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***Barić I, Fumić K, Glenn B, Ćuk M, Schulze A, Finkelstein JD, et al. S-adenosylhomocysteine hydrolase deficiency in a human: a genetic disorder of methionine metabolism. Proc Natl Acad Sci U S A. 2004;101:4234-9.**

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The authors report studies of a Croatian boy, a proven case of human S-adenosylhomocysteine (AdoHcy) hydrolase deficiency. Psychomotor development was slow until his fifth month; thereafter, virtually absent until treatment was started. He had marked hypotonia with elevated serum creatine kinase and transaminases, prolonged prothrombin time and low albumin. Electron microscopy of muscle showed numerous abnormal myelin figures; liver biopsy showed mild hepatitis with sparse rough endoplasmic reticulum. Brain MRI at 12.7 months revealed white matter atrophy and abnormally slow myelination. Hypermethioninemia was present in the initial metabolic study at age 8 months, and persisted (up to 784 microM) without tyrosine elevation. Plasma total homocysteine was very slightly elevated for an infant to 14.5-15.9 microM. In plasma, S-adenosylmethionine was 30-fold and AdoHcy 150-fold elevated. Activity of AdoHcy hydrolase was approximately equal to 3% of control in liver and was 5-10% of the control values in red blood cells and cultured fibroblasts. The authors found no evidence of a soluble inhibitor of the enzyme in extracts of the patient's cultured fibroblasts. Additional pretreatment abnormalities in plasma included low concentrations of phosphatidylcholine and choline, with elevations of guanidinoacetate, betaine, dimethylglycine, and cystathionine. Leukocyte DNA was hypermethylated. Gene analysis revealed two mutations in exon 4: a maternally derived stop codon, and a paternally derived missense mutation. The reasons for biochemical abnormalities and pathophysiological aspects of AdoHcy hydrolase deficiency are discussed.

Četković H, Muller WE, Gamulin V. Bruton tyrosine kinase-like protein, BtkSD, is present in the marine sponge Suberites domuncula. Genomics. 2004;83:743-5.

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Sponges, the simplest and most ancient phylum of *Metazoa*, encode in their genome complex and highly sophisticated proteins that evolved together with multicellularity and are found only in metazoan animals. We report here the finding of a Bruton tyrosine kinase (BTK)-like protein in the marine sponge *Suberites domuncula* (*Demospongiae*). The nucleotide sequence of one sponge cDNA predicts a 700-aa-long protein, which contains all of the characteristic domains for the Tec family of protein tyrosine kinases (PTKs). The highest homology (38% identity, 55% overall similarity) was found with human BTK and TEC PTKs. Sponge PTK was therefore named BtkSD. Human BTK is involved in the maturation of B cells and mutations in the BTK gene cause X-linked agammaglobulinemia. Kinases from the Tec family are not present in Caenorhabditis elegans and, until now, they were found only in insects and higher animal taxa. The finding presented in this paper implies that the BTK/TEC genes are of a very ancient origin.

***Vlak T, Eldar R. Disability in rheumatoid arthritis after monotherapy with DMARDs. Int J Rehabil Res. 2003;26:207-12.**

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Rheumatoid arthritis (RA) is a progressive disease that leads to an increasing loss of functional ability. Its management should be multidisciplinary, focused primarily at the prevention of functional loss. The aim of the present study was to investigate the effectiveness of monotherapy with disease-modifying antirheumatic drugs (DMARDs) on the prevention of functional loss in RA patients. Of 188 patients with RA, 95 had received DMARD monotherapy (mainly gold salts, but also antimalarials and sulfasalazin) for at least 36 months; 93 patients had not received DMARDs because of their inability to attend the rheumatology clinic regularly because of accessibility difficulties. All 188 patients were examined at the start of the follow-up and at its completion, some 42 months later. The following parameters were determined at the two examinations: tenderness and pain in individual joints, functional independence, functional and working status, and the results of ancillary tests. At the end of the follow-up there was a decrease in functional independence and deterioriation in the functional and working status in both groups. Long-term monotherapy with DMARDs had not prevented functional loss or the ensuing disability in RA patients.

Dujić Z, Duplančić D, Marinović-Terzić I, Baković D, Ivančev V, Valić, et al. Aerobic exercise before diving reduces venous gas bubble formation in humans. J Physiol. 2004;555(Pt 3):637-42.

