

International publications of authors from Bosnia and Herzegovina in Current Contents indexed publications in 2007

1. Simunovic VJ, Hren D, Ivanis A, Dørup J, Krivokuca Z, Ristic S, Verhaaren H, Sonntag HG, Ribaric S, Tomic S, Vojnikovic B, Seleskovic H, Dahl M, Marusic A, Marusic M. Survey of attitudes towards curriculum reforms among medical teachers in different socio-economic and cultural environments. *Med Teach.* 2007;29(8): 33-5.

Mostar University School of Medicine, Bosnia and Herzegovina.

BACKGROUND: Curriculum reforms in medical schools require cultural and conceptual changes from the faculty. **AIMS AND METHODS:** We assessed attitudes towards curriculum reforms in different academic, economic, and social environments among 776 teachers from 2 Western European medical schools (Belgium and Denmark) and 7 medical schools in 3 countries in post-communist transition (Croatia, Slovenia, Bosnia and Herzegovina). The survey included a 5-point Likert-type scale on attitudes towards reforms in general and towards reforms of medical curriculum (10 items each). **RESULTS:** Teaching staff from medical schools in Bosnia and Herzegovina had a more positive attitude towards reforms of medical curriculum (mean score 36.8 out of maximum 50 [95% CI 36.1 to 37.3]) than those from medical schools in Croatia or Slovenia (30.7 [29.8 to 31.6]) or Western Europe (27.7 [27.1 to 28.3]) ($P < 0.001$, ANOVA). Significant predictors of positive attitudes towards medical curriculum reform in post-communist transition countries, but not in Western European schools, was younger age, as well as female gender in Bosnia and Herzegovina. **CONCLUSIONS:** Factors influencing faculty attitudes may not be easy to identify and may be specific for different settings. Their identification

and management is necessary for producing sustainable curriculum reform.

2. Brekalo Z, Kvesić A, Galić G, Kukić-Brusić S, Martinović V, Jonovska S. Burkitt's lymphoma in the boy: infiltration in the stomach, colon and the retroperitoneum-ileocecal invagination. *Coll Antropol.* 2007;31(4):1183-6.

Clinic of Surgery and Urology, University Hospital, Mostar, Bosnia and Herzegovina.

A 4-year-old boy was hospitalised because showing signs of weakness, slight pain in the abdomen and while urinating. The symptoms occurred 7 days before hospitalisation. The boy did not vomit, nor did he have the urge to vomit, the defecation was regular showing no traces of blood. The physical visit a soft and painless tumefaction was confirmed ileoceally. The echography tests and the computed tomography suggested invagination, not excluding the second substrate. Barium enema showed irreducible invagination. The operative test showed that it was about the ileocolic invagination with extreme thickening of the cecum, the ascendant colon, the intestine and the retroperitoneum walls. A resection of the small intestine and a ileocolic anastomosis was performed. The pathological test shows the primary abdominal Burkitt's lymphoma. In spite of the subsequent therapy the boy dies three weeks after the first symptoms' manifestation. We, herewith, suggest at the importance of the echography analysis when diagnosing the Burkitt's tumor and give advantage to this analysis against the computerized tomography. We also point at the huge level of malignancy of the Burkitt's tumor in this boy.

3. Uzunović-Kamberović S, Zorman T, Heyndrickx M, Smole Mozina S. Role of poultry meat in sporadic Campylobacter infections in Bosnia and Herzegovina: laboratory-based study. Croat Med J. 2007;48(6):842-51.

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AIM: To investigate genetic diversity and specificity of Campylobacter jejuni and Campylobacter coli strains isolated from humans, retail poultry meat, and live farm chickens in Zenica-Doboj Canton, Bosnia and Herzegovina, and identify the role of poultry meat in sporadic Campylobacter infections. METHODS: We determined the type of Campylobacter species using standard microbiological methods and multiplex polymerase chain reaction (PCR), and performed pulsed field gel-electrophoresis (PFGE) and restriction fragment length polymorphism (RFLP) typing of the flaA gene to investigate genetic diversity among the isolates. RESULTS: We isolated C jejuni and C coli from 75 (5.2%) of 1453 samples of consecutive outpatients with sporadic diarrhea; from 51 (34.7%) of 147 samples of poultry meat; and from 15 out of 23 farm chicken samples. The proportion of C coli found among human (30.1%), poultry meat (56.9%), and farm chicken isolates (53.3%), was greater than the proportion of C jejuni. Fourteen and 24 PFGE genotypes were identified among 20 C coli and 37 C jejuni isolates, respectively. Identical PFGE genotypes were found in two cases of human and poultry meat isolates and two cases of poultry meat and farm chicken isolates. CONCLUSION: Only a minority of human Campylobacter isolates shared identical PFGE type with poultry meat isolates. Although poultry is the source of a certain number of human infections, there may be other more important sources. Further research is required to identify the environmental reservoir of Campylobacter spp responsible for causing human disease and the reason for the high prevalence of C coli human infections in this region.

4. Tahirovic H, Toromanovic A, Bacaj D, Hasanovic E. Ketoacidosis at onset of type 1 diabetes mellitus in children in Bosnia and Herzegovina: frequency and clinical presentation. J Pediatr Endocrinol Metab. 2007;20(10):1137-40.

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5. Redžić SS. The ecological aspect of ethnobotany and ethnopharmacology of population in Bosnia and Herzegovina. Coll Antropol. 2007;31(3): 869-90.

