

**Abram M, Vučković D, Wraber B, Dorić M. Plasma cytokine response in mice with bacterial infection. *Mediat Inflamm* 2000;9:229-34.**

*Department of Microbiology, Rijeka University School of Medicine, Rijeka, Croatia*

This study was undertaken to quantify the plasma levels of pro-inflammatory cytokines during the course of primary *Listeria monocytogenes* and *Campylobacter jejuni* infection. C57BL/6 mice were infected by the intraperitoneal route. At different time points we determined the number of colony-forming units of bacteria in the liver of infected animals and paralleled these with the plasma levels of interferon-gamma (IFN-gamma), tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) measured by enzyme immunoassays. *L. monocytogenes* infection lasted 10-11 days. IFN-gamma production occurred in the early phase but was more pronounced after day 4, following the appearance of specific immunity. The duration of experimental campylobacteriosis was 15 days. Early IFN-gamma production was not significant but a progressive rise of this cytokine in plasma was seen during the second week post infection. Mice produced measurable amounts of plasma TNF-alpha immediately after being given viable *L. monocytogenes*, peaking on day 2-3 when the greatest number of bacteria was present in the examined organs. During *C. jejuni* infection plasma TNF-alpha was produced in a similar manner, but the highest concentrations were found a few days later than in listeriosis, in correlation with the different course of campylobacteriosis. The quantity of IL-6 increased and decreased in concordance with clearance of *L. monocytogenes* and the clinical status of the animals. *C. jejuni* did not promote the induction of this cytokine. In conclusion, during systemic bacterial infection, a network of pro-inflammatory cytokines is activated and blood levels of these cytokines are elevated, albeit inconsistently, with large individual variations and depending on microbial characteristics and structure.

**Alli OAT, Gao LY, Pedersen LL, Zink S, \*Radulić M, \*Dorić M, et al. Temporal pore formation-mediated egress from macrophages and alveolar epithelial cells by *Legionella pneumophila*. *Infect Immun* 2000;68:6431-40.**

*\*Department of Microbiology and Parasitology, Rijeka University School of Medicine, Rijeka, Croatia*

The authors show that, similar to the protozoan host, the induction of necrosis and cytolysis of macrophages by *L. pneumophila* is mediated by the pore-forming toxin or activity. This activity is temporally and maximally expressed only upon termination of bacterial replication and correlates with cytolysis of macrophages and alveolar epithelial cells in vitro. They have identified five *L. pneumophila* mutants defective in the pore-forming activity. The phagosomes harboring the mutants do not colocalize with the late endosomal or lysosomal marker Lamp-1, and the mutants replicate intracellularly similar to the parental strain. Interestingly, despite their prolific intracellular replication, the mutants are defective in cytotoxicity and are "trapped" within and fail to lyse and egress from macrophages and alveolar epithelial cells upon termination of intracellular replication. However, the mutants are subsequently released from the host cell, most likely due to apoptotic death of the host cell. Data derived from cytotoxicity assays, confocal laser scanning microscopy, and electron microscopy confirm the defect in the mutants to induce necrosis of macrophages and the failure to

egress from the host cell. Importantly, the mutants are completely defective in acute lethality (24 to 48 h) to intratracheally inoculated A/J mice. The authors conclude that the pore-forming activity of *L. pneumophila* is not required for phagosomal trafficking or for intracellular replication. This activity is expressed upon termination of bacterial replication and is essential to induce cytolysis of infected macrophages to allow egress of intracellular bacteria. In addition, this activity plays a major role in pulmonary immunopathology in vivo.