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The authors previously showed in a rat model that a single bout of high-intensity aerobic exercise 20 h before a simulated dive reduces bubble formation and after the dive protects from lethal decompression sickness. The present study investigated the importance of these findings in man. Twelve healthy male divers were compressed in a hyperbaric chamber to 280 kPa at a rate of 100 kPa min(-1) breathing air and remaining at pressure for 80 min. The ascent rate was 9 m min(-1) with a 7 min stop at 130 kPa. Each diver underwent two randomly assigned simulated dives, with or without preceding exercise. A single interval exercise performed 24h before the dive consisted of treadmill running at 90% of maximum heart rate for 3 min, followed by exercise at 50% of maximum heart rate for 2 min; this was repeated eight times for a total exercise period of 40 min. Venous gas bubbles were monitored with an ultrasonic scanner every 20 min for 80 min after reaching surface pressure. The study demonstrated that a single bout of strenuous exercise 24h before a dive to 18 m of seawater significantly reduced the average number of bubbles in the pulmonary artery from 0.98 to 0.22 bubbles cm(-2)($P = 0.006$) compared to dives without preceding exercise. The maximum bubble grade was decreased from 3 to 1.5 ($P = 0.002$) by pre-dive exercise, thereby increasing safety. This is the first report to indicate that pre-dive exercise may form the basis for a new way of preventing serious decompression sickness.

Hren D, Lukić IK, Marušić A, Vodopivec I, Vujaklija A, Hrabak M, et al. Teaching research methodology in medical schools: students' attitudes towards and knowledge about science. Med Educ. 2004;38:81-6.

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OBJECTIVE: To explore the relationship between teaching scientific methodology in Year 2 of the medical curriculum and student attitudes towards and knowledge about science and scientific methodology. DESIGN: Anonymous questionnaire survey developed for this purpose. SETTING: Zagreb University School of Medicine, Croatia. PARTICIPANTS: A total of 932 students (response rate 58%) from all 6 years were invited to participate. MAIN OUTCOME MEASURES: Score on attitude scale with 45 Likert-type statements and score on knowledge test consisting of 8 multiple choice questions. RESULTS: The average attitude score for all students was 166±22 out of a maximum of 225, indicating a positive attitude towards science and scientific research. The students' average score on the knowledge test was 3.2±1.7 on 8 questions. Students who had finished Year 2 had the highest mean attitude (173±24) and knowledge (4.7±1.7) scores compared with other year groups ($P < 0.001$, anova and Tukey posthoc test). For students who had attended a mandatory Year 2 course on the principles of scientific research in medicine (Years 3 to 6), multiple linear regression analysis showed that knowledge test score ($B = 3.4$; $SE = 0.4$; 95% confidence interval 2.5-4.2; $P < 0.001$) and average grades ($B = 7.6$; $SE = 1.5$; 95% CI 4.6-10.6; $P < 0.001$) were significant predictors of attitude towards science, but not sex or failure to pass a year ($B = -0.6$; $SE = 1.7$; 95% CI -3.9-2.6; $P = 0.707$; and $B = -3.1$; $SE = 1.9$; 95% CI -6.8-5.7; $P = 0.097$, respectively). CONCLUSION: Medical students have generally positive attitudes towards science and scientific research in medicine. Attendance of a course on research methodology is related to a positive attitude towards science.

Labar B, Rudan I, Ivanković D, Biloglav Z, Mrsić M, Strnad M, et al. Haematological malignancies in childhood in Croatia: investigating the theories of depleted uranium, chemical plant damage and 'population mixing'. Eur J Epidemiol. 2004;19:55-60.

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Some of potential causes proposed to explain the reported increase of haematological malignancies in childhood during or after the war period in several countries include depleted uranium, chemical pollution and population mixing theory. The aim of this study was to define the population of Croatian children aged 0-14 years who were potentially exposed to each of those risks during the war and to investigate any possible association between the exposure and the incidence of haematological malignancies. The authors analyzed the data reported by the Cancer Registry of Croatia during the pre-war period (1986-1990), war period (1991-1995) and post-war period (1996-1999). In the group of 10 counties potentially exposed to depleted uranium and two counties where chemical war damage occurred, no significant difference in incidence of the studied haematological malignancies was noted in comparison to pre-war period. The incidence of lymphatic leukaemia significantly increased in four counties where population mixing had occurred during the war period, supporting the 'mixing theory'. In those counties, the incidence of Hodgkin's lymphoma decreased during and after the war. In Croatia as a whole, decreases in incidence of myeloid leukaemias during war and non-Hodgkin lymphoma after the war were noted.