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This paper contains first systematical revision of the results on traditional use of wild medicinal and aromatic herbs on the territory of Bosnia and Herzegovina (B&H)--west of Balkan Peninsula; Southeast of Europe. There have been detected 227 plants belonging to 71 different plant families, which are being used with ethno therapeutic purpose. Results were obtained by method of open ethno botanical interview which comprised 150 persons, whose average age was 63. Medicinal plants in ethno therapy are being used either in fresh, raw or dried condition. Different herbal parts, depending on period of vegetation season, sometimes even in winter, are basis for preparation of infusions (59%), decoct (19%), tinctures (4%). Especially original are balms known as Bosnian "mehlems", which are fresh cutted herbal parts mixed with lukewarm resin, raw cow butter or honey. In ethno therapy are mostly being used aerial plant organs. Majority of herbs is being used for treatment of illnesses of respiratory (22%), gastrointestinal (19%) and urinary and genital system (9%), for treatment of skin conditions (11%), as well as for nervous system and heart diseases (16%). The most original plants on the field of ethno pharmacology, comparing with ethno therapy practice of other regions, are as follows: Ballota nigra, Aesculus hippocastanum, Calluna vulgaris, Centaurea cyanus, Euphrasia rostkoviana, Geranium robertianum, Gentiana asclepiadea, Helichrysum italicum, Lycopodium clavatum, Marrubium vulgare, Nepeta cataria, Populus tremula, Ruta graveolens, Tamus communis, Teucrium montanum, T. chamaedrys, and endemic plants Gentiana lutea subsp. symphyandra, Teucrium arduini, Micromeria thymifolia, Satureja montana, S. subspicata, Rhamnus fallax and Viola elegantula. There haven't been noticed significant differences in the frequencies of medicinal plants use among different ethnical groups. But, it has been perceived that longer ethno therapeutic tradition possess inhabitants of sub- and Mediterranean areas, as well as inhabitants of the mountain areas of B&H, regardless their ethnicity.

6. Tahirovic I, Sofic E, Sapcanin A, Gavrankapetanovic I, Bach-Rojecky L, Salkovic-Petrusic M, Lackovic Z, Hoyer S, Riederer P. Brain antioxidant capacity in rat models of betacytotoxic-

induced experimental sporadic Alzheimer's disease and diabetes mellitus. J Neural Transm Suppl. 2007; (72):235-40.

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It is believed that oxidative stress plays a central role in the pathogenesis of metabolic diseases like diabetes mellitus (DM) and its complications (like peripheral neuropathy) as well as in neurodegenerative disorders like sporadic Alzheimer's disease (sAD). Representative experimental models of these diseases are streptozotocin (STZ)-induced diabetic rats and STZ-intracerebroventricularly (STZ-icv) treated rats, in which antioxidant capacity against peroxy (ORAC(-ROO)*) and hydroxyl (ORAC(-OH)*) free radical was measured in three different brain regions (hippocampus, cerebellum, and brain stem) by means of oxygen radical absorbance capacity (ORAC) assay. In the brain of both STZ-induced diabetic and STZ-icv treated rats decreased antioxidant capacity has been found demonstrating regionally specific distribution. In the diabetic rats these abnormalities were not associated with the development of peripheral diabetic neuropathy. Also, these abnormalities were not prevented by the icv pretreatment of glucose transport inhibitor 5-thio-D-glucose in the STZ-icv treated rats, suggesting different mechanism for STZ-induced central effects from those at the periphery. Similarities in the oxidative stress alterations in the brain of STZ-icv rats and humans with sAD could be useful in the search for new drugs in the treatment of sAD that have antioxidant activity.

7. Pranjic N, Brkovic A, Beganlic A. Discontent with financial situation, self-rated health, and well-being of adolescents in Bosnia and Herzegovina: cross-sectional study in Tuzla Canton. Croat Med J. 2007;48(5):691-700.

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AIM: To examine the relationship between quality of life, self-rated health, and well-being and to establish the relationship between discontent with familial financial situation and health in adolescents living in the Tuzla Canton. **METHOD:** The study comprised a random sample of 356 high school students aged 16, coming from 15 different classes of 16 high schools in the Tuzla municipality. Data were obtained using a validated self-reporting questionnaire on demographic and socioeconomic background, structure, and dynamics of the adolescent's family, life-style, perception, and satisfaction with the financial situation and

current health status, as well as social relationships and health care provided in school settings. **RESULTS:** In 11% (n=40) of students' households several poverty indicators were present. Twenty three percent (n=82) of the examinees were dissatisfied with the financial situation in their families, and 73% of them came from local, non-refugee families. They presented with progressive symptoms of unhappiness and expressed discontent with their health condition, and even self-hate in comparison with adolescents who were satisfied with the financial situation in their families ($\chi^2=21.5$; $P=0.001$). The prevalence of self-rated mental symptoms was significantly lower among adolescents who were satisfied with their financial situation than in those who were dissatisfied (symptoms of depression 57/274 vs 40/82, $P=0.001$; sadness 73/274 vs 45/82, $P=0.001$; moroseness 34/274 vs 19/82, $P=0.001$; under-sedation 29/274 vs 18/82, $P=0.001$; bad marks and school failures 31/274 vs 20/82, $P=0.001$; suicidal attempts 11/274 vs 7/82, $P=0.001$, respectively). Using linear regression analysis we found that adolescents' satisfaction with the financial situation was a major factor predicting depression (OR, 1.57; 95% CI, 1.158-1.855), loss of appetite (OR, 0.82; 95% CI, 0.561-1.235), distraction (OR, 1.19; 95% CI, 0.837-1.154), unhappiness (OR, 1.05; 95% CI, 0.686-1.405), and inability to perform at school as expected (OR, 1.24; 95% CI, 0.903-1.581). **CONCLUSION:** Discontent with the financial situation significantly reduces the quality of mental health, leads to inappropriate patterns of behavior, and endangers future perspectives and well-being of adolescents.

8. Zaciragic A, Leparo O, Valjevac A, Arslanagic S, Fajkic A, Hadzovic-Dzuvo A, Avdagic N, Alajbegovic A, Mehmedika-Suljic E, Coric G. Elevated serum C-reactive protein concentration in Bosnian patients with probable Alzheimer's disease. J Alzheimers Dis. 2007;12(2):151-6.

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Studies indicate that inflammatory mechanisms may play an important role in the pathogenesis of Alzheimer's disease (AD). C-reactive protein (CRP), marker and mediator of inflammation, has been detected in lesions typical for the affected areas of AD brain. There have been conflicting reports on serum CRP concentration in AD. Scarce data exist on association of CRP and measures of adiposity in AD patients. Thus, we investigated serum CRP concentration in fifteen overweight institutionalized patients with probable AD and fifteen age-matched control subjects. Body mass index (BMI) and waist/hip ratio (WHR) were calculated for

each subject included in the study. Age, systolic and diastolic blood pressure, BMI and WHR did not differ significantly between the two groups. Serum CRP concentration was significantly higher in patients with AD compared to controls ($p < 0.0001$). Although not significant, positive correlations between serum levels of CRP and BMI and WHR were found. Obtained results support the notion that low-grade inflammation is present in patients with AD. Absence of significant association between CRP and measures of total and central adiposity in overweight AD patients needs further investigation and explanation.

