Vitamin C-Dependent Hypertyrosinemia in Small Premature Babies: Diagnosis Through Routine Metabolic Screening in Urine

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High-protein feeding of newborns frequently produces transient elevations of tyrosin in plasma. Up to 30% of small premature babies will show this metabolic abnormality. In some cases, neurological symptoms have been observed; the long-term prognosis has not yet been defined. Reduced protein intake or supplementation with 75 to 100 mg vitamin C daily has been effective in normalizing plasma tyrosin.

Inadequate metabolism of protein in newborns leads mainly to elevated tyrosin and phenylalanine levels. The rate-limiting enzyme for tyrosin metabolism seems to be the p-hydroxypyruvic acid oxidase, an enzyme that is itself inhibited by its substrate. In vitro vitamin C and other reducing substances can protect the enzyme from substrate inhibition.

In the case of hypertyrosinemia, various metabolic products of this amino acid appear in urine, the main ones being p-hydroxyphenylpyruvic acid as well as the acetic acid derivative. A semiquantitative one-dimensional high-voltage electrophoresis used for metabolic screening purposes can easily detect signs of plasma hypertyrosinemia.

From 1976 to 1985, 158 surviving, very small premature babies (birth-weight <1,150 g) were screened for metabolic diseases. One morning, urine was evaluated as soon as full oral feeding had been established. All babies received breast milk, the target being 200 ml/kg/day, equivalent to a protein load of approximately 2.2 g/kg/day.

Eighteen babies (11.4%) had elevated urine excretion of p-hydroxypyruvic acid; some of them had mild generalized hyperaminoaciduria. Mean age at diagnosis was 8.2 days. Oral therapy with vitamin C 50 mg/day normalized...
this finding within 3 to 8 days without any reduction in protein supply. This survey indicates that breast milk feeding of small premature babies, despite its low protein load, will in some cases produce signs of hypertyrosinemia. This metabolic disturbance can easily be detected in routine urinary metabolic screening programs. Vitamin C supplementation will normalize urinary chromatograms and hence plasma tyrosin levels.