

1. Gerenèè M, \*Burek V, Crowe BA, Barrett NP, Dorner F. The role of complement and gp120-specific antibodies in virus lysis and CD4+ T cell depletion in HIV-1-infected patients. *Microb Pathog* 1998;25:253-66.  
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The substantial virus lysis was induced by HIV-1-infected patient serum and normal human complement serum in the presence of purified patient IgG. Non-infected CD4+ T cells coated with the whole virus or with a recombinant HIV-1 envelope gp120 and sensitized with patient IgG were also shown to be susceptible to complement-dependent lysis. The serum level of complement regulatory protein in a fluid phase, the C1- esterase inhibitor, was significantly correlated with serum concentration of C1q-circulating immune complexes ( $p=0.0062$ ), but inversely with CD4+ T cell count ( $p<0.0001$ ). Accordingly, the disease progression in HIV-1-infected patients was significantly correlated with the level of complement activation as determined by serum level of C1-esterase inhibitor ( $p=0.0001$ ), and inversely correlated with CD4+ cell count ( $p<0.001$ ) and gp120-specific antibody titre ( $p=0.0086$ ). These results strongly suggest that the complement activation by gp120-specific antibodies play a very important role in virus clearance, but also in depletion of infected as well as gp120-coated non-infected CD4+ bystander T cells during the course of HIV-1 infection.
2. \*Thaller V, Buljan D, Breitenfeld D, Marušiæ S, Breitenfeld T, De Syo D, Zorièiæ Z. Anthropological aspects of alcohol consumption and alcohol related problems. *Coll Antropol* 1998;22:603-11.  
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Authors believe that drinking alcoholic beverages can be associated with customs and habits specific to small communities, societies and even entire nations. The primary family, as the foundation of customs and habits of the first generation, has a role in stimulating drinking and alcoholism. The authors have examined some sociocultural factors, mostly taking into consideration relations in the primary family, by means of a questionnaire filled out by alcoholics (N=200) and non-alcoholics (N=100). The alcoholics usually have their first drink earlier, start drinking regularly earlier, and in the primary family there is a high tolerance towards the use of alcoholic beverages. The authors believe that the prevention should be directed primary towards the primary family with a view to changing their customs and habits as well as attitudes towards the use of alcoholic beverages.
3. Novick WM, Gurbuz AT, Watson DC, Lazorishinets VV, Perepeka AN, \*Malèiæ I, Marinoviæ B, Alpert BS, DiSessa TG. Double patch closure of ventricular septal defect with increased pulmonary vascular resistance. *Ann Thorac Surg* 1998;66:1533-8.  
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The authors designed a fenestrated flap valve double VSD patch in an effort to decrease the morbidity and mortality associated with the closure of a large VSD with elevated pulmonary vascular resistance. Eighteen children (mean age, 5.7 years) with a large VSD and elevated pulmonary vascular resistance (mean, 11.4 Wood units) underwent double patch VSD closure using moderately hypothermic cardiopulmonary bypass and cardioplegic arrest. The routine VSD patch was fenestrated (4 to 6 mm) and on the left ventricular side of the patch, a second, smaller patch was attached to the fenestration along its superior margin before closure of the VSD. All children survived operation and were weaned from inotropic and ventilator support within 48 hours postoperatively. Postoperative pulmonary artery pressures were significantly lower than preoperative values. One child died 9 months postoperatively. In conclusion, closure of a large VSD in children with elevated pulmonary vascular resistance can be performed with low morbidity and mortality when a flap valve double VSD patch is used.
4. \*Aniæ K, Soldo I, Periæ L, Karner I, Barac B. Tick-borne encephalitis in eastern Croatia. *Scand J Infect Dis* 1998;30:509-12.  
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92 patients treated for tick-borne encephalitis(TBE) in the Department for Infectious Diseases, University Hospital Osijek, over a 22-year period (1973-1995) were analyzed. The patients

were mostly forestry workers. The appearance of the disease followed the biological activity of the tick, with the largest number of affected individuals recorded between April and August. In a smaller number (9.8%) of cases the clinical picture was aseptic meningitis, while in the majority of patients (90.2%) it presented as an acute meningoencephalomyelitic form. The course was relatively severe in the majority of the patients analyzed, with disturbances of consciousness (32.6%) and transitory neurological signs (61.9%). Three patients died (3.3%) in the early phase of the disease. A monophasic course dominated. The clinical and epidemiological data were compared with the cases described in other parts of Croatia and regional differences were seen in the severity of illness. These variations could be due to the previously hypothesized different virus subtypes, or to some other unknown factors.