9. Redžić A, Hadžihalilović J. Influence of some socio-economic factors on growth and development of the boys in the Tuzla region (Bosnia and Herzegovina). Coll Antropol. 2007;31(2):427-34.

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The impact of certain exogenous factor (socio-economic, ecological) has been investigated with special attention paid to the parents' living standard, and number of family members on some anthropometric parameters like: body height, body mass, chest circumference, upper leg circumference, upper arm circumference, sitting height, arm length, leg length, pelvis width, shoulders width, length of head and width of head on the sample of 698 boys aged 11 to 16 (17) years in the Tuzla region (the northeastern Bosnia, Western Balkan peninsula). Anthropometric measurements have been carried out using methodology proposed by the International Biological program (IBP). The results of these investigations have shown that there is a certain impact of the socio-economic conditions on the growth and development of boys. Children from families that have better living standard are, as a rule, taller, which is indicated by the statistical significant differences ($P > 0.01$). This trend indicates also value of Body Mass Index (BMI), which is in younger children from the families with lower living standard 16, while in the same category in the children from the families with better living standard it has value 18.5. The real impact of living conditions on the dynamics of development could be the best seen in the period of puberty. The number of children in the family has negative relationship with anthropometric features. Statistically significant differences ($P > 0.001$) have been detected in numerous analysed features in families with one or two children in comparison with families with three, four, or five children. Therefore, BMI has been significantly lower (16) in children from families with several children, while in the families with one child in the same growth class (11 years) it was significantly higher (17.4). Similar value of BMI (17.9) have chil-

dren from the families with five children and which are 17 years old. Besides socio-economic conditions, high level of environmental pollution which is typical for Tuzla region for a long time, has also significant impact on the growth and development of children.

10. Klupka-Sarić I, Ristić S, Sepčić J, Kapović M, Peterlin B, Materljan E, Jurisić T, Mamić DM, Burina A, Sulentić V. Epidemiology of multiple sclerosis in western Herzegovina. Clin Neurol Neurosurg. 2007;109(9):779-83.

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OBJECTIVES: To determine epidemiological rates of multiple sclerosis (MS) in western Herzegovina. **PATIENTS AND METHODS:** We analysed data from 81 MS patients (49 females, 32 males) on the prevalence day, 31 December 2003. Patient information was obtained from a search of all available medical records from the period 1994-2003 in the investigated area. **RESULTS:** Crude prevalence of MS was 27/100,000 (95% confidence interval (CI) 20-34). Prevalence was highest in the mountainous municipality of Posusje (56/100,000) and lowest in the coastal municipality of Neum (0 incidence). The annual incidence of MS was 1.6/100,000 (95% CI 0-3.3). The female/male ratio of MS was 1.5. The mean age of the patients on prevalence day was 40.0±11.6 years, and the mean age at disease onset was 31.0±7.1 years. Eight (10%) of the patients had a first-degree relative with MS. The primary progressive (PP) disease course was observed only in females. Visual symptoms were the initial symptom of MS in 6 (7%) of the patients. **CONCLUSIONS:** Western Herzegovina is an area of moderate risk for MS, and the distribution of MS in western Herzegovina is heterogeneous. PP-MS occurred only in females, and involvement of the visual pathways as the initial symptom of MS was low.

11. Zerem E, Hadžić A. Sonographically guided percutaneous catheter drainage versus needle aspiration in the management of pyogenic liver abscess. AJR Am J Roentgenol. 2007;189(3):W138-42.

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OBJECTIVE: The purpose of this study was to determine the effectiveness of percutaneous catheter drainage (PCD) and to compare PCD with percutaneous needle aspiration in the management of liver abscess. **SUBJECTS AND METHODS:** Sixty patients with pyogenic liver abscess were randomly assigned to two groups in a prospective study. Antibiotics were

administered for 10 days, starting the day of the beginning of percutaneous treatment. One group was treated with sonographically guided PCD and the other group with repeated percutaneous needle aspiration. Percutaneous needle aspiration was attempted a maximum of three times. Lack of response to the third aspiration was considered failure of treatment; these patients were treated with PCD but were not included in the PCD group for analysis. Patient demographics, duration of hospital stay, treatment outcome, and complications were analyzed. RESULTS: Percutaneous needle aspiration was successful in 20 (67%) of the 30 patients after one (n = 12), two (n = 7), or three (n = 1) aspirations. PCD was curative in all 30 patients after one (n = 24) or two (n = 6) procedures. All abscesses 50 mm or less in longest diameter were successfully managed, 10 by percutaneous needle aspiration and 12 by PCD. None of patients in the percutaneous needle aspiration group with multiloculated abscesses (n = 5) was successfully treated. Hospital stay did not differ significantly between the groups. There were no complications related to the procedure. CONCLUSION: PCD is more effective than percutaneous needle aspiration in the management of liver abscess. Percutaneous needle aspiration can be used as a valid alternative for simple abscesses 50 mm in diameter or smaller.

12. Marjanović D, Durmić-Pasić A, Bakal N, Haverić S, Kalamujić B, Kovacević L, Ramić J, Pojskić N, Skaro V, Projić P, Bajrović K, Hadziselimović R, Drobnić K, Huffine E, Davoren J, Primorac D. DNA identification of skeletal remains from the World War II mass graves uncovered in Slovenia. Croat Med J. 2007;48(4):513-9.

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AIM: To present the joint effort of three institutions in the identification of human remains from the World War II found in two mass graves in the area of Skofja Loka, Slovenia. METHODS: The remains of 27 individuals were found in two small and closely located mass graves. The DNA was isolated from bone and teeth samples using either standard phenol/chloroform alcohol extraction or optimized Qiagen DNA extraction procedure. Some recovered samples required the employment of additional DNA purification methods, such as N-buthanol treatment. Quantifiler Human DNA Quantification Kit was used for DNA quantification. PowerPlex 16 kit was used to simultaneously amplify 15 short tandem repeat (STR) loci. Matching probabilities were estimated using the DNA View program. RESULTS: Out of all processed samples, 15 remains

were fully profiled at all 15 STR loci. The other 12 profiles were partial. The least successful profile included 13 loci. Also, 69 referent samples (buccal swabs) from potential living relatives were collected and profiled. Comparison of victims' profile against referent samples database resulted in 4 strong matches. In addition, 5 other profiles were matched to certain referent samples with lower probability. CONCLUSION: Our results show that more than 6 decades after the end of the World War II, DNA analysis may significantly contribute to the identification of the remains from that period. Additional analysis of Y-STRs and mitochondrial DNA (mtDNA) markers will be performed in the second phase of the identification project.

