hypoallergenic formula for 6 weeks. They were then readmitted for cows milk challenge studies as previously described.[1] At the time of readmission the infants were clinically well and had registered satisfactory weight gains on pregestimil. The stools from all three were negative for enteropathogens. Jejunal biopsies were performed immediately before and 24 h after CMP provocation. Informed consent was obtained from all parents of the infants for jejunal biopsy.

The histological appearances of the pre- and post-challenge biopsies were normal. However, the electron microscope showed mild but recognizable and quantifiable changes in the enterocytes, particularly in the microvilli. Compared to the pre-challenge, the microvilli in the post-challenge biopsies were shorter, sparser and malaligned. Some of the microvilli were fractured. The infants continued to thrive on the CMP formula without clinical reactions when reviewed at 1, 7, and 30 days after challenge.

Mucosal response to antigenic food protein challenge may range from severe villous atrophy associated with clinical symptoms, to mild histological changes without symptoms.[3] The current study suggests that the spectrum of mucosal injury may include subcellular changes in the microvilli without any overt histological changes under the light microscope. These observed subcellular changes may explain the impaired xylose absorption, probably due to the depletion of mucosal oligosaccharidases, despite normal histological appearance of the jejunal mucosa.

We suggest that the intestinal mucosa thriving in a hypoallergenic environment will react when it is suddenly exposed to antigenic CMP. However, the severity of the reaction is most probably due to the outcome of a combination of multiple factors related to the competency of the immuno-digestive function, interplay between Th1 and Th2 immune-regulatory response, and the interaction of CMP antigens with living organisms in the gut.[4]

Earlier we hypothesized that the intestinal mucosa of young infants recovering from acute gastroenteritis when exposed to CMP, may become sensitized to CMP and develop secondary CMA and lead to protracted diarrhoea and intractable diarrhoea of infancy syndrome.[5] However, this observation raises the possibility that the converse may also be possible. Thus, minimal injury to the microvilli induced by CMP in bottle-fed infants may render the enterocyte vulnerable and facilitate its colonization and infection by viral, bacterial, and parasitic enteropathogens. Enteric colonization may remain subclinical or may progress to overt clinical disease, unmasking the underlying CMA. The enteric infection may in turn potentiate the progression of CMA by causing further damage to the mucosa thereby increasing its permeability to CMP. This results in a vicious cycle that ultimately leads to intractable diarrhoea of infancy syndrome.

It is generally well known that bottle-fed infants have a higher incidence of gastrointestinal infections due to absence of breastmilk-protective factors. It is possible that the subtle structural damage to the microvilli could contribute to the vulnerability of the enterocytes to enteropathogenic colonization. The subcellular changes may also have other implications such as the reduced absorptive capacity of the enterocytes for macro- and micronutrients. Further studies are clearly indicated to confirm these observations.

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Investigating for Inborn Errors of Metabolism with Tandem Mass Spectrometry in Ankara Region, Turkey: A 2 Years Evaluation

The prevalence of inborn errors of metabolism is relatively high in Turkey, at least in part due to frequent consanguineous marriages.[1]

Tandem mass spectrometry (MS/MS) is an analytical technique, by which not only the structure, but perhaps more importantly, the concentration of many compounds can easily and quickly be determined.[2] In Gazi University Hospital Department of Pediatric Metabolism and Nutrition, all the babies who were born in our hospital, as well as the babies and children that were considered to be at risk for metabolic diseases, were investigated with tandem mass spectrometry 24 months ago. Gazi University Hospital is located in central Ankara, the capital, to

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which about 50 000 patients a year are admitted from Ankara and other cities in Turkey. Between September 1999 and October 2001, a total of 2607 babies were investigated. A total of 2120 were newborns, born in Gazi University Hospital or followed-up in the newborn unit with any diagnosis, and 487 were at-risk babies referred to our hospital between the ages of 5 days and 96 days who had symptoms or signs pointing to an inborn error of metabolism. Blood samples were drawn by lancets on Guthrie Cards when the babies were 3 days old.[2,3] The sample preparation procedure for MS/MS analysis of amino acids and acylcarnitines was made according to the consensus procedure.[4] All the results were confirmed by GC/MS, enzymatic, or genetic analysis.

Among the 487 at-risk infants, eight infants with phenylketonuria, five with propionic acidemia, two with glutaric aciduria type 2, one with type 1, two with hydroxymethylglutaryl CoA lyase deficiency, one with maple syrup urine disease, one with methylmalonic acidemia, and one with holocarboxylase synthase deficiency were diagnosed. No metabolic disease was noticed among the 2120 babies who were born uneventfully in our hospital and those followed-up in the newborn unit until now.

The incidence of inborn errors of metabolism is reported to be 1 in every 3500–4500 newborns screened by MS/MS.[3,5] In our laboratory, 21 children out of 487 at-risk babies (about 4.5 per cent) were found to have a metabolic disease. This could be considered as a high but not unexpected frequency compared with the other reports of 'high risk' screening by MS/MS,[5] as it is known that consanguineous marriages are frequent in Turkey (about 21 per cent).[1] Of course the small population of babies investigated in the Ankara region cannot reflect the real incidence of inborn errors of metabolism for the whole of Turkey, but we consider it worthwhile to report the first investigation results with MS/MS from Turkey. The incidence of metabolic diseases would probably be greater with a greater number of babies screened.[6,7]

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