and apoptosis of CD4 positive cells refers to increased destruction of these cells via apoptosis, which may lead to the detected decrease in the CD4/CD8 ratio resulting in abnormalities in the regulation of immune responses.

**P.5.11.62** Functional alterations of the macrophage system of autoimmune BXSB mice

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**Introduction:** At an age of 8 weeks, male BXSB mice spontaneously develop an autoimmune disease that resembles human systemic lupus erythematosus (SLE). During lifetime, BXCD mice show an increasing monocytosis in the peripheral blood and macrophage proliferation in organs like liver and spleen. In order to analyse functional reactions of macrophages from male and female BXSB mice in comparison to healthy C57Bl/6 we examined the production of nitric oxide (NO), interleukin-6 (IL-6) and interleukin-10 of bone marrow derived macrophages, thioglycollate induced peritoneal macrophages (PE-MO) and spleen cells after in vitro stimulation.

**Materials and Methods:** IL-6 and IL-10 concentrations in supernatants were measured using an ELISA test system. RT-PCR was used to amplify IL-10 mRNA. 3H-Thymidine incorporation was used to determine the proliferative response of macrophage enriched cell preparations of liver and spleen to colony stimulating factors.

**Results:** The cells of liver and spleen of the autoimmune mice showed an increased proliferation after the incubation with colony stimulating factors. The IL-6 secretion of PE-MO and BM-MO was decreased compared to age matched female BXSB and C57BL/6 mice. Measured the IL-10 secretion and IL-10 mRNA expression of BM-MO no differences comparing male and female BXSB mice to C57BL/6 mice could be shown. The NO-concentration in supernatants of PE-MO was decreased in male BXSB mice compared to the other groups tested. No differences for inducible nitric oxide synthase (iNOS) gene expression, measured by northern blotting, could be detected.

**Conclusion:** Our results show that in addition to the increasing number of macrophages in BXSB mice there might be further changes in functional reaction of the macrophage system, which may be involved in the development of SLE in male BXSB mice.

**P.5.11.63** Soluble CD4 (sCD4), CD8 (sCD8) and cytokine levels in rheumatoid arthritis complicated by vasculitis

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**Introduction:** Rheumatoid vasculitis (RV) is a multi-system disease with a broad spectrum of clinical features. A damage to internal organs occurs through a widespread disorder of the microvasculature.

**Materials and Methods:** The aim of the study was to investigate a possible association between local microvascular capillaroscopic abnormalities, systemic extra-articular involvement and immunological alterations in 80 RA patients. Serum levels of soluble CD4 (sCD4), soluble CD8 (sCD8), interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF-α) were determined by enzymelinked immunosorbent assay (ELISA). In all patients nailfold capillaroscopy was performed.

**Results:** Vasculitis of the skin was demonstrated in 51 (63.7%) of cases, whereas 33 (41.3%) of patients had signs of extraarticular manifestation. In all patients with signs of systemic vasculitis, severe or moderate changes in nailfold capillaroscopy were found. Serum levels of IL-6, TNF-α, sCD4 and sCD8 were higher in RA patients than in healthy subjects. RA patients with clinical signs of systemic vasculitis showed significantly elevated serum levels of IL-6 and TNF-α as compared to those without vascular involvement. Besides, a positive correlation was found between serum sCD4 levels and vascular changes in nailfold capillaroscopy.

**Conclusion:** Our results point to a pathogenic role of the cytokine network in RV and further suggest an important role of cellular immune activation in the etiopathogenesis of microvascular damage.

**P.5.11.64** The effect of Solcoseryl on chosen parameters in patients intoxicated with heavy metals

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**Introduction:** Chronic intoxication with heavy metals has resulted in patient’s hear and teeth loss. Extensive not healing ulceration posses a direct threat for the patient’s life. Skin autografts are rejected. Thus the aim of the study was to assess the effect of toxic metals on the immunological system parameters and to assess Solcoseryl as an immunomodulatory agent.

**Material and Methods:** The examination involved a patient chronically intoxicated with thallium, cadmium, lead and bismuth, the doses exceeding hundred times the concentrations found in healthy people. There were five people in the control group.