13. Huel RL, Basić L, Madacki-Todorović K, Smajlović L, Eminović I, Berbić I, Milos A, Parsons TJ. Variant alleles, triallelic patterns, and point mutations observed in nuclear short tandem repeat typing of populations in Bosnia and Serbia. Croat Med J. 2007;48(4):494-502.

International Commission on Missing Persons, Sarajevo, Bosnia and Herzegovina.

AIM: To present a compendium of off-ladder alleles and other genotyping irregularities relating to rare/unexpected population genetic variation, observed in a large short tandem repeat (STR) database from Bosnia and Serbia. METHODS: DNA was extracted from blood stain cards relating to reference samples from a population of 32800 individuals from Bosnia and Serbia, and typed using Promega's PowerPlex16 STR kit. RESULTS: There were 31 distinct off-ladder alleles were observed in 10 of the 15 STR loci amplified from the PowerPlex16 STR kit. Of these 31, 3 have not been previously reported. Furthermore, 16 instances of triallelic patterns were observed in 9 of the 15 loci. Primer binding site mismatches that affected amplification were observed in two loci, D5S818 and D8S1179. CONCLUSION: Instances of deviations from manufacturer's allelic ladders should be expected and caution taken to properly designate the correct alleles in large DNA databases. Particular care should be taken in kinship matching or paternity cases as incorrect designation of any of these deviations from allelic ladders could lead to false exclusions.

14. Milos A, Selmanović A, Smajlović L, Huel RL, Katzmarzyk C, Rizvić A, Parsons TJ. Success rates of nuclear short tandem repeat typing from different skeletal elements. Croat Med J. 2007;48(4):486-93.

International Commission on Missing Persons, Sarajevo, Bosnia and Herzegovina.

AIM: To evaluate trends in DNA typing success rates of different skeletal elements from mass graves originating from conflicts that occurred in the former Yugoslavia (Bosnia and Herzegovina and Kosovo) during the 1990s, and to establish correlation between skeletal sample age and success of high throughput short tandem repeat (STR) typing in the large data set of the International Commission on Missing Persons. METHOD: DNA extraction and short tandem repeat (STR) typing have been attempted on over 25000 skeletal samples. The skeletal samples originated from different geographical locations where the conflicts occurred and from different time periods from 1992 to 1999. DNA preservation in these samples was highly variable, but was often significantly degraded and of limited quantity. For the purpose of this study, processed samples were categorized according to skeletal sample type, sample age since death, and success rates tabulated. RESULTS: Well-defined general trends in success rates of DNA analyses were observed with respect to the type of bone tested and sample age. The highest success rates were observed with samples from dense cortical bone of weight-bearing leg bones (femur 86.9%), whereas long bones of the arms showed significantly lower success (humerus 46.2%, radius 24.5%, ulna 22.8%). Intact teeth also exhibited high success rates (teeth 82.7%). DNA isolation from other skeletal elements differed considerably in success, making bone sample selection an important factor influencing success. CONCLUSION: The success of DNA typing is related to the type of skeletal sample. By carefully evaluating skeletal material available for forensic DNA testing with regard to sample age and type of skeletal element available, it is possible to increase the success and efficiency of forensic DNA testing.

15. Davoren J, Vanek D, Konjhodžić R, Crews J, Huffine E, Parsons TJ. Highly effective DNA extraction method for nuclear short tandem repeat testing of skeletal remains from mass graves. Croat Med J. 2007;48(4):478-85.

International Commission on Missing Persons, Sarajevo, Bosnia and Herzegovina.

AIM: To quantitatively compare a silica extraction method with a commonly used phenol/chloroform extraction method for DNA analysis of specimens exhumed from mass graves. METHODS: DNA was extracted from twenty randomly chosen femur samples, using the International Commission on Missing Persons (ICMP) silica method, based on Qiagen Blood Maxi Kit, and compared with the DNA extracted by the standard phenol/chloroform-based method. The efficacy of extraction methods was compared by real time polymerase chain reaction (PCR) to measure DNA quantity and the presence of inhibitors and by

amplification with the PowerPlex 16 (PP16) multiplex nuclear short tandem repeat (STR) kit. RESULTS: DNA quantification results showed that the silica-based method extracted on average 1.94 ng of DNA per gram of bone (range 0.25-9.58 ng/g), compared with only 0.68 ng/g by the organic method extracted (range 0.0016-4.4880 ng/g). Inhibition tests showed that there were on average significantly lower levels of PCR inhibitors in DNA isolated by the organic method. When amplified with PP16, all samples extracted by silica-based method produced 16 full loci profiles, while only 75% of the DNA extracts obtained by organic technique amplified 16 loci profiles. CONCLUSIONS: The silica-based extraction method showed better results in nuclear STR typing from degraded bone samples than a commonly used phenol/chloroform method.

16. Zukanović A, Kobaslija S, Ganibegović M. Caries risk assessment in Bosnian children using Cariogram computer model. Int Dent J. 2007;57(3):177-83.

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AIM: To examine caries risk using the Cariogram model, interactive PC program for caries risk evaluation in 12-year-old children and to correlate caries risk in children of different socioeconomic backgrounds. MATERIAL AND METHODS: 109, Sarajevo 12-year-olds in three groups based on socioeconomic background. Baseline data on general health condition, diet frequency and use of fluoride were obtained. DMFT and plaque scores were calculated. Saliva analyses included lactobacillus and mutans streptococci levels in saliva, saliva secretion and buffer capacity. Scores were entered into the Cariogram model and risk was calculated for each child. RESULTS: Most 12-year-old children have a medium risk of caries, with a 59.4% chance of avoiding future caries. In an average caries risk profile of children from Sarajevo the dominant sector is diet, with 12.5% risk; bacteria sector (plaque and mutans streptococci level) 10.8% risk; susceptibility (fluoride, saliva secretion and buffering capacity) 9.7% risk; circumstances (caries experience and medical history) 7.4% risk. Caries risk profiles showed that there are differences in the socioeconomic status of children with significantly greater risk in children with poor living conditions who also have the most unfavourable caries risk profiles. CONCLUSIONS: The Cariogram model can successfully determine caries risk profiles for 12-year-old children of different socioeconomic status and can be used in developing preventive strategies for reducing caries risk in children.

