

---

**Cekinović D, Golemac M, Pugel EP, Tomac J, Čičin-Šain L, Slavuljica I, et al. Passive immunization reduces murine cytomegalovirus-induced brain pathology in newborn mice. *J Virol.* 2008;82:12172-80.**

*Department of Histology and Embryology, Rijeka University School of Medicine, Rijeka, Croatia.*

The authors used a recently established model of mouse cytomegalovirus CMV (MCMV) infection in newborn mice to analyze the contribution of humoral immunity to virus clearance from the brain. In brains of MCMV-infected newborn mice treated with immune serum, the titer of infectious virus was reduced below detection limit, whereas in the brains of mice receiving control (nonimmune) serum significant amounts of virus were recovered. Moreover, histopathological and immunohistological analyses revealed significantly less CNS inflammation in mice treated with immune serum. Treatment with MCMV-specific monoclonal antibodies also resulted in the reduction of virus titer in the brain. Recipients of control serum or irrelevant antibodies had more viral foci, marked mononuclear cell infiltrates, and prominent glial nodules in their brains than mice treated with immune serum or MCMV-specific antibodies. In conclusion, these data indicate that virus-specific antibodies have a protective role in the development of CNS pathology in MCMV-infected newborn mice, suggesting that antiviral antibodies may be an important component of protective immunological responses during CMV infection of the developing CNS.

---

**Žuškin E, Mustajbegović J, Schachter EN, Kern J, Dečković-Vukres V, Trošić I, et al. Respiratory function in pesticide workers. *J Occup Environ Med.* 2008;50:1299-305.**

*Andrija Štampar School of Public Health, Zagreb University School of Medicine, Zagreb, Croatia.*

Pesticide aerosols are frequently toxic irritants associated with respiratory symptoms and lung function impairment. A cross-sectional study examined the prevalence of acute and chronic respiratory symptoms and lung function abnormalities in 82 workers employed in processing pesticides

and in 60 control workers not exposed to irritants and employed in a soft drink bottling plant. The prevalence of almost all chronic respiratory symptoms was greater among pesticide workers than among controls. A logistic regression analysis shows differences between men and women. There was a high prevalence of acute symptoms during the work shift in pesticide workers. The data on ventilatory capacity indicates significant reductions in all tests compared to predicted. Multivariate analysis of lung function showed differences in smoking and work exposure effects in men and women. These data indicate that duration of work exposure in the pesticide processing industry may be associated with the development of acute and chronic respiratory symptoms and lung function changes. These effects appear to be aggravated by smoking.

---

**Eterović D, Antunović Z, Marković V, Grošev D. Planning of <sup>131</sup>I therapy for Graves disease based on the radiation dose to thyroid follicular cells. *J Nucl Med.* 2008;49:2026-30.**

*Department of Nuclear Medicine, University Hospital Split, Split University School of Medicine, Split, Croatia.*

The authors evaluated the effects on the absorbed dose to thyroid follicular cells of self-absorption of <sup>131</sup>I radiation (specifically, beta-rays) in the follicular colloid. Thyroid follicles were modeled as colloid-filled spheres, containing a uniform concentration of <sup>131</sup>I and surrounded by a concentric monolayer of cells. Assuming close packing of identical follicles, the authors Monte Carlo simulation to assess the absorbed dose to follicular cells. Because of beta-ray self-absorption in colloidal spheres with radii larger than 50 μm, the absorbed dose to follicular cells is less than the average thyroid absorbed dose. In conclusion, for the same thyroid mass, radioiodine thyroid uptake, and effective half-life, patients with follicles with colloidal sphere radii of 100, 200, 300, and 400 μm should be administered 9%, 15%, 21%, and 30% more <sup>131</sup>I, respectively, than patients with colloidal sphere radii of less than 50 μm, to yield the same absorbed dose to follicular cells.

**Aurer I, Mitrović Z, Nemet D, Radman I, Sertić D, Serventi-Seiwerth R, et al. Treatment of relapsed or refractory aggressive non-hodgkin lymphoma with two ifosfamide-based regimens, IMVP and ICE. J Chemother. 2008;20:640-4.**

*Department of Internal Medicine, Zagreb University Hospital Center and Zagreb University School of Medicine, Zagreb, Croatia.*

The authors report the outcomes of 45 patients with relapsed or refractory aggressive non-Hodgkin's lymphoma (NHL) treated with a combination of ifosfamide, carboplatinum and etoposide (ICE) and 28 patients treated with a combination of ifosfamide, methotrexate and etoposide (IMVP) during two 5-year periods. The response rate (RR) to ICE was 47%, 2-year overall survival (OS) 31% and 2-year event-free survival (EFS) 22%. These results were similar to those obtained with IMVP (RR 39%, 2-year OS 23%, 2-year EFS 13%;  $p=0.355$  for RR, 0.275 for OS, 0.668 for EFS). Higher IPI scores and refractoriness to treatment were negative prognostic factors, immunophenotype (B vs. T) had no influence on prognosis. Changing from IMVP to ICE does not substantially improve the outcome of patients with relapsed or refractory aggressive NHL. Patients with relapsed/refractory aggressive B-NHL do not have a superior outcome in comparison to those with T-NHL if treated with chemotherapy alone.