Irha E, Vrdoljak J, Vrdoljak O. Evaluation of ultrasonographic angle and linear parameters in the diagnosis of developmental dysplasia of the hip. J Pediatr Orthop B. 2004;13:9-14.

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Angle parameters proposed by Graf and linear parameters introduced by Morin are the most common currently in use for quantification and classification of ultrasonographic findings in the diagnosis of developmental dysplasia of the hip. The aim of this study was to determine which of the two parameters is more suited to routine clinical use. Investigation was carried out on 100 hips of 50 infants by the same examiner who obtained two separate sonograms for each hip. Based on the results of our study, angle parameters appear to be more functional in identifying and classifying pathology, and more adequate for screening and diagnosis.

Boras A, Jeren T, Sacchi CT, Schmink S, Božinović D, Baršić B, et al. Establishment of an active laboratory-based surveillance for bacterial meningitis in Croatia and molecular characterization of *Neisseria meningitidis* isolates causing meningococcal disease that were collected in the year 2000, the first year of activity. J Clin Microbiol. 2004;42:1803-6.

University Hospital for Infectious Diseases, Zagreb, Croatia

In 2000, 23 Neisseria meningitidis (meningococcal [Men]) isolates were collected in Croatia through an active laboratory-based surveillance for bacterial meningitis (17 Men serogroup B [MenB], 4 MenC, 1 MenW135, and 1 nongroupable isolate). Molecular characterization revealed a substantial level of diversity with only six isolates belonging to electrophoretic type 5 (ET-5) and ET-37 hypervirulent complexes.

Martić M, Tatić I, Markovic S, Kujundžić N, Kostrun S. Synthesis, biological activity and molecular modeling studies of novel COX-1 inhibitors. Eur J Med Chem. 2004;39:141-51.

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Synthesis of new potential COX-1 and/or COX-2 inhibitors, derivatives of 1,1-di-(3-carboxyphenyl)ethane, their biological activity, docking results on COX-1 enzyme and absorption, distribution, metabolism, excretion (ADME) properties are presented. In addition to known interactions between ketoprofen and ibuprofen, leading NSAID agents and COX-1 active site, the possibility of formation of additional interactions is explored. Interactions with Ala527, and with one of the water molecules situated within the active site are identified. Molecular mechanics and DFT calculations for studied compounds have revealed free rotation around two central bonds (C1-C3' and C1-C3"), making them flexible, thus easier to enter and adjust to the active site. Further modifications of core structure have been undertaken to optimize biological activity and ADME properties. As a result, two of the compounds are indicated as novel COX-1 inhibitors.

Hrabak M, Vujaklija A, Vodopivec I, Hren D, Marušić M, Marušić A. Academic misconduct among medical students in a post-communist country. Med Educ. 2004;38:276-85.

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AIM: To assess the prevalence of, attitudes towards and willingness to report different forms of academic dishonesty among medical students in a post-communist transitional country. METHODS: An anonymous, self-administered questionnaire was distributed to medical students in Years 2-6 at the Zagreb University School of Medicine; 827 (70%) valid questionnaires were returned and analysed. RESULTS: Most of the students (94%) admitted cheating at least once during their studies. The most frequent type of misconduct was 'signing in an absent student on a class attendance list' (89.1%), and the least frequent 'paying for passing an examination' (0.7%). The number of committed types of misconduct out of 11 listed types increased from Year 2 (median 2) to Year 6 (median 4). Cheating behaviours could be clustered into 4 groups based on self-reported cheating, perceived prevalence of cheating, attitude towards cheating, and willingness to report cheating. The clustered behaviours that most students admitted to were perceived as the most frequent, more approved of and less likely to be reported. The strongest predictors of dishonest behaviour were attitude, perception of peer group behaviour and study year. Almost half (44%) the students said they would never report any form of cheating. CONCLUSION: Academic misconduct is widespread among medical students at the largest medical school in

Croatia and its prevalence is greater than that reported for developed countries. This may be related to social and cultural factors specific to a country in the midst of a post-communist transition to a market economy, and calls for measures to be instigated at an institutional level to educate against and prevent such behaviour.

Zuntar I, Kalanj-Bognar S, Topić E, Petlevski R, Stefanović M, Demarin V. The glutathione S-transferase polymorphisms in a control population and in Alzheimer's disease patients. Clin Chem Lab Med. 2004;42:334-9.