17. Vranić S, Bilalović N, Lee LM, Kruslin B, Lilleberg SL, Gatalica Z. PIK3CA and PTEN mutations in adenoid cystic carcinoma of the breast metastatic to kidney. Hum Pathol. 2007;38(9):1425-31.

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Adenoid cystic carcinoma (ACC) of the breast rarely metastasizes and has been associated with excellent prognosis. We describe a patient with renal metastasis of primary breast ACC 5 years after the mastectomy. A detailed molecular genetic analysis of the primary and metastatic tumors demonstrated somatic mutations in 2 well-known cancer genes associated with regulation of PI3K/AKT signaling pathway: (1) PIK3CA, which encodes the catalytic alpha subunit of the phosphoinositide-3-kinase, and (2) PTEN, which encodes phosphatase and tensin homolog. The mutation identified in PIK3CA (Ex1+169 A>C) predicts an amino acid change from isoleucine to methionine at codon 31 (I31M) and resides in the p85-binding domain of exon 1. The mutation identified in PTEN (IVS4-3 C>T) resides in intron 4 near the splice acceptor site of exon 5 and was associated with an aberrant PTEN transcript lacking exon 5, which is necessary for protein tyrosine phosphatase function and tumor suppressor properties of PTEN. Increased promoter methylation of PTEN was present in renal metastasis, coinciding with the decrease in the level of normal PTEN transcript. These coexistent mutations/epigenetic inactivations in PI3K/AKT pathway may be responsible for the unusually aggressive course of ACC.

18. Tahirovic I, Sofic E, Sapcanin A, Gavrankapetanovic I, Bach-Rojecky L, Salkovic-Petrisic M, Lackovic Z, Hoyer S, Riederer P. Reduced brain antioxidant capacity in rat models of betacytotoxic-induced experimental sporadic Alzheimer's disease and diabetes mellitus. Neurochem Res. 2007;32(10):1709-17.

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It is believed that oxidative stress (OS) plays a central role in the pathogenesis of metabolic diseases like diabetes mellitus (DM) and its complications (like peripheral neuropathy) as well as in neurodegenerative disorders like sporadic Alzheimer's disease (sAD). Representative experimental models of these diseases are streptozotocin (STZ)-induced diabetic rats and STZ-intracerebroventricularly (STZ-icv) treated rats, in which antioxidant capacity (AC) against peroxyl (ORAC(-ROO) (*)) and hydroxyl (ORAC(-OH)

(*)) free radicals (FR) was measured in three different brain regions: the hippocampus (HPC), the cerebellum (CB), and the brain stem (BS) by means of oxygen radical absorbance capacity (ORAC) assay. In the brain of both STZ-induced diabetic and STZ-icv treated rats decreased AC has been found demonstrating regionally specific distribution. In the diabetic rats these abnormalities were not associated with the development of peripheral diabetic neuropathy (PDN). Also, these abnormalities were not prevented by the intracerebroventricularly (icv) pretreatment of glucose transport inhibitor 5-thio-D: -glucose (TG) in the STZ-icv treated rats, suggesting different mechanism of STZ-induced central effects from those at the periphery. Similarities of the OS alterations in the brain of STZ-icv rats and humans with sAD could be useful in the search for the new drugs in the treatment of sAD that have antioxidant activity. In the STZ-induced diabetic animals the existence of PDN was tested by the paw pressure test, 3 weeks following the diabetes induction. Mechanical nociceptive thresholds were measured three times at 10-min intervals by applying increased pressure to the hind paw until the paw-withdrawal or overt struggling was elicited. Only those diabetic animals which demonstrated decreased withdrawal threshold values in comparison with the control non-diabetic animals (C) were considered to have developed the PDN.

19. Brekalo Z, Kvesić A, Nikolić H, Tomić D, Martinović V. Snodgrass' urethroplasty in hypospadias surgery in Clinical Hospital Mostar-preliminary report. Coll Antropol. 2007;31(1):189-93.

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Amongst the various methods of reconstructing the hypospadiac urethra such as the MAGPI, Mathieu's and Preputial island flap urethroplasty method and the Snodgrass method, the latter is being used more frequently nowadays in patients with the urethral meatus located in the proximity of the penis. In the Pediatric ward at Mostar Clinical Hospital, we have recently adopted the Snodgrass method when reconstructing the hypospadiac urethra. We herewith present our research regarding the successful results in adopting the aforementioned method. Success was evaluated according to the frequency of post-operative complications, as well as the patients' satisfaction with the functional and the cosmetic result of the urethra reconstruction. The conclusions relating to our research result in an addition basis from which to evaluate whether the Snodgrass method should receive privileged preference in future operative treatment of the hypospadias over others methods, as can be seen from our research.

20. Uzunovic-Kamberovic S, Bedenic B, Vranes J. Predominance of SHV-5 beta-lactamase in enteric bacteria causing community-acquired urinary tract infections in Bosnia and Herzegovina. Clin Microbiol Infect. 2007;13(8):820-3.

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The beta-lactamases produced by 14 non-duplicate *Klebsiella pneumoniae* isolates and five *Escherichia coli* isolates from urine samples obtained from outpatients were characterised by isoelectric focusing, substrate profile determination, PCR and sequencing of bla(SHV) genes. Three *E. coli* A15 R(+) transconjugants were identified as isolates that produced SHV-5 beta-lactamase. This report is the first description of SHV-5 beta-lactamase among community isolates. Since the isolates showed distinct pulsed-field gel electrophoresis patterns, it was concluded that there was no clonal spread of bla(TEM) and bla(SHV) genes, and that dissemination of the bla(TEM) and bla(SHV) genes was the result of exchange of plasmids among different clones.

21. Ibrulj S, Rahmanovic A, Haveric S, Haveric A, Pasic AD. Cytogenetic evaluation of paracetamol effects in human lymphocytes culture. Drug Chem Toxicol. 2007;30(2):133-43.

