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Begovac J, Kuzmanovic N, Bejuk D. Comparison of clinical characteristics of group-A Streptococcal bacteremia in children and adults. Clin Infect Dis 1996;23:97-100.

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This report reviews 55 cases of bacteremia due to group A streptococci (GAS) in patients treated at the University Hospital of Infectious Diseases, Zagreb, Croatia, 1974-1994. Clinical findings for 27 children (age, <18 years) were compared with those for 28 adults. A predominance of the respiratory tract as a primary focus of infection in younger patients was observed (p=.00006). Children were more frequently colonized by GAS in their throats than were adults (p=.04). Suppurative osteoarticular metastatic foci were more often found in children (p=.02). Acute underlying conditions were more common in children (p=.04), whereas chronic underlying conditions were more common in adults (p=.00005). The case fatality rate was 23% among children (6 of 27) and 50% among patients aged >60 years (5/10). The course of bacteremia due to GAS was benign in eight children (29.6%) and 12 adults (42.8%). Our experience suggests that there are significant differences in the presentation of GAS bacteremia in children and adults.

Gudelj L, Deniz G, *Rukavina D, Johnson PM, Christmas SE. Expression of functional molecules by human CD3(-) decidual granular leukocyte clones. Immunology 1996;87(4):609-15.

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Cell surface and cytoplasmic antigen expression by 35 CD3(-) decidual granular leucocyte (DGL) clones derived from human endometrial tissue in the first trimester of pregnancy, has been compared with both that of fresh CD3(-) decidual leucocytes and that of CD3(-) peripheral blood natural killer (PBNK) cell clones (n=12). The majority of DGL clones retained the antigenic phenotype of fresh cells, although CD103 (HML-1) was expressed on 50% of DGL clones but only 17% of fresh DGL. Both cytoplasmic CD3z and CD3e were detected in >90% of DGL clones in the absence of cell surface CD3. Cytoplasmic CD3z was present in almost all fresh CD3(-) DGL, whereas CD3e was not. Most DGL clones did not express surface Fcg-receptors I-III (CD64, -32 and -16, respectively) and complement receptors (CR1 and CR2), but 43% expressed CR3 (CD11b/18); in contrast, all PBNK clones were CR3(+). The NK cell-associated molecules Kp43 (CD94) and p58 (Mo. ab HP3E4) were both present on a higher proportion of CD3(-) PBNK (91% and 50%, respectively) than DGL clones (31% and 14%, respectively), despite expression of CD94 by >90% of fresh CD56(+) decidual leucocytes. Five of 35 CD3(-) DGL clones expressed cyt. CD3z in the absence of expression of CD2, CD16 or the p58 molecule recognized by HP3E4. These variations between CD3(-) DGL and PBNK cell clones may be related to previously reported differences in MHC-non-restricted cytotoxic activities between these two cell types.

Haberstock H, *Marotti T, Banfic H. Neutrophil signal-transduction in Met-enkephalin modulated superoxide anion release. Neuropeptides 1996;30(2):193-201.

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The study explored the involvement of signal transduction system(s) in Met-enkephalin (MENK) modulated superoxide anion O^{-2}(-) release from human neutrophils. This opioid pentapeptide stimulated the O^{-2}(-) release at 10^{-8} M concentration, while in lower concentrations the stimulatory concentration was donor-dependent. The most abundant product of MENK degradation, Tyr-Gly-Gly (TGG), suppressed O^{-2}(-) release over a wide range of concentrations (10^{-12}-10^{-8} M). MENK induced O^{-2}(-) release was associated with a dose-dependent increase of diacylglycerol (DAG) and protein-kinase C (PKC) translocation to the neutrophil membranes, with an increase of cytosolic Ca^{2+}, and could be abolished by H7, a PKC inhibitor. On the contrary, the suppressive effect of TGG was not associated with alteration of DAG concentration in neutrophil membranes. Superoxide anion release

induced by low concentrations of MENK (10^{-12}-10^{-10} M), could be blocked by NDGA, an inhibitor of the lipooxygenase pathway. We conclude that MENK-induced O^{-2}(-) release is mainly due to DAG /PKC pathway activation, although other secondary messengers might be involved.

