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A

KARDIOVASKULARNA OBOLJENJA I SRČANI MARKERI

CARDIOVASKULAR DISEASES AND CARDIAC MARKERS

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A1
ZNAČAJ ADENOZIN DEZAMINAZE KOD BOLESNIKA SA AKUTNIM INFARKTOM MIOKARDA

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Kod infarkta miokarda dolazi do varijabilnog obima nekroze tkiva miokarda, kao posledica opstrukcije aterosklerotičnih koronarnih arterija. Jedan od najvećih faktora rizika koji dovodi do ateroskleroze i koronarne bolesti srca je dijabetes melitus. Adenozin dezaminaza (EC.3.5.4.4) (ADA) enzim je koji katalizuje dezaminaciju adenozina do inozina i amonijaka. Adenozin, degradacioni produkt ATP-a, ima zaštitu ulogu kod oštećenja srca u ishemiji-reperfuziji. Kod 55 bolesnika sa akutnim infarktom miokarda (AIM), koji su imali pozitivan troponin I, ispitivali smo aktivnost ADA. Trideset devet zdravih osoba istih godina starosti činili su kontrolnu grupu. Značajno povećana aktivnost ADA ($p<0,001$) nađena je u serumu bolesnika sa AIM u odnosu na zdrave dobrovoljce. Takođe bolesnici iz AIM grupe koji su imali dijabetes (50%) pokazali su visoke nivoe ADA ($p<0,01$) u poređenju sa bolesnicima koji nisu imali dijabetes. Rezultati pokazuju da porast aktivnosti ADA nakon akutnog infarkta miokarda dovodi do pada adenozina koji je endogeni celularni aktivator antioksidanasa. Ovo istraživanje pokazuje da je određivanje aktivnosti ADA važno kod bolesnika sa AIM i može imati vitalnu ulogu kod oštećenja u ishemiji-reperfuziji.

A1
THE SIGNIFICANCE OF ADENOSINE DEAMINASE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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In myocardial infarction ischemic necrosis of a variable amount of myocardial tissue occurs as a result of atherosclerotic coronary artery obstruction. One of the major risk factors leading to atherosclerosis and coronary heart disease is diabetes mellitus. Adenosine deaminase (EC.3.5.4.4) (ADA) is the enzyme which catalyzes the deamination of adenosine to inosine and ammonia. Adenosine, a degradation product of ATP, has been attributed to exert a protective effect on injury caused by ischemia-reperfusion in the heart. In 55 patients with acute myocardial infarction (AMI) who were troponin I positive, we investigated serum ADA activity. Thirthy nine age-matched healthy persons served as a control group. A highly significant increase ($p<0.001$) in the activity of ADA was found in the sera of AMI patients as compared to healthy donors. Also, AMI patients, with diabetes (50%) showed high levels of ADA ($p<0.01$) when compared to non-diabetic patients. The results indicate that increased levels of ADA activity in patients after AMI lead to the depletion of adenosine that is an endogenous activator of cellular antioxidants. These findings show that the estimation of ADA activity is important in patients with AMI and may play a vital role in ischemia-reperfusion injury.

A2
ULOGA KATALAZE KOD PACIJENATA SA STABILNOM I NESTABILNOM ANGINOM PEKTORIS

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Ishemijska bolest srca – stabilna i nestabilna angina pectoris i infarkt miokarda – jedan je od najčešćih i najvažnijih uzroka morbiditeta i mortaliteta danas. Slobodni radikali nastali u ishemijskoj bolesti srca dovode do ireverzibilnog oštećenja funkcije srca uzrokujući promenu nivoa glavnih endogenih antioksidativnih komponenata kao što su katalaza, superoksid dizmutaza, redukovani glutation i glutation peroksidaza. Cilj ovog rada bio je da se pokaže na koji način merenje aktivnosti katalaze može da se iskoristi za procenu ishemijskog oštećenja miokarda u pacijenata sa stabilnom (SAP) i nestabilnom (NSAP) anginom pektoris. Ispitivana je aktivnost katalaze u plazmi i eritrocitima (Er) u 40 pacijenata sa potvrđenom SAP i 45 pacijenata sa NSAP. Kontrolnu grupu činilo je 30 zdravih dobrovoljaca. Aktivnost katalaze u Er merena je metodom po Beutleru, a u plazmi po Gothu. Utvrđeno je da postoji značajno povećanje aktivnosti katalaze u plazmi u pacijenata sa NSAP ($p<0,01$), dok kod pacijenata sa SAP ta razlika ima manju značajnost u odnosu na kontrolnu grupu ($p<0,05$). Aktivnost katalaze u Er u obe grupe pacijenata nije pokazala značajne razlike u odnosu na zdrave ispitanike. Ovi rezultati pokazuju značajan porast aktivnosti katalaze što je posledica hroničnog oksidativnog stresa, stoga praćenje nivoa ovog enzima može biti korisno u dijagnostici i terapiji stabilne i nestabilne angine pektoris.

A2
THE ROLE OF CATALASE IN PATIENTS WITH STABLE AND UNSTABLE ANGINA PECTORIS

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Ischemic heart disease (IHD) – stable and unstable angina pectoris and myocardial infarction – is the most frequent cause of morbidity and mortality today. Generation of reactive oxygen species-free radicals in IHD contributes to irreversible myocardial tissue injury with concomitant changes of certain key endogenous antioxidant compounds, e.g. catalase, superoxide dismutase, reduced glutathione and glutathione peroxidase. The purpose of this study is to show in which way we can use catalase activity in the evaluation of ischemic heart damage, in patients with stable (SAP) and unstable (USAP) angina pectoris. In the study we observed the activity of catalase in the plasma and erythrocytes (Er) of 40 patients with assessed SAP and 45 patients with USAP. The control group consisted of 30 healthy volunteers. The activity of catalase in Er was determined according to the Beutler method, and in plasma it was measured by the method of Goth. We noted a significant increase in catalase activity in the plasma of patients with USAP ($p<0.01$), while in patients with SAP we noted less significant increase compared with the control group ($p<0.05$). The catalase activity in Er in both groups did not show any significant difference compared with healthy volunteers. These results show an increase in catalase activity, which is a consequence of chronic oxidative stress, so we believe that the follow-up of this enzyme could be useful in the diagnosis and treatment of patients with USAP and SAP.

A3
KORELACIJA IZMEĐU INTIMOMEDIJALNOG KOMPLEKSA I NIVOA HOLESTEROLA I TRIGLICERIDA U BOLESNIKA SA ZNAČAJNOM STENOZOM KORONARNIH ARTERIJA KOJI SU PREBOLELI INFARKT MIOKARDA

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Debljina kompleksa intimomedije zida ekstrakarnijalnih karotidnih arterija predstavlja merljiv pokazatelj ateroskleroze. Ukazano je na značajnu udruženost karotidne bolesti sa hiperlipidemijom. Ispitivanja su potvrdila povezanost ishemične bolesti srca i karotidne bolesti. Ispitivana je povezanost debljine intimomedijalnog kompleksa (IMC) zida zajedničke karotidne arte-

A3
CORRELATION BETWEEN INTIMA-MEDIA THICKNESS AND THE LEVELS OF CHOLESTEROL AND TRIGLYCERIDES IN PATIENTS WHO RECOVERED FROM ACUTE MYOCARDIAL INFARCTION

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The growth of the intima-media complex is a widely accepted parameter in studies related to the process of atherosclerosis. A large number of clinical studies showed that the intima-media thickness (IMT) of the extracranial segments of arteriae carotis communis presents a measurable index of the presence of atherosclerosis. The aim of this study was to investigate

rije (ACC) i nivoa holesterola i triglicerida u serumu bolesnika koronarografski potvrđenom okluzivnom bolešću koronarnih arterija koji su preboleli infarkt miokarda. Ispitivanjem je obuhvaćeno 28 bolesnika sa infarktom miokarda, prosečne starosti $\bar{x}$=60,28+ 7,39 godina, 22 (78,58%) muškarca i 6 (21,42%) žena. Svim ispitanicima je urađen »color duplex« ehosonografski pregled karotidnih arterija. Ispitivanje je obavljeno na ultrazvučnom aparatu firme »SONOACE 8000 SE« sa linearnom sondom od 7,5 MHz i dubine 5,0 cm. Intimomedijalna debljina je merena na posteriornom zidu zajedničke karotidne arterije (ACC), 2 cm od vrha bifurkacije, i uzimana prosečna vrednost tri uzastopna merenja tokom dijastole. Svim bolesnicima je izmeren nivo ukupnog holesterola, LDL holesterola i triglicerida. Kod svih bolesnika je prethodno urađena selektivna koronarografija. Trosudovnu koronarnu bolest imalo je 10 (35,7%), dvosudovnu 16 (57,1%) i jednosudovnu 2 (7,2%) bolesnika. Prosečna vrednost debljine IMC zajedničke karotidne arterije iznosila je $\bar{x}$=1,67+0,13 mm. Prosečna vrednost ukupnog holesterola iznosila je $\bar{x}$=7,40+1,81 mmol/L, triglicerida $\bar{x}$=3,10+2,41 mL/L i LDL holesterola $\bar{x}$=5,89+ 1,50 mmol/l. Postoji pozitivna, niska i nesignifikantna korelacija između debljine IMC-a i nivoa ukupnog holesterola (r=0,35, p>0,05). Takođe postoji pozitivna, niska i nesignifikantna korelacija između debljine IMC-a i nivoa LDL holesterola (r=0,31, p>0,05). Postoji pozitivna, niska i signifikantna korelacija između debljine IMC-a i nivoa triglicerida (r=0,45, p<0,05). Dobijeni rezultati ukazuju na povezanost lipida i ateroskleroze, kao i na to da su lipidi značajan, ali ne i jedini faktor rizika ateroskleroze merene debljinom intimomedijalnog kompleksa.

A4
NIVO IZOENZIMA KREATIN KINAZE MB MASE U BOLESNIKA SA AKUTNIM INFARKTOM MIOKARDA

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Određivanje koncentracije CK MB mase ističe se kao rani i veoma senzitivan marker akutnog infarkta miokarda (AIM), posebno kod bolesnika sa odsutnim EKG promenama ili malim infarktnim područjima. Porast koncentracije CK MB mase nakon AIM nastaje znatno ranije u odnosu na aktivnost CK MB izoenzima i aktivnost ukupne CK. Cilj rada je bio da se odredi nivo CK MB mase u serumu bolesnika sa AIM i sagleda njegov značaj u dijagnostici AIM. Ispitivanjem je obuhvaćeno 47 bolesnika sa AIM, prosečne starosti $\bar{x}$=61.7 +9.0 godina, 12 (25.5%) žena i 35 (74.5%) muškaraca, i 20 zdravih osoba, 10 žena i 10 muškaraca, kao kontrolna grupa. Kod svih bolesnika krv za analizu uzimana je odmah po prijemu i određivane su koncentracije CK MB mase, CK, CK MB, AST, LDH, hsCRP, holesterol, HDL, LDL, trigliceridi i glikemija. CK MB mase je određivan na principu elektrohemiluminiscencije na aparatu »ELECSYS 1010«, »Roche« dijagnostika, sa normalnim vrednostima 0,1–0,5 ng/mL. Pro-

the relation between the IMT of the arteriae carotis communis and the levels of cholesterol and triglycerides in patients who recovered from acute myocardial infarction. The study involved 28 patients who recovered from acute myocardial infarction, 22 (78.6%) men and 6 (21.4%) women, average age $\bar{x}$=60.3+ 7.4 years. IMT was measured in the end-diastole on the back wall of a. carotis communis; for detection we used a high resolutive color-Doppler ultrasonic system frequency of 7.6 MHz. Total cholesterol, HDL cholesterol and triglycerides were determined. The average value of the IMT of a. carotis communis in patients who recovered from acute myocardial infarction is $\bar{x}$=1.67+0.13 mm. The average value total cholesterol is $\bar{x}$=7.4+1.8 mmol/L, LDL $\bar{x}$=5.89+1.50 mmol/l and triglycerides $\bar{x}$=3.10+2.40 mmol/L. We found a positive but insignificant corelation between total cholesterol and IMT (r=0.35 p>0.05). We found a significant positive correlation between IMT and triglycerides (r=0.45, p<0.05).

A4
THE LEVEL OF CK-MB MASS ISOENZYMES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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The determination of the level of CK-MB mass isoenzymes is important in the early diagnosis of acute myocardial infarction. The aim of this study was to determine the levels of plasma CK-MB mass in patients with acute myocardial infarction. The study involved 47 patients with acute myocardial infarction, 12 (25.5%) women and 35 (74.5%) men, average age $\bar{x}$=61.7+ 9.0 years, and 20 healthy persons, as a control group. CK-MB mass, CK, CK-MB, LDH, AST, ALT, hsCRP, cholesterol, HDL, LDL and triglycerides were determined. CK-MB mass was determined using an electrochemiluminescent method on an Elecsys 1010, »Roche Diagnostics«. Reference ranges were from 0.1 to 0.5 ng/mL. The average values of CK-MB mass in patients with acute myocardial infarction and persons control group are: $\bar{x}$=95.6 + 103.9 ng/mL and $\bar{x}$=2.3 = 0.7 ng/mL (t=6.1, p<0.01); CK $\bar{x}$=1930+1401.04 U/L and $\bar{x}$= 91.1+40.0 U/L (t=8.9, p<0.01); CK MB $\bar{x}$=969.5

sečne koncentracije CK MB mase i drugih markera oštećenja miokarda kod bolesnika sa AIM i kontrolne grupe su: CK MB masa $\bar{x}$ = 95,6 + 103,9 ng/mL i $\bar{x}$ = 2,3 + 0,7 (t=6,1, p<0,01); CK $\bar{x}$ = 1930,5 + 1401,0 U/L i $\bar{x}$ = 91,1 + 40,0 U/L (t=8,9, p<0,01); CK MB $\bar{x}$ = 969,5 + 140,2 U/L i 10,6 = 3,5 U/L (t = 8,0 p<0,01); AST $\bar{x}$ = 188 + 176,1 U/L i $\bar{x}$ = 20,7 + 5,4 U/L (t = 6,5, p<0,01); LDH $\bar{x}$ = 989,2 + 521,9 U/L i $\bar{x}$=303,8 + 80,7 U/L (t=8,7, p<0,01). Relativni indeks koji se dobija iz odnosa CK MB mass/CK MB aktivnost iznosio je prosečno $\bar{x}$=54,5%. Vrednosti više od 2,5 % ukazuju pre na srčano poreklo, nego na poreklo iz skeletnih mišića i nađene su kod 45/47 (95,7%) bolesnika sa AIM. Postoji vrlo visoka pozitivna korelacija između nivoa CK MB i CK MB mase (r=0,85, p<0,01). Postoji pozitivna i niska, ali statistički značajna korelacija između nivoa CK i CK MB mase (r=0,45, p<0,01). Postoji pozitivna i visoka korelacija između CK i CK MB (r=0,67, p<0,01). Određivanje koncentracije CK MB mase u serumu je značajno u dijagnostici pacijenata sa akutnim bolom u grudima i ranoj dijagnostici akutnog infarkta miokarda.

A5
ANTROPOMETRIJSKI INDEKSI, CRP I KORONARNA ARTERIJSKA BOLEST KOD ODRASLIH ŽENA U SRBIJI

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C-reaktivni protein (CRP) nezavisni je faktor rizika za koronarnu arterijsku bolest (KAB) i u snažnoj je korelaciji sa gojaznošću. Cilj ovog rada je bio da se ispita veza između CRP-a i antropometrijskih indeksa: odnosa struk/kuk (WHR) i indeksa telesne mase (BMI) kod zdravih žena i žena sa angiografski dokazanom KAB. Grupu ispitanika činilo je 111 zdravih žena i 63 pacijentkinje starosti od 31 do 75 godina. Visina, težina i obim struka i kuka su izmereni dok su BMI i WHR izračunati. CRP je određen upotrebom ultrasenzitivne imunoturbidimetrijske metode. U zavisnosti od godina, sve žene su klasifikovane u četiri grupe: zdrave ≤ 50 godina (grupa 1), zdrave ≥ 51 godina (grupa 2), pacijentkinje ≤ 50 godina (grupa 3), pacijentkinje ≥ 51 godina (grupa 4). Rezultati dobijeni upotrebom studentovog t-testa su pokazali da ne postoji statistički značajna razlika u BMI između mlađih i starijih zdravih žena. Starije zdrave žene imale su značajno veći WHR (0,82 prema 0,77) i CRP (1,47 prema 0,9 mg/L) u odnosu na mlađe zdrave žene. S druge strane, nije bilo značajne razlike ni za jedan ispitivani parametar između starijih i mlađih pacijentkinja (p>0,05). Statistički značajna pozitivna korelacija je dokazana između koncen-

A5
ANTHROPOMETRIC INDICES, CRP AND CAD IN ADULT SERBIAN WOMEN

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C-reactive protein (CRP) is an independent risk factor for coronary artery disease (CAD) that is strongly associated with measures of obesity. Our purpose was to explore the relationship between CRP, body mass index (BMI) and waist-to-hip ratio (WHR) in healthy women and women with angiographically assessed CAD. A total of 63 patients and 111 healthy subjects, aged 31 to 75, were included in the study. Height, weight and waist and hip circumferences were measured. BMI and WHR were computed. CRP was assayed using an ultra-sensitive immunoturbidimetric method. According to age, women were classified into four groups: healthy ≤ 50 years of age (group 1), healthy ≥ 51 years (group 2), patients ≤ 50 years (group 3), patients ≥ 51 years (group 4). The results obtained by using Student's t-test have shown that there was no significant difference in BMI, but that there was a statistically significant difference in WHR and CRP between groups 1 and 2. Elderly healthy women had significantly higher WHR (0.82 vs 0.77) and CRP (1.47 vs. 0.9 mg/L) compared to the younger group. On the other hand, there was no difference for any of the mentioned parameters between younger

tracije CRP-a i mera gojaznosti kod zdravih žena (BMI p<0,001 i WHR p<0,01, linearna regresiona analiza), dok je statistički značajna korelacija između pomenutih paramatara izostala kod pacijentkinja. Rezultati ove studije ukazuju na to da se gojaznost nalazi u snažnoj vezi s koncentracijom CRP-a kod zdravih odraslih žena u populaciji Srbije. Na osnovu toga može se zaključiti da je gojaznost važan faktor koji utiče na hroničnu inflamaciju niskog stepena. Starije žene imaju više vrednosti odnosa struk/kuk i CRP-a u poređenju sa mlađim ženama najverovatnije zbog odsustva protektivnog efekta estrogena.

A6
VEZA IZMEĐU VISOKO-NORMALNOG KRVNOG PRITISKA I FAKTORA RIZIKA ZA KARDIOVASKULARNU BOLEST

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Prema klasifikaciji JNC VI i WHO-ISH, osobe bez hipertenzije koje imaju sistolni pritisak od 130 do 139 mmHg, dijastolni pritisak od 85 do 89 mmHg, ili oba kategorisane su u grupu visoko-normalnog krvnog pritiska. Nema dovoljno informacija o tome koliki je rizik za obolevanje od kardiovaskularne bolesti (KAB) kod tih osoba. Cilj rada je bio ispitivanje veze između kategorija normalnog pritiska i faktora rizika za KAB. Grupu ispitanika je činilo 99 zdravih osoba, 53 muškarca i 46 žena. Ispitanici su klasifikovani u tri nehipertenzivne grupe: optimalan (sistolni pritisak manji od 120 mmHg ili dijastolni pritisak manji od 80 mmHg, grupa 1), normalan (sistolni pritisak od 120 do 129 mmHg ili dijastolni pritisak od 80 do 84 mmHg, grupa 2) i visoko-normalan (sistolni pritisak od 130 do 139 mmHg ili dijastolni pritisak od 85 do 89 mmHg, grupa 3). Informacije o starosti, konzumiranju alkohola, statusu pušenja i fizičkoj aktivnosti ispitanici su dali samoizjašnjavanjem. Indeks telesne mase (BMI) i odnos struk/kuk (WHR) su izračunati. U uzorcima su određeni hsCRP, mokraćna kiselina i lipidni parametri (ukupan holesterol, HDL-H, LDL-H, trigliceridi, Lp(a), apoA-I, apoB) standardnim laboratorijskim metodama. Fibrinogen je izmeren Klausovom metodom. Statistička analiza je urađena upotrebom ANOVE i dokazano je da postoji značajna razlika između ispitivanih grupa za sledeće faktore rizika: WHR (grupa 2 prema grupi 3, *Tuckey* test p=0,008), HDL-H (grupa 1 prema grupi 2, p=0,024 i grupa 1 prema grupi 3, p=0,034), mokraćna kiselina (grupa 1 prema grupi 3, p=0,039). Nije bilo značajne razlike ni za jedan drugi ispitivani parametar (p>0,05). Dobijeni rezultati ukazuju na to da sniženje HDL-holes-

and older patients (p>0.05). A strong positive relationship was found between CRP and measures of obesity in healthy subjects (BMI p<0.001 and WHR p<0.01 by linear regression analysis), but the statistically significant relationship disappeared in the group of patients. The results of this study indicate that adiposity is strongly associated with CRP in healthy adult women. Also, these data suggest that adipose tissue is an important determinant of a low level, chronic inflammatory state as reflected by CRP levels. Elderly women have higher WHR and CRP levels than younger women probably because of a lack of the protective influences of estrogen.

A6
THE ASSOCIATION BETWEEN HIGH-NORMAL BLOOD PRESSURE AND RISK FACTORS FOR CARDIOVASCULAR DISEASE

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According to the classification approaches developed by the joint JNC VI and WHO-ISH, nonhypertensive persons with a systolic pressure of 130 to 139 mmHg, diastolic pressure of 85 to 89 mmHg, or both are categorized as having high-normal blood pressure. Information is limited regarding the risk of cardiovascular disease (CAD) in these subjects. We investigated the association between blood pressure category and the risk factors for CAD in these persons. A total of 99 healthy persons, 53 men and 46 women, were included in the study. The subjects were classified into one of the three nonhypertensive blood pressure categories: optimal (systolic pressure of less than 120 mmHg and diastolic pressure of less than 80 mmHg, group 1), normal (systolic pressure of 120 to 129 mmHg or diastolic pressure of 80 to 84 mmHg, group 2), or high-normal (systolic pressure of 130 to 139 mmHg or diastolic pressure of 85 to 89 mmHg, group 3). We collected information such as age, smoking status, alcohol consumption and exercise from self-reports. Body mass index (BMI) and waist-to-hip ratio (WHR) were calculated. In the blood samples, hsCRP, uric acid and lipid parameters (total cholesterol, HDL-H, LDL-H, triglycerides, Lp(a), apoA-I, apoB) were determined by standard laboratory procedures. Fibrinogen was measured by Clauss method. The results obtained by using an ANOVA have shown that there was a significant difference in WHR (group 2 vs. group 3, *Tuckey* test p=0.008), HDL-H (group 1 vs. group 2, p=0.024 and group 1 vs. group 3, p=0.034) and uric acid (group 1 vs. group 3, p=0.039). There was no difference for any of the other examined risk factors (p>0.05). These data suggest that the lowering of HDL-cholesterol and

terola, povećanje mokraćne kiseline i gojaznost mogu da dovedu do razvoja hipertenzije. U primarnoj prevenciji, odnos struk/kuk je bolji parametar od BMI za detektovanje i praćenje stepena gojaznosti kod osoba bez povišenog krvnog pritiska.

A7
INCIDENCA HIPERHOMOCISTEINEMIJE I MTHFR C677T POLIMORFIZAM KOD MLADIH BOLESNIKA SA AKUTNIM INFARKTOM MIOKARDA

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Hiperhomocisteinemija (HHcy) smatra se nezavisnim faktorom rizika za preuranjeni razvoj kardiovaskularnih bolesti. Snižena enzimska aktivnost metilentetrahidrofolat reduktaze (MTHFR), usled prisustva C677T mutacije, jedan je od uzroka HHcy. Određeni su incidenca HHcy, koncentracija homocisteina (Hcy) i raspodela MTHFR 677 genotipova (C/C, C/T i T/T) kod grupe mladih bolesnika sa akutnim infarktom miokarda (AIM) i upoređeni sa vrednostima dobijenim kod zdravih osoba odgovarajuće starosti. Studija je obuhvatila 86 bolesnika sa AIM, mlađih od 45 godina (77 muškaraca i 9 žena), i kontrolnu grupu od 35 osoba. Homocistein je određivan u serumu, HPLC metodom uz fluorescentnu detekciju. PCR amplifikacija i digestija sa restriktivnom endonukleazom Hinf I korišćene su za genotipizaciju MTHFR. Podaci su statistički obrađeni *Mann-Whitney U* i *Chi-square* testom. HHcy, definisana kao nivo Hcy viši od 12 μmol/L, bila je prisutna kod 32,6% bolesnika i kod 14,3% kontrola, što je predstavljalo značajnu razliku (p=0,038). Medijane Hcy mladih ljudi sa AIM (10,4 μmol/L) i zdravih mladih ljudi (9,6 μmol/L) bile su značajno različite (p=0,035). Genotip C/C je bio prisutan kod 50,0%, C/T kod 41,9% i T/T kod 8,1% bolesnika. Nije uočena značajna razlika u raspodeli genotipova MTHFR između bolesnika i kontrola, kao ni u incidenci HHcy i nivou Hcy između genotipova MTHFR. Može se zaključiti da mladi bolesnici imaju višu incidencu HHcy i viši nivo Hcy nego zdrave osobe iste starosti, pri čemu nema značajne razlike u raspodeli genotipova MTHFR C677T.

a rise of uric acid level may lead to a subsequent development of hypertension. Also, we found a progressive increase in blood pressure with the increasing of adipose tissue. In primary care WHR is better tool than BMI for screening and following obesity in subjects with optimal to high-normal blood pressure.

A7
INCIDENCE OF HYPERHOMOCYSTEINEMIA AND MTHFR C677T POLYMORPHISM AMONG YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Hyperhomocysteinemia (HHcy) is considered an independent risk factor for premature cardiovascular diseases. The reduction of the methylentetrahydropholate reductase (MTHFR) activity, due to the presence of C677T mutation, is one of the causes of HHcy. We assessed the HHcy incidence, homocysteine (Hcy) level and distribution of all the three MTHFR 677 genotypes (C/C, C/T and T/T) in a group of young patients with acute myocardial infarction (AMI) and compared them with those obtained in healthy persons, matched for age. Thes study involved 86 patients younger than 45 years of age (77 men and 9 women) and 35 healthy controls. Homocysteine was measured in serum, using an HPLC method with fluorescent detection. PCR amplification and digestion with restrictive endonuclease Hinf I were employed for the determination of MTHFR 677 genotype. Statistical analyses included *chi-square* and *Mann-Whitney U* tests. HHcy, defined as Hcy higher than 12 μmol/L, was present in 32.6% patients and in 14.3% controls, which was a significant difference (p=0.038). Medians of Hcy in young adults with AMI (10.4 μmol/L) and in healthy young adults (9.6 μmol/L) were significantly different (p=0.035). Among the patients, 50.0% had C/C, 41.9% had C/T and the remaining 8.1% had T/T genotype. No significant difference in the distribution of MTHFR genotypes was observed between the patients and controls. MTHFR genotype had no influence on HHcy incidence and Hcy level, both in patients and controls. We conclude that young patients with AMI have higher incidence of HHcy and a higher Hcy level than healthy young adults, while there is no significant difference in the distribution of MTHFR C677T genotypes.

A8
PARAMETRI FIBRINOLIZE KOD PACIJENATA SA INFARKTOM MIOKARDA

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U nastanku infarkta miokarda (IM) izvesnu ulogu mogu imati i poremećaji fibrinolitičkog sistema, pa se procena njegove funkcije smatra veoma značajnom za prognozu. U studiji su upoređene aktivnosti inhibitora aktivatora plazminogena (PAI) i plazminogena, kao i nivoi fibrinogena između grupe od 50 bolesnika sa IM, mlađih od 50 godina (30 muškaraca i 20 žena), i kontrolne grupe od 50 zdravih osoba, odgovarajuće starosti (30 muškaraca i 20 žena). Navedeni parametri su određeni u uzorcima plazme, standardnim metodama, a rezultati upoređeni *Mann-Whitney U* testom. Aktivnosti PAI i plazminogena nisu pokazale statistički značajnu razliku, dok su nivoi fibrinogena bili značajno viši (p=0,000) kod bolesnika nego u kontrolnoj grupi. Muškarci sa IM su imali značajno više vrednosti fibrinogena (p=0,000) u odnosu na zdrave muškarce, a takva razlika nije uočena kod žena. Može se zaključiti da između bolesnika sa IM i zdravih osoba nema razlike u aktivnostima PAI i plazminogena, a bolesnici imaju više nivoe fibrinogena nego zdrave osobe. Mladi muškarci sa IM imaju veću koncentraciju fibrinogena u odnosu na zdrave muškarce odgovarajuće starosti, dok se takva razlika ne uočava kod žena.

A8
THE PARAMETERS OF FIBRINOLYSIS IN PATIENTS WITH MYOCARDIAL INFARCTION

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The disturbances in various components of the fibrinolytic system may account for the development of myocardial infarction (MI) and are considered as valuable prognostic factors. Our study compared plasminogen activator inhibitor (PAI), plasminogen and fibrinogen levels between the group of 50 patients with MI, younger than 50 (30 men and 20 women), and a control group of 50 healthy persons (30 men and 20 women), matched for age. Plasma samples were analyzed by standard methods. The results were compared using *Mann-Whitney U* test. PAI and plasminogen levels showed no statistically significant difference, while fibrinogen levels were significantly higher (p=0.000) in patients than in controls. Men with myocardial infarction had significantly higher fibrinogen levels (p=0.000) than healthy men, while such differences did not exist between healthy women and women with myocardial infarction. We conclude that there was no difference in PAI and plasminogen levels, while fibrinogen levels were higher in all patients with myocardial infarction compared with the control group. Young men with myocardial infarction have higher fibrinogen levels than healthy young men, while there is no such difference for women.

A9
NIVO C-REAKTIVNOG PROTEINA NEPOSREDNO PO PRIJEMU U INTERNISTIČKU AMBULANTU KOD PACIJENATA KOD KOJIH SE SUMNJA NA INFARKT MIOKARDA

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C-reaktivni protein (CRP) jedan je od najosetljivijih markera inflamacije a istovremeno i biomarker ateroskleroze, koja se danas smatra hroničnom inflamatornom bolešću. Cilj rada je da se odredi nivo CRP-a kod pacijenata kod kojih se sumnja na akutni infarkt miokarda i izvrši ispitivanje korelacije između inflamatornog

A9
LEVELS OF C-REACTIVE PROTEIN AT ADMISSION TO AN INTERNIST OUT-PATIENT CLINIC IN PATIENTS SUSPECTED OF HAVING ACUTE MYOCARDIAL INFARCTION

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C-reactive protein (CRP) is one of the most sensitive markers of inflammation and at the same time a biomarker of atherosclerosis, that is considered a chronic illness. The aim of this project is to determine the CRP level in patients suspected of having acute myocardial infarction, and also to establish the presence of

odgovora izraženog serumskom koncentracijom C-reaktivnog proteina i akutnog infarkta miokarda, te korelacije između C-reaktivnog proteina i lipidskih parametara. Studija je obuhvatila 94 pacijenta, neposredno po prijemu u internističku ambulantu Kliničkog centra »Banjaluka« kod kojih se sumnjalo na infarkt miokarda. Standardnim biohemijskim metodama određivane su vrednosti ukupnog, HDL i LDL holesterola, aminotransferaza (AST, ALT), kreatin kinaze (CK), i glikemija. C-reaktivni protein određivan je visokosenzitivnom imunoturbidimetrijskom metodom na aparatu »Hitachi 902«, reagensima firme »Roche«. Prosečna starost pacijenata bila je 59 godina. U grupi je bio 71 muškarac i 23 žene. Na osnovu kasnije postavljene dijagnoze za svakog pacijenta, oformljene su grupe od 22 pacijenta sa infarktom miokarda i 72 pacijenta bez infarkta miokarda. U grupi pacijenata koji su imali infarkt miokarda, srednja vrednost C-reaktivnog proteina bila je 12,89 mg/L, ukupnog holesterola 5,13 mmol/L, HDL holesterola 1,02 mmol/L, LDL holesterola 3,17 mmol/L, triglicerida 2,00 mmol/L, a u grupi bez infarkta srednja vrednost C-reaktivnog proteina bila je 8,50 mg/L, ukupnog holesterola 5,34 mmol/L, HDL holesterola 1,26 mmol/L, LDL holesterola 3,16 mmol/L, triglicerida 2,03mmol/L. Statističkom obradom podataka utvrđeno je da postoji vrlo značajna povezanost ($p<0,01$) između vrednosti C-reaktivnog proteina i HDL holesterola, kao i CRP-a i ukupnog holesterola. Nije nađena korelacija između koncentracija CRP-a unutar dve grupe ispitanika. Postoji statistički veoma značajna razlika između vrednosti HDL kod ispitanika sa i bez infarkta miokarda ($p<0,01$).

A10
POREĐENJE TRI RAZLIČITA BODOVNA SISTEMA ZA PROCENU 10-GODIŠNJEG RIZIKA ZA NASTANAK KORONARNE BOLESTI SRCA

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Budući da je ateroskleroza multifaktorijalna bolest i da faktori rizika imaju multiplikativno dejstvo, u cilju identifikacije i lečenja asimptomatskih osoba sa visokim rizikom za razvoj koronarne bolesti srca (KBS) u praksi se koriste različiti bodovni sistemi za procenu rizika. Cilj istraživanja bio je poređenje procenjenog 10-godišnjeg rizika za KBS prema Framinghamskom (FHS), PROCAM i SCORE bodovnom sistemu kod 110 asimptomatskih osoba oba pola, starosti 30–80 godina, prilikom prvog pregleda i godinu dana posle lečenja lipidskog poremećaja. Faktori rizika koji su uključeni u izra-

correlation between an inflammatory response expressed in C-reactive protein and acute myocardial infarction and to establish the presence of correlation between C-reactive protein and the lipid profile. The project involved 94 patients who were admitted into the Internist Out-Patient Clinic of the Clinical Centre in Banjaluka, with suspected myocardial infarction. The values of total cholesterol, HDL and LDL cholesterol, aminotransferase (AST, ALT), creatine kinase (CPK), and glucose were determined by standard laboratory methods. C-reactive protein was measured by a high-sensitivity immunoturbidimetric method (Latex) on a »Hitachi 902« analyzer using »Roche« diagnostic reagents. The average age of the patients was 59 years. There were 71 men and 23 women in the group. After a diagnose for each patient was established, two groups were formed: a group of 22 patients with the diagnosis of myocardial infarction and a group of 72 without myocardial infarction. In the group of patients with myocardial infarction the mean value of C-reactive protein was 12.89 mg/L, total cholesterol 5.13 mmol/L, HDL cholesterol 1.02 mmol/L, LDL cholesterol 3.17 mmol/L, triglycerides 2.00 mmol/L. In the group of patients without myocardial infarction the mean value of C-reactive protein was 8.50 mg/L, total cholesterol was 5.34 mmol/L; HDL cholesterol 1.26 mmol/L, LDL cholesterol 3.16 mmol/L and triglycerides 2.03 mmol/L. Statistical analyses showed that there is a statistically significant relation between CRP values and HDL cholesterol, and also between CRP and total cholesterol. No connection was found between the concentrations of CRP within the two examined groups. There is a statistically important difference in the HDL values of the examinees with or without myocardial infarction ($p<0.01$).

A10
COMPARISON OF THREE DIFFERENT RISK SCORES FOR A 10-YEAR CORONARY HEART DISEASE RISK EVALUATION

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Considering that atherosclerosis is a multifactorial disease and that risk factors have multiplicative effects, in the everyday routine identification and treatment of asymptomatic individuals at high risk for developing coronary heart disease (CHD) different risk scoring schemes are used. The aim of this study was to compare the estimated 10-year CHD risk according to Framingham (FHS), PROCAM and SCORE risk scores in 110 asymptomatic individuals of both sexes, 30–85 years old, at first examination and after a one-year lipid disorder treatment. The risk factors involved in the cal-

čunavanje su pol, starost, ukupni, LDL i HDL holesterol, sistolni krvni pritisak, pozitivnost porodične anamneze, kao i podatak o uzimanju antihipertenzivne terapije i pušačkom statusu. Od 110 ispitanika, nizak rizik imalo je prema FHS 60 osoba (54,55%), PROCAM-u 86 (78,18%) i SCORE-u 48 (43,64%), srednji rizik prema FHS 35 (31,82%), PROCAM-u 15 (13,64%) i SCORE-u 37 (33,64%), i visok rizik prema FHS 15 (18,18%), PROCAM-u 9 (8,18%) i SCORE-u 25 (22,73%) osoba. Posle godinu dana lečenja lipidskog poremećaja niskorizičnih je bilo prema FHS 86 (78,18%), PROCAM-u 97 (88,18%) i SCORE-u 61 (55,45%), srednjerizičnih prema FHS 17 (15,45%), PROCAM-u 11 (10,00%) i SCORE-u 36 (32,73%), a visokorizičnih prema FHS 7 (6,36%), PROCAM-u 2 (1,82%) i SCORE-u 13 (11,82%). Postoji statistički značajna razlika ($p<0,05$) u pripadnosti određenoj kategoriji rizika i to prilikom prvog pregleda između FHS i PROCAM-a, kao i između PROCAM-a i SCORE-a, za sve kategorije rizika, a posle godinu dana između FHS i PROCAM-a, FHS i SCORE-a za kategorije s niskim i srednjim rizikom, a između PROCAM-a i SCORE-a za sve kategorije rizika. Razlike u pripadnosti određenoj kategoriji rizika koje se dobijaju korišćenjem tri različita bodovna sistema mogu se objasniti različitim faktorima rizika koji su uključeni u svaki algoritam kao i statističkim hazard modelima koji su u osnovi svakog od njih.

culation are gender, age, total cholesterol, HDL and LDL cholesterol, systolic blood pressure, treatment of hypertension and positive family history. Among 110 individuals, there were 60 persons at low risk according to FHS (54.55%), PROCAM 86 (78.18%) and SCORE 48 (43.64%); intermediate according to FHS 35 (31.82%), PROCAM 15 (13.64%) and SCORE 37 (33.64%) and high risk according to FHS 15 (18.18%), PROCAM 9 (8.18%) and SCORE 25 (22.73%). After a one-year lipid disorder treatment 86, persons were at low risk according to FHS (78.18%), PROCAM 97 (88.18%) and SCORE 61 (55.45%); intermediate according to FHS 17 (15.45%), PROCAM 11 (10.00%) and SCORE 36 (32.73%) and high risk according to FHS 7 (6.36%), PROCAM 2 (1.82%) and SCORE 13 (11.82%). There were significant differences ($p<0.05$) in the risk category assignment at first examination between FHS and PROCAM as well as between PROCAM and SCORE, and after a one-year lipid disorder treatment between FHS and PROCAM and FHS and SCORE in low and intermediate risk categories and between PROCAM and SCORE for all risk categories. The differences in risk category assignment using the three different risk scoring schemes can be explained by the use of different risk factors involved in algorithm calculation as well as different statistic hazard models used for their construction.

A11
PARAMETRI AKTIVACIJE TROMBOCITA KOD PACIJENATA PODVRGNUTIH PERKUTANOJ TRANSLUMINALNOJ KORONARNOJ ANGIOPLASTICI

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Trombociti igraju važnu ulogu u razvoju i formiranju tromba kod pacijenata koji su podvrgnuti perkutanoj transluminalnoj koronarnoj angioplasici (PTCA), zbog efekta PTCA na ćelije endotela na mestu implantacije stenta. Shodno tome, antikoagulantna i antitrombocitna terapija se često koriste kod tih pacijenata. Cilj ove studije je bio da se ispita novi parametar trombocitne aktivacije (MPC, srednja gustina trombocita, g/L), za utvrđivanje aktivacije tormbocita i njihovog odgovora na antiagregacionu terapiju (klopidogrel) šest meseci posle PTCA intervencije. Parametri trombocita MPC, srednji volumen trombocita (MPV, fL), distribucija širine trombocitne gustine (PCDW, g/L), srednja masa trombocita (MPM, pg) i broj trombocita (PC $\times 10^9$/L) analizirani su na automatskom hematološkom sistemu »ADVIA 120.« Za merenje ADP (%), kao parametra agregabilnosti trombocita, korišćen je komercijalni test firme »Dade Behring«. Krv je saku-

A11
PLATELET ACTIVATION PARAMETERS IN PATIENTS UNDERGOING PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY

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Platelets play a major role in the development of thrombus formation in patients undergoing percutaneous transluminal coronary angioplasty (PTCA), because PTCA has an effect of damaging the endothelial cells on the spot when the stent is present. Consequently, anticoagulant and antiplatelet therapies are widely used for those patients. The aim of the study was to investigate the usefulness of new activating platelet parameters (MPC, mean platelet component concentration, g/L) for evaluating the platelet activation and the platelet response to antiplatelet therapy (clopidogrel) in patients six months after PTCA. The platelet research parameters MPC and other related parameters i.e., the mean platelet volume (MPV, fL), platelet component distribution width (PCDW, g/L), mean platelet mass (MPM, pg) and platelet count (PC $\times 10^9$/L) were analyzed on an automated ADVIA 120 Hematology System. A commercial Dade Behring test

pljena od 26 pacijenata pre (bazalno) i posle ergometrije. Sniženje u gustini trombocita, mereno redukcijom u MPC (srednja vrednost ±SD, 242,8±13,56, 225,8±15,37, p<0,001) je znak trombocitne aktivacije. Vrednost MPV je značajno povećana (9,7± 1,11, 10,25±1,08, p<0,001), reflektujući promenu oblika trombocita. ADP je blago snižen (52,8±10,48, 48,9±12,22) kao odgovor pacijenata na anti-agregacionu terapiju koja modifikuje aktivaciju trombocita. Naši podaci pokazuju da upotreba parametara aktivacije trombocita kod pacijenata podvrgnutih PTCA može biti korisna alatka u otkrivanju rizika za aktivaciju trombocita i sledstveno tome rani indikator rizika za razvoj tromboze.

was used for measuring the platelet aggregometry parameter, ADP (%). Blood samples were collected from 26 patients before (baseline) and after an ergometric test. A decrease in platelet density, measured by reduction in MPC (means ± SD, 242.8±13.56, 225.8 ±15.37, p<0.001) is indicative of the platelet activation. The values of MPV increased significantly (9.7±1.11, 10.25±1.08, p<0.001), reflecting a shape change. ADP values was mildly decreased (52.8±10.48, 48.9±12.22) reflecting the response in patients on antiaggregation therapy which modified the platelet activation. Our data show that the use of platelet activation parameters in patients undergoing the PTCA may be helpful in detecting the risk of platelet activation, and hence as an indicator of patients at risk of thrombosis.

