

## CIP

**Brugiatelli M, Holowiecka B, Dmoszynska A, Krieger O, \*Planinc-Peraica A, Labar B, et al. 2-Chlorodeoxyadeno-sine treatment in non-Hodgkin's lymphoma and B-cell chronic lymphocytic leukemia resistant to conventional chemotherapy: results of a multicentric experience. Ann Hematol 1996;73:79-84.**

*\*Merkur University Hospital and University Hospital Center Zagreb, 10000 Zagreb, Croatia*

2-chlorodeoxyadenosine (2-CDA) is effective for the treatment of hairy cell leukemia and Waldenström's macroglobulinemia. Thirty cases, mainly refractory, 16 affected with CLL, were included from six centers of the International Society for Chemo-Immunotherapy (IGCI). 2-CDA was administered in a 2 h iv. infusion for 5-7 days at the standard dose of 0.1 mg/kg/day every 4 weeks. The median number of cycles was 3. Of 30 cases, eight (26.7%) achieved a complete remission (CR), nine (30%) a partial remission (PR), and two (6.7%) a minor response, while five cases (16.6%) did not respond, and six (20%) were considered early deaths. The overall response rate (CR+PR) was 56.7%, with a median response duration of 12 months (range 3-28) and a better response in CLL patients. Considering that the majority of patients were heavily pretreated, toxicity was acceptable, with 40% of cases not presenting any toxic effect. The main toxicity consisted in infectious complications. The present study confirms that 2-CDA is an effective drug in these lymphoproliferative disorders, suggesting its possible use either alone or in combination, also as first-line therapy.

**\*Gregurek R, Labar B, Mrsic M, Batinic D, Ladika I, Bogdanic V, et al. Anxiety as a possible predictor of acute GVHD. Bone Marrow Transplant 1996;18:585-9.**

*\*Department of Psychological Medicine, University Hospital Center Zagreb, 10000 Zagreb, Croatia*

In order to determine the influence of anxiety on the development of BMT complications and survival, we analysed data in 35 consecutive patients undergoing BMT in our Center between June 1992 and December 1994. All patients received bone marrow from HLA-identical MLC non-responsive siblings. The patients were tested with the Spielberger STAI test as a measure of anxiety as a state (STAI-S) and as a trait (STAI-T). The STAI-S/1 and STAI-T/1 were performed during the first week of isolation (day -5 to day -3 prior to BMT) and STAI-S/2 and STAI-T/2 at the end of the discharge from laminar air flow units (day +35 to day +40 post-transplant). The level of anxiety at the beginning of isolation as measured by STAI-S/1 and STAI-T/1 tests had been significantly higher in patients who subsequently developed acute grade II-IV GVHD as compared to patients with GVHD grade 0-I ( $P < 0.001$ ), irrespective of age, sex or stage of the disease prior to BMT. In those patients who died, the STAI-S/1, STAI-T/1 and STAI-T/2 tests had been almost identical to those of surviving patients, while STAI-S/2 had been significantly higher ( $P = 0.034$ ). These data indicate an association between the level of anxiety and the risk for BMT complications.

**\*Vukicevic S, Kopp JB, Luyten FP, Sampath TK. Induction of nephrogenic mesenchyme by osteogenic protein 1 (bone morphogenetic protein 7). Proc Natl Acad Sci USA 1996;93: 9021-6.**

*\*Department of Anatomy, University of Zagreb Medical School, 10000 Zagreb, Croatia*

As osteogenic protein 1 (OP-1/bone morphogenetic protein 7), a member of the TGF-beta superfamily of proteins, is expressed predominantly in the kidney, we examined its involvement during metanephric induction and kidney differentiation. OP-1 mRNA was expressed in the ureteric bud epithelium before mesenchymal condensation and was subsequently seen in the condensing mesenchyme and during glomerulogenesis. Mouse kidney metanephric rudiments cultured without ureteric bud epithelium failed to undergo mesenchymal condensation and further epithelialization, while exogenously added recombinant OP-1 was able to substitute for ureteric bud epithelium in restoring the induction of metanephric mesenchyme. Blocking OP-1 activity using either neutralizing

antibodies or antisense oligonucleotides in mouse embryonic day 11.5 mesenchyme, cultured in the presence of metanephric inducers or in intact embryonic day 11.5 kidney rudiment, greatly reduced metanephric differentiation. It appears that OP-1 is required for metanephric mesenchyme differentiation and plays a functional role during kidney development.

