,57% (2 patients) and all had achieved moderate disease activity. With the notable exception of one patient who developed pneumonia because of which application of tocilizumab was ended, all others responded well to therapy and there was no decrease of efficiency of tocilizumab during the treatment.

Conclusion: Tocilizumab has been shown to have significant efficiency in patients with RA. Treatment with this agent can rapidly induce remission in RA in a high proportion of patients and is generally well tolerated. Tocilizumab would seem to be a promising treatment option, even as a possible first-line choice in the management of RA. Studies, on a large scale, analyzing its effects in varied populations of RA patients, as well as greater detail concerning its long-term efficiency and safety of tocilizumab is needed to more precisely define its role in the treatment of RA.

APPROPRIATE MARKERS FOR OXIDATIVE STRESS LEVEL IN HEMODIALYSIS PATIENTS

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Background: Oxidative stress (OS) is common in hemodialysis (HD) patients that may lead to atherosclerosis, hypertension and other related disorders. The aim of the study was to examine the appropriate markers for oxidative stress determination.

Material and method: A number of 55 HD patients (20 female and 35 male, at mean age of 43±17 years) were examined. They were exposed on hemophane (n=21) and polusulphone (n=34) HD membranes. A control group of healthy subjects (n=38) was examined as a control one. For determination of antibodies against oxidazed LDL, an enzymatic immunoassay was used (Biomedica gruppe, Austria). Lipid peroxidation (LP) was used by Yagi fluorimetric method. Lipid profile was determined by determination of cholesterol and tryglycerids by enzymatic color test Vitros 250 (dry chemistry Ortho Diagnostic Johnson-Johnson, USA) and HDL and LDL determination by photometric method (Chod-pap Merck, Germany). For all the patients undergoing HD with average duration of 4 to 5 hours, bicarbonate buffer was used and none of them was given antioxidative agents.

Results: In HD patients, LDL-ox antibodies showed increased levels: 356±259 mU/ml on hemophane membrane ($p<0.01$) and 220±125 mU/ml on polysulphone membrane ($p<0.05$). Lipid peroxidation level has also showed increased values of 5.36±0.98 μmol/L for hemophane ($p<0.01$) and 4.52±0.22 μmol/L for polysulphone membrane ($p<0.05$). For tryglicerids, a significant increased level was found in all HD patients on both membranes: hemophane 2.37±0.7 mmol/L ($p<0.01$) and polysulphone 2.28±0.7 mmol/L ($p<0.01$) as well as decreased HDL level, 088±0.4 mmol/L for both HD membranes ($p<0.01$). No significant difference was noticed for both markers, cholesterol and LDL in all HD patients.

Conclusion: Due to obtained results, increased values for LDL-ox antibodies and LP (for both used membranes) show that OS is present in HD patients compared to the control group, although no statistical difference for some lipid profile markers was found. According to this, more recommended OS markers would be the LDL-ox antibodies and LP for the examination of OS appearance and for its follow-up, respectively.

PREHOSPITAL TREATMENT OF SUPERFICIAL BURNS OF FACE AND NECK

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Background: When heat trauma happens on a face and neck what is very important is the proper prehospital treatment. Often in the initial phase of burns of the first degree found on the face and neck are easily understood which represents vitium artis. Knowing that the face and neck are with predominantly loose tissue, it is typical that with superficial burns of this region edema is quickly created. In the burnt surface within the first 12 hours there exists an uninterrupted blood flow, but during 24 hours hypoperfusion occurs and area of hyperemia with extravasations. Survival of these burns is not brought into question and the scars do not exist.

Methods: In our material we have treated 42 people from 16 to 75 years of age. We went by the principal: to create optimal physiological conditions for epithelization and to actively influence the course of treatment.

Results: Twenty six patients from people we examined came at 2 to 6 hours since the occurence of trauma depending on the growth of pain and swelling. Important factor in prehospital treatment of facial and neck burns is to decrease the pain because it is a neurogenic area, which we did through constant infusion of analgesics in ringer lactate and local application of gauze packs with 0,9% NaCl. Conjunctivitis rinse (treatment) with 0,9% NaCl, in case of pain local anesthetic in form of an eye drops and after that local application of antibiotic ointment for eyes. In the other category of patients which came at the first or second day after the injury, additional and more aggressive treatment was implied, especially if signs of local contamination or infection are visible. Within 16 patients of this kind we were more persistent with wound cleaning from extravasations i.e. secretion with preserved potential of spontaneous healing. In these cases enzyme necrolytics have been applied in hospital conditions. With all 16 patients the smear of a wound was positive. On this second category of patients who came in late, systemic antibiotics were applied.