**Sabol I, Matovina M, Gašperov NM, Grce M. Identification of a novel human papillomavirus type 16 E1 gene variant with potentially reduced oncogenicity. J Med Virol. 2008;80:2134-40.**

*Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia.*

The human papillomavirus (HPV) 16 genome has been studied extensively, although no study has focused on the E1 gene that is implicated in viral DNA replication. After analyzing the E1 region of HPV 16 genomes in 429 cervical samples, 11.2% were found to contain a 63 nucleotide duplication in this region. Sequence analysis of the E6 and the E7 regions has shown that all samples containing this duplication were related to E6-G350 variant of the HPV 16 (Chi square test,  $P=0.0012$ ). A comparison of cervical lesion severity of the examinees having regular or variant E1 genes has shown that the variant group had a significantly (Fischer's exact test,  $P=0.0401$ ) lower percentage of high grade disease cases, suggesting that this particular duplication might reduce the oncogenic potential of HPV 16, and also might clarify the differences of E6-G350 variant on-

cogenicity observed in European populations. Albeit, a decreased incidence of high grade cervical lesions can be linked to the prevalence of multiple HPV infection, the additional decrease of those cases with the variant E1 gene versus those without (10.5% and 18.6%, respectively) can only be ascribed to the effect of this particular HPV variant. Further research is needed to clarify the biology of these HPV 16 E1 variants.

**Jonjić S, Polić B, Krmpotić A. Viral inhibitors of NKG2D ligands: Friends or foes of immune surveillance? Eur J Immunol. 2008;38:2952-6.**

*Rijeka University School of Medicine, Rijeka, Croatia.*

NKG2D is a potent activating receptor on NK cells and a co-stimulatory receptor on CD8(+) T cells. Through its ability to recognize a panel of ligands inducible by stress or infection, it plays an important role in the control of viral infections. The viruses have evolved robust mechanisms to counteract NKG2D-dependent immune response. The functions of these viral inhibitors are well characterized during the early days post-infection but less so during the chronic viral infection.

**Boraska V, Škrabić V, Čulić VC, Becić K, Kapitanović S, Zemunik T. Association of TNF promoter polymorphisms with type 1 diabetes in the South Croatian population. Biol Res. 2008;41:157-63.**

*Department of Medical Biology, Split University School of Medicine, Split, Croatia.*

Type 1 diabetes mellitus (T1DM) is an autoimmune disease characterized by the destruction of pancreatic  $\beta$  cells. Tumor necrosis factor (TNF) is a pleiotropic cytokine with potent immunomodulatory and inflammatory activity. Association studies of TNF polymorphisms and type 1 diabetes (T1DM) frequently demonstrated TNF involvement with T1DM. Although TNF may play an important role in the pathogenesis of T1DM, the genetic association of TNF region with the disease has not been conclusive because of the strong linkage disequilibrium with HLA genes. In this study, the authors examined two TNF promoter variants (rs 1800629 at position -308, and rs361525 at position -238) for T1DM association in 233 patients and 144 controls from the population of South Croatia. A higher frequency of TNF -308 A allele and also, a more frequent specific -308A -238G haplotype in T1DM patients were observed with a limited significance. However, the authors did not find strong evidence of association of TNF promoter poly-

morphisms with T1DM. In order to elucidate the contribution of TNF to T1DM susceptibility in investigated population, more comprehensive studies with HLA adjustment in a larger sample are required.

---

**Miličević G, Gavranović Z, Bakula M, Pazur V, Frank B. Successful conversion of recent-onset atrial fibrillation by sequential administration of up to three antiarrhythmic drugs. Clin Cardiol. 2008;31:472-7.**

*Intensive Cardiac Care Department, Division of Cardiology, Osijek University School of Medicine, Zagreb, Croatia.*

