The primary immune response in patients with chronic nonspecific lung disease (CNSLD). The role of hydrocortisone in the regulation of te cell-mediated response.

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Summary and conclusions

Aim of the study

Patients with chronic nonspecific lung disease (CNSLD) are characterized by increased airway reactivity to both specific (allergic) and non-specific environmental triggers, leading to dyspnea and/or cough.

Immunological processes play an important role in the reactions to specific factors. Especially the role of elevated levels of allergen specific IgE class antibody has been studied extensively in the past. The first question is whether increased levels of antibody result from increased exposure to the allergen in question to the immunocompetent cells, possibly due to increased permeability of the bronchial membrane, or from different immune regulation. The next question is whether a possible difference in immune regulation only applies to the IgE class antibody response, or has also consequences for antibody responses in other immunoglobulin classes and for the cell-mediated immune response.

The latter aspect is of particular interest as cell-mediated immune reactions are very sensitive to corticosteroid hormones. This is clearly illustrated by the inverse correlation between endogenously produced corticosteroid hormones and the number of immunocompetent cells in animal experiments (Del Rey, 1984). These hormones are known to show beneficial effects in patients with CNSLD, even in relatively low doses. The therapeutic success of corticosteroid medication was found to correlate with the sensitivity of the lymphocytes of the same patients to the dampening influence of the steroid hormone on in vitro proliferative responses (Poznansky, 1985). In vitro lymphocyte proliferation to allergens was found to be increased in patients with CNSLD (Rawle, 1984). Furthermore the number of mononuclear cells in (Godard, 1981) and round (Dunnill, 1984) the bronchi appeared to be increased in CNSLD. The relevance of cell-mediated immune reactions for the pathogenesis of CNSLD is increasingly recognized, as lymphocyte derived factors may play a role in inducing proliferation (Razin, 1984), attraction (Mitchell, 1984) and degranulation (Sedgwick, 1981) of mediator cells.

This study was designed to measure the humoral and cell-mediated immune response in patients with CNSLD after a carefully standardized immunological trigger. The function of the adrenal cortex was measured under basal and ambulant conditions. Furthermore the relation between the function of the adrenal cortex and the amplitude of the immune response was evaluated in patients with CNSLD and controls.
Summary of the results

Young, male, allergic patients with CNSLD, showing the clinical picture of bronchial asthma, were tested during a symptom free period. These patients were compared with an age matched control group. The immune response was measured after subcutaneous immunization with the primary immunogen Helix pomatia Haemocyanin (HPH), thus offering a direct, standardized trigger to the immune system.

The antibody responses to HPH in the IgE and IgG classes appeared to be highest in the patient group (chapter 1). IgA class antibody responses in the patients tended to be higher as well, though this was not statistically significant. IgM class antibody responses were normal in the patient group, apart from temporarily elevated values in the early phase of the response. Thus antibody responses after standardized immunization tended to be elevated in the patients, suggesting a disturbance in immune regulation which is expressed increasingly in the order IgM-IgA-IgG/IgE.

Antibody responses in the IgG, IgE and IgA classes appeared to be correlated. IgM class antibody responses, however, were not correlated with the responses in the other antibody classes.

Elevated primary IgE class antibody responses to HPH were also observed in patients with CNSLD, who are skin test negative to allergens (disc I.B).

Anti-HPH IgE class antibody levels appeared to be correlated with the diameters of HPH-induced skin reactions at 15 minutes and 8 hours, but not with the reaction at 24 and 48 hours after skin testing (disc II.C).

HPH-induced skin reactions at 24 and 48 hours, and HPH-induced in vitro lymphocyte proliferation responses were compared between patients and controls in chapter 2. No differences could be observed between the two groups with respect to these parameters for the cell-mediated immune response. In vitro lymphocyte proliferation appeared to be correlated with the skin test diameter at 24 hours. In vitro and in vivo cell mediated responses were correlated only with IgM class antibody responses, but not with the responses in IgG, IgE or IgA antibody classes.

The HPH-specific IgE antibody response in patients and controls was compared with the IgE class antibody levels to the allergen housedustmite and a major allergen from this extract (P1). This comparison revealed a much larger difference in anti P1 antibody levels between patients and controls, due to the absence of anti-P1 antibody in the control group. This observation could not be explained by the differences in immunoregulation, as reflected in the HPH response, alone (disc I.C). Furthermore other studies revealed that in vitro cell-mediated responses to antigen P1 could be induced in patients with CNSLD, but were low or absent in controls. Therefore it was