Conclusion: Regular prehospital care of superficial facial and neck burns requires a very careful approach and it always begins right after the patient has been taken in. Our recommendation is that this group of patients gets hospitalized right after receiving appropriate prehospital care. Thereby in making such decision we go by certain parameters: condition of the injured, anatomic details of the injury, mechanism of injury (flame or water) and comorbid factors. Finally, the aim of this recommendation with this kind of analysis in the initial examination is to follow these rules which provide safe procedure during the treatment.

EFFECTS OF TYR-MIF-1'S ANALOGUES ON NITRIC OXIDE SYNTHASE IN PAG

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The question of the role of nitric oxide (NO) in physiological functions has been studied intensely in recent years. It's now clear that NO system affects the secretion of stress hormones and fulfils the main criteria of a stress-limiting system. NO is synthesized by the enzyme nitric oxide synthase (NOS), which had widespread distribution in the brain. Also, NO is involved in NO-molecular ways, which affect through auto regulation different signaling molecules – like opioids, endocanabiotics and others.

It's known that periaqueductal gray (PAG), a midbrain region surrounding the aqueduct, is a major module in the circuitry mediating stress-induced analgesia, as it sends descending inhibitory fibers to the medulla, which in turn modulates incoming noxious signals in the spinal cord.

One of the mechanisms known to play a part in the response of an organism to stress is activation of the endogenous opioid system. Neuropeptide Tyr-MIF-1 takes part in various functions as hormone or neuromodulator and inhibits the expression of some forms of stress.

The aim of our study was to investigate the effects of newly synthesized Tyr-MIF-1 analogues containing citrulline (Tyr-Cit-MIF-1) and canavanine (Tyr-Cav-MIF-1) on NOS expression in PAG after immobilization stress in rats.

The obtained results revealed that investigated peptides mentioned above decreased NOS expression in PAG of rats set on immobilization.

THE USEFULNESS OF BIO FM MEDIUM IN COMPARISON WITH LOWENSTEIN JENSEN FOR RAPID DIAGNOSING OF TB IN CHILDREN

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Background: The objective of the study was to assess the ability of Mycobacteria growth on Bio FM medium as a diagnostic technique for Mycobacteria in sputum and to compare sensitivity to Lowenstein Jensen culture.

Methods: A prospective clinical study of 24 Mycobacterium – positive samples on conventional medium were tested on Bio FM liquid medium.

Results: 23/24 samples (95,84%)showed growth on Bio FM medium, while 24/24 (100%) on Lowenstein Jensen.
The average days in Bio FM to positivity is 16,8 days, than in Lowenstein Jensen 28,9 days.

Conclusion: Bio FM is useful, timesaving culture for detecting Mycobacteria, with identical sensitivity as Lowenstein Jensen (p>>0,05).
It is very important in pediatrics cases where smear positivity is low, and Bio FM is a good way for rapid and significant diagnosing of TB in children.

THE ROLE OF HOSPITAL MANAGER IN APPLICATIONS OF DISINFECTION AND STERILIZATION

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Background: Outline the issues related to role of hospital manager in application of D&S (disinfection and sterilization);Analyze the qualifications of the hospital manager;
Review the challenges of hospital managers are facing; What is needed for functional hospital management?.

Method: We analyzed the current data about issues, qualifications and challenges of the hospital managers in applications of disinfection and sterilization.

Results: Safety (patient, occupational, standards), quality (policy, management, documentation, training and permanent schooling, information and knowledge and certification)

Conclusions: The success of the D&S is the result of the work done on the floor with the help of the H.M. (hospital manager);
H.M. is the link with the industrial partners;
Without industrial scientific research D&S would not have made the progress it has made;The goal is to minimize the risk of infection within the healthcare setting world wide through development of a network of infection control organizations for communication, consensus building , education , and sharing expertise;
For functional hospital management is needed: Good structure, Training, Duties and responsibilities, Operating procedures.