**Badovinac AR, Buretić-Tomljanović A, Starčević N, Kapović M, Vlastelić I, Randić L. Chromosome studies in patients with defective reproductive success. *Am J Reprod Immunol* 2000;44:279-83.**

*Department of Biology, Rijeka University School of Medicine, Rijeka, Croatia*

The objective of the study was to evaluate the contribution of chromosomal anomalies to decreased fertility in humans. A total of 782 persons (259 couples, 158 male and 106 female) with different clinical diagnoses of sterility and infertility were analysed cytogenetically. The overall frequency of major chromosomal aberration was 13.1% (103/783), which suggests that fertility or sterility problems in this population are due to chromosomal aberrations. Couples experiencing repeated spontaneous abortions, having malformed children or having sterility problems had chromosomal abnormalities in 18.0% (47/259 couples) of the population studied, and constituted chromosomal disorders occurred in couples seeking IVF and ICSI with prevalence of 22.2% (8/38 couples), especially minor mosaicism of sex chromosomes in the female partners. The prevalence of chromosome abnormalities in infertile men was 17.7% (28/158), and in subfertile females, it was 26.4% (28/106). The results could indicate an increased tendency to mitotic sex chromosome non-disjunction in humans.

**Ban J, Maysinger D, Kovač V, Galetić I, Matulić M, Hadžija M, et al. Molecular mechanisms involved in the antiproliferative action of protein tyrosine phosphatase inhibitor potassium bisperoxo (1,10-phenanthroline) oxovanadate. *Life Sci* 2000;68:165-75.**

*Department of Molecular Biology, Faculty of Science, Zagreb, Croatia*

Potassium bisperoxo(1,10-phenanthroline)oxovanadate, bpV(phen), a powerful protein phosphotyrosine phosphatase inhibitor and a potent insulinomimetic, influenced three fundamental cellular processes in HL-60 human leukemic cells: 1) inhibition of proliferation, 2) induction of differentiation and 3) apoptotic cell death. In the presence of micromolar concentrations of bpV(phen) cell number and DNA synthesis decreased progressively with time of incubation. A single treatment with bpV(phen) (3 μM) activated a differentiation program; after 6 days of incubation 82% of cells were differentiated, but differentiation started already within the first 24 h. Concentrations of 5-10 μM bpV(phen) caused the characteristic DNA ladder pattern, starting after 4.5 h. Differentiation in HL-60 cells appear to be associated with activation of extracellular signal-regulated kinase while apoptosis is connected with phosphorylation and activation of both extracellular signal-regulated kinase and c-Jun N-terminal kinase in a concentration and time-dependent

manner. The antiproliferative and apoptotic action of bpV(phen) could be exploited in combination chemotherapy in leukemia.

**Begovac J, Kniewald T, Ugarković N, Lisić M, Sonicki Z, Jazbec A. Survival of AIDS patients in Croatia prior to the introduction of combined antiretroviral therapy with protease inhibitors. Eur J Epidemiol 2000;16:741-4.**

*University Hospital for Infectious Diseases "Dr Fran Mihaljević", Zagreb, Croatia*

The authors report on survival of adults with AIDS, treated at the University Hospital of Infectious Diseases, Zagreb, Croatia from October 1986 to December 1998. The median survival of our 116 patients was 15.8 months. Multivariate analysis showed that factors independently associated with survival were type of presenting AIDS indicator disease and CD4+ cell count.

**Bosukonda D, Shih MS, Sampath KT, \*Vukičević S. Characterization of receptors for osteogenic protein-1/bone morphogenetic protein-7 (OP-1/BMP-7) in rat kidneys. Kidney Int 2000;58:1902-11.**