**Huskic J, Kulenovic H, \*Culo F. Serum angiotensin-converting enzyme activity in patients with endemic nephropathy. *Nephron* 1996;74:120-4.**

*\*University of Zagreb Medical School, Department of Physiology, Salata 3, 10000 Zagreb, Croatia*

Serum angiotensin-converting enzyme was measured in 60 patients with endemic nephropathy and in 30 healthy individuals. The patients with endemic nephropathy were further divided into groups with arterial hypertension (n=30) and without arterial hypertension (n=30). The activity of angiotensin-converting enzyme was determined by a spectrophotometric method using hippuryl-L-histidyl-L-leucine as a substrate. The serum activity of angiotensin-converting enzyme was significantly increased in the patients with endemic nephropathy ( $28.51 \pm 1.64$  U/L) as compared with healthy individuals ( $20.83 \pm 1.33$  U/L). The level of the enzyme was further increased if the endemic nephropathy was accompanied by arterial hypertension ( $37.09 \pm 1.45$  U/L).

**\*Nola M, Babic D, Ilic J, Marusic M, Uzarevic B, Petroveckii M, et al. Prognostic parameters for survival of patients with malignant mesenchymal tumors of the uterus. *Cancer* 1996;78:2543-50.**

*\*Department of Gynecological and Perinatal Pathology, Zagreb University School of Medicine, 10000 Zagreb, Croatia*

Flow cytometric cell cycle analysis was performed on archival paraffin embedded blocks from 80 patients with malignant mesenchymal uterine neoplasms (endometrial stromal sarcomas, malignant smooth muscle tumors, and malignant Mullerian mixed tumors). The Cox proportional hazards regression model used to assess relative effects on the patient's survival, in univariate analysis for stromal sarcomas revealed a statistical significance for DNA ploidy+proliferative activity ( $P < 0.001$ ), histologic type ( $P = 0.005$ ), and DNA index ( $P < 0.001$ ). In multivariate analysis, DNA index appeared to be the only significant parameter influencing patient survival ( $P = 0.005$ ). In univariate analysis for malignant smooth muscle neoplasms, statistical significance was detected for mitotic activity ( $P = 0.049$ ) and International Federation of Gynecology and Obstetrics classification ( $P = 0.021$ ), but in multivariate analysis, clinical stage appeared to be the only significant parameter of survival ( $P = 0.032$ ). In univariate analysis for malignant Mullerian mixed tumors, statistical significance was found for the depth of myometrial invasion ( $P = 0.039$ ), DNA index ( $P = 0.037$ ), and clinical stage ( $P = 0.013$ ), but in multivariate analysis, only the depth of myometrial invasion ( $P = 0.036$ ) and clinical stage ( $P = 0.025$ ) were of statistical significance. Thus, DNA index was the most powerful prognostic indicator for stromal sarcomas.

**\*Klajic-Turkalj M, Cvorisec B, Tudoric N, Stipic-Markovic A, Rabatic S, et al. Decrease in CD23+ B lymphocytes and clinical outcome in asthmatic patients receiving specific rush immunotherapy. *Int Arch Allergy & Immunol* 1996;111:188-94.**

*\*Department of Pulmonary Diseases and Clinical Immunology, Sveti Duh General Hospital, 10000 Zagreb, Croatia*

Rush immunotherapy (RIT) mechanisms in patients with allergic bronchial asthma were studied according to the changes in the serum levels of total IgE, allergen-specific IgE and IgG4, and expression of CD23 on peripheral blood B cells. Twenty patients were evaluated before the beginning of RIT, as well as 6 weeks and 6 months later. Compared to pretreatment values, the level of Der-p-specific IgG4 and IgE significantly increased after 6 weeks and 6 months of RIT, while the total serum IgE remained unchanged. After 6 months of RIT, the percentage of CD23+B cells and its CD23 receptor density significantly decreased. The symptom score improved and the need for medication decreased. After 6 months, 30% of patients did not have an asthma attack, without using any

medications in the last month, while 10% of them were asthma free for the last 3 months. No significant correlation between the clinical improvement, and *in vitro* changes was found. These findings suggest that the inhibition of IL-4-induced B cell stimulation may be hypothesized as the most important mechanism of RIT.