DELAYED GRAFT FUNCTION IN RENAL TRANSPLANTATION: RISK FACTORS AND SHORT AND LONG-TERM SIGNIFICANCE

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Background: Delayed graft function (DGF) is a common complication of renal transplantation. The short-term consequences of DGF are well known, but the long-term relationship between DGF and patient and graft survival is controversial in

the published literature. We analyzed the risk factors of DGF and its association with acute rejection (AR), and histological evidence of subclinical (SR) and borderline changes (BC) in protocol biopsies performed early after transplantation (Tx), as well as its impact on graft function and survival at 1 and 5 years after transplantation.

Methods: Forty-two consecutive living related kidney transplant recipients were included. Protocol biopsies were performed at 1-month after transplantation. Patients without evidence of DGF (N=12, non-DGF group), and those with DGF (N=28, DGF group), were compared.

Results: The groups differed significantly in the mean cold ischemic time (CIT) and time on dialysis (3.2±1.1 vs. 4.0±1.3 hours, $p<0.05$; 8.0±6.9 vs. 34.7±40.9 months, $p<0.01$) for non-DGF vs. DGF group, respectively. The DGF group had a significantly higher percentage of acute rejection (AR), borderline (BR) and subclinical rejection (SR) at 1-month biopsies 39% vs. 8% ($p<0.05$); 89% vs. 58% ($p<0.01$); and 75% vs. 32% ($p<0.01$); respectively. DGF was associated with a 38% relative increase in the risk of acute rejection (RR 1.38, 95% CI 1.29-1.47).

Patient with DGF had significantly higher mean serum creatinine (181.6±60.3 vs. 127.0±53.4 mmol/l; $p<0.05$) when compared to patients without DGF at 1-year follow-up. However, there was no significant difference in the graft function and survival between the two groups at 5 years after Tx.

Conclusion: The results of this study confirmed prolonged cold ishemia time and time on dialysis as risk factors for DGF, as well as its association with significantly higher evidence of subclinical rejection and borderline changes in the first post-transplant month. Although DGF was found to be one of the several risk factors of acute rejection and suboptimal function at one year, it had no influence on the graft function and survival at 5 years after transplantation.

GIANT MUCINOUS EPITHELIAL CYST OF THE SPLEEN ASSOCIATED WITH SPLENIC PSEUDOCYST - A CASE REPORT

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Introduction: Splenic mucinous cysts are exceptionally rare. A derivation from ectopic tissue (endodermal epithelium - pancreatic or intestinal, mesonephric structures or mesothelium) has been proposed to be their histogenesis.

Case report: We report a case of 56-year-old woman presented with atypical pain and sensation of fullness in the epigastrium. Physical examination revealed 15 cm large palpable mass in the left upper quadrant of the abdomen. All laboratory tests were normal, and serological tests gave no evidence of parasitic infection. Ultrasonography of the abdomen showed two adjacent cysts in the spleen. All other possible sites of primary tumor appeared normal clinically and radiologically. It was therefore regarded as a tumor of primary splenic origin and splenectomy was performed. The surgical specimen consisted of spleen measuring 28x17x8cm and weighing 920gm. The splenic

capsule was smooth and intact. The cut surface revealed presence of two adjacent cysts surrounded by a peripheral rim of splenic tissue of variable thickness. The larger cyst 13x8x6cm was multiloculated, filled with mucinous material, without communication with the second cyst that measured 4x2x2cm. Microscopically, the larger cyst was lined by a single layer of columnar mucinous epithelium without atypia. A collagenous fibrous wall of variable thickness supported the epithelium. The second cyst was without epithelial lining. The surrounding splenic parenchyma was regular. Immunohistochemically, the mucinous epithelium showed strong staining for cytokeratin 18, 19, 20 and CEA, but not for CK7. Mucin stained strongly with Alcian blue.

Conclusions: The immunophenotype of the cyst epithelium excluded ovarian origin and was suggestive to be of a gastrointestinal origin.

BRONHODILATATION TEST (BDT) IN PATIENTS WITH DIFFERENT TYPE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

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Dr. Jordan Spasevski: Bolnica „Jasenovo" Veles.

Introduction: The aim of this prospective study was to assess the reversibility of bronchial obstruction in different form of chronic obstructive pulmonary disease (COPD) and justification of the therapy with β-2 agonist.