5. \*Baršić B, Beus I, Marton E, Himbele J, Klinar I. Nosocomial infections in critically ill infectious disease patients: results of a 7-year focal surveillance. *Infection* 1999;27:16-22. Intensive Care Unit, University Hospital for Infectious Diseases Dr. Fran Mihaljevic, Zagreb, Croatia.  
An incidence study on nosocomial infections in critically ill infectious disease patients was carried out in the intensive care unit (ICU) of a university hospital for infectious diseases over a 7-year period (1 January 1990 to 31 December 1996). A total of 660 patients who stayed in the ICU for over 48 h were prospectively observed. The patients were divided into two groups: one with central nervous system infections (442 patients) and the other with other severe infections (218 patients). The risk of nosocomial sepsis and pneumonia was significantly higher in patients suffering from severe central nervous system infections. The incidence of sepsis was 24.2% vs. 11.4% (relative risk 1.95; 95% confidence interval 1.32-2.89); the incidence of pneumonia was 30.5% vs. 14.7% (relative risk 2.09; 95% confidence interval 1.47-2.96). The incidence of urinary tract infection was 14.3% vs. 13.3% (relative risk 1.07; 95% confidence interval 0.71-1.61). Density rates of nosocomial septic episodes were  $21.1 \pm 37.1$  vs.  $11.7 \pm 32.4$  episodes/100 central venous-line days ( $p < 0.006$ ). Nosocomial pneumonia occurred only in mechanically ventilated patients ( $36.9 \pm 61.2$  vs.  $28.5 \pm 65.8$  episodes per 1000 ventilatory days,  $p = 0.012$ ). Nosocomial urinary tract infection occurred only in patients with urinary catheters ( $11.6 \pm 60.7$  episodes/1000 urinary catheter days vs.  $18.7 \pm 90.1$ ,  $p = 0.886$ ). Multivariate regression analysis identified age, diagnosis of CNS infection, duration of urinary tract catheterization, the use of central venous lines and mechanical ventilation as independent risk factors of nosocomial sepsis. duration of mechanical ventilation, use of steroids and diagnosis of CNS infection were independent risk factors of nosocomial pneumonia. A subanalysis identified tetanus patients to be at particular risk of nosocomial infections.
6. \*Eterović D, Juretić-Kušević L, Ćepkun V; Dujic Z. Pyelolithotomy improves while extracorporeal lithotripsy impairs kidney function *J Urol* 1999; 161:39-44. Department of Physiology, Medical School, Clinical Hospital Split, Croatia  
Extracorporeal shock wave lithotripsy (ESWL) causes acute depression of kidney function, which chronically returns to baseline levels. This sequel could indicate chronic regression of acute lesions or a balance between lesions and relief of obstruction. We compared changes in kidney function 1 week and 3 months after ESWL and pyelolithotomy. **MATERIALS AND METHODS:** A group of 17 women and 13 men 28 to 71 years old with 0.6 to 3 cm stones received 1,800 to 3,200 shock waves by an electromagnetic lithotripter. Another group of 21 women and 9 men 35 to 76 years old with 2.5 to 3.8 cm. stones underwent Gil-Vernet intrasinus pyelolithotomy. Split renal plasma flow, glomerular filtration rate and mean parenchymal transit times of nonreabsorbable filtrate solutes were measured by dual gamma camera renography, and plasma clearances of <sup>99m</sup>technetium diethylenetriaminepentaacetic acid and <sup>131</sup>orthoiodohippurate acid. **RESULTS:** ESWL caused acute deterioration and chronic restoration of baseline parameters of the treated kidney, and small but sometimes irreversible damage to plasma flow to the untreated kidney, especially in obese patients. In contrast, pyelolithotomy acutely and chronically improved function of the treated kidney, and normalized parenchymal transit times of radiotracers. **CONCLUSIONS:** ESWL does not achieve substantial improvements in kidney function, which can be achieved by other methods of stone removal.
7. \*Gabrić N, Dekaris I, Šuman L, Karaman Z, Mravić I. The influence of tissue culture on corneal immunogenicity. *Exp Eye Res* 1999;68:277-82. General Hospital "Sveti Duh", Department of Ophthalmology, Zagreb, Croatia  
In this study we examined whether immunization with heterotopic corneal graft can be suppressed by usage of cultured corneal tissue. Starting from the hypothesis that the corneal

antigenicity might change during long-time storage, we compared, in a mouse model, the immunization obtained with fresh and stored corneas. Heterotopic (chest wall) mice corneal allografts were exchanged between donors and hosts: (1) mismatched at multiple minor H loci and (2) only H-Y mismatched animals. Median survival time (MST) of primary and secondary skin grafts exchanged between mentioned donors and hosts was recorded. Recipient mice were immunized with either: (a) tail-skin graft, (b) fresh cornea graft or (c) corneal graft stored for three weeks in tissue culture. Three weeks later, recipients were challenged with skin graft placed at the opposite side of the chest wall and MST of these skin grafts was recorded. MST of secondary skin grafts in animals that had been immunized by skin served as a control. Our results suggest that stored corneas do not lose ability to sensitize the multiple minor H disparate host. They also show both cultured and fresh corneas, when placed in non-privileged site, have same immunizing capacity as skin. No significant difference in MST of secondary skin grafts between recipients of fresh (19 days) and stored corneal grafts (18 days) was recorded. Accordingly, the ability of corneal tissue to immunize both multiple minor H mismatched, as well as only H-Y mismatched host, was not influenced by storage in a tissue culture.

