

DIFFERENTIATION OF CHRONIC GALACTOSEMIA AND MILK ALLERGY IN EARLY CHILDHOOD

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AMONG causes for vomiting, colic, and diarrhea in the newborn infant, food allergy is common, especially that due to cow's milk. The relief of the child's difficulties by the elimination of milk need not necessarily lead to the diagnosis of milk allergy, however.

This paper aims to call attention to a disease which has recently become quite well known in pediatric circles. In 1908 von Reuss⁷ and in 1917 Goeppert¹ observed galactosemia and galactosuria in certain children after the ingestion of milk and other foods containing galactose. This disease seems to be of hereditary origin, the result of a single recessive gene or of a more complex genetic pattern.⁴ The specific enzymatic defect in galactosemia is the absence of an enzyme, phosphate-galactose-uridyl-transferase, which is responsible for the transfer of galactose-1-phosphate to glucose-1-phosphate.^{5, 6}

These children frequently present themselves with gastrointestinal disorders such as diarrhea, vomiting, or abdominal distention.² Malnutrition, hepatomegaly, jaundice, splenomegaly, lamellar cataracts, mental retardation, and proteinuria are all occasional features of this disease called galactosemia or galactose diabetes.³

The diagnosis is frequently missed, because such a child in the hospital is given only glucose water, parenteral fluids, or nothing by mouth, leading therefore to the absence of reducing substances in the urine.

Some of the defects mentioned occur only if the disease has been allowed to progress undetected for any length of time. The usual disappearance of all subjective and objective symptoms on a milk-free diet, with substitution by soybean, meat-base, or protein formulas, is dramatic and leads to the need for pointing out differential diagnostic points between this disease and milk allergy, as described in Table I.

The diagnosis of chronic galactosemia is proved by the presence of abnormal amounts of galactose in the urine and blood, present only if the child has ingested foods containing galactose. Galactose is not fermented by yeast in contradiction to glucose and thus can be differentiated from the latter. The addition of phenylhydrazine to galactose yields typical galactosazone crystals.

Many of these points are illustrated by the following case from U. S. Army Hospital, Fort Knox, Kentucky.

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TABLE I. DIFFERENTIAL DIAGNOSTIC POINTS

SYMPTOMS	CHRONIC GALACTOSEMIA	MILK FOOD G.I. ALLERGY
Nausea	May be present	May be present
Vomiting	May be present	May be present
Colic	May be present	May be present
Diarrhea	May be present	May be present
Failure to gain weight	May be present	May be present
Jaundice	Usually present	Absent
Hepatomegaly	Usually present if disease of longer duration	Absent
Lamellar cataracts	Usually present if disease of longer duration	Absent
Mental retardation	Usually present if disease of longer duration	Absent
Proteinuria	Usually present	Absent
Galactosuria	Present if child on milk	Absent
Symptoms present if child is fed	Any milk, including human milk	Only one species-specific milk
Symptoms disappear on cessation of milk feedings	Yes	Yes
Galactose tolerance test	Elevated, abnormal	Normal
Skin test to cow's milk	Negative	Sometimes positive
Family history of allergy	Usually no	Usually yes
Family history of galactosemia	Sometimes yes	No

H. A. W. was a full-term white male infant, born on July 31, 1956, to a primiparous mother. The past history of the parents, the prenatal course, and the delivery were non-contributory except that the mother's catheterized urine specimen taken at the delivery table contained a trace of sugar. There was no family history of allergies or of symptoms which could have been the result of chronic galactosemia.

The physical examination of the infant one day after delivery failed to reveal any physical abnormalities.

The child was breast-fed by the mother and received no supplemental cow's milk feedings. There was no fever, diarrhea, or excessive crying. On August 3, the child appeared jaundiced, but this was judged to be due to physiologic jaundice and the child was discharged on the fourth day. Laboratory work-up showed no evidence of Rh, ABO, MN, or any other blood incompatibility; both the child and the mother were O, Rh positive, and the direct Coombs' test was negative. On August 10, the child was readmitted to the hospital because of diarrhea for three days and inability to take an evaporated milk formula (breast-feeding was discontinued after discharge from the hospital), and jaundice of six days' duration. Physical examination at this time showed a weight of 6 pounds, 1½ ounces, compared with a birth weight of 7 pounds, 2½ ounces. The child appeared jaundiced and malnourished, but liver and spleen were not enlarged; the lenses appeared clear and an ophthalmologist failed to detect any lamellar cataracts. The diagnosis on admission was acute gastroenteritis.

