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This Week's Citation Classic®

Gitzelmann R. Hereditary galactokinase deficiency, a newly recognized cause of juvenile cataracts. *Pediat. Res.* 1:14-23, 1967.
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The report describes the first patient known to have hereditary galactokinase deficiency, his equally affected sisters, and his family. It establishes that the disorder causes juvenile cataracts and galactose-galactitol-glucose diabetes. [The *SCI*® indicates that this paper has been cited in over 145 publications.]

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In 1956 in Berne, Carl Cori and Herman Kalckar lectured on disorders of carbohydrate metabolism. I was a young intern asked to present excerpts of my doctoral thesis. British colleagues reported the first cases of galactosemia, which we had never seen at the Children's Hospital in Zürich. Before long, I diagnosed our first case, began to read old records, and came upon those of a nine-year-old blind gypsy boy seen in 1932. The charts had been carefully handwritten by Guido Fanconi, then a young chairman of the department he was still heading. The boy, a presumed diabetic, had *galactose* diabetes, a unique anomaly Fanconi identified while studying the effects of a fruit and vegetable diet. The boy had melituria only after drinking milk,[1] which, to my amazement, he had tolerated well! Was he indeed a galactosemic?

In 1963, after three years of fellowship in the US, I was given my own small laboratory. After losing time installing a water still (the first in our hospital), as well as our administrator's goodwill (for buying a mechanical calculator, considered an extravagance), I was able to locate the patient in a home for the blind. He was now 40 years old, drank two liters of milk daily, and had *normal* transferase but no galactokinase.[2] I spent many months (and developed a detective's skills) tracking down his family in their caravans and mobile homes to obtain blood for galactokinase assays. In the process, I learned some gypsy history and how to negotiate a gypsy's permission to draw blood from his wife, who was usually hidden in the rear when I approached.

The publication interested biologists, probably because the *Escherichia coli lac* operon was still very much in the air. Bob Guthrie heard of my discovery and on his first visit rounded the corner to my lab and curtly asked, "OK, what's his transferase?" and only then shook hands with me. As I had speculated, the disorder was later discovered in newborns through mass screening (although it did not appear in over 1.5 million young Swiss) and thus became an early example of a preventable hereditary disease. It shed far more light on the pathogenesis of galactosemia than had two years of my previous work on dozens of galactose-poisoned rats. And of course, it had a mildly exotic flavor as a "gypsy disease." To date, of the 21 European children diagnosed in my lab, 16 are either gypsy, Bulgarian, Yugoslavian, or all three.

Although I have not received any awards for this work, discovery of galactokinase deficiency gave me credit as a researcher and helped my academic career. It also taught me that human mutations can be predicted. Indeed, the first mutant for the last of the three steps in the Leloir pathway[3,4] was soon to be discovered.[5]

1. **Fanconi G.** Hochgradige Galaktose-Intoleranz (Galaktose-Diabetes) bei einem Kinde mit Neurofibromatosis Recklinghausen (Severe galactose intolerance (galactose diabetes) in a child with Recklinghausens neurofibromatosis). *Jahrb. Kinderheilk.* 138:1-8, 1933.
2. **Gitzelmann R.** Deficiency of erythrocyte galactokinase in a patient with galactose diabetes. *Lancet* 2:670-1, 1965. (Cited 90 times.)
3. **Segal S.** Disorders of galactose metabolism. (Stanbury J B, Wyngaarden J B, Fredrickson D S, Goldstein J L & Brown M S, eds.) *The metabolic basis of inherited disease.* New York: McGraw-Hill, 1983. p. 167-91.
4. **Gitzelmann R & Hansen R G.** Galactose metabolism, hereditary defects and their clinical significance. (Burman D, Holton J B & Pennock C A, eds.) *Inherited disorders of carbohydrate metabolism.* Lancaster, England: MTP Press, 1980. p. 61-101.
5. **Gitzelmann R.** Deficiency of uridine diphosphate galactose 4-epimerase in blood cells of an apparently healthy infant. *Helv. Paediat. Acta* 27:125-30, 1972.

CC/ 1-14