A12
AKTIVNOST KASPAZE-3 U LIMFOCITIMA BOLESNIKA SA ISHEMIJSKOM BOLEŠĆU SRCA

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Smrt ćelija apoptozom može imati kritičnu ulogu u različitim kardiovaskularnim oboljenjima. Apoptoza se može indukovati kao odgovor na ishemiju, toksine i fizičke stimuluse. Ključni fenomen u apoptozi je aktivacija jedne od efektorskih kaspaza – kaspaze-3, koja se može aktivisati indukcijom i spoljašnjeg i unutrašnjeg puta apoptoze. Njena aktivacija vodi fragmentaciji DNK i smrti ćelije. U ovom radu određivana je aktivnost kaspaze-3 u limfocitima periferne krvi, koji su izolovani pomoću separacionog medijuma. Aktivnost kaspaze-3 merena je komercijalnim, kolorimetrijskim ELISA testom koji se bazira na razgradnji sintetskog tetrapeptida DEVD-pNa. Aktivnost enzima je određivana u limfocitima bolesnika sa stabilnom anginom (SAP, 30), sa nestabilnom anginom pektoris (NSAP, 26) i sa akutnim infarktom miokarda (AIM, 38). Dobijeni rezultati su poređeni sa vrednostima kaspaze-3 u kontrolnoj grupi (zdravi ispitanici). U limfocitima bolesnika sa SAP aktivnost enzima je bila 0,093±0,035 μmol/mg proteina, a kod bolesnika sa AIM 0,106±0,061 μmol/mg proteina, (to su neznačajno više vrednosti u odnosu na one u kontolnoj grupi (0,092±0,022 μmol/mg proteina). U limfocitima bolesnika sa NSAP aktivnost kaspaze-3 (0,118±0,061 μmol/mg proteina) bila je značajno povišena (p<0,05) u odnosu na kontrolnu i ostale dve grupe bolesnika. Može se zaključiti da aktivnost kaspaze-3 može biti validan parametar u proceni aktivnosti aterosklerotičnog plaka, ali i nova mogućnost za terapijsku intervenciju.

A12
CASPASE-3 ACTIVITY IN THE LYMPHOCYTES OF PATIENTS WITH ISCHEMIC HEART DISEASE

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Apoptotic cell death may play a critical role in a variety of cardiovascular diseases and may occur in response to ischemia, toxins and physical stimuli. A key phenomenon of apoptotic cell death is the activation of one of the effector caspases – caspase-3, which may be activated by both extrinsic and intrinsic apoptotic pathways. The caspase-3 activation leads to DNA fragmentation and cell death. In this study, the activity of caspase-3 was determined in the lymphocytes of peripheral blood isolated using a lymphocyte separation medium. Caspase-3 activity was measured by a colorimetric commercially available ELISA kit based on the degradation of synthetic tetrapeptide DEVD-pNa. Enzyme activity was determined in the lymphocytes of patients with stable angina (SAP, 30), with unstable angina pectoris (USAP, 26), and with acute myocardial infarction (AMI, 38). The obtained results were compared to the caspase-3 values in the control group (healthy individuals). In the lymphocytes of patients with SAP the enzyme activity was 0.093±0.035 μmol/mg protein, but in patients with AMI 0.106±0.061 μmol/mg protein, and both values were insignificantly higher in comparison with controls (0.092±0.022 μmol/mg protein). In the lymphocytes of NSAP patients the caspase-3 activity (0.118±0.061 μmol/mg protein) was significantly higher (p<0.05) compared to the control as well as to both other patient groups. In conclusion, the caspase-3 activity may be a valid parameter for assessing atherosclerotic plaque activity, and a new target for therapeutic intervention.

A13
KORISNOST BIOMARKERA I KLINIČKIH ANALITAKAO PREDIKTORA U KARDIOHIRURGIJI

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Kardiohormon BNP je dragocen dijagnostički marker kod pacijenata sa kongestivnom srčanom slabošću (HF), ali BNP je i važan prognostički indikator za pacijente koji podležu kardiohirurgiji na otvorenom srcu. Hirurgiju na otvorenom srcu prate značajni postoperativni kardio-događaji, a prisutna je uvek i inflamatorna faza sa različitim stepenom težine. Mogućnost predviđanja efektivnih postoperativnih komplikacija, dužine hospitalizacije i morbiditeta još uvek je nesigurna, jer zasad ne postoji »zlatni standard«. Cilj ove studije bio je da predloži varijetet »multifaktornih indeksa« za preoperativni rizik pacijenata kod kojih treba da se izvrši kardiohirurški zahvat. Za ovaj deo studije izabrani su sledeći testovi: BNP i »inflamatorni indeks« zasnovan na analizama prokalcitonina (PCT) i C-reaktivnog proteina (CRP) u odnosu na renalnu funkciju pacijenta. Takav izbor pruža značajan doprinos za preoperativnu kvantitativnu evaluaciju. Stodvoje pacijenata sa CHF (13,7% žena, 86,3% muškaraca starosne dobi 62,9±7,8 vs. 59±9,7 godina) podeljeni su u tri grupe na bazi hirurške intervencije: CABG – grupa 1 (*coronary artery bypass grafting*), *valve* rekonstrukcija – grupa 2, i kombinacija obe, CABG+*valve* – grupa 3. Za sve testove su korišćene imunohemijske metode: PCT (ILMA), CRP (imunoturbidimetrijska), BNP direktna imunohemiluminiscenca (»Bayer ACS180Plus«). Analize su izvođene preoperativno, 6 časova, 24 časa i 48 časova posle operacije. Dobijeni rezultati su sledeći:

Klinički status	CABG (group 1)				VALVE (group 2)				CABG+VALVE (group 3)			
	Infl.	BNP	GFR	creat(S)	Infl.	BNP	GFR	creat(S)	Infl.	BNP	GFR	creat(S)
index (odnos)	Index	ng/L		μmol/L	Index	ng/L		μmol/L	Index	ng/L		μmol/L
srednje vrednosti					srednje vred.				srednje vred.			
pre-op	54,4	585	61,9	118,7	36,7	515	72,2	99	90	346	63,7	109,8
0 day postop	120,2				181,2				211,3			
24h postop	354,1				379,3				399,7			
48h postop	389,6				381,1				458,8			
range: (CI: 95%)					range: (CI: 95%)				range: (CI: 95%)			
GFR mL/min/1.73 m^2 (MDRD)									Infl.index =			

Inflamatorni proces predviđa i kartkoročne i dugoročne kardio-rizike. Srednja vrednost inflamatornog indeksa bila je najniža u grupi 2, a najviša u grupi 3. Postoperativno su sve vrednosti Inflamatornog indeksa bile povišene. Inflamatorni markeri PCT i CRP imaju značajnu prediktivnu vrednost. Ova studija pokazuje da je Inflamatorni indeks jači prediktor za rizike komplikacija. Četrdesetosam časova posle operacije oni ostaju još veoma visoki (cutoff < 10) u sve tri grupe. To pokazuje da inflamatorni proces još uvek nije završen, i korisno ih je primeniti za izbor adekvatne terapije i

A13
THE UTILITY OF BIOMARKERS AND CLINICAL ANALYTES AS PREDICTORS IN CARDIAC SURGERY

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The cardiac hormone BNP is a valuable diagnostic marker in patients with congestive heart failure (CHF), but BNPis also an important prognostic indicator for patients undergoing open heart surgery. Open heart surgery is asssociated with significant risks for postoperative cardiac events and an inflammatory phase with different degrees of severity is always present. The ability to effectively predict postoperative complications, the duration of hospital stay and mortality is yet uncertain, and no gold standard currently exists. The purpose of the present study was to propose a variety of multifactor indexes for preoperative risk assessment in patients undergoing cardiac surgery. This part of the study focuses on the following tests: BNP and the »Inflammatory index« based on procalcitonin (PCT) and C-reactive protein (CRP) analysis, and the relation to renal function of the patients. This choice offers an important addition to the preoperative quantitative evaluation. One hundred and two patients with CHF (13.7% female, 86.3% male; ages: 62.9±7.8 vs 59± 9.7 years) were divided into three groups, on the basis of the surgical intervention: CABG – group 1, valve reconstruction – group 2, and the combination of both, CABG+valve procedures – group 3. We introduce and define the »inflammatory index« established on the basis of the PCT-ILMA method and CRP immunoturbidimetric analysis, BNP (P) by a direct immunochemiluminiscent automatic assay, measured on an ACS180Plus (Bayer) analyzer. GFR was calculated with MDRD. The analyses were performed preoperatively, 6 hours, 24 hours and 48 hours after the intervention. Results for BNP, the Inflammatory index, creatinine and GFR are:

Clinical status	CABG (group 1)				VALVE (group 2)				CABG+VALVE (group 3)			
	Infl.	BNP	GFR	creat(S)	Infl.	BNP	GFR	creat(S)	Infl.	BNP	GFR	creat(S)
ratio	Index	ng/L		μmol/L	Index	ng/L		μmol/L	Index	ng/L		μmol/L
mean values					mean values				mean values			
pre-op	54.4	585	61.9	118.7	36.7	515	72.2	99	90	346	63.7	109.8
0 day postop	120.2				181.2				211.3			
24h postop	354.1				379.3				399.7			
48h postop	389.6				381.1				458.8			
range: (CI: 95%)					range: (CI: 95%)				range: (CI: 95%)			
GFR mL/min/1.73 m^2 (MDRD)									Infl.index =			

The inflammatory process predicts both short-term and long-term cardiac risks. The mean Inflammatory index was lowest in group 2 and highest in the group 3. Postoperatively, all the inflammatory index values were increased. The inflammatory markers PCT and CRP have significant predictive values. This study shows that the inflammatory index is a stronger pre-

dalju kontrolu iste. BNP srednje (mean) vrednosti, a naročito srednje vrednosti koreliraju sa inflamatornim indeksom. GFR i kreatinin (i mean i median) vrednosti (uključeni zbog kontrole renalne funkcije pacijenata) bile su < 90 mL/min /1,73 m^2 u sve tri grupe. BNP srednje vrednosti bile su najviše u grupi 2, a najniže u grupi 1. Odnos između niskih i visokih BNP cutoff vrednosti stratificira preporučene GFR (naše sledeće saopštenje, drugi deo). Gornje i donje granične vrednosti inflamatornog indeksa su se striktno i stalno značajno pomerale u toku celog 48-časovnog postoperativnog perioda. Shifting graničnih limita ukazuje na poboljšanje maksimalnog scattering-a analiza (kompaktnost postoperativnih zbivanja). Predloženi set prediktora je veoma pouzdan, ekonomski efikasan, štedi vreme i primenjiv je u urgentnoj službi.

dictor for risks of complications. Forty-eight hours after operation, they remain very high (cutoff < 10) in all three groups. This proves that the inflammatory process is not finished after 48 hours which is very useful for the choice of adequate therapy as well control measures for this therapy. The mean BNP levels, and particularly the median levels, correlate with the inflammatory indexes. GFR and creatinine (included for the control of renal dysfunction) mean and median levels were < 90 mL/min/m^2 in all three groups. The median BNP level was the highest in group 2, the lowest in group 1. Nevertheless, the relation between the lower and higher BNP cutoffs stratifies the recommended GFR (our next communication, part 2 of this study). The upper and lower range limits of the inflammatory index shifted strikingly and continuously during the complete 48-hour postoperative study phase. The shifting of the range limits points at an improvement of the maximal analysis scattering. The proposed set of predictors is very reliable, cost-effective, time-efficient and applicable in emergency services.

A14
PRIMENA REYNOLDS RIZIK SKORA U PROCENI KARDIOVASKULARNOG RIZIKA KOD ŽENA

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Starost, hipertenzija, pušenje, dijabetes i hiperlipidemija su uključeni u globalne rizik skorove za procenu kardiovaskularnog rizika. Međutim, kod žena, do 20% svih koronarnih bolesti se javlja u odsustvu svih ovih glavnih faktora rizika, a kod mnogih žena sa prisutnim tradicionalnim faktorima rizika ne dolazi do koronarnih komplikacija. Takođe, skoro 70% svih kardiovaskularnih bolesti se javlja kod osoba sa intermedijarnim rizikom (rizik od 5–20% određen *Framingham* rizik skorom (FRS) ili rizik od 1–5% određen na osnovu SCORE sistema). *Reynolds* rizik skor (RRS), novi model procene globalnog kardiovaskularnog rizika, razvijen samo za žene, uključuje visoko osetljivi C-reaktivni protein (hsCRP) i pojavu infarkta miokarda pre 60. godine kod jednog od roditelja, pored glavnih faktora rizika – sistolnog krvnog pritiska, pušenja, ukupnog i HDL holesterola. Cilj ovog rada je bio poređenje kardiovaskularnog rizika određenog na osnovu FRS, SCORE i RRS kod 138 zdravih, asimptomatskih žena, starih 30–85 godina. Ukupan i HDL holesterol i hsCRP su određeni na analizatoru »Olympus AU2700«, u serumima izdvojenim iz uzoraka krvi uzetih posle 12h gladovanja. FRS je izračunavan pomoću programa *ATP III Risk Estimator*, rizik na osnovu SCORE-a je dobijen pomoću *HeartScore* programa, a RRS je određen korišćenjem

A14
APPLICATION OF THE REYNOLDS RISK SCORE IN CARDIOVASCULAR RISK ASSESSMENT IN WOMEN

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Age, hypertension, smoking, diabetes and hyperlipidemia are incorporated into global risk scores for assessment of cardiovascular risk. However, in women, up to 20% of all coronary events occur in the absence of these major risk factors and many women with traditional risk factors do not experience coronary events. Also, almost 70% of all cardiovascular disease (CVD) events occur among individuals at intermediate risk (5-20% of risk determined using *Framingham* Risk Score (FRS) or 1–5% of risk determined using SCORE). *Reynolds* Risk Score (RRS), the new risk prediction model for global cardiovascular risk, developed exclusively for women, includes high sensitivity C-reactive protein (hsCRP) and parental history of myocardial infarction before age 60 next to major risk factors: systolic blood pressure, smoking, total and HDL cholesterol. The aim of this study was to compare CVD risk assessed using FRS, SCORE and RRS in 138 healthy, asymptomatic women, 30–85 years old. Total and HDL cholesterol and hsCRP were determined in sera collected after a 12h fasting period using an Olympus AU2700 analyzer. FRS was calculated using the *ATP III Risk Estimator* and risk status according to SCORE was obtained using the HeartScore Programme for populations at high risk. RRS was determined using *Reynolds Risk Score*

Reynolds Risk Score kalkulatora. Upotrebom RRS 6 (5%) učesnica je pomereno u višu, a 7 (5%) učesnica je pomereno u nižu kategoriju rizika u odnosu na rizik određen po FRS-u. U poređenju sa svojim rizikom po SCORE-a, 25 (18%) učesnica je klasifikovano u nižu kategoriju rizika, a samo 3 (2%) učesnica je klasifikovano u višu kategoriju rizika na osnovu RRS-a. Razlika između raspodela rizika u odabranoj populaciji je značajna kada se uporede SCORE i RRS (χ^2=21,53; p<0,001; df=2). Raspodele rizika na osnovu FRS i RRS nisu statistički značajno različite (χ^2=3,08; p=0,214; df=2), što se ne slaže sa objavljenim podacima. Mogući razlog je veliki broj učesnica sa niskim inicijalnim rizikom (desetogodišnji rizik <5% na osnovu FRS-a, odnosno <1% na osnovu SCORE-a) u odabranoj populaciji.

Calculator. With RRS, 6 (5%) participants were moved to a higher and 7 (5%) were moved to a lower risk category compared with their FRS. In comparison with their SCORE results, 25 (18%) participants were reclassified into a lower risk category and only 3 (2%) were reclassified into a higher risk category according to their RRS. The difference between risk distribution in the selected population was significant when SCORE and RRS were compared (χ^2= 21.53; p<0.001; df=2). Risk distributions according to FRS and RRS showed no statistical difference (χ^2=3.08; p=0.214; df=2), which is in disagreement with published data. The reason for this might be the large number of participants with low initial risk (<5% 10-year risk based on FRS or <1% according to SCORE) in the selected population.

A15
PACIJENTI SA BUBREŽNOM INSUFICIJENCIJOM I FAKTORI KOJI POVEĆAVAJU RIZIK OD KARDIOVASKULARNIH BOLESTI

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Oboljenja bubrega su udružena sa značajno povećanim rizikom za nastanak kardiovaskularnih obolenja. Mnoga istraživanja su pokazala da je smanjena bubrežna funkcija udružena sa poremećajem koncentracije triglicerida, a zapaža se i snižavanje HDL holesterola. Promene u koncentraciji markera inflamacije (CRP, fibrinogen), malnutricije (albumin) i koagulacije (fibrinogen) takođe su udružene sa povećanim mobiditetom i mortalitetom usled kardiovaskularnih bolesti kod bubrežnih pacijenata. Koncentracije ukupnog holesterola (TC), LDL holesterola, triglicerida (TG), apolipoproteina AI (Apo AI), apolipoproteina B (Apo B), lipoprotein a (Lpa), CRP, fibrinogen, albumin određivani su u 100 uzoraka pacijenata sa oštećenom funkcijim bubrega (65 hemodijaliziranih pacijenata i 35 pacijenata sa hroničnom bubrežnom insuficijencijom) i 100 zdravih pacijenata. Parametri su određivani komercijalnim testovima automatizovanim metodama. LDL holesterol je izračunat Friedewaldovom formulom. Aterogeni rizik je izračunat kroz odnos TC/ HDL-c i LDL/HDL-c. TG, CRP, fibrinogen, TC, LDL, Apo B su značajno viši kod bubrežnih pacijenata, dok su HDL-c, Apo AI niži nego u kontrolnoj grupi. Prevalenca hipertenzije kao faktora rizika za nastanak koronarnih bolesti takođe je prisutna kod pacijenata sa bubrežnom insuficijencijom.

A15
PATIENTS WITH END STAGE RENAL DISEASE AND FACTORS WHICH INCREASE THE RISK OF CARDIOVASCULAR MORBIDITY

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Renal failure is accompanied with significantly increased risk of cardiovascular morbidity and mortality. Previous studies have revealed that progressive renal failure is accompanied by abnormalities of plasma tryglyceride, and a decrease in HDL cholesterol concentrations with smaller change in the levels of cholesterol rich lipoproteins. Also, markers of inflammation (CRP, fibrinogen), malnutrition (albumin) and hipercoagulability (fibrinogen) have been linked to an excessive morbidity and mortality. The concentrations of total cholesterol (TC), low density lipoprotein cholesterol (LDL), tryglycerides (TG), apolipoprotein AI (ApoAI), apolipoprotein B (Apo B), lipoprotein a (Lpa), CPR, fibrinogen, albumin were measured in the samples of 100 patients (65 hemodialysed (HD), 35 with chronic renal failure (CRF)) and 100 age and sex-matched healthy patients as controls. Parameters were examined by standard automated assays using commercial reagents. LDL was calculated according to the Friedewald formula. Atherogenic risk factors were calculated as TC/HDL-c and LDL/HDL-c ratio. TC, TG, CRP, fibrinogen, LDL cholesterol, Apo B levels were significantly higher (p>0.05) and HDL-c and ApoAI were lower than in healthy persons (p<0.05). Cardiovascular events were noted in 21 patients. Prevalence of hypertension and the CRP concentration were also higher in CRF and HD patients with CVD.

B

METODE U KLINIČKOJ HEMIJI

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Poster sessions

B16
RAZVIJANJE METODE ZA ISTOVREMENO ODREĐIVANJE REDUKOVANOG I OKSIDOVANOG GLUTATIONA U KRVI BEZ DERIVATIZACIJE KORIŠĆENJEM KAPILARNE ELEKTROFOREZE I FAKTORSKOG DIZAJNA

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Glutation (GSH) ima važne uloge u celokupnom metabolizmu, uključujući hemostazu ćelije, radioprotekciju i antioksidativnu odbranu. U prisustvu slobodnih radikala kiseonika on se oksiduje u disulfidnu formu (GSSG). Stoga je njegovo merenje korisno za određivanje oksidativno/anitoksidativnog statusa u raznim fiziološkim i patofiziološkim stanjima. Kako koncentracija glutationa u krvi može da odražava glutationski status u drugim tkivima manje dostupnim za analizu, određivanje GSH i GSSG u krvi se smatra kao dobar pokazatelj oksidativnog statusa osobe, koji predstavlja koristan indikator rizika za razvoj bolesti. Do sada korišćene metode uglavnom mere samo GSH, dok se nivo GSSG izračunava. Kapilarna elektroforeza pruža mogućnost za njihovo istovremeno određivanje, a dosad razvijene metode obično zahtevaju njihovu derivatizaciju. Korišćenjem faktorijalnog dizajna za variranje odgovarajućih parametara (pH i koncentracija elektrolita, temperatura separacije), mi smo razvili jednostavnu i brzu metodu za istovremeno analiziranje GSH i GSSG bez njihove prethodne derivatizacije. Dobijeni rezultati su pokazali da njihovo razdvajanje zavisi od pH elektrolita u kom se vrši separacija, a u manjoj meri od koncentracije rastvora ili temperature. Najbolje razdvajanje ispitivanih komponenti je postignuto u 10 mmol/L fosfatnom puferu, pH 2,90–2,95, na temperaturi od 180 °C i pri naponu od 15 kV. Pod optimalnim uslovima analiza traje 30 minuta. Dobijen je linearan odnos između površine pika i koncentracije (r=0,995 i 0,999) uz dobru preciznost određivanja (9,7 i 12,1% za GSH i GSSG). Metoda je testirana analiziranjem hemolizata humane krvi. Dobijeni rezultati pokazuju da je u krvi zdravih odraslih osoba (n=10) nivo GSH (1340 ± 292 μmol/L) skoro petnaest puta veći od nivoa GSSG (80 ± 36 μmol/L). Rezultati naših ispitivanja su takođe pokazali da je fak-

B16
THE DEVELOPMENT OF A METHOD FOR THE SIMULTANEOUS MEASUREMENT OF GLUTATHIONE AND GLUTATHIONE DISULFIDE IN BLOOD WITHOUT DERIVATIZATION EMPLOYING CAPILLARY ELECTROPHORESIS AND INCLUDING A FACTORIAL DESIGN

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Glutathione (GSH) has important roles in the overall metabolism, including cell homeostasis, radioprotection and antioxidant defense. In the presence of free oxygen radicals it is oxidized to the disulfide form (GSSG). Thus, their measurement is useful for determining the oxidative/antioxidative status in various physiological and patophysiological conditions. Since blood glutathione concentrations may reflect glutathione status in other less accessible tissues, measurement of both GSH and GSSG in blood has been considered essential as an index of the whole subject oxidative status and as a useful indicator of disease risk in humans. Usually, GSH is measured, while GSSG is calculated. The capillary electrophoresis permits their separation, but needs their derivatization. Using a full factorial design for screenning important variables (i.e. carrier electrolyte pH, concentration and separation temperature), we developed a simple and rapid method for the simultaneous analysis of GSH and GSSG without any derivatization procedures for the examined compounds. The obtained results indicated that their separation was mainly influenced by the pH of the running electrolyte, while its concentration as well as temperature had little effect upon their resolutions. The best separations of the examined compounds were obtained with a 10 mmol/L phosphate buffer, pH from 2.90 to 2.95, 180 °C temperature and 15kV voltage. It was achieved within less than 30 minutes. A linear relationship between peak area and concentrations (r=0.995 and 0.999) with good precisions (9.7 and 12.1% for GSH and GSSG, respectively) were obtained. The method was used to analyze human capillary blood needing only its hemolyses. The obtained results have shown that in the blood of healthy subjects (n=10) GSH (1340 ±292 μmol/L) was almost fifteen times greater than the GSSG (80 ±

torijalni dizajn korisan postupak za definisanje promenljivih koje omogućavaju najbolje razdvajanje komponenti iz smeše pomoću kapilarne elektroforeze.

B17
POREĐENJE DVE METODE ZA KVANTITATIVNO ODREĐIVANJE FERITINA U HUMANOM SERUMU

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Feritin je veliki makromolekul (450kDa) koji se sintetiše u jetri i drugim tkivima i ima glavnu ulogu u deponovanju gvožđa. Feritin je osetljiv pokazatelj nedostatka gvožđa u organizmu, jer koncentracija feritina opada pre smanjenja nivoa serumskog gvožđa, hemoglobina ili veličine eritrocita. Stoga je osnovni klinički značaj određivanja feritina dijagnostikovanje anemije. Koncentracija feritina može biti povećana usled preopterećenja organizma gvožđem (kod hemohromatoza ili hemosideroza), infekcija ili inflamacija, malignih oboljenja i oštećenja tkiva jetre. U ovom radu izvršeno je poređenje dva komercijalna testa za određivanje koncentracije feritina, zasnovana na različitim principima: 1) lateks test »FERITINA LATEX L«, »Globe Diagnostics«, Italija i 2) ELISA test »Ferritin«, »DIMA Diagnostika«, Getingen, Nemačka. Koncentracija feritina određena je prema uputstvu proizvođača u 30 uzoraka seruma. Dve metode su upoređene primenom linearne regresione i korelacione analize, a razlika između dve metode je testirana t-testom za parove određivanja. Dobijeni rezultati pokazali su dobro slaganje između dve metode (r^2=0,9950). Razlika između dve grupe rezultata nije bila statistički značajna. Koncentracije feritina određene lateks testom bile su generalno niže od vrednosti dobijenih ELISA testom. U opsegu koncentracija feritina nižih od referentnih vrednosti, ELISA test je osetljiviji od lateks testa, koji daje više vrednosti u opsegu niskih koncentracija. Rezultati pokazuju da ispitani ELISA test ima bolju analitičku osetljivost od ispitanog lateks testa i da je kao takav osetljiviji u otkrivanju pacijenata sa nedostatkom gvožđa, kod kojih se obično očekuju vrednosti feritina u serumu niže od referentnih.

36 μmol/L) level. This study also confirms factorial design as a suitable procedure in screening important variables leading to the best separation of the compounds present in a mixture employing capillary electrophoresis.

B17
A COMPARISON OF TWO METHODS FOR THE QUANTITATIVE DETERMINATION OF FERRITIN IN HUMAN SERUM

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Ferritin is a large macromolecule (450kDa) which is synthesized in the liver and other tissues and plays a major role in iron storage. Ferritin is a sensitive indicator of iron deficit in the body, since ferritin concentration falls prior to a decrease in serum iron level, haemoglobin or size of erythrocytes. Thus, the main clinical application of ferritin measurement is in the diagnosis of anaemia. The ferritin concentration may increase in the case of iron overload (haemochromatosis or haemosiderosis), infection or inflammation, malignancies and destruction of liver tissue. In this work, two commercial kits for the determination of ferritin concentration, based on different immunochemical principles, were compared: 1) a latex test »FERITINA LATEX L«, »Globe Diagnostics«, Italy and 2) ELISA test »Ferritin«, »DIMA Diagnostika«, Goettingen, Germany. The ferritin concentration was determined in 30 serum samples, according to the manufacturer's instructions. Linear regression and correlation analysis were used to compare the two methods and the difference between the methods was tested by a t-test: paired two sample for means analysis. The obtained results exhibited a good correlation between the two methods (r^2=0.9950). There was no significant difference between two groups of results. A latex test gives generally lower values then an ELISA test. However, in the ranges bellow the reference limit, an ELISA test is more sensitive than a latex test, which gives higher values in the low concentration range. The results presented here show that the analysed ELISA test has better analytical sensitivity than the analysed latex test and as such is more sensitive in detecting patients with iron deficiency, whose ferritin levels in serum are often expected to be lower than the reference range.

B18
KONTROLA KVALITETA LABORATORIJSKOG ISPITIVANJA U INEP-U

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Institut za primenu nuklearne energije – INEP je multidisciplinarna naučnoistraživačka organizacija, koja se, pored istraživanja kroz projekte u osnovnim i primenjenim naukama, već godinama bavi razvojem i proizvodnjom imunodijagnostičkih kompleta, kao i brojnim laboratorijskim ispitivanjima, koja uključuju endokrinološke, imunološke, biohemijske i hematološke analize, kao i ispitivanje kontaminacije radionuklidima i agroekologiju. Takva opredeljenost Instituta zahteva stalnu brigu o kvalitetu proizvoda, kao i pouzdanosti rezultata ispitivanja. Zbog toga je u INEP-u tokom 2001. godine uspostavljen sistem upravljanja kvalitetom prema zahtevu standarda ISO 9001:1994, a u 2004. godini i prema zahtevu standarda ISO 9001:2000. Sertifikaciju je obavila međunarodna organizacija »IQNet OQS« (Austrija). Laboratorija za ispitivanje je akreditovana prema zahtevu standarda ISO/IEC 17025 u toku 2003. godine. Analitički kvalitet rada laboratorije obezbeđuje se kontinuiranim sprovođenjem unutrašnje i spoljašnje kontrole kvaliteta. Unutrašnja kontrola kvaliteta (IQA) obuhvata sve aktivnosti koje redovno sprovodi osoblje u laboratoriji za proveru rada, kako bi se omogućila pouzdanost rezultata koji se izdaju korisniku usluga. Sa svakom serijom uzoraka paralelno se testiraju kontrolni serumi i izvodi statistička obrada rezultata. Program za automatsku i grafičku analizu vrednosti koncentracija kontrolnih seruma (Levey-Jennings kontrolne karte) implementiran je u kompjuteru vezanom za gama brojač, a dobijeni podaci se redovno analiziraju. U INEP-u postoji veliki broj interno razvijenih metoda, koje pre primene prolaze kroz postupak validacije, kako bi se potvrdilo da metoda zadovoljava sve pojedinačne zahteve za predviđenu primenu. Za svaku novu metodu urađena je procena merne nesigurnosti. INEP redovno učestvuje u spoljašnjoj kontroli kvaliteta (EQA) koju organizuje DMBS i KCS (SNEQAS – medicinska biohemija), a učestvovao je i u projektu IMEP 17 »Elementi u tragu i minorni konstituenti humanih seruma« ispitivanjem jedinog predviđenog hormona, T4. Dobijeni rezultat merenja T4 u INEP-u je za manje od 5% odstupao od tačne vrednosti određene referentnom metodom, masenom spektrometrijom. Kako u Srbiji nisu uspostavljene EQA za određivanje hormona, tumorskih markera i drugih analita koji se određuju imunotestovima, INEP redovno organizuje međulaboratorijska uporedna ispitivanja sa laboratorijama sličnog profila. Institut se opredelio za stalno poboljšanje postojećeg sistema kvaliteta.

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QUALITY CONTROL OF LABORATORY TESTING IN INEP

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The Institute for the Application of Nuclear Energy (INEP) is a multidisciplinary research organization contributing to biological, medical and agricultural research through projects both in pure and applied science. Scientific results in INEP are used for the development and production of a range of immunodiagnostic sets, together with various laboratory examinations, such as endocrinological, immunological, biochemical and hematological analyses, the monitoring of contamination by radionuclides, and agroecology. Such diverse activity at the Institute demands a permanent concern about the quality of both diagnostic kits and laboratory testing. In order to attain such a goal, a quality management system according to standard ISO 9001:1994 was established at INEP during 2001 and recertification according to standard ISO 9001:2000 was done in 2004. The certification was performed by the international organization »IQNet OQS« (Austria). The laboratory was accredited according to standard ISO/IEC 17025 during 2003. The analytical quality of laboratory testing is provided by applying continuous internal (IQA) and external (EQA) quality assesment. IQA includes all activities of laboratory staff in the quality control of analyses: control sera are tested with each group of patients sera, and the results are statisticaly processed. A program for an automatic graphical analyses of control sera concentrations (Levey-Jennings control cards) is implemented in the gamma counter computer, and the obtained data are regularly analysed. A validation of the methods developed at INEP is necessary in order to confirm that the new methods fulfill all demands for the intended application. For every new analysis, the uncertainty of measurement was determined. INEP participates in the EQA organized by DMBS and KCS (SNEQAS – medical biochemistry), and also took part in the project IMEP 17 »Trace elements and the minor constituents of human serum«, by measuring the concentration of the only hormone included in this project, T4. The result of T4 determination at INEP was by less than 5% different from the exact value determined by the refferent method, mass spectrometry. Due to the lack of such organized EQA for measuring concentrations of hormones, tumor markers and other analytes by immunoassays in Serbia, INEP has been organizing interlaboratory testing of the same analytes with laboratories of a similar profile. The institute is orientated towards constant improvement of the quality system.

B19
UPOREDNO ODREĐIVANJE HEMATOLOŠKIH PARAMETARA NA ANALIZATORIMA ADVIA 120® I HmX-AL®

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U radu hematoloških laboratorija većeg kapaciteta može se pojaviti potreba za korišćenjem analizatora različitih proizvođača. Cilj rada je bio da se uporede vrednosti osnovnih hematoloških parametara dobijene na analizatorima *ADVIA 120-BAYER®* i *HmX-AL-BECKMAN COULTER®*. U 180 uzoraka venske krvi, prikupljenih sa K_2EDTA kao antikoagulansom, paralelno su određeni: leukociti (WBC), eritrociti (RBC), hemoglobin (HGB), hematokrit (HCT), srednji volumen eritrocita (MCV) i trombociti (PLT). Statistička obrada podataka je obuhvatila Studentov t-test i regresionu i korelacionu analizu. Na osnovu dobijenih vrednosti može se zaključiti da pri određivanju leukocita, eritrocita, hemoglobina, hematokrita i trombocita nema statistički značajnih razlika. Poređenjem vrednosti MCV uočeno je neslaganje između analizatora, koje je ukazalo na činjenicu da u uzorcima gde je MCV<83 fL ADVIA 120-BAYER® daje više rezultate od HmX-AL®, dok je iznad te vrednosti odnos obrnut.

B19
PARALLEL DETERMINATION OF HAEMATOLOGICAL PARAMETERS ON ADVIA 120® AND HmX-AL® ANALYZERS

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Haematology laboratories with a high throughput of samples may need analyzers from different manufacturers. The aim of this study was to compare values of basic haematological parameters determined by *ADVIA 120-BAYER®* and *HmX-AL-BECKMAN COULTER®* analyzers. In 180 samples of venous blood, collected with K_2EDTA as an anticoagulant, the following parameters were simultaneously measured: leukocytes (WBC), erythrocytes (RBC), haemoglobin (HGB), haematocrit (HCT), mean cell volume (MCV) and platelets (PLT). The results were compared using a Student's t-test and regression correlation analysis. On the basis of the obtained values we can conclude that there is no statistically significant difference in the determination of leukocytes, erythrocytes, haemoglobin, haematocrit and platelets on the analyzers mentioned above. A comparison of MCV values revealed a significant discrepancy between the obtained results, which drove us to the conclusion that in the samples with microcytosis (MCV<83 fL), the values obtained on the *ADVIA 120* ® are higher than those measured on the *HmX-AL*.

B20
MERENJE KONCENTRACIJE HEMOGLOBINA IZ KAPILARNE I VENSKE KRVI

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Koncentracija hemoglobina određuje se kako iz kapilarne tako i iz venske krvi. Upoređivana je koncentracija hemoglobina iz uzoraka kapilarne krvi hemoglobinometrom sa parametrima uzoraka iz venske krvi rađenih na automatizovanom hematološkom analizatoru. Ispitivanje je rađeno na uzorku od 90 zdravih dobrovoljnih davalaca krvi. Uzorci su uzimani neposredno pre davanja krvi. Kapilarna krv ispitivana je na aparatu *HaemoCue* a uzimana je iz prsta, a iz venske krvi rađene su sledeće analize: koncentracija hemoglobina, broj eritrocita i hematokrit iz uzorka u epruveti sa K_2EDTA na aparatu *Nihon Kohden AVL* i određivanje nivoa gvožđa, TIBC, UIBC i feritina iz seruma na aparatu *Olympus AU400*. Vrednosti hemoglobina kretale su se od 128 g/L do 168 g/L. Iz uzoraka venske krvi, broj

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A COMPARISON BETWEEN THE CONCENTRATION OF HEMOGLOBIN FROM CAPILLARY AND VENOUS BLOOD

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The measurement of the hemoglobin concentration has been done from capillary blood taken from the pulp of the finger or from samples of venous blood. A comparison of the concentration of hemoglobin from capillary blood by hemoglobin meter with parameters from venous blood using an automated hematological analyzer was made. The analysis was done on a sample of 90 healthy voluntary blood donors. The samples had been taken immediately before blood giving. Capillary blood was examined on a HemoCue device taken from the pulp of the finger, and from venous blood we did the following analysis: concentration of hemoglobin, number of erythrocytes, and hematocrite from samples in test tubes with K_2EDTA on a Nihon Kohden AVL device and determination of the level of iron, TIBC, UIBC and

eritrocita je bio na granici od 3,8 x 10^{12}/L do 5 x 10^{12}/L, a u tri slučaja vrednosti su bile ispod normalnih vrednosti. Vrednosti hemoglobina iz venske krvi bile su od 120 do 165 g/L a u dva slučaja su bile ispod normalne granice. Kod ove dve osobe gvožđe je bilo ispod granica normale, a feritin je bio normalan. Ne postoji značajana razlika između rezultata koncentracije hemoglobina, bilo da je krv uzeta kapilarno ili venski. Adekvatnom analizom i praćenjem vrednosti hemoglobina iz kapilarne krvi obezbeđeni su validni rezultati hemoglobina za urgentna stanja, tokom operacija, kod bolesnika sa malignim bolestima kod kojih se vene čuvaju za primenu terapije i svih ostalih pacijenata kod kojih je teško doći do površinskih vena ili su one osetljive.

ferritine from sera on an Olympus AU 400 analyzer. The values of hemoglobin were from 128 g/L to 168 g/L. From samples of venous blood, the number of erythrocytes was close to the limits of from 3.8 x 10^{12}/L to 5.5 x 10^{12}/L, and in three cases the values were below the normal limits. The values of hemoglobin from venous blood were from 120 to 165 g/L, and in two cases they were under normal limits. In these two persons, iron was below the normal limits, and ferritin was within the normal limits. There was no significant difference between the results of hemoglobin concentration from capillary and venous blood. With adequate training and monitoring, the value of hemoglobin from capillary blood supplies valid results of hemoglobin in urgent states, surgery states and in patients with malignant diseases in whom we need to preserve the veins for later therapy, and in all patients who have bad veins or veins that are difficult to reach.

B21
ZNAČAJ ODREĐIVANJA LDL HOLESTEROLA DIREKTNOM METODOM U PRIMARNOJ ZDRAVSTVENOJ ZAŠTITI

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Dom zdravlja Bačka Palanka

Određivanje odnosa između LDL i HDL holesterola po Friedewaldu, tj. izračunavanjem koncentracije LDL holesterola na osnovu koncentracije triacilglicerola, ukupnog i HDL holesterola, predstavlja već skoro 40 godina osnovnu metodu za procenu rizika za aterosklerozu u primarnoj zdravstvenoj zaštiti. Kada se krajem devedesetih godina pojavila mogućnost za direktno merenje koncentracije LDL-a, mnogi su autori utvrdili značajne razlike između direktno izmerene koncentracije i one izračunate po Friedewaldu. Takođe su se pojavile i druge, tačnije metode izračunavanja koncentracije LDL holesterola na osnovu koncentracije triacilglicerola. Cilj ovoga rada je bio da se utvrdi kolike su navedene razlike u uslovima primarne zdravstvene zaštite, i da li one iziskuju napuštanje Friedewaldove metode i direktnog određivanja LDL holesterola ili njenu zamenu nekom boljom metodom izračunavanja. U tu svrhu izvršeno je kod 140 ambulantnih bolesnika određivanje serumskih koncentracija ukupnog holesterola, HDL holesterola i triacilglicerola, na osnovu kojih je izračunata koncentracija LDL holesterola upotrebom Friedewaldove metode i novije metode po Anandaraji, LDLCh=(0,9× Ukupni Ch) – (0,9×TG/2,2) – 0,73. Vrednosti dobijene pomoću obe metode upoređene su zatim sa vrednostima koncentracija LDL holesterola određenih u istim tim uzorcima seruma direktnom enzimatskom metodom, i izračunate razlike i korelacija između njih. Rezultati su prikazani u tabeli:

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THE SIGNIFICANCE OF LDL CHOLESTEROL MEASUREMENT BY USE OF THE DIRECT METHOD IN PRIMARY HEALTH CARE

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The determination of the ratio between LDL and HDL cholesterol according to Friedewald, i.e. by the calculation of LDL cholesterol concentration on the basis of triacylglycerol, total and HDL cholesterol concentration, was for 40 years the basic method for the evaluation of the risk for atherosclerosis in primary health care. From the late nineties, when a direct method for the measurement of LDL concentration was developed, many authors reported significant differences between the directly measured concentrations and those calculated according to Friedewald. Also, several better methods were introduced for the calculation of LDL cholesterol on the basis of triacylglycerol concentration. The aim of this study was to establish how big are these differences in the conditions of primary health care, and also whether they demand abandoning of Friedewald's method and the measurement of LDL cholesterol by the direct method, or its replacement by some better method of calculation. To establish that, measurements of serum concentrations of total cholesterol, HDL cholesterol and triacylglycerol were carried out in 140 outpatients, and on the basis of the obtained results the concentrations of LDL cholesterol were calculated by the use of Friedewald's, and a newer method of Anandaraya: LDLCh=(0.9×Total Ch) – (0.9×TG/2.2) – 0.73. The values obtained by both methods were then compared with the values of LDL cholesterol measured in the same samples by use of the direct enzymatic method, and the differences and correlations between them were calculated. The results are shown in the table:

Pokazatelj	Po Friedewaldu	Po Anandaraji
Razlika srednje vrednosti u odnosu na izmereni LDLCh	–0,40 mmol/L	–0,20 mmol/L
t-test	0,21 (NS)	0,11 (NS)
Koeficijent korelacije u odnosu na izmereni LDLCh	0,824019	0,902479
Veliki uticaj koncentracije TG 1. grupa2. grupa	Iznad 6,0 mmol/L	Iznad 12 mmol/L

Iz dobijenih rezultata se vidi da se računskim metodama, i po Friedewaldu i po Anandaraji, dobijaju niže vrednosti za LDL holesterol, ali da one u obe metode nisu statistički značajne. Vrednosti izračunate pomoću obe metode imaju dobru korelaciju sa vrednostima LDL holesterola izmerenim direktnom metodom, međutim, pri vrednostima triacilglicerola iznad 6,0, odnosno iznad 12,0 mmol/L pojavljuju se neprihvatljivo velike razlike, preko 100%. Iz ovih rezultata proizilazi da se u primarnoj zdravstvenoj zaštiti mogu i dalje upotrebljavati računske procene koncentracije LDL holesterola po Friedewaldu ili po Anandaraji (druga metoda je nešto tačnija i ne iziskuje određivanje HDL holesterola), ali da se pri znatnije povišenim vrednostima triacilglicerola kao i u složenijim tipovima hiperlipoproteinemija mora vršiti direktno određivanje koncentracije LDL holesterola pri proceni rizika za aterosklerozu.

Parameter	Friedewald	Anandaraya
Difference of the mean compared to the direct method	–0.40 mmol/L	–0.20 mmol/L
t-test	0.21 (NS)	0.11 (NS)
Coefficient of correlation compared to the direct method	0.824019	0.902479
Influence of TG concentration	Iznad 6.0 mmol/L	Iznad 12 mmol/L

From the obtained results it is visible that lower values for LDL cholesterol were obtained by calculation with both Friedewald and Anandaraya methods, but these differences were not statistically significant in both methods. The values calculated by the use of both methods showed good correlation with the corresponding values of LDL cholesterol measured by the direct method, meanwhile at values of triacylglycerol concentration above 6.0 and respectively 12.0 mmol/L, unacceptably high differences, above 100%, were found. From these results it can be concluded that calculations of LDL cholesterol according to Friedewald of Anandaraya (which is more accurate and does not need the determination or HDL cholesterol) may be further used in primary health care, but at remarkably elevated triacylglycerol concentrations, as well as in complex types of hyperlipoproteinemias, direct measurement of LDL concentrations should be used for the evaluation of the risk for atherosclerosis.

