Glucose Appearance Rate After the Ingestion of Galactose

M.C. Gannon, M.A. Khan, and F.Q. Nuttall

Galactose is one of the monosaccharides of importance in human nutrition. It is converted to glucose-1-phosphate in the liver and subsequently stored as glycogen, or is converted to glucose and released into the circulation. The increase in plasma glucose is known to be modest following galactose ingestion. Whether this is due to a small increase in hepatic glucose output, or to a relatively large increase in hepatic glucose output but a concomitant increase in glucose disposal, is not known in humans. Therefore, the rates of glucose appearance (R_a) and disappearance (R_d) were determined over an 8-hour period in normal subjects using an isotope dilution technique. The subjects ingested 50 g galactose or water alone in random order at 8 AM on separate occasions. Plasma glucose, glucagon, lactate, urea nitrogen, total amino acids, and uric acid and serum insulin and triglycerides also were determined. Following galactose ingestion, there was a modest transient increase in peripheral glucose and insulin concentrations. This was associated with a modest increase in the glucose R_a. The calculated amount of glucose appearing in the circulation as a result of galactose ingestion was 9.8 g, while the amount of glucose disappearing over the 8 hours was 9.9 g. Thus, following ingestion of 50 g galactose by overnight-fasted men, approximately 20% appears as additional glucose in the circulation. Data obtained in animals suggest that a large amount of the galactose is stored as glucose in glycogen. Nevertheless, the conversion of galactose to glucose in the liver may have been greater than suggested by the increase in glucose appearance in the circulation due to substitution for other gluconeogenic substrates.
Copyright © 2001 by W.B. Saunders Company

G LUCOSE, GALACTOSE, AND FRUCTOSE are the major monosaccharides absorbed following the ingestion of a mixed meal. Galactose (milk sugar) is quantitatively the least important of the three, except in infancy. It is almost always ingested in the form of lactose, a disaccharide composed of glucose and galactose. The hydrolysis of lactose in the intestine is so rapid that in the circulation the rate of increase of the products of its hydrolysis (ie, glucose and galactose) is largely dependent on the rate at which they can be absorbed,[1] except in people with lactose deficiency. The latter is uncommon in Caucasians.[2] The absorbed galactose also is readily removed by the liver.[3] Indeed, in the past, it has been used to assess the general functional capacity of this organ.[4]

In the liver, galactose is readily converted to glucose-1-phosphate and subsequently stored as glucose in glycogen.[5-7] It also may be converted to glucose and released into the circulation.[5-7] However, galactose increases the plasma glucose concentration only modestly. Ingestion of relatively large amounts of galactose (25 to 50 g) results in a mean increase of the peripheral circulating glucose of only 1 mmol/L (18 mg/dL) or less in normal adults and in people with type 2 diabetes.[1,8-11] However, ingested galactose is relatively potent in stimulating insulin secretion in both normal subjects[10,11] and subjects with type 2 diabetes.[1]

In people with type 2 diabetes, galactose had little effect on the circulating glucagon concentration but attenuated the expected decrease in glucagon by ingested glucose.[1] We are not aware of similar data in nondiabetic subjects.

The modest increase in the glucose concentration after galactose ingestion may be due to a small conversion to glucose and subsequent release of this glucose into the circulation. Alternatively, it may be due to a relatively large conversion to glucose, but because of substitution for other gluconeogenic substrates, only a small increase in glucose production and release occurs. The modest increase in glucose also could be due to an insulin-mediated increase in the glucose disposal rate, which prevents a large increase in glucose production from being translated into a large increase in the circulating glucose concentration. To determine if a modest increase in the appearance rate of glucose or a decrease in its removal rate are primarily responsible for the observed small increase in glucose, we have determined both using an isotope dilution technique. On a separate occasion, the same subjects ingested only water during the same period. Thus, each individual served as their own control.

SUBJECTS AND METHODS

Six normal males were studied in the Special Diagnostic and Treatment Unit (SDTU). The subjects were in excellent health and had a mean age of 31 years, with a range of 21 to 42. All were within 10% of their ideal body weight using the 1959 Metropolitan Life Insurance tables[12] (mean weight, 85 kg; range, 67 to 97). They provided written informed consent, and the study was approved by the VA Medical Center Committee on Human Subjects. All of the men ingested a diet containing at least 200 g carbohydrate per day, as well as their usual food energy intake, for the 3 days preceding the study.

