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# Serum antibodies to dietary antigens in patients with HIV-1 infection

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Diarrhoea is a common complication of HIV-1 infection [1], but in a considerable proportion of patients, especially in earlier stages of the disease, the cause of diarrhoea remains unclear despite extensive investigation [2]. Increased levels of serum antibodies against food proteins have been described in HIV-infected children [3], similar to patients with non-IgE-mediated gastrointestinal food hypersensitivity [4], coeliac disease [5], or chronic inflammatory bowel disease [6]. These abnormalities are thought to result from increased gut permeability leading to increased uptake of dietary antigens and an aberrant mucosal IgG response in these patients [7]. Increased intestinal permeability [8] and an increase of IgG in mucosal secretions [9] have also been found in patients infected with HIV-1. Since abnormal immunity to dietary antigens may contribute to the pathogenesis of diarrhoea, we investigated serum antibodies to food proteins in HIV-1-infected patients with and without diarrhoea.

Sera from 70 consecutive HIV-infected patients (65 men, five women) attending the HIV outpatient clinic were studied. Forty-three patients had AIDS. The median age was 44 years (range, 29-64 years) and the median CD4 T-cell count was 65 × $10^6$/l (range, 4-987 × $10^6$/l). Eleven HIV-infected patients had diarrhoea. In six of these patients an enteric pathogen was found (*Salmonella* sp. and microsporidia infection each in two patients, *Mycobacterium avium* complex and *Isospora belli* infection in one patient, and one patient with microsporidia had additional coronavirus infection). Blood samples from 20 healthy controls (15 men, five women; mean age, 55.5 years; range, 18-73 years) not at risk for HIV infection and without evidence for immune defect served as controls.

Serum IgG, IgA and IgM titres against the dietary antigens β-lactoglobulin, α-lactalbumin, ovalbumin, and soy protein, and the non-dietary antigen tetanus toxoid were measured by enzyme-linked immunosorbent assay. Because serum immunoglobulins are unspecifically increased in HIV-infected patients compared with controls, antibody titres were corrected for serum immunoglobulin concentrations as measured by single radial immunodiffusion. Serum IgG, IgA and IgM antibody levels against all food proteins (except anti-β-lactoglobulin IgM) were significantly higher in HIV-infected patients than in controls. In contrast, IgG antibody titres against tetanus toxoid were decreased in HIV-infected patients compared with controls (each $P < 0.05$; Fig. 1). No differences were found for IgA and IgM antibody titres against tetanus toxoid. When antibody titres were expressed in relation to the respective serum immunoglobulin concentration, IgG antibody levels against all food proteins tested were still increased (each $P < 0.01$), although IgG against tetanus toxoid was decreased in HIV-infected patients compared with controls. Relative IgA and IgM titres against the tested proteins were similar in HIV-infected patients and controls. No differences were found between HIV-infected patients with and without AIDS. Median antibody titres for IgG, IgA, and IgM against all tested food proteins were higher in HIV-infected patients with diarrhoea than in patients who had no diarrhoea, but a significant difference was found only for IgG antibodies against ovalbumin ($P < 0.05$).

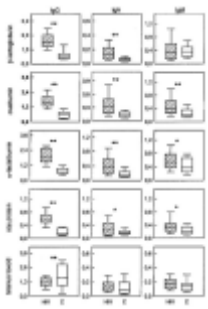

**Fig. 1**. Serum IgG, IgA and IgM antibodies to the dietary proteins β-lactoglobulin, ovalbumin, α-lactalbumin, soy protein and the non-dietary protein tetanus toxoid. Antibodies were measured by enzyme-linked immunosorbent assay in 70 HIV-infected patients, of whom 43 had AIDS, and in 20 healthy controls. IgG, IgA and IgM antibody levels against all food proteins (except IgM anti-β-lactoglobulin antibodies), but not against tetanus toxoid, were significantly higher in HIV-infected patients than in controls (C). *$P$ < 0.05, compared with controls; **$P$ < 0.01, compared with controls.

Our results show an increase of serum antibodies against four common food proteins in HIV-infected patients. This is not due to unspecific polyclonal B-cell activation because immunoglobulin levels were still increased when antibody levels were corrected for total immunoglobulin concentration. In addition, no increase of serum antibodies against the non-dietary protein tetanus toxoid was observed. The appearance of antibodies to food proteins in serum indicates an abnormal access of these antigens to the mucosal immune system, probably due to an impaired epithelial barrier function [8]. Although we did not specifically investigate local humoral immunity, the increased mucosal production of IgG in HIV-infected patients [10] and the high IgG levels in duodenal secretions of HIV-infected patients [11] indicate considerable transudation of serum antibodies into the gut. In contrast to the immune exclusion mediated by secretory IgA, IgG antibodies to food proteins will form immune complexes if their respective antigens are present in the mucosa and will activate complement [12]. The resulting mucosal inflammation that is frequently observed in the intestine of HIV-infected patients [13] may not only establish a vicious circle perpetuating impairment of epithelial barrier function but could also contribute to the pathogenesis of diarrhoea. The increased immunity to food proteins in HIV infection shown in our study suggests that HIV-infected patients might benefit from nutritional interventions. This should be tested primarily in HIV-infected patients with high titres of serum antibodies to dietary antigens.

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