**\*Kolacek S, Grguric J, Percl M, Booth IW. Home-made modular diet versus semi-elemental formula in the treatment of chronic diarrhea of infancy: a prospective randomized trial. Eur J Pediatr 1996;155:997-1001.**

*\*Department of Gastroenterology and Nutrition, Children's Hospital Zagreb, 10000 Zagreb, Croatia*

We developed a home-made modular diet (MD) based on boiled minced chicken meat, sunflower oil emulsion, sucrose and cornflower, with full range of vitamins and minerals. The value of this MD was compared to a semi-elemental formula (SF) Pregomin. Eighteen infants with severe chronic diarrhea were randomly assigned to receive either MD or SF. After 4 weeks of treatment: (1) diarrhea was significantly shorter (3 vs 7 days;  $p < 0.001$ ) and nutritional recovery started earlier (5 vs 9 days;  $p < 0.001$ ) in MD group; (2) median weight gain in the SF group was 100 g/week, compared to 171g/week in MD group ( $p < 0.005$ ); (3) in two patients from the SF group, diarrhea persisted, but they achieved a complete recovery when changed to MD.

**Stimac D, Rubinic M, Lenac T, Kovac D, Vcev A, Miletic D. Biochemical parameters in the early differentiation of the etiology of acute pancreatitis. Am J Gastroenterol 1996;91:2355-9.**

*Internal Clinic, University Hospital Center Rijeka, 51000 Rijeka, Croatia*

Biochemical differentiation between alcoholic and nonalcoholic acute pancreatitis was performed retrospectively. 167 patients were divided into groups A (alcoholic pancreatitis) and NA (nonalcoholic pancreatitis). Group NA was further subdivided into groups B (biliary pancreatitis) and NANB (nonalcoholic, nonbiliary pancreatitis). Serum amylase, ALT, AST, alkaline phosphatase ( $p < 0.001$ ), and urine amylase ( $p < 0.01$ ) were significantly lower in patients with alcoholic pancreatitis. Erythrocyte mean corpuscular volume and lipase/amylase ratio were significantly higher in patients with alcoholic pancreatitis ( $p < 0.001$ ). Multivariate analysis showed that a combination of lipase/amylase ratio, erythrocyte mean corpuscular volume, and alkaline phosphatase differentiated between alcoholic and nonalcoholic pancreatitis.

**\*Primorac D, Anđelinovic S, Definis-Gojanovic M, Drmic I, Rezic B, Baden MM et al. Identification of war victims from mass graves in Croatia and Bosnia and Herzegovina by use of standard forensic methods and DNA typing. J Forensic Sci 1996;41:891-4.**

*\*Department of Pathology and Forensic Medicine, Zagreb University School of Medicine in Split, 21000 Split, Croatia*

The postmortem remains of sixty-one war victims were excavated from 6 mass graves in Bosnia and Herzegovina one and a half years after interment. By matching of medical and dental records, the recognition of distinguishing characteristics such as the use of clothing and belongings, and video superimposition, 35 persons were identified. For the remaining 26 persons identification efforts have continued. DNA typing was performed at the HLA DQA1 locus and five PM loci. Results from DNA typing were confirmed by other methods.

**Stanimirovic A, Skerlev M, Gacina P, Beck T, Stipic T, Basta-Juzbasic A. Leprosy in Croatia in the twentieth century. Lepr Rev 1995;66:318-23.**

*Department of Dermatology and Venereology, Zagreb University Medical School, 10000 Zagreb, Croatia*

During the twentieth century, 17 cases of leprosy were registered in Croatia. However, due to the loss of medical documentation concerning the cases from Metkovic, the total number was obviously slightly greater. Among 17 cases, 4 patients were most probably infected during their travels abroad;

3 patients developed leprosy after a prolonged close contact with infected family members, while the exact source of infection remains unsettled for the remaining 10. Two of these patients originated from the area of Cazin in Bosnia and Herzegovina, which is known to be an endemic focus of leprosy. The remaining 8 patients came from the small area of the village of Blizna in the Croatian municipality of Trogir, which thus seems to be the endemic focus of leprosy in Croatia. The last case of leprosy in Blizna was registered in 1956. The sporadic cases of leprosy can reappear in Croatia, originating either from this endemic focus of Blizna, or from an infected person who returned to Croatia from abroad.