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Paracetamol is a common analgesic and antipyretic drug. It has been recognized as one of the most ordinary medications taken in overdoses. We examined the possible genotoxic effects of high paracetamol concentrations expected to occur after overdose. Paracetamol was added to the cultures at the beginning of the cultivation period. Separate cultures for three tested concentrations of paracetamol (50 microg/mL, 100 microg/mL, and 200 microg/mL) were set. Effects of paracetamol were evaluated by micronucleus cytokinesis-block assay, chromosome aberration analysis, and nuclear division index. Results demonstrate that paracetamol concentration of 200 microg/mL expresses certain genotoxic effects in human peripheral blood lymphocytes.

22. Pilav A. A view from Bosnia and Herzegovina. Interview by Emma Wilkinson. Circulation. 2007; 24;115(16):f73-4.

23. Rifatbegović M, Assunção P, Poveda JB, Pasić S. Isolation of *Mycoplasma bovis* from the respiratory tract of cattle in Bosnia and Herzegovina. Vet Rec. 2007;160(14):484-5.

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24. Brkić F, Umihanić S. Tracheobronchial foreign bodies in children. Experience at ORL clinic Tuzla, 1954-2004. Int J Pediatr Otorhinolaryngol. 2007;71(6):909-15.

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OBJECTIVE: To determine the clinical characteristics and the results of bronchoscopic treatment of children due to foreign body aspiration in a university hospital. **SETTING:** Department of Otorhinolaryngology and Maxillofacial Surgery, University Clinical Center Tuzla, Bosnia and Herzegovina. **METHOD:** The analysis of the cases of aspirated foreign bodies within the period from January 1954 to December 2004. The analyzed patients were the children up to 14 years of age. All cases underwent the bronchoscopy. Each patient was analyzed for age, sex, nature and location of the foreign body, results of bronchoscopic removal, complications of bronchoscopy and presence of foreign bodies in the airways. **RESULTS:** Six hundred and sixty-two children who underwent bronchoscopy for removal of foreign body in the airways were evaluated. From evaluated children 66.8% were boys, ages ranging from 9 months to 14 years. Foreign bodies were more frequent in children under 3 years of age (65.2%). Most of the foreign bodies removed were organic (87.1%) and more frequently found in the right bronchial tree (53%). **CONCLUSIONS:** More attention is necessary to the prevention of aspirations. Prevention of aspiration of foreign bodies is better than cure. Public awareness through mass media needs attention to prevent foreign body inhalation.

25. Tahirovic H, Imsiragic-Zovko S, Toromanovic A, Begic L. Assessment of the success of implementation of new rule book on salt iodination in Federation of Bosnia and Herzegovina. J Endocrinol Invest. 2007;30(1):9-12.

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The aim of this study was to determine the success of an increase in the level of salt iodization which was

increased to 20-30 mg iodine per kilo of salt, 2 yr after the introduction of the new mandatory salt iodination. This prospective study was performed at level of Federation of Bosnia and Herzegovina (FBH). We singled out 60 cluster school-based surveys (6 cluster surveys in each canton) with equal representation of urban and rural areas. Within each cluster, between 10 to 30 subjects (both males and females) aged 11, 12, 13 and 14 were randomly selected. The study included a total of 962 schoolchildren. The mean iodine level per 1 kg of salt for whole FBH was 21.4+/-5.2. It ranged from 2.1 to 41.3 mg/kg. A significant improvement in urinary iodine excretion medians was detected in the current survey in all cantons and on the entire territory of FBH, compared to results from a previous study conducted in 1999. The urinary iodine excretion in schoolchildren in the whole FBH varied from 50.6 to 303.8 mug/l with a median of 139.5 mug/l. Values of urinary iodine <100.0 mug/l were found in 15.9% of samples of schoolchildren, whereas no values <50.0 mug/l were found. In conclusion, the results of the study indicate that increased iodine supplementation of salt in 2001 was successful and that FBH is presently iodine sufficient. In the future, however, program for monitoring of iodine prophylaxis has to have two major aims: firstly, control of iodine content in salt at different levels especially at retail shops and at imported salt and secondly, iodine deficiency disorders control. Also, a periodic measurement of urinary iodine excretion needs to be planned together with the neonatal TSH screening and the establishment of a notification system for cases of hyperthyroidism.

26. Prohic A, Ozegovic L. Malassezia species isolated from lesional and non-lesional skin in patients with pityriasis versicolor. Mycoses. 2007;50(1):58-63.

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Pityriasis versicolor (PV) is a superficial fungal infection where *Malassezia* species play a definite causative role, but the clinical significance of each of these species is not fully understood. The aim of our study was to analyse the prevalence of *Malassezia* species in PV lesions and to examine if the range of species varies with patient sex, age, direct microscopy findings and some clinical data. Ninety patients with PV completed the study. The samples were obtained by scraping the skin surface, both from lesional and non-lesional skin and then incubated on Sabouraud dextrose agar and modified Dixon agar. The yeast isolated were identified according to their macroscopic and microscopic features and physiological characteristics. In PV lesions, the most common species was *M. globosa* (63%),

followed by *M. sympodialis* (14%), *M. furfur* (10%), *M. obtusa* (8%) and *M. slooffiae* (4%). The most frequently isolated species from clinically healthy skin were *M. globosa* (49%), *M. sympodialis* (37%) and *M. furfur* (5%). We found significant difference in the distribution of *Malassezia* species between lesional and non-lesional skin and in the distribution of *Malassezia* species according to the direct microscopy findings. *M. globosa* in its mycelial phase is the predominant species involved in the aetiology of PV.

27. Salkic NN, Zildzic M, Muminhodzic K, Pavlovic-Calic N, Zerem E, Ahmetagic S, Mott-Divkovic S, Alibegovic E. Intrafamilial transmission of hepatitis B in Tuzla region of Bosnia and Herzegovina. Eur J Gastroenterol Hepatol. 2007;19(2):113-8.

