spectrophotométrie UV ou par la méthode de Burton[8]. Le contenu total en ADN du cervelet des animaux traités de 6 et 35 jours, est significativement inférieur à la normale excepté pour le groupe 5. Il n'y a pas de différence significative entre les animaux du groupe 2 et ceux des groupes 3 et 4. Chez les animaux traités de 6 jours, la concentration en ADN du cervelet est généralement supérieure à la normale mais la différence n'est pas significative. A 35 jours, la concentration en ADN du cervelet des animaux traités est supérieure à la normale, excepté pour le groupe 5.

A 6 jours comme à 35 jours, l'administration de 0,5 µg de LT3 tous les 2 jours n'entraîne aucune modification des paramètres étudiés. Cette dose d'hormone ne semble donc pas suffisante pour créer une hyperthyroïdie. Par contre l'administration de 5 µg/j de DLT4 ou de 25 µg de LT3 à la naissance suivis ou non de 0,5 µg tous les 2 jours, provoquent une diminution significative du contenu en protéines, ARN et ADN du cervelet à 6 comme à 35 jours. La diminution significative à 6 et 35 jours du contenu en ARN et ADN du cervelet, est comparable à celle observée par Balázs et coll.[4], chez les animaux rendus hyperthyroïdiens par l'injection de 25 µg de LT3 à la naissance suivis de 0,5 µg tous les 2 jours. On ne relève à 6 jours aucune différence significative entre le contenu total en ADN du cervelet des animaux traités par la DLT4 et celui des animaux traités par la LT3.

Par contre à 35 jours on observe que le contenu en ADN est significativement plus abaissés chez les animaux traités par 5 µg/j de DLT4 que chez ceux qui reçoivent 25 µg de LT3 à la naissance suivis ou non par 0,5 µg de LT3 tous les 2 jours. Les doses d'entretien de 0,5 µg de LT3 tous les 2 jours ne semblent donc pas plus efficaces pour accentuer l'hyperthyroïdie qu'elles ne le sont à elles seules pour la susciter. Par contre l'injection d'une dose unique de 25 µg de LT3 à la naissance semble suffisante pour créer une hyperthyroïdie durable. Cependant l'administration d'une dose journalière de 5 µg/j de DLT4 paraît plus efficace que l'administration de 25 µg de LT3 à la naissance, contrairement à ce qui avait été observé précédemment[7]. Toutefois la technique d'extraction des acides nucléiques est différente dans les 2 cas, et une nouvelle expérimentation est nécessaire pour vérifier si les différences de résultats sont imputables aux techniques utilisées.

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Induction of an intestinal epithelial sugar transport system by high blood sugar[1]

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Summary. Intravenous infusion of glucose produces a marked increase of the mucosal-to-serosal sugar flux in the isolated everted small intestine of rats. The phenomenon is partially substrate specific, is inhibited by phloretin but not by phlorizin and is completely abolished by cycloheximide. The results suggest that sustained hyperglycemia may stimulate the synthesis of new transport receptors (carriers).

It has been known for some time that the mucosal-to-serosal sugar (glucose, galactose, 6-deoxyglucose) transport is markedly enhanced in the isolated intestine of alloxan- and streptozotocin-diabetic rats[3–8]. Recent studies conducted in our laboratory indicate that the enhancement is the consequence of hyperglycemia and not a direct pharmacological action of the provoking drug, alloxan or streptozotocin. Rats were given continuous intravenous infusion of a glucose solution; after the blood glucose was maintained about 400 mg%, or higher, for over 4 h, or longer, the mucosal-to-serosal transport of glucose, galactose and 3-O-methylglucose in the isolated small intestine increased (table 1). This increased transport was not appreciably inhibited by 10^{-3} M phlorizin but was eliminated by phloretin (10^{-4} M). There was a certain degree of specificity in the induction of the intestinal transport: sustained hyperglycemia or hypergalactosemia enhanced the transport of glucose, galactose and 3-O-methylglucose but not that of fructose; sustained hyperfructosemia, on the other hand, enhanced the transport of fructose (table 2). The effect is not due to the expansion of the extracellular space caused by the

Table 1. Effect of continuous glucose infusion on the mucosal-to-serosal (M → S) glucose flux in the isolated small intestine

Time after start of infusion	n	Blood glucose mg %	Glucose flux (M → S)
Control	6	84.4± 5.0	86.8± 7.3
1 h	4	400 ±59.3	69.4±21.0 (n.s.)
2 h	4	460 ±59.0	105 ±21.8 (n.s.)
4 h	4	420 ±19.8	172 ±37.9 $p < 0.05$
6 h	4	490 ±88.8	220 ±44.1 $p < 0.01$
12 h	4	460 ±19.8	251 ±54.5 $p < 0.01$

A 30% (w/v) glucose solution was infused i. v. into 200–300 g nonanesthetized rats at rate of 2.0 ml/h. At the end of the infusion period the glucose content of the arterial blood was determined[9], the animal killed, the small intestine removed, everted and incubated in a Krebs-Ringer-bicarbonate solution. 2.8 mM uniformly ^{14}C-labeled glucose was placed in the mucosal bath and its appearance in the serosal compartment measured. The glucose flux was expressed in µM/g dry gut per h. n = number of experiments; n. s. = not significant. Mean values ± standard error of the mean (SEM).