Methods: In a period of 6 months we evaluated 68 patients with COPD. Every one of them was assessed with pulmonary obstruction before the inhalation of β-2 agonist. We evaluated the change of: FEV-1; FVC; Tiffeneau; PEF and the subjective feeling of improvement.

Results: out of the whole group of patients 75% were men more then 54 years old. Bronchodilatation test (BDT) was assumed positive when FEV-1 is more than 12% improved after 2 inhalation of β-2 agonist. BDT was positive in 63% of patients. Most successful were patients with asthma – 100%, and chronic obstructive bronchitis - 59%, while least effective were patients with emphysema - 28%. Subjective feeling of improvement was found in 72% of patients. Majority of them had asthma - 95% and 57% had emphysema. In patients with positive tests 88% had a subjective feeling of improvement, while in negative tests – 44% had this feeling. FEV-1 was increased on average of 19%, being highest in asthma patients - 27% and minimal in those with emphysema 5%. Tiffeneau increase 9% on average (13% in asthma and 1% in patients with emphysema. Finally, PEF was maximally increased in asthma - 21%, minimally in emphysema patients.

Conclusion: BDT is positive in 63% of patients and 100% in asthmatics. In COPD patients it is positive in 60% thus justifying the therapy with β-2 agonist. It is negative in 72% of emphysema patients. The cost effectiveness of BDT in every day practice in COPD seems justified.

ОТКРИТИ ФРАКТУРИ НА КРАЙНИЦИ – ЗНАЧЕНИЕ НА СЪВРЕМЕННИЯ СТАНДАРТ ЗА СПЕШНОСТ (ТРАВМА СИСТЕМА)

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Въведение.Откритите фрактури на крайниците са тези, при които има нарушение целостта на кожата (с видима кожна рана). Представляват както диагностичен, така и терапевтичен проблем.Поведението и опитът на лекуващите имат огромно значение за добрия краен резултат. Последният е много различен, в зависимост от бързината на точната диагностика и началото на дефинитивното лечение.Ако последните се извършват според правилата и изискванията на съвременния стандарт за спешност, т. нар. травма система, лечебният резултат е много добър.Травма системата е организиран отговор (лечебен) на всички травми и тежки състояния.

Основен проблем при реакцията е недостигът на време. Това е най-важният фактор в лечението - особено началото му.При тежки травми, непосредствено заплашващи живота, има нужда от незабавно действие. Това формулира правилото на „десетте златни минути“ (ten golden minutes).Главен проблем е избягването на „предотвратимата смърт“ (preventable death). Избягва се чрез добра система на лечение на пострадалите, като целта е да оживеят. Смъртността обаче статистически никога не достига нула.В едно писмо до губернатора на щата Мериленд през 1963г. R. Adams Cowly обяснява необходимостта от намаляване на времето от травмата до началото на дефинитивното лечение до един час. От тогава е дефинирано правилото за „първия златен час“ (first golden hour) - условие за постигане на възможно най-добър резултат.Организационният модел на травма системата е започнал да се формира в отделните си детайли в далечното минало по време на военни конфликти поради поява на голям брой пострадали за кратко време. Военните хирурзи са първите, които започват да създават принципи на клиничните и системни грижи за травмирани пациенти. Опитът от военните конфликти налага мнението, че най-важно за пострадалите е намаляване на времето от травмата до дефинитивното лечение. Тази концепция се предава и преминава от военната травма система в организацията на цивилната травма през 70-те години, когато поетапно се оформя моделът на съвременната травма система.Още по време на войни френският хирург Доминик Ларей (Ларе) развива концепцията за бърза евакуация и ранно лечение на пострадалите. За целта създава „летяща болница“, която силно скъсява рамото на евакуация (в пространство и време). Нещо повече - той разполага полевите болници близо до мястото на бойните действия.Преди въвеждането на тези прости правила пострадалите военни оставали често с часове и дни на мястото на инцидента преди да получат някаква медицинска помощ.

