ethanol, and diluted with Krebs bicarbonate solution. The results were evaluated statistically using Student's paired and unpaired t-tests and regression analysis.

Results and discussion. The plasma disappearance rate of glucose decreased, and the fasting plasma glucose level rose considerably and lastingly under the influence of alloxan treatment. Urinary glucose excretion increased to a corresponding degree, but no acetone was excreted. Decrease of body weight by about 25% followed alloxan treatment, while blood urea nitrogen did not change significantly (table).

$PGF_{2\alpha}$ (1–30 µmoles) produced a similar, concentration-dependent increase in the tone of coronary strips both from healthy and alloxan-diabetic dogs. Indomethacin (3 µmoles) enhanced considerably the contractile response to $PGF_{2\alpha}$ in both groups of arteries, but the enhancing effect of indomethacin was significantly greater in alloxan-diabetic vessels than in normal ones (table). A close, inverse correlation was found between the plasma disappearance rate of glucose and the indomethacin-induced percent potentiation of response to $PGF_{2\alpha}$ (figure).

PGI_2 did not alter or only slightly diminished the basic tone of coronary strips, but when the arteries were precontracted by $PGF_{2\alpha}$, PGI_2 (0.03–0.43 µmoles) produced a similar and marked, concentration-dependent relaxation in arteries from healthy and alloxan-diabetic animals (table). To explain the enhancing effect of indomethacin on the contractile responses to $PGF_{2\alpha}$ it may be assumed that $PGF_{2\alpha}$ releases PGI_2 in coronary strips in the same way as in rat heart[15]. In this case, indomethacin would reduce PGI_2 release[13,14], and the diminished release of PGI_2 would counteract the contractile effect of $PGF_{2\alpha}$ to a lesser extent. It is kown that PGI_2 release[14] and coronary blood flow[13] are higher in diabetic hearts. Consequently, it may be supposed that in diabetic coronary arteries $PGF_{2\alpha}$ exerts a more prominent PGI_2 release, and after indomethacin treatment it exerts a more pronounced contractile effect. On the other hand, the relaxant effect of PGI_2 on strips from diabetic dogs was similar to that on strips from healthy animals when PGI_2 was added to the bath. This finding is evidence against an enhanced responsiveness of diabetic coronary arteries to PGI_2. To the extent that it is permissible to extrapolate from in vitro studies to the more complex situation in vivo, an unfavourable effect of indomethacin on the coronary circulation of diabetic animals would be predicted.

1 H. Keen, Postgrad. med. J. *52*, 445 (1976).
2 W.R. Timperley, J.D. Ward, F.E. Preston, T. Duckworth and B.C. O'Maley, Diabetologia *12*, 237 (1976).
3 S.S. Ahmed, G.A. Jaferi, R.M. Narang and T.J. Regan, Am. Heart J. *89*, 153 (1975).
4 T. Karlefors, Acta med. scand. *180*, suppl. 449, 45 (1966).
5 S. Afonso, G.T. Bandow and G.G. Rowe, J. Physiol., Lond. *241*, 299 (1974).
6 R.J. Kraemer and J.D. Folts, Fedn Proc. *32*, 454 (1973).
7 R.W. Alexander, K.M. Kent, J.J. Pisano, H.R. Keiser and T. Cooper, J. clin. Invest. *55*, 1174 (1975).
8 G.J. Dusting, S. Moncada and J.R. Vane, Eur. J. Pharmac. *49*, 65 (1978).
9 C.G. Strong and D.F. Bohr, Am. J. Physiol. *213*, 725 (1967).
10 M.L. Ogletree, J.B. Smith and A.M. Lefer, Am. J. Physiol. *235*, H400 (1978).
11 K. Schrör, S. Moncada, F.B. Ubatuba and J.R. Vane, Naunyn-Schmiedebergs Arch. Pharmac. *297*, R31 (1977).
12 K. Schrör, S. Moncada, F.B. Ubatuba and J.R. Vane, Eur. J. Pharmac. *47*, 103 (1978).
13 H. Stam and W.C. Hülsmann, Basic Res. Cardiol. *72*, 365 (1977).
14 P. Rösen and K. Schrör, Diabetologia *18*, 391 (1980).
15 E.A.M. de Deckere and F. Ten Hoor, Advances in Prostaglandin and Thromboxane Research, Vol.7, p.655. Ed. B. Samuelsson, P.W. Ramwell and R. Paoletti. Raven Press, New York 1980.
16 A. Hyvärinen and E.A. Nikkilä, Clin. chim. Acta *7*, 140 (1962).
17 W. Neuweiler, Klin. Wschr. *12*, 869 (1933).
18 J.J. Coulomba and L. Favreau, Clin. Chem. *9*, 102 (1963).
19 V. Conard, J.R.M. Franckson, P.A. Bastenie, J. Kestens and L. Kovács, Archs int. Pharmacodyn. *93*, 277 (1953).