Cvitkovic E, Eschwege F, Rahal M, Dosen-Mersic Z, *Krajina Z, Armand JP, et al. Preliminary results of a randomized trial comparing neoadjuvant chemotherapy (Cisplatin, Epirubicin, Bleomycin) plus radiotherapy vs. radiotherapy alone in stage-IV (greater-than-or-equal-to-N2, M0) undifferentiated nasopharyngeal carcinoma - a positive effect on progression-free survival. Int J Radiat Oncol Biol Phys 1996;35(3):463-9.

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Purpose: To establish the value of bleomycin, epirubicin and cisplatin (BEC) regimen as neoadjuvant chemotherapy in the treatment of locoregionally advanced undifferentiated nasopharyngeal carcinoma (UCNT) we initiated a large international phase III trial in 1989. Methods and Materials: From November 1989 to October 1993, 339 patients with negative metastases workup have been randomized, 168 to radiotherapy alone and 171 to chemotherapy plus radiotherapy. All patients' characteristics were well balanced in both arms. Results: With a median follow-up of 49 months (range: 23-70), despite an excess of treatment-related deaths in the neoadjuvant chemotherapy arm (8 vs. 1%), there was a significant difference in disease free survival favoring the chemotherapy arm ($p < 0.01$). The proportion of local and/or regional metastases was comparable in both arms. No difference in overall survival was evident but the numbers of events needed for analysis has not yet been reached. Conclusions: BEC type neoadjuvant chemotherapy has a significant impact in the natural history of UCNT.

Herak-Kramberger CM, Spindler B, Biber J, Murer H, *Sabolic I. Renal type-II Na/P-i-cotransporter is strongly impaired whereas the Na/Sulphate-cotransporter and aquaporin-1 are unchanged in cadmium treated rats. Pflugers Arch 1996;432(2):336-44.

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We investigated the cellular causes of the Cd-induced phosphaturia in the rat. Compared to controls, Cd-treated rats (2 mg Cd/kg body weight, s.c. for 14 days) showed a marked polyuria, proteinuria and phosphaturia. Na^+ gradient-driven uptake of phosphate [(P32(i)] and of [H-3] glucose were markedly decreased in Cd-treated rats, whereas uptake of sulphate (S35) remained unchanged. By Western blotting and immunocytochemistry, using an antibody against the type II Na/P-i-cotransporter (NaPi-2), we found a diminished expression of this protein in the brush-border membrane from Cd-treated rats. However, the expression of the water channel aquaporin 1, estimated from the specific antibody staining in brush-border membranes, remained unchanged by Cd. Northern blot analysis showed a strong reduction of 2.7 kb NaPi-2-related mRNA in Cd-affected kidneys. In conclusion, Cd may reduce reabsorption of P-i in proximal tubules by affecting the expression of the functional Na/P-i-cotransporters in the luminal membrane, and Cd effects on brush-border transporters are selective.

Knotek M, Jaksic O, Selmani R, Skoric B, *Banfic H. Different endothelin receptor subtypes are involved in phospholipid signaling in the proximal tubule of rat kidney. Pflugers Arch 1996;432(2):165-73.

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Phospholipid signalling mediated by endothelin (ET) receptor subtypes was studied in the rat proximal tubule. In freshly isolated proximal tubule cells, ET-1, ET-2 and sarafotoxin S6c (S6c) evoked an increase in 1,2-diacylglycerol (DAG), inositol 1,4,5-trisphosphate (InsP(3)) and phosphocholine (PCho), suggesting stimulation of both phosphatidyl-inositol 4,5-bisphosphate- and phosphatidyl-choline-specific phospholipase C (PLC), while ET-3 increased only DAG and PCho, presumably via phosphatidyl-choline-dependent PLC. In brush border membranes (BBM), DAG increased in response to ET-1, ET-2 and ET-3, and was followed by protein kinase C (PKC) translocation to the BBM, while in basolateral membranes (BLM), DAG formation and translocation of PKC were observed only in response to ET-3. Tyrphostine, pertussis toxin (PTX) or cholera toxin (CTX) did not

influence ET-mediated signalling in either of the membranes, suggesting PTX- and CTX-insensitive G-protein-mediated stimulation of PLC beta by ET receptors. BQ123, an inhibitor of ET(A) receptors, did not prevent ET-l-mediated signalling in BBM, but an ET(A,B) antagonist, bosentan, inhibited ET-3-mediated signalling in BBM. Neither BQ123 nor bosentan inhibited ET-3 signalling in BLM. Our data strongly suggest the presence of ET(B) receptors coupled to phosphatidyl-inositol 4,5-bisphosphate- and phosphatidyl-choline-dependent PLC in BBM and ET(C) receptors linked to phosphatidyl-choline-dependent PLC in BLM.