8. \*Plavec D, Godniæ-Èvar J. Lack of correlation between nonspecific nasal and bronchial reactivity in allergic rhinitis subjects. *Lung* 1999;177:169-77.  
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A link between allergic rhinitis and asthma has long been suspected, allergic rhinitis being considered a precursor of asthma. The hypothesis is that if such a link exists, then nonspecific nasal and bronchial reactivity are already correlated in acute rhinitis patients. To test for this correlation, we compared nonspecific nasal and bronchial reactivity in two groups of rhinitis subjects: 37 rhinitis pollinosis patients tested during the pollen season and 35 rhinitis pollinosis patients tested outside the pollen season. We also assessed how smoking affects this link. We found no correlation between nonspecific nasal and bronchial reactivity in the two nonasthmatic rhinitis groups. During active allergic inflammation (pollinosis season) no shift toward a stronger link between upper and lower airways can be found compared with the latent period (out of pollinosis season). Unexpectedly, among smokers we found a significant relationship between nonspecific nasal and bronchial reactivity. Thus, there is not yet sufficient evidence for a straightforward link between nasal and bronchial hyperreactivity in nonasthmatic pollinosis rhinitis subjects. The development of asthma seems to be crucial for this link.
9. Reusch U, Muranyi W, \*Luèin P, Burgert HG, Hengel H, Koszinowski UH. A cytomegalovirus glycoprotein re-routes MHC class I complexes to lysosomes for degradation. *EMBO J* 1999;18:1081-91.  
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Mouse cytomegalovirus (MCMV) early gene expression interferes with the major histocompatibility complex class I (MHC class I) pathway of antigen presentation. Here we identify a 48 kDa type I transmembrane glycoprotein encoded by the MCMV early gene m06, which tightly binds to properly folded  $\beta$ 2-microglobulin-associated MHC class I molecules in the endoplasmic reticulum (ER). This association is mediated by the luminal/transmembrane part of the protein. gp48-MHC class I complexes are transported out of the ER, pass the Golgi, but instead of being expressed on the cell surface, they are redirected to the endocytic route and rapidly degraded in a Lamp-1(+) compartment. As a result, m06-expressing cells are impaired in presenting antigenic peptides to CD8(+) T cells. The cytoplasmic tail of gp48 contains two di-leucine motifs. Mutation of the membrane-proximal di-leucine motif of gp48 restored surface expression of MHC class I, while mutation of the distal one had no effect. The results establish a novel viral mechanism for downregulation of MHC class I molecules by directly binding surface-destined MHC complexes and exploiting the cellular di-leucine sorting machinery for lysosomal degradation.
10. Rohrer J, Minegishi Y, \*Richter D, Eguiguren J, Conley ME. Unusual mutations in Btk: an insertion, a duplication, an inversion, and four large deletions. *Clin Immunol* 1999;90:28-37.  
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Mutations in Bruton's tyrosine kinase (Btk) result in the immunodeficiency X-linked agammaglobulinemia (XLA). In a previous study of 101 patients with presumed XLA, we identified seven patients with large genomic alterations in Btk. The recent completion of 100 kb of contiguous DNA sequence at the Btk locus has allowed us to characterize these mutations in detail and to identify four different types of alterations. These alterations included

a 253-bp retroposon insertion at position +5 within intron 9, an inversion of greater than 48 kb that disrupted Btk between exons 4 and 5, a 12.9-kb duplication including Btk exons 2 to 5, and four deletions ranging from 2.8 to 38 kb in size. The duplication and three of the deletions resulted from unequal crossovers of Alu repeats. Further, three of the deletions terminated within a repeat-rich cluster spanning 30 kb of sequence 3' of Btk exon 19, suggesting that this region was more susceptible to unequal crossovers than the rest of the Btk gene. These studies describe the first reports of an insertion, an inversion, and a duplication in Btk and demonstrate the utility of large-scale sequencing in the elucidation of disease-causing mutations.

