Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 10 (3—4), pp. 303—313 (1969)

Lactose Absorption in Growth Retarded Newborn Infants

By

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(Received April 19, 1969)

Lactose and glucose/galactose tolerance tests were performed in term, preterm and small for date newborn infants. The absorption of lactose compared to that of glucose and galactose and expressed as a percentage, was found to be less than 50 in the severely growth retarded infants and in some of preterm infants growing at a normal rate. It is suggested that, similarly to extrauterine malnutrition, severe intrauterine growth retardation caused by placental insufficiency might also cause a transient malabsorption of lactose in the neonatal period.

Holzel in 1959 [11] reported a malabsorption syndrome caused by congenital lactase deficiency and characterized by defective lactose absorption with consequent malnutrition. It has since been found that, in addition to the congenital type, acquired transient forms of lactose malabsorption such as those observed in marasmus and kwashiorkor may also be encountered [3, 4, 5, 7, 14, 20].

Observations made in extrauterine malnutrition raise the question as to whether foetal malnutrition causes similar transient lactase deficiency, unfavourably affecting the adaptation of underweight newborns to extrauterine life. Since clinically and biochemically striking similarities exist between marasmus and intrauterine malnutrition, lactose malabsorption might possibly be a further disturbance indicating that in both conditions essentially identical pathophysiological mechanisms are involved. It was therefore studied to what extent, if at all, lactose malabsorption occurs in foetal growth retardation. The present paper reports such investigations using glucose + galactose and lactose tolerance tests which suggest a transient disturbance of lactose absorption in severely malnourished newborn infants.

Material and Methods

Three groups of newborn infants aged less than 14 days were studied.

(i) 10 small for date full term infants (8 single born and a set of monoplacental, monochorionic twins) born at or after 37 weeks gestation.

(ii) 10 normally grown full term infants (gestational age ≥ 37 weeks)

(iii) 9 normally grown preterm infants (gestational age < 37 weeks) whose birth weight roughly corresponded to that of the malnourished full term infants.

The rate of growth in utero was determined by our local standard [10] and a

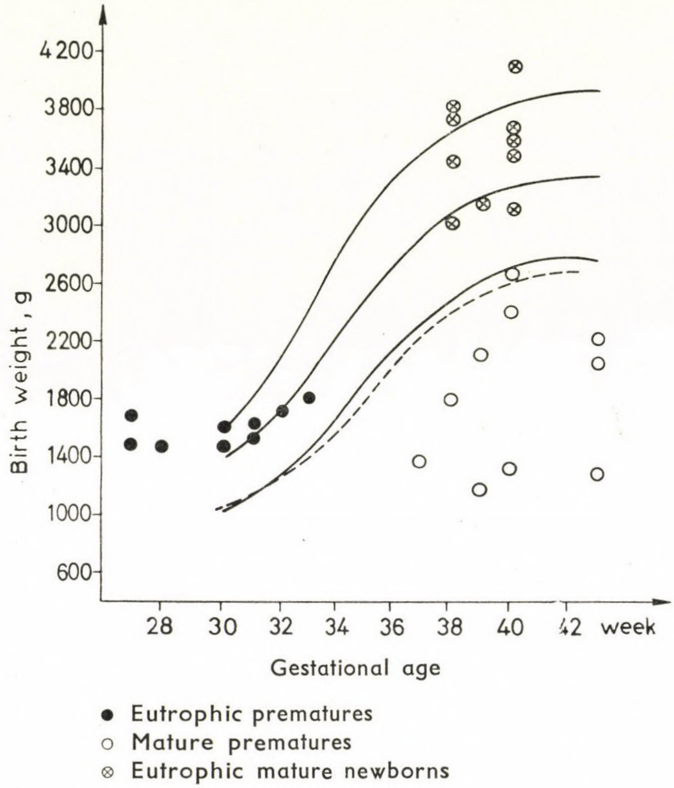

FIG. 1. The position of newborn infants included in the present study on a local intrauterine growth chart. The dotted curve represents the 10 percentile values of Lubchenco's standard [15]

newborn whose birth weight fell below the 10th percentile curve was rated as underweight for gestational age. The position of the three groups of newborn infants on our local intrauterine growth chart is shown in Fig. 1.