The initial laboratory results were: *urine*: trace of albumin, sugar 3 plus, being a nonglucose reducing sugar, 13 to 16 W.B.C. and 4 to 5 R.B.C.; *blood*: R.B.C. 5, 45 W.B.C. 14,550, neutrophils 64, leukocytes 36, hemoglobin 18.6, with no nucleated red cells on the peripheral smear. The total bilirubin on admission was 27.4 mg. per cent, with 20.9 mg. per cent being indirect and 6.5 mg. per cent being direct; the stools appeared yellow and bile-stained.

The child was placed on a mixture of equal parts of 10 per cent Arobon solution and Lytren feedings,* which led to the control of the diarrhea in two days. The child appeared "quiet between feedings" on the third day of treatment and also appeared less jaundiced.

*Arobon is carob powder produced commercially by Nestlé products, White Plains, New York; Lytren is an electrolyte solution produced commercially by Mead Johnson & Co., Evansville, Indiana.

Urinalyses on August 13 and 14 were negative for sugar, and on August 14, the child was placed on Nutramigen* feedings ad lib. He started to gain some weight and there was no jaundice present on August 16. Evaporated cow's milk formula was started on August 16 and within three hours galactosuria was noted and was present in each urine specimen while the child was given milk.

On this diagnostic trial the diarrhea and vomiting recurred and the child stopped gaining weight. Frequent crying and colicky behavior were noted. After seven days on milk there was, however, no recurrence of the jaundice. The trial was stopped and the urine became negative for sugar. The child was first placed on equal parts of 10 per cent Arobon-Nutramigen, and, after cessation of the diarrhea, on plain Nutramigen. Two galactose tolerance tests were performed. On one occasion 1.75 Gm. of galactose per kilogram of body weight was administered by bottle in form of a galactose-water solution after the bladder was emptied. A four-hour total urinary output yielded 1.24 Gm. of galactose (normal for newborn infants, less than 1 Gm). On another occasion the same procedure was employed. The results are seen in Table II.

TABLE II

	BLOOD GALACTOSE IN MG. PER CENT	URINE "SUGAR"
Fasting	0	Negative
½ hour	142	+++
1 hour	76	+++
2 hours	151	+++

The blood galactose levels were obtained by first determining total blood sugar levels and then subjecting this blood sugar to yeast fermentation. The undigested component was interpreted to be galactose. Multiple blood and urinary specimens were also examined with phenylhydrazine and yielded typical galactosazone crystals.

On discharge August 31, he was placed on a milk-free diet and has done well other than for a minor U.R.I. and diarrheal episode in October. He is alert and cooperative; no mental defect is apparent, the eyes show no evidence of cataracts, and periodic urinalyses reveal no sugar. At no time was there hepatomegaly or splenomegaly. A recent emergency operation for an incarcerated inguinal hernia was performed. His only problem at present is difficulty in gaining weight and a slight hypochromic microcytic anemia.

DISCUSSION

Since early diagnosis of galactosemia can prevent irreparable damage such as mental retardation, cataracts, and hepatomegaly, practicing physicians should be on the alert for such a possibility. The initial symptoms may mimic milk allergies in infants, and it is wise to do urinalyses in every case of suspected milk allergy and galactosemia. Since children admitted for diarrhea or gastroenteritis are usually placed on milk-free electrolyte feedings, a negative urine analysis may be misleading. Galactosuria occurs only when the child has ingested galactose; therefore, the diagnosis will be easily missed on a milk-free diet. Just as a diagnostic trial on milk is used to prove milk allergy, it is used likewise to prove galactosemia, and the importance of urinalysis and galactose tolerance tests should be equally important as specific allergy test procedures.

*Nutramigen is a commercially prepared hypoallergenic formula, containing a pancreatic hydrolysate of casein combined with carbohydrate, fat, and minerals but free of lactose or galactose. (Manufactured by Mead Johnson & Co., Evansville, Indiana.)

Jaundice aids in the diagnosis of galactosemia and its occurrence in the presence in a milk allergy would require a work-up involving studies for galactosemia as well as liver disease. A child with milk allergy, failure to gain weight, and appearance of mental retardation or cataracts should likewise be studied for galactosemia.

Helpful features in the diagnosis of galactosemia are the usual absence of a family history of allergies and sometimes a history of similar members of the family being blind or jaundiced in early childhood, pointing to familial galactosemia. Galactosemia occurs in children who are fed any milk, including human milk, which is obviously not the case in milk allergies to a species-specific milk antigen.

SUMMARY

Gastrointestinal milk allergies in early childhood should be differentiated from chronic galactosemia, which is characterized by galactosuria and usually by vomiting, colic, diarrhea, failure to gain weight, jaundice, hepatomegaly, lamellar cataracts, and mental retardation. One case has been presented. The early diagnosis of chronic galactosemia may prevent most of the serious complications.

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