Galactose and leucine transport in the developing rat small intestine

Juana M. Planas[1], M. Moretó and J. Bolufer

Departamento de Fisiología Animal, Facultad de Farmacia, Universidad de Barcelona, Barcelona-28 (Spain), 17 October 1980

Summary. Jejunal transport of galactose and leucine was studied in 9–45-day-old rats by means of the everted sac technique. Maximum transport was observed in 9–10-day-old rats, but then decreased until the 22nd day, and remained unchanged from then on. There were no remarkable differences in the pattern of galactose and leucine transport over this period.

Intestinal ability to transport non-electrolytes changes with age. In the rabbit[2], mouse[3] and human[4], the active transport systems develop before birth, In the chick, maximum transport capacity for galactose occurs soon after hatching[4] and in the guinea-pig maximum transport for α-methyl glucoside and many aminoacids is detected the first day after birth[5]. In rats, Younoszai and Linch[6] observed that the maximum absorption of glucose was at 21–23 days after birth. These experiments were done in vivo with no distinction between the active and diffusional components of sugar absorption.

The active transport of galactose and leucine in the jejunum of the rat at various age periods was studied. Our results indicate that the maximum transport of both substrates occurs before the time of weaning.

Methods. Male Wistar rats 9–42 days old were used. After weaning animals were fed a standard rat chow (U.A.R., A03) and water ad libitum. Rats were starved for 8 h (9–21-day-old, suckling animals) or 16 h (22–45-day-old) before the experiment. The study was done on everted sacs of mid jejunum, as described by Wilson and Wiseman[7]. The pieces of small intestine were removed under urethane anesthesia. Sacs were filled with Krebs-Henseleit bicarbonate buffer[8] and incubated in 10 ml of the same at 37 °C for 45 min. The mucosal solution was continuously gassed with 95% oxygen and 5% carbon dioxide. D-galactose (5 mM) and ^{14}C-

Changes in active transport of D-galactose and L-leucine according to age

Age (days)	Body weight (g)	D-Galactose µmole/100 mg wet tissue/45 min	S/M	L-Leucine µmole/100 mg wet tissue/45 min	S/M
9-10	21.07±0.39	6.26±0.59 (8)[a]	6.63±0.53 (8)	4.19±0.64 (8)[g]	5.32±0.58 (8)
11-14	28.85±0.56	3.78±0.33 (20)[b]	4.82±0.35 (20)	3.95±0.21 (6)[h]	4.67±0.29 (6)
15-21	34.64±1.17	2.55±0.16 (19)[c]	3.71±0.20 (19)	1.15±0.12 (8)[i]	2.39±0.14 (8)
22-28	42.80±1.05	1.99±0.14 (20)[d]	2.89±0.14 (20)	0.81±0.07 (15)[j]	2.04±0.10 (15)
35	87.40±3.81	2.09±0.15 (7)[e]	2.88±0.19 (10)	0.99±0.09 (8)[k]	2.21±0.14 (8)
45	155.26±4.54	1.85±0.20 (7)[f]	3.09±0.09 (7)	-	-

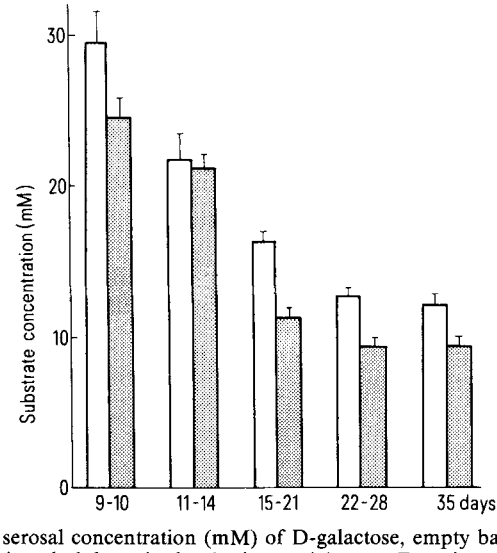
Net transport and serosal to mucosal concentration ratio (S/M) of galactose and leucine by everted sacs, is shown. The data are the mean±SEM. Number of experiments in brackets. Statistical significance: a vs b, $p<0.001$; b vs c, $p<0.05$; d vs e, e vs f, N.S.; g vs h, N.S.; h vs i, $p<0.01$; i vs j, $p<0.05$; j vs k, N.S.

labelled L-leucine (Amersham; 5 mM) were employed as transport substrates. Galactose was determined by the Somogyi method[9] and leucine by the ^{14}C-activity in a liquid scintillation counter.