B22
LABORATORIJSKI INFORMACIONI SISTEM – POMOĆ ILI SMETNJA

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Glavni princip laboratorijskog informacionog sistema (LIS) je da se stavi informacija u red. LIS mora obezbediti podršku i ne sme biti smetnja u dnevnom radu laboratorijskih radnika. Instituti primaju oko 2000 uzoraka ili 15000 analiza dnevno. Starija verzija LIS je ažurirana u 2000. godini. Mi smo počeli sa razvojem LIS, koji je produkt bliske saradnje između naše laboratorije i kompjuterskih eksperata. Glavni cilj i očekivanja od ažuriranja LIS su sledeća: kraće TAT, manje grešaka u administraciji, povećanje u broju elektronskih zahteva od strane odeljenja i klinika, bolja sledivost uzoraka i rezultata, kao i cilj grafičkog prezentovanja rezultata, povezivanje većine analizatora (bi- ili monousmereni), posedovanje što je više moguće informacija o pacijentu i njegovim/njenim zahtevima u jednom elektronskom zapisu. Neki ciljevi su postignuti na samom početku, neki od njih su kasnije razvijeni sa delimičnom reorganizacijom našeg instituta. Teško da je iznenađujuće da nismo na samom početku bili u mo-

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LABORATORY INFORMATION SYSTEM – SUPPORT OR NUISANCE

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The main principle of the laboratory information system (LIS) is to put information in order. LIS must provide support and not be a nuisance in the daily work of laboratory workers. The institute receives around 2000 samples or 15000 analyses daily. The older version of LIS was updated in the year 2000. We started to develop LIS, which is a product of close collaboration between our laboratory and computer experts. The main goals and expectations from the updated LIS were as follows: a shorter TAT, fewer errors at the admission, an increase in the number of electronic orders from wards and clinics, better traceability of the samples and results, as well as the aim to present results graphically, to connect most of the analysers (bi- or mono-directional), to have as much information as possible from the patient and his/her orders in one electronic record. Some goals were attained at the very beginning, some of them were developed later with a partial reorganisation of our institute. It is hardly sur-

gućnosti da predvidimo sve probleme na koje se nailazilo za vreme implementacije novog LIS. U toku ovih perioda odlična komunikacija između laboratorije i kompjuterskih eksperata je bila neophodna, kao i razvoj »nedostajućih« delova LIS u najkraćem mogućem vremenu. Ali najvažnija stvar od svega je bio stalan napor da se održi motivacija laboratorijskih radnika. Posle 9 godina iskustva i primene LIS u našem dnevnom radu, promenili smo fokus razvoja i počeli smo da radimo na autoverifikaciji, autovalidaciji i automatizaciji svih nivoa (zasnovanim na Laboratorijskoj medicini zasnovanoj na dokazima). Postoji mogućnost za prijem zahteva ili slanje rezultata u elektronskoj formi u druge zdravstvene centre u Sloveniji i u inostranstvo. Klinička hemija i biohemija konstantno razvijaju naučno polje gde progres ne može biti zaustavljen. U isto vreme, ako želimo da predamo naše znanje pacijentima, LIS mora takođe da napreduje kako se ne bi pretvorio u smetnju za laboratorijske ljude, što je veoma čest događaj u mnogi medicinskim laboratorijama.

prising that at the very outset we were unable to predict all the problems which were encountered during the implementation of the new LIS. During those periods excellent communication between the laboratory and computer experts was essential, as was the development of the 'missing' parts of LIS in the shortest possible time. But the most important thing of all was the persistent effort to keep laboratory workers motivated. After 9 years of experience and the use of LIS in our daily work we have changed the focus of development and have started to work on autoverification, autovalidation, and automation on all the levels (based on Evidence-based Laboratory Medicine). There is a possibility to receive orders or send results in electronic form to other health centers in Slovenia and abroad. Clinical chemistry and biochemistry is constantly developing scientific field where progress cannot be stopped. At the same time, if we want to pass on our knowledge to the patients, also LIS has to progress lest it should turn into a nuisance to laboratory people, which is a very common occurance in many medical laboratories.

B23
INFORMACIONI SISTEM LABORATORIJSKE SLUŽBE KAO DEO BOLNIČKOG INFORMACIONOG SISTEMA

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Informacioni sistem laboratorijske službe funkcioniše kao deo informacionog sistema Instituta za neonatologiju od 1996. godine. U serveru su deponovane sve informacije i preko njega se ostvaruje veza između svih šest kliničkih odeljenja u Institutu, kabineta za ultrazvuk, rentgen, enteralnu i parenteralnu ishranu, konsultativne ambulante i laboratorije. Sistem ima aplikacije za elektronsku istoriju bolesti pacijenta, anamnezu, status na prijemu, laboratorijske rezultate, CRIB skor I i II i ponderalni indeks, preračunavanje pripreme obroka za novorođenčad, volumena obroka i izračunavanje energetskog i proteinskog unosa po detetu. Svaki pacijent na prijemu dobija jedinstveni broj koji koriste sve službe. Kada se uzorak biološkog materijala preda u laboratoriju, unosi se broj pacijenta te se istovremeno pojavljuju osnovni demografski podaci, memoriše se vreme uzimanja uzorka, uzorak dobija laboratorijski broj i na ponuđenoj listi analiza markiraju se one koje su tražene. Posle manuelnog unošenja rezultata, oni se mogu neposredno videti od strane lekara. Postoji mogućnost štampanja samo rezultata urgentnih analiza i po odeljenjima, naloga za pojedina radna mesta, ili dobijanja izveštaja sa svim rezultatima jednog pacijenta u definisanom vremenu za željenu grupu analiza. Moguće je dobiti različite statističke izveštaje u vezi sa

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LABORATORY SERVICE INFORMATION SYSTEM AS PART OF THE HOSPITAL INFORMATION SYSTEM

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The information system of the laboratory service has been functioning as a part of the information system of the Institute of Neonatology since 1996. All the pieces of information are stored in the server which connects all six clinical departments of the Institute, the ultrasound and X-ray units, units for enteral and parenteral nutrition, out-patient department for consultation and laboratory. The system has applications for electronic patient records, case history, condition at admission, laboratory results, CRIB score I and II and the ponderal index, the calculation of meal preparation for newborns, of the volume of meals and the calculation of energetic and protein intake per child. At admission, each patient receives a unique number to be used by all units. When a sample of biologic material is delivered to the laboratory, the patient's number is entered and simultaneously the basic demographic data appear, time of sampling is recorded, the sample gets a laboratory number and on the available list of analyses the ones that are requested are marked. Upon manual entering of the results they can be directly seen by a physician. There is a possibility of printing of the results of urgent analyses only and for the particular departments, of the orders for individual work positions, or a possibility to receive a report with all the

svim vrstama usluga, dijagnoza, morbiditeta i mortaliteta, urađenih laboratorijskih analiza određenog tipa, razvrstane po odeljenjima, po smenama, o broju pacijenata i zdravstvenim filijalama iz kojih pacijenti dolaze. Izveštaji se koriste na zahtev zdravstvenog fonda.

results of a patient in a defined period for the desired group of analyses. It is possiblSe to receive different statistic reports regarding all types of services, diagnoses, morbidity and mortality, conducted laboratory analyses of certain type, classified per departments, per shifts, on the number of patients and health affiliates from which the patients come. The reports are used at the request of the Health Insurance Fund.

B24
ODREĐIVANJE BAKRA METODOM AAS I SPEKTROFOTOMETRIJSKOM METODOM

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Za određivanje bakra u serumu do sada se koristila metoda atomske apsorpcione spektrofotometrije (AAS), što je preporučena metoda za određivanje metala u biološkom materijalu. Pošto takav uređaj većina laboratorija ne poseduje smatrali smo da je potrebno uporediti rezultate dobijene AAS-om i kolorimetrijskim testom određivanja bakra u serumu bez deproteinizacije. Tačnost i preciznost smo proverili i potvrdili korišćenjem kontrolnih seruma. Upoređivanjem eksperimentalnih rezultata pomoću obe metode utvrdili smo da je kolorimetrijski test uporediv sa metodom AAS tako da se može koristiti u svim laboratorijama koje poseduju spektrofotometar koji pokriva talasnu dužinu od 580 nm. Određivanje smo vršili u serumu, dok se za određivanje bakra u urinu preporučuje metoda AAS zbog niskih referentnih vrednosti (0,40–1,10 μmol/L).

B24
COPPER DETERMINATION BY THE AAS METHOD AND SPECTROPHOTOMETRY

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The method of atomic absorption spectrophotometry (AAS) was used so far for the determination of copper in serum, and was the method of choice for the determination of metals in biological material. Since such an apparatus is not available to most laboratories we considered it necessary to compare the results obtained by AAS and by a colorimetric test for the determination of copper in serum without deproteinisation. Accuracy and precision were checked and confirmed by use of control serums. Comparing the experimental results of both methods we have concluded that the colorimetric test is comparable to the AAS method and can be used in all laboratories that have a spectrophotometer, covering a wavelength range of 580 nm. These analyses were conducted in serum while for the determination of copper in urine the AAS method is recommended due to low reference values (0.40–1.10 μmol/L).

B25
POREĐENJE ČETIRI METODE ZA ODREĐIVANJE FERITINA

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Koncentracija feritina u serumu odražava telesne rezerve gvožđa i zbog toga se imunotestovi za određivanje koncentracije feritina često koriste u dijagnostikovanju poremećaja vezanih za gvožđe i u praćenju statusa gvožđa u populaciji. Cilj ovog rada je bio da se uporede metode za određivanje serumskog feritina koje se zasnivaju na četiri različita principa: CMIA (chemiluminescent microparticle immunoassay), ECLIA (electrochemiluminescence immunoassay), PEINA

B25
COMPARISON OF FOUR METHODS FOR FERRITIN MEASUREMENT

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The concentration of serum ferritin reflects body iron stores and therefore ferritin immunoassays have been widely used in diagnosing iron related disorders and in population surveys of iron status. The aim of this study was to compare the methods for the determination of serum ferritin which were based on four different principles: CMIA (chemiluminescent microparticle immunoassay), ECLIA (electrochemiluminescence immunoassay), PEINA (particle-enhanced immunone-

(particle-enhanced immunonephelometric assay) and ITA (immunoturbidimetric assay). Ove metode se koriste na sledećim sistemima: CMIA na »Architect ci8200« (Abbott Diagnostics, Vizbaden, Nemačka), ECLIA na Elecsys 2010 (Roche Diagnostics, Mannheim, Nemačka), PEINA na BNII nefelometru (Dade Behring, Marburg, Germany) i ITA na »Olympus AU2700« (Olympus Diagnostica, Hamburg, Nemačka). U ispitivanju nepreciznosti pri rastućoj koncentraciji feritina u serumu, koeficijenti varijacije unutar i između serija su bili u opsegu: 3,4–5,0%, 1,8–6,0%, 1,9–3,9% i 2,7–4,5%, za Abbott, Olympus, Roche i Dade Behring metode ponaosob. Korelacija vrednosti feritina određenih tim metodama je procenjena primenom regresione analize najmanjih kvadrata i dijagramom apsolutnih razlika prema Bland i Altmanu. Dobijeni koeficijenti korelacije (nagib, odsečak) bili su: Dade Behring vs Abbott metodi, 0,9954 (1,051, 7,415); Dade Behring vs Olympus metodi, 0,9948 (0,935, 1,195); Abbott vs. Olympus metodi, 0,9933 (1,004, 1,996); Olympus vs. Roche metodi, 0,9958 (1,334, 2,736); Dade Behring vs. Roche metodi, 0,9979 (1,341, 12,928) i Abbott vs. Roche metodi, 0,9947 (1,250, 9,319). Srednje vrednosti (Sd) apsolutnih razlika iz Bland-Altmanovog dijagrama su bile: 21,0 (43,8) μg/L, –7,5 (13,1) μg/L, 2,5 (13,3) μg/L, 47,8 (40,5) μg/L 91,1 (108,6) μg/L i 70,8 (92,7) μg/L, pri poređenju: Dade Behring i Abbott metoda, Dade Behring i Olympus metoda, Abbott i Olympus metoda, Olympus i Roche metoda, Dade Behring i Roche metoda i Abbott i Roche metoda. Koncentracije feritina određene Roche metodom su bile 25–33% više od koncentracija feritina određenih sa ostale tri metode, što odgovara višem referentom intervalu datom od strane Roche proizvođača. Rezultati ovog ispitivanja su pokazali da postoji dobro slaganje između vrednosti feritina određenih sa ove četiri metode.

phelometric assay) and ITA (immunoturbidimetric assay). These methods are used on the following systems: CMIA on Architect ci8200 (Abbott Diagnostics, Wiesbaden, Germany), ECLIA on Elecsys 2010 (Roche Diagnostics, Mannheim, Germany), PEINA on BNII nephelometer (Dade Behring, Marburg, Germany) and ITA on Olympus AU2700 (Olympus Diagnostica, Hamburg, Germany). In imprecision studies at increasing serum ferritin concentration, intra-assay and inter-assay CVs ranged: 3.4–5.0%, 1.8–6.0%, 1.9–3.9% and 2.7–4.5%, for Abbott, Olympus, Roche and Dade Behring methods, respectively. The correlation of ferritin values, determined with these methods, was evaluated using least-square regression analysis and absolute difference plot according to Bland and Altman. Obtained correlation coefficients (slope, intercept) were: Dade Behring vs. Abbott method, 0.9954 (1.051, 7.415); Dade Behring vs. Olympus method, 0.9948 (0.935, 1.195); Abbott vs. Olympus method, 0.9933 (1.004, 1.996); Olympus vs. Roche method, 0.9958 (1.334, 2.736); Dade Behring vs. Roche method, 0.9979 (1.341, 12.928) and Abbott vs. Roche method, 0.9947 (1.250, 9.319). Mean (SD) absolute differences from the Bland-Altman plot were: 21.0 (43.8) μg/L, –7.5 (13.1) μg/L, 2.5 (13.3) μg/L, 47.8 (40.5) μg/L 91.1 (108.6) μg/L and 70.8 (92.7) μg/L, for the comparison of: Dade Behring and Abbott methods, Dade Behring and Olympus methods, Abbott and Olympus methods, Olympus and Roche methods, Dade Behring and Roche methods and Abbott and Roche methods, respectively. Ferritin concentrations measured with Roche method were 25–33% higher than the ferritin concentrations measured with the other three methods, which corresponded with higher reference intervals given by Roche manufacturer. The results of this study showed that there was good agreement among ferritin values determined with these four methods.

B26
POREĐENJE DVE METODE ODREĐIVANJA PROKALCITONINA

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Prokalcitonin (PCT) jeste prohormon kalcitonina koji luče C-ćelije tireoidee. Nakon proinflamatorne stimulacije izazvane bakterijskom infekcijom, PCT produkuju mnoge ćelije različitih tkiva, posebno ćelije jetre. Povišene vrednosti PCT ukazuju na bakterijsku infekciju. Velika prednost PCT u odnosu na druge parametre sepse je rano i specifično povećanje vrednosti kod sistemskih bakterijskih infekcija i stanja sepse. Koncentra-

B26
COMPARISON OF TWO METHODS FOR PROCALCITONIN DETERMINATION

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Procalcitonin (PCT) is the prohormone of calcitonin and PCT is secreted by the C-cells of the thyroid gland. PCT can be produced by numerous cell types, especially liver cells, after proinflammatory stimulation. Elevated PCT levels indicate bacterial infection accompanied by a systemic inflammatory reaction. One major advantage of PCT compared to other parameters is its early and specific increase in response to severe sys-

cije PCT < 0,5 ng/mL ukazuju na nizak rizik od nastanka sistemske infekcije, vrednosti 0,2–2,0 ng/mL predstavljaju umereni rizik za razvoj sepse, dok koncentracije PCT >2,0 ng/mL predstavljaju visok rizik, odnosno ukazuju na veliku verovatnoću za prisustvo sepse. Vrednosti PCT su normalne kod virusnih infekcija i autoimunih poremećaja. Rana detekcija i adekvatna klinička terapija su od velikog vitalnog značaja za pacijente obolele od sepse. Cilj ovog rada je bio poređenje vrednosti PCT dobijenih pomoću dve različite metode - ELFA (Enzyme Linked Fluorescent Assay), primenjene na analizatoru »mini VIDAS®« (bioMérieux Industry, Hajzelvud, Misuri, SAD), i TRACE tehnologije (Time Resolved Amplified Cryptate Emission) na analizatoru »KRYPTOR®« (BRAHMS Aktiengesellschaft, Henigsdorf, Nemačka). Na oba anlizatora su korišćeni originalni testovi: BRAHMS PCT sensitive na »KRYPTOR®«-u i VIDAS BRAHMS PCT na mini »VIDAS®«-u. Nepreciznost u seriji (N=15) određena je pomoću komercijalnih kontrolnih uzoraka: BRAHMS PCT sensitive Kryptor - Control 1 (K1, koncentracija PCT 1,32-2,10 ng/mL) i VIDAS BRAHMS PCT – Control 2 (K2, koncentracija PCT 0,22–0,34 ng/mL), i dobijeni koeficijenti varijacije su bili za K1 2,12% i 0,79%, a za K2 7,86% i 7,10% na »mini VIDAS®«-u i »KRYPTOR®«-u redom. Za ispitivanje slaganja dve metode, koncentracije PCT su određene u svežim serumima 50 pacijenata na oba anlizatora simultano. Dobijene su sledeće regresione jednačine: y = 1,200x – 0,096 linearnom regresionom analizom, i y = 1,045x – 0,025 Passing-Bablok regresionom analizom. U oba slučaja koeficijent korelacije je bio r = 0,99. Srednja vrednost razlike između metoda dobijena analizom po Altmanu i Blandu je bila 0,636 (Sd = 0,322). Na osnovu dobijenih rezultata može se zaključiti da su nepreciznosti obe metode i njihova međusobna korelacija zadovoljavajuće i da se oba aparata mogu koristiti za određivanje PCT-a u ranom otkrivanju bakterijskih infekcija i sepse.

temic bacterial infections and sepsis. PCT levels are low in viral infections or autoimmune processes. PCT concentrations < 0.5 ng/mL indicate low risk for progression to severe systemic infection, concentrations 0.2–2.0 ng/mL represent moderate risk for progression to severe sepsis, while PCT concentrations >2.0 ng/mL represent high risk and indicate high likelihood of sepsis. Early detection and specific clinical intervention has been shown to be crucial for patients with sepsis. The aim of this study was the comparison of PCT values obtained using two different methods – ELFA (Enzyme Linked Fluorescent Assay), used by mini VIDAS® analyzer (bioMérieux Industry, Hazelwood, Missouri, USA), and TRACE technology (Time Resolved Amplified Cryptate Emission) used by KRYPTOR® analyzer (BRAHMS Aktiengesellschaft, Hennigsdorf, Germany). Both analyzers used original test kits: BRAHMS PCT sensitive for KRYPTOR® and VIDAS BRAHMS PCT for mini VIDAS®. Within-run imprecision (N=15) was determined using commercial control samples: BRAHMS PCT sensitive Kryptor – Control 1 (K1, PCT concentration 1.32–2.10 ng/mL) and VIDAS BRAHMS PCT – Control 2 (K2, PCT concentration 0.22-0.34 ng/mL), and obtained coefficients of variation were: for K1 2.12% and 0.79%, and for K2 7.86% and 7.10%, on mini VIDAS® and KRYPTOR®, respectively. For method comparison study, PCT concentrations were determined in 50 fresh serum samples on both analyzers, simultaneously. Obtained regressions were: y = 1.200x – 0.096 with linear regression analysis, and y = 1.045x – 0.025 with Passing-Bablok regression analysis. The coefficients of correlation in both cases were r = 0.99. Mean bias and SD for Bland-Altman plot were 0.636 and 0.322, respectively. Based on the obtained results we can conclude that both methods showed satisfactory imprecision and gave comparable results. Therefore, both analyzers can be used for PCT determination in the early detection of bacterial infection and sepsis.

B27
LEKOVI KAO VAŽAN FAKTOR U PREANALITIČKOJ FAZI

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Lekovi se smatraju važnim faktorima pri stvaranju pogrešnih laboratorijskih laboratorijskih rezultata. Iako je ta mogućnost stalno prisutna, lekovi su dosta često van kontrole. Oni mogu da utiču na biohemijske i druge analize *per se* ili preko svojih derivata ili metabolita, delujući sami ili u kombinaciji sa jednim, dva ili više lekova. Ovaj rad na primeru kreatinifokinaze (dejstvo diklofenaka), kreatinina (dejstvo askorbinske kiseline) i natrijuma (dejstvo triglicerida) i samih pacijenata

B27
DRUGS AS IMPORTANT FACTORS IN THE PREANALYTICAL PHASE

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Although they have an important role in the creation of potentially misleading laboratory results,which is a constant possibility, drugs are often beyond control. They could influence biochemical and other analyses *per se* or through their derivates and metabolites acting alone or in combination with one, two or more drugs. The paper presents a few parameters (creatine phosphokinase – influenced by diclofenac, creatinine the influenced by ascorbic acid, sodium – influenced by

sa problemima interferencije želi da skrene pažnju na tumačenje patoloških ili čak »normalnih« laboratorijskih rezultata. Ne smemo uzeti pravo da osporavamo značaj ovog problema u vreme kada ne postoji usvojena strategija za njegovo rešavanje.

triglycerides) and some patients with impressive interfering problems with the idea to take more attention to the commenting of pathological or even »normal« laboratory results. No general approach to the solution of this problem does not give the right to neglect it.

B28
OSETLJIVOST I SPECIFIČNOST LATEKS AGLUTINACIONOG TESTA ZA ODREĐIVANJE KONCENTRACIJE D-DIMERA U DIJAGNOSTICI PLUĆNE EMBOLIJE

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Dijagnostikovanje plućne embolije je veoma komplikovan proces, jer znaci i simptomi nisu strogo specifični. Testovi koji isključuju plućnu emboliju su vrlo korisni u njenoj dijagnostici. Koncentracija D-dimera određivana je u citratnoj krvi pomoću lateks aglutinacionog testa, norveške firme NYCOMED. Referentna vrednost D-dimera je do 0,5 g/L. Kod 81 pacijenta (64% muškarci), sa plućnom embolijom (30–64 godine), određivali smo D-dimer. Srednja vrednost koncentracije D-dimera je bila 4,2 g/L. Osetljivost ove metode je 93,9% a specifičnost 88,6%. Ovaj lateks aglutinacioni test za određivanje koncentracije D-dimera u citratnoj krvi je vrlo specifičan i osetljiv i treba ga usvojiti kao algoritam u dijagnostici plućne embolije.

B28
SENSITIVITY AND SPECIFICITY OF A LATEX AGGLUTINATION TEST FOR THE DETERMINATION OF D-DIMER CONCENTRATION IN THE DIAGNOSIS OF PULMONARY EMBOLISM

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The diagnosis of pulmonary embolism remains a complicated issue for physicians because the signs and symptoms of this condition are not specific. Tests that allow confident exclusion of pulmonary embolism are very useful. The concentration of D-dimer in citrate blood was determined with a latex agglutination test, n.v. 0.5 g/L. We determined the D-dimer in 81 patients (64% men) with pulmonary embolism (30–64 years). Median concentration of D-dimer was 4.2 g/L. The sensitivity of this method is 93.0 % and specificity is 88.6%. The latex agglutination method is very specific and sensitive and the D-dimer assay should therefore be incorporating as an algorithm for the diagnosis of pulmonary embolism.

B29
POREĐENJE DVE IMUNOHEMIJSKE METODE ZA ODREĐIVANJE INTAKTNOG PARATIREOIDNOG HORMONA

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Određivanje paratireoidnog hormona (PTH) ima veliki klinički značaj u proceni poremećaja metabolizma kalcijuma, daje direktnu informaciju o aktivnosti paratireoidnih žlezda i indirektnu informaciju o koštanom metabolizmu. Iako je PTH jedan od prvih hormona koji je određivan imunohemijskim metodama, postoje mnogi problemi, pre svega velike razlike izme-

B29
COMPARISON OF TWO INTACT PARATHYROID HORMONE IMMUNOASSAYS

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The determination of parathyroid hormone (PTH) is of great clinical relevance in the assessment of calcium metabolic disorders, as it provides direct information about parathyroid activity and indirect information about bone turnover. Although PTH was one of the first hormones measured by immunoassay, there are still many difficulties in its determination,

đu komercijalnih testova za određivanje intaktnog PTH (iPTH) i sledstvena neadekvatnost primene algoritama iz vodiča kliničke prakse kod pacijenata sa sekundarnim paratireoidizmom. Cilj ovog rada je bio da se odredi varijabilnost u rezultatima PTH, dobijenim pomoću dve metode druge generacije: CMIA (*chemiluminescent microparticle immunoassay*) i ECLIA (*electrochemiluminescence immunoassay*). Ove metode se koriste na sledećim sistemima: CMIA na »Architect ci8200« (Abbott Diagnostics, Vizbaden, Nemačka), ECLIA na Elecsys 2010 (Roche Diagnostics, Manhajm, Nemačka). U ispitivanju nepreciznosti iz dana u dan, koristeći tri nivoa kontrole (PreciControl Bone, Roche i IntactPTH Controls, Abbott) koeficijenti varijacije su bili u opsegu: 3,9–5,5% i 2,5–6,7% za Roche i Abbott metode, redom. Poređenje metoda je određeno Passing-Bablok regresionom analizom, kao i vizuelno, dijagramom apsolutnih razlika po Blandu i Altmanu. Rezultati dva imunotesta su u dobroj korelaciji, (korelacioni koeficijent je 0,995, N=83). Nagib od 1,225 i odsečak od 3,0 nisu bili neočekivani usled razlika u standarizaciji imunotestova, zbog prisustva različitih PTH fragmenata i promenljivog afiniteta antitela za te PTH fragmente. Srednja vrednost apsolutnih razlika iz Bland-Altmanovog dijagrama je bila 62,3 pg/mL (95% interval pouzdanosti: 47,9 do 76,7) sa jasnim dokazom pozitivnog odstupanja CMIA metode koje zavisi od koncentracije. Neprihvatljiva posledica velike varijabilnosti između metoda može biti različita klinička i terapijska odluka kod istoga pacijenta zavisno od korišćenog iPTH testa. Prema tome, rezultati iPTH su zavisni od metode i potrebno je nastaviti napore da se imunotestovi harmonizuju. Dostupnost internacionalnog referentnog materijala može doprineti tim nastojanjima.

especially due to large differences between commercial iPTH assays and, consequently, the inappropriate use of algorithms from Clinical Practice Guidelines on patients with secondary hyperparathyroidism. The aim of this study was to determine the variability in results obtained with two second generation assays for PTH: CMIA (chemiluminescent microparticle immunoassay) and ECLIA (electrochemiluminescence immunoassay). These methods are used on the following systems: CMIA on the Architect ci8200 (Abbott Diagnostics, Wiesbaden, Germany), ECLIA on Elecsys 2010 (Roche Diagnostics, Mannheim, Germany). The imprecision study yielded between-days CVs of 3.9–5.5% and 2.5–6.7% for Roche and Abbott methods, respectively, using three control levels (PreciControl Bone, Roche and IntactPTH Controls, Abbott). Method comparison was performed using the Passing-Bablok regression method and visually, using the Bland-Altman plot. The results of two immunoassays correlated well according to the correlation coefficient, which was 0.995. The slope of 1.225 and intercepts of 3.0 were not unexpected due to differences in immunoassay standardization, and due to the presence of different PTH fragments and a variable affinity of the used antibodies to these PTH fragments. Mean of the absolute differences from the Bland-Altman plot was 62.3 pg/mL (95% CI 47.9 to 76.7) with clear evidence of concentration related positive bias for CMIA method. The unacceptable consequence of this is that opposite therapeutic attitudes may be reached in a single patient depending on the PTH assay used. Thus, iPTH results are method-dependent, and continuing efforts to harmonize assays are needed. The availability of the international reference material could facilitate this effort.

B30
POREĐENJE TRI AUTOMATIZOVANE METODE ZA ODREĐIVANJE TIREOSTIMULIRAJUĆEG HORMONA

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Određivanje koncentracije tireostimulirajućeg hormona (TSH) ima superiornu dijagnostičku osetljivost za detekciju primarnog hiper- i hipotireoidizma kod ambulantne populacije pacijenata, terapeutski je »end-point« za titriranje supstitucione doze L-tiroksina (L-T4) kod primarnog hipotireoidizma i monitoring supresione terapije kod diferenciranog karcinoma štitne žlezde. Komparabilnost različitih metoda koje se koriste za određivanje koncentracije ovog parametra od velikog je značaja kako za lekare tako i za pacijente. Mi smo poredili rezultate za TSH dobijene

B30
COMPARISON OF THREE AUTOMATED METHODS FOR THYROID SIMULATING HORMONE IMMUNOASSAYS

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Thyroid Stimulating Hormone (TSH) measurement is the most diagnostically sensitive test for detecting primary hypo- or hyperthyroidism in ambulatory patients and it is a therapeutic endpoint for titrating the L-thyroxin (L-T4) replacement dose for primary hypothyroidism and monitoring LT4 suppression therapy for differentiated thyroid carcinoma. Between-method comparability for this parameter is of great importance for physicians and patients. We compared the TSH results of three different methods: acridinium derived chemiluminescence (»ARCHI-

trima različitim metodama: imunohemiluminiscencijom koja potiče od akridinijuma (»ARCHITECT i2000sr«), imunoelektrohemiluminiscencijom koja se zasniva na upotrebi rutenium(II)-tris(bipiridil)-a i tripropilamina (»ELECYS 2010«) i mikročestičnom enzimimunotehnikom koja koristi 4-metil-umbeliferil fosfat kao supstrat (»AxSYM«). Koncentracija TSH određivana je u 157 uzoraka. Preciznost metoda testirana je u periodu od 30 dana, upotrebom po tri nivoa komercijalno dostupnih kontrolnih seruma: za »ARCHITECT i2000sr« (Ar1, Ar2, Ar3), »ELECSYS 2010« (PUTSH, PU1, PU2) i za »AxSYM« (Ax1, Ax2 and Ax3). CV za Ar1 (0,10 mU/L) bio je – 6,6%, Ar2 (6,00 mU/L) – 6,4% i Ar3 (30,00 mU/L) – 4,3%. CV za PUTSH (0,20 mU/L) bio je – 5,3%, PU1 (1,28 mU/L) – 6,9% i PU2 (8,05 mU/L) – 6,3%. CV za Ax1 (0,10 mU/L) bio je – 7,0%, Ax2 (3,00 mU/L) – 5,6% i Ax3 (29,00 mU/L) – 7,2%. Linearnom regresionom analizom dobili smo sledeće rezultate: ARCHITECT=0,89ELECYS-0,20 (r=0,996), ARCHITECT=0,78 AxSYM-0,23 (r=0,994) i ELECYS=0,98 AxSYM-0,70 (r=0,996). Ova evaluaciona studija pokazala je dobru međusobnu korelaciju metoda koje se široko koriste za određivanje koncentracija TSH.

TECT i2000sr«), electrochemiluminescence based on the use of ruthenium(II)-tris(bypiridil) complex and trpropylamin (»ELECSYS 2010«) and microparticle enzyme immunoassay using 4-methyl-umbelliferyl phosphate as substrate (AxSYM). Precision was assayed during 30 days, using three levels of commercial control serums for ARCHITECT i2000sr (Ar1, Ar2, Ar3), »ELECSYS 2010« (PUTSH, PU1, PU2) and »AxSYM« (Ax1, Ax2 and Ax3). TSH was measured in 157 serum samples. CV for Ar1 (0.10 mU/L) was – 6.6%, Ar2 (6.00 mU/L) – 6.4% and Ar3 (30.00 mU/L) – 4.3%. CV for PUTSH (0.20 mU/l) was – 5.3%, PU1 (1.28 mU/L) – 6.9% and PU2 (8.05 mU/L) – 6.3%. CV for Ax1 (0.10 mU/L) was – 7.0%, Ax2 (3.00 mU/L) – 5.6% and Ax3 (29.00 mU/L) – 7.2%. Linear regression analysis gave the following results ARCHITECT=0.89, ELECYS-0.20 (r=0.996), ARCHITECT=0.78 AxSYM-0.23 (r=0.994) and ELECYS=0.98, AxSYM-0.70 (r=0.996). This evaluation study confirms the overall good correlation of the results obtained with assays for TSH.

C

PROTEINI I ENZIMI

PROTEINS AND ENZYMES

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C31
ZNAČAJ ODREĐIVANJA HUMANOG PLACENTALNOG LAKTOGENA U TREĆEM TRIMESTRU TRUDNOĆE

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Humani placentalni laktogen (hPL) jeste hormon koji produkuje placenta i regulator je feto-placentalnog rasta. Određivanje koncentracije hPL-a u serumu trudne žene koristi se kao pokazatelj placentalne funkcije. U radu su prikazani rezultati određivanja hPL-a u trećem trimestru trudnoće, sa ciljem da se ispita senzitivnost tog biohemijskog markera za otkrivanje poremećaja funkcije placente, fetalnog vitaliteta i rizika za loš ishod. hPL se određuje ELISA metodom testovima *Bioserv Diagnostics*, a rezultati se očitavaju na rideru *STAT-FAX 303+*. Ispitivanje je obavljeno na uzorku od 370 rizičnih trudnoća između 20 i 36 nedelje trudnoće. Indikacije za određivanje hPL su bila stanja rizična za preeklampsiju, hipertenzija, dijabetes melitus, toksemiju, edeme, bubrežnu insuficijenciju kao i ultrazvučno uočen intrauterini zastoj rasta ploda, placentalni trofoblasni tumor, krvarenje i preteći pobačaj. Rezultate hPL markera poredili smo sa standardnim referentnim vrednostima po nedeljama trudnoće. U normalnim okolnostima koncentracija hPL u serumu trudnice raste sa napredovanjem trudnoće. Uočeno je značajno opadanje hPL kod pretećih pobačaja, krvarenja, kalcifikacije placente, intrauterinog zastoja rasta, intrauterine smrti ploda i trudnoćama iz kojih je rođeno dete sa fetalnim distresom i asfiksijom. Nagli porast hPL utvrđen je kod trudnica sa dijabetes melitusom trudnice i fetalne makrosomije. Rezultati istraživanja su pokazali da hPL u trećem trimestru trudnoće može da se koristi kao pokazatelj placentalne insuficijencije i poremećaja fetalnog vitaliteta. Budući da je disfunkcija placente povezana sa poremećajem oksigenacije ploda, određivanje hPL u trećem trimestru trudnoće moglo bi da ima izvesna prediktivna svojstva.

C31
THE IMPORTANCE OF DETERMINING HUMAN PLACENTAL LACTOGEN IN THE THIRD TRIMESTER OF PREGNANCY

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Human placental lactogen (hPL) is a hormone produced by the placenta and a regulator of fetoplacental growth. The determination of hPL concentration in the serum of pregnant women is used as an indicator of placental function. In this paper, the results of the determination of hPL in the third trimester of pregnancy are presented with the aim of testing the sensitivity of this biochemical marker for detecting placental dysfunction decline in, fetal vitality and risk of bad outcome. hPL is determined by an ELISA method using *Bioserv Diagnostics* tests and the results are read by a *STAT-FAX 303+* reader. The tests have been done on 370 women with high risk pregnancy, between the 20^{th} and 36^{th} week of pregnancy. The indications for determining hPL were states associated with a risk of preeclampsia, hypertension, diabetes mellitus, toxemia, edema, kidney insufficiency, as well as an ultrasonic detection of intrauterine fetal growth halt, placental trophoblast tumor, bleeding and a threatened abortion. The results of hPL marker were compared to the standard reference values according to the weeks of pregnancy. Normally, the concentration of hPL in the serum of a pregnant woman increases as the pregnancy progresses. A significant decrease of hPL has been identified in threatened abortions, bleeding, placental calcification, intrauterine fetal growth halt, intrauterine letal death and in pregnancies which resulted in children born with fetal distress and asphyxia. A rapid increase in hPL was determined in pregnant women suffering from diabetes mellitus and in cases of fetal macrosomia. The results of research showed that hPL in the third trimester of pregnancy can be used as an indicator of placental insufficiency and disturbed fetal vitality. Since placental dysfunction is related to a disturbed oxygenation of the fetus, the determination of hPL in the third trimester of pregnancy could have some predictive characteristics.

C32
PROKALCITONIN KAO MARKER SEPSE

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Brze i adekvatne dijagnostičke procedure neophodne su za postizanje rane dijagnoze i odgovarajuće terapije sepse. Među najnovijim biomarkerima sepse prokalcitonin (PCT) pokazao se kao jedan od najkorisnijih. Nakon infekcije sa sistemskim posledicama, unutar 6–12h, nivo PCT-a značajno raste. Fiziološka, odnosno patofiziološka uloga tog proteina u procesima sistemskih infekcija, kao i u posttraumatskim stanjima, ostaje još uvek nepoznanica. Cilj naše studije bio je poređenje vrednosti nivoa PCT-a kod pacijenata sa klinički dokazanom sepsom i pacijenata sa lokalnom infekcijom, radi provere značaja i stepena pouzdanosti PCT-a kao biomarkera. Za određivanje vrednosti PCT-a korišćen je standardno izdvojen serum iz krvi 20 pacijenata podeljenih u dve grupe. Prvu grupu je činilo 10 pacijenata sa lokalnom infekcijom, odabranih prema sledećem kriterijumu: povišeni leukociti, povišen CRP, klinički znaci lokalne infekcije i bakteriološka potvrda. Drugu grupu su činili pacijenti sa kliničko-laboratorijskom i mikrobiološkom potvrdom septičkog stanja različitog uzroka. PCT je određivan na *Brahms* Kriptoru-u, tehnologijom TRACE. Prosečna vrednost PCT-a u prvoj grupi pacijenata bila je 0,0574 ng/mL ± 0,0196, a u drugoj grupi 0,7542 ng/mL ± 0,6578. Razlika u srednjim vrednostima između dve grupe je 0,6968 ng/mL, što je statistički značajno ($p<0,01$). Na osnovu dobijenih rezultata može se zaključiti da postoji značajna razlika između dve grupe pacijenata, mada je ona bila na donjoj granici očekivanih vrednosti. Naša je pretpostavka da je antibiotska terapija razlog sniženih nivoa PCT-a. Pored njegove uloge kao markera sepse, PCT se u našim istraživanjima pokazao kao dobar potencijalni pokazatelj težine bolesti, njenog toka i uspešnosti terapije.

C32
PROCALCITONIN AS A MARKER OF SEPSIS

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Urgent and adequate diagnostic procedures are necessary to achieve early diagnosis and correct therapeutic treatment of sepsis. Among the latest biomarkers of sepsis, procalcitonin (PCT) has been proved to be one of the most useful. After an infection with systemic manifestations the level of PCT significantly increases in the first 6–12h. The physiological, namely pathological role of this protein in the processes of systemic infection, as well as in posttraumatic conditions remains still unknown. The aim of our study was to compare the value of the levels of PCT in patients with clinically proved sepsis to that of patients with local infection. The goal was to prove the importance and reliability of PCT as a biomarker. For obtaining the PCT value, a standard procedure of taking blood from 20 patients, divided into two groups was used. The first group consisted of 10 patients with local infection chosen by the following criteria: leukocytosis, raised CRP, clinical signs of local infection and bacteriologically tested. The second group were the patients with laboratory and microbiological confirmation of a septic state of different origin. PCT was measured on a *B.R.A.H.M.S*. KRYPTOR, by a TRACE method. The mean value of PCT in the first group was 0.0574 ng/mL ± 0,0196, and in the second 0.7542 ng/mL ± 0.6578. The difference between the mean values of the two groups was 0.6968 ng/mL, which is statically significant ($p<0.01$). On the basis of the obtained results we can deduce that there is a noticeable difference between the two groups of patients. The mean value was between the expected levels, though on a lower level than was expected. We believe that the reason for the lower level is antibiotic therapy. PCT was recognized as a good marker of sepsis, as well as an indicator of therapeutic monitoring.

C33
RECEPTORI I VEZUJUĆI PROTEINI ZA INSULIN I INSULINU SLIČNE FAKTORE RASTA U PLACENTI ZDRAVIH I DIJABETIČNIH MAJKI

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IGF sistem humane placente sačinjavaju insulinu slični faktori rasta (IGF) - I i -II, receptori za koje se oni vezuju (IGF1R i IGF2R), kao i njihovi vezujući proteini

C33
RECEPTORS AND BINDING PROTEINS FOR INSULIN AND INSULIN-LIKE GROWTH FACTORS IN THE PLACENTA OF HEALTHY AND DIABETIC MOTHERS

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The IGF system in the human placenta consists of insulin-like growth factors (IGF) -I i -II, their receptors (IGF1R i IGF2R), and binding proteins (IGFBP-1 to -6).

(IGFBP-1 do -6). Takođe, usled strukturnih i metaboličkih sličnosti sa insulinom, IGF sistem se ne može izučavati izdvojeno od insulina i insulinskog receptora. U ovom radu gel filtracija je korišćena kako bi se detektovali membranski proteini iz solubilizata membrana dobijenih iz terminskih placenti tri zdrave i tri dijabetične majke. Pojedinačni uzorci solubilizata preinkubirani su sa tri ^{125}I- liganda: ^{125}I-IGF-I, ^{125}I-IGF-II i ^{125}I-insulinom. Nakon toga uzorci su razdvajani na koloni »Sephadexa G-100«, a hromatografija je praćena merenjem radioaktivnosti ^{125}I-liganada u frakcijama eluiranim sa kolone. Gel filtracijom solubilizata inkubiranog sa ^{125}I-IGF ili ^{125}I-IGF-II dobijaju se međusobno slični elucioni profili, pri čemu prvi pik sa hromatograma potiče od kompleksa radioliganda sa odgovarajućim receptorom, drugi pik od kompleksa radioliganda sa IGFBP, dok treći pik potiče od slobodnih radioliganada. Gel filtracijom solubilizata inkubiranog sa ^{125}I-insulinom dobija se hromatogram koji, za razliku od prethodnih, ne sadrži pik koji bi odgovarao kompleksu sa IFGBP. Integracijom površina ispod pika utvrđeno je da se količine IGF i insulinskih receptora u solubilizatima iz membrana placente zdravih i dijabetičnih majki neznatno razlikuju, dok je količina IGFBP u solubilizatu zdrave, u odnosu na dijabetičnu majku, značajno manja. Na osnovu ovih rezultata može se pretpostaviti da se mehanizmi regulatorne funkcije vezujućih proteina u placenti zdrave i dijabetične majke međusobno razlikuju.

Due to many structural and metabolic similarities with insulin, the IGF system cannot be examined separately from insulin and its receptor. In this study gel filtration was used to detect solubilised membrane proteins of placenta obtained from 3 healthy and 3 diabetic mothers. Solubilised placental membranes were preincubated with three ^{125}I- ligands: ^{125}I-IGF-I, ^{125}I-IGF-II and ^{125}I-insulin, and further chromatographed on a »Sephadex G-100« column. Radioactivity was measured in each collected fraction. Gel filtration of the solubilised membranes incubated with ^{125}I-IGF or ^{125}I-IGF-II resolved in comparable elution profiles, whereby the first eluted peak represented complexes of radioligands with receptors, the second peak representeds radioligand bound to IGFBP, while the third maximum represented free radioligands. To the contrary, gel filtration of the solubilised membranes incubated with ^{125}I-insulin produced a profile lacking a peak that included IGFBP. By measuring the area under peaks it was found that there was no significant difference in the content of IGF and insulin receptors in the solubilised placental membranes of healthy and diabetic mothers, while the amount of IGFBP in the placenta of healthy mothers was significantly lower. Based on these results, different regulatory mechanisms of binding proteins in the placenta of healthy and diabetic mothers can be suggested.