It can be seen that the small for date full term infants (7 males and 3 females)

TABLE I

	Number of cases		Gestational age, week	
	Males	Females	Average	Range
Malnourished infants	7	3	40	37—43
Normal full term infants	8	2	39	38—40
Normal premature infants	1	8	30	27—33

exhibited a marked weight deficit whether the local or Lubchenco's standard [15] were used for determining intrauterine growth rate. The severity of foetal malnutrition is also shown by the fact that in three infants the blood glucose level fell below 20 mg, and in other three between 20 and 31 mg per 100 ml on the first day of extrauterine life. In seven of these infants, pregnancy was complicated by severe toxaemia and in four extensive placental lesions (infarction) were observed. Two infants were delivered by Bracht extraction.

In the second group all infants were delivered after a normal pregnancy. In one instance Caesarean section was performed. Seven infants were admitted on account of an uncomplicated constellation in the AB0 or Rh system, but neither the clinical course nor laboratory analysis confirmed isoimmunisation. One baby was admitted on account of hare-lip, another for social reasons, and a third because of a cyanotic attack developed shortly after birth. Eight infants in this group were males and two females.

All infants in the third group (7 single born, one set of twins) had been admitted in good condition, and no signs and symptoms indicating any complication during the neonatal period were observed. In one instance pregnancy had been complicated by mild toxaemia, and one infant was delivered by Bracht extraction. The sex distribution of this group was eight females to one male.

Lactose and glucose/galactose tolerance tests were performed. The sugars were administered orally after a 6—8 hr fast as a 20% solution in a dose of 2 g/kg. Venous blood samples were obtained at 30 min. intervals during a period of 3 hours. Blood sugar levels were estimated by the glucose oxydase method. The pH of the stools was determined by means of Merck's indicator paper during the first 24 hrs following the tolerance test. The clinical condition and postnatal growth of the infants was also recorded. The carbohydrate tolerance tests were always done in the above order with 2 or 3 days between the two tests.

In every instance the absorption ratio was calculated from the blood glucose-curves obtained by the carbohydrate tolerance test as described by Cuatrecasas [8]. According to this technique the ratio is calculated by measuring the area under each resultant blood-glucose curve from zero time to 60 min. The ratio:

$$AR = \frac{T_L}{T_{G+G}} \cdot 100$$

expresses lactose absorption as percentage of glucose + galactose absorption. T_L = area below the lactose tolerance curve from zero time to 60 min; T_{G+G} = area below the glucose + galactose tolerance curve from zero time to 60 min. Malabsorption of lactose is assumed if the ratio is less than 50 [8].

Results

Results obtained in the three groups of newborn infants are summarized in Table I.

Birth weight, g		Postnatal age at tolerance test, days				Absorption ratio	
Average	Range	Lactose		Glucose + galactose		Average	Range
		Average	Range	Average	Range		
1880	1200—2700	7	4—11	9	6—13	84	11—173
3570	3050—4150	6	3—11	8	5—13	86	57—168
1620	1500—1820	6	3—12	8	5—14	61	22—157

The average absorption ratio was definetely lower in the normally grown preterm infants [61] than in the preterm newborn infants are less homogeneous than the group of well-nourished full term infants. This is