Results and discussion. Results of galactose and leucine transport in the developing rat jejunum are shown in the table (S/M ratio; µmole/100 mg wet tissue/45 min) and in the figure (final serosal concentration, mM). The values indicate that the younger the animals the higher the rate of absorption of both substrates. The high transport observed in the 9-10-day-old rats (with a serosal to mucosal concentration ratio above 6 for galactose and above 5 for leucine) decreases significantly in the 2nd (11-14-day-old) and 3rd (15-21-day-old) groups. The maximum decrease in galactose transport (40%) occurs between 9 and 14 days after birth, and in leucine transport (70%) between 11 and 21 days after birth. In all groups, except the 11-14-day-old, galactose accumulation by rat jejunum is significantly higher than that of leucine, which supports previous experiments in adult animals[10]. Transport of both substrates shows no age dependency from the 22-28-day-old group of rats onwards.

Many intestinal transfer mechanisms are widely distributed in the whole intestine shortly after birth and subsequently restricted to adult sites, e.g. hexose transport can be detected both in small intestine and colon in newborn rats, whereas in adult animals this ability is restricted to the proximal half of the small intestine[11]. In this study we have used jejunum because it is the segment where the active transport systems are most efficient in the adult rat[12]. The decrease in the net absorption of galactose and leucine we observe cannot, therefore, be ascribed to a change in the location of these transport systems. In vivo studies by Younoszai and Linch[6] indicate that glucose is absorbed twice as much at the time of weaning (21-23 days) as at the suckling period (7-15-day-old). This finding is not in agreement with the results presented here, in which the serosal accumulation of galactose and leucine in the suckling animals is higher. Since the in vivo method does not distinguish between active and passive absorption, it is possible that the higher rate of absorption observed by Younoszai and Linch reflects an increase in the diffusional component of absorption. Batt and Schachter[11] observed that slices from mid jejunum of 31-day-old rats accumulate 30% more 3-O-methyl-glucose than rats aged 1-2 days. However, it is probable that the tissue from the younger rats was damaged by long incubation (60 min) and shaking (100 cycles/min), as the low accumulation ratios found by these authors suggests[11].

Our results are in agreement with what has been described for other species, such as guinea-pig[13], lamb[14,15] and chick[16], showing greater ability to transport non-electrolytes in early stages of development. These changes might be explained by an increased number of active transport sites for both sugars and aminoacids, or by an increased affinity of substrates for the carrier, in the suckling period.



Final serosal concentration (mM) of D-galactose, empty bars, and L-leucine, dark bars, in developing rat jejunum. Experiments were done on everted sacs. Initial substrate concentration was 5 mM in both serosal and mucosal compartments. The abscissa shows the age-groups studied. The SEM(+) is indicated.

1 Holder of a grant from Fundación Juan March.
2 J.J. Deren, E.W. Strauss and T.H. Wilson, Devl Biol. *12*, 467 (1965).
3 A. Calingart and A. Zorzoli, J. Geront. *20*, 211 (1965).
4 O. Koldovský, A. Heringová, V. Jirsová, J.E. Jirásek and J. Uher, Gastroenterology *48*, 185 (1965).
5 P.H. Bogner and I.A. Haines, Am. J. Physiol. *207*, 37 (1964).
6 M.K. Younoszai and A. Linch, Pediat. Res. *9*, 130 (1975).
7 T.H. Wilson and G. Wiseman, J. Physiol., Lond. *123*, 116 (1954).
8 H.A. Krebs and K. Henseleit, Hoppe-Seylers Z. Physiol. Chem. *210*, 33 (1932).
9 H. Somogyi, J. biol. Chem. *195*, 19 (1952).
10 J. Bolufer and J. Larralde, Comp. Biochem. Physiol. *58*, 75 (1977).
11 E.R. Batt and D. Schachter, Am. J. Physiol. *216*, 1064 (1969).
12 R.B. Fisher and D.S. Parsons, J. Physiol., Lond. *119*, 224 (1953).
13 J.M. Butt and T.H. Wilson, Am. J. Physiol. *215*, 1468 (1968).
14 E. Scharrer, Pflügers Arch. *366*, 147 (1976).
15 E. Scharrer, H.G. Liebich, W. Raab and N. Promberger, Zentbl. VetMed. *26a*, 95 (1979).
16 K.L. Raheja, J. Tepperman and H.M. Tepperman, Comp. Biochem. Physiol. *58*, 245 (1977).