Горните формирования са били де факто първите травма центрове. По време на Кримската война Н. Пирогов въвежда сортировката. Разделя пострадалите в 3 групи: тежко пострадали- за незабавно лечение, тежко пострадали - критични с наранявания, несъвместими с живота - без лечение и леко пострадали - за по-късно лечение. Това увеличило процента на оцелелите. Пръв описва травматичния шок.През Гражданската война в Америка военните болници биват инкорпорирани в самата структура на армията, като фронтови лечебни звена с нарастващо ниво на компетентност от фронта към тила. По време на Първата световна война системното лечение на ранените чрез прогресивни медицински ешелони вече е стандартен протокол. Пострадалите са били евакуирани към батальонния медицински пункт, където са обработвани и връщани в батальона (по-леките) или стабилизирани и насочвани към болници с по-високо ниво на лечение в тила.През Втората световна война системата се подобрява. Чрез санитарни автомобили се намалява времето на евакуация до 4-6 часа. Проучванията върху шока и широкото използване на

кръвопреливането при лечението му, намаляват смъртността и усложненията от остра бъбречна недостатъчност. За допълнително намаляване на смъртността допринасят антисептиката и откриването на антибиотиците. В архивите на Армията на САЩ се пазят медицински документи на ранени от времето на Гражданската война до днес и този травма регистър позволява разработването на алгоритми за най-доброто лечение при специфични наранявания.След появата на хеликоптерите по време на войните в Корея и Виетнам времето за евакуация от мястото на битката до напълно оборудвани болници става за по-малко от час. Ранените са сортирани и обслужвани от добре обучен медицински персонал в система, която осигурява дефинитивно лечение за най-кратко възможно време. Това довежда до 97.5% преживяемост на пострадалите, които достигат до военната болница живи.По време на Първата световна война времето между нараняването и операцията е между 12 и 18 часа, с обща смъртност 8.5%. През Втората световна война същото време е 6-7 часа, а смъртността е 5.8%. По време на Корейската война времето е 2-4 часа и смъртността 2.4%. Във Виетнамската война пострадалите постъпват до 1 час в болницата, а смъртността сеснижава до 1.7%. Тези данни ясно показват необходимостта от бърз транспорт на пострадалия до мястото на дефинитивно лечение.Докато военните медици в САЩ развиват и прилагат правила за лечение на ранените, подобни грижи за цивилните граждани въобще не съществуват. Въпреки големите медицински загуби от пътно-транспортни инциденти, повече от колкото във Виетнамската война, в страната почти липсва обществен интерес. За разлика от военните, цивилните граждани на САЩ често попадат в лошо оборудвани бази и в ръцете на неопитен персонал.Развитието на цивилната травма система започва със създаването на „American College of Surgeons Committee on Trauma" (Ch. L. Scudder - 1992). Докато обаче в армията е постигнат голям напредък в евакуация, сортировка и дефинитивно лечение, при цивилните липсвал организиран подход при лечението на травмата. Ситуацията започва да се променя едва след 1966г. след публикация на Националната академия на науките, озаглавена „Accidental Death and Disability, the Neglected Diseaseof Modern Society". Този основополагащ материал описва недоброто лечение на остро травмирани пациенти и дава тласък за развитие на цивилните травма системи. Описани са недостатъците и са дадени специфични препоръки за доболничното и болничното лечение на травмите.

Следващият важен момент е завръщането на хирурзите, пилотите на хеликоптери и добре тренирания останал персонал от Виетнамския конфликт - всички с огромен опит в лечението на пациенти с остра травма.Споменатите по-горе принципи са адаптирани в Западна Германия през 1970г. с разполагане на травма центрове покрай автомагистралите. Това води до намаление на смъртността след пътни травми с около 25%.Травма системите подлежат на непрекъснато развитие. Основните правила са установени от American College of Surgery Committee on Trauma в 1976г. като „Optimal Hospital Resources for Care of the Injured Patients".Този документ маркира съществените компоненти на различните по степен травма центрове и фиксира необходимостта от развитие на системата. Основните правила се ревизират и осъвременяват на всеки 4-5 години. През същия период комитетът (комисията) въвежда курса ATLS (Advance Trauma Life Support). В САЩ фактически първите травма центрове (без още да се наричат така) стават градските болници, осигуряващи спешна медицинска помощ за неосигурени пациенти. По- късно се оформят т.нар. „ексклузивни" травмасистеми от центровете за лечение само на тежка травма, които обхващат в дейността си всички фази на лечението - доболнично, спешно болнично лечение, рехабилитация. Тези системи се наричат ексклузивни (външни), поради факта, че са независими от лечебните заведения за неспешни пациенти.Работещите днес съвременни системи са развити на базата на The Model Trauma Care System Plan,написан през 1992г. от Health Resources Services Administration.Описан е инклузивният модел на травма системата, при който освен главния травма център като ключов компонент са включени и другите болници от региона. Така пострадалите получават оптимално лечение с наличните