C34
PROTEIN S-100β KOD PACIJENATA SA TEŠKOM SEPSOM

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Uticaj sepse na mozak nije u potpunosti razjašnjen. Direktni efekti posredstvom delovanja toksičnih medijatora i indirektni efekti kao što su hipotenzija, povišena telesna temperatura, povišen intrakranijalni pritisak, doprinose konfuznoj slici o mozgu u toku sepse. U ovom radu, ispitivali smo vrednosti proteina S100β, kao biomarkera oštećenja mozga, kod pacijenata obolelih od teške sepse. Cilj rada je bio da se utvrdi da li su vrednosti proteina S100β povišene na samom početku bolesti i da li se na osnovu njih može predvideti ishod. Ispitano je 30 pacijenata sa teškom sepsom, koji su lečeni u jedinici intenzivne terapije. Pacijenti su bili podeljeni u dve grupe: preživeli (n=8) i umrli (n=22). Za analizu je uzimana venska krv u prvih 24h od pojave simptoma. Koncentracija proteina S100β merena je pomoću imunološkog testa metodom elektrohemiluminiscencije na aparatu *Elecsys 2010* (*Roche Diagnostics*). Od 30 ispitanih pacijenata,

C34
S-100β PROTEIN IN PATIENTS WITH SEVERE SEPSIS

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The effects of sepsis on the brain have not been fully elucidated. The interplay between direct effects resulting from toxic mediators and indirect effects, such as hypotension, hyperthermia and increased intracranial pressure, contribute to the unclear image of the brain during sepsis. This study investigated the serum levels of S100β protein in patients with severe sepsis, as a biomarker of brain damage. The aim of the study was to determine whether the levels of S100β are increased early, at the onset of sepsis, and if this protein is a good early predictor of outcome. We studied 30 patients with severe sepsis, treated in the Intensive Care Unit. The patients were divided into survivors (n=8) and norsurvivors (n=22). Venous blood was sampled within the first 24h after the onset of symptoms. The concentrations of S100β protein were measured using an electrochemiluminescence immunoassay on an *Elecsys 2010 analyzer* (*Roche Diagno-*

74,4% (n=22) imalo je povišene vrednosti proteina S100β (6 preživelih i 16 umrlih), dok je 8 pacijenata (2 preživela i 6 umrlih) imalo vrednosti u okviru referentnog opsega. Između preživelih i umrlih nije bilo statistički značajne razlike u srednjoj vrednosti proteina S100β (0,390±0,515 *vs.* 0,415±0,508 μg/L). Povišene vrednosti tog proteina ukazuju na verovatna difuzna okultna oštećenja mozga, koja mogu biti i reverzibilna. Osim toga, protein S100β nije dovoljno pouzdan marker za ranu predikciju ishoda kod pacijenata obolelih od teške sepse.

stics). Out of 30 examined patients, 74.4% (n=22) had increased levels of S100β protein (6 survivors and 16 nonsurvivors), while 8 patients (2 survivors and 6 nonsurvivors) had values within the reference range. The mean value of S100β protein did not differ significantly between the survivors and nonsurvivors (0.390±0.515 vs. 0.415±0.508 μg/L). The increased levels of this protein indicate possible occult diffuse brain injury, that can be reversible. Moreover, the study showed that S100β protein is not a good early predictor of outcome in severe sepsis.

C35
IMUNSKI KOMPLEKSI I KOMPLEMENT U SERUMU I SINOVIJALNOJ TEČNOSTI KOD BOLESNIKA SA REUMATOIDNIM ARTRITISOM

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Reumatoidni artritis (RA) jeste predominantno intraartikularna zapaljenska i autoimunska bolest koja uključuje različita autoantitela i efektorne mehanizme. Cilj ispitivanja je bio da se ustanovi značaj cirkulišućih imunskih kompleksa (CIK) i komponenti komplementa (C3, C4), kao pokazatelja stepena aktivnosti RA za laboratorijsku dijagnostiku. U studiji preseka stanja je ispitano 59 bolesnika koji su prema kliničkim kriterijumima za aktivnost RA podeljeni u dve grupe: grupa sa umerenom (UA, n=24) i grupa sa visokom aktivnošću (VA, n=35) RA. Koncentracije CIK, C3c i C4 u serumu i sinovijalnoj tečnosti (ST) određivane su imunonefelometrijskom metodom (»DADE – Behring«) u obe grupe ispitanika i upoređene sa vrednostima u kontrolnoj grupi od 15 pacijenata sa povredama meniskusa. Rezultati su pokazali da nije bilo statistički značajnih razlika u koncentracijama za C3c i C4 u oba biološka uzorka između ispitivanih grupa. Statistički značajne razlike nađene su u koncentracijama CIK testiranjem vrednosti ($\bar{x}$±SD, IU/mL), a dobijene vrednosti u serumu grupe sa VA i grupe sa UA RA bile su: 7,43±13,40; 3,01±2,92 ($p<0,05$) i za vrednosti u ST: 13,47±21,1, 5,33±7,53 ($p<0,001$). Te razlike su bile još više izražene između grupe sa VA RA i KG. Rezultati koncentracija CIK su bili značajno viši u ST u odnosu na serum u obe grupe bolesnika: u grupi sa UA za 77% a u grupi sa VA RA za 82%. Ovi podaci idu u prilog potvrdi hipoteze o lokalnoj, intraartikularnoj produkciji autoantitela, odnosno CIK. Može se zaključiti da je laboratorijsko određivanje koncentracije CIK korisan pokazatelj stepena aktivnosti RA, što se ne odnosi na ispitivane komponente komplementa. To ne

C35
IMMUNE COMPLEXES AND COMPLEMENT IN THE SERUM AND SYNOVIAL FLUID OF RHEUMATOID ARTHRITIS PATIENTS

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Rheumatoid arthritis (RA) is predominantly an intraarticular inflammatory and autoimmune disease in which different auto antibodies and effector mechanisms are involved. The aim of the study was to determine the utility of circulating immune complexes (CIC) and complement components (C3c, C4) as possible markers for disease activity in laboratory diagnostics. In a cross-section study 59 patients were categorized into two groups according to the clinical criteria: a group with moderate (MA, n=24), and a group with severe (SA, n=35) RA activity. The concentrations of CIC, C3c and C4 in the sera (S) and synovial fluids (SF) were examined by the immunonephelometric (»DADE Behring«) method in both groups and compared with the values in the control group (n=15) of patients with lesions of the menisci. The obtained results showed that there was no statistical significance of the values of C3c and C4, in both biological fluids, in all tested groups. Significant differences were found for the levels of CIC in both fluids, testing the parameters ($\bar{x}$±SD, IU/mL) in the sera of the groups with SA and MA of RA: 7.43 13.40; 3.01±2.92 ($p<0.05$) and SF: 13.47±21.1, 5.33±7.53 ($p<0.001$), respectively. These differences were more pronounced in the group with SA and CG. The results for the concentrations of CIC were significantly higher in the SF compared to the sera: in the RA group with SA by 77% and in the group with MA by about 82%. These data could provide a confirmation of the hypothesis about the local, intraarticular autoantibodies and the subsequent CIC production. It could be concluded that the examination of the CIC concentration in serum, and where it is possible in

isključuje njihovu aktivnost u okviru efektornog imunskog mehanizma, ali ukazuje na to da bi anafilaktički, manji molekulski fragmenti (C3a, C4a) mogli biti bolji pokazatelji stepena aktivnosti RA.

SF, is a useful marker of disease activity in RA patients, in contrast to the tested components of the complement. This statement does not exclude their activity as immune effector mechanisms, but suggests the possibility that lower molecular fragments (C3a, C4a) could be better disease activity markers in RA patients.

C36
DIJAGNOSTIČKI ZNAČAJ ODREĐIVANJA PROSTATIČNOG SPECIFIČNOG ANTIGENA (PSA) I PROSTATIČNE KISELE FOSFATAZE (PAP) KOD OBOLJENJA PROSTATE

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Karcinom prostate je najčešća maligna bolest muškaraca starijih od 50 godina pa je rano otkrivanje od vitalnog značaja za prevenciju i terapiju bolesti. Glavnu ulogu u tome imaju tumorski markeri za oboljenja prostate: PSA i PAP. Cilj ovog rada je da se utvrdi odnos nivoa PSA i aktivnosti PAP između grupa pacijenata sa adenomom i karcinomom prostate u odnosu na zdrave muškarce, kao i da se ispita korelacija PSA i PAP u datim grupama. Ispitanici su muškarci starosti od 56 do 78 godina, svrstani u grupe sa verifikovanim karcinomom prostate (32), adenomom prostate (47), i grupa zdravih muškaraca (30). PSA je određivan na imunološkom analizatoru »IMMULITE-1000«, a PAP standardnom biohemijskom metodom (»Biosystems«). Statističkom obradom dobijenih rezultata utvrđeno je da postoji statistički značajna razlika u koncentracijama PSA u grupi pacijenata sa karcinomom prostate, a i u grupi sa adenomom ta koncentracija je značajno viša. Vrednosti aktivnosti PAP značajno su više u grupi pacijenata sa karcinomom, dok kod pacijenata sa adenomom ta razlika nije statistički značajna. Urađena je i korelaciona analiza tih parametara kod sve tri grupe ispitanika. U grupi sa karcinomom takva korelacija je najveća (r=0,632), u grupi sa adenomom nešto niža (r=0,421), dok je u kontrolnoj grupi ona niska (r=–0,222), to jest, nema povezanosti između PSA i PAP. Na osnovu dobijenih podataka može se zaključiti da postoji značajna povezanost PSA i PAP kod karcinoma prostate, da je nešto manja kod adenoma, i da je korisno određivati oba parametra u dijagnostičkoj proceduri.

C36
THE DIAGNOSTIC SIGNIFICANCE OF DEFINING PROSTATE SPECIFIC ANTIGEN (PSA) AND PROSTATIC ACID PHOSPHATASE (PAP) WHEN AN ILLNESS OF THE PROSTATE GLAND IS DIAGNOSED

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Prostate gland cancer is the most common malignant illness in males aged fifty and more. Therefore early detection is crucial for the prevention and treatment of this illness. The main role in this belongs to tumor markers for prostate gland illness: PSA and PAP. The aim of this study is to establish the relation of the level of PSA and activity of PAP between a group of patients suffering from adenoma and prostate gland cancer and a group of healthy males, as well as to examine the correlation of PSA and PAP in these groups. Test subjects are males aged from 56 to 78 divided into groups diagnosed with prostate gland cancer (32) and adenoma (47) and a group of healthy males (30). PSA was determined on an immunological analyzer »IMMULITE-1000«, while PAP was determined by standard biochemical methods (»Biosystems«). The results were statistically processed and it was determined that there is a statistically significant difference in the concentrations of PSA in the group of patients suffering from prostate gland cancer, and in the group of patients suffering from adenoma that concentration is considerably higher. The values of PAP activity are considerably higher in the group of patients suffering from cancer, while in the group of patients with adenoma that difference is not statistically significant. Correlation analysis of these parameters was also done in all three groups. In the group with cancer this correlation is the highest, while in the control group it is low, that is, there is no connection between PAP and PSA. Based on the obtained data, it can be concluded that there is a significant connection between PSA and PAP in cases of prostate gland cancer, that it is slightly lower in cases of adenoma, and therefore that it is useful to determine both parameters in the diagnostic procedure.

C37
KLINIČKI ZNAČAJ ODREĐIVANJA FERITINA U HEMATOLOŠKIM MALIGNIM OBOLJENJIMA

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Serumski feritin je sekretorna komponenta intracelularnog feritina sintetisanog na endoplazmatičnom retikulumu. Kod hematoloških malignih oboljenja, po jednoj hipotezi, povišena koncentracija serumskog feritina je posledica sinteze neoplastičnih ćelija, ali takođe može biti uzrokovana oštećenjem tkiva bogatih feritinom (jetra, slezina i koštana srž). Cilj rada je da se odredi povezanost nivoa feritina i enzima značajnih za procenu funkcije jetre kod limfoma, plazmocitoma i hronične limfocitne leukemije. Kod ovih pacijenata su pored feritina ispitivani jetreni enzimi (ALT, AST, GGT), kao i Fe. Feritin je određivan hemiluminiscentnom metodom (testom firme »DPC« na analizatoru »Immulite 1000«), pri čemu su referentne vrednosti 6–195 ng/mL. ALT, AST i GGT određivani su enzimskim metodama na biohemijskom analizatoru »Dimension Rxl«, dok je Fe određivano metodom sa ferenom. Visoke vrednosti feritina nađene su kod plazmocitoma i limfoma, dok je kod HLL koncentracija feritina blago povišena. Rezultati pokazuju da postoji statistički značajna korelacija između feritina i GGT ($p<0,01$), dok nije uočena statistički značajna korelacija feritina sa nivoima AST i ALT ($p>0,05$). Budući da GGT može poslužiti kao marker maligne infiltracije jetre, povećanje koncentracije feritina može nastati usled destrukcije hepatocita. Takođe je uočeno da ne postoji statistički značajna korelacija između gvožđa i feritina ($p>0,05$), što ide u prilog hipotezi da je feritin u tim oboljenjima sintetisan od strane malignih ćelija.

C37
CLINICAL IMPORTANCE OF FERRITIN DETERMINATION IN HEMATOLOGIC MALIGNANCIES

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Serum ferritin is a secretory component of intracellular ferritin synthesized on the endoplasmic reticulum. A recent hypothesis suggested that an increased concentration of serum ferritin in hematologic malignancies is the result of synthesis by neoplastic cells, but it can also be caused by damage to ferritin-rich tissues (liver, spleen and bone marrow). The aim of this study was to determine the relationship between serum ferritin and enzymes important for the estimation of liver function in lymphomas, plasmacytomas and chronic lymphocytic leukemia. In all patients we measured the concentrations of ferritin, iron and liver enzymes (ALT, AST, GGT). Ferritin was examined using a chemiluminescent assay (»DPC« reagents applied on a »Immulite 1000« analyzer), with a reference range of 6–195 ng/mL. ALT, AST, GGT were determined using enzyme methods applied on a »Dimension Rxl« biochemical analyzer, and iron was determined using the Feren method. High levels of serum ferritin were found in plasmacytomas and lymphomas, while the concentration of serum ferritin in CLL was slightly increased. The results showed a significant correlation between the levels of ferritin and GGT ($p<0.01$). No significant correlation was found between ferritin levels and ALT or AST ($p>0.05$). Considering that GGT can be used as a marker of liver malignant infiltration, high levels of serum ferritin might be caused by the destruction of hepatocytes. Results also showed that there was no significant correlation between the levels of ferritin and iron ($p>0.05$), which supports the hypothesis that an increase in ferritin is the result of its production by malignant tissues.

C38
ODREĐIVANJE AKTIVNOSTI ALKALNE FOSFATAZE KOD PACIJENATA SA ANEURIZMOM ABDOMINALNE AORTE

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Alkalna fosfataza (EC 3.1.3.1) široko je rasprostranjen enzim i nalazi se u svim ćelijama a posebno na ili u membranama. Cilj istraživanja je da se utvrdi da li se na osnovu određivanja nekih biohemijskih parametara može uspešnije proceniti rizik od rupture aneurizme abdominalne aorte (AAA). Parametri koji se za

C38
DEFINING THE ACTIVITY OF ALKALINE PHOSPHATASE IN PATIENTS WITH ABDOMINAL AORTIC ANEURYSM

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Alkaline phosphatase (EC 3.1.3.1) is a widely spread enzyme. It can be found in all cells, especially in or on all cell membranes. The aim of this research was to establish whether some biohemical parameters could be certain more successfully for the estimation of the risk of aneurisym rupture. Parameters used so far,

sada koriste u praksi, kao što su veličina anurizme, godine života i dr, nisu se pokazali sigurnim u predviđanju preteće rupture AAA. Pošlo se od pretpostavke da aktivnost endotelnih enzima u plazmi, odnosno u serumu, može biti pomoćni dijagnostički kriterijum u proceni rizika od rupture AA. Određivana je aktivnost AP u grupi pacijenata sa rupturiranom aneurizmom AA i u grupi operisanih pacijenata kod kojih nije došlo do rupture aneurizme. Kontrolnu grupu predstavljaju zdave osobe sa vrednostima AP u referentnim granicama. Aktivnost AP izražena je u U/mL i na mg ukupnih proteina seruma. Prvo je određivana aktivnost AP u serumima pomoću IFCC metode i sa 4-fenilfosfatom kao supstratom, korišćen je »Randoks Kit 132« za AP. Apsorbanca je čitana na 405 nm na 37 °C na spektrofotometru »Evolution 3000«. Potom je određena koncentracija ukupnih proteina istih uzoraka biuretskom metodom (modifikacija po Benediktu) i aktivnost AP izražena na mg ukupnih proteina. Pojedinačni t-testovi su pokazali da nema statistički značajne razlike ni na jednom nivou značajnosti ($p>0,05$) između grupe pacijenata sa rupturiranom AA i grupe pacijenata kod kojih nije došlo do rupture AA, kao ni značajne razlike između svake te grupe ponaosob i kontrolne grupe. Na osnovu dobijenih podataka izvodi se zaključak da se aktivnost AP ne može koristiti kao dijagnostički parametar za procenu rizika od rupture AAA.

such as aneurysm size, have not been proved in the anticipation of a rupture of AAA. It has been assumed that the activity of endothelial enzymes in plasma, that is serum, could aid in the estimation of the risk of AA rupture. The activity of AP as an endothelial enzyme was defined, considering that a common cause ateriosclerosis is, and in base of ateriosclerosis, the integrity of the cells of the intimate matter, that is endobodz cells,is endangered. No activity of AP in the group of patients with a ruptured aneurysm was found. Control group was a group of healthy persons with values of AP within reference limits. The activity was expressed in U/mL and per mg of total serum proteins. First, the activity of AP in serum was defined with the IFCC method and 4-phenylphosphate as substrate. A Randox Kit 132 for AP was used. Absorbent was read at 405 nm at 37 °C on a spectrophotometer Evolution 3000. The concentration of total proteins in the same samples was thendetermined with a biuretic method (modification by Benedict) No statistically significant difference was found on neither level of significance ($p>0.05$) between the patients with ruptured AA and the patients who had no such rupture. There are no significant differences between each of these groups and the control group, as well. According to these data we came to a conclusion that the activity of AP cannot be used as a diagnostic parameter for the anticipation of the risk of AAA rupture.

C39
ZNAČAJ KISELE FOSFATAZE KAO MARKERA RENALNE OSTEODISTROFIJE KOD DIJALIZIRANIH PACIJENATA

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Renalna osteodistrofija predstavlja patološke promene koštanog tkiva izazvane poremećajem metabolizma kalcijuma tj. sekundarnim hiperparatireoidizmom u hroničnoj bubrežnoj insuficijenciji (HBI). Ispoljava se stanjima sa pojačanom i smanjenom koštanom izmenom od kojih svako zahteva odgovarajući terapijski pristup uz naglašen značaj dijagnostike. Ovoj studiji je bio cilj da utvrdi mesto kisele fosfataze (AP) u monitoringu renalne osteodistrofije kod dijaliziranih pacijenata. Utvrđena je laboratorijska pouzdanost fotometrijskog određivanje aktivnosti AP na automatskom analizatoru, i to: preciznost u seriji uzoraka u opsegu normalnih i visokih vrednosti (izražena sa CV=6,9% odn. CV=3,5%), tačnost izražena kao procenat odstupanja (BIAS) od ciljne vrednosti primarnog standarda (CV=3,1%) i recovery testom (odstupanje do 1,24%), te ukupna greška merenja od 3,89%. Potom je izvršeno poređenje srednjih vrednosti AP u serumu ispitivane grupe (40 pacijenata na dijalizi) i kontrolne grupe zdravih osoba primenom studentovog t-testa sa rezultatom t=8,768, p=0,000 ($p<0,001$) i koreliranje

C39
THE IMPORTANCE OF ACID PHOSPHATASE AS A MARKER OF RENAL OSTEODISTROPHY IN PATIENTS ON DIALYSIS TREATMENT

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Acid phosphatase (AP) encloses a group of enzymes which catalyse the hydrolitic process of many phosphoric acid monoestars. It is present in every human cell. Serum AP comes from blood cells, osteoclasts and from prostate cells in males. There are at least five isoenzymes in the human body. This study aims: firstly to prove the clinical importance of AP as a biochemical marker of osteoclastic activity which is raised in all patients with increased bone destruction (patients with chronic kidney failure, CKF) and secondly to define the ratio of the correlation of AP and the marker of hyperparathyroidism HBI parathormone (PTH) level in patients with CKF. Ca+ metabolism is seriously changed in CKF and clinically manifests as renal osteodistrophy. Renal osteodystrophy presents with increased or decreased bone Ca^+ exchange which demands different therapeutic approaches. The sample used was: a group of 40 patients on dialysis treatment in the Center for dialysis of the P.H.C. »Dr M. Stojanović« and a control group of 30 healthy persons. Total AP was measured by the photometric method

vrednosti AP i vrednosti parathormona (rutinski test u monitoringu dijaliziranih pacijenata) sa koeficijentom korelacije r=0,750 (rezultat na granici srednje i jake korelacije, a testiranjem nulte hipoteze po Fisheru sa t=6,9, ova korelacija je visoko signifikantna sa p=0,01). Zlatni standard za procenu oba poređena markera (histološki nalaz) nije bio dostupan. Većina studija ukazuje na nedostatke u dijagnostici ako se koriste izolovani biohemijski markeri koštanog metabolizma u komplikovanim i promenljivim metaboličkim uslovima HBI, a shodno potrebi za izbegavanjem agresivnog dijagnostičkog pristupa (biopsija kosti sa histomorfometrijom), preporučuje se uporedno korišćenje većeg broja markera među kojima ima mesto i kisela fosfataza.

with 1-naftil phosphate as a substrate on an automatic analyzer Mira Cobas Plus. The compared results of the median values of AP in the sera of two groups showed adifference which was highly statistically important (p<0.001). The values of AP and PTH are between a medium and a strong correlation measured by correlation coefficient r=0.750, tested by the Fisher hypothesis and is highely significant, p=0.01. Cytology as the gold standard for the valuation of both marker was not available. The study proved that AP has its place as a selfsufficient biomarker of increased osteoclastic activity but (acording to a number of studies) usage of other markers of osseal metabolism is highely recommended in cases of complicated and easily changed metabolism in CKF patients. This comes with the need to avoid aggressive a diagnostic aproach (osseal biopsy).

C40
NIVO CISTATINA C KOD PACIJENATA SA ENDEMSKOM NEFROPATIJOM

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Balkanska endemska nefropatija (BEN) jeste hronična tubulointersticijalna bolest koja dovodi do progresivnog oštećenja bubrega. BEN se javlja u izolovanim selima Balkana oko reke Dunav. Maksimalan broj pacijenata zapažen je u periodu između 1965. i 1970. godine. Bolest zahvata ne više od dve generacije. Uzrok je još uvek nepoznat. Epidemiološki podaci koji su dobijeni nakon biopsije govore o primitivnim glomerulima i opstrukciji tubula. Jačina glomerulske filtracije (JGF) najbolji je indeks bubrežne funkcije. Koncentracija cistatina C u serumu uglavnom zavisi od jačine glomerulske filtracije. Shodno tome, cistatin C se nameće kao dobar interni parametar za procenu jačine glomerulske filtracije. Cilj rada je bio da istraži nivoe i povezanost između koncentracije cistatina C, koncentracije kreatinina i klirensa kreatinina kod pacijenata sa BEN. Ispitivanje je obuhvatilo 40 osoba oba pola (17 žena i 23 muškarca) sa BEN čija je srednja vrednost starosne dobi bila 47,76±9,93 godina. Cistatin C u serumu je određivan PENIA metodom na laserskom nefelometru testovima firme »Dade-Behring«. Srednja vrednost cistatina C bila je 3,69±1,39 mg/L. Srednja vrednost kreatinina je bila 309,68±145,28 μmol/L a srednja vrednost klirensa kreatinina 38,8±24,3 mL/min. Statistička analiza je obuhvatila srednju vrednost, Studentov t-test i Spirmanov test korelacije. Kod pacijenata sa BEN postoji statistički veoma značajna pozitivna korelacija izme-

C40
CYSTATIN C LEVEL IN PATIENTS WITH BALKAN ENDEMIC NEPHROPATHY

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Balkan endemic nephropathy (BEN) is a chronic tubulointerstitial disease which leads to progressive renal failure. BEN occurs in isolated villages in the Balkan region around the Danube river. Maximum number of patients were seen during 1965–1970. The disease affects no more than two generations. The etiology of BEN is still unknown. The epidemiological data show primitive glomeruli and obstructed tubules after kidney biopsy. GFR is traditionally considered the best overall index of kidney function. Cystatin C concentration in serum depends mainly upon the glomerular filtration rate. Accordingly, serum cystatin C is a favorable internal (endogenous) parameter for the measurement of glomerular filtration rate (GFR). The aim of this study was to examine the association of serum cystatin C concentration, creatinine concentration and creatinine clearance in BNE patients. The study included 40 individuals of both sexes (17 females and 23 males), mean age 47.76±9.93 years, who had BEN. Cystatin C in serum was determined by a PENIA method, Dade Behring. The mean value of cystatin C was 3.69± 1.39mg/L. The mean value of serum creatinine was 309.68±145.28 μmol/L and the mean value of creatinine clearance was 38.8±24.3 mL/min. Statistical analysis of the results was performed by the average, student t-test and Spearman test for rang correlation. In BNE, patients there is a statistically highly significant

đu koncentarcije kreatinina i cistatina C, kao i statistički visoko značajna negativna korelacija između cistatina C i klirensa kreatinina (p<0,01). Cistatin C je dobar parametar za procenu jačine glomerulske filtracije.

positive correlation between the creatinine concentration and cystatin C concentration (p<0.01) and there is a statistically highly significant negative correlation between the creatinine clearance and cystatin C concentration (p<0.01). Cystatin C is a good parameter to determination the glomerular filtration rate in BNE patients.

C41
KOŠTANA ALKALNA FOSFATAZA I ESTRODIOL KAO MARKERI KOŠTANOG REMODELOVANJA U POSTMENOPAUZALNOJ OSTEOPOROZI

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Poremećaj koštanog remodelovanja kod žena u postmenopauzi sa osteoporozom nastaje usled smanjenja koštanog formiranja i povećanja koštane resorpcije. Cilj studije bio je da se utvrdi da li su serumski nivoi alkalne fosfataze specifične za kosti (Bone-ALP) i estradiola (E2) povišeni kod žena u postmenopauzi koje imaju osteoporozu. Odredili smo serumske nivoe Bone-ALP-a i E2 kod žena u postmenopauzi sa osteoporozom (dve grupe pacijenata, u zavisnosti od gubitka estrogena) i uporedili ih sa kontrolnim uzorcima (žena u menopauzi bez osteoporoze). Serumski nivoi markera mereni su ELISA tehnikom dok je gustina minerala u kostima (BMD) analizirana DEXA metodama procenom T-spine skora (sT spine). U grupi 1 (manje od 15 godina gubljenja estrogena) serumski nivoi Bone-ALP bili su 13,76±0,6 μg/ml, serumski nivoi E2 bili su 28,32±1,78 pg/mL, a vrednosti sT spine bile su –3,63±0,65. U grupi 2 (preko 15 godina gubljenja estrogena) serumski nivoi Bone-ALP bili su 11,88± 0,38 μg/mL, serumski nivoi E2 19,66±1,23 pg/mL, a vrednosti sT spine –3,78±0,36. U kontrolnoj grupi, serumski nivoi Bone-ALP bili su 8,68±0,44 μg/mL, serumski nivoi E2 43,07±4,04 pg/mL a vrednosti sT spine 1,78±0,11. Povišeni serumski nivoi Bone-ALP ukazuju na aktivaciju osteoblasta, što znatno pojačava koštani promet, a kada su oni povezani sa niskim BMD ukazuju na povećanu koštanu resorpciju kod žena u postmenopauzi sa osteoporozom u poređenju sa ženama u menopauzi bez osteoporoze. Serumski nivoi E2 su značajno povišeni i ukazuju na smanjenu funkciju receptora za estrogen Erα kao što je izraženo u osteoblastima.

C41
BONE ALKALINE PHOSPHATASE AND ESTRADIOL AS MARKERS OF BONE REMODELING IN POSTMENOPAUSAL OSTEOPOROSIS

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The bone remodeling imbalance in postmenopausal women with osteoporosis is produced by decreased bone formation and increased bone resorption. The aim of this study is to determine whether serum levels of bone specific alkaline phosphatase (Bone-ALP) and estradiol (E2) are elevated in postmenopausal women with osteoporosis. We determined the serum levels of Bone-ALP and E2 in postmenopausal women with osteoporosis (two cohorts of patients, depending on the estrogenic deprivation) as compared to controls (menopausal women without osteoporosis). The serum levels of the markers were measured by the ELISA technique and the evaluation of Bone Mineral Density (BMD) as analyzed using the DEXA methods assessment of T spine scores (sT spine). In cohort 1 (under 15 years of estrogenic deprivation) serum levels of Bone-ALP were 13.76±0.6 μg/mL, serum levels of E2 were 28.32±1.78 pg/mL, and sT spine values were –3.63± 0.65. In cohort 2 (over 15 years of estrogenic deprivation) serum levels of Bone-ALP were 11.88±0.38 μg/mL, serum levels of E2 were 19.66±1.23 pg/mL, and sT spine values were –3.78±0.36. In the control group the serum levels of Bone-ALP were 8.68±0.44 μg/mL, serum levels of E2 were 43.07±4.04 pg/mL, and sT spine values were –1.78±0.11. Increased serum levels of Bone-ALP demonstrate osteoblast activation, which increases significantly bone turnover, and when associated with low BMD demonstrates increased bone resorption in postmenopausal women with osteoporosis compared to menopausal women without osteoporosis. The serum levels of E2 are significantly decreased and demonstrate decreased functions of the estrogen receptor ERα as expressed in the osteoblasts.

C42
KONCENTRACIJE UKUPNOG ANTIGENA SPECIFIČNOG ZA PROSTATU I SLOBODNOG ANTIGENA SPECIFIČNOG ZA PROSTATU, AKTIVNOSTI KISELE FOSFATAZE, PROSTATIČNE KISELE FOSFATAZE I ALKALNE FOSFATAZE U SERUMU PACIJENATA OBOLELIH OD KARCINOMA PROSTATE

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Kod 70 pacijenata starosti 50–80 godina, obolelih od karcinoma prostate određivane su koncentracije ukupnog antigena specifičnog za prostatu (tPSA), slobodnog antigena specifičnog za prostatu (free PSA), aktivnosti kisele fosfataze (ACP, EC 3.1.3.2), prostatične kisele fosfataze (pACP) i alkalne fosfataze (AP, EC 3.1.3.1) u serumu, sa ciljem utvrđivanja značaja tih biohemijskih parametara u proceni prisustva karcinoma prostate i praćenja daljeg toka maligne bolesti. Određivanja su vršena kod 34 pacijenta obolelih od karcinoma prostate, kod kojih još nije primenjena nijedna vrsta terapije, kod 19 pacijenata posle urađene radikalne prostatektomije (pacijenti u ranijim stadijumima bolesti, I i II) i 17 pacijenata posle primljene radioterapije ili hormonalne terapije (pacijenti u kasnijim stadijumima bolesti). Tumori su dokazani histopatološki, koncentracije tPSA i freePSA određene su elektrohemiluminiscentnim imunoodređivanjem (»ECLIA«) na imunohemijskom analizatoru »Roche Elecsys 2010«, aktivnost ACP i neprostatične ACP određena je modifikovanom kolorimetrijskom metodom koju je opisao Hillman, aktivnost pACP je izračunata (pACP=ACP-neprostatična ACP), aktivnost AP je određena IFCC kinetičkom metodom. Kontrolnu grupu je sačinjavalo 60 zdravih muškaraca starosti 50–65 godina. ANOVA testom su upoređeni nivoi ispitivanih parametara kontrolne grupe i pacijenata obolelih od karcinoma, pre početka lečenja, posle urađene radikalne prostatektomije i posle primljene radioterapije ili hormonalne terapije. Koncentracije tPSA i freePSA značajno su bile više kod sve tri grupe obolelih od karcinoma prostate. Aktivnosti ACP, pACP i AP značajno su bile više kod pacijenata pre početka lečenja i posle primljene terapije ili hormonalne terapije. Koncentracije tPSA i freePSA bile su iznad gornjih granica očekivanih vrednosti kod normalnih zdravih muškaraca, a bile su prisutne i veće individualne razlike. Aktivnosti ACP, pACP i AP su ponekad bile iznad gornjih granica očekivanih vrednosti kod normalnih zdravih muškaraca. Dobijeni rezultati pokazuju da povišene koncentracije PSA i freePSA mogu biti značajan pokazatelj karcinoma prostate. Aktivnosti ACP, pACP i AP mogu biti od koristi pri dijagnostici i praćenju daljeg toka karcinoma prostate.

C42
CONCENTRATIONS OF TOTAL PROSTATE-SPECIFIC ANTIGEN AND FREE PROSTATE-SPECIFIC ANTIGEN, ACTIVITES OF ACID PHOSPHATASE, PROSTATIC ACID PHOSPHATASE AND ALKALINE PHOSPHATASE IN THE SERUM OF PATIENTS SUFFERING FROM PROSTATE CARCINOMA

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In 70 patients, aged 50-80 years, with prostate carcinoma, the concentrations of total prostate- specific antigen (tPSA) and free prostate-specific antigen (free PSA), activities of acid phosphatase (ACP, EC 3.1.3.2), prostatic acid phosphatase (pACP) and alkaline phosphatase (AP, EC 3.1.3.1) in the serum were determined. The aim of the study was to emphasize the important role of these biochemical parameters in the evaluation of prostate carcinoma. These biochemical values were determined in 34 patients with prostate carcinoma so far without any therapy, in 19 patients after radical prostatectomy (patients in earlier stages of diseases, I and II) and in 17 patients receiving radiotherapy or hormonal therapy (patients in later stages of diseases). Prostate carcinoma were identified histopathologically. The tPSA and free PSA concentrations were determined by an electrochemiluminescence immunoassay (»ECLIA«), intended for use on the »Roche Elecsys 2010«. The ACP activity and non-prostatic ACP activity were determined with a modification of the colorimetric method described by Hillmann, the pACP activity was calculated (Activity pACP = Activity ACP-Activity non-prostatic ACP). The AP activity was determined by IFCC kinetic method. The control group consisted of 60 healthy males, aged 50–65 years. ANOVA test was used to compare the values of the control group and the patients with prostate carcinoma without any therapy, the patients after radical prostatectomy and the patients receiving radiotherapy or hormonal therapy. The concentrations of tPSA and free PSA in patients in all three groups were significantly increased. The ACP, pACP and AP activity in patients with prostate carcinoma without therapy and in patients receiving radiotherapy or hormonal therapy were significantly increased. The values of tPSA and free PSA were above the upper limits of expected values in normal healthy males and great individual differences were also noted. The activities of ACP, pACP and AP were occasionally above the upper limits of expected values in normal healthy males. The obtained results indicate that the tPSA values and free PSA values may be a sign of the presence of prostate carcinoma. The activity of ACP, pACP and ALP may be used in the evaluation of prostate carcinoma.

C43
PROKALCITONIN U DIJAGNOZI ABDOMINALNE SEPSE

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Prokalcitonin (PCT) jeste potvrđeni marker teških sistemskih bakterijskih infekcija i sepse. Autoimuna, alergijska i virusna oboljenja kao i lokalizovane bakterijske infekcije i hronična inflamacija ne dovode do povećanja prokalcitonina. Ključnu ulogu u procesu indukcije PCT imaju bakterijski endotoksini. Nivo prokalcitonina povećava se u stanjima poznatim pod imenom sindrom sistemskog inflamatornog odgovora (engl. SIRS) kao što su bakterijska infekcija, pankreatitis, groznica ili politrauma. U normalnim metaboličkum stanjima, koncentracija prokalcitonina u plazmi je veoma mala (< 0,1 ng/mL) i raste u teškim infekcijama, gde se mogu detektovati i nivoi prokalcitonina iznad 0,5 ng/mL. Cilj ove studije bio je da se utvrdi dijagnostički značaj prokalcitonina u akutnim abdominalnim stanjima. U studiju je bilo uključeno 50 pacijenata, sa dijagnozom akutnog abdominalnog stanja, podeljenih u dve grupe zavisno od toga da li su se kod njih razvili SIRS ili sepsa. Grupe pacijenata su oblikovane nakon operativnog zahvata u zavisnosti od pozitivnog tj. negativnog mikrobiološkog nalaza intra-abdominalne infekcije. Uzorci krvi u kojima je određivan nivo PCT uzimani su pre operativnog zahvata. Prokalcitonin je određivan imunoluminometrijskim testom firme »BRAHMS Diagnostica« (Berlin, Nemačka). Dobijene vrednosti za prokalcitonin, po prijemu pacijenta, bile su statistički značajno više u grupi pacijenata kod kojih se razvila sepsa (2,45±7,32 ng/mL) u odnosu na pacijente sa dijagnozom SIRS (0,45±2,52 ng/mL, p<0,001). Srednja vrednost za PCT kod septičnih pacijenata bila je pet puta veća od vrednosti PCT kod neinfektivnih pacijenata. Nivoi prokalcitonina kod pacijenata sa sepsom su bili povećani, dok su vrednosti za neinfektivne pacijente i pored povećanja ostale u opsegu normalnih vrednosti. Naši rezultati pokazali su veliku korist od određivanja PCT za ranu, preoperativnu dijagnozu abdominalne sepse, gde je prokalcitonin i potvrđen kao rani indikator i vrlo koristan marker i za dijagnozu kao i za terapiju sepse i septičnog šoka.

C43
PROCALCITONIN IN THE DIAGNOSIS OF ABDOMINAL SEPSIS

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Procalcitonin (PCT) is an established marker for severe systemic bacterial infection and sepsis. Autoimmune, allergic and viral diseases, locally limited bacterial infections and chronic inflammation do not induce a rise in PCT. Bacterial endotoxins play a crucial role in the induction process. Levels of procalcitonin are elevated in many conditions leading to a systemic inflammatory response syndrome (SIRS) such as bacterial infection, pancreatitis, burns or polytrauma. Under normal metabolic conditions, the plasma concentration of PCT is very low but is raised in several infections, where increased levels of PCT (>0.5 ng/ml) have been detected. The aim of our study was to identify the diagnostic significance of procalcitonin in acute abdominal conditions. The study included 50 patients with acute abdominal conditions, divided into sepsis and SIRS group. Group were formed after the operations depending on the positive or negative microbiological evidence of intraabdominal infection. Blood samples for determination were obtained before surgical procedures. PCT was measured using an immunoluminometric assay, BRAHMS Diagnostica, Berlin, Germany. Concentrations of PCT on admission were significantly higher in the sepsis group (2.45±7.32 ng/mL) than in the SIRS group (0.45±2.52 ng/mL, p<0.001). The mean value of PCT in septic patients was about five times higher than the PCT values in non-infected patients. PCT values in the septic patients were increased, while values in non-septic patients were still within the normal range. Our results suggest that the PCT measurement may be useful for early, preoperative diagnosis of abdominal sepsis and PCT has been established as an early indicator and useful marker for the diagnosis and therapy monitoring of sepsis, severe sepsis and septic shock.

C44
PRODUKTI UZNAPREDOVALE OKSIDACIJE PROTEINA KOD PACIJENATA NA HEMODIJALIZI

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Oksidativni stres se smatra značajnim faktorom rizika za razvoj kardiovaskularnih bolesti i zajedničkim mehanizmom delovanja drugih faktora rizika za razvoj koronarne bolesti. Pacijenti na hemodijalizi su zbog visokog nivoa oksidativnog stresa pod visokim rizikom za razvoj kardiovaskularnih bolesti. U ovoj studiji je meren oksidativni stres određivanjem koncentracija produkata uznapredovale oksidacije proteina (engl. *advanced oxidation protein products*, AOPP) zajedno sa drugim kliničkim i biohemijskim parametrima. Sakupljani su serumi pripadnika kontrolne grupe (n=102), kao i serumi pacijenata na hemodijalizi (n=63), pre same procedure dijaliziranja. Koncentracije AOPP, malondialdehida (MDA), lipidnih hidroperoksida (LOOH), superoksidnog anjona ($O_2^{\cdot -}$), ukupnih SH grupa i aktivnosti enzima superoksid-dizmutaze (SOD) određivane su odgovarajućim metodama. Značajno povećanje koncentracija AOPP uočeno je kod pacijenata na hemodijalizi u odnosu na zdrave osobe ($p<0,001$). Takođe je uočeno povećanje MDA ($p<0,01$), $O_2^{\cdot -}$ ($p<0,05$) i smanjenje sadržaja ukupnih SH grupa ($p<0,001$) i aktivnosti enzima SOD ($p<0,05$) kod pacijenata. Zabeležena je značajna korelacija između koncentracija AOPP i ukupnih proteina ($\rho=0,465$, $p<0,001$) kao i AOPP i koncentracija triglicerida ($\rho=0,682$, $p<0,001$) kod pacijenata. Ova studija je pokazala da je kod pacijenata na hemodijalizi evidentno povećan oksidativni stres i smanjena sposobnost antioksidativne zaštite i takvo stanje izlaže pacijente povećanom riziku od kardiovaskularnih bolesti.

C44
ADVANCED OXIDATION PROTEIN PRODUCTS (AOPP) IN HEMODIALYSIS PATIENTS

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Oxidative stress is considered a significant cardiovascular risk factor and the unifying mechanism for other cardiovascular risk factors. Hemodialysis patients develop high levels of oxidative stress and therefore are at high risk for cardiovascular disease (CVD). In the present study oxidative stress was assessed using advanced oxidation protein products (AOPP) along with other clinical and biological parameters. Sera of a control group (n=102) as well as sera of patients (n=63) before hemodialysis session were collected. Serum AOPP, malondialdehyde (MDA), lipid hydroperoxide (LOOH), superoxide anion ($O_2^{\cdot -}$), total SH groups and superoxide dismutase (SOD) activity were estimated by appropriate assays. A significant increase in AOPP value was observed in hemodialysis patients as compared to healthy subjects ($p<0.001$). Also, a significant increase was observed for MDA ($p<0.01$), $O_2^{\cdot -}$ ($p<0.05$) and decrease in SH groups content ($p<0.001$) and SOD activity ($p<0.05$) in the patients. Significant correlation was noted for AOPP and total protein content ($\rho=0.465$, $p<0.001$) and AOPP and triglyceride concentration ($\rho=0.682$, $p<0.001$) in a patient group. This study shows that the increased oxidative stress in hemodialysis patients is evident as well as diminished antioxidative capability and such a situation exposes patients to a higher risk of cardiovascular disease.

D

LIPIDI I LIPOPROTEINI

LIPIDS AND LIPOPROTEINS

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Poster sessions

D45
KONCENTRACIJA LIPIDNIH PARAMETARA KOD PACIJENATA SA SENILNOM DEGENERACIJOM MAKULE

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Lipidna peroksidacija, naročito polinezasićenih masti, česta je pojava u tkivima, koja predstavlja odgovor na povećan oksidativni stres i produkciju slobodnih radikala. Cilj ovog rada je bio da se analiziraju koncentracije serumskih lipoproteina, i to ukupnog holesterola, triglicerida, HDL- i LDL-holesterola, kao i koncentracije apolipoproteina A1, B i Lp(a) kod pacijenata sa senilnom degeneracijom makule (SDM), kako bi se ispitala uloga lipidnih parametara kao faktora rizika za nastanak i razvoj bolesti. U ispitivanje je uključeno 48 pacijenata sa senilnom degeneracijom makule, starosti 70,7±6,76 godina, i 17 zdravih ispitanika iste starosne dobi, koji su činili kontrolnu grupu. Pacijenti su prošli kompletan oftalmološki pregled uključujući pregled fundusa i fluorescentnu angiografiju. Lipidni status je analiziran na biohemijskom analizatoru *Olympus AU400*. Obrada statističkih podataka vršena je pomoću statističkog paketa *SPSS v10.0*, koristeći Mann-Whitney U test, χ^2 i ANOVA test. Statističkom obradom podataka utvrđeno je da su vrednosti ukupnog holesterola, triglicerida i LDL-holesterola ($p<0,05$), kao i vrednosti apolipoproteina A1 i B ($p<0,001$) bile značajno više kod pacijenata sa SDM u poređenju sa kontrolnom grupom zdravih ljudi. Od ukupnog broja pacijenata sa SDM, 78% je imalo poremećaj lipidnog statusa: 44% je imalo tip 2a, 28% tip 2b a 6% tip 4 hiperlipoproteinemije. Na osnovu dobijenih rezultata može se zaključiti da poremećaj serumskih lipida može igrati značajnu ulogu u nastanku i razvoju senilne degeneracije makule kod starijih ljudi.