*\*Department of Anatomy, Zagreb University School of Medicine, Zagreb, Croatia*

Osteogenic protein-1/bone morphogenetic protein-7 (OP-1/BMP-7), a member of the transforming growth factor-beta superfamily, has been shown to prevent kidney damage from ischemia/reperfusion injury in rats. The molecular events involved in OP-1 action on kidney are not yet understood. In this study, the authors evaluated the biodistribution of I-125-labeled OP-1 in rat kidneys. At 10 and 180 minutes following injection, the relative uptake of I-125-labeled OP-1 was consistently higher in kidney cortex than in medulla region. Upon autoradiography, kidney tissue sections revealed that OP-1 bound to the convoluted tubule epithelium, glomeruli, and collecting ducts. Moreover, in situ hybridization and immunostaining methods have shown localization of mRNA transcripts and the protein for BMP receptor type II in the cortex and medulla in similar areas as I-125-labeled OP-1. Scatchard analysis of quantitative binding data indicated that the OP-1 receptors of kidney contained a single class of high-affinity binding sites for OP-1 with an association constant ( $K_a$ ) of  $2.26 \times 10^9$  mol/L<sup>-1</sup> and a binding capacity of 1.01 pmol of OP-1 per mg membrane protein. When analyzed by a ligand blot technique, plasma membranes isolated from kidney cortex and medulla each showed the presence of a prominent specific band with a relative molecular mass (Mr) of 100 kD. Further analysis by Western blotting indicated that an antibody raised against BMP type II receptor effectively recognized the 100 kD OP-1 binding component of kidney plasma membranes. In conclusion, the authors demonstrated for the first time the presence of membrane-bound, specific, high affinity OP-1 receptors in rat kidney tissues, which are likely to mediate OP-1 actions in the kidney. The major OP-1-binding component of the kidney appears to be a long form of BMP type II receptor with a Mr of 100 kD. In vivo and in vitro evidence suggests that the cellular targets for OP-1 are convoluted tubule epithelium, glomeruli, and collecting ducts. OP-1 does not share receptor binding properties with other growth factors, including BMP-2 and CDMP-1, suggesting that its mode of action in kidney appears to be specific.

**Brkić H, Strinović D, Kubat M, Petrovečki V. Odontological identification of human remains from mass graves in Croatia. Int J Legal Med 2000;114:19-22.**

*Department of Dental Anthropology, Zagreb University School of Dental Medicine, Zagreb, Croatia*

The paper reports the results of dental identification of 1000 human remains exhumed from mass graves in Croatia up to July 1998. Personal identification of the victims was performed at the Department of Forensic Medicine and Criminology at the School of Medicine in Zagreb. A total of 824 victims were positively identified, while 176 victims remained unidentified. Dental identification based on available dental antemortem data was achieved in 25% of the cases. Dental identification based on dental charts was achieved in 35%, on x-rays in 15%, on photographs of teeth in 22%, on interviews in 18%, and on confirmation by odontologists in 10% of the cases. Teeth, in combination with anthropological pa-

rameters, age, sex and height, as well as other specific characteristics such as tattoos, personal identification cards, clothes, jewellery and DNA, were helpful for identification of 63% of the victims, but the significance for the identification was not dominant. Only in 11% of the cases was identification achieved by other relevant means and teeth not used at all. Identification procedures in Croatia will continue until another 1700 people who are still missing or kept as prisoners of war since the aggression on Croatia in 1991 are found and/or identified.

**Dmitrović R. Transvaginal color Doppler study of uterine blood flow in primary dysmenorrhea. Acta Obstet Gynecol Scand 2000;79:1112-6.**

*Šulekova 4, 10000 Zagreb, Croatia*

The aim of the study was to determine if vasoconstriction of the uterine vessels in patients with primary dysmenorrhea is detectable by transvaginal color Doppler ultrasound. Forty-two women with primary dysmenorrhea and fifty healthy controls were included in this prospective study. Women were examined with transvaginal color Doppler ultrasound on first day of the cycle, once in the follicular and once in the luteal phase. Measurements of pulsatility index in uterine, arcuate, radial and spiral arteries were performed. Student's t-test was used to establish statistical significance between groups. Women in dysmenorrhea group had significantly higher uterine blood flow indices than healthy controls in all three measurements periods. This includes all vessels studied on the first day of the cycle, the radial and spiral arteries during the follicular phase and the arcuate, radial and spiral arteries during the luteal phase. Women with primary dysmenorrhea have elevated Doppler indices in uterine arteries not only on first day of the cycle but throughout the whole cycle. It is postulated that primary dysmenorrhea is not only the disorder of menstruation but also a disease of a menstrual cycle as a whole.