***Labar B, Masszi T, Morabito F, Mistrik M, Holowiecki J, Bogdanic V, et al. Allogeneic bone marrow transplantation for acute leukemia - Igci experience. Bone Marrow Transplant 1996;17(6):1009-12.**

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From October 1984 to December 1994, 142 patients from six IGCI-BMT centers (78 AML and 64 ALL) received allogeneic bone marrow from their HLA-identical sibling. The probability of LFS at 60 months was 41% for AML patients and 39% for ALL patients. A better LFS was documented in patients allografted in first CR compared to the patients treated in advanced stage of the disease. The overall relapse rate was 27% for AML patients and 45% for ALL patients. The relapse rate was higher for patients allografted in dvanced stage of the disease (47 vs 26% at 60 months for AML and 55 vs 38% at 60 months for ALL). The incidence of moderate to severe acute GVHD was between 45-50% for both AML and ALL patients. Chronic GVHD was documented in 30% of AML patients and 38% of ALL patients. Transplant-related mortality for both AML and ALL was 25%. Relapse and GVHD with or without infection were the main causes of death. These results confirm that allogeneic BMT is very effective therapy for patients with acute leukemia, especially for patients transplanted in first CR.

***Marusic-Galesic S, Sparbier K, Knezevic N, Walden P. Altered allogeneic response in neonatally anti-MHC class I-treated mice. Scand J Immunol 1996;43(3):321-8.**

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Neonatal treatment of C3H mice [H-2(k)] with anti-K-k monoclonal antibodies results in altered cytotoxic responses against allogeneic targets. After 2-3 weeks of antibody treatment, no difference in the number of CD4(+)8(-) or CD4(-)8(+) T cells was observed between the antibody- and saline-treated mice. However, antibody-treated mice had a significantly reduced cytotoxic response against various allogeneic MHC class I-expressing targets. The strongest reduction was observed in very young mice (up to 2 weeks of age). As the mice got older, the allo MHC-specific responses reached control levels. No significant changes in T-cell receptor (TCR)-V-region usage was observed even in young antibody-treated mice. The results suggest that the reduction in the number of positively selecting elements reduces alloreactivity and most likely also the diversity of TCR-repertoire. However, the reduced alloresponsiveness was not restricted to either allogeneic K- or D-encoded molecules, suggesting that self MHC D-region-encoded molecules can mediate positive selection of T cells able to react against both K and D region-encoded allogeneic MHC class-I molecules.

***Muck-Seler D, Jakovljevic M, Pivac N. Platelet 5-HT concentrations and suicidal behavior in recurrent major depression. J Affect Disord 1996;39(1):73-80.**

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Platelet 5-HT concentrations were determined in 84 male and 82 female psychotic and non-psychotic depressed patients with various degrees of suicidal behavior, and in 175 healthy controls. Psychotic patients had higher platelet 5-HT concentrations than non-psychotic depressed patients and healthy controls. A sex difference, i.e., lower platelet 5-HT concentrations in females were found in healthy controls, depressed patients, non-psychotic patients and non-suicidal depressed patients. A negative relationship was shown between platelet 5-HT concentrations and suicidal behavior. The lowest platelet 5-HT concentrations were associated with the most pronounced suicidal behavior. The results

suggest that the differences in platelet 5-HT concentrations found in depressed patients might be used as a biological marker for suicidal behavior.

Radulovic S, Feng HM, *Morovic M, Djelalija D, Popov V, Crocquetvaldes P, Walker DH. Isolation of Rickettsia-akari from a patient in a region where Mediterranean spotted fever is endemic. Clin Infect Dis 1996;22(2):216-220.

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Rickettsia akari was isolated from blood collected from a patient in Croatia in 1991. We believe this is the first human isolate of R. akari to be reported in more than 40 years, and the first ever from southern Europe. The Croatian isolate was antigenically and genetically indistinguishable from the prototype American strain and a Ukrainian strain. Rickettsial pox would be diagnosed more frequently and in a broader geographic area if physicians gave greater consideration to the diagnosis and if laboratory diagnostic methods were more efficient in distinguishing among spotted fever group rickettsioses.