

THE CHEMOKINE AND PROINFLAMMATORY CYTOKINE RESPONSE IN HUMAN NEUROCYSTICERCOSIS.

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Neurocysticercosis is a major cause of epilepsy in developing nations. For example, this infection causes approximately 20% of adult-onset epilepsy in Peru. Morbidity and mortality result from inflammation around degenerating *T. solium* larvae and are associated with immune cell, particularly eosinophil, influx to the brain during anti-parasitic therapy. Little is known about the immunopathology of infection and current anti-inflammatory therapy has limited efficacy.

We analysed serum from 9 patients and 20 controls as well as cerebrospinal fluid (CSF) from 14 patients and 9 controls. ELISAs were used to measure concentrations of the eosinophil-selective cytokines eotaxin and Interleukin (IL)-5 and of IL-8, a neutrophil attractant. In addition, bioassays were used to measure concentrations of the proinflammatory cytokine TNF- α and the acute phase cytokine IL-6.

Eotaxin was detected in the serum of all patients compared with 23.5% of controls and the serum eotaxin concentration was significantly higher in patients (geometric mean 69.9pg/ml, $p=0.01$). Eotaxin was not detected in CSF. Serum IL-5 concentrations were elevated in 78% of patients compared to 29% of controls and mean concentrations were higher in patients ($p=0.05$). CSF IL-5 was detected in 43% of patients (geometric mean 35pg/ml) but not in controls ($p=0.03$). Serum IL-6 concentrations were similar in patients and controls but CSF IL-6 was elevated in all patients compared with 44% of controls and mean levels were significantly higher in patients (geometric means 81.3pg/ml and 9.5pg/ml respectively, $p=0.02$). In contrast, TNF- α and IL-8 were rarely detectable and there were no differences between patients and controls.

This is the first report of elevated eotaxin concentrations in a human infectious disease. These findings suggest that the eosinophil-selective mediators eotaxin and IL-5 may have a role in either host defense or inflammatory injury in cysticercosis. In addition, patients with neurocysticercosis mount an acute phase response to the pathogen.

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before than after treatment ($P=0.002$) and this difference was only significant in the females ($P=0.002$).

In conclusion, we believe that hormones play a role in the changing clinical spectrum of tuberculous disease during adolescence. IL-10, known to downregulate production of type I cytokines after infection with *Mtb*, warrants further study with respect to the male/female epidemiology of TB.

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PRENATAL IMMUNE PRIMING WITH HELMINTH INFECTIONS: PARASITE SPECIFIC CELLULAR RESPONSIVENESS AND CYTOKINE PRODUCTION IN NEONATES

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The present investigation was aimed at determining the effects of prenatal exposure to helminth antigens in newborns from intestinal helminth- and filaria-infected mothers. Umbilical cord mononuclear blood cells (UCBC) responded in a dose dependent manner to mitogens (PHA, ConA) and bacterial (*Streptococcus pyogenes*, SL-O) as well as helminth-derived antigens (*Necator americanus*, *Oesophagostomum bifurcum*, *Onchocerca volvulus*). Cellular reactivity was of a similar magnitude in both mothers and their neonates when mononuclear cells were stimulated with intestinal helminth-derived antigens. Proliferative responses to filarial antigens were however significantly higher in mothers than their offspring. Several TH1-

type (IL-2, IFN- γ) and TH2-type (IL-5, IL-10, IL-13) cytokines were produced by UCBC in neonates or PBMC in mothers. Low levels of IFN- γ were elicited by UCBC in response to helminth and bacterial antigens while secretion of IL-2 was pronounced and similarly high in neonates and their mothers. Amounts of IL-5 produced by UCBC in response to bacterial SL-O and mitogenic stimulation (PHA) were low, but equivalent of levels IL-5 were induced by intestinal helminth and filaria-derived antigens in neonates and mothers. A pronounced production of IL-10 by UCBC was observed-spontaneous IL 10 secretion by UCBC was higher in neonates than by PBMC from mothers - but net amounts of IL-10 elicited by helminth antigens were similar in mothers and their offspring.

Our results indicate that maternal helminth infection will sensitize *in utero* parasite-specific cellular responsiveness in offspring and also activate specific production of several TH1- and TH2-type cytokines.

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DEVELOPMENT OF DIAGNOSTICS AND DIAGNOSTIC STRATEGIES AND THE CONTRIBUTION TO DISEASE CONTROL

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The review of the advances made in the field of diagnostics at both (1) the more conventional and (2) the molecular levels, reveals an impressive plethora of tools available for the various diseases and conditions that are of high priority in international health. These important, mainly technological, developments have substantially changed the possibilities of strategies for the diagnosis and surveillance of endemic and epidemic diseases. There is no doubt that advances in diagnostics have positively influenced disease control strategies in many areas. While the progress at the level of individual diagnosis is impressive, there are still comparatively few advances in the field of rapid population-based diagnoses. Tools and approaches that can rapidly (in relation to the needs in health planning and public health action) identify communities or population groups at risk have become essential for informed decision-making in health planning that is, in turn, a cornerstone of a decentralised health systems management. Combined with the problems of integrating diagnostic tools into health systems management, the developments of many new diagnostic tools also lead to the discussion of technology transfer issues. While we were more concerned with assuring acceptability (by addressing socio-cultural and technological issues) and applicability in the past, the field of diagnostics is now increasingly confronted with the areas of adequacy and affordability, i.e. with the socio-cultural, socio-economic and technological issues against the background of health systems factors. Using examples of individual and population-based diagnostic approaches from the field of communicable diseases, the position and application of new tools as part of strategies to achieve high community effectiveness in disease control will be presented. The discussion will also address the role of diagnostics in achieving sustainable health systems and development.

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VALIDITY, REPEATABILITY AND REPRODUCIBILITY OF THE DIRECT AGGLUTINATION TEST FOR KALA-AZAR

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Background: The serological Direct Agglutination Test (DAT) for Visceral Leishmaniasis (VL) has been recommended for field use based on its high validity and ease of implementation. For the first time, repeatability and reproducibility of the DAT were evaluated with aqueous antigen in a multicentric study carried out in VL endemic areas together as well as in an external reference laboratory (ITMA, Belgium).

Methods: DAT antigen and kits were provided by ITMA. Plain blood

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