**Grahovac B, Bingulac-Popović J, Vucelić B, Hrستی I, Ostojić R, Džajić V, et al. Hypervariable region 1 of hepatitis C virus genome and response to interferon therapy. Clin Chem Lab Med 2000;38:905-10.**

*Department of Molecular Immunogenetics, Croatian Institute of Transfusion Medicine, Zagreb, Croatia*

The relationship between the complexity of the hypervariable region 1 (HVR1) quasispecies of hepatitis C virus (HCV) and responsiveness to interferon-alpha (IFN) therapy was studied in patients with chronic hepatitis C. Twelve HCV-RNA-positive patients were treated daily with high dose IFN and ribavirin for 4 weeks, and then with IFN 3 MIU (Million International Units) TIW (three times per week) and ribavirin for 6 months. The HVR1 quasispecies complexity was analyzed by nested polymerase chain reaction-mediated single-strand conformation polymorphism (SSCP). The baseline HCV-RNA levels in the study group ranged from  $10^6$  to  $10^7$  copies/mL. All patients exhibited HCV genotype 1b. Initial SSCP analysis revealed four (33.3%) patients with a low complexity pattern (SSCP bands less than or equal to 4) and eight (66.6%) patients with high complexity pattern (SSCP bands >4). After 4 weeks of IFN therapy, one patient became HCV negative, and among those remaining positive, the HCV-RNA levels decreased by 2 to 3 logs and the number of SSCP decreased by 2 to 3 bands per sample. After 6 months of IFN therapy, five (41.7%) patients became HCV-RNA-negative. Seven (58.3%) patients did not respond to IFN therapy with sustained viral load from  $10^3$  to  $10^5$  copies/mL, and high complexity SSCP patterns. Our data support the HVR quasispecies complexity to be an independent predictive factor for IFN responsiveness in patients infected with HCV.

**Grčević D, Lee SK, Marušić A, Lorenzo JA. Depletion of CD4 and CD8 T lymphocytes in mice in vivo enhances 1,25-dihydroxyvitamin D-3-stimulated osteoclast-like cell formation in vitro by a mechanism that is dependent on prostaglandin synthesis. Journal of Immunology 2000;65:4231-8.**

*Department of Physiology and Immunology, Zagreb University School of Medicine, Zagreb, Croatia*

To investigate the role of T lymphocytes in osteoclastogenesis, the authors performed in vivo depletion of CD4 and/or CD8 T lympho-

cyte subsets and evaluated *in vitro* osteoclast-like cell (OCL) formation, T lymphocyte depletion (TLD) with mAbs was confirmed 24 h later by flow cytometry, OCL formation was stimulated with 1,25-dihydroxyvitamin D-3 (1,25-(OH)(2)D-3) in bone marrow and with recombinant mouse (rm) receptor activator of NF-kappa B ligand (RANK-L) and rmM-CSF in bone marrow and spleen cell cultures, OCL formation was up to 2-fold greater in 1,25-(OH)(2)D-3-stimulated bone marrow cultures from TLD mice than in those from intact mice. In contrast, TLD did not alter OCL formation in bone marrow or spleen cell cultures that were stimulated with rmRANK-L and rmM-CSF, The effects of TLD seemed to be mediated by enhanced PG synthesis, because the PGE(2) concentration in the medium of 1,25-(OH)(2)D-3-stimulated bone marrow cultures from TLD mice, was 5-fold higher than that in cultures from intact mice, and indomethacin treatment abolished the stimulatory effect of TLD on OCL formation. There was a 2-fold increase in RANK-L expression and an almost complete suppression of osteoprotegerin expression in 1,25-(OH)(2)D-3-stimulated bone marrow cultures from TLD mice compared with those from intact mice. Although there was a small (20%) increase in IL-1 alpha expression in 1,25-(OH)(2)D-3-stimulated bone marrow cultures from TLD mice, TLD in mice lacking type I IL-1R and wild-type mice produced similar effects on OCL formation. Our data demonstrate that TLD up-regulates OCL formation *in vitro* by increasing PG production, which, in turn, produces reciprocal changes in RANK-L and osteoprotegerin expression. These results suggest that T lymphocytes influence osteoclastogenesis by altering bone marrow stromal cell function.