D45
LIPID PARAMETER VALUES IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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The peroxidation of lipids, especially polyunsaturated lipids, is a frequent occurence in stressed tissues, being particularly common as a response to increased oxidative stress and free radical production. The aim of this study was to analyse the concentration of serum lipoproteins (total cholesterol, triglycerides, HDL- and LDL-cholesterol), as well as apolipoproteins A1, B and Lp(a), in age-related macular degeneration, in order to explore the role of lipid parameters as risk factors for the development of age-related macular degeneration (AMD). A total of 48 AMD patients aged 70.7±6.76 and 17 age-matched healthy control subjects were included in the study. The patients underwent a complete ophtalmological examination, including visual acuity, color fundus photography and fluorescein angiography. The patients' lipid status was estimated an *Olympus AU400* biochemical analyzer. Statistical analyses were performed by an *SPSS v10.0* statistical package using a Mann-Whitney U test, Chi-Square and ANOVA tests. A statistical processing of the data revealed significantly higher values of total cholesterol, triglycerides and LDL-cholesterol ($p<0.05$), as well as apolipoproteins A1 and B ($p<0.001$) in AMD patients, compared to healthy control subjects. Seventy eight percent of the tested AMD patients had lipid status disorders: 44% had type 2a hyperlipoproteinemia, 28% had type 2b and 6% type 4 hyperlipoproteinemia. Based on the obtained results, it may be concluded that plasma lipid disorders could play an important role in the development of age-related macular degeneration in elderly subjects.

D46
MALE GUSTE LDL I HDL ČESTICE SU UDRUŽENE SA POVIŠENOM KONCENTRACIJOM MOKRAĆNE KISELINE I INFLAMACIJOM NISKOG STEPENA

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U ovoj studiji ispitivana je međusobna povezanost koncentracija mokraćne kiseline (MK), visoko osetljivog C-reaktivnog proteina (hsCRP) i fibrinogena sa veličinom LDL i HDL čestica kod zdravih sredovečnih osoba. Koncentracije MK, hsCRP i fibrinogena su merene standardnim laboratorijskim metodama u uzorcima seruma i plazme 194 zdrava dobrovoljca (112 muškaraca i 82 žene). Veličina LDL i HDL čestica je određena gradijent gel elektroforezom. Ispitanici sa vrednostima MK u najvišem tercilu imali su manje LDL i HDL čestice (P<0,05 i P<0,01) i više koncentracije fibrinogena i hsCRP (P<0,05 i P<0,01). Povišena MK je bila značajan prediktor prisustva malih, gustih LDL i HDL čestica (OR = 3,09; P<0,01 i OR = 4,40; P<0,001). Utvrđena veza između povišene koncentracije MK i manje veličine HDL-a ostala je statistički značajna i u prisustvu tradicionalnih faktora rizika za KVB. Povećane koncentracije hsCRP su bile u korelaciji sa manjom veličinom LDL čestica (P<0,05), dok su više koncentracije fibrinogena bile u korelaciji sa manjim dijametrima HDL čestica (P<0,05). Rezultati studije ukazuju da su povišena koncentracija MK i inflamacija niskog stepena povezane sa poremećajima u metabolizmu lipoproteina, što može biti rani pokazatelj ateroskleroze kod asimptomatskih osoba.

D46
SMALL DENSE LDL AND HDL PARTICLES ARE ASSOCIATED WITH HIGHER SERUM URIC ACID LEVELS AND LOW-GRADE INFLAMMATION

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This study investigates the interrelationships between serum uric acid (UA), high sensitivity C-reactive protein (hsCRP) and fibrinogen concentrations with LDL and HDL sizes in healthy middle-aged subjects. Serum UA, hsCRP and plasma fibrinogen concentrations were measured by standard laboratory methods in a sample of 194 healthy volunteers (112 men and 82 women). The diameters of LDL and HDL particles were determined by gradient gel electrophoresis. The participants in the highest UA tertile had significantly smaller LDL and HDL particle sizes (P<0.05 and P<0.01, respectively) and higher concentrations of fibrinogen and hsCRP (P<0.05 and P<0.01, respectively). Elevated UA was a significant predictor of smaller, denser LDL and HDL particles (OR = 3.09; P<0.01 and OR = 4.40; P<0.001, respectively). The observed relationship of higher UA with smaller HDL size persisted after adjustment for conventional cardiovascular risk factors. Higher hsCRP concentration correlated with smaller LDL size (P<0.05), while fibrinogen concentration was inversely related to HDL size (P<0.05). In conclusion, higher serum UA and low-grade inflammation are closely linked to alterations in lipoprotein metabolism, which may represent an early sign of atherosclerosis in asymptomatic subjects.

D47
UTICAJ RAZLIČITIH IZOFORMI APOLIPOPROTEINA (a) I SUBKLASA LIPOPROTEINA MALE GUSTINE NA KONCENTRACIJU LIPOPROTEINA (a)

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Povišena koncentracija lipoproteina (a) Lp(a) jedan je od faktora rizika za razvoj koronarne arterijske bolesti (KAB). Taj lipoprotein se sastoji od apolipopro-

D47
THE INFLUENCE OF DIFFERENT APOLIPOPROTEIN (a) ISOFORMS AND LOW DENSITY LIPOPROTEIN SUBCLASSES ON LIPOPROTEIN (a) CONCENTRATION

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An elevated concentration of lipoprotein (a) Lp(a) is a risk factor for the development of coronary artery disease (CAD). Lp(a) consists of a low density lipopro-

teina (a) [apo(a)] koji je vezan za česticu lipoproteina male gustine (LDL). Poznato je da su manje izoforme apo(a) i male, guste LDL čestice povezane sa povećanim rizikom za razvoj KAB. Takođe je poznato da je povišena koncentracija Lp(a) u cirkulaciji praćena prisustvom malih apo(a) izoformi. Međutim, još uvek nije jasno da li promene u veličini i raspodeli LDL čestica u krvi imaju uticaja na promene u koncentraciji Lp(a). U ovoj studiji smo ispitivali povezanost prisustva malih apo(a) izoformi i malih LDL subklasa sa promenama u koncentraciji Lp(a) u krvi 109 pacijenata sa KAB i 102 zdrava ispitanika. Koncentracija Lp(a) u plazmi je merena imunoturbidimetrijski. Izoforme apo(a) su određene elektroforetski na SDS-agaroznom gelu, nakon čega je primenjen imunobloting. Subklase LDL čestica su određene gradijent (3–31%) gel elektroforezom na poliakrilamidnom gelu. Veličina LDL i apo(a) čestica bila je značajno manja kod pacijenata ($P<0,001$ i $P<0,01$). Kod pacijenata je uočeno značajno veće prisustvo malih apo(a) izoformi ($P<0,01$), dok se zastupljenost malih LDL čestica nije razlikovala u ispitivanim grupama. Dalje smo ispitivali zastupljenost malih izoformi apo(a) i malih subklasa LDL u odnosu na koncentraciju Lp(a) (≥300 mg/L ili <300 mg/L). Dobijeni rezultati pokazali su značajno veće prisustvo malih apo(a) izoformi u krvi ispitanika sa koncentracijom Lp(a) ≥300 mg/L, kako u KAB ($P<0,01$), tako i u kontrolnoj grupi ($P<0,01$). S druge strane, najveća zastupljenost malih LDL čestica bila je u grupi KAB pacijenata sa Lp(a) koncentracijom ≥300 mg/L, ali bez statistički značajne razlike u odnosu na zastupljenost tih subklasa u ostalim ispitivanim grupama. Naši rezultati pokazuju da je kod pacijenata sa KAB povišena koncentracija Lp(a) praćena povećanim prisustvom malih izoformi apo(a) i malih, gustih LDL čestica u krvi. Odnos između komponenti Lp(a) treba dalje analizirati u budućim studijama.

tein (LDL) particle to which a glycoprotein apolipoprotein (a) [apo(a)] is attached. Smaller apo(a) isoforms and LDL subclasses are associated with an elevated risk for CAD. It has been documented that the presence of smaller apo(a) isoforms is related to a high Lp(a) level, while it is unclear if changes in the size and distribution of circulating LDL particles have any impact on Lp(a) concentration. In this study, we examined the presence of smaller apo(a) isoforms and LDL subclasses in circulation with respect to the concentration of Lp(a) in 109 patients with CAD and 102 controls. The plasma concentration of Lp(a) was measured using immunoturbidimetry. Apo(a) size isoforms were determined by high resolution SDS-agarose gel electrophoresis followed by immunoblotting. LDL subclasses were determined by polyacrylamide gradient (3–31%) gel electrophoresis. Mean LDL and apo(a) sizes were lower in patients than in controls ($P<0.001$ and $P<0.01$, respectively). The prevalence of small apo(a) isoforms was significantly higher among the patients ($P<0.01$). However, we found no differences in the prevalence of small LDL particles. Next, we examined the predominance of smaller apo(a) isoforms and LDL subclasses with respect to the concentration of Lp(a) (≥300 mg/L or<300 mg/L). The obtained results showed significantly higher presence of smaller apo(a) isoforms in individuals with Lp(a) level ≥300 mg/L, in CAD ($P<0.01$), as well as in the control group ($P<0.01$). The highest proportion of small LDL particles was seen in CAD patients with Lp(a) levels ≥300 mg/L, but with no statistically significant difference ($P>0.05$) when compared to the other groups. Our results indicated that CAD patients with elevated Lp(a) concentration had an abundance of smaller apo(a) isoforms and small LDL subclasses in the circulation. This topic should be further elucidated by future studies.

D48
LIPIDNI STATUS U POPULACIJI ROMA OPŠTINE INĐIJA

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Dom zdravlja »Dr Milorad Mika Pavlović«, Inđija

U okviru projekta »Dekada Roma«, Dom zdravlja Inđija radio je na samostalnom projektu »Monitoring i sekundarna prevencija koronarne bolesti kod populacije Roma u opštini Inđija«. Tim istraživanjem obuhvaćeno je 174 pripadnika romske populacije SO Inđija, od kojih je metodom slučajnog izbora izdvojeno njih ukupno 33–18 žena i 15 muškaraca prosečne starosti 50±7 godina. Kontrolnu grupu je obuhvatila 31 zdrava osoba prosečne starosti 49±7. Iz uzoraka krvi određivana je koncentracija triglicerida, ukupnog holesterola, HDL holesterola i LDL holesterola primenom

D48
THE DETERMINATION OF LIPID STATUS IN THE ROMANI POPULATION OF INĐIJA MUNICIPALITY

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The Health Centre of Inđija has been actively participating in the project called »The Decade of Roma« with its own project »Monitoring and Secondary Prevention of Cardiac Diseases in the Romani Population of Inđija«. The research included 174 Romani subjects from the territory of the town of Inđija. Thirty three subjects were chosen the method of free selection, 18 women and 15 men average age 50±7. A control group included healthy adults, average age 49±7. In the blood samples we determined triglycerides, total, HDL and LDL cholesterol using standard enzymatic

standardne enzimske metode. U radu su korišćeni komercijalni reagensi za određivanje lipidnog statusa, firme »Roche Diagnostics GmbH«, na diskretnom biohemijskom analizatoru »Roche/Hitachi 912«, a indeks ateroskleroze je određen računski. Rezultati pokazuju da postoji statistički značajna razlika (P<0,01) u koncentracijama triglicerida, holesterola, LDL holesterola i indeksa ateroskleroze između ispitivane i kontrolne grupe, dok (P>0,05) u koncentracijama HDL holesterola ne postoji statistički značajna razlika (*Tabela I*). To ukazuje na mogućnost preventivnog delovanja na sprečavanje razvitka kardiovaskularnih bolesti i daljeg porasta koncentracije triglicerida, holesterola, LDL holesterola kao i na povećanje HDL holesterola. Postoji jasna indikacija za sekundarnu prevenciju kardiovaskularnih bolesti među pripadnicima romske populacije na teritoriji opštine Inđija.

Tabela I. Prosečna koncentracija parametara lipidnog statusa po grupama.

	Holesterol	LDL-H	HDL-H	Trigliceridi	IA
Kontrolna grupa	4,44 +/– 0,50	2,38 +/– 0,50	1,57 +/– 0,28	1,14 +/–0,35	1,61 +/– 0,62
Ref. vrednosti	Do 5,2	Do 3,4	Preko 1,6	Do 1,7	Do 3,0
Ispitivana grupa	5,92 +/– 1,24	3,45 +/–1,22	1,48 +/– 0,27	1,74 +/– 0,86	2,46 +/– 1,11

methods, calculating the atherosclerosis index (AI). Lipid concentration was examined using »Roche Diagnostics GmbH« reagents on a discrete biochemical automat »Roche/Hitachi 912« analyzer. The results showed a statistically significant difference (P<0.01) in the concentrations of triglycerides, total and LDL cholesterol (LDL-C) and atherosclerosis index between the examined population and control group. No statistically significant difference (P>0.05) was found in the values of HDL holesterol (HDL-C) in both groups (*Table 1*). The obtained results confirme the possibility that prevention activities can help to decrease the levels of triglycerides, total and LDL cholesterol, atherosclerosis index, and elevate the HDL cholesterol level. There is clear indication for the secondary prevention of cardiac diseases in the Romani population of Inđija.

Table II. Mean concentration of lipid status and AI in the examined and control group.

	Total Cholesterol	LDL-C	HDL-C	Triglyceride	AI
Control group	4.44 +/– 0.50	2.38 +/– 0.50	1.57 +/– 0.28	1.14 +/–0.35	1.61 +/– 0.62
Reference values	Do 5.2	Do 3.4	Preko 1.6	Do 1.7	Do 3.0
Examined group	5.92 +/– 1.24	3,45 +/–1.22	1.48 +/– 0.27	1.74 +/– 0.86	2.46 +/– 1.11

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VEZA IZMEĐU VELIČINE HDL ČESTICA I PARAOKSONAZNE AKTIVNOSTI KOD PACIJENATA SA DIABETES MELLITUS-OM TIPA 2

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Dobro je poznato da su niske koncentracije HDL holesterola udružene sa povećanim rizikom za razvoj kardiovaskularnih bolesti. Mnoge studije su pokazale da su HDL čestice strukturno izmenjene kod pacijenata sa dijabetes melitusom tipa 2. Paraoksonaza (PON1) enzim je na HDL-u koji štiti LDL čestice od oksidativne modifikacije. Ova studija se bavi ispitivanjem veze između zastupljenosti HDL2 i HDL3 lipoproteinskih fenotipova i statusa PON1. U serumu 91 zdrave osobe i 85 pacijenata sa dijabetes melitusom tipa 2 određivana je aktivnost PON1 metodom po Richteru i Furlongu. Veličina HDL čestica je određivana elektroforezom na poliakrilamidnom gelu. Aktivnost PON1 je značajno manja kod pacijenata u poređenju sa kontrolnom grupom (P<0,001), ali nije pronađena razlika u

D49
THE ASSOCIATION BETWEEN HDL PARTICLE SIZE AND PARAOXONASE ACTIVITY IN TYPE 2 DIABETES MELLITUS PATIENTS

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HDL-cholesterol is recognized as a factor that protects against the development of cardiovascular diseases, and low HDL-cholesterol is associated with increased risk of cardiovascular diseases in subjects with and without diabetes. Many studies showed that HDL composition is abnormal in type 2 diabetic patients. Paraoxonase (PON1) is a serum esterase associated with HDL which protects LDL particles from oxidative modifications. Our study examined the association of HDL2 and HDL3 particles distribution in type 2 diabetes mellitus patients and controls with PON1 status. PON1 activities were measured spectrophotometrically in the sera according to the method described by Richter and Furlong in 91 control subjects and 85 type 2 diabetes mellitus patients. HDL particle size was determined by

distribuciji PON1 Q192R fenotipa u ispitivanim grupama. Poređenjem aktivnosti PON1 između kontrole i pacijenata sa predominantno zastupljenim većim HDL2 česticama, kao što se i očekivalo, dobijene su značajno veće aktivnosti PON1 u kontrolnoj grupi ($P<0.001$). Međutim, statistički značajna razlika u aktivnosti PON1 između kontrole i pacijenata nije dokazana kada su upoređene osobe sa predominantno zastupljenim HDL3 česticama. Aktivnost PON1 kod osoba sa predominantnim HDL2 česticama bila je značajno veća u kontrolnoj grupi ($P<0,05$) u odnosu na osobe sa predominantnim HDL3, dok kod pacijenata te razlike nije bilo. Ovi rezultati nas navode na zaključak da HDL2 čestice imaju jači antioksidativni efekat, ali je on značajno umanjen zbog izmenjene strukture HDL čestica kod dijabetesa. Smanjena aktivnost PON1 udružena sa strukturno izmenjenim HDL česticama predstavlja značajan faktor za progresivni razvoj kardiovaskularnih bolesti kod pacijenata sa dijabetes melitusom tipa 2.

D50
PROVERA TAČNOSTI DVE NOVE JEDNAČINE ZA IZRAČUNAVANJE KONCENTRACIJE LDL HOLESTEROLA POREĐENJEM SA VREDNOSTIMA DOBIJENIM DIREKTNIM ODREĐIVANJEM

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Pouzdano i tačno određivanje koncentracije LDL holesterola (LDL-H) od velikog je značaja zbog pravilnog razvrstavanja pacijenata u rizične kategorije predložene od strane NCEP ATP-III. U kliničkoj praksi koncentracija LDL-H se najčešće određuje računanjem pomoću Friedewaldove formule. Cilj ove studije je da proveri tačnost dve nove formule za izračunavanje LDL-H u odnosu na vrednosti dobijene direktnim određivanjem. U studiju je uključeno 1640 pacijenata (srednja vrednost godina 54 ± 15, 52,4% žena) koji su imali koncentraciju triglicerida ≤ 4,5 mmol/L. LDL-H je određen direktnom metodom (D-LDL-H) i izračunat pomoću dve nove formule. Prva formula predstavlja modifikovanu Friedewaldovu jednačinu a druga je izvedena primenom multiple regresione analize. Iz dobijenih rezultata izračunata je srednja vrednost LDL-H i to: 3,86 ± 1,09 mmol/L za direktnu metodu, 3,86 ± 1,1 mmol/L za prvu formulu (F1-LDL-H) i 3,83±1,06 mmol/L za drugu formulu (F2-LDL-H). Linearna regresiona analiza je pokazala dobre i istovetne korelacije između direktnog LDL-H i LDL-H izračunatog iz obe jednačine (R

D50
TESTING THE ACCURACY OF TWO NEW FORMULAS FOR THE DETERMINATION OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL CONCENTRATION COMPARED WITH A DIRECT ASSAY

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Reliable and accurate determination of low-density lipoprotein cholesterol (LDL-C) concentration is very important for the classification of patients into proper risk categories based on cut-off points given by NCEP ATP-III. The Friedewald formula for the estimation of LDL-C concentrations is the most often used formula in clinical practice. In the present study, we attempted to derive and validate more accurate formulas to determine LDL-C levels. Our study included 1640 patients (mean age 54 ± 15, 52.4% women) with triglyceride concentration ≤4.5 mmol/L. LDL-C was determined by the direct method and also calculated with two new formulas. The first formula represents a modified Friedewald formula and the second was derived using multiple linear regression analysis. In the studied population, the mean LDL-C levels was 3.86±1.09 mmol/L measured by the direct assay (D-LDL-C), 3.86 ± 1.1 mmol/L calculated using the first formula (F1-LDL-C) and 3.83±1.06 mmol/L using the second formula (F2-LDL-C). Linear regression analysis shows good and equal correlations between D-LDL-C and LDL-C calcu-

=0,97). Razlika između srednjih vrednosti D-LDL-H i F1-LDL-H nije statistički značajna, dok je razlika srednjih vrednosti D-LDL-H i F2-LDL-H od 0,02±0,25 mmol/L pokazala statističku značajnost (P<0,01). Slaganje rezultata po NCEP ATP-III kategorijama rizika između direktno određenog i izračunatog holesterola je 81,1% za prvu formulu i 80% za drugu formulu. Tačnost rezultata u odnosu na direktno određen LDL-H bila je zadovoljavajuća: 90% rezultata za prvu i 93% rezultata za drugu formulu bilo je u opsegu ±10% razlike. Nove jednačine za izračunavanje LDL-H treba dodatno testirati na većoj populaciji pre nego što se počne sa njihovom implementacijom u biohemijskim laboratorijama.

lated by both equations (R=0.97). The mean difference between D-LDL-C and F1-LDL-C showed no statistic significance, while the mean difference between D-LDL-C and F2-LDL-C of 0.02±0.25 mmol/L was significant (P<0.01). Concordant results for NCEP ATP-III risk categories were present in 81.1% of results calculated by the first formula and directly measured LDL-C, and in 80% of the results calculated by the second formula and directly measured LDL-C. The results calculated by both formulas revealed a satisfactory level of accuracy, 90% of results for the first formula and 93% of results for the second formula were within the difference range of ±10%. New equations for the determination of LDL-C levels need to be tested on a bigger population before we can start with their implementation into biochemical laboratories.

D51
ZNAČAJ ODREĐIVANJA LDH I DRUGIH BIOHEMIJSKIH MARKERA KAO PREDIKTORA PREVREMENOG PORODAJA I POBAČAJA

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Incidenca prevremenog porođaja se kreće od 3 do 5% i najčešće je posledica infekcije. Intraamnionske infekcije, i predstavljaju najčešći uzrok morbiditeta i mortaliteta. Ova prospektivna studija sprovedena je sa ciljem da se uporede vrednosti biohemijskih, hematoloških i mikrobioloških parametara u amnionskoj tečnosti (glukoze, laktat dehidrogenaze, leukocita i bojenja po Gramu) sa pozitivnom kulturom amnionske tečnosti u predikciji intraamnionske infekcije i preterminskog porođaja. Na Institutu za ginekologiju i akušerstvo u periodu od novembra 2003. do aprila 2004. ispitano je 125 trudnica. Njima je pri rutinskim ranim amniocentezama (između 16. i 18. gestacione nedelje) uzimana plodova voda za mikrobiološku, biohemijsku i hematološku obradu. Mikrobiološka obrada je podrazumevala zasejavanje na standardnim podlogama za aerobne bakterije i bojenje po Gramu. Senzitivnost, specifičnost, pozitivna i negativna prediktivna vrednost za LDH, glukozu, Gram bojenje, izračunati su u odnosu na pozitivnu kulturu amnionske tečnosti. Za statističku obradu rezultata korišćeni su neparametarski Mann-Whitney U-test, ROC-kriva i t-test. Prevalenca pozitivnih kultura amnionskih tečnosti bila je 13% (15 od 125). Srednja vrednost aktivnosti enzima LDH (414 U/L) u grupi sa pozitivnom kulturom bila je značajno veća od one u grupi čija je kultura bila negativna (LDH 143 U/L; p<0,01). Granice odlučivanja (»cut-off« vrednosti) za sve parametre su izračunate u odnosu na predikciju pozitivne kulture amnionske tečnosti i iznosile su za LDH ≥ 205 U/L, za broj leukocita ≥10 cells/mm^3

D51
HIGH LEVEL OF LDH AND OTHER BIOCHEMICAL MARKERS IN THE PREDICTION OF PRETERM LABOR AND ABORTION

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The incidence of preterm labor is 3–5 % and it is most frequently caused by infection. Bacterial infections of the amniotic cavity (chorioamnionitis) is a significant cause of perinatal morbidity and mortality. Our objective was to analyze the value of an amniotic fluid test for the detection of microbial invasion of the uterine cavity. Amniotic fluid was obtained by amniocentesis from one hundred and fifteen consecutive patients, from 16 to 18 gestational weeks. Fluid was analyzed for leukocyte count, glucose level, lactate dehydrogenase level (LDH), and Gram stain. Cultures for aerobes and anaerobes were performed. Sensitivity, specificity, and positive and negative predictive value were calculated for LDH, leukocyte count, glucose, and Gram stain in the prediction of positive amniotic fluid culture. Receiver-operator characteristic curve analysis, t-test, and nonparametric test (Mann Whitney U-test) were used. The prevalence of positive amniotic fluid cultures was 13% (14 of 115). The median LDH level (414 U/L) was significantly greater for women with a positive amniotic fluid culture than for those with a negative culture (median LDH 143 U/L; p<0.01). Critical values of LDH ≥ 205 U/L, leukocyte count ≥10 cells/mm^3 (10×10^6/L) and glucose ≤ 1.15 mmol/L were selected for optimal performance in the prediction of a positive amniotic fluid culture. LDH level had the best sensitivity (71%) in contrast to leukocyte count (51%), glucose (65%) and positive Gram stain (36%). Amniotic fluid LDH level has diagnostic value in the

(10×10^6/L), a za glukozu ≤1,15 mmol/L. Najsenzitivniji test za detekciju mikrobiološke infekcije u amnionskoj tečnosti je aktivnost LDH (71%), za razliku od ostalih dijagnostičkih markera: glukoze (65%), broja leukocita (51%) i pozitivnog Gram bojenja (36%). Nivo LDH u amnionskoj tečnosti ima dijagnostičku vrednost u predikciji pozitivnog nalaza kulture amnionske tečnosti. Određivanje nivoa LDH u amnionskoj tečnosti, kao ranog prediktora infekcije, jednostavna je, brza i pouzdana metoda, lako dostupna svim bolničkim laboratorijama.

prediction of a positive amniotic fluid culture. Considering that amniotic fluid infection in a majority of pregnant women may cause preterm labor or abortion the determination of amniotic fluid LDH might be of great importance. Lactate dehydrogenase is a readily available, inexpensive, rapid amniotic fluid marker that can be measured in any hospital laboratory.

D52
ISPITIVANJE UTICAJA POVIŠENE FIZIČKE AKTIVNOSTI NA NEKE LIPIDSKE PARAMETRE ZDRAVIH MLADIH OSOBA

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Brojne studije pokazale su povoljan efekat fizičke aktivnosti na parametre lipidskog statusa. Ipak, nedovoljno je ispitano kakav efekat ima intenzivirani fizički trening. Cilj ovog istraživanja bio je da se ispita uticaj povišene fizičke aktivnosti na serumske nivoe ukupnog holesterola (TC), triglicerida (TG), HDL holesterola (HDL-C), LDL holesterola (LDL-C), apolipoproteina (apo) A1 i B i lipoproteina (a) (Lp(a)). Ispitivanjem je obuhvaćeno 28 aktivnih članova Sportske sekcije Medicinskog fakulteta Univerziteta u Novom Sadu (19 muškaraca i 9 žena), i 25 zdravih studenata slične životne dobi (12 muškaraca i 13 žena) koji se ne bave aktivno sportom. TC, TG, HDL-C i LDL-C određivani su standardnim biohemijskim metodama, a apo A1 i B (»Olympus«, Lismehan, Irska) i Lp(a) (»Sentinel«, Milano, Italija) imunoturbidimetrijski. Uzorci ispitanika uzeti su pre i posle osam meseci aktivnog sportskog treninga (septembar–maj). Dobijeni su sledeći rezultati:

Ispitivani parametri	Sportisti (n = 28)			Zdrave osobe (n = 25)		
	bazalno Xsr.±SD	posle 8 m. Xsr.±SD	% promena	bazalno Xsr.±SD	posle 8 m. Xsr.±SD	% promena
mmol/L						
TC	4,05±0,56	4,13±0,63	+2,03	4,19±0,50	4,43±0,61	+5,63
TG	0,93±0,36	1,09±0,41	+18,28	0,82±0,43	1,07±0,52	+29,71
HDL-C	1,51±0,38	1,42±0,30	–5,88	1,56±0,43	1,47±0,39	–5,90
LDL-C	2,12±0,69	2,15±0,70	+1,38	2,22±0,62	2,42±0,67	+8,83
g/L						
Apo A1	1,45±0,19	1,45±0,16	+0,15	1,48±0,19	1,48±0,16	–0,35
Apo B	0,65±0,17	0,75±0,22	+15,41	0,71±0,14	0,79±0,19	+11,99
Lp(a)	0,08±0,11	0,10±0,13	+35,24	0,09±0,11	0,11±0,16	+22,27

D52
EXAMINATION OF THE INFLUENCE OF ENHANCED PHYSICAL ACTIVITY ON SOME LIPID PARAMETERS IN HEALTHY YOUNG ADULTS

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Numerous studies have demonstrated the positive effect of physical activity on some lipid parameters. However, what kind of effect intensified physical practice has is insufficiently examined. The aim of this study was to examine the influence of enhanced physical activity on the serum levels of total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL-C), LDL cholesterol (LDL), apolipoproteins (apo) A1 and B and lipoprotein (a) (Lp(a)). In this study 28 active members of the Sports Section of the Medical Faculty, University of Novi Sad (19 males and 9 females), and 25 healthy students matched for age (12 males and 13 females) who did not practise sport actively were included. TC, TG, HDL-C and LDL-C were determined by standard biochemical methods, and apo A1 and B (»Olympus«, Lismeehan, Ireland) and Lp(a) (»Sentinel«, Milano, Italy) by immunoturbidimetry. Samples were taken before and after eight months of active sport practise (September to May). The following results were obtained:

Examined parameters	Sportsmen (n = 28)			Healthy subjects (n = 25)		
	basal Xsr.±SD	after 8 m. Xsr.±SD	% difference	basal Xsr.±SD	after 8 m. Xsr.±SD	% difference
mmol/L						
TC	4.05±0.56	4.13±0.63	+2.03	4.19±0.50	4.43±0.61	+5.63
TG	0.93±0.36	1.09±0.41	+18.28	0.82±0.43	1.07±0.52	+29.71
HDL-C	1.51±0.38	1.42±0.30	–5.88	1.56±0.43	1.47±0.39	–5.90
LDL-C	2.12±0.69	2.15±0.70	+1.38	2.22±0.62	2.42±0.67	+8.83
g/L						
Apo A1	1.45±0.19	1.45±0.16	+0.15	1.48±0.19	1.48±0.16	–0.35
Apo B	0.65±0.17	0.75±0.22	+15.41	0.71±0.14	0.79±0.19	+11.99
Lp(a)	0.08±0.11	0.10±0.13	+35.24	0.09±0.11	0.11±0.16	+22.27

U našoj grupi ispitanika nisu ustanovljene značajne promene u nivoima ispitivanih lipidskih parametara posle perioda od 8 meseci aktivnog treninga. Neočekivano, nivoi HDL-C u obe podgrupe i apo A1 kod osoba koje se ne bave aktivno sportom su se snizili, dok su se svi ostali ispitivani parametri bili povišeni.

In the examined group, there were no significant differences in lipid parameter levels after the period of eight months of active sport practise. Surprisingly, HDL-C levels in both subgroups as well as apo A1 in the subjects who do not practise sport actively were reduced, while the other examined parameter values increased.

D53
UTICAJ HRONIČNE *HELICOBACTER PYLORI* INFEKCIJE NA PARAMETRE LIPIDSKOG STATUSA, APOLIPOPROTEINE A1 I B I Lp(a) LIPOPROTEIN

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Dosadašnja saznanja pokazuju da hronična infekcija s *Helicobacter pylori* (HP), kao niskostepeni perzistentni inflamatorni stimulus, ima određeni uticaj na razvoj ateroskleroze. Istovremeno, podaci o nastanku proaterogenih promena u lipidskom statusu u sklopu te hronične infekcije su kontradiktorni. Cilj istraživanja bio je da se ispitaju razlike u lipidskom statusu, apolipoproteinima (apo) A1 i B i Lp(a) lipoproteinu (Lp(a)) kod osoba s hroničnom HP infekcijom i bez nje. Ispitivanjem je obuhvaćeno 55 osoba (20 muškaraca i 30 žena) s hroničnom HP infekcijom (IgG >50 U/mL i IgA <20 U/mL) i 55 (20 muškaraca i 30 žena) HP negativnih osoba (IgG i IgA <20 U/mL). IgG i IgA antitela protiv HP određivana su ELISA metodom (»Virion/Serion«, Vircburg, Nemačka). Parametri lipidskog statusa određivani su standardnim biohemijskim metodama, a apo A1 i B (»Olympus«, Lismehan, Irska) i Lp(a) (Sentinel, Milano, Italija) imunoturbidimetrijski. Vrednosti ukupnog holesterola (TC), triglicerida (TG), LDL-holesterola (LDL), non-HDL holesterola (non-HDL), kao i apo B i Lp(a) bile su povišene kod HP pozitivnih u odnosu na HP negativne osobe. Promene su bile značajne za TC, LDL i non-HDL u ukupnoj grupi ispitanika (6,01±1,04 vs. 5,18±0,97 mmol/L, p<0,001; 3,69±1,14 vs. 3,23±0,78 mmol/L, p<0,02 i 4,62 ±0,98 vs. 3,87±0,97 mmol/L, p<0,001) i kod žena (5,98±1,07 vs. 5,10±0,82 mmol/L, p<0,001; 3,79 ±1,11 vs. 3,14±0,66 mmol/L, p<0,01 i 4,58±1,06 vs. 3,75±0,86 mmol/L, p<0,001), za TG u ukupnoj grupi (1,86±1,16 vs. 1,42±0,78 mmol/L, p<0,05) i kod muškaraca (2,28±1,29 vs. 1,57±0,75 mmol/L, p<0,05), a za apo B u ukupnoj grupi (1,10±0,26 vs. 0,90±0,23 mmol/L, p<0,001), kod muškaraca (1,13 ±0,22 vs. 0,93±0,23 mmol/L, p<0,01) i kod žena (1,08±0,28 vs. 0,89±0,23 mmol/L, p<0,005). Povišenje Lp(a) nije bilo značajno, dok se nivoi HDL holesterola i apo A1 nisu značajno razlikovali između HP pozitivnih i HP negativnih osoba. Naši rezultati podržavaju hipotezu da bi hronična infekcija s HP mogla modifikovati metabolizam lipida u pravcu formiranja proaterogenog lipidskog statusa.

D53
THE INFLUENCE OF CHRONIC *HELICOBACTER PYLORI* INFECTION ON SERUM LIPID PROFILE PARAMETERS, APOLIPOPROTEINS A1 AND B AND Lp(a) LIPOPROTEIN

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Recent studies unequivocally show that chronic Helicobacter pylori (HP) infection, as a low-grade persistent inflammatory stimulus, has an influence on atherosclerosis development. Simultaneously, data on proatherogenic alterations in the serum lipid profile due to this chronic infection are contradictory. The aim of this study was to look for differences in the lipid status, apolipoproteins (apo) A1 and B and Lp(a) lipoprotein of the subjects with and without chronic HP infection. Fifty five subjects (20 male and 30 female) with chronic HP infection (IgG>50 U/mL and IgA <20 U/mL) and 55 (20 male and 30 female) HP negative subjects (IgG and IgA <20 U/mL) were examined. IgG and IgA antibodies were determined from serum samples by the ELISA method (Virion/Serion, Würzburg, Germany). Lipid profile parameters were determined by standard biochemical methods, apo A1 and B (Olympus, Lismeehan, Ireland) and Lp(a) (Sentinel, Milano, Italy) by immunoturbidimetry. Levels of total cholesterol (TC), triglycerides (TG), LDL cholesterol (LDL), non-HDL cholesterol (non-HDL) as well as apo B and Lp(a) were higher in HP positive in comparison to HP negative subjects. Differences were significant for TC, LDL and non-HDL in all subjects (6.01±1.04 vs. 5.18± 0.97 mmol/L, p<0.001; 3.69±1.14 vs. 3.23±0.78 mmol/L, p<0.02 i 4.62±0.98 vs. 3.87 ±0.97 mmol/L, p<0.001) and in female group (5.98 ±1.07 vs. 5.10±0.82 mmol/L, p<0,001; 3.79±1.11 vs. 3.14±0.66 mmol/L, p<0.01 i 4.58±1.06 vs. 3.75±0.86 mmol/l, p<0.001) and for TG in whole subject group (1.86± 1.16 vs. 1.42±0.78 mmol/L, p<0.05), in male group (2.28±1.29 vs. 1.57±0.75 mmol/L, p<0.05) and for apo B in all subjects (1.10±0.26 vs. 0.90±0.23 mmol/L, p<0.001), in males (1.13±0.22 vs. 0.93± 0.23 mmol/L, p<0.01) and the female (1.08 ±0.28 vs. 0.89±0.23 mmol/L, p<0.005) group. The increase in Lp(a) levels were not significant, while there were no diferences in HDL-cholesterol and apo A1 levels between HP positive and negative subjects. Our results confirm the hypothesis that chronic HP infection could modify lipid profile in a way that would promote the formation of a proatherogenic lipid profile.

D54
EFEKTI SINTETSKE ŽUČNE SOLI KAO MODULATORA LIPIDSKOG METABOLIZMA ZDRAVIH I DIJABETIČNIH PACOVA

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Otkriće da su žučne kiseline važni signalni molekuli uključeni i u regulaciju metabolizma lipida dalo je osnov za ispitivanje njihovih sintetskih derivata kao potencijalno novih hipolipidemijskih agenasa. U ovom istraživanju ispitivan je uticaj sintetske Na-monoketoholne kiseline (Na-MKHA), aplikovane peroralno (p.o.), subkutano (s.c.) i intravenski (i.v.), 2 mg/kg TT, jednokratno i tokom 7 dana, na lipidski status zdravih (n=30) i dijabetičnih (n=30; dvokratna intraperitonealna aplikacija 100 mg/kg TT aloksana) »Wistar« pacova. Odgovarajuće kontrolne grupe (KG, n=5) zdravih i dijabetičnih pacova primale su 10 mL/kg TT fiziološkog rastvora p.o, jednokratno ili tokom 7 dana. Parametri lipidskog statusa određivani su standardnim biohemijskim metodama. Jednokratna primena Na-MKHA dovela je do neznatnih promena ukupnog i HDL holesterola, dok je sedmodnevna primena izazvala značajno sniženje ukupnog (KG 1,93±0,45 mmol/L; p.o. 1,21±0,14 mmol/L, p<0,01; s.c. 1,38±0,05 mmol/L, p<0,05; i.v. 1,13±0,08 mmol/L, p<0,01) i LDL holesterola (KG 0,49±0,31 mmol/L; p.o. 0,03±0,04 mmol/L; s.c. 0,04±0,04 mmol/L; i.v. 0,03±0,07 mmol/L; p<0,02 svi) kod dijabetičnih, i sniženje HDL holesterola i kod zdravih (KG 0,91±0,16 mmol/L; i.v. 0,63±0,12 mmol/L, p<0,02) i kod dijabetičnih (KG 1,08±0,13 mmol/L; s.c. 0,87±0,06 mmol/L, p<0,02; i.v. 0,77± 0,06 mmol/L, p<0,01) životinja. Trigliceridi su se snizili posle jednokratne primene Na-MKHA, značajno samo kod dijabetičnih pacova (KG 1,38±0,50 mmol/L; s.c. 0,66±0,28 mmol/L, p<0,05; i.v. 0,58±0,44 mmol/L, p<0,05), dok je sedmodnevna primena dovela do porasta triglicerida kod zdravih (KG 0,53±0,09 mmol/L; s.c. 1,63±0,39 mmol/L, p<0,001; i.v. 0,87±0,11 mmol/L, p<0,001) i neznačajnog sniženja kod dijabetičnih pacova. Dobijeni rezultati upućuju na potrebu daljih ispitivanja modulacijskog efekta sintetskih žučnih soli na metabolizam lipida, pre svega putem nuklearnih farnesoid X receptora.

D54
THE EFFECTS OF SYNTHETIC BILE SALT AS A MODULATOR OF THE LIPID METABOLISM OF HEALTHY AND DIABETIC RATS

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The finding that bile acids as important signal molecules are also involved in lipid metabolism regulation give rise to an examination of their synthetic derivates as potentially new hypolipidemic agents. In this study, the influence of synthetic sodium-monoketocholate (Na-MKHA), perorally (p.o.), subcutaneously (s.c.) and intravenously (i.v.) applied, 2 mg/kg b.w., in one-dose and during 7 days, on the lipid status of healthy (n=30) and diabetic (n=30; two-time intraperitoneal application of 100 mg/kg b.w. of Aloxane) »Wistar« rats was examined. Corresponding control groups (CG, n=5) of healthy and diabetic rats received 10 mL/kg b.w. of physiological saline p.o., in one-dose or during 7 days. Lipid status parameters were determined using standard biochemical methods. One-dose application of Na-MKHA provoked insignificant changes in total and HDL cholesterol, while a seven-day application provoked a significant decrease in total (CG 1.93± 0.45 mmol/L; p.o. 1.21± 0.14 mmol/L, p<0.01; s.c. 1.38±0.05 mmol/L, p<0.05; i.v. 1.13±0.08 mmol/L, p<0.01) and LDL cholesterol (CG 0.49±0.31 mmol/L; p.o. 0.03±0.04 mmol/L; s.c. 0.04±0.04 mmol/L; i.v. 0.03±0.07 mmol/L; p<0.02 respectively) in diabetic, and a decrease in HDL cholesterol in healthy (CG 0.91±0.16 mmol/L; i.v. 0.63 ±0.12 mmol/L, p<0.02) and diabetic (CG 1.08±0.13 mmol/L; s.c. 0.87±0.06 mmol/L, p<0.02; i.v. 0.77± 0.06 mmol/L, p<0.01) animals. Triglycerides significantly decreased after the one-dose application of Na-MKHA only in diabetic rats (CG 1.38±0.50 mmol/L; s.c. 0.66±0.28 mmol/L, p<0.05; i.v. 0.58±0.44 mmol/L, p<0.05), while the seven-day application provoked an increase in triglycerides in the healthy (CG 0.53±0.09 mmol/L; s.c. 1.63±0.39 mmol/L, p<0.001; i.v. 0.87±0.11 mmol/L, p<0.001) and an insignificant decrease in the diabetic rats. The obtained results point to the need for further examination of the modulation effect of synthetic bile salts on lipid metabolism, especially through nuclear farnesoid X receptors.

D55
LIPOPROTEIN (a) U HRONIČNOJ BUBREŽNOJ INSUFICIJENCIJI

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Kardiovaskularne komplikacije predstavljaju vodeći uzrok mortaliteta kod pacijenata sa hroničnom bubrežnom insuficijencijom (HBI). Lp(a) lipoprotein kao nezavisni faktor rizika za razvoj prevremene ateroskleroskleroze mogao bi imati značajnu doprinosnu ulogu. Ova studija izvedena je s ciljem ispitivanja odnosa između funkcione rezerve bubrega i serumskih koncentracija Lp (a) kod bolesnika u različitim stadijumima HBI. U studiju je uključeno 74 ispitanika, 42 (27 muškaraca, 15 žena) sa HBI i 32 (9 muškaraca, 23 žena) na hroničnom programu hemodijalize, kao i 53 (31 muškaraca, 22 žena) zdrave osobe, odgovarajuće životne dobi (kontrolna grupa). Standardizovanim biohemijskim metodama, a u cilju procene funkcionalne rezerve bubrega, kod bolesnika su određivani klirens endogenog kreatinina (osim kod bolesnika na hemodijalizi), serumski kreatinin i urea. Bolesnicima na hemodijalizi krv je vađena neposredno pre samog tretmana dijalize, prvog dana u nedelji. Osim toga, kod svih ispitanika, određivan je serumski nivo Lp(a) imunoturbidimetrijskom metodom na analizatoru »Olympus AU 400« (Sentinel, Milano, Italija). Povišene vrednosti Lp(a) (iznad 0,25 g/l) ustanovljene su kod 31% hemodijaliziranih pacijenata, 14% bolesnika sa HBI koji nisu na hemodijalizi, kao i kod 11% zdravih osoba. Izuzetno povišene Lp(a) koncentracije, ≥0,50 g/L, postojale su kod 16% bolesnika na hemodijalizi, 9% HBI pacijenata, ali ne i kod zdravih osoba. Ustanovljena je statistički značajna razlika između srednjih vrednosti Lp (a) ispitanika na hemodijalizi i kontrolne grupe (0,22±0,25 vs. 0,08±0,1 g/L, $p<0,01$), kao i nedijaliziranih HBI pacijenata i kontrolne grupe (0,18±0,21 vs. 0,08±0,1 g/L, $p<0,05$). Između srednjih vrednosti Lp(a) kod bolesnika na hemodijalizi i onih sa HBI koji nisu na dijalizi ne postoji statistički značajna razlika. Takođe, nije postignuta statistički značajna korelacija između klirensa kreatinina i nivoa Lp (a). Na osnovu dobijenih rezultata može se zaključiti da bolesnici sa hroničnom bubrežnom insuficijencijom, naročito na hemodijalizi, imaju značajno više vrednosti lipoproteina (a) u poređenju sa zdravom kontrolnom grupom.