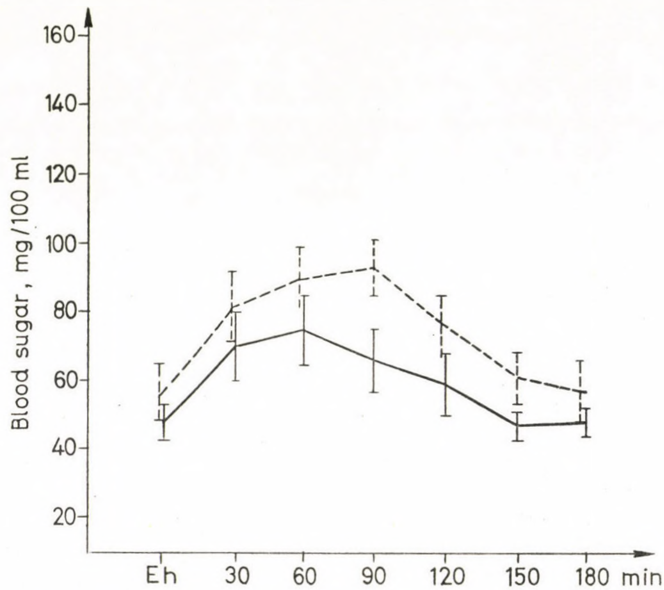

FIG. 2. Mean blood glucose levels obtained in small for date term infants during lactose (solid line) and glucose/galactose (dotted line) tolerance tests. Vertical bar represents SE

growth retarded and normal full term infants (84 and 86).

In order to visualize the magnitude and the time-course of the response to the carbohydrate loads, the average blood sugar curves with SE are shown in Figs. 2, 3 and 4.

It can be seen that the blood glucose levels obtained during the lactose tolerance test in growth retarded and premature infants showed greater variations than those observed in normal full term infants. This marked variation suggests the possibility that, as far as lactose absorption is concerned, the groups of malnourished and borne out by Fig. 5 showing the relationship between absorption ratio and gestational age.

While 5 of the 9 preterm infants had an absorption ratio less than 50, of the full term infants lactose absorption appeared to be impaired only in 4. It is important that all non-absorber full term infants were foetally malnourished and none of the normally grown mature infants showed an impairment of lactose absorption.

In order to demonstrate the relation of the severity of undernutrition to the absorption ratio, the results obtained in the undernourished newborn in-

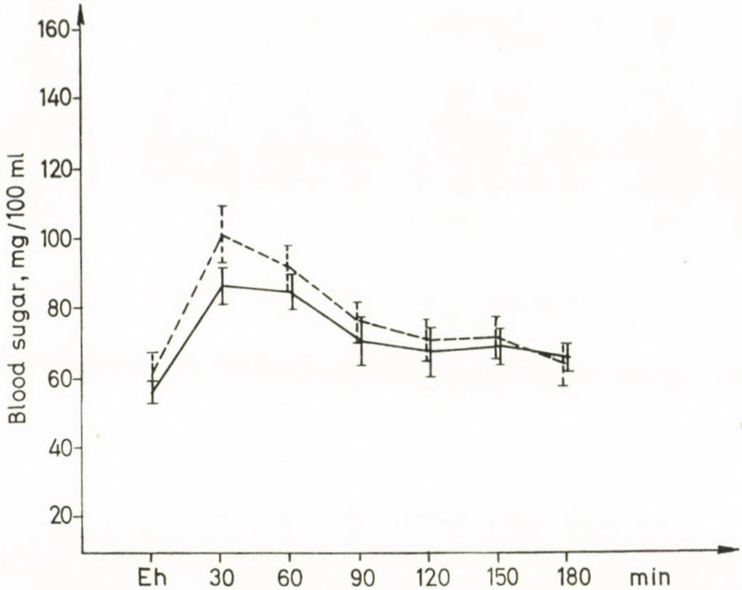

FIG. 3. Lactose (solid line) and glucose/galactose (dotted line) tolerance curves obtained in normal full term newborn infants

