

### Cows' milk and diabetes

There are, apparently, rats which when reared on cows' milk develop diabetes but they remain free of the disease if they are not given cows' milk in the first three months of life. A case-control study in Finland showed that children who received no cows' milk in the first four months had a reduced risk of diabetes up to the age of 7 years (odds ratio 0.48).<sup>1</sup>

Cows' milk contains bovine serum albumin (BSA) and the diabetes-prone rats can be made resistant to the effect of cows' milk feeding by inducing immunotolerance to BSA. Immunisation against BSA makes them develop diabetes all the faster. Why should anti-BSA antibodies bring on diabetes? Well, it seems that these antibodies cross react with a protein found on the surface of the pancreatic beta cell, called p69. At this point the plot thickens because the expression of p69 on the surface of the beta cells is induced by interferon gamma. Ah-ha, you say, herein lies the makings of a very neat little hypothesis. Babies fed cows' milk ... immune system develops 'memory' for BSA ... later infection ... interferon released ... p69 induced ... p69 itself stimulates production of more BSA/p69 antibodies ... beta cells destroyed ... repeat process several times ... diabetes! Hold onto your hats we're in exciting territory.

Finnish workers have collaborated with workers in Toronto to study 142 children with newly diagnosed diabetes and 79 control children matched for age, sex, and region of residence (Jukka Karjalainen and colleagues, *New England Journal of Medicine* 1992; 327: 302-7). At the onset of diabetes serum concentrations of IgG antibodies to BSA ranged from 3.6 to 18.2 kilofluorescence units/ $\mu$ l in the patients. The range in controls was 0.7 to 3.5 ( $p < 0.001$ ). For IgA antibodies the ranges were 1.4 to 7.6 in patients and 0.8 to 3.5 in controls ( $p < 0.001$ ). Concentrations of serum IgM antibodies to BSA were significantly lower in the patients than in controls ( $p < 0.05$ ). There was no difference between patients and controls when IgG antibodies to other milk proteins (casein and  $\beta$  lactoglobulin) were measured. Anti-BSA antibody concentrations declined slowly over one or two years after the onset of diabetes.

Previous work by these authors has identified a 17 amino acid sequence in the BSA molecule which differs from the analogous sequence in human, rat, and mouse albumins. This peptide is called ABBOS and anti-ABBOS antibodies have been shown to react with p69. When serum from patients in the present study was incubated with ABBOS the concentration of anti-BSA antibodies fell by about two thirds indicating that much of the anti-BSA antibody reacted specifically with the ABBOS peptide and the follow up studies showed that anti-ABBOS antibody was the first to decline. Most of the anti-BSA antibodies found in normal children and in adult blood donors were not directed against ABBOS.

The authors postulate that at the time of onset of diabetes the antigen responsible for the generation of anti-BSA antibodies is p69 and the gradual destruction of remaining beta cells explains the decline in antibody concentrations over the next year or two. They do not speculate about the significance of their findings as regards prospects for the prevention of diabetes. Not giving cows' milk to babies can't be the complete answer otherwise no baby fully breast fed for the first few months would ever develop the disease and some in the Finnish case-control study clearly did. Could it lead to the prevention of some cases? Would adding anti-ABBOS antibody to infant formulas do any good? We can live in hope.

ARCHIVIST

<sup>1</sup> Virtanen SM, Räsänen L, Aro A, *et al.* Infant feeding in Finnish children 7 years of age with newly diagnosed IDDM. *Diabetes Care* 1991; 14: 415-7.