D55
LIPOPROTEIN (a) IN CHRONIC RENAL FAILURE

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In patients with chronic renal failure (CRF) cardiovascular events are a major cause of mortality. Lp (a) lipoprotein as an independent risk factor for the development of premature atherosclerosis could have an important contributing role. The aim of this study was to determine the relationship between the functional kidney reserve and serum Lp(a) level in different CRF stadiums. This study included 74 patients, 42 (27 males, 15 females) of them with CRF and 32 (9 males, 23 females) on a chronic hemodialysis program, as well as 53 healthy individuals (31 males, 22 females) matched for age as a control group. To evaluate the functional kidney reserve serum urea, creatinine and endogenous creatinine clearance (except in patients on a chronic hemodialysis program) were determined by standard biochemical methods. Blood was taken directly before dialysis treatment in patients on chronic hemodialysis program on the first day of the week. Moreover, in all subjects Lp(a) serum levels were determined by immunoturbidimetry, analyzer Olympus AU 400 (Sentinel, Milano, Italy). Elevated Lp(a) levels (above 0.25 g/L) were found in 31% of hemodialysed patients, 14% of non-hemodialysed patients with CRF as well as in 11% of healthy subjects. Extremely elevated Lp(a) levels ≥0.50 g/L were determined in 16% of hemodialysed patients, 9% of non-hemodialysed patients with CRF and 0% of healthy subjects. Significant differences were found between mean Lp(a) levels in hemodialysed patients and control group (0.22±0.25 vs. 0.08±0.1 g/L, $p<0.01$) as well as in the non-hemodialysed patients with CRF and the control group (0.18±0.21 vs. 0.08±0.1 g/L, $p<0.05$). There were no statistical differences between mean Lp(a) levels in hemodialysed patients and non-hemodialysed patients with CRF and no statistical correlation between creatinine clearance and Lp(a) levels. From our results it can be concluded that patients with CRF, especially ones on a chronic hemodialysis program, have significantly higher Lp(a) levels in comparison with the healthy control group.

D56
LIPIDNI STATUS DAVALACA NA PROGRAMU PLAZMAFEREZE

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Plazmafereza je skup postupaka koji omogućavaju odvajanje plazme tj. tečnog dela krvi od ostalih elemenata krvi. Davaocu se reinfuzijom vraćaju svi ćelijski elementi kao autologna krv. Cilj plazmafereze je da se dobije plazma koja se koristi za proizvodnju stabilnih lekova iz krvi (albumina i imunoglobulina za intravensku i intramuskularnu primenu). Radi zaštite zdravlja davalaca plazme primenjuje se redovna kontrola u koju spada i praćenje biohemijskih parametara. Prati se funkcionalno stanje jetre određivanjem sadržaja ukupnih proteina, albumina, ALT, AST,GGT, kao i lipidnog statusa. Ovim ispitivanjem obuhvaćeno je 100 davalaca plazme kojima je određivan lipidni status. Ispitivane su vrednosti ukupnog holesterola (UH), triglicerida (TG), HDL i LDL holesterola, indeks ateroskleroze (IA) i utvrđeni su faktori rizika (FR). Određivanja UH i TG su vršena standardnim enzimskim metodama, HDL-hol određen je u supernatantu nakon precipitacije plazme magnezijum-hloridom i fosfovolframovom kiselinom. LDL-hol je izračunat preko Friedwaldove formule. Vrednosti IA i FR su dobijene računskim putem. Dobijene su sledeće vrednosti: ukupni holesterol $\bar{x}$ = 5,47±1,089 mmol/L, trigliceridi $\bar{x}$ = 1,587±0,957 mmol/L, HDL-holesterol $\bar{x}$=1,276±0,304 mmol/L i LDL – holesterol 3,45±1,144 mmol/L. Dobijene vrednosti ukazuju na prisustvo aterogenog rizika lipidnog porekla kod davalaca na programu plazmafereze, iako oni pripadaju najzdravijem delu populacije. Neophodno je primeniti higijensko-dijetetski režim ishrane i odgovarajuću fizičku aktivnost. Redovnim davanjem plazme obezbeđena im je stalna lekarska kontrola i briga o zdravlju.

D56
PLASMAPHERESIS DONORS' LIPID STATUS

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Plasmapheresis is a set of procedures that enables separation of plasma, i.e. the liquid part of blood from other blood elements. Donors are then reinfused with all blood cell elements as the autologous blood. Goal of plasmapheresis is to obtain plasma used for the preparation of stable blood products (albumins and immunoglobulins for intravenous and intramuscular use). In order to protect plasma donors' health, regular medical check-ups are carried, including biochemical parameters follow-up. Functional liver condition is monitored by the determination of the total protein content, albumin, ALT, AST, GGT, as well as the lipid status. This investigation included 100 plasma donors in which the lipid status had been determined. Total cholesterol (TCH) values, triglycerides (TG), HDL and LDL cholesterol, index of atherosclerosis (IA) were investigated and risk factors were determined. Determination of TCH and TG was performed using standard enzyme methods, HDL cholesterol was determined in the supernatant following plasma precipitation by $MgCl_2$ and phosphotungstic acid. LDL cholesterol was calculated using Friedwald formula. IA and FR values had been calculated. The following values were obtained: total cholesterol $\bar{x}$ = 5.47±1.089 mmol/L, triglyceride $\bar{x}$ =1.587±0.957 mmol/L, HDL cholesterol $\bar{x}$ = 1.276±0.304 mmol/L and LDL – cholesterol 3.45±1.144 mmol/L. The obtained values point to the presence of the lipid originating an atherogenous risk in the plasmapheresis donors, despite the fact that they belong to the healthiest part of the population. A dietary nutrition regime and adequate physical activities are necessary. Regular plasma donation provides them with continuous medical check-up and health care.

D57
LIPIDNI PROFIL GOJAZNE DECE I ADOLESCENATA PRE I POSLE ZNAČAJNOG GUBITKA TELESNE MASE

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Kod gojazne dece mogu se javiti povišeni nivoi ukupnog holesterola, triglicerida i lipoproteina male gustine (LDL) u serumu. Cilj ovog rada bio je praćenje lipidnog profila kod gojazne dece pre i posle značajnog gubitka telesne mase. Ispitano je 60 gojazne dece (37 devojčica i 23 dečaka), prosečnog uzrasta

D57
LIPID PROFILE CONCERNING OBESE CHILDREN AND ADOLESCENTS BEFORE AND AFTER SIGNIFICANT WEIGHT LOSS

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The obesity in children can be associated with the higher level of total cholesterol, triglycerides and low-density lipoproteins (LDL) in serum. The arm of the study was to monitored the lipid profile of obese children before and after significant weight loss. Sixty obese children (37 girls and 23 boys), average age

11,37± 2,48 god. koja su bila uključena u program za redukciju telesne mase u Savetovalištu za unapređenje ishrane Instituta za javno zdravlje u Nišu. Merenja su rađena na početku ispitivanja i nakon 10 nedelja. Za sve ispitanike beležene su antropometrijske promene, kao i promene nivoa lipida u serumu (ukupnog holesterola, triglicerida i LDL holesterola). Tokom 10 nedelja sprovođenja redukcione dijete, telesna masa kod ispitane dece je značajno smanjena ($p<0,01$). Nađena je statistički značajna redukcija svih ispitivanih parametara lipidnog statusa ($p<0,01$). Dobijeni rezultati pokazuju da je kombinacija dijeto-terapije, povećane fizičke aktivnosti i promene životnih navika efikasna u snižavanju ukupnog holesterola, triglicerida i LDL holesterola kod gojazne dece.

11,37±2,48 year, who took part in the weight reduction program in The Counseling Service for well-balanced diet of the Institute for Public Health in Nis, were examined. The measurements were taken at the beginning of the research and 10 weeks later. Anthropometric changes and the changes of the level of lipids in serum (total cholesterol, triglycerides and LDL-cholesterol) were recorded for all participants in the study. Carrying out of the reduced diet during the period of 10 weeks showed that body weight in the examined children had been greatly reduced ($p<0,01$). Statistical significant reduction of all the examined parametres of the lipid profile was detected ($p<0,01$). Results show that the combination of the diet-therapy, increased physician activity and behavior modification is efficient in reducing of the total cholesterol, triglycerides and LDL-cholesterol as far as obese children are concerned.

E

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E58
PRENATALNI BIOHEMIJSKI SKRINING U II TRIMESTRU TRUDNICA STARIJIH OD 30 GODINA

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Trizomija 18 i trizomija 21 (Dounov sindrom – DS) najčešće su hromozomopatije. Danas se u laboratorijama izvodi test za rano otkrivanje tih anomalija, tzv. tripel test, koji obuhvata određivanje tri markera: alfa-fetoproteina (AFP), nekonjugovanog estriola i horioni gonadotropnog hormona (β HCG). Pomoću softvera se izračunava individualni koeficijent MOM prema karakteristikama trudnoće i ultrazvučnim parametrima fetusa. Cilj je bio da se ispita da li postoji uvećan rizik da plod ima hromozomsku anomaliju (trizomija 21, ili DS) kod trudnica starijih od 30 g. Određivani su biohemijski markeri: AFP, βHCG i slobodni estriol u venskoj krvi trudnica od 16 do 20 nedelje gestacije, principom iluminescencije na imunoanalizatoru »Immulit1000«. Ispitivana grupa je brojala 89 trudnica starijih od 30 godina što se još uvek ne smatra dobnim rizikom. Dobijene su vrednosti: AFP 13,6–93,7 IU/mL (MoM 0,48–2,57); estriol 0,412–9,79 ng/mL, (MoM 0,23–3,39); βHCG 8270–128700 mIU/mL (MoM 0,44–4,46). Povećan rizik za DS dokazan je u 9 slučajeva (1<50–1<257), 10%. Podgrupu sa visokim dobnim rizikom prosečne starosti 37 godina (35–44,9), činilo je 12 trudnica, tri su imale povećan rizik od DS-a (1:50–1:96), 25%. Visokodobni rizik (1:33) i najveći rizik za DS (1:50) i trizomiju 18 (1<102) pokazao je tripel test kod jedne trudnice, što je potvrđeno i amniocentezom, dok je u 8 slučajeva nalaz bio uredan. Rano testiranje trudnica biohemijskim markerima, ultrazvučni pregled i amniocenteza, kada je to indikovano, umnogome smanjuju procenat rađanja dece sa hromozomskim defektom.

E58
SECOND-TRIMESTER PRENATAL BIOCHEMICAL SCREENING IN PREGNANT WOMEN ABOVE THE AGE OF 30

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Trisomy 18 and trisomy 21 are the most common chromosome anomalies. Nowadays a test for the early detection of these anomalies, called the triple test, is performed, that involves three markers: alpha-fetoprotein (AFP), unconjugated estriol and chorionic gonadotropin hormone (β HCG). The software calculates the individual coefficient MOM, related to the characteristics of pregnancy and ultrasound parameters of the fetus. The aim was to find out if there was an increased risk of the fetus developing a chromosome anomaly (trisomy 21, DS or neural tube defect) in pregnant women above the age of 30. Biochemical markers were determined: AFP, βHCG and free estriol in the venal blood of pregnant women in the period from 16–20th week of gestation, using a method of luminescence, »Immulit 1000«. The studied group included 89 pregnant women above the age of 30, which is still considered an age risk. None of them had diabetes mellitus, 28 were active smokers, and all of them had conceived naturally. The following values were acquired: AFP 13.6–93.7 IU/mL (MoM 0.48–2.57); estriol 0.412–9.79 ng/mL (MoM 0.23–3.39) and βHCG 8270–128700 mIU/mL (MoM 0.44–4.46). An increased risk of trisomy 21 was proved in 9 cases (1<50–1<257), 10%. The subgroup of high age risk involved 12 pregnant women whose average age was 37 (35– 44.9). The risk of DS in this group was heightened in 3 cases (1:50 – 1:96), 25%. The triple test showed high age risk (1:33) and the highest risk of DS (1:50) and trisomy 18 (1<102) in 1 case. All the pregnants who with an increased risk of chromosome anomaly for the fetus were tested were sent to amniocentesis. In 8 cases the findings were normal. Early testing of pregnant women using biochemical markers, an ultrasound check and amniocentesis, when indicated, largely reduces the percentage of children born with chromosomal defects.

E59
PREVREMENI PORODJAJI – PROINFLAMATORNI CITOKINI KAO POTENCIJALNI MARKERI INFEKCIJE

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Prevremeni porođaji su najznačajniji uzrok perinatalnog mortaliteta i morbiditeta. Bakterijska invazija u horiodecidualni prostor podstiče deciduu i fetalne membrane da proizvode citokine, i to u prvom redu: interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8) i interferon-γ (INT-γ). Interleukin-6 i interleukin-8 su proinflamatorni citokini, čije je povećanje u cervikalnom brisu povezano sa bakterijskom vaginozom i bakterijskim intrauterinim infekcijama, dok je skok interferona-γ opisan kod virusnih vaginalnih infekcija. Proinflamatorni citokini mogu indukovati sintezu i oslobađanje prostaglandina i stimulisati uterusne kontrakcije i metaloproteinaze, koje dovode do omekšavanja cerviksa i slabljenja amnionskih membrana, te njihove prevremene rupture. Cilj studije je bio da se ispita moguća primena serumskog nivoa IL-8 i γ-interferona kao markera lokalne infekcije kod pacijentkinja sa kliničkim simptomima prevremenog porođaja i infekcije. Ispitivanje je obuhvatilo 74 gravidne pacijentkinje sa simptomima prevremenog porođaja i potvrđenom infekcijom. Citokini su određeni u serumu pacijentkinja ELISA metodom (*Beckman Coulter, R&D Quantikine*). Vrednost citokina IL-8 u ispitivanoj grupi je bila 18,13 +/–30,87, u odnosu na 5,02 +/– 4,91 (p< 0,08) u kontrolnoj grupi. Vrednost γ-interferona u grupi pacijenata sa potvrđenom infekcijom i simptomima prevremenog porođaja je 14,22 +/–28,26, u odnosu na 4,66 +/–6,45 (p< 0,172) u kontrolnoj grupi. IL-8 i γ-interferon predstavljaju neinvazivne markere koji mogu da ukažu na prisustvo infekcije u trudnoći, kao i na povećanje rizika od prevremenog porođaja kod pacijentkinja sa takvim rizikom.

E59
PRETERM DELIVERIES – PROINFLAMMATORY CYTOKINES AS POSSIBLE MARKERS OF INFECTION

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Preterm deliveries are the most significant cause of perinatal mortality and morbidity. Bacterial invasion of the choriodecidual space stimulates the decidua and the fetal membrane to produce cytokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), and interferon-γ (INT-γ). Interleukin 6 and interleukin 8 are proinflammatory cytokines whose levels in the cervical mucus have been reported to be associated with bacterial vaginosis and intrauterine infections, while interferon-γ is reported in viral infections. Inflammatory cytokines may induce the synthesis and release of prostaglandins that stimulate uterine contractions and metalloproteinases that soften the cervix and weaken the chorioamniotic membranes leading to their rupture. The aim of the study was to investigate the possibility of the application of the level of proinflammatory cytokine IL-8, and interferon-γ as biochemical markers of local infections in patients with clinical symptoms of preterm delivery. The investigation comprised 74 pregnant women at 24–36 weeks' gestation with symptoms of preterm delivery and confirmed infections. Cytokine levels were determined in the patients serum using an ELISA method (*Becman Coulter, R&D Quantikine*). The values of cytokine IL-8 in the investigated group were 18.13 +/–30.87 vs. 5.02 +/–4.91 (p< 0.08) in the control group. The values of γ-interferon in the group of patients with confirmed infection were 14.22 +/–28.26 versus 4.66 +/–6.45 (p<0.172) in the control group. Cytokine IL-8 and interferon-γ are diagnostic markers which could point to the presence of infection in pregnancy, as well as to an increased risk of preterm deliveries in these patients. A combination of these proinflammatory cytokines could be added to the group of predictors of preterm delivery.

E60
KONCENTRACIJA SERUMSKOG LEPTINA KOD PACIJENATA NA DIJALIZI

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Veliki broj bolesnika u uznapredovaloj fazi hronične bubrežne insuficijencije (HBI) pokazuje biohemijske manifestacije hroničnog inflamatornog stanja,

E60
SERUM LEPTIN CONCENTRATION IN DIALYSIS PATIENTS

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Health Care Center Kruševac

A large number of patients in the progressive phase of renal insufficiency (HBI) show biochemical manifestations of a chronic inflammation condition,

koje se odlikuje porastom cirkulišućeg nivoa reaktanata akutne faze kao što je C-reaktivni protein (CRP). Anoreksija je dobro poznati efekat inflamacije. Jedan od mehanizama koji indikuje anoreksiju u uslovima inflamacije može biti povišeni nivo serumskog leptina. Leptin, produkt ob gena, peptidni je hormon, koji se smatra ključnim regulatorom unosa hrane i telesne težine. Cilj rada je da se utvrdi razlika u nivou leptina kod zdravih ljudi i bolesnika na dijalizi, kao i da se ustanovi da li dužina dijaliziranja utiče na koncentraciju leptina u krvi. Ispitano je 80 bolesnika (47 muškaraca i 33 žene) sa terminalnim stadijumom HBI, prosečne životne starosti 56 godina, koji se u proseku 66 meseci nalaze na hroničnom programu dijalize. Od biohemijskih parametara određivani su: urea, CRP i leptin (ELISA metod). Rezultati pokazuju da su vrednosti uree, CRP i leptina znatno više u ispitivanoj grupi u odnosu na kontrolnu grupu ($p<0,001$). Analizom vrednosti CRP i leptina razvrstanih po dužini lečenja dijalizom (do 1 godine, do 5 godina i više od 5 godina), može se reći da se rizik od hronične inflamacije (CRP) povećava sa dužinom lečenja dijalizom ($p<0,05$), što nije slučaj sa leptinom ($p>0,05$). Tačni uzroci povišenog nivoa leptina u uremiji nisu sa sigurnošću objašnjeni, iako dosadašnji podaci upućuju na mogućnost povećane produkcije zbog inflamacije ili hiperinsulinemije.

followed by an increase in the circulation level of acute phase reactants such as C-reactive protein (CRP). Anorexia is a well known effect of inflammation. One of the mechanisms indicating anorexia in conditions of inflammation could be an increased level of serum leptin. Leptin, an ob gene product, is a peptide hormone that is considered the basic regulator of food intake and body weight. The aim of the study was to determine difference in the leptin level between healthy subjects and dialysis treated patients, as well as to determine if the duration of dialysis treatment has any influence on the leptin concentration in blood. A cross-sectional study included 80 patients, average age 56 (47 men and 33 women) with end-stage HBI, mostly undergoing a chronic dialysis program for 66 months. The biochemical parameters determined were: urea, CRP and leptin (by an ELISA method). The results show that the values of urea, CRP and leptin are significantly higher in the examined group than in the control group ($p<0.001$). Having analyzed CRP and leptin values classified according to the duration of dialysis treatment (up to 1 year, up to 5 years and above 5 years), we can say that the risk of chronic inflammation (CRP) increases with the duration of dialysis treatment ($p<0.05$), which is not the case with leptin ($p>0.05$). Precise causes of increased leptin levels in uremia have not been explained thoroughly, although actual data point at the possibility of increased production due to inflammation or due to hiperinsulinemia.

E61
EFEKTI KONZUMIRANJA GAZIRANIH NAPITAKA NA SERUMSKE LIPIDE I LIPOPROTEINE

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Promene u lipidnom profilu mogu se smatrati aterogenim faktorima rizika i voditi razvoju kardiovaskularnih bolesti. Prateći sve veću učestalost poremećaja lipidnog profila, došli smo na ideju da potražimo vezu sa konzumiranjem gaziranih napitaka. Cilj ovog rada je bio da se utvrdi uticaj konzumiranja velike količine gaziranih napitaka na lipidni profil. Izabrana je grupa od 55 osoba (30 žena i 25 muškaraca), starosti između 20 i 45 godina, koji su konzumirali gazirana pića u količini većoj od 1 litra dnevno duže od mesec dana. Kontrolna grupa od 46 osoba (26 žena i 20 muškaraca) uopšte ne konzumira gazirana pića. Svima su ukupni holesterol i trigliceridi određivani enzimski, HDL holesterol direktno enzimski, LDLholesterol je određivan pomoću Friedewaldove jednačine, a APO A-1 I APO B imunoturbidimetrijski. Statističke razlike između grupa su testirane Studentovim t-testom i p-vrednosti od 0,05 i niže su izabrane za nivo statističke značajnosti. Kod osoba koje konzumiraju gazirana pića ukupni holes-

E61
THE EFFECTS OF A CONSUMPTION OF CARBONATED BEVERAGES ON SERUM LIPIDS AND LIPOPROTEINS

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Changes in the lipid profile can be considered as atherogenic risk factors and can lead to the development of cardiovascular diseases. Monitoring the increased frequency of disturbances in the lipid profile, we came to the idea to look for a connection with the consumption of carbonated beverages. The purpose of this study is to evaluate the effects of a consumption of carbonated beverages on the lipid profile. A group of 55 individuals (30 females and 25 males) was formed, aged between 20 and 45 years, who consumed large amounts of carbonated beverages, more than one liter per day, longer than one month. The control group comprised 46 individuals (26 females and 20 males), who do not consume carbonated beverages at all. For all individuals we determined total cholesterol and triglyceride concentrations enzymatically, HDL cholesterol by a direct enzymatic method, LDL cholesterol was derived by the Frieldewald equation and APO A-1 and APO B imunoturbidimetrically. Statistical differ-

terol je povišen u odnosu na kontrolnu grupu ($p<0,05$), trigliceridi su takođe povišeni ($p<0,05$), LDL holesterol je statistički značajno povišen u odnosu na kontrolnu grupu ($p<0,05$), dok je HDL holesterol statistički značajno snižen ($p<0,05$). Kod apolipoproteina promene vrednosti nisu statistički značajne ($p>0.05$). Na osnovu rezultata našeg rada moguće je povezati povećano konzumiranje gaziranih napitaka sa promenama u koncentraciji serumskih lipida kao jednog od faktora rizika za nastanak kardiovaskularnih bolesti. Dalje i obimnije studije su potrebne da bi se potvrdili ovi rezultati.

ences between the groups were tested by a Studentžs t-test and a p-value of 0.05 or less was selected as the level of statistical significance. In the group that consumed carbonated beverages, total cholesterol increased in comparison with the control group ($p<0.05$), triglycerides also increased ($p<0.05$), LDL cholesterol increased in relation to the control group statistically significantly ($p<0.05$), and HDL cholesterol decreased statisticaly significantly ($p<0.05$). Changes in the values of apolipoproteins were not statistically significant ($p>0.05$). On the basis of the results of our work it can be possible to associate increased consumption of carbonated beverages with changes in the concentration of serum lipids and lipoproteins as one of the risk factors for cardio-vascular diseases. Further studies are needed to confirm these results.

E62
ISPITIVANJE ANEMIJE KOD PACIJENATA NA HEMODIJALIZI

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Nedovoljna sinteza eritropoetina i nedostatak gvožđa su osnovni uzroci razvoja normocitne normohromne anemije kod hronične bubrežne insuficijencije (HBI). U cilju prevencije brojnih posledica anemije bubrežnog porekla, prema preporukama, neophodna je adekvatna terapija primenom eritropoetina, preparata gvožđa, folne kiseline. Ispitivanje anemije i procena terapije obuhvataju određivanje hematoloških parametara (eritrocita, hemoglobina, hematokrita, indeksa eritrocita: MCV, MCH, MCHC), serumskog Fe, feritina, kapaciteta vezivanja gvožđa (T.I.B.C.), procenta saturacije transferina (TSAT), C-reaktivnog proteina. U našem radu ispitivan je efekat korekcije doze iv. preparata Fe kod pacijenata na hemodijalizi koji su primali eritropoetin. Praćeno je 68 pacijenata u periodu od 18 meseci. Hematološki parametri određivani su na brojaču *Coulter Beckman*, a biohemijski na *Synchron Beckman* automatskom analizatoru. TSAT je izračunat. U ispitivanom periodu, rezultati hematoloških parametara i vrednosti T.I.B.C. nisu pokazali statističku značajnost. Vrednosti za Fe su bile značajno niže ($p<0,001$) posle promene (smanjenja) terapije. Rezultati za TSAT ($p<0,01$) i feritin ($p<0,001$) značajno su se snizili i ušli u opseg preporučenih vrednosti za HBI, što je bio cilj korekcije terapije. Dobijeni rezultati su potvrdili neophodnost praćenja navedenih parametara, posebno TSAT i feritina, za procenu primene adekvatne supstitucione terapije u bubrežnoj anemiji.

TE62
HE EXAMINATION OF ANEMIA IN HEMODIALYSIS PATIENTS

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Insufficient erythropoietin synthesis and iron shortage are the main causes of normocytic normochrome anemia in chronic renal insufficiency (CRI). To prevent numerous consequences caused by anemia of renal failure, an adequate therapy with erythropoietin, iron preparations and folic acid is recommended as necessary. The examination of anemia and estimation of therapy effectiveness involve the determination of hematological parameters (erythrocyte, hemoglobin, hematocrit, index erythrocyte: MCV, MCH, MCHC), serum Fe, ferritin, total iron-binding capacity (T.I.B.C.), percentage of transferrin saturation (TSAT) and C-reactive protein. The study examines the effect of IV iron dosage correction phase in hemodialysis patients treated with erythropoietin. Sixty eight patients were examined over the period of 18 months. Hematological parameters were determined by using a *Beckman Coulter* automated analyzer and biochemical ones using a *Beckman Synchron* analyzer. TSAT was calculated. During the period of examination the results of hematological parameters and T.I.B.C. values did not reveal any statistical significance. Fe values were considerably lower ($p<0.001$) as a result of the change (decrease) in therapy. There was a considerable decrease in TSAT results ($p<0.01$) and ferritin results ($p<0.001$) and they were now within the range of recommended CRI values, which was the aim of the therapy correction. The obtained results confirmed the necessity of monitoring the cited parameters, especially TSAT and ferritin, in order to estimate the adequate substitution therapy in renal anemia.

E63
SERUMSKI BIOMARKERI U BOLESTIMA JETRE

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Mnogi proteini krvi sintetišu se u jetri. Nivoi tih proteina u serumu mogu usled poremećaja u jetri biti sniženi ili povišeni, stoga neki od njih mogu poslužiti kao korisni biomarkeri. Određivanje koncentracije različitih biomarkera u serumu ima važnu ulogu u dijagnostici oboljenja jetre i u praćenju toka bolesti. U ovom radu izvršeno je poređenje tri serumska markera koji su povezani sa oboljenjima jetre: α-fetoproteina (AFP), feritina i insulinu-sličnog faktora rasta I (IGF-I). Visoke koncentracije AFP u serumu ukazuju na primarni hepatocelularni karcinom (HCC), a vrednosti feritina u serumu često su povećane kod neoplazija u jetri. Komponente IGF sistema su takođe uključene u hepatokarcinogenezu. Cilj ovog rada je bio da se proceni da li pomenuti biomarkeri, sintetisani u jetri, ispoljavaju specifičnu distribuciju u različitim oboljenjima jetre: virusnom hepatitisu, parazitarnoj infekciji izazvanoj ehinokokusom i primarnom HCC. Kontrolnu grupu činile su zdrave osobe. Koncentracije AFP i IGF-I u serumu određene su IRMA, odnosno RIA testom (INEP, Beograd, Srbija), a koncentracija feritina određena je pomoću ELISA testa »Ferritin« (»DIMA Diagnostika«, Getingen, Nemačka). Statistička analiza izvršena je primenom programa »Primer of Biostatistics«. Vrednosti AFP i feritina u serumu ispoljile su sličan obrazac kod pacijenata sa virusnim hepatitisom ili primarnim HCC, a koncentracije ta dva markera bile su značajno više u odnosu na kontrolnu grupu ($p<0,05$). S druge strane, koncentracija IGF-I bila je značajno snižena kod pacijenata sa primarnim HCC ili ehinokokozom u odnosu na kontrolnu grupu ($p<0,01$ odnosno $p<0,05$). Kod pacijenata sa primarnim HCC sva tri analizirana serumska biomarkera pokazala su bilo povišene, bilo snižene koncentracije u odnosu na kontrolnu grupu. Rezultati su pokazali da određivanje IGF-I diferencira virusni hepatitis od primarnog HCC i da može pomoći u proceni oštećenja jetre kod pacijenata sa ehinokokozom i primarnim HCC.

E63
SERUM BIOMARKERS IN LIVER DISEASES

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Many human blood proteins are synthesized in the liver. Their serum levels may decrease or increase due to liver disorders, therefore some of them could serve as useful biomarkers. The determination of the serum concentration of different biomarkers has an important role in the diagnosis of liver diseases and in monitoring the course of disease. In this work three serum markers, linked to liver disorders, were compared: α-fetoprotein (AFP), ferritin and insulin-like growth factor I (IGF-I). High serum concentrations of AFP are strongly predictive of primary hepatocellular carcinoma (HCC) and serum ferritin levels are often increased in liver neoplasia. Components of the IGF axis are also involved in hepatocarcinogenesis. The aim of this work was to assess whether the above-mentioned liver biomarkers exhibit a specific distribution pattern in different types of liver disease: viral hepatitis, parasitic infection echinococcosis and primary HCC. The control group consisted of healthy subjects. Serum concentrations of AFP and IGF-I were determined using IRMA and RIA assays, respectively (INEP, Belgrade, Serbia), while the concentration of ferritin was determined using a Ferritin ELISA test (»DIMA Diagnostika«, Goettingen, Germany). Statistical analysis was performed using program »Primer of Biostatistics«. Serum AFP and ferritin levels exhibited similar patterns in patients with viral hepatitis or primary HCC, and concentrations of these two markers were significantly increased compared to the control group ($p<0.05$). On the other hand, the concentration of IGF-I was significantly decreased in patients with HCC or echinococcosis compared to the control group ($p<0.01$ and $p<0.05$, respectively). In patients with HCC, all three analysed serum biomarkers exhibited either elevated or reduced concentrations compared to the control group. Our results showed that the determination of IGF-I differentiates between viral hepatitis and primary HCC and may aid in assessing hepatic damage in patients with echinococcosis and primary HCC.

E64
KRETANJE TPOAt I TgAt TOKOM LEČENJA GRAVESOVE BOLESTI RADIOJODNOM I MEDIKAMENTOZNOM TIREOSUPRESIVNOM TERAPIJOM

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Cilj ovog istraživanja je bio da se uporede vrednosti TPOAt i TgAt u grupi pacijenata obolelih od Mb. Graves-Basedowi (MGB) koji su lečeni radiojodnom terapijom (RAJTh) sa vrednostima tih antitela kod pacijenata lečenih medikamentoznom tireosupresivnom terapijom (MTh), te da se utvrdi eventualna povezanost između nivoa TPOAt i TgAt i funkcijskog stanja štitaste žlezde u tim grupama pacijenata. U istraživanju je učestvovalo 15 osoba ženskog pola obolelih od MGB lečenih RAJTh. Sve pacijentkinje su primile jednu dozu RAJ, srednje veličine 202 MBq. U drugoj grupi je bilo 15 žena kojima je tek dijagnostikovana MGB i uvedena MTh. Kontrolnu grupu sačinjavalo je 15 zdravih žena slične životne dobi. Kod obe grupe bolesnica određivane su vrednosti TT3, TT4, TSH, TPOAt i TgAt visokoosetljivom elektrohemiluminiscentnom metodom na automatizovanom aparatu »Elecsys 2010«. Svi navedeni parametri određivani su bazalno, pre uvođenja MTh i RAJTh, te nakon 3 i 6 meseci. Pre MTh, 93,3% pacijenata imalo je povišen nivo TPOAt, $\bar{x}$=332,2 IU/mL koji konstantno opada u toku MTh dostižući $\bar{x}$=217,4 IU/mL posle šest meseci terapije. Pre aplikacije RAJTh, 86,6% pacijenata je imalo povišene vrednosti TPOAt, $\bar{x}$= 814,3 IU/mL, za 3 meseca vrednosti antitela dvostruko rastu na 1579,3 IU/mL, a 6 meseci od primene RAJTh snižavaju se na $\bar{x}$=1352 IU/mL. U obe ispitivane grupe 46,6% pacijenata imalo je povišene bazalne vrednosti TgAt. Nema značajne razlike između prosečnih bazalnih vrednosti TgAt (193 IU/mL) pre MTh i vrednosti nakon šest meseci po započetoj MTh ($\bar{x}$=199 IU/mL). Bazalna vrednost TgAt u grupi lečenoj RAJTh iznosi prosečno 260,7 IU/mL i raste konstantno u toku šest meseci po primenjenoj RAJTh dostižući prosečne vrednosti od 533 IU/mL. Bazalne vrednosti TPOAt i TgAt u osoba obolelih od MGB značajno su više u odnosu na nivo antitela u kontrolnoj grupi zdravih. MTh dovodi do smanjenja titra TPOAt, a RAJTh do značajnog povišenja vrednosti TPOAt nakon tri meseca, sa tendencijom smanjenja nivoa antitela nakon šest meseci posle RAJTh. Nivo TgAt se ne menja u toku MTh, a konstantno raste nakon primene RAJTh. Nema korelacije vrednosti nivoa tireoidnih hormona i TSH sa nivoima TPOAt i TgAt u obe grupe pacijenata.

E64
TPOAb AND TgAb DURING THE TREATMENT OF GRAVES DISEASE WITH RADIOIODINE THERAPY AND MEDICAMENTOSE THYROSUPPRESSIVE THERAPY

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The aim of the study was to compare TPOAb and TgAb values in patients (pts) with Graves disease (GD) treated with radioiodine therapy (RAITh) and those once who were treated with medicamentose thyrosuppressive therapy (MTh), and to evaluate the connections between TPOAb and TgAb levels and indicators of thyroid gland function. We investigated 15 females with GD treated with RAITh and 15 females newly diagnosed with GD treated with MTh. Fifteen healthy sex and age-matched persons made up the control group. All pts treated with RAITh received only one dose, average 202 MBq. Levels of TPOAb, TgAb, TT3, TT4 and TSH were measured by an electrochemiluminescence immunoassay, using an »Elecsys 2010«. These parameters were estimated before treatment, 3 and 6 months after RAITh or MTh. Before treatment, 93.3% of pts on MTh had increased levels of TPOAb compared to the controls, the average was 332.2 IU/mL. During MTh, TPOAb constantly decreased and 6 months after MTh their average was 217.4 IU/mL. Before RAI application, 86.6% of pts had increased levels of TPOAb, average was 814.3 IU/mL, 3 months after, they increased twice, average 1579.3 IU/mL, and 6 months after the treatment we noticed some decrement, average was 1352 IU/mL. In both groups 46.6% pts had increased basal levels of TgAb. We did not notice any significant change between the levels of TgAb at the beginning of MTh ($\bar{x}$=193 IU/mL) and after six monts of MTh ($\bar{x}$=199 IU/mL). Basal levels of TgAb in the group treated with RAITh were average 260.7 IU/mL and they increased to an average level of 533 IU/mL after 6 months of RAITh. Basal levels of TPOAb and TgAb in GD in the analysed groups are significantly higher compared to the controls. There was a significant difference between the basal levels of TPOAb and TgAb in the group treated with RAITh and with MTh. MTh decreased levels of TPOAb. TPOAb levels rose after RAITh, but showed some decrement after six months of RAITh. TgAb levels rose constantly after RAITh, but there was no change in TgAb during MTh. There was no direct correlation of TPOAb and TgAb levels with thyroid hormone levels and TSH in either group of patients.

E65
PROMENE REDOKS STATUSA VITAMINA C U TOKU ASEPTIČNOG MENINGITISA

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Moždano tkivo je zbog svog sastava i fizioloških osobenosti izuzetno osetljivo na dejstvo slobodnih radikala. U inflamatornoj reakciji koja prethodi i prati meningealnu lokalizaciju bolesti, aktivirani fagociti i drugi učesnici inflamacije stvaraju veliku količinu slobodnih radikala kiseonika. U cerebrospinalnom likvoru (CSF) aktivnost enzima antioksidativne zaštite je niska, zbog čega se odbrana subarahnoidnog prostora zasniva uglavnom na antioksidantnom dejstvu vitamina C. U ovoj studiji su određivane koncentracije redoks para vitamina C (vit C), askorbata (Asc) i dehidroaskorbata (DHAsc) u cerebrospinalnom likvoru (CSF) i serumu kod 53 pacijenata sa aseptičnim meningitisom, na prijemu, zatim 2–3. dana i 7–8. dana hospitalizacije. Kontrolnu grupu činilo je 15 pacijenata sličnog uzrasta i istog pola sa dijagnozom meningizma. Osim toga, određivane su koncentracije ukupnih proteina u likvoru, albumina, albuminski koeficijent, kao i koncentracija stabilnog produkta lipidne peroksidacije malondialdehida (MDA). Rezultati pokazuju da u toku aseptičnog meningitisa ne dolazi do promene koncentracije ukupnog vit C, već do značajnog povećanja odnosa redoks para DHAsc/Asc ($p<0,01$). Normalizacija tog odnosa zapažena je na kraju hospitalizacije, izuzev kod pacijenata sa početnom proteinorahijom većom od 1,01 g/L, kod kojih takođe postoji i stalni pad odnosa CSF/serum za askorbat ($p<0,05$). Dobijeni rezultati sugerišu da pacijenti sa virusnim meningitisom imaju različite brzine intratekalne akumulacije askorbata koja zavisi ne samo od aktuelnih koncentracija Asc u serumu, već i od brzine cerebralnog protoka krvi i očuvanosti mehanizama aktivnog transporta tog vitamina. Nešto više vrednosti odnosa askorbata CSF/serum na otpustu kod grupe sa proteinorahijom do 1,00 g/L u odnosu na kontrolne vrednosti ($p<0,05$) verovatno predstavljaju kompenzatornu akciju horioidnog pleksusa, koja kod pacijenata sa značajnim oštećenjem krvno-likvorske i krvno-moždane barijere izostaje.

E65
CHANGES IN THE VITAMIN C REDOX STATUS DURING ASEPTIC MENINGITIS

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Due to its specific composition and physiological functions, cerebral tissue is extremely sensitive to the free radical injury. In inflammatory reactions that proceed and accompany the meningeal localization of disease, activated phagocytes and other inflammatory response effectors produce huge amounts of oxygen-derived free radicals. In cerebrospinal fluid (CSF) the activities of antioxidative enzymes are low, therefore the antioxidative defense of the subarachnoid space is mostly based on protective actions of vitamin C. In this study we have followed up the concentration changes of vitamin C redox pair, ascorbate (Asc) and dehydroascorbate (DHAsc) in CSF and serum of 53 patients with aseptic meningitis on admission, between the 2nd and 3rd day, and between the 7th and 8th day of hospitalization. The results were compared with a group of 15 sex- and age-matched meningismus patients. The concentrations of CSF total protein, as well as concentrations of albumin, malondialdehyde (MDA) and albumin quotient in CSF and serum were also measured. Results show that during the course of viral meningitis no significant changes occur in total vitamin C concentrations in CSF and serum, but a significant increase in DHAsc/Asc ratio was found on admission ($p<0.01$). During hospitalization that increase reversed towards control values, except in cases with initial proteinorachia above 1.01 g/L where, besides a permanent increase in DHAsc/Asc ratio, a permanent decrease in Asc CSF/serum ratio also occurred ($p<0.05$). The obtained results suggest that patients with aseptic meningitis have different swiftness of intrathecal ascorbate accumulation that depends not only on the actual ascorbate serum concentration, but also on the cerebral blood-flow and conserved active transport mechanisms of this vitamin. Somewhat higher values of ascorbate CSF/serum ratio were observed on dismissal within the group with proteinorachia up to 1.00 g/L ($p<0.05$ vs. control) which probably represents a compensatory action of the chorioid plexus, absent in patients with severe blood-CSF and blood-brain barrier dysfunction.

E66
UTICAJ TIREOIDNE DISFUNKCIJE NA NIVO HOMOCISTEINEMIJE

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Hiperhomocisteinemija (HHcy) faktor je rizika za nastanak ubrzane ateroskleroze i trombotskih komplikacija. Hipotireoidizam je jedan od stečenih uzroka HHcy. U radu je ispitivano 68 bolesnika sa hipotireoidizmom, 64 bolesnika sa hipertireoidizmom i 68 eutiroidnih ispitanika ekvivalentne starosne dobi. Homocistein (Hcy) je određivan u serumu, HPLC metodom uz fluorescentnu detekciju. U statistickoj analizi korišćeni su sledeći testovi: *ANOVA, Post Hoc, Chi-square, Mann-Whitney U* i *Student's t*. Nivo Hcy kod bolesnika sa hipotireoidizmom (12,75±7,18 μmol/L) viši je nego kod kontrola (11,26±4,39 μmol/L) i kod bolesnika sa hipertireoidizmom (9,49±3,34 μmol/L), pri čemu je razlika bila značajna samo između hipotireoidnih i eutireoidnih osoba (p=0,001). Incidencija HHcy (Hcy>12 μmol/L) bila je značajno veća (p=0,008) kod bolesnika sa hipotireoidizmom (46,4%) nego kod u eutireoidnih kontrola (27%) i hipertireoidnih bolesnika (21%). Grupa hipotireoidnih bolesnika teškog stepena (TSH>50 mU/L) imala je značajno višu (p=0,008) koncentraciju homocisteina (14,23±5,6 μmol/L) u odnosu na koncentraciju homocisteina u eutireoidnih osoba. Poređenjem vrednosti Hcy između hipotireoidnih bolesnika umerenog stepena (TSH≤50mU/L) (11,36 μmol/L) i eutiroidnih osoba nije dobijena statistički značajna razlika. Poređenjem vrednosti Hcy u bolesnika sa subkliničkim hipotireoidizmom sa eutireoidnim kontrolama, kao i bolesnika sa klinički ispoljenim hipotireoidizmom i eutireoidnih kontrola, nisu uočene statistički značajne razlike. Smanjenje tireoidne funkcije, kao i stepen smanjenja tireoidne funkcije u grupi bolesnika sa hipotireoidizmom utiče na povišenje nivoa homocisteinemije. Kod bolesnika sa hipotireoidizmom, naročito ako je prisutan u višem stepenu, veća je verovatnoća ispoljavanja negativnih uticaja HHcy na indukciju aterotrombotskih događaja i nastanak venskog tromboembolizma. U navedenim rizičnim grupama potrebno je primeniti odgovarajuće dijagnostičke i terapijske procedure radi sprečavanja nastanka oboljenja u čijoj patogenezi HHcy ima definisano mesto.