11. \*Šebečić B, Nikolaić V, Sikirić P, Seiwerth S, Šoša T, Patrlj L, et al. Osteogenic effect of a gastric pentadecapeptide, BPC-157, on the healing of segmental bone defect in rabbits: a comparison with bone marrow and autologous cortical bone implantation. *Bone* 1999;24:195-202.  
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It has been previously shown that a stomach pentadecapeptide, BPC-157, improves wound and fracture healing in rats in addition to having an angiogenic effect. In present study, using a segmental osteoperiosteal bone defect, the osteogenic effect of pentadecapeptide BPC-157 was further studied. Pentadecapeptide BPC-157 significantly improved the healing of segmental bone defects. For instance, the effect of pentadecapeptide BPC-157 was shown to correspond to improvement after local application of bone marrow or autologous cortical graft. Moreover, a comparison of the number of animals with unhealed defects (all controls) or healed defects (complete bony continuity across the defect site) showed that besides pentadecapeptide intramuscular application for 14 days (i.e., local application of bone marrow or autologous cortical graft), also following other pentadecapeptide BPC-157 regimens (local application, or intermittent intramuscular administration), the number of animals with healed defect was increased. Hopefully, in the light of the suggested stomach significance for bone homeostasis, the possible relevance of this pentadecapeptide BPC-157 effect (local or intramuscular effectiveness, lack of unwanted effects) could be a basis for methods of choice in the future management of healing impairment in humans, and requires further investigation.
12. Rudan I. Inbreeding and cancer incidence in human isolates. *Hum Biol* 1999;71:173-87.  
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This study investigates the incidence of cancer in isolate populations. The number of cancer cases on 5 islands (Brač, Hvar, Korčula, Vis, and Lastovo) over a 20-year period (1971-1990) has been extracted from the data of the Croatian Cancer Registry. The population of coastal Dalmatia, characterized by similar environmental factors but a different population genetic structure, was used as a control population. The leading hypothesis was that, if there were genes or gene complexes (especially with recessive inheritance) responsible for genetic susceptibility to certain types of cancer, then the incidence of those cancer types should be greater in reproductively isolated island populations than in a control population because of increased manifestation of such genes or gene complexes caused by inbreeding. After adjusting the data for sex and age, I confirmed the hypothesis: Island populations have greater total cancer incidence than the control population for both sexes. The excess incidence on the islands shows an almost linear correlation with geographic distance from the mainland. The cancer sites primarily responsible for the excess incidence are bladder cancer in males, and breast, ovarian, brain, and large bowel cancer in females, predominantly in the younger age groups.
13. \*Šturlan S, Kapitanović S, Kovačević D, Lukač J, Spaventi Š, Spaventi R, Pavelić K. Loss of heterozygosity of APC and DCC tumor suppressor genes in human sporadic colon cancer. *J Mol Med* 1999;77:316-21.  
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The authors examined 36 cases of human sporadic colon carcinoma and corresponding normal tissue samples to evaluate loss of heterozygosity at the APC and DCC tumor suppressor genes loci using restriction fragment length polymorphism polymerase chain reaction and variable nucleotide tandem repeat analysis. Observed informativity was 83% for APC and 75% for DCC. DNA from 6 (20%) of 30 informative tumors exhibited loss of heterozygosity at the APC locus. Loss of heterozygosity at the DCC locus was observed in 7 (26%) of 27 informative tumor DNAs. Our results support the view that malignant progression is a consequence of more than one genetic change and suggest that inactivation of APC and DCC genes plays a role in a multistep process of colon tumor progression.

14. \*Vidas I, Delajlija M, Temmer-Vuksan B, Stipetiæ-Mravak M, Cindriæ N, Marièiæ D. Examining the secretor status in the saliva of patients with oral pre-cancerous lesions. *J Oral Rehabil* 1999;26:177-82.  
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A total of 122 subjects were examined, half of whom suffered from oral pre-cancerous lesions (excluding *Candida albicans* in oral smears), while the other half were the healthy control group. All were subjected to clinical oral examinations and standard evaluation tests in order to establish the secretor status of their saliva. In the group of patients with oral pre-cancerous lesions (experimental group), a pathohistological examination of the oral mucosa was performed. The results have demonstrated that the large majority of the people examined in both groups were secretors and no significant difference between secretors and non-secretors was found in the comparison between the experimental group and the healthy control group. However, a) we found a higher intensity of oral disease in the non-secretor group, and b) the occurrence of epithelial dysplasia was found exclusively in the non-secretor group.
15. \*Vodopija I, Baklaiæ Z, Vodopija R. Rabipur: a reliable vaccine for rabies protection. *Vaccine* 1999;17:1739-41.  
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Rabipur, a vaccine propagated on chick embryofibroblasts, is one of the "second generation" rabies vaccines produced by cell culture techniques. It compares in tolerance, immunogenicity and efficacy with the human diploid cell culture vaccines and is significantly more economical to be produced. It has proven to be an excellent vaccine, particularly when employed by the 2-1-1 schedule vaccination. This approach combines economy of vaccine with increased safety of treatment. Rabipur was investigated in all immunological parameters and can be recommended as a vaccine of choice for postexposure rabies treatment.