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OBJECTIVE: To determine (i) the prevalence of HBV infection in families of confirmed chronic carriers, (ii) possible routes of transmission and risk factors for the intrafamilial transmission, (iii) vaccination rate among family members of chronic carriers and (iv) family members with highest risk for infection. **METHODS:** A total of 172 family members of 67 hepatitis B surface antigen chronic carriers were tested for hepatitis B markers; 716 first-time blood donors from the same area were used as controls. **RESULTS:** Prevalence of hepatitis B surface antigen was higher (12.2%; 21/172) than among controls (3.6%; 26/716) with relative risk of 3.3 (95% confidence Intervals=1.9-5.8; $P<0.05$). Rate of exposure among family members was 37.8% (65/172); only 8.7% (15/172) had been vaccinated for hepatitis B virus. Difference ($P<0.001$) in exposure existed among family members; exposure increased with age ($\rho=0.34$; $P<0.001$). Prevalences of hepatitis B surface antigen positivity and hepatitis B virus exposure were higher among parents of index cases ($P<0.005$) and among offspring of female index cases ($P<0.001$). There were more ($P<0.001$) hepatitis B surface antigen-positive family members among those with mother-children relationship with index case (13/31; 41.9%) than among those with father-children (19/85; 22.4%) and horizontal (siblings and spouses) relationship (2/56; 3.6%). Significantly more ($P<0.001$) hepatitis B surface antigen-positive and hepatitis B virus-exposed offspring were found in families where only mother was hepatitis B surface antigen positive. Among family members of HBeAg-positive cases more hepatitis B surface antigen-positive cases and hepatitis B virus-exposed cases have been found ($P<0.001$). Combination of HBeAg positivity

and female sex of index case significantly increased risk for chronic carriage among family members (relative risk=24.06; 95% confidence interval=8.88-65.21; $P<0.05$). CONCLUSION: In the area studied, both horizontal and vertical transmission exists, but maternal route is predominant. Female sex, HBeAg positivity of index carrier and presence of hepatitis B surface antigen-positive mother inside family increased risk for hepatitis B surface antigen positivity and exposure among family members. Vaccination rate of family members of index cases is alarmingly low.

28. Bergsland J, Kabil E, Mujanovic E, Terzic I, Røislien J, Svennevig JL, Fosse E. Training of cardiac surgeons for Bosnia and Herzegovina: outcomes in coronary bypass grafting surgery. *Ann Thorac Surg.* 2007;83(2):462-7.

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BACKGROUND: Bosnia and Herzegovina did not have invasive cardiac diagnosis or cardiac surgery before the recent war. With assistance from the United States and Norway, a cardiovascular clinic was developed. This study reports center-specific and surgeon-specific clinical outcomes. Since off-pump coronary bypass grafting surgery was prioritized in the treatment of coronary disease, a comparison was made between operations performed with and without cardiopulmonary bypass. METHODS: Surgeons and key staff members were trained in the United States. A Norwegian data management system for cardiac surgery was implemented and cases entered after quality review of the data. A total of 1276 patients were entered; operations were performed with cardiopulmonary bypass in 540 and without in 736. The primary surgeon was entered as a variable in an anonymous fashion. RESULTS: Overall mortality for coronary bypass grafting surgery was 1.6%, and the major complication rate was 4.5%. Patients operated on off-pump received fewer grafts and had a shorter length of stay. Unfavorable outcome was more common in patients when cardiopulmonary bypass was used in the operation. Regression analysis demonstrated that the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and use of cardiopulmonary bypass were predictors of poor outcome. The individual surgeon factor did not impact on outcomes. CONCLUSIONS: Our study confirms that coronary artery bypass grafting surgery may be performed safely in a poor country in a hospital without experience with cardiac surgery. Selection of talented staff and cooperation with international cardiac centers are crucial. Off-pump coronary artery bypass grafting surgery is

suitable for a new center and does not require more training than standard procedures.

29. Kurić L. The digital language of amino acids. *Amino Acids.* 2007;33(4):653-61.

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The subject of this paper is a digital approach to the investigation of the biochemical basis of genetic processes. The digital mechanism of nucleic acid and protein bio-syntheses, the evolution of biomacromolecules and, especially, the biochemical evolution of genetic language have been analyzed by the application of cybernetic methods, information theory and system theory, respectively. This paper reports the discovery of new methods for developing the new technologies in genetics. It is about the most advanced digital technology which is based on program, cybernetics and informational systems and laws. The results in the practical application of the new technology could be useful in bioinformatics, genetics, biochemistry, medicine and other natural sciences.

30. Jelavic B, Bevanda M, Ostojic M, Leventic M, Vasilj M, Knezevic E. Tonsillar colonization is unlikely to play important role in *Helicobacter pylori* infection in children. *Int J Pediatr Otorhinolaryngol.* 2007;71(4):585-90.

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OBJECTIVE: To determine (i) seroprevalence of *Helicobacter pylori* (HP) infection in children undergoing tonsillectomy, (ii) possible HP colonization on tonsils of children and its importance in HP transmission, and (iii) if four examined socio-economic factors are the risk factors for HP transmission and HP colonization on tonsils in children. METHODS: Rapid urease test (RUT) of tonsils, and serologic blood tests for HP were performed in 77 children (aged 4-14 years) in Bosnia and Herzegovina (B-H), undergoing tonsillectomy. RUT positive tonsils were cultured for HP. RUT positive children were tested using (13)Carbon-urea breath test ((13)C-UBT). Information about socio-economic potential risk factors was obtained from the parents. RESULTS: Out of 139 pharyngeal and palatine tonsils, 17 palatine tonsils in 14 children were RUT positive and had negative HP culture. Eight children had positive both RUT and (13) C-UBT. There was no significant difference between children with hypertrophy and those with recurrent tonsillitis comparing their serologic tests results. There was no significant difference between seronegative (n=61) and

seropositive (n=16) children comparing their age, sex, parental education level, owning a family courtyard, attending a children's collective, and owning a pet cat. CONCLUSIONS: The results in this prospective study do not support the notion that tonsils are an important reservoir for HP transmission in children in B-H. The examined socio-economic factors did not enhance HP seropositivity rate in children.

31. Zerem E, Salkic N, Imamovic G, Terzić I. Comparison of therapeutic effectiveness of percutaneous drainage with antibiotics versus antibiotics alone in the treatment of periappendiceal abscess: is appendectomy always necessary after perforation of appendix? Surg Endosc. 2007;21(3):461-6.