Short-term conversion attempt of recent-onset atrial fibrillation (AF) in the emergency room fails too often. Many patients and doctors still prefer pharmacological to electrical solutions in such cases. The hypothesis of this study is that sequential administration of up to 3 antiarrhythmic drugs of different classes of action (amiodarone, propafenone, and quinidine) may achieve conversion in such patients. One hundred and forty consecutive patients with recent-onset AF were transferred to the intensive cardiac care unit after a failed 2-h conversion attempt in the emergency room. First-line drug for conversion was continued up to a full dose, and was chosen by AF etiology, or in recurrent AF episodes, empirically. In nonresponders, the failed drug was replaced by a drug of another class, and if the second-line drug failed it was replaced by a drug of the third-line. Electrical cardioversion was the final solution for nonresponders. Sixty percent of patients reached sinus rhythm by the first-line drug therapy, 34% by the second-line, and 4% by the third-line. Seventy-five percent of patients achieved conversion within 26 h, and 95% of patients achieved conversion within 40 h. Three patients were electrically cardioverted due to hemodynamical instability. Two episodes of Torsade de Pointes ventricular tachycardia were self-terminated. In conclusion, sequential usage of up to 3 antiarrhythmic drugs of different classes of action provides almost complete success in conversion of recent-onset AF in patients refractory to short-term conversion attempt in the emergency room.

---

**Dmitrović R, Vlaisavljević V, Ivanković D. Endometrial growth in early pregnancy after IVF/ET. J Assist Reprod Genet. 2008;25:453-9.**

*Nova Gradiška General Hospital, Nova Gradiška, Croatia.*

The purpose of this work was to detect the endometrial volume change in conception cycles. Additionally the authors measured endometrium in three planes, to see if the hypothesized endometrial volume differences will be detectable by

this surrogate technique. Following the embryo transfer, a three-dimensional ultrasound exam was performed on average days 22 and 28 of the cycle. Seventy-eight subjects signed the informed consent form, and 63 completed the study. A significant difference was observed between Visit 1 and Visit 2, for endometrial volume, thickness, length and width in the pregnant group, and for endometrial volume, thickness and width in the non-pregnant group. In this study the authors have shown that in normal intrauterine pregnancy after IVF/ET, prominent endometrial volume growth can be detected by a three-dimensional ultrasound over the course of several days. Moreover, in patients who did not conceive in a particular cycle, a decrease in endometrial volume can be seen.

---

**Bašić Kes V, Šimundić AM, Nikolac N, Topić E, Demarin V. Pro-inflammatory and anti-inflammatory cytokines in acute ischemic stroke and their relation to early neurological deficit and stroke outcome. Clin Biochem. 2008;41:1330-4.**

*University Department of Neurology, Sisters of Mercy University Hospital, Zagreb, Croatia.*

The aim of this study was to explore (i) the difference in concentration of IL-6, TNF-alpha and IL-10 between acute ischemic stroke patients and control individuals; (ii) the association of plasma cytokine concentration with stroke severity at admission assessed by NIHSS and stroke outcome in 90 days assessed by Barthel index (BI) and modified Rankin scale (mRS). Study included 68 stroke patients admitted within 12 h of symptoms onset and 71 controls. IL-6 was increased in patients relative to controls ( $P=0.035$ ) and this increase was associated with severe stroke ( $P=0.007$ ) and worse outcome ( $P=0.030$  and  $0.019$ ; assessed by BI and mRS, respectively), whereas IL-10 was decreased ( $P=0.044$ ) and associated with better outcome ( $P=0.043$ ). TNF-alpha did not differ between studied groups ( $P=0.302$ ). In conclusion, increased IL-6 and reduced IL-10 concentrations are present in early stroke period and are associated with a degree of neurological deficit and/or stroke outcome.

---

**Gužvinec M, Tešović G, Tambić-Andrašević A, Židovec-Lepej S, Vukić BT, Begovac J. The epidemiology of invasive Streptococcus pneumoniae disease in Croatian children. Med Sci Monit. 2008;14:PH59-64.**

*University Hospital for Infectious Diseases, Zagreb, Croatia.*

Invasive pneumococcal disease (IPD) is a major medical problem in childhood. Pneumococcal conjugate vaccines

(PCVs) offer a new possibility to reduce the incidence of pneumococcal infections, especially IPD. The aim of this study was to describe the characteristics of IPD among Croatian children and examine the possibilities of introducing different PCVs in our population. *Streptococcus pneumoniae* isolates causing IPD during three years (2001, 2005, 2006) in Croatian children younger than 14 years old were collected prospectively. Epidemiological and clinical parameters, results of serotyping, and antimicrobial susceptibility data were evaluated. One hundred strains were collected during the study period. The ages of the patients ranged from 30 days to 13 years (median: 25.5 months). Seventy-

nine percent of the isolates were from patients younger than five years old. The incidence of IPD was highest among children younger than two years of age (33.9/100,000). Serotypes 14, 6B, 18C, and 23F accounted for 67% of all serotypes. The overall coverage rates of PCV7, PCV10, and PCV13 were 72%, 80%, and 90%, respectively. Low-level resistance to penicillin was found in 20% of the isolates and high resistance to erythromycin in 33.8%. PCV7 covered 85% of the penicillin-resistant strains and 80% of the erythromycin-resistant strains. The inclusion of a PCV in the immunization program could have a considerable effect on IPD-associated morbidity among Croatian children.