**Kos M, Matijević R, Stipoljev F, Mijković B, Kurjak A. Does an isolated choroid plexus cyst or cysts really indicate fetal karyotyping? *Prenat Neonatal Med* 2000;5:311-5.**

*Department of Obstetrics and Gynecology, Holy Gost Hospital, Zagreb, Croatia*

Fetal choroid plexus cysts (CPCs) are hypoechoic structures within the choroid plexus of the lateral brain ventricles. They are symmetrical in appearance, have sharply circumscribed margins and may be either unilateral or bilateral. On the follow-up examination, they are rarely found after 24 weeks of pregnancy. In anatomical and structural terms, CPCs are of no serious significance for the pregnancy; however, they have been associated with trisomies (mostly 18 and less commonly 21) and other chromosomal abnormalities. Several authors have suggested further evaluation of pregnancy for an additional risk factor before undertaking further invasive diagnostic tests. Recent studies have suggested that isolated choroid plexus cysts are not an absolute indication for invasive prenatal diagnosis. A choroid plexus cyst associated with other ultrasonographic markers or with other risk factors such as advanced maternal age should be an indication for offering prenatal diagnosis.

**Krmpotić-Nemanić J, Vinter I, Jalšovec D, Hat J. Relation of the ethmoidal cells to the floor of the anterior cranial fossa. *Ann Anat-Anat Anz* 2000;182:533-6.**

*"Drago Perović" Department of Anatomy, Zagreb University School of Medicine, Zagreb, Croatia*

The shape of the anterior part of the anterior cranial fossa undergoes important changes in the postnatal life depending on the degree of pneumatization of the ethmoid labyrinth and/or the frontal sinus. There exist three possibilities in these relations: 1) from the newborn period up to 9 years of age, in the majority of the cases the cribrous plate is situated at the level of the roof of the ethmoid labyrinth with the width of the ethmoid incisure corresponding to the width of the cribrous plate. 2) in the period from 9-35 years of age, in the majority of cases, the ethmoidal cells are partly or completely incorporated into the floor of the anterior cranial fossa with the width of the ethmoid incisure corresponding to the number of cells forming the floor of the anterior cranial fossa. 3) in the period from 35-80 years of age, the cribrous lamina is in the majority of cases lowered due to the intensive development of the frontal sinus. The medial wall of the ethmoid labyrinth consists of a thin bony strip, the width

of which depends upon the degree of lowering of the cribrous plate. Adequate CT imaging may clarify the situation.

**Ljubičić N, Spajić D, Vrkljan MM, Altabas V, Doko M, Zovak M, et al. The value of ascitic fluid polymorphonuclear cell count determination during therapy of spontaneous bacterial peritonitis in patients with liver cirrhosis. *Hepato-Gastroenterol* 2000;47:1360-3.**

*Department of Internal Medicine, Sisters of Mercy University Hospital, Zagreb, Croatia*

