

Association Of *Escherichia coli* Sepsis And Galactosemia In Neonates

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Family physicians frequently care for neonates who have jaundice and sepsis. There is a strong association between serious infection and galactosemia in infants. A case is presented describing a neonate with jaundice and sepsis caused by *Escherichia coli* who was found to be galactosemic in the first week of life. The symptoms of galactosemia are discussed together with biochemical abnormalities leading to an increased frequency of infection and sepsis in these infants.

Case Report

A 20-year-old woman, gravida 2, para 1, abortus 0, gave birth to a 3800-g (8 lb, 3 oz) girl by spontaneous vaginal delivery. Her prenatal course was unremarkable. The same couple also had a 20-month-old healthy boy.

The new baby thrived on house formula until day 2 of life, when the mother noted poor feeding and frequent emesis. Initial evaluation was remarkable only for the infant's bilirubin level (258 $\mu\text{mol/L}$ [15.2 mg/dL]). Phototherapy was initiated. After 24 hours, the baby appeared pale, lethargic, and continued to feed poorly. An evaluation for sepsis was performed, and intravenous administration of gentamicin and ampicillin was begun. Laboratory studies indicated elevated liver function tests, abnormal clotting factors, and urine positive for reducing substances. A presumptive diagnosis of galactosemia was entertained. Later blood and urine cultures grew *Escherichia coli*.

At 5 days of life, vomiting had ceased, and the infant was fed a lactose-free formula. On day 11 of life, metabolic screening confirmed the diagnosis of galactosemia. The infant completed 14 days of intravenous antibiotics and tolerated the lactose-free formula. She was discharged home on day 17 of life feeding well with steady weight gain.

Follow-up care has been carried out in the Department of Family Practice of the Naval Hospital, Camp Pendleton, California, and the Pediatric Metabolic Clinic of University of California, San Diego. Electrophoresis subsequently showed a low galactose-1-phosphate uridyl transferase level (0.1 U/g hemoglobin; normal range 18.5–28.5 U/g hemoglobin) as the cause of the galactosemia. Well-baby checkups at 2 and 4 months have shown her to be a vigorous infant in the 25th to 50th percentile for weight and length and the 50th percentile for circumference. Bilateral small cataracts developed but are expected to resolve on the lactose-free diet. The adequacy of the dietary therapy has been assessed by monitoring the galactose-1-phosphate level in red cells. A good prognosis exists because of early diagnosis.

Discussion

A review of the pertinent literature from 1960 to the present shows an association of galactosemia with life-threatening infection, particularly *E. coli* sepsis. In 1960 Donnell, et al.¹ described an increased susceptibility to infection in infants with galactosemia. In 1963 neonatal screening for galactosemia was instituted in Massachusetts. Levy, et al.² analyzed the information obtained, discovering that *E. coli* was the cause of most of these infections in galactosemic newborns. Twenty-nine percent of galactosemic infants became infected. Of these, 90 percent had *E. coli* infections with an 89 percent mortality rate.

Galactosemia, first described in 1908, is an autosomal recessive congenital disorder.¹ The gene abnormality produces a deficiency of either galactose-1-phosphate uridyl transferase or galactokinase (Figure 1). The incidence of galactosemia resulting from the transferase deficiency ranges from 1 in 60,000 to 1 in 80,000. The frequency of the galactokinase deficiency is approximately 1 in 250,000.³ These inborn errors of galactose metabolism result in an inability to metabolize the galactose derived from lactose to glu-

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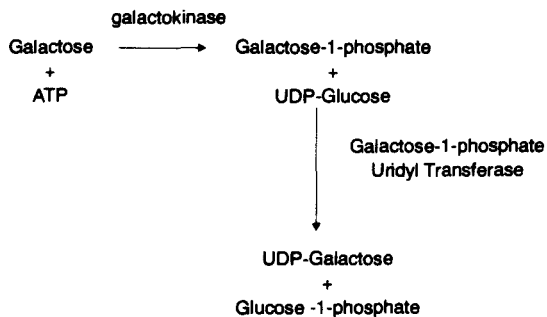


Figure 1. Galactose metabolism. ATP = adenosine triphosphate, UDP = uridine diphosphate. Used with permission from Bondy PK, Rosenberg LE, editors. *Metabolic control and disease*. Philadelphia: W.B. Saunders, 1980:370.

cose metabolites. When galactose is administered to patients with the deficiency of galactose-1-phosphate uridyl transferase, clinical consequences in neonates include vomiting, failure to thrive, liver disease, cataracts, and jaundice. In more advanced untreated cases, cirrhosis of the liver, ascites, mental retardation, and death occur.⁴ Accumulation of galactose-1-phosphate in red cells and tissue can be responsible for the liver abnormalities, cataracts, and renal changes. In addition, galactose depresses the glucose level, causing seizures and mental retardation.⁴ Toxicity in galactokinase deficiency is less severe and mainly manifests as cataracts.⁵

According to Bondy and Rosenberg,⁶ the absent enzyme causes galactose-1-phosphate and galactitol to accumulate in blood and tissues, including liver, spleen, lens of the eye, kidney, heart,

and cerebral cortex. This accumulation is responsible for many of the clinical manifestations. Notably, uncontrolled galactosemic pregnant women can produce affected infants.⁶ In addition, Levy, et al.² noted that both bacterial infections and the clinical signs can relate to the severity of the biochemical abnormalities (Table 1).

In 1971 Kelly⁷ suggested that the concomitant infections associated with galactosemia follow a mechanical route. Infants with galactosemia can be susceptible to septicemia as a result of excessive vomiting or diarrhea. The urinary tract might be the source of infection. The substrate for the bacteria would be accumulation of galactose in the tissue. This theory is supported by the isolation of only lactose-fermenting organisms. In addition, broth suspensions of *E. coli* isolated from feces grew greater numbers of galactose- and lactose-enriched media.⁷ Litchfield and Wells⁸ studied the biochemical effects of galactosemia. They suggested that impaired bacteriocidal activity of polymorphonuclear leukocytes was responsible for the association of galactosemia and sepsis. They found that both phagocytosis and bacteriocidal activity are impaired in polymorphonuclear leukocytes when galactose accumulates. Phagocytosis depends upon energy from glycolysis. The bacteriocidal activity requires both an increase in the hexose monophosphate shunt and reduction of oxygen to a free radical intermediate. Both of these reactions are impaired by the accumulation of galactose and contribute to the observed increased morbidity and mortality.⁸

Summary

Galactosemia in newborns and infants is associated with the following symptoms: jaundice, hepatomegaly, failure to thrive, feeding difficulties, hypoglycemia, convulsions, lethargy, aminoaciduria, cataracts, hepatic cirrhosis, ascites, and mental retardation.⁹ If the preliminary evaluation indicates galactosemia, there is high risk for *E. coli* sepsis and death. Strong consideration should therefore be given for early antibiotic therapy in infants with suspected galactosemia in spite of the absence of clinical signs or symptoms of sepsis.

References

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Table 1. Comparison of the Signs and Symptoms of Galactosemia with Galactose-1-Phosphate Uridyl Transferase versus Galactokinase Deficiency.*

Enzyme Deficiency	Tissue Distribution	Signs and Symptoms
Galactose-1-phosphate uridyl transferase	Liver Erythrocytes Intestine	Vomiting Hypoglycemia Hepatomegaly Hepatic cirrhosis Splenomegaly Jaundice Cataracts Aminoaciduria Glucosuria Mental retardation
Galactokinase	Erythrocytes Liver	Cataracts

*Used with permission from Hug.⁹

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