

# This Week's Citation Classic

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Durand P. Lattosuria idiopatica in una paziente con diarrea cronica ed acidosi.  
(Idiopathic lactosuria in a patient with chronic diarrhea and acidosis.)

*Minerva Pediat.* 10:706-11, 1958.

[G. Gaslini Institute, Genova-Quarto, Italy]

This paper provides support for the suggestion that a lactose intolerance might be a cause of chronic diarrhoea and failure to thrive in infancy. The interest stimulated by this suggestion has resulted in the accumulation of a considerable amount of knowledge on intestinal disaccharide absorption and malabsorption. [The *SCI*<sup>®</sup> indicates that this paper has been cited in over 120 publications since 1961, making it the most-cited paper published in this journal, 1961-80.]

Paolo Durand  
Third Department of Pediatrics  
G. Gaslini Institute  
16148 Genova-Quarto  
Italy

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"Twenty-four years ago, when this paper was published, it was not clear whether the tempo would justify the publication. In the intervening years, it has become apparent that the rate of accumulation of new knowledge on the absorption and malabsorption of carbohydrates and its relevance to man has exceeded all my expectations.

"The paper reported the case of a 13-month-old girl, daughter of consanguineous and unaffected parents, who was weak and malnourished, and suffered from chronic diarrhoea, abdominal pain, dehydration, and symptoms of vomiting. She showed severe lactosuria, renal acidosis, and intermittent proteinuria. A galactose tolerance test showed normal results and a lactose tolerance test showed a low rise in blood sugar with an increase of lactosuria. On a lactose-free diet she improved temporarily, but died at 15 months. Postmortem examination revealed atrophic enteritis as well as hepatic and adrenal atrophy and renal tubular degeneration. I suggested that the patient was affected by a congenital deficiency of intestinal lactase.

"It seemed to me that the diarrhoea developed because the lactose failed to undergo hydrolysis, remained in the lumen,

and, by its osmotic effect, moved water into the lumen from the absorptive cells. Lactose passing through an abnormally permeable enteric mucosa led to lactosuria. The clinical syndrome lacked a biochemical demonstration of lactase deficiency but at that time the methods were not available for obtaining and assaying peroral biopsies of the small intestine.<sup>1</sup> However, a reason for the slow development of these methods was a general acceptance of the erroneous concept that digestive enzymes are excreted from the intestinal wall into the lumen.

"Since 1958 some additional cases having similar clinical manifestations have been reported and the number of papers on lactose intolerance has been increasing logarithmically.

"The contributors and I<sup>2</sup> came to the conclusion that there are two categories of carbohydrate intolerance: the first, rare, of congenital absence of a disaccharidase or of the transport mechanism, and the second, frequent, of one or more disaccharidases and of transport mechanism, secondary to many intestinal diseases. My first patient was probably affected by lactose intolerance without lactase deficiency; the etiology is unknown but a gastrogenic origin of the disorder is likely.<sup>3</sup> Other types of lactose intolerance are the very rare lactase deficiency in infants and young children; the lactase deficiency in adults, especially in black Americans, Asians, African Bantus, and Indians; and the frequent secondary and transient lactase deficiency in a variety of diseases in which the small intestine is or is not directly involved.

"There was a polite polemic about the priority of discovery of lactose intolerance by myself (1958) and by Holzel *et al.*<sup>4</sup> Certainly these first studies contributed to the creation of the chapter on intestinal disaccharidase deficiencies and to development of pediatric gastroenterology with many clinical, laboratory, and commercial implications.

"These factors contribute to the unexpected frequency of citation of my paper. Finally, this experience convinced me to publish in English the successive papers that I and my friends and colleagues judged of some interest."

1. Dahlqvist A. Method for assay of intestinal disaccharidases. *Anal. Biochem.* 7:18-25, 1964.

2. Durand P. *Disorders due to intestinal defective carbohydrate digestion and absorption.* Rome: Il Pensiero Scientifico, 1964. 190 p.

3. Berg N O, Dahlqvist A & Lindberg T. A boy with severe infantile gastrogen lactose intolerance and acquired lactase deficiency. *Acta Paediat. Scand.* 68:751-8, 1979.

4. Holzel A, Schwarz V & Sutcliffe K W. Defective lactose absorption causing malnutrition in infancy. *Lancet* 1:1126-8, 1959.