The following immunological parameters were assessed: the subpopulations of lymphocytes by flow cytometry, IL-1β, IL-2, IL-6, TNF cytokine concentrations and soluble receptors for interleukine IL-6 and TNF by ELISA method with the use of Genzyme kits (USA).

The peripheral blood mononuclear cells (PBMC) cultures were done in standard conditions with the use of PHA, Con-A, LF-7 as stimulators and Solcoseryl as an immunomodulator.

**Results:** The study found normal distribution of lymphocyte subpopulation in the peripheral blood of the examined patient. No differences between the concentrations of IgG, IgA, IgM and the tested cytokines and soluble receptors for IL-6 and TNF in the serum of the patient and the controls were found. PBMC cultures examined the synthesis of IL-1β and IL-6 without stimulation and with stimulation induced by PHA, Con-A, LF-7 and in the presence of different Solcoseryl doses. The synthesis of the examined cytokines affected by stimulation was found normal. The presence of Solcoseryl decreased the synthesis of IL-6 to the degree depending on the used dose.

**Conclusion:** High concentrations of heavy metals were found not to affect significantly the examined parameters of the immunological system. Solcoseryl added to the PBMC culture induced by Con-A caused dose depending immunomodulatory activity both in patient and the control.

**P.5.11.65** Infection and apoptosis in NOD mice

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Most female NOD mice spontaneously develop insulin-dependent diabetes mellitus (IDDM) after the 6th month of age, with T cells playing a pivotal role in the pathogenesis of the disease. NOD's T cells display a defect in apoptosis that is mediated through several pathways. This apoptosis-resistance may be involved in the pathogenesis of IDDM in NOD mice. There are several ways in which T cell tolerance could be established and maintained. In these work we tried to determine the means by which development of 'T cell tolerance' is achieved. Previous work from our lab showed that infection of 2-months-old NOD mice with Mycobacterium avium prevents the onset of diabetes in these mice, a phenomenon that is not observed when heat-killed (HK) Avicac are used. We searched here for qualitative changes in the lymphocyte subpopulations associated with the vaccination effect afforded by M. avium infection. We found that M. avium-infected mice presented a significant increase in CD4+ T cells and B220+ B cells, at days 14 and 30 of infection, changes that were not observed in control and HK-bacilli-injected mice. Infected NOD mice showed increased numbers of CD8+ T cells, by the 7th day of infection. NOB mice that reached old age because of being protected from diabetes (due to M. avium infection) presented enhanced numbers of B220+ B cells. We conclude that the M. avium-induced protection from diabetos is associated with the triggering of an early elevation in helper T cells and in IgM- and B220+ B cells, being consistent with a Th2 dominated immune response. We also investigated the expression of cell cycle molecules involved in glucocorticoid-induced cell death, and we compared the expression of these molecules in NOD mice and non-autoimmune strains of mice: NON, BALB/c and C57Bl16 mice. We state here similarities and differences observed between these strains and the possible relation of our findings with the pathogenesis of IDDM. This investigation was supported by grants from the Portuguese Research Council (JNICT) and a Concerted Action from the EEC.

**P.5.11.66** Mercuric chloride and IL-4 differentially modify expression of MHC class II molecules RT1.B and RT1.D on B lymphocytes

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**Introduction:** Injection of HgCl₂ into BN rats induces systemic autoimmunity, involving high production of (auto-) antibodies and IgE, multi-organ inflammation, and proteinuria. Induction of disease is dependent on activation of Th2 cells. In contrast, Lewis rats are a generalized immunosuppression upon exposure to HgCl₂, which probably involves activation of Th1 cells. In both rat strains, HgCl₂ induces an early and transient increase in expression of the MHC class II (MHCII) molecule RT1.B (HLA-DQ/H-2 I-A homolog) on B cells. In vivo, HgCl₂ was shown to induce enhanced expression of RT1.B but not of RT1.D (HLA-DR/H-2 I-E homolog) on splenic B cells from BN and Lewis rats, which was partially inhibited by anti-IL-4 only in cell cultures from BN rats. We compared the effects of HgCl₂ and IL-4 on expression of RT1.B and RT1.D.

**Materials and Methods:** Expression of RT1.B and RT1.D was measured by dual color flow cytometry on lymphnode (LN) B cells from BN and Lewis rats.