The aim of this study was to demonstrate whether it is possible, on the basis of ascitic fluid polymorphonuclear cell count in patients with liver cirrhosis and spontaneous bacterial peritonitis, to determine the optimal duration of cefotaxime therapy, as the most frequently applied empirical therapy, and possibly anticipate the disease recurrence. In 16 patients with alcoholic liver cirrhosis and confirmed diagnosis of spontaneous bacterial peritonitis, cefotaxime therapy was administered 2g t.i.d. during 5 days. Before the therapy, at 48 hours, 5 days and 15-20 days after the cefotaxime therapy was started, in all patients with spontaneous bacterial peritonitis diagnostic abdominal paracentesis was performed, each time determining the ascitic fluid polymorphonuclear cell count together with microbiological analysis. A significant association was found between the ascitic fluid polymorphonuclear cell count determined 48 hours after the therapy and the recurrence of spontaneous bacterial peritonitis. A recurrence occurred in only 1 patient with the number of ascitic fluid polymorphonuclear cell count <250/mm<sup>3</sup>, 48 hours after the therapy was started. A recurrence of spontaneous bacterial peritonitis occurred in all the patients who had an ascitic fluid PMN cell count greater than or equal to 250/mm<sup>3</sup>, 48 hours after the therapy was started. By monitoring the ascitic fluid PMN cell count it seems to be possible to determine the efficacy and optimal duration of cefotaxime therapy in patients with spontaneous bacterial peritonitis when it is of most importance that the number of ascitic fluid PMN cell count should decrease below 250/mm<sup>3</sup> during the therapy.

**Ljubin T, Milas DZ, Mimica N, Folnegović-Šmalc V, Makarić G. A preliminary study of the comparative effects of olanzapine and fluphenazine on cognition in schizophrenic patients. *Hum Psychopharmacol-Clin Exp* 2000;15:513-9.**

*Departments of Forensic Psychiatry and Clinical Psychophysiology, Zagreb University Psychiatric Hospital Vrapče, Zagreb, Croatia*

The aim of the study was to compare the effect of olanzapine versus fluphenazine treatment on cognitive functioning. Eighteen schizophrenic outpatients, aged 25-61 (average 37 years), all meeting DSM-IV diagnostic criteria for schizophrenia, were included in the study. They were randomly assigned to 22 weeks of either olanzapine or fluphenazine treatment. Certain subscales of the Wechsler Adult Intelligence Scale, the Stroop Neuropsychological Screening Test and the Wisconsin Card Sorting Test were performed. Olanzapine treatment proved to have a beneficial effect on digit-symbol performance and some aspects of executive function. In comparison to the fluphenazine treatment, the olanzapine treatment only showed a beneficial effect in increased percentage of conceptual level responses. Although the results are preliminary, they could implicate that the benefit of olanzapine treatment is primarily related to certain aspects of executive function, i.e. frontal lobe functioning.

**Marušić A, Grčević D, Katavić V, Kovačić N, Lukić IK, Kalajzić I, Lorenzo JA. Role of B lymphocytes in new bone formation. *Lab Invest* 2000;80:1761-74.**

*Zagreb University School of Medicine and Croatian Institute of Brain Research, Zagreb, Croatia*

The authors compared *in vivo* new bone induction in mice homozygous for the B-cell deficient (muMT) gene knockout, which lack functional B lymphocytes, with bone induction in control wild-type (C57BL/6) mice. The comparison used two models of new bone induction *in vivo*: endochondral osteoinduction by subcutaneous implantation of recombinant human bone morphogenetic protein (rhBMP-2) and osteogenic regeneration af-

ter tibial bone marrow ablation. Ossicles induced by rhBMP-2 were larger in volume and mass in muMT knockout mice, but relative volumes of the newly induced bone, cartilage, and bone marrow were similar in the two groups. Six days after tibial bone marrow ablation, muMT knockout mice resorbed the initial blood clot faster and formed more trabecular bone, paralleled by greater levels of bone sialoprotein mRNA than in the wild-type mice. muMT knockout and wild-type mice also differed in the expression pattern of inflammatory/immunomodulatory cytokines during the development of the newly induced bone, suggesting that a genetic lack of B lymphocytes may create a change in the immunological milieu at the site of new bone induction, which stimulates the initial accumulation and proliferation of mesenchymal progenitor.