ресурси, като чрез сортировъчните критерии, съобразно тежестта на травмата се извършва трансфер до болницата с по-високо (или по-ниско) ниво на лечение. Травма системата става широка мрежа от болници (травма центрове), сред които травма центровете I и II степен са източник на информация за оценка на системата. Този механизъм позволява малките болници (III степен, най-ниска) да трансферират пациенти към по-големите болници (I и II степен), които имат заделен персонал и ресурси за онези 15% критично травмирани, нуждаещи се от по-високо ниво на обслужване. Нещо повече - някои проучвания показват, че концентрирането на лечението на тези 15% критично травмирани в ръцете на няколко добре тренирани хирурзи се отплаща с по-добри резултати.

Resources for the Optimal Care of the Injured Patients е последното издание за изискванията и основните правила за развитие на травма системата, публикувано от American College of Surgeons Committee on Trauma. Според него първата крачка при всяко планиране е оценката на нуждите. Броят и гъстотата на населението, раждаемостта и нивото на травматизма определят колко травма центрове са необходими за нуждите на дадена област.

Откритите фрактури се разглеждат от различни автори като се класифицират различно с минимални различия. Най-използвана е класификацията на Gustilo and Anderson:

I степен: кожна рана до 1 см; видимо чиста; минимална мускулна контузия; причинена от натиск отвътре навън; напречни или коси фрактури;

II*степен*: кожна рана над 1 см; минимална мекотъканна повреда; без смачквания или минимални; напречни и коси фрактури;

III степен: кожна рана над 1см; размачквания на меки тъкани; често високоенергийни раздробени фрактури;

- ***III-A***: възможно покритие с кожа или ламбо; няколко фрагмента;
- ***III-B:***невъзможно тъканно покритие; увреда на периост; масивно замърсени;
- ***III-C***: всяка открита фрактура с артериална увреда.

Забележка: Ако до 8 часа I и II не са обработени, преминават в IIIстепен.

Огнестрелните наранявания в тази класификация се приравняват към: III-A степен-куршумните, III-B и III-C - експлозивните и от голямокалибрени балистично детерминирани проектили.

Скъсяването на времето между нараняването и началото на дефинитивното лечение е ключов и решаващ фактор за:

1.Избора на лечебно поведение;

2.За добрия краен резултат;

3.За ефективен „damage control".

Например при I и II степен, ако лечението започне до 2 часа от травмата, дебридманът е най-ефективен, а фиксацията се решава по целесъобразност - първична външна фиксация или отсрочена във времето вътрешна фиксация (след 1 до 4 седмици).

За III степен - A и B фиксацията (след дебридмана) е винаги външна. Понеже се касае за раздробени фрактури почти винаги се налага отстраняване на костни парчета, което води до оформяне на дефект (липса на част от костта). Този дефект трябва да се запълни с кост - чрез авто-, ало-, или ксено-остеопластика. Последната според П.Минчев е:

1. Първична остеопластика (ПОП) - в деня на нараняването;
2. Първично-отсрочена остеопластика (ПООП) - до 30 дни от нараняването;
3. Вторична остеопластика (ВОП) - извършена след повече от 30 дни от нараняването.

Колкото по-рано започне дефинитивното лечение, толкова по-радикален ще бъде хирургичният подход, съответно - по-късо по време ще е лечението. Това се постига чрез стриктното спазване правилата на съвременния стандарт за спешност (травма система). Обратно - изчакването, недобрият подход и недостатъчното хирургично лечение удължават възстановяването, а често то не е пълно.

Дискусия:Ясно е, че където се работи по правилата на травма системата, резултатите са по-добри, възстановяването е по-бързо, а усложненията са по-редки.Извършването на дейността от опитни хирурзи е наложително.

Изводи:1.Травма системата е инструмент за получаване на по-добри лечебни резултати;

2.Гласуването на закон за травма система в България е наложително. Прилагането на отделни детайли само на системата е недостатъчно.

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