E66
THE INFLUENCE OF THYROID DYSFUNCTION ON THE HOMOCYSTEINEMIA LEVEL

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Hyperhomocysteinemia (HHcy) is a risk factor for the development of premature atherothrombosis and thrombotic complications. Hypothyroidism is one of the acquired causes of HHcy. Our study comprised 68 patients with hypothyroidism, 64 patients with hyperthyroidism and 68 euthyroid persons, matched for age. Homocysteine (Hcy) was measured in serum, using an HPLC method with fluorescent detection. Statistical analyses included *ANOVA, Post Hoc, Chi-square, Mann-Whitney U* and *Student's t* tests. The Hcy level in patients with hypothyroidism (12.75±7.18 μmol/L) was higher compared to that in controls (11.26±4.39 μmol/L) and patients with hyperthyroidism (9.49± 3.34 μmol/L), but the difference was significant only in the comparison between hypothyroid and euthyroid persons (p=0.001). The incidence of HHcy (Hcy>12 μmol/L) was significantly higher (p=0.008) in patients with hypothyroidism (46.4%), than in euthyroid controls (27%) and hyperthyroid patients (21%). The group of patients with severe hypothyroidism (TSH> 50 mU/L) had a significantly higher (p=0.008) Hcy level (14.23±5.6 μmol/L) compared with the Hcy level in euthyroids. A comparison of Hcy levels in patients with moderate hypothyroidism (TSH≤50 mU/L) (11.36 μmol/L) and euthyroids revealed no significant difference. The Hcy levels in euthyroid patients showed no significant difference compared to the Hcy levels in patients with subclinical and clinical forms of hypothyroidism. We can conclude that the increase in the Hcy level is influenced by the decrease of thyroid function, as well as the degree of reduction of thyroid activity in patients with hypothyroidism. The probability that HHcy will express its deleterious effects on the induction of atherothrombotic events and venous thromboembolism is rather high in patients with hypothyroidism, especially if it has a severe form. In the aforesaid risk groups it is necessary to perform all the adequate diagnostic and therapeutic procedures in order to prevent the development of diseases in whose patogenesis HHcy has a important role.

E67
DIFERENCIJACIJA ANEMIJE U HRONIČNIM BOLESTIMA (ACD) OD ANEMIJE USLED DEFICIJENCIJE Fe (IDA)

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Problemi u dijagnostici anemije nastaju kada je rezerva gvožđa ispražnjena, a nema kliničkih simptoma. To je, u stvari, deficijencija gvožđa bez ikakvih kliničkih simptoma (tzv. deficijencija gvožđa bez anemije). Drugi problem javlja se kod hroničnih inflamacija, infekcija i neoplazmi. Tu je često teško postaviti dijagnozu nedostatka gvožđa, i time se možda propušta primena adekvatne terapije. Određivanje koncentracije gvožđa u serumu bez TIBC i transferina u serumu je od malog kliničkog značaja. Zato se istovremeno moraju određivati koncentracije Fe i TIBC, odnosno transferina. Vrednost TIBC korelira sa koncentracijom transferina, pa služi za indirektnu procenu količine transferina u krvi. Glavni problem je što su Fe i TIBC relativno neosetljivi, jer koncentracija Fe pada a TIBC raste već kada se javi hipohromna anemija, kao kasna klinička manifestacija deficita gvožđa. Samo kad je odnos Fe/TIBC manji od 15% pouzdan je dijagnostički pokazatelj deficijencije Fe. Zato je veoma bitno određivanje feritina. Koncentracija feritina opada vrlo rano kod deficijencije gvožđa pre nego što dođe do promene u koncentraciji hemoglobina, veličini eritrocita ili nivou Fe i TIBC. Feritin je glavni depo oblik gvožđa u organizmu i prisutan je u svim ćelijama. U ovoj studiji određivane su vrednosti Fe, TIBC, odnos Fe/TIBC i feritin u serumu kod 30 pacijenata sa deficijencijom Fe (IDA) i 20 pacijenata sa anemijom u hroničnim bolestima (ACD). Određivanje je vršeno *Biosystem*-ovim testovima na automatskom analizatoru BTI 2000. Fe i TIBC su izražavani u μmol/L a feritin u μg/L. Rezultati pokazuju da je Fe značajno sniženo i kod pacijenata sa IDA anemijom i kod pacijenata sa ACD anemijom ($p<0,05$). Feritin je značajno viši kod pacijenata sa ACD anemijom ($p<0,05$) a niži kod pacijenata sa IDA anemijom ($p<0,05$). TIBC je značajno viši kod pacijenata sa IDA anemijom ($p<0,05$) a niži kod pacijenata sa ACD anemijom ($p<0,05$). Diferencijalna dijagnoza te dve anemije je veoma bitna jer se njihova terapija znatno razlikuje. Zato se pri tumačenju rezultata koncentracije feritina u anemiji usled deficijencije Fe mora isključiti postojanje reakcije akutne faze određivanjem markera inflamacije (CRP, sedimentacije i fibrinogena).

E67
ANAEMIA DIFFERENTIATION IN CHRONIC DISEASES (ACD) CAUSED BY ANAEMIA AS RESULT OF Fe DEFICIENCY (IDA)

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Problems in the diagnostic of anaemia occur when the iron reserves are depleted and no clinic symptoms found. This is actually iron deficiency without any clinic symptoms (also known as iron deficiency without anaemia). A second problem is connected to chronic inflammations, infections and neoplasm. In these situations it is often difficult to make an iron insufficiency diagnosis which is important for determining proper therapy. A quantitative analysis of iron in the serum without TIBC and transferrin in the serum is of little importance. This is the reason why quantitative analysis of Fe and TIBC, namely transferrin, must occur simultaneously. The amount of TIBC correlates with the concentration of transferrin, wherewith it serves for direct quantitative analysis of transferrin in the blood. Them main problem is that bout iron and TIBC are relatively senseless, as a result of descending concentration of iron and ascending concentration of TIBC when the hypochronic anaemia appears as a clinic manifestation of iron deficit. When the ratio of Fe/TIBC is less than 15%, we have a certain diagnostic indicator of iron deficiency. This is why quantitative analysis of ferritin is important. The amount of ferritin descends in the early stages of iron deficiency, before changes in the concentration of haemoglobin, size of erythrocytes or amount of Fe and TIBC occur. Ferritin is a main depot of iron formation in the organism and is immanent in every cell. In this research the values of iron, TIBC, Fe/TIBC ratio and ferritin in serum were measured in 30 patients with iron deficiency (IDA) and 20 patients with anaemia in chronic diseases (ACD) in this research. Measuring was performed using *Biosystem* tests on an automatic analyzer BTI 2000. Fe and TIBC are expressed in μmol/L and ferritin in μg/L. The results shows that iron is significantly lower in patients with ACD anaemia and patients with IDA anaemia ($p<0.05$). Ferritin is considerably higher in patients with ACD anaemia ($p<0.05$) and lower among patients with IDA anaemia ($p<0.05$). TIBC is noticeably higher among patients with IDA anaemia but lower among patients with ACD anaemia ($p<0.05$). Differential diagnosis of these two anaemia formations is highly important because of the treatment which is significantly different depending of what kind of anaemia we are dealing with. The existence of an acute reaction phase must be excluded during the result examination of the quantitative analysis of ferritin in anaemia, as a result of iron deficiency, by determining inflammation markers (CRP, sedimentation and fibrinogen).

E68
PRIMENA ZAKONA O LEKOVIMA I MEDICINSKIM SREDSTVIMA U PRIVREDNOM DRUŠTVU »SPEKTAR« D.O.O. ČAČAK

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»Spektar« d.o.o, Dr Dragiše Mišovića 144/1, 32000 Čačak

Cilj rada je da ukaže na značaj Zakona o lekovima i medicinskim sredstvima (»Sl. glasnik RS« 84/04) za proizvođače medicinskih sredstava. Kao materijal je korišćena dokumentacija »Spektra« d.o.o. kao i podaci dobijeni od Privredne komore Srbije i Agencije za lekove i medicinska sredstva Srbije. Korišćena je deskriptivna epidemiološka metoda. Praćenjem usklađivanja načina rada sa važećim standardima i direktivama EU u »Spektru« d.o.o., analiziran je kompletan tok prilagođavanja proizvodnje medicinskih sredstava zakonskim odredbama, sve do dobijanja sertifikata ISO 9001, ISO 13485 kao i CE znaka za medicinska sredstva. Predhodna procedura je olakšala registraciju naših proizvoda kod ALIMS-a. Na osnovu podataka dobijenih iz PKS i ALIMS-a, samo 15% proizvođača medicinskih sredstava u Srbiji ima Rešenje za puštanje u promet medicinskog sredstva, neophodno da bi se proizvod plasirao na tržištu Srbije. Analizom korišćenog materijala utvrdili smo da je neophodno usaglašavanje uslova proizvodnje i kvaliteta medicinskih sredstava sa zakonskom regulativom. Očekujemo da će nam dobijena Rešenja za puštanje u promet medicinskih sredstava i posedovanje CE znaka za proizvode omogućiti bolji plasman proizvoda na domaćem i stranom tržištu, ostvariti konkurentsku prednost na domaćem tržištu i unaprediti rad u zdravstvenim ustanovama koje koriste naše proizvode.

E68
THE APPLICATION OF THE LAW ON MEDICINES AND MEDICAL DEVICES IN »SPEKTAR« LTD., ČAČAK

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The purpose of this thesis is to point out the significance of the Law on Medicines and Medical Devices (»Official Herald« No. 84/04) for medical device manufacturers. The material used was obtained from »Spektar« Ltd., as well as from the Serbian Chamber of Commerce and the Medicines and Medical Devices Agency of Serbia. A method of descriptive epidemiology was used. By monitoring the harmonization of the work process with valid standards and directives of the EU in »Spektar« Ltd., the entire course of adjusting the medical devices production procedure according to current legislation and up to obtaining the ISO 9001, ISO 13485 certificates and the CE sign for medical devices, was analyzed. The above procedure made the registration of our products at the Medicines and Medical Devices Agency of Serbia much easier. According to the Serbian Chamber of Commerce and ALIMS data, only 15% of medical device manufacturers in Serbia have the Permit to distribute a medical device despite the necessity of such a permit when distributing a product in the Serbian market. Having analyzed the material used, we concluded that manufacturing conditions and the quality of medical devices have to be harmonized with the current legislation. We expect that the obtained permit for distributing our medical devices, as well as the CE sign they carry, will enlarge our distribution in both the domestic and foreign market, provide us with a competitive advantage in the domestic market and improve the work process in the health facilities that use our products.

E69
BIOHEMIJSKE PROMENE FOLATNOG I METIL-TRANSFERNOG PUTA U CEREBROSPINALNOJ TEČNOSTI PACIJENTA SA HRONIČNOM NEUROTOKSIČNOSTI ASOCIRANOM SA PRIMENOM METOTREKSATA

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Metotreksat (MTX) antifolat je koji se često primenjuje u visokim dozama i/ili intratekalno u terapiji maligniteta poput akutne limfoblastične leukemije

E69
BIOCHEMICAL ALTERATIONS OF THE FOLATE AND METHYL-TRANSFER PATHWAY IN THE CSF OF A PATIENT WITH METHOTREXATE ASSOCIATED CHRONIC NEUROTOXICITY

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Methotrexate (MTX) is a widely used antifolate, administered in a high-dose and/or intrathecally in the treatment of malignancies such as acute lymphoblastic

(ALL). Slučajevi neurotoksičnosti koja se klasifikuje kao akutna, subakutna i hronična dovedeni su u vezu s primenom MTX kod malignih oboljenja. Patofiziološki mehanizam nastanka neurotoksičnosti još nije rasvetljen, moguće je da u njemu važnu ulogu igraju biohemijske promene folatnog i metil-transfernog metaboličkog puta za koje se smatra da su uzrokovane dejstvom MTX. Opisan je slučaj odrasle pacijentkinje na terapiji recidiva ALL sa simptomima hronične leukoencefalopatije za koju se smatra da je uzrokovana primenom MTX. U cilju procene folatnog i metil-transfernog puta u cerebrospinalnoj tečnosti (CST) pacijentkinje merena su smo koncentracije 5-metiltetrahidrofolata (5-metil-THF), MTX, S-adenozilmetionina (SAM) i S-adenozilhomocisteina (SAH). Tri uzorka CST su dobijena lumbalnom punkcijom u periodu od četiri meseca. Koncentracije su merene pomoću validiranih bioanalitičkih metoda zasnovanih na primeni HPLC sa ultraljubičastom i fluorescentnom detekcijom. Rezultati su pokazali dvostruko sniženje koncentracije 5-metil-THF (29,3–31,8 nmol/L) u poređenju sa referentnim vrednostima u svim uzorcima, dok su koncentracije SAM bile više od pet puta manje u dva uzorka (5–34,2 nmol/L). Koncentracije SAH su bile u rasponu 7,5–14,3 nmol/L. Pacijentkinja je imala izražene promene u folatnom i metil-transfernom metaboličkom putu koje ukazuju na to da biohemijske promene ovih metaboličkih puteva za koje se smatra da su uzrokovane dejstvom MTX mogu imati važnu ulogu u razvoju leukoencefalopatije.

leukaemia (ALL). Cases of neurotoxicity classified as acute, subacute and chronic were associated with MTX-treatment of malignant diseases. The pathogenic mechanism of neurotoxicity is not yet clear, and possibly the MTX associated biochemical alterations of the folate and methyl-transfer metabolic pathway may play an important role. A case is reported of an adult patient treated for ALL recidive with signs of chronic leukoencephalopathy associated with MTX administration. In order to asses the folate and methyl-transfer pathway in the cerebrospinal fluid (CSF) of the patient, 5 methyltetrahydrofolate (5-methyl-THF), MTX, S-adenosylmethionine (SAM) and S adenosylhomocysteine (SAH) were determined. Three CSF samples were obtained by lumbar punction within four month period. The measurement was performed using validated bioanalytical methods based on HPLC with UV and fluorescence detection. The results showed a two-fold decrease in 5-methyl-THF levels (29.3–31.8 nmol/L) in all obtained samples compared to reference values, whereas SAM concentrations were more than five-fold lower in two samples (5–34.2 nmol/L). SAH was in the range 7.5–14.3 nmol/L. The patient had pronounced alterations in the folate and methyl-transfer pathway which indicate that MTX-associated biochemical alterations of these pathways may play an important role in the development of leukoencephalopathy.

E70
HIPERKALEMIJA KOD PACIJENATA NA HEMODIJALIZI

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Bubreg ima ključnu ulogu u homeostatskom mehanizmu i održava eksterni balans kalijuma (K^+) konstantnim podešavanjem urinarne ekskrecije kalijuma (bubreg izlučuje 92% K^+). Organizam je veoma osetljiv čak i na male promene K^+ u serumu. Uzroci hiperkalemije su mnogi i veoma značajni po posledicama te se zbog toga lečenju pristupa ozbiljno. Dijaliza dovodi do brzog odstranjivanja K^+ iz organizma. Cilj ovoga rada je bio da se ispita hiperkalemija kod pacijenata u terminalnoj fazi bubrežne insuficijencije koji se leče hemodijalizom, i povezanost tog katjona sa koncentracijama kreatinina. Ispitivana grupa je imala 122 bolesnika (Ž=46; M=76). Prosečna životna dob bolesnika je bila 59,2±12,0 godina, minimalno 20 god, maksimalno 81 god. (M=58,7±12,6, Ž=59,6±11,0). Dužina dijalize kod muškaraca iznosila je 4,6±4,1 god, kod žena 4,5±4,3 god. Određivani su: urea, kreatinin i kalijum u serumu (pre uključenja na aparat za dijalizu) na analizatoru »Bayer Advia« standardnim metodama a kalijum jonselektivnom elektrodom. Prema nivou K^+

E70
HYPERPOTASSEMIA IN THE SERA OF PATIENTS ON DIALYSIS

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The kidney has a vital role in the homeostatic mechanism and it regulates the external balance of potassium (K^+) by the constant adjustment of urinary excretion of potassium. The causes of hyperpotassemia are many and very significant concerning their consequences. This is the reason why we must seriously deal with the treatment. Dialysis leads to a very fast removal of K^+ from the organism. The aim of this work is to confirm the presence of hyperpotassemia in the serum of patients in the terminal phase of kidney insufficiency who are on a hemodialysis treatment, and to check the connection of this cation with the concentration of creatinine. The examined group comprised 122 patients (W=46, M=76). Average age of the patients was 59.2±12.0 years old. The duration of dialysis in men was 4.6±4.1 years and in women 4.5±4.3 years. We determined urea, nitrogen, creatinine and potassium in the serum (before starting dialysis) on a »Bayer Advia« analyzer using standard methods, and for potassium the ionselective electrode was used. According

u serumu svi ispitanici su razvrstani u dve grupe: I grupa (N=78) sa konc. K^+ do 5,5 mmol/L, II grupa (N=42) konc. K^+>5,6 mmol/L. Pacijenti u II grupi ($\bar{x}$kalijum=6,261 mmol/L, medijana 5,93) imali su više vrednosti uree ($\bar{x}$=27,84 mmol/L, medijana 26,80) i kreatinina (901,7 μmol/L, medijana 878,2) u odnosu na grupu ispitanika koja je imala K^+ u referentnim granicama ($\bar{x}$kalijum=4,832 mmol/L, $\bar{x}$urea= 26,0 mmol/L, $\bar{x}$ kreat=857,8 μmol/L). Dobijeni rezultati pokazuju da porast vrednosti uree i kreatinina u serumu pacijenata u HBI prati hiperkalemija (na nivou P=0,05) i stoga je neophodno njihovo redovno laboratorijsko kontrolisanje.

to the level of K^+ in the serum all the tested patients were divided into two groups: the first group (N=78) with a concentration of potassium K^+ of up to 5.5 mmol/l, the second group (N=42) with a concentration of K^+>5.6 mmol/L. The patients in the second group ($\bar{x}$potas= 6.261 mmol/L, median 5.93) had higher levels of urea ($\bar{x}$=27.84 mmol/L, median 26.8) and creatinine (901.7 μmol/L mediane, 878.2) in relation to the group of tested patients who had K within the reference range ($\bar{x}$potas=4.832 mmol/L, $\bar{x}$urea= 26.0 mmol/L, $\bar{x}$creat=857.8 μmol/L). The given results show that the increase of urea and creatinine in the serum is followed by hyperpotassemia in patients in the terminal phase of CRF who are on a chronic hemodialysis programme (at the level of P=0.05).

E71
KALCIJUM, FOSFOR, MAGNEZIJUM I INTAKTNI PARAT HORMON KOD PACIJENATA NA HEMODIJALIZI

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Kod pacijenata sa hroničnom renalnom insuficijencijom javlja se sekundarni hiperparatireodizam kao rezultat stimulacije paratireoidnih žlezda usled niskog nivoa kalcijuma. Predmet rada je praćenje biohemijskih parametara – kalcijuma (Ca), fosfora (P), magnezijuma (Mg) i intaktnog parat hormona kod hemodijaliziranih pacijenata pre dijalize. Grupa uključuje 74 pacijenta oba pola – 28 žena i 46 muškaraca, podvrgnutih hemodijalizi tokom 1–24 godine. Parametri su određivani u serumu: Ca, P i Mg određivani su na biohemijskom analizatoru »Advia 1650« komercijalnim testovima »Advia chemistry«. Intaktni parat hormon je određivan na analizatoru »Immulite 1000« hemiluminiscencijom (»Immulite-Siemens« testovima). Rezultati pacijenata poređeni su sa rezultatima kontrolne grupe od 20 dobrovoljnih davalaca krvi. Srednje serumske vrednosti Ca i Mg pacijenata dobijene su u okviru normalnih referentnih vrednosti, a fosfora iznad gornje referentne granice. Medijana iPTH bila je 269,5 pg/mL. Srednje vrednosti kalcijuma niže su kod pacijenata (p<0,001). Srednja vrednost fosfora viša je kod pacijenata (p<0,001). Vrednosti magnezijuma se statistički značajno ne razlikuju u ispitivanim grupama. Srednja vrednost iPTH je u kontrolnoj grupi 41,61±11,15, a medijana pacijenata je 296,5 pg/mL. Parat hormon može biti potencijalno dijagnostičko sredstvo u prevenciji koštanih oboljenja hemodijaliziranih pacijenata i kao takav se pominje u literaturi. Mada su vrednosti iPTH u ovoj grupi višestruko povišene u odnosu na normalne vrednosti, kliničke manifestacije na kostima ih ne prate u istom stepenu. One su u ovoj grupi diskretne i ume-

E71
CALCIUM, PHOSPHORUS, MAGNESIUM AND INTACT PARATHYROID HORMONE IN HAEMODIALYSED PATIENTS

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In chronic renal failure patients secondary hyperparathyroidism occurrs as a result of stimulation of the parathyroid gland by low calcium levels. The purpose of the study was the follow-up of laboratory parameters: calcium (Ca), phosphorus (P), magnesium (Mg) and intact parathyroid hormone (iPTH) in haemodialysed patients before dialysis. The group included 74 patients of both sexes – 28 females and 46 men, the duration of haemodialysis was 1–24 years. Parameters were determined in the serum: Ca, P and Mg concentrations were measured using a biochemical analyzer »Advia 1650« and »Advia Chemistry« tests. IPTH was defined on an »Immulite 1000« analyzer (Immulite 1000 iPTH is a solid phase, to-site chemiluminescent enzyme labeled immunometric assay). The results of patients were compared with those obtained from the control group. Mean serum levels of Ca and Mg in patients were within the normal reference range, but of P were higher than the normal reference range. The median of iPHT was 269.5 pg/mL. Mean serum levels of calcium were significantly lower in patients (p< 0.001). Mean serum levels of phosphorus were also significantly lower in patients (p<0.001). Mean serum levels of phosphorus were significantly higher in patients (p<0.001). Magnesium levels were not significantly different. Mean serum levels of iPTH were in the control group 41.61±11.15 pg/mL, the median of iPTH in patients was 296.5 mg/mL. IPTH is a potential diagnostic tool in the prediction of renal bone diseases in haemodialysed patients, as is known in literature. Although levels of iPTH were many times higher

rene. Izgleda da postoji neka vrsta rezistencije koštanog tkiva na parat hormon kod obolelih od hronične bubrežne insuficijencije, pa su promene na kostima male i pored velikog lučenja paratireoidnih žlezda.

E72
INFLAMATORNI MARKERI I OKSIDATIVNI STRES U DIJABETES MELITUSU TIPA-2

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Najnovije teorije o aterosklerozi ukazuju na to da je inflamatorni odgovor arterijskog zida značajan patogenetski faktor. Inflamacija ne samo da doprinosi akutnom kardiovaskularnom događaju, već je ključ inicijacije i progresije ateroskleroze. Međutim, karakteristike inflamatornog procesa u dijabetes melitusu tipa 2 još uvek su nedovoljno poznate, budući da to oboljenje karakteriše udruženost brojnih proinflamatornih, prooksidativnih i prokoagulacionih faktora rizika. Kod bolesnika sa dijabetes melitusom tipa 2 (DM tipa 2), pored lipidnog statusa i stepena glikoregulacije, određivani su: lipidna peroksidacija – malondialdehid (MDA), reaktant akutne faze – visokoosetljivi C-reaktivni protein (hsCRP), intracelularni adhezivni molekul-1 (ICAM-1) i vaskularni ćelijski adhezivni molekul-1 (VCAM-1). Vrednosti MDA su određivane po metodi Andreeve i sar. (1988), hsCRP komercijalnim testom firme »Dade Behring« na analizatoru »Dimension-Xpand«, a ICAM-1 i VCAM-1 ELISA metodom, komercijalnim testom firme »Beckman Coulter Company« na »ByoSistems« ELISA rideru. Ispitanici su podeljeni u grupe bolesnika sa: DM tipa 2 i revaskularizacijom miokarda, DM tipa 2 bez revaskularizacije, bolesnici sa ishemičnom srčanom bolešću, i grupu zdravih ispitanika. Nivoi HbA1c, koncentracija lipidnih parametara, MDA, hsCRP, ICAM-1 i VCAM-1 bili su znatno viši kod pacijenata sa dijabetesom u odnosu na ostale ispitanike ($p<0,05$). Kod grupe pacijenata sa dijabetesom postojala je negativna korelacija između vrednosti hsCRP i HDL holesterola ($p<0,05$). Pozitivna korelacija postojala je između vrednosti hsCRP i ICAM-1 ($p<0,05$). Povećani nivo oksidativnog stresa i proinflamatornih markera javlja se u DM tipa 2 i ima značajnu ulogu u pojavi kardiovaskularnih oboljenja.

than the normal reference interval in the examined group, clinical manifestations on the bones do not have the same gravity. In our patient group renal bone changes were discrete and moderate. It seems that there is some kind of bone resistence to iPTH in chronic renal failure patients.

E72
INFLAMMATION MARKERS AND OXIDATIVE STRESS IN DIABETES MELLITUS TYPE 2

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Recent theories of atherosclerosis have revealed that the inflammatory response of the artery wall is a significant pathogenesis factor. Not only does this inflammation process contribute to a cardiovascular change, but it also initiates and helps atherosclerosis progress. However, the characteristics of the inflammatory process in type 2 diabetes mellitus are still vague taking into account that the disease is characterised by a coexistence of myriads of proinflammatory, prooxidative and procoagulating risk factors. Besides the lipid status and glicoregulation levels in patients with type 2 diabetes mellitus, the following aspects have been determined: lipid peroxidation – malondialdehyde (MDA), high-sensitivity C-reactive protein – acute phase reactant (hsCRP), intracellular adhesive molecule-1 (ICAM-1), and vascular cellular adhesive molecule-1 (VCAM-1). MDA values have been determined using the Andreev et al. method (1988), hsCRP values by a commercial test of the Dade Behring Company with a Dimension-Xpand analyzer, and ICAM-1 and VCAM-1 values by the ELISA method, commercial test of the Beckman Coulter Company with the BioSystems-ELISA reader. The subjects were divided into the following groups: type 2 DM and myocardial revascularization patients, type 2 DM without revascularisation, patients with ischemic cardiac disease, and a healthy control group. The levels of HbA1c, lipid parameters, MDA, hsCRP, ICAM-1 and VCAM-1 were significantly elevated in the diabetic patients compared to the other groups ($p<0.05$). There was a negative correlation between the values of hsCRP and HDL cholesterol ($p<0.05$). A positive correlation was found between the hsCRP and ICAM-1 values ($p<0.05$). Elevated oxidative stress and proinflammatory marker values were found in the type 2 DM patients and have a significant role in the occurence of cardiovascular diseases.

E73
MEĐUZAVISNOST VREDNOSTI BCL-2 I RAZLIČITOG ŽIVOTNOG DOBA

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Bcl-2 predstavlja familiju gena i proteina koji su uključeni u homeostatske mehanizme ćelijske proliferacije i smrti. Bcl-2 verovatno ostvaruje sopstvene efekte regulacijom permeabilnosti prolaznih pora mitohondrija koje su uključene u održavanje Ca^{2+}, pH i voltaže. Poznato je da sniženje nivoa Bcl-2 vodi u ćelijsku smrt putem procesa apoptoze dok povećana produkcija Bcl-2 štiti ćelije od smrti. Bcl-2 gen ima učešća u pojavi brojnih kancera, uključujući melanome, karcinome dojke, prostate kao i pojavi šizofrenije i različitih autoimunih bolesti. On takođe igra važnu ulogu u smanjivanju rezistencije na tradicionalnu onkološku terapiju. U ovoj studiji praćen je uticaj godina starosti i pola na anti-apoptotični protein – Bcl-2. Nivo Bcl-2 određivan je ELISA metodom, u serumu dve grupe zdravih ispitanika: prvoj grupi starijih osoba (58±5,6 god.) i drugoj grupi mlađih osoba (30±6,8 god.). Ustanovljen je statistički značajan niži nivo Bcl-2 vrednosti kod starijih osoba u odnosu na mlađe osobe (0,250±0,067ng/mL prema 0,294±0,67ng/mL; $p<0,05$). Istovremeno, zabeležena je neizmenjena vrednost Bcl-2 između različitih polova obe ispitivane grupe. Možemo zaključiti da nizak Bcl-2 nivo kod starijih osoba može biti jedan od mogućih rizika za neadekvatnu regulaciju apoptoze, uključujući proces onkogeneze kao i rezistenciju na onkološku terapiju u odnosu na mlađe osobe.

E73
INTERDEPENDENCE BETWEEN VALUES OF BCL-2 AND DIFFERENT AGE

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The Bcl-2 presents a family of genes and proteins which are involved in the homeostasis of cell proliferation and death. The Bcl-2 probably realizes its effects by the regulation of mitochondrial permeability transition pore which is involved in the maintenance of Ca^{2+}, pH and voltage. It is known that decreases in Bcl-2 levels lead to cell death by apoptosis while an overexpression of Bcl-2 protects cells from death. The Bcl-2 gene has been implicated in a number of cancers, including melanoma, breast, prostate, and lung carcinomas, as well as schizophrenia and autoimmunity diseases. It is also may be involved in resistance to conventional cancer treatment. In this study we investigated the effects of age and sex on anti-apoptotic protein – Bcl-2. The values of Bcl-2 were measured by the ELISA method in the serum of two healthy groups of volunteers: the first, older group (58±5.6 years) and a second, younger group (30±6.8 years). We observed statistically significant lower Bcl-2 values in older persons compared with younger persons 0.250± 0.067ng/mL vs. 0.294±0.67ng/mL; $p<0.05$). Simultaneously, we noted unchanged values of Bcl-2 between different sexes in both investigated groups. We can conclude that a low level of Bcl-2 in aged persons may be one of possible risks in the adequate regulation of apoptosis, including oncogenesis as well as resistance to therapy of cancer in comparison with younger person.

E74
OKSIDATIVNI STRES U JETRI VISTAR PACOVA IZAZVAN KLOFIBRATOM

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Poznato je da klofibrat, kao i drugi peroksizomalni proliferatori, mogu izazvati peroksizomalnu proliferaciju i u vezi s tim brojne druge efekte kod glodara. Otkriveno je da dugotrajan tretman glodara peroksizomalnim proliferatorima izaziva hepatocancerogenezu a ima izveštaja i o nastanku tumora u drugim organima. Jedan od navedenih potencijalnih mehanizama hepatokancerogenosti peroksizomalnih proliferatora jeste hipoteza o oksidativnom stresu. Cilj naše studije bio je da se utvrdi da li je došlo do modulacije antioksidantnih enzima koji olakšavaju uklanjanje reak-

E74
OXIDATIVE STRESS IN WISTAR RAT LIVER CAUSED BY CLOFIBRATE

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It is well known that clofibrate, as well as other peroxisomal proliferators, can induce peroxisomal proliferation and a variety of associated effects in rodents. Long-term treatment of rodents with peroxisomal proliferators has been found to cause hepatocarcinogenesis and there are also reports of tumor formation in other organs. One of the proposed mechanisms underlying the hepatocarcinogenicity of peroxisomal proliferators is the hypothesis of oxidative stress. The aim of our study was to determine whether antioxidant enzymes that facilitate the removal of reactive oxygen

tivnih kiseoničnih vrsta (ROS) posle kratkotrajne primene klofibrata i da li takva modulacija ima isti obrazac kao i prooksidantna. Studija je sprovedena na mužjacima Vistar pacova, težine 250–350 g, podeljenim u dve grupe: kontrolnu, N=14 (injekcije i. p. fiziološkog rastvora) i eksperimentalnu N= 14 (injekcije i. p. 250 mg/1000 g/24h 12 dana). U homogenatima jetre, kao i subcelularnim frakcijama, određene su aktivnosti oksidaze D-aminokiselina, urat oksidaze i palmitoil CoA oksidaze kao prooksidantnih enzima, kao i aktivnosti katalaze, superoksid dismutaze i glutation peroksidaze kao antioksidantnih enzima. Standardne spektrofotometrijske metode korišćene su za merenje aktivnosti enzima. Specifična aktivnost prooksidantnih enzima pokazala je statistički značajan porast, sa izuzetkom D-aminooksidaze. Nasuprot tome, samo je katalaza pokazala blag porast aktivnosti. Aktivnosti superoksid dismutaze i glutation peroksidaze bile su statistički značajno smanjene. Zaključujemo da tretman klofibratom može izazvati oksidativni stres u jetri Vistar pacova.

species (ROS) were modulated following short-term administration of clofibrate and whether the modulation had the same pattern as the prooxidant one. The study was performed in male Wistar rats weighting 250–350 g, divided into two groups: control one, N=14 (injected i.p. with sterile saline) and experimental one N= 14 (injected i.p. 250 mg/1000 g/24h for 12 days). Whole liver homogenates, as well as subcellular fractions, were assayed for activity of D-amino acid oxidase, urate oxidase and palmitoyl CoA oxidase as prooxidant enzymes, and for the activity of catalase, superoxide dismutase and glutathione peroxidase as the antioxidant enzymes. Standard spectrophotometer methods were employed for the measurement of the enzyme activities. Specific activity of prooxidant enzymes showed a statistically significant increase, with the exception of D-aminoxidase. On the contrary, only catalase showed a slight increase in activity. Superoxide dismutase and gluthatione peroxidase showed a statistically significant decrease of the activity. We may conclude that clofibrate treatment might lead to oxidative stress in Wistar rat liver.

E75
ADHEZIONI MOLEKULI I SISTEMSKI LUPUS ERITEMATODES

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Sistemski lupus eritematodes (SLE) jeste poremećaj kompleksne etiologije koji obuhvata inicijalne faktore spoljašnje sredine koji reaguju sa zaleđem jasno prisutne poligene podložnosti. Jedan od osnovnih uslova za njegov nastanak je poremećaj imunološke regulacije uz neadekvatno odstranjivanje imunih kompleksa koji dovode do oštećenja tkiva i funkcije organa. Budući da adhezioni molekuli predstavljaju značajne produkte aktivacije ćelija sa ključnom ulogom u procesu interćelijske signalizacije, cilj ovog rada je bio odrediti koncentracije intercelularnog (ICAM) i vaskularnog adhezionog molekula (VCAM-1) kod bolesnika sa različitim kliničkim manifestacijama SLE u fazi kliničkog pogoršanja bolesti: kožni (K-SLE); neurolupus (N-SLE); zglobni (Z-SLE) i vaskularni (V-SLE). Kontrolnu grupu su sačinjavali uzorci zdravih osoba, dobrovoljnih davaoca krvi. Merenje vrednosti adhezionih molekula je vršeno ELISA metodom, komercijalnim testom R&D. ICAM, kao jedan od integralnih činilaca ćelija-ćelija i ćelija-matriks receptora i inicijalni marker inflamatornog odgovora, pokazuje samo neznatan porast bez statistički značajne razlike u odnosu na kontrolne vrednosti. Što se tiče VCAM, koga stvaraju ćelije endotelijuma, postoji statistički značajan porast ($P<0,05$) u grupi »ukupni SLE« u odnosu na kontrolne vrednosti. Do-

E75
ADHESION MOLECULES AND SYSTEMIC LUPUS ERYTHEMATODES

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Systemic lupus erythematodes (SLE) is a disorder of complex etiology, involving initial factors in the environment reacting with the background of clear polygene susceptibility. One of the most important pre-conditions of SLE is the disturbance of immune regulation with inadequate removal of immune complexes leading to tissue damage and organ function disorders. Since adhesion molecules are important products of cell activation with a key role in the intracellular signalling process, this paper aims to determine the concentration of intercellular (ICAM) and vascular adhesion molecule (VCAM-1) in patients with different clinical manifestations of SLE in the clinical exacerbation phase of the disease: skin (S-SLE); neurolupus (N-SLE); joint (J-SLE); and vascular (V-SLE). Healthy blood donor volunteers comprised the control group. Adhesion molecule values were measured by the ELISA method, with a commercial R&D assay. ICAM, as one of the integral factors in cell-cell and cell-matrix receptors and an initial marker of inflammatory response, shows only a slight increase, without statistical significance compared to control values. As for VCAM, produced by endothelial cells, there was a marked increase ($P<0.05$) in the group of total SLE compared to con-

bijeni rezultati sugerišu da VCAM može biti obećavajući marker za praćenje bolesnika sa SLE. Takođe, VCAM je jedan od markera aktivacije NADP-H oksidaze u endotelnim ćelijama koja je neophodna u procesu migracije limfocita. Transkripciju VCAM-1 promotera podržava NF-κB sastavljen od p50 i p65 subjedinica, pri čemu p-50 subjedinica ima inhibitornu ulogu u supresiji aktivacije VCAM-1 različitim citokinima, dok je p65 subjedinica predstavljena kao pozitivan, citokin-inducibilan specifičan regulator ekspresije gena za VCAM-1. Otuda buduće određivanje vrednosti NF-κB može biti od posebnog značaja kod bolesnika sa SLE.

trols. The results we obtained suggest that VCAM can be an appropriate marker for surveillance of SLE patients. VCAM is also one of the NADP-H oxidase activation markers in endothelial cells, necessary in the lymphocyte migration process. VCAM-1 promoter transcription is supported by NF-κB composed of p50 and p65 subunits, with p50 subunit having an inhibitory role in the suppression of VCAM-1 activation by various cytokines, and with the p65 subunit being a positive, cytokine-inducible specific regulator of VCAM-1 gene expression. Future determination of NF-κB value can thus be of special importance in SLE patients.

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PRIMENA HOMA MODELA ZA PROCENU INSULINSKE REZISTENCIJE KOD PACIJENATA SA SINDROMOM POLICISTIČNIH OVARIJUMA

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Insulinska rezistencija (smanjen efekat date doze insulina na homeostazu glukoze) često je prisutna kod žena sa sindromom policističnih ovarijuma (PCOS) i smatra se odgovornom za pojavu reproduktivnih poremećaja kao i komplikacija PCOS (*diabetes mellitus* tip 2, hipertenzija, dislipidemija, ateroskleroza). Zlatni standard za procenu insulinske rezistencije (IR) predstavlja euglikemijski hiperinsulinemijski klamp. Zbog zametnog postupka klampa, širu kliničku primenu ima HOMA (*Homeostasis Model Assessment*) koji za procenu IR koristi bazalne vrednosti glukoze i insulina. Po preporuci SZO vrednosti HOMA indeksa >2,5 ukazuju na pojavu insulinske rezistencije. Rad je obuhvatio 67 pacijentkinja sa PCOS i 46 ispitanica koje su činile kontrolnu grupu. Obe grupe su prema vrednosti BMI podeljene u dve podgrupe: negojazne, BMI ≤ 25 kg/m^2 (A1 – PCOS (n=36) i B1 – KONT (n=32)) i gojazne, BMI > 25 kg/m^2 (A2 – PCOS (n=31) i B2 – KONT (n=14)). Kod svih ispitanica određivani su glukoza (enzimskom metodom), insulin (ELISA metodom) i testosteron (RIA metodom). HOMA je izračunata primenom formule [insulin (mU/L) x glukoza (mmol/L)] / 22,5. Dobijene su sledeće vrednosti HOMA indeksa (izražene kao Xsr±Sd): A1-PCOS 2,62±1,18; A2-PCOS 3,93±2,65; B1-KONT 1,68±0,60; B2-KONT 1,97± 1,04. Statističkom obradom podataka nisu dobijene značajne razlike određivanih parametara unutar kontrolne grupe (B1 prema B2). Unutar grupe PCOS pacijenata (A1 prema A2) statistički značajnu razliku su pokazivale vrednosti insulina i HOMA indeksa (p<0,005), dok se vrednosti glukoze i testosterona nisu razlikovale. Međusobnim poređenjem podgrupa pacijenata i odgo-

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THE USE OF HOMA MODELING IN THE ASSESSMENT OF INSULIN RESISTENCE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Insulin resistance (reduced actions of insulin on glucose homeostasis) is present in many PCOS (polycystic ovary syndrome) women and plays a role in the pathogenesis of the reproductive disturbances as well as PCOS complications (diabetes, hypertension, dyslipidaemia, atherosclerosis). The »gold standard« for the evaluation of insulin resistance (IR) is euglycemic hyperinsulinemic clamp, but it is not feasible for the routine screening of patients. The HOMA (homeostasis assessment model) index uses the basal glucose and insulin levels for assessment of IR. The aim of this study was to identify PCOS in women who are most insulin resistant using the HOMA index. We investigated 67 PCOS women and 46 healthy, age- and BMI-matched controls. Based on the BMI (body mass index), both PCOS and control groups were divided into two subgroups: normal weight, BMI ≤ 25 kg/m^2 (A1-PCOS (n=36) and B1-CONT (n=32)) and overweight, BMI > 25 kg/m2 (A2-PCOS (n=31) and B2-CONT (n=14)). Blood samples were collected in the follicular phase of the cycle for the determination of basal glucose (enzymatic method), insulin (ELISA method) and testosterone (RIA method). HOMA was calculated using the formula [fasting insulin (mU/L) x fasting glucose (mmol/L)]/22.5. We have found no significant differences in these parameters between control subgroups (B1 vs. B2). Analyzing the PCOS subgroups (A1 vs. A2), we have found significant differences in the levels of insulin (p<0.005) and HOMA (p<0.005). Normal weight PCOS women and controls (A1 vs. B1) showed statistically significant differences in insulin levels (p<0.001) and HOMA index (p<0.001) as well as

varajućih kontrolnih podgrupa nisu dobijene značajne razlike u vrednostima glukoze u obe podgrupe, dok su se vrednosti HOMA indeksa i insulina značajno razlikovale ($p<0,001$ u grupi negojaznih i $p<0,005$ za insulin i $p<0,01$ za HOMA u grupi gojaznih ispitanica). Na osnovu dobijenih rezultata može se zaključiti da je IR prisutna i kod velikog broja negojaznih žena sa PCOS, a da se HOMA indeks može koristiti kao screening test za IR i selekciju žena sa PCOS koje bi dale dobar odgovor na primenu terapije u cilju poboljšanja insulinske senzitivnosti.

overweight patients and controls (A2 vs. B2): $p<0.005$ for insulin and $p<0.01$ for the HOMA index. There were no differences in glucose levels between groups and subgroups. Based on these results, we can conclude that IR is present in a significant number of normal weight PCOS women. The HOMA index can be used as a screening test for IR and for selecting PCOS women most likely to respond to therapy for improvement of insulin sensitivity.

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NEFROTOKSIČNI EFEKTI GENTAMICINA KOD PACIJENATA U NEONATALNOM PERIODU

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Rezultati naše ranije studije su pokazali da čak i normalne doze gentamicina izazivaju, kod pacijenata starosti od 3 do 10 godina oba pola, nefrotoksične efekte praćene povećanjem aktivnosti enzima dominantno lokalizovanih u proksimalnim tubulama u urinu, alaninaminopeptidaze (AAT, EC 3.4.11.2), gama-glutamiltransferaze (GGT, EC 2.3.2.1) i N-acetil-beta-D-glukozaminidaze (NAG, EC 3.2.1.30). Kod pacijenata u neonatalnom periodu manje je izražena renalna akumulacija aminoglikozida što može da se objasni morfološkim i funkcionalnim karakteristikama bubrega u tom periodu i zbog toga bi se moglo očekivati manje nefrotoksično delovanje gentamicina, uz iste uslove primene, u odnosu na decu starijeg uzrasta. Mi smo, u uzorku 12-časovnog urina, pratili aktivnosti enzima proksimalnih tubula, AAP, GGT i NAG, kod 30 pacijenata kojima je u okviru terapije apliciran gentamicin i kod 30 pacijenata iz kontrolne grupe. U sastav ispitanika bila su uključena oba pola, u neonatalnom periodu. Tretman je sprovođen do 10 dana uz davanje gentamicina u dozama od 2,5 mg/kg telesne mase dnevno. Utvrđena je značajna razlika između AAP i GGT, u U/mmol kreatinina, osmog dana sprovođenja terapije između ispitanika u eksperimentalnoj i kontronoj grupi ($p<0,01$) (kod odrasle dece je do porasta aktivnosti, pri ranijem ispitivanju, došlo drugog dana sprovođenja terapije) i nije utvrđena značajna razlika u aktivnosti NAG između ispitanika u eksperimentalnoj i kontrolnoj grupi (u odrasle dece, signifikantna razlika je ranije utvrđena osmog dana nakon sprovođenja terapije). Dobijeni rezultati pokazuju da je nefrotoksično delovanje gentamicina kod pacijenata u neonatalnom periodu manje izraženo, verovatno zbog nepotpune morfološke razvijenosti bubrega i brže glomerularne filtracije, nego kod dece uzrasta od 3 do 10 godina. Kod dece tog uzrasta rani i veoma osetljivi indikatori nefrotoksičnosti gentamicina su AAP i GGT.