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BACKGROUND: The present study was designed to compare the therapeutic effectiveness of percutaneous drainage with antibiotics versus antibiotics alone in the treatment of appendicitis complicated by periappendiceal abscess. METHODS: In a prospective study, 50 patients with acute appendicitis complicated by periappendiceal abscess > or = 3 cm in size were randomly assigned to two groups. The first group received treatment with ultrasound guided-percutaneous drainage and i.v. antibiotics (ampicillin, cefuroxime, and metronidazole), and the other group received antibiotics only. Patient's baseline characteristics, duration of hospital stay, and treatment outcome and complications were analyzed. RESULTS: Appendectomy was avoided in 16/25 patients in the drainage group and 2/25 patients in the non-drainage group during follow-up with RR of 0.39 (95% CI = 0.22-0.62; p < 0.05). One patient in the drainage group and 8 patients in the non-drainage group underwent surgery in the first month after the beginning of treatment. Eight patients in the drainage group and 15 in the non-drainage group underwent interval appendectomy. There was no statistically significant difference between the two groups regarding patient demographics, abscess size, and pretreatment clinical symptoms. Hospital stay up to the subsidence of clinical and sonographic signs was significantly shorter (p < 0.001) in the drainage group, with a mean difference of 6.4 days (95% CI = 5.0-7.9; p < 0.05). CONCLUSIONS: Percutaneous drainage with antibiotics is a safe and effective way of treating acute perforated appendicitis. The recurrence rate for these patients is relatively low, and very often interval appendectomy is not required. For patients with periappendiceal abscess > or = 3 cm in diameter, antibiotic therapy alone is insufficient and the recurrence rate is high.

32. Kapur E, Vuckovic I, Dilberovic F, Zaciragic A, Cosovic E, Divanovic KA, Mornjakovic Z, Babic M, Borgeat A, Thys DM, Hadzic A. Neurologic and histologic outcome after intraneural injections of lidocaine in canine sciatic nerves. Acta Anaesthesiol Scand. 2007;51(1):101-7.

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BACKGROUND: Inadvertent intraneural injection of local anesthetics may result in neurologic injury. We hypothesized that an intraneural injection may be associated with higher injection pressures and an increase in the risk of neurologic injury. METHODS: The study was conducted in accordance with the principles of laboratory animal care, and was approved by the Laboratory Animal Care and Use Committee. Fifteen dogs of mixed breed (16-21 kg) were studied. After general endotracheal anesthesia, the sciatic nerves (n=30) were exposed bilaterally. Under direct vision, a 25-gauge, long-beveled needle (30 degrees) was placed either epineurally (n=10) or intraneurally (n=20), and 4 ml of preservative-free lidocaine 20 mg/ml was injected using an automated infusion pump (4 ml/min). Injection pressure data were acquired using an in-line manometer coupled to a computer via an analog-to-digital conversion board. After injection, the animals were awakened and subjected to serial neurologic examinations. One week later, the dogs were killed, the sciatic nerves excised and histologic examination was performed by pathologists blind to the purpose of the study. RESULTS: All perineural injections resulted in low pressures (< or = 5 psi). In contrast, eight of 20 intraneural injections resulted in high pressures (20-38 psi) at the beginning of the injection. Twelve intraneural injections, however, resulted in pressures of less than 12 psi. Neurologic function returned to baseline within 3 h after perineural injections and within 24 h after intraneural injections, when the measured injection pressures were less than 12 psi. Neurologic deficits persisted throughout the study period after all eight intraneural injections that resulted in high injection pressures. Histologic examination of the affected nerves revealed fascicular axonolysis and cellular infiltration. CONCLUSIONS: The data in our canine model of intraneural injection suggest that intraneural injections do not always lead to nerve injury. High injection pressures during intraneural injection may be indicative of intrafascicular injection and may predict the development of neurologic injury.

33. Tahirović H, Toromanović A. Incidence of type 1 diabetes mellitus in children in Tuzla Canton between 1995 and 2004. Eur J Pediatr. 2007;166(5):491-2.

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34. Mulaomerović A, Halilbasić A, Cickusić E, Zavasnik-Bergant T, Begić L, Kos J. Cystatin C as a potential marker for relapse in patients with non-Hodgkin B-cell lymphoma. *Cancer Lett.* 2007; 18;248(2):192-7.

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The concentration of cysteine protease inhibitor cystatin C was determined in sera from 59 patients with non-Hodgkin B-cell lymphoma using ELISA. The sera from 43 age and sex matched healthy blood donors served as controls. Cystatin C was significantly increased in sera of patients without therapy (mean 1136+/-SE 105.7ng/ml, p=0.00001) and with therapy (mean 1073+/-52ng/ml, p=0.001) compared to controls (mean 819+/-28ng/ml). The highest levels were determined in sera of patients with a relapse (mean 1680+/-196ng/ml). By using immunofluorescence staining and confocal microscopy we determined immature dendritic cells as a major population of cystatin C positive cells in affected lymph nodes. Our study reports for the first time that cystatin C is a potential marker for relapse in patients with non-Hodgkin B-cell lymphoma.

35. Pilav A, Nissinen A, Haukkala A, Niksic D, Laatikainen T. Cardiovascular risk factors in the Federation of Bosnia and Herzegovina. *Eur J Public Health.* 2007;17(1):75-9.

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BACKGROUND: Federation of Bosnia and Herzegovina (FBiH) has high cardiovascular disease mortality as other countries in Eastern Europe and situation has even deteriorated in the post war period. Reliable information on risk factor levels and patterns needed in prevention planning and disease management has been lacking. **METHODS:** A cross sectional population survey was conducted in the FBiH in autumn 2002. A random sample of population, aged 25-64 years, was taken using a three stage stratified sampling methodology. Altogether, 2750 persons participated in the survey (1121 men and 1629 women). The survey was done according to internationally established standards and protocols. **RESULTS:** The mean systolic blood pressure was 132 mmHg among men and 135 mmHg among women. The mean diastolic blood pressure was 84 mmHg in both genders. Almost 40% of the participants were recognized as hypertensive (blood pressure level over 140/90 mmHg). The prevalence of hypertension among men was 36% and among women 45%. The mean Body Mass Index (BMI) was 26.5 kg/m(2) among males and 27.0 kg/m(2) among females. About 75% of both men and women were overweight (BMI > 25 kg/m(2) and 16% of men and 20% of women were obese (BMI > 30 kg/m(2)). About 50% of men and 30% of women reported to be daily smokers. **CONCLUSIONS:** As a whole the non-communicable disease risk factor levels in the FBiH seems to be relatively high. The data can be utilized in health promotion planning and as a baseline for future monitoring activities with possibility of international comparison of results.

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