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Table 2. In vitro mucosal-to-serosal sugar flux

	Flux Glucose	Galactose	3-O-methylglucose	Fructose
Control	86.8 ± 7.3	41.1 ± 9.2	19.8 ± 2.2	13.4 ± 3.6
Glucose infused	248.0 ± 29.4	110.0 ± 15.3	39.4 ± 4.7	11.3± 2.3
Galactose infused	218.3 ± 20.8	94.2 ± 18.7		15.9 ± 3.9
Fructose infused	179.8 ± 34.0			32.9 ± 6.5
Control + cycloheximide	90.0 ± 11.5			
Glucose infused + cycloheximide	68.8 ± 16.9	33.7 ± 6.0	15.1 ± 5.3	
Fructose infused + cycloheximide				10.7 ± 3.6

Method and calculation as in table 1. n = 6–11. Cycloheximide was given intravenously in a dose of 1.5 mg/kg at the beginning of the i.v. sugar infusion; in the control: 4 h prior to the killing of the animal.

glucose infusion because there was no increase in the mucosal-to-serosal flux of sugars in the intestine of control animals infused with the same concentration and volume of mannitol. The protein synthesis inhibitor, cycloheximide, completely inhibited the enhancement of hexose transport following hyperglycemia, hypergalactosemia and hyperfructosemia, without any effect upon the basal sugar transport (table 2).

The stimulation of the mucosal-to-serosal flux of sugars was not necessarily accompanied by an intracellular accumulation, particularly in the gut of animals with moderate hyperglycemia. This agrees with the finding of Olsen and Rosenberg[7] that the intestine of rats which were maintained in a hyperglycemic state (degree not specified) for 5 days by intravenous glucose infusion did not display an increased tissue accumulation of 3-O-methylglucose.

These findings support the following hypothesis: the increase of the sugar level in the blood enhances the transepithelial sugar transport. It is most likely that the enhancement is the consequence of an induced synthesis of new transport carriers which would explain why the high blood sugar has to be maintained for several hours before it takes effect. It was also observed that the enhanced sugar transport is maintained for a few hours after the blood sugar returned to a normal level. The complete inhibition by cycloheximide of the increased sugar transport produced by hyperglycemia, hypergalactosemia and hyperfructosemia strongly indicates that the transport enhancement is connected with the synthesis of additional transport receptors (carriers).

The interesting finding of the present study is the existence of a substrate-specific adaptive transport system which is rather rapidly activated, presumably through the synthesis of new transport receptors (carriers). The system is not localized in the brush border but most probably in the basolateral membrane; hence its inhibition by phloretin but not by phlorizin.

The effect of cobra venom factor (CVF) activation of the complement cascade on leukocyte circadian variation in the rat[1]

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Summary. Administration of cobra venom factor (CVF) at different time periods over a 24-h-period produced a leukocytic response which varied according to the time of day the factor was given. The resulting leukocytic circadian rhythm was achieved by a marked variation and increase in the neutrophil population.

Serum complement consists of 9 separate protein macromolecules (C_1–C_9) and is sequentially activated by a series of enzymatic reactions in the presence of antigen-antibody complexes. An alternate pathway in the complement cascade can be activated by purified cobra venom factor (CVF) or the polysaccharide inulin[2]. Biological activities resulting from activation of the various components of the complement cascade include chemotaxis (C_{3a}, $C_{5a,6,7}$), opsonization (C_{3b}), anaphylaxis (C_{3a}, C_{5a}), and lysis and lesion formation at the cell membrane (C_8, C_9)[3]. Recently a new biological activity of complement has been described following activation by inulin and purified cobra venom factor of the alternate pathway[4]. An immediate neutropenia followed by a marked neutrophilia occurred. Accordingly, this response was studied to determine it might be time sensitive and display a circadian rhythm. This investigation determined the effects of CVF administered equally at different time periods over a 24-h-period on leukocyte response and rhythm.

Materials and methods. 45-day-old male Holtzman rats weighing between 200 and 250 g were housed 5 per cage and allowed free access to food and water. The rats were maintained rigidly on a 12-h-light(7.00 a.m. to 7.00 p.m.)-

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