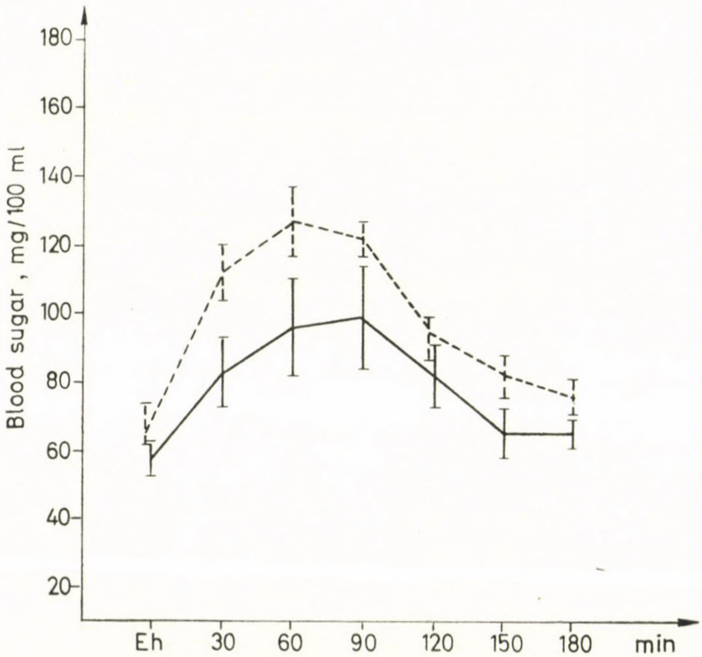

FIG. 4. Mean blood glucose levels obtained in preterm infants during lactose (solid line) and glucose/galactose (dotted line) load

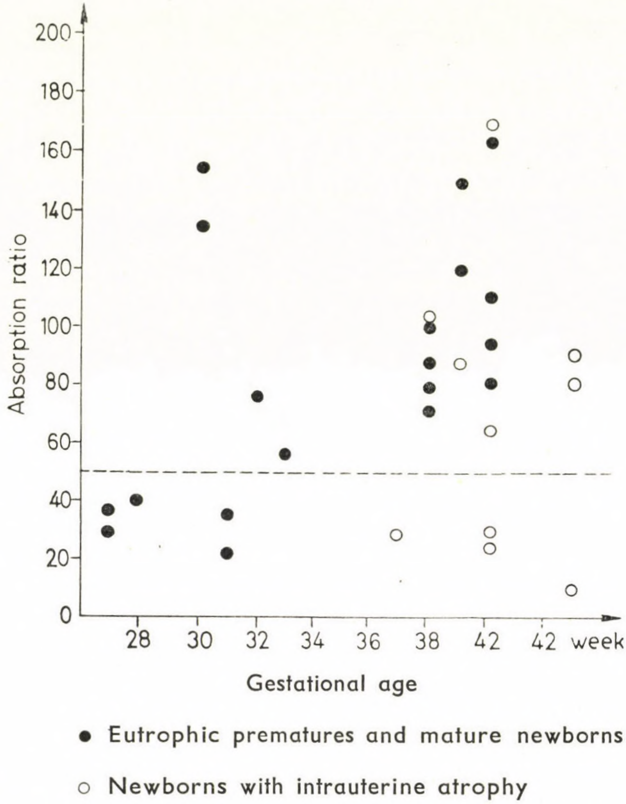

FIG. 5. Absorption ratios observed in the three groups of infants in relation to gestational age

fants were grouped according to weight groups (Fig. 6).

Lactose malabsorption occurred only in infants severely underweight for their gestational age. The average birth weight and absorption ratio of the four nonabsorber growth retarded infants was 1320 g and 24, respectively. In these infants pregnancy was complicated with severe toxaemia and in three of them the placenta was extensively infarcted.

The carbohydrate tolerance tests performed in both groups of full term infants has also been analysed according to the maximum rise in blood glucose level. It has been suggested that an increment of more than 30 mg per 100 ml indicates satisfactory absorption, while one of less than 20 mg per 100 ml can be regarded as a consequence of defective disaccharide absorption [12]. The mean maximum increase in blood glucose obtained during the carbohydrate tolerance tests in the four weight-groups of full term infants is shown in Fig. 7.