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The authors investigated the role of glutathione S-transferase P1 (GSTP1) polymorphisms in the pathogenesis of Alzheimer's disease (AD). They genotyped the GSTP1 polymorphisms in exon 5 (A313G) and exon 6 (C341T) by PCR-restriction fragment length polymorphism (PCR-RFLP) in 56 Croatian patients with AD and 231 controls. Distributions and frequencies of GSTP1 genetic variants were not statistically different between AD patients and healthy controls. Higher frequencies of the mutant genotypes were observed in AD patients (13% for both A313G and C341T) when compared with control subjects (7% for A313G and 8% for C341T), but association of GSTP1 GG (OR 2.057, 95% CI 0.796-5.315, p = 0.094) and TT (OR 1.691, 95% CI 0.669-4.270, p = 0.514) genotypes with an increased risk of AD was not confirmed by statistical analysis. The frequencies of GSTP1 alleles (A, B, C, D) did not significantly differ between AD patients and controls. The estimation of the GSTP1 haplotype distribution showed that GSTP1*A/GSTP1*B and GSTP1*A/GSTP1*C haplotypes were less frequent, while GSTP1*B/GSTP1*B and GSTP1*C/GSTP1*D haplotypes were more frequent in AD patients than in controls. In conclusion, the involvement of GSTP1 alleles in individual susceptibility to AD was not confirmed as statistically significant in the tested Croatian Caucasian population. A possible role of GSTP1 in the etiopathogenesis of AD is discussed, based on observed differences in haplotype distribution and higher frequencies of mutant genotypes in AD patients.

Mrsić-Pelčić J, Pelčić G, Vitezić D, Antončić I, Filipović T, Simonić A, et al. Hyperbaric oxygen treatment: the influence on the hippocampal superoxide dismutase and Na^+,K^+-ATPase activities in global cerebral ischemia-exposed rats. Neurochem Int. 2004;44:585-94.

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The influence of hyperbaric oxygen (HBO) treatment on the activities of superoxide dismutase (SOD) and Na^+K^+-ATPase was determined during different time periods of reperfusion in rats exposed to global cerebral ischemia. Ischemic animals were either sacrificed or exposed to the first HBO treatment 2, 24, 48 or 168 h after ischemic insult (for SOD activities measurement) or immediately, 0.5, 1, 2, 6, 24, 48, 72 or 168 h after ischemic procedure (for Na^+K^+-ATPase activities measurement). Hyperbaric oxygenation procedure was repeated for seven consecutive days. The results demonstrated the statistically significant increase in the hippocampal SOD activity 24 and 48 h after global cerebral ischemia followed by a decrease in the enzymatic activity 168 h after ischemic insult. In the ischemic rats treated with HBO the level of hippocampal SOD activity was significantly higher after 168 h of reperfusion in comparison to the ischemic, non HBO-treated animals. In addition, it was found that global cerebral ischemia induced a statistically significant decrease of the hippocampal Na^+K^+-ATPase activity starting from 1 to 168 h of reperfusion. Maximal enzymatic inhibition was obtained 24 h after the ischemic damage. Decline in Na^+K^+-ATPase activity was prevented in the animals exposed to HBO treatment within the first 24 h of reperfusion. The results suggest that global cerebral ischemia induces significant alterations in the hippocampal SOD and Na^+K^+-ATPase activities during different periods of reperfusion. Enhanced SOD activity and preserved Na^+K^+-ATPase activity within particular periods of reperfusion, could be indicators of a possible beneficial role of HBO treatment in severe brain ischemia.

Škrobonja A, Muzur A, Čulina T. The cult of St. Lucia, patroness of the eyes: some examples from Croatian ethnomedical tradition. On the occasion of the 1700th anniversary of her martyrdom. Int Ophthalmol. 2004;25:37-41.

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In the introductory part, the authors present several patrons/patronesses of the eyes and sight, as well as the protectors from eye diseases. In addition, presented is a short hagiography of St. Lucia, the most famous among the patrons of the eyes. The second part is dedicated to the cult of St. Lucia, which has existed among the Croats from the 10th century until present day. Testimonies to this are numerous churches, chapels, altars, paintings, sculptures, processions, pilgrimage, prayers, votive gifts, and many other forms of folk piety. By reviewing several characteristic examples from Istria and the region of Kvarner, the importance of this veneration is indicated, for general and religious tradition as well as for the history of medicine, especially the history of ethno-ophthalmology.