**Prpić K. The publication productivity of young scientists: an empirical study. *Scientometrics* 2000;49:453-90.**

*Institute of Social Research, Zagreb, Croatia*

The research was conducted on a sample of 840 respondents who represent half of the Croatian population of young scientists. There are three main features which define the publication productivity of young scientists: 1) despite the worsened position of R & D, they publish more scientific papers than the young generations of scientists at the beginning of the nineties; 2) differences between a highly-productive minority, which produces on average half of all scientific publications, and a low-productive majority is already apparent in young scientists, and 3) the productivity of young scientists is formed according to productivity patterns typical of particular scientific fields and disciplines. With regard to the explanation of productivity, the following has been found: a) an expansion of the set of predictors resulted in an improvement in the explanation of the productivity of young scientists compared with previous surveys; b) among the factors which contribute significantly to the explanation of the quantity of scientific publications, the most powerful predictor is attendance at conferences abroad, followed by scientific qualifications and some gatekeeping variables; and c) besides certain similarities, scientific fields also show a specific structure of determinants of young scientists' productivity.

**Siest G, Bertrand P, Qin B, Herbeth B, Serot JM, Masana L, Ribalta J, Passmore AP, Evans A, Ferrari M, Franceschi M, Shepherd J, Cuchel M, Beisiegel U, Zuchowsky K, \*Rukavina AS, \*Sertic J, et al. Corporate Author ApoEurope Grp. Apolipoprotein E polymorphism and serum concentration in Alzheimer's disease in nine European centres: The ApoEurope study. *Clin Chem Lab Med* 2000;38:721-30.**

*\*Institute of Clinical Laboratory Diagnosis, Zagreb University School of Medicine, Zagreb, Croatia*

As part of the ApoEurope Project, apolipoprotein E (apo E) common polymorphism and serum concentration were determined in 489 Alzheimer's disease patients and 429 controls. Patients and controls were recruited through nine centres in eight European countries. Age, sex ratios and education levels of both case and control populations were similar, although discrete differences appeared between centres. The prevalence of the epsilon4 allele was higher in Alzheimer's disease than in controls (increased by 140%), while serum apo E concentration was lower by 11.2% ( $p < 0.001$ ). In addition, serum total cholesterol and triglyceride concentrations were lower in Alzheimer's disease ( $p < 0.001$ ), while that of apo AI was not affected. The decrease in serum apo E concentration was not accounted for by the epsilon4 allele, age or gender, suggesting that apo E concentration might represent an additional risk factor for Alzheimer's disease, complementary and independent of the epsilon4 allele. Further analysis will be aimed at determining whether the quantitative link between apo E concentration and Alzheimer's disease occurs through the effect of apo E genotype on lipid parameters or by other mechanisms.

**Svoboda-Beusan I, Kušec R, Bendelja K, Tudorić-Ghemo I, Jakšić B, Pejša V, Rabatić S, Vitale B. The relevance of multidrug resistance-associated P-glycoprotein expression in the treatment response of B-cell chronic lymphocytic leukemia. *Haematologica* 2000;85:1261-7.**

*Department of Cellular Immunology, Institute of Immunology, Zagreb, Croatia*

The aim of the study was to determine whether expression of P-glycoprotein (Pgp) is an intrinsic feature of B-lymphocytes in B-cell chronic lymphocytic leukemia (B-CLL) and how it correlates with hematologic indices and tumor load. Furthermore, the change of Pgp expression under cytotoxic treatment and its correlation to treatment outcome were studied. In 42 patients, of whom 13 were sequentially monitored, expression of extracellular (MRK-16) and intracellular (C-219) Pgp epitopes on peripheral blood lymphocytes was determined by flow cytometry and quantified by ratio of the mean fluorescence (RMF). Median RMF values in B-CLL patients were higher than in age-matched controls. Pgp expression did not correlate with any of the hematologic features or clinical stage of the disease, patients who received some type of cytoreductive treatment prior to the study had lower Pgp values for both measured epitopes. In 13 patients monitored during treatment the decrease in RMF was noted after treatment with chlorambucil, with RMF values for both Pgp epitopes decreasing in responders. This was in contrast to unchanged or even increased RMF values in those patients who did not respond to therapy. The study confirms the importance of quantitative evaluation of Pgp expression by flow cytometry.