It can be seen that only in the mature newborns weighing less than 1500 g was there a striking difference in the

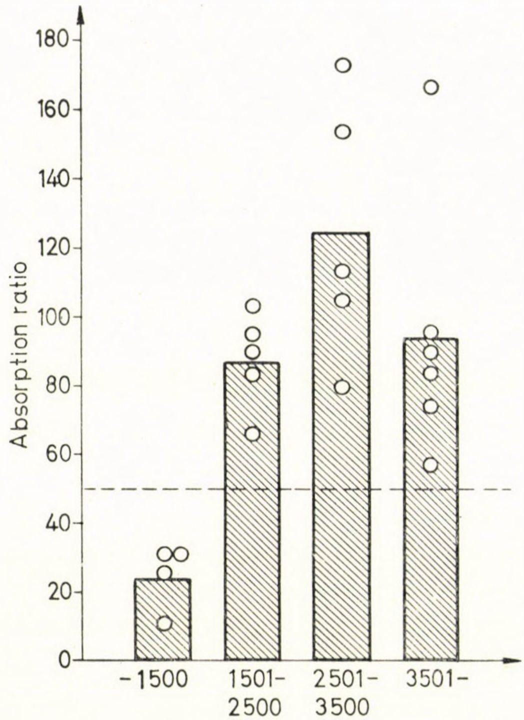

FIG. 6. Absorption ratio in full term infants belonging to different weight groups

maximum increment of blood glucose following the ingestion of lactose and glucose + galactose. This difference is even more striking if the whole time course of the blood glucose curves obtained in these severely underweight infants are compared (Fig. 8).

As regards the pH of the stools of the nonabsorber infants following the lactose tolerance test, no unequivocal fall could be observed. Furthermore, no episode of fermentative diarrhoea followed any of the tests resulting in a flat lactose tolerance curve, and weight gain during the first 3 or 4 weeks of extrauterine life did not significantly differ from that recorded in infants showing normal lactose tolerance curves.

DISCUSSION

DAHLQUIST and LINDBERG [9] reported that intestinal lactase, cellobiase and maltase activities of the small intestine appear between the 22nd and 37th gestational week. Of these disaccharidases lactase is the last to reach maximum activity, at about 40 weeks gestation. Similar observations were made by AURICCHIO et al. [1]. In contrast, JARETT and HOLMANN [13] observed normal lactose tolerance tests in premature infants aged 13–17 days; however, prematurity was defined by birth weight (< 2500 g) by these authors. BOELLNER et al. [2] reported that while in premature infants flat lactose tolerance curves oc-

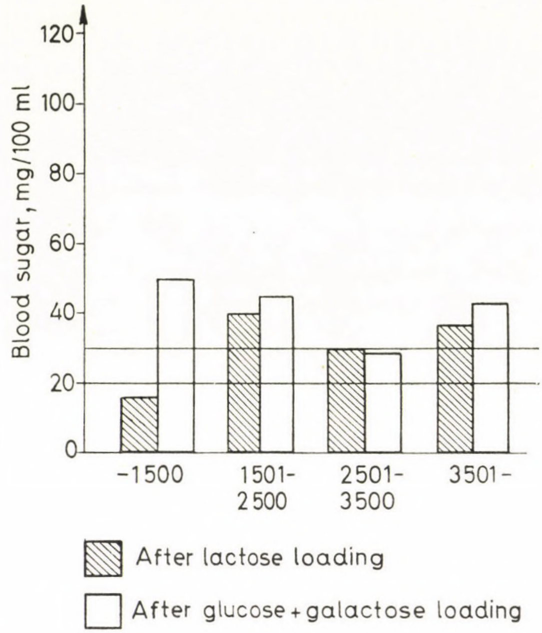

FIG. 7. Maximum increment in blood glucose during lactose and glucose/galactose tolerance test performed in newborn infants of different weight groups

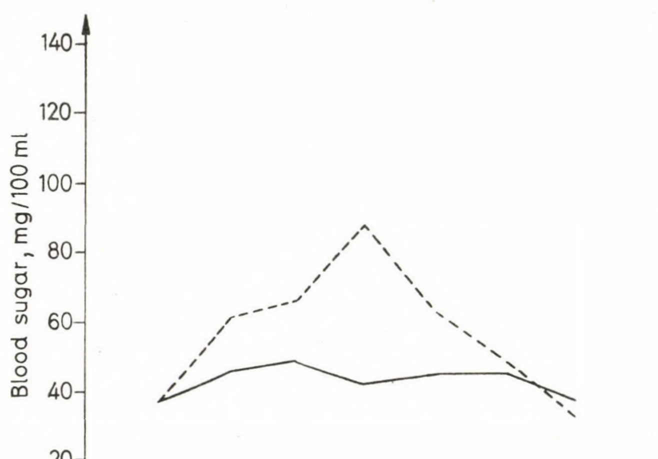

FIG. 8. Lactose (solid line) and glucose/galactose (dotted line) tolerance curves in full term infants weighing less than 1500 g.

cur during the first 7 days of extrauterine life, in mature infants abnormal tests may be encountered only during the first 3 days. The flat lactose tolerance curve and hence the low absorption ratio obtained in premature infants in the present study are more or less in accordance with the observations of BOELLNER et al.