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NEPHROTOXIC EFFECTS OF GENTAMICIN IN PATIENTS IN THE NEONATAL PERIOD

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From the results obtained throughout our earlier study it can be concluded that even normal gentamicin doses in children patients aged 3–10 years old of both sexes, express nephrotoxic effects followed by elevated enzymatic activities of alaninaminopeptidase (AAT, EC 3.4.11.2), gamma-glutamyltransferase (GGT, EC 2.3.2.1) and N-acetyl-beta-D-glucosaminidase (NAG, EC 3.2.1.30) i.e. enzymes dominantly localized within the proximal tubules. Patients in the neonatal period show lower renal accumulation of aminoglycosides, which can be explained by the morphometric and functional characteristics, and there would be less renal toxicity. We studied the enzyme activities in 12-hour urine samples of the proximal tubular enzymes, AAP, GGT and NAG, in 30 patients who received gentamicin and in 30 similar control patients. The patients were of both sexes, all in the neonatal period. The tretment was conducted during a period of 10 days using gentamicin in doses of 2.5 mg/kg body weight daily. A significant difference in AAP and GGT, in units/mmol creatinine, between the experimental and control group was noted on the 8th day ($p<0.01$) (earlier, in adults on the 2nd day) and no significant differences in NAG activities were noted between the experimental and control group (in adults we had noted a significant difference on the 8th day). The date indicate that the renal toxicity of aminoglycosides seems to be less frequent in newborn infants compared to adults even though glomerular filtration mechanisms are subjected to adaptive processes during the neonatal period, and in patients in the neonatal period only high urinary AAP and GGT levels are among the earliest and extremely sensitive indicators of nephrotoxicity.

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BIOMARKERI RENALNE INSUFICIJENCIJE KOD BOLESNIKA SA DIJABETES MELITUSOM TIPA II

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Renalna insuficijencija (RI) jeste hronična manifestacija dijabetes melitusa (DM). Značajno je pravovremeno prepoznavanje faktora koji ubrzavaju nastanak RI kod obolelih od DM. Ovom presek studijom obuhvatili smo pacijente sa DM tip II i hipertenzijom (25), od kojih je sa RI bilo 13 pacijenata (Gr1), prosečne starosne dobi 64,67 god, prekomerne telesne mase (BMI=28,79 kg/m^2) sa tenzijom 151,67/91,67 mmHg, i 12 pacijenata bez RI (Gr2), prosečne starosti 70,0 god, slične, prekomerne telesne mase (BMI= 28,50 kg/m^2) sa tenzijom 138,33/78,33 mmHg. Kontrolnu grupu (Gr3) činili su dobrovoljni davaoci krvi (12) bez DM, prosečne starosti 51,57 god, sa blagom do umerenom hipertenzijom (TA=153/96 mmHg). Od svih određivanih biohemijskih parametara u serumu značajno su se razlikovali glukoza (p1/3=0,06; p2/3= 0,007), urea (p1/3=0,009), kreatinin (p1/3=0,02), mikroalbuminurija/proteinurija (p1/3=0,007) kao i starosno doba (p1/3=0,002; p1/2=0,02). Nezavisni prediktori za nastanak RI, u ispitivanoj populaciji DM tipa 2, bili su, posle prilagođavanja za životno doba i prisustvo hipertenzije, glikemija, urea, kreatinin i mikroalbuminurija/proteinurija (R2=0,943).

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RENAL INSUFFICIENCY BIOMARKERS IN DIABETES MELLITUS TYPE II PATIENTS

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Renal failure (RF) is a chronic manifestation of diabetes melitus (DM). Early recognition of factors that speed up RF development in DM patients is very important. This cross-sectional study included DM type II patients with hypertension (25), 13 patients with RF (Gr1), average age 64.67 years, elevated body mass (BMI=28.79 kg/m^2) with blood pressure 151.67/91.67 mmHg) and 12 patients without RF (Gr2), average age 70 years, similar elevated body mass (BMI= 28.50 kg/m^2) with blood pressure 138.33/78,33 mmHg. The control group (Gr3) included 12 voluntary blood donors without DM presence, average age 51.57 years, with mild to moderate hypertension (TA=153/96 mmHg). Amongst all tested biochemical serum parameters. We found significant differences in glucose (p1/3=0.06; p2/3= 0.007), urea (p1/3= 0.009), creatinine (p1/3=0.02), microalbuminuria/ proteinuria (p1/3= 0.007) and age (p1/3=0.002; p1/2=0.02). Independent predictors of RF development, in the tested population with DM type II, were (after age and hypertension presence adjustments) glycemia, urea, creatinine and microalbuminuria/proteinuria (R2=0.943).

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SINERGISTIČKI EFEKTI ISHRANE, FIZIČKE AKTIVNOSTI I BIHEVIORALNE TERAPIJE NA GLUKOREGULACIONE PARAMETRE KOD BOLESNIKA SA SINDROMOM X

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Sindrom X (Sy X) jeste maksimalno potentni aterogeni faktor rizika za veliki broj KVB. Zbog obavezne insulinske rezistencije (IR) sindrom X čini prefazu DM tipa 2, tj. predijabetesa. Gerald Reaven je 1988. godine postavio hipotezu o sindromu X kao klasteru obavezne insulinske rezistencije (IR) i najmanje jednog aterogenog faktora rizika (ATFR), ali 1998. godine kriterijumi za dijagnozu promenjeni su od strane SZO: obavez-

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SYNERGISTIC EFECTS OF NUTRITION, PHYSICAL ACTIVITY AND BEHAVIORAL THERAPY ON GLUCOREGULATION PARAMETERS IN PATIENTS WITH SYNDROME X

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Syndrome X (Sy X) is estremely potent atherogenic risk factor for most CVD. With its insulin resistance (IR), Syndrom X is a prephase of DM type 2, ie. prediabetes. Gerald Reaven in 1988 made a hypothesis that syndrome X is a cluster of insulin resistance (IR) and at least one atherogenic risk factor (ATRF), but in 1998 the diagnostic criteria (DG) were changed by the WHO: insulin resistance and at least two ATRF (Alberti

na insulinska rezistencija i najmanje dva ATFR (Alberti KG, 1998. i SZO, 1999.) Mi smatramo da je Sy X odgovor tela na egzogene stimuluse: prejedanje, smanjena fizička aktivnost i stres uz uticaj podignutog praga osetljivosti hipotalamičkih glikoreceptora i povećane količine abdominalnog (visceralnog) masnog tkiva. Naš cilj je bio da istražimo sinergističke efekte fizičke aktivnosti, ishrane i bihevioralne terapije na glukoregulacione poremećaje kod bolesnika sa sindromom X. Pacijenti: sedamdeset patijenata sa Sy X, starosti 51 14,7 godina stari podeljeni su u dve grupe (DIJ i BIH). Svaka grupa je sadržala 35 bolesnika (27 ž i 8 m). Zdrava kontrolna grupa je brojala 35 osoba (27 ž. i 8 m.), 47 11,2 god. Dva kombinovana terapijska programa (DIJ and BIH) bili su korišćeni. Bila su slična u dijetoterapiji i aerobno acikličnim vežbama. Program BIH je imao jednu komponentu više: bihevioralnu terapiju. Istražili smo dve različite faze terapije: prva je trajala dva meseca (intenzivni dijetoterapijski program sa paralelnim programom fizičkih vežbi), druga faza je trajala dve godine. Terapijski program u celini trajao je dve godine i dva meseca. Svi parametri su mereni paralelno tri puta: inicijalno, onda na prvoj kontroli (posle dva meseca) i konačno (posle 26 m. od početka terapije). Koncentracije serumskog insulina (I) bile su merene RIA komercijalnim testom (n. vrednosti od 5 do 25 mIU/L). Glukoza (Gly) je bila određivana kolorimetrijskom GOD-PAP tehnikom. Normalne vrednosti bile su 3,6–6,1 mmol/L. Koncentracije (STH), bile su merene spektrofluorimetrijski, donja i gornja kvartila (0,762–6,345 μmol/L) i »Quicki index« senzitivnosti periperalnih tkiva na delovanje insulina je računat (Katz A, 2000). Mediana kontrolne grupe je bila 0,338, s nižom i višom kvartilom: 0,307 i 0,348. Pored inicijalnih vrednosti, klasičnim Anova i Manova tehnikama istražili smo intragrupne i intergrupne promene koncentracija: glukoze Gly, insulina (I) i hormona rasta (STH) i vrednosti »Quicki indexa«. Prosečna koncentracija glucoze bila je inicijalno viša u obe grupe ($p<0,05$). I prosečna koncentracija insulina bila je povišena u obe grupe: medijana i (niža i viša kvartila) bile su: u grupi BIH = 26,20 (22–34,3) i u DIJ: 27,92 (24,6–31,1); zdrava kontrola (med. 16,20 i (11,8–18,9) – donja i gornja kvartila). U obe grupe prosečna vrednost »Quicki indexa« inicijalno bila je niža (u grupi BIH: 0,286±0, 0012, i 0,287±0,008 u DIJ). U normalnoj kontroli bila je 0,326±0,018 tj. (0,313 niža i 0,335 viša 0,335 kvartila). Koncentracija STH bila je snižena u obe grupe takođe (medijana; niža i viša kvartila) bile su: (u grupi BIH: 0,711 (0,264–0,65 i 0,728 (0,304–2,09) u DIJ. U zdravoj kontroli bila je 1,55, tj. (0,762–6,35), niža i viša kvartila. Napravili smo grupnu tabelu koja pokazuje statističku značajnost razlika prosečnih vrednosti između dve eksperimentalne grupe u prvoj fazi terapije (inicijalno-prva kontrola) na nivou ($p<0,05$) i tokom čitavog perioda od 26 meseci (pošto program terapije se smatra uspešnim samo ako bolesnici očuvaju dobre rezultate najmanje dve godine (stat. značajnost razlika između inicijalnog i finalnog merenja na nivou $p<0,05$). Nažalost nije bilo stat. zna-

KG, 1998 and WHO, 1999). We presume that functional Sy X that is the body's answer to exogenous stimulances: overeating, lowered physical activity and stress with the contribution of elevated insensitivity of hypothalamic glycoreceptors and elevated amount of abdominal (visceral) fat tissue. Our purpose was to investigate the sinergistic effects of physical activity, nutrition and behavioral therapy on glucoregulatiory disturbances in patients with syndrome X. Seventy patients with Sy X, 51 14.7 y. old were divided in two groups (DIJ and BIH). Each group consisted of 35 patients (27 f and 8 m). Healthy control numbered 35 persons (27 F and 8 M), 47 11.2 y. old. Two combined therapy programs (DIJ and BIH) used were. The patients had similar dietotherapy and aerobic acyclic exercises programs. The program BIH had one component more: behavioral therapy. We investigated two different phases of therapy: first one last two months (intensive dietotherapy program with parallel physical exercises), second phase lasted two years. The therapy programs lasted two years and two months in total. All parameters were measured paralelly three times: initialy, then on the first control (after two months) and finally (after 26 m. from the beginning of therapy). Concentration of serum insulin (I) were mesured with RIA commercial test (n. values from 5 to 25 mIU/L). Glycose (Gly) was measured with colorimetric GOD-PAP technicque. Normal values were 3.6–6.1 mmol/L. Concentration of STH was measured spectrofluorimetrically, Lower-upper qu.(0.762–6.345 μmol/L) and Quicki index of pertipheral tissue sensitivity to insulin action were calculated (Katz A, 2000). The median in the healthy controls was 0.338, lower and upper quart were 0.307 and 0.348. Beside the initial values, using classic Anova and Manova technics, we investigated inter- and intragroup changes of the conc.: of glycose (Gly), insuline (I) and growth hormone (STH) and the value of Quicki index. Mean conc. of glucose were higher in both exp. groups initialy ($p<0.05$). Mean conc of insulin were higher in both exp. groups: (medians and lower and upper quartile) were: in group BIH = 26.20 (22–34.3) and in DIJ: 27.92 (24.6–31.1), respectively; healthy control med. 16.20 (11.8–18.9) up-low quartile. In both exp. groups, means of Quicki index initialy were lowered (in BIH group: 0.286 ± 0, 0012, and 0.287±0.008 in DIJ), respectively. In normal controls it was 0.326 ± 0.018 (ie. 0.313 lower and 0.335 upper quartile). Conc. of STH were lowered too in both exp. Groups (med.; lower and upper quartile) in BIH group: 0.711 (0.264–1.65), and 0.728 (0.304–2.09) in DIJ, respectively. In normal controls in median was 1.55 ie. (0.762–6.35, lower and upper quartile). We made a group table which represents the stat. significance of the differencies of means beetwen two exp. in groups in the first phase of th. (initial-first control) at level $p<0.05$ and during the whole period of 26 months (because the therapy program is efficient only if the patient keeps good results for two years (stat. significances of stat differences beetwen inicial-final measurement, at level $p<0.05$). Unfortunately there is no

čajne razlike između inicialnog i finalnog prosečnih vrednosti Gly, I, »Quicki indeksa« i STH u grupi DIJ, ali ista merenja dala su značajne razlike u grupi BIH (bihevioralna terapija.) Na prvom jugoslovenskom kongresu o gojaznosti (1992) prof. M. Pecelj-Gec rekla je da sva nastojanja da se eliminišu glukoregulacione disturbancije kod bolesnika sa sindromom X samo su Sizifov posao bez stalne promene ponašanja. Ovo istraživanje je to dokazalo.

statistically significant difference beetwen the inicial and final value of means of Gly, I, Quicki index and STH in Group DIJ but the same measurements were significantly different in group DIJ (behavioral therapy). At The first Yugoslav Congress on obesity (1992) prof. M. Pecelj-Gec said that all intentions to eliminate glucoregulation disturbances in patients with Sy X are only Sisyphean work bringing no permanent bihevioral changes. This examination proved that.

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GOJAZNOST KAO FAKTOR RIZIKA ZA POJAVU ŽUČNIH KAMENACA

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Holelitijaza je jedna od najčešćih bolesti digestivnog trakta. Gojaznost predstavlja značajan faktor u razvoju žučnih kamenaca. Cilj ovog rada bio je da se proceni povezanost gojaznosti i standardnih biohemijskih parametara sa pojavom žučnih kamenaca. Ispitivanje je obuhvatilo grupu pacijenata sa holelitijazom (19 muškaraca/37 žena) i kontrolnu grupu (20 muškaraca/41 žena) približno istih demografskih karakteristika: starosne dobi, obrazovanja i bračnog statusa. Procena uhranjenosti ispitanika izvršena je na osnovu antropometrijskih i biohemijskih parametara. Stanje uhranjenosti izraženo je preko indeksa telesne mase (BMI), a standardne biohemijske analize (albumin, protein, CRP, glukoza, gvožđe, TIBC, ukupan, HDL i LDL holesterol, trigliceridi, bilirubin, mokraćna kiselina, kao i aktivnosti enzima AST, ALT, ALP, γ-GT, α-amilaze) urađene su na aparatu »Vitros 350« (»Ortho-Clinical Diagnostics«, Johnson & Johnson company). Utvrđena je statistički značajna razlika u vrednostima BMI između dve ispitivane grupe ($p<0,01$), a bolesnici sa holelitijazom su imali prosečno veći BMI u odnosu na kontrolnu grupu. Snižen nivo HDL holesterola i visok nivo triglicerida su značajno povezani sa povećanim rizikom za nastanak žučnih kamenaca. Hiperurikemija 2,5 puta povećava šansu za nastanak te bolesti (Exp (B) = 2,519; p=0,046), a hiperglikemija čak 3 puta kod osoba sa holelitijazom, u poređenju sa zdravim osobama. Nivo CRP-a iznad 3 mg/L značajno povećava šansu za nastanak kalkuloze žučne kese. Može se zaključiti da je u cilju smanjenja rizika važno sprečiti pojavu gojaznosti i održavati ukupan energetski unos u preporučenim granicama.

E80
OBESITY – RISK FACTOR FOR GALLSTONE DEVELOPMENT

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Cholelitiasis is one of the most common diseases of the digestive system. Obesity is an important risk factor for gallstone development. The aim of this study was to evaluate the impact of obesity and standard biochemistry parameters on gallstone development. Cholelitiasis patients (19 male and 37 female) were evaluated as well as control grupu (20 male and 41 female), with similar demographic characteristics: stature, education, and marriedge status. The allimentation was estimated based on antropometric and biochemistry parameters. Level of allimentation was expressed through body mass index (BMI). Standard biochemistry parameters (albumine, proteins, CRP, glucose, iron, TIBC, cholesterol, HDL- and LDL- cholesterol, tryglicerides, bilirubin, uric acid, and enzyme activities AST, ALT, ALP, γ-GT, α-amilase) were analyzed on Vitros 350 Ortho Clinical Diagnostics system (Johnson & Johnson company). There were confirmed a statistical difference in BMI values between two evaluated groups (p 0,01). Patients with cholelitiasis were with higher levels of BMI compared to control group. Lower HDL level and high tryglicerides were connected with high risk for gallstone development. Hiperuricemia increase risk for gallstone development 2.5 times (Exp (B) = 2.519; p=0.046), and hyperglicemia increase risk for 3 times in cholelitiasis patients compared to control group. CRP level higher than 3 mg/L increase risk for gallstone development. In conclusion, it is very important to keep from obesity to decrease a risk for gallstone development and keep total energy diet in recommended levels.

E81
NOVA TEHNOLOGIJA U UPRAVLJANJU MEDICINSKIM OTPADOM U SLUŽBI LABORATORIJSKE DIJAGNOSTIKE DOMA ZDRAVLJA »NOVI SAD«

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Služba laboratorijske dijagnostike,
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Brojne analize stanja životne sredine u Republici Srbiji pokazale su da neadekvatno postupanje sa otpadom predstavlja jedan od najvećih ekoloških problema na ovom prostoru. Po preporuci Evropske agencije za rekonstrukciju i Ministarstva zdravlja RS i nakon karakterizacije, uvedena je trijaža čvrstog zaraznog zdravstvenog otpada u Domu zdravlja, te tako i u Službi laboratorijske dijagnostike. Kako Služba laboratorijske dijagnostike uzima uzorke biološkog materijala za oko 1000 pacijenata, nametnuo se problem na koji način upravljati zaraznim zdravstvenim otpadom, a ne dozvoliti štetan uticaj na zdravlje ljudi i životnu sredinu. Nakon višegodišnjih bezuspešnih pokušaja spaljivanja igala, Dom zdravlja je nabavio sistem za dezinfekciju i sterilizaciju čvrstog zaraznog zdravstvenog otpada – »SINTION« sa drobilicom »SHREDTION«. Tehnologija rada tog aparata se zasniva na kombinaciji vakuuma, mikrotalasne energije i zasićene pare, što omogućava efikasno uništavanje mikroorganizama u različitim materijalima i u najužim šupljinama. Svi ciklusi rada su potpuno automatizovani. Sistem je zatvoren i operater na uređaju nije izložen nikakvoj opasnosti od emisija, otpadnih voda ili struje. Proces upravljanja otpadom u našoj laboratoriji započinje trijažom, pakovanjem u specijalne plastične kese i transportom do sistema specijalnim namenskim vozilom, gde pomoću pomenutog aparata na zdravstveno i ekološki najprihvatljiviji način rešavamo problem zagađivanja životne sredine. Praktična iskustva u rešavanju problema adekvatnog upravljanja otpadom govore da se ova pitanja mogu rešiti samo stalnom i kontinuiranom saradnjom i edukacijom svih subjekata na celom prostoru, a u okviru sistema zaštite životne sredine.

E81
A NEW TECHNOLOGY FOR MANAGEMENT MEDICAL WASTE IN THE LABORATORY SERVICE OF HEALTH CENTER »NOVI SAD«

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Many analyses of evironmental conditions in the Republic of Serbia have led to the conclusion that inadequate dealing with the waste is one of the greatest ecological problems in this area. Following the recommendation from the European Agency of Reconstruction and the Ministry of Health of the Republic Serbia and after caracterisation we made a selection of hard infectious medical waste both in the »Novi Sad« Health Center and also in the Laboratory Service. Our service of laboratory diagnostics prepares the biological material of about 1000 people and it has become a problem to remove tall infectious medical waste to aviod its harmful influence on people's health and on the environment. After many years of unsuccessful attempts to burn the needles, our Health Center has purchased the disinfection and sterilization system for all kinds of infectious medical waste – »SINTION« with the division part SHREDTION. It is based on a combination of vacuum, microwave energy and saturated steam and this combination allows for effective destruction of microorganisms in different materials and in the tightest of hollows. All work cycles are completely automated. The system is closed and the technician operating the apparatus is not exposed to the influence of bad emissions, foul water or the current. The waste management in our laboratory begins with the division, packing in to special plastic bags and transportation to the system in a specially designed vehicle where this modern new system helps us to solve the problem. In practice we have learned that the management of waste is a big problem for the whole community. The adequate removal of waste can be achieved only through permanent cooperation and education of the all subjects in the community and within the system of environmental protection.

E82
TRIJAŽA MEDICINSKOG OTPADA U DOMU ZDRAVLJA »NOVI SAD«

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Služba laboratorijske dijagnostike,
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Dosadašnja praksa upravljanja, rastuća produkcija, i prateći zdravstveni rizici aktuelizovali su i potencirali neophodnost rešavanja problema medicinskog otpada. Zabrinutost javnosti zbog odlaganja medicinskog otpada raste usled straha od širenja krvno preno-

E82
MEDICAL WASTE DIVISION IN THE HEALTH CENTER »NOVI SAD«

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Former inadequate management practice, growing production and health risks have brought the problem of medical waste to the open line. The public is worried about the transmission of blood diseases and about toxic materials. Medical waste is all waste from

sivih bolesti, kao i izlaganja toksičnim materijama. Medicinski otpad se definiše kao sav otpad koji nastaje u zdravstvenim institucijama, istraživačkim ustanovama i laboratorijama. U Domu zdravlja »Novi Sad« vrši se razdvajanje celokupnog otpada, prema preporukama Evropske agencije za rekonstrukciju i Ministarstva zdravlja RS, u pet kategorija: komunalni, komunalni koji je moguće reciklirati, zarazni zdravstveni otpad, štetni otpad i otpad koji se zatrpava. Komunalni otpad se odlaže u plastične kante sa crnim kesama, a zatim u kontejnere koje komunalno preduzeće transportuje do deponije. Čvrsti komunalni otpad koji je moguće reciklirati sakuplja se u odgovarajuće kese ili kutije i prosleđuje na reciklažu. Čvrsti zarazni zdravstveni otpad se po službama odlaže u adekvatno označene metalne, pedalne kante sa poklopcem i crnom kesom kao uloškom, dok se oštri predmeti (igle) odlažu u namenske, kartonske kutije. Celokupan zarazni zdravstveni otpad se odlaže u centralne tipske kante, odakle se transportuje namenskim vozilom do sistema za upravljanje otpadom, gde se specijalnim tehnološkim postupkom prevodi u komunalni. Štetni otpad se čuva zaključan u apoteci i posebno obeležen. Budući da evropske studije pokazuju da zarazni zdravstveni otpad čini najviše 10% ukupne količine medicinskog otpada, neophodno je ozbiljno shvatiti značaj pravilne trijaže otpada i uvesti je u svakodnevnu praksu.

health institutions, research institutes and laboratories. In the health center »Novi Sad«, we perform medical waste division, as advised by the European Agency for Reconstruction and the Ministry of Health of the Republic of Serbia into five categories: communal waste, communal recyclable waste, infectious health waste, harmful waste and waste to be buried. The communal waste is placed into plastic cans with black bags inside, and then taken to containers for transportation to the waste depot. The recyclable communal waste is collected into bags or boxes and is then sent to be recycled. Infectious health waste is placed into appropriately marked metall pedal cans with black bags inside, and sharp things (needles) are moved to suitable carton boxes. All infectious waste is removed into specific central cans and from there the waste is transported by suitable vehicles to the system for waste management. There waste is transported into communal waste by a special technology. Harmful waste is specially marked, locked and protected in the pharmacy. Some European studies have supplied the data that only about 10% of all medical waste is potentially infectious and dangerous and, because many medical institutions have no sufficient financial means and equipment for adequate waste management, it is necessary to work very seriously on waste division and make it a part of the daily work routine.

E83
BIOHEMIJSKI MARKERI KAO SMERNICA U PRAĆENJU EFEKTA TERAPIJE KOD PACIJENATA SA REUMATOIDNIM ARTRITISOM

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Biohemijski markeri (enzimi u urinu, albuminurija i cistatin C u serumu) ispitivani su kod pacijenata sa RA kako bi se procenila moguća toksičnost nesteroidnih antiinflamatornih lekova (NSAID). Enzimska aktivnost β-NAG, AAP, γ-GT u urinu određena je standardizovanim kinetičkim metodama. Koncentracije albumina u urinu i cistatina C u serumu merena je imunoturbidimetrijskim metodama primenom »DAKO« testova. Srednje vrednosti ± Sd NAG, AAP i γ-GT u urinu kod seropozitivnih (N=56), seronegativnih RA (N=32) pacijenata i zdravih osoba (N=30) pronađene su: β-NAG 2,27±0,65; 1,26±0,34; 0,75±0,43 U/mmol kreatinina; AAP 2,98±0,36; 1,30±0,74; 0,50±0,35 U/mmol kreatinina; γ-GT (3,84±0,30; 1,36±0,28; 1,32±0,50 U/mmol kreatinina). Utvrđene srednje

E83
BIOCHEMICAL MARKERS AS A TRACER IN FOLLOW-UP OF THERAPY EFFECT ON PATIENTS WITH RHEUMATOID ARTHRIT

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The biochemical markers (urinary enzymes, albuminuria and serum Cystatin C) was investigated in patients with RA to evaluate the eventually toxicity of non-steroidal anti-inflammatory drugs(NSAIDs). Urinary enzyme activity of β-NAG,AAP, γ-GT was determined with standardised kinetic methods. Urinary albumin concentration and serum Cystatin C was measured immunoturbidimetric methods using DAKO tests. Mean +/– SD values of urinary NAG, AAP and γ-GT In seropositive (N=56), in seronegative RA(N=32) patients and in normally subjects (N=30) were found to be: β-NAG (2,27+/–0.65, 1.26+/– 0.34,0.75+/–0.43 U/mmol creatinine); AAP(2.98+/–0.36,1.30+/–0.74,0.50+/–0.35 U/mmol creatinine), γ-GT(3.84+/– 0.30,1.36+/–

vrednosti NAG i γ-GT u urinu kod RA pacijenata su bile značajno više ($p<0,01$) u poređenju sa srednjim vrednostima kod seronegativnih RA pacijenata i normalnih zdravih osoba kada su analizirani *one-way* ANOVA testom. Kod pacijenata koji su tretirani metatreksatom i dekortinom pokazano je da su koncentracije cistatina C u serumu značajno povišene u toku terapije (2,85± 0,56 vs. 0,70±0,50 mg/L). Koncentracija albumina u urinu je bila povećana, ali ne značajno, u toku prvih dana tretmana. Određivanje enzima β-NAG i γ-GT u urinu, kao i koncentracije cistatina C u serumu može prema tome služiti kao osetljiviji test za oštećenje bubrega kod pacijenata sa reumatoidnim artritisom. Rano otkrivanje visokih NAG enzimurija i povećanja nivoa albumina u urinu pre primene MTX terapije može biti korisno za predviđanje moguće toksičnosti MTX koja je verovatno povezana sa smanjenim renalnim klirensom MTX.

E84
RAZLIKE U HEMATOLOŠKIM PARAMETRIMA KOD PACIJENATA SA DIJABETESOM

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Ova studija bavi se ispitivanjem razlika u hematološkim parametrima kod pacijenata sa dijabetes melitusom (tipa 1 i tipa 2). Objavljen je mali broj studija koje se odnose na dobru kontrolu dijabetes melitusa i broja trombocita ili kontrolu funkcije krvnih ćelija. Povećanje kontrolne glikemije kod pacijenata sa tipom 2 dijabetesa prouzrokuje redukciju u trombogenosti. Dobra kontrola glikemije može pomoći u korelaciji visokog povećanja koagulobilnosti. U ovoj studiji ispitivani su broj eritrocita, leukocita i trombocita, kao i drugih parametara za razlikovanje dva tipa dijabetesa (tip 1 N=160, tip 2 N=180) kod dijabetičnih pacijenata i poređeni sa kontrolnom populacijom. Uzorci krvi (K3EDTA) pacijenata sa dijabetesom tipa 1 ili 2 i kontrolne grupe (N=50) sa referentnim vrednostima glukoze su korišćene u ovoj studiji. Koncentracija glukoze je određena pomoću GOD metode, a hematološki parametri na »Sysmex KX-21« i »PENTRA 120« analizatorima. Rezultati su pokazali povećanje vrednosti hematokrita, broja leukocita, limfocita i monocita kod pacijenata sa dijabetesom, dok su MCV, MCH (osetljiv na koncentraciju glukoze) i broj neutrofila bili smanjeni. Pacijenti sa dijabetesom tipa 1 pokazali su povećanje eritrocita, Hct, leukocita, limfocita ($p<0,05$) i koncentracije glukoze ($p<0,01$), u poređenju sa kontrolnom.

0.28,1.32+/–0.50 U/mmol creatinine. The mean urinary NAG and γ-GT values in RA patients was found to be a significant higher ($p< 0.01$) compared to the mean values in seronegative RA patients and normal healthy subjects when analysed by one way ANOVA. In patients who were treated with Methatrexat and Decortin the serum Cystatin C concentration showed significantly elevated values in the therapeutic days (2.85+/– 0.56; v.c.g. 0.70 +/–0.50 mg/L). Urinary albumin concentration increased, but not significantly in the first days of treatment. Determination of the urinary enzymes β-NAG and γ-GT, as well as the serum concentration of Cystatin C me therefore serve a more sensitive test for kidney injury in patients with Rheumatoid arthrit.Early detection of high NAG enzymuria and elevated albumin levels in urine before the initiation of MTX therapy could be helpful in predicting possible MTX toxicity probably related to impaired renal clearence of MTX.

E84
DIFFERENCES IN HEMATOLOGY PARAMETERS IN DIABETIC PATIENTS

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This study is related to the investigation differences in hematology parameters in patients with diabetes mellitus (type 1 and type 2). Few studies relating good control of diabetes mellitus and thrombocyte number, or the control of the function of blood cells have been reported so far. A rise a glycemic control in patients with type 2 diabetes causes a reduction in thrombogenicity. Good glycemic control can help in the correlation of increased coagulability. In this study erythrocyte, leukocyte and thrombocyte counts were investigated, as well as other parameters for differentiating between the two types of diabetes (type 1 N=160, type 2 N=180) in relation to a control population. Blood samples (K_3EDTA) from two diabetic and one control group (N=50) with reference values for glucose were used in this study. The glucose concentration was analyzed with the GOD method and hematologic parameters with the »Sysmex KX-21« and »PENTRA 120« analyzers. Our results showed an increase in hematocrit, leukocyte, lymphocyte and monocyte number in diabetic patients, while MCV, MCH (affected by the glucose concentration) and neutrophils number were decreased. Patients with type 1 diabetes showed an increase in erythrocytes, Hct, leukocytes, lymphocytes ($p<0.05$)

Hematokrit i trombociti su značajno povišeni ($p<0,05$), dok su neutrofili i monociti sniženi ($p<0,05$) kod pacijenata sa dijabetesom tipa 2 u poređenju sa dijabetesom tipa 1.

and glucose ($p<0.01$) concentration compared with the control. Hematocrit and thrombocytes are significantly increased ($p<0.05$) while neutrophils and monocytes are decreased ($p<0.05$) in patients with type 2 diabetes in relation to type 1 diabetes.

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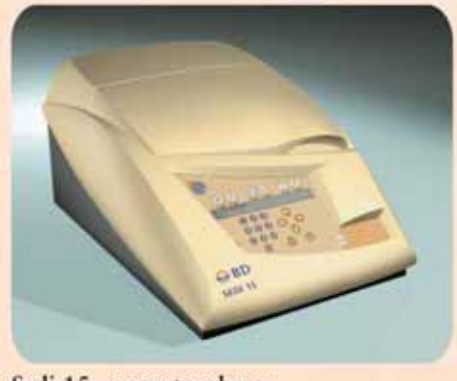

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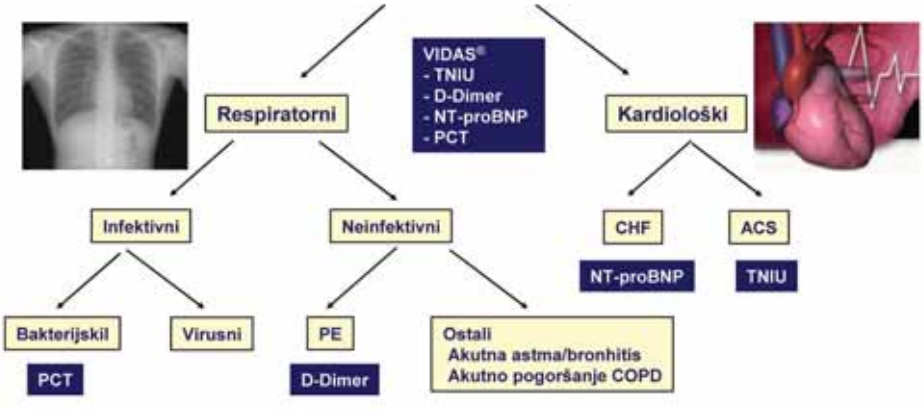

SOB: shortness of breath (otežano disanje)
CHF: congestive heart failure (kongestivni srčani zastoj)
ACS: acute coronary syndromes (akutni koronarni sindromi)
PE: pulmonary embolism (plućna embolija)
COPD: chronic obstructive pulmonary disease (hronična opstruktivna plućna bolest)

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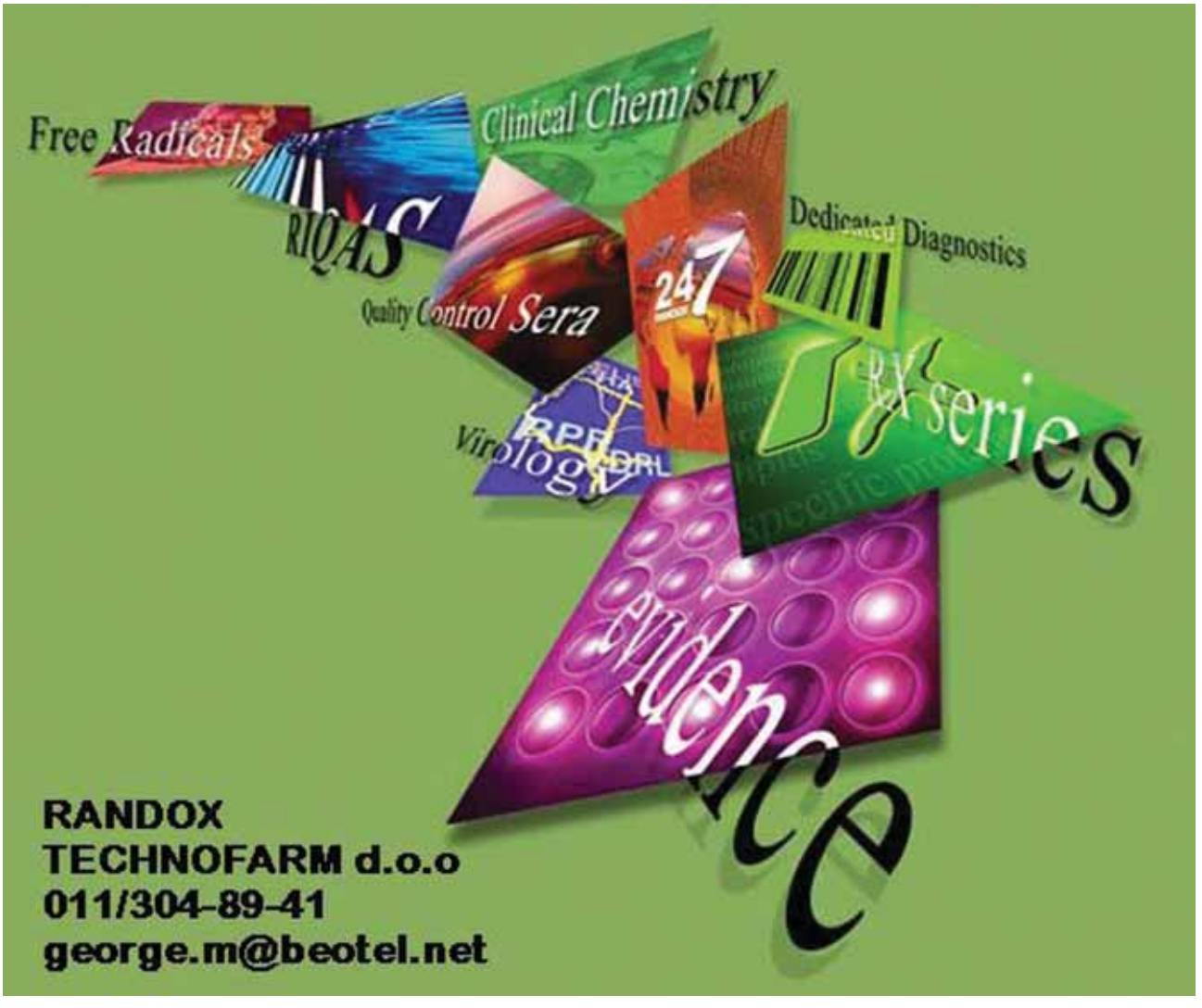
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TEST-TRAKE ZA ANALIZU URINA

URiSCAN

Urinske trake omogućavaju brz i pouzdan dokaz patoloških promena u sastavu urina.

Rutinska analiza urina test-trakama je prvi korak u uspostavljanju dijagnoze što omogućuje kasnije selektivno ispitivanje kvantitativnim laboratorijskim testovima. Istovremeno test-trake su sredstvo izbora prilikom većih kampanja u preventivnoj medicini (razne vrste sistematskih pregleda i sl.).

Reagensi su impregnirani u test-zoni koja omogućuje dobru penetraciju urina što osigurava dobar razvoj obojenja prilikom hemijske reakcije.

Test zona ima dimenzije 5x5 mm što omogućava dobru vidljivost.
Promene boja su jasne i pri najmanjim gradacijama se uočavaju.

Upotreba je veoma jednostavna:

-necentrifugirani urin se sipa u čiste i suve posude i dobro se promeša pre upotrebe
-uzeti test-traku iz bočice i bočicu ponovo dobro zatvoriti
-traku u potpunosti ne duže od jedne sekunde uroniti u urin

-višak urina odstraniti na papirnoj vati tako što se ivica trake lagano obriše o papirnu vatu

-očitavanje se vrši posle 60 sekundi (izuzev leukocita 90-120 sekundi) tako što se obojenje na traci uporedi sa skalom boja na bočici; sigurniji način očitavanja je na analizatoru urina.

Sve URISCAN trake poseduju evropsku oznaku kvaliteta **CE** i imaju dozvolu za stavljanje u promet izdatu u Agenciji za lekove i medicinska sredstva Srbije.

URISCAN TRAKE NUDE RAZLIČITE KOMBINACIJE PARAMETARA:

Ime proizvoda	Krv	Bilirubin	Urobilinogen	Ketoni	Proteini	Nitriti	Glukoza	pH	Specifična težina	Leukociti	Askorbinska kiselina	Veličina pakovanja
URISCAN GLUKETO				■			■					50
URISCAN HEMOKETO	■			■	■		■	■				100
URISCAN GEN 9SG	■	■	■	■	■	■	■	■	■			100
URISCAN GEN 10SGL	■	■	■	■	■	■	■	■	■	■		100
URISCAN 11 STRIP	■	■	■	■	■	■	■	■	■	■	■	100

URiSCAN PRO II

- **-kapacitet :** 720 testova/h (po jedan uzorak na svakih 5 sekundi)
- **-memorija :** do 1 000 poslednjih merenja
- -očitavanje boje i bistrine urina
- -displej sa auto alarmom
- -interni štampač, mogućnost povezivanja sa eksternim štampačem
- -analizator se može povezati u kompjuterski sistem zdravstvene ustanove
- **-dimenzije :** 465 x 400 x 246 mm, težina 7 kg

UVOZNIK:

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PRIMAX d.o.o. Vodovodska 158a 11000 Beograd
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BIOHEMIJSKI ANALIZATOR

RT-1904C

Ovaj aparat, iako mali i jednokanalni, poseduje sve osobine velikih analizatora. U prvom redu njegov softver značajno je drugačiji od ostalih aparata u njegovoj klasi, u prvom redu mislimo na organizaciju programa, koja korisniku pruža velike mogućnosti, a da pritom rad na aparatu čini jednostavnim i preglednim.
Pored toga RT-1904 odlikuje se i velikom pouzdanošću što je postignuto ugradnjom proverenih, mehaničkih komponenti koje su se do sada pokazale više nego dobre.

ProMedia je zastupnik italijanske firme Globe diagnostics, koja se bavi proizvodnjom reagenasa za kliničku biohemiju

MicroTest 1, AliFax

MicroTest 1 i ostali aparati iz grupe Test 1 proizvođača AliFax određuju sedimentaciju eritrocita metodom agregacije, iz uzorka zapremine 30ul, za samo 20 sec, i uz upotrebu EDTA kao antikoagulansa.
Ovakvim određivanjem sedimentacije izbegnut je uticaj velikog broja najrazličitijih faktora koji utiču na tačnost i preciznost rezultata, znatno je skraćeno vreme izvođenja ovog testa.
Nabrojane prednosti, stotine uporedo odrađenih testova sa svim komercijalno prisutnim sistemima na našem tržištu, veliki broj instaliranih aparata porodice Test 1 širom sveta, dali su našem radu potpuni smisao i uverenje da je ovakav način određivanja sedimentacije preko vremena agregacije metoda izbora za kliničke laboratorije.

ELISA SISTEM

ProMedia u svojoj ponudi ima nekoliko izvanrednih ELISA sistema koji svojim tehničkim karakteristikama mogu da odgovore zahtevima svih korisnika.
Za male laboratorije tu je poluautomatski sistem sa odvojenim
"reader-om" i "washer-om"
dok za velike laboratorije, predlažemo nabavku PersonalLab, već godinama najprodavanijeg automatskog ELISA sistema na svetu

Hematološki brojači proizvođača DIAGON

- 3-part i 5-part diff hematološki brojači
- Napredni upravljački softver za jednostavno rukovanje
- Pouzdani i precizni
- Niska potrošnja reagenasa
- Ne zahtevaju održavanje

ProMedia je generalni distributer i zastupnik vodećih svetskih proizvođača biohemijskih i ELISA testova (Fujirebio, EUROIMMUN, IBL, Adaltis, The Binding Site, DSL, Biomerica, LDN, Trinity Biotech, Immunodiagnostic, R&D...) i potrošnog materijala za laboratorije (Deltalab, Vitrex...) i urinskih traka E77

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