Although a difference of two weeks existed in gestational age between the lactose absorber and nonabsorber premature infants (29 weeks versus 31 weeks), our findings did not justify a definite conclusion concerning the effect of gestational age on intestinal lactose absorption capacity. It must be borne in mind that the difference of 3 days in postnatal age may equally or even more contribute to the difference in the lactose absorption ratio in the two groups of premature infants.

It has been reported that the rate of postnatal increase of intestinal lactase activity is more or less dependent on the amount of ingested milk. Some authors deny, however, that external factors such as milk intake might influence the postnatal development of lactase activity.

In the average absorption ratio no significant difference has been found between the normal and foetally malnourished full term infants (86 and 84, respectively). If, however, the results obtained in the most severely growth-retarded newborns are considered separately, it becomes apparent that severe intrauterine malnutrition may considerably affect lactose absorption. In these extremely underweight full term infants lactose loading led only to a small increase in the blood glucose level, while the glucose plus galactose absorption test induced a marked rise in the blood glucose curve. In two of these infants the lactose tolerance test repeated at a postnatal age of one month resulted in a normal absorption ratio indicating that defective lactose absorption associated with severe intrauterine malnutrition improves rapidly during the first few weeks of extrauterine life.

It is known [16, 17] that the disaccharidases are concentrated in the brush border of the intestinal epithelial cells and hence are easily damaged by a variety of agents and illness. Lactase, the clinically most important disaccharidase, is vulnerable and regains its activity slowly after recovery. Lactose malabsorption has been demonstrated in different forms of malnutrition (marasmus, kwashiorkor) suggesting that a markedly reduced calorie or protein intake may cause mucosal cell damage, leading to a secondary lactase deficiency [3, 5, 7, 14]. Studying the mitotic index of Lieberkühn's crypts in infants suffering from marasmus and kwashiorkor, BRUNSER et al. [6] found the index to be considerably lower in calorie than in protein malnutrition; they concluded that the reduction of the mitotic rate was due to a reduced calorie supply rather than an inadequate protein intake.

Among the different factors causing or contributing to intrauterine malnutrition, placental insufficiency is undoubtedly the most important and most frequently encountered condition. Hence, it is not unrealistic to suppose that a deficient transplacental transport of plasma nutrients starting at different stages of foetal growth and persisting for different periods may affect growth, maturation and body composition of the foetus. The somatic signs and symptoms of severely wasted newborn infants show striking similarities to those characteristic of extrauterine calorie malnutrition (marasmus). In addition to the nutritional state, a close similarity exists in respect of the common occurrence of hypoglycaemia. NAEYE's [18, 19] quantitative histological studies have shown identical changes taking place in the both conditions. All these similarities between marasmus and intrauterine malnutrition strongly point to an insufficient transplacental supply of nutrients as a potential factor capable of producing a transient postnatal disturbance in lactose absorption.

Besides the mucosal damage resulting in histological and biochemical abnormalities, some other effects such as a delayed maturation of lactase activity may also be responsible for the transient absorption defect.

It is interesting that in spite of the low lactose absorption ratio no fermentative diarrhoea occurred. The absence of any clinical and biochemical signs suggestive of bacterial lactose fermentation might to some extent have been due to the relatively sterile intestines of the newborn infant. Although the lactose tolerance test and the absorption ratio appear useful for detecting an absorption defect of lactose, further biochemical and histological examinations appear to be necessary for precisely defining the nature of the transient disturbance caused by severe intrauterine malnutrition.

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