The subjects were admitted to the SDTU on the evening prior to the study and received a standardized meal at 5 PM. Subsequently, only water ad libitum was allowed. The following morning at 3 AM, two indwelling venous catheters were inserted, one in the antecubital vein and the other in the dorsum of the contralateral hand. The hand was kept warm with a heating pad. The catheters were maintained patent with a slow infusion of 0.9% saline. An infusion of tritium-labeled glucose ^{3}H-carbon 3 (New England Nuclear, Boston, MA) was started at 3 AM at a constant rate of approximately 3.5 nCi/min/kg. This was continued until 4 PM.
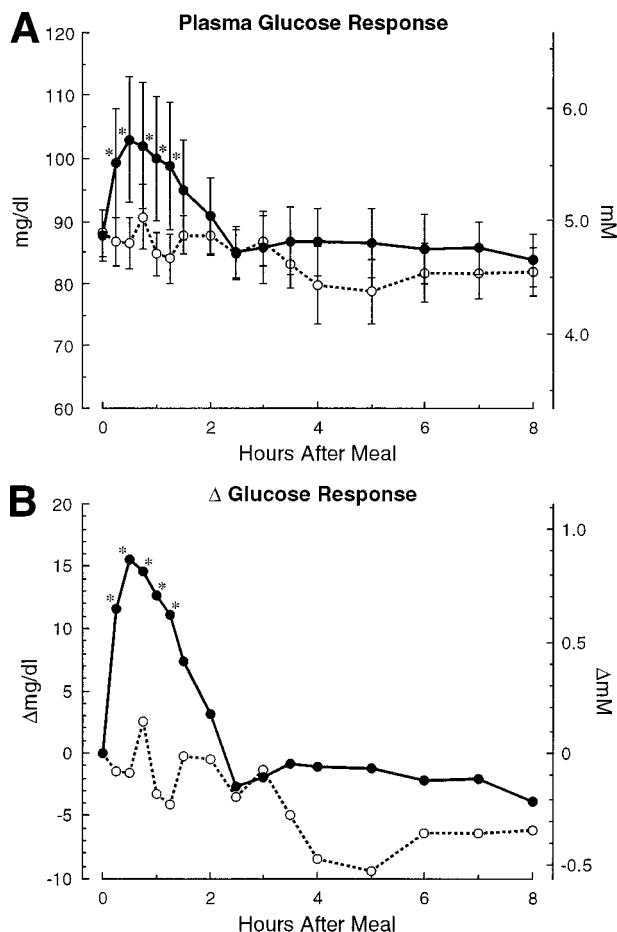
Fig 1. (A) Mean arterialized plasma glucose concentration following ingestion of 50 g galactose (●) or water alone (control, ○) in 6 normal male subjects. The mean baseline glucose was 4.9 ± 0.2 mmol/L (88 ± 4 mg/dL) for both water and galactose. Values are the mean ± SEM. (B) Change in glucose concentration (B). *P < .05 v control (water).

At 8 AM, either 50 g galactose in 500 mL water or water alone was administered in random order. During the subsequent 8-hour period, the subjects were allowed to consume water ad libitum. Arterialized blood samples were drawn from the hand hourly from 3 to 7 AM and then every 15 minutes until 8 AM. Subsequently, blood samples were drawn at 15-minute intervals for 90 minutes, at 30-minute intervals for 150 minutes, and every hour for the final 4 hours of the study. Subjects were studied over an 8-hour period to ensure complete absorption of the 50 g galactose.

Plasma glucose was determined by a glucose oxidase method using a Beckman glucose analyzer with an O_2 electrode (Beckman Instruments, Fullerton, CA). Glucose oxidase does not have detectable galactose oxidase activity. The serum level of immunoreactive insulin was measured by a standard double-antibody radioimmunoassay (RIA) method using kits produced by Endotech (Louisville, KY). Glucagon was determined by RIA using 30K antiserum purchased from Health Sciences Center (Dallas, TX). The C-peptide level was measured using a double-antibody RIA method with kits produced by Incstar (Stillwater, MN); the antibody to C-peptide has only a 4% cross-reactivity with proinsulin. Serum nonesterified fatty acids (NEFAs) were determined by the colorimetric assay of Duncombe.[13] Triglycerides and urea ni-

trogen were determined using an EktaChem analyzer (Eastman Kodak, Rochester, NY). Plasma lactate was determined by the method of Hohorst[14] using lactate dehydrogenase. The total α-amino nitrogen was determined by the method of Goodwin.[15] This is an index of the total amino acid concentration in serum. Urine galactose was determined by the method of Kurz and Wallenfels[16] using galactose dehydrogenase.

^{3}H-3-glucose in plasma was determined by drying a protein-free plasma filtrate under forced air and resuspending it in water. An aliquot of the resulting sample was added to Ultima Gold (Packard Instrument, Meriden, CT) scintillation cocktail and analyzed in a beta-counter. Plasma samples obtained prior to isotope infusion and an aliquot of the radioactive infusate were treated in a similar manner to serve as negative and positive controls, respectively.

The rate of peripheral glucose appearance (R_a) was calculated using the non–steady-state equations of Steele et al[17] as modified by de-Bodo.[18] To correct for noninstantaneous mixing of glucose, a correction factor (Vp) of 0.65 was used.[19] The volume of distribution for glucose was considered to be 26% of body weight. The fasting baseline used in the presentation of the results represents the mean for data obtained from the 4 blood samples obtained from 7 to 8 AM for each individual. The fasting R_a was calculated using the steady-state equation over the 7- to 8-AM period. The non–steady-state equation was then used for the remainder of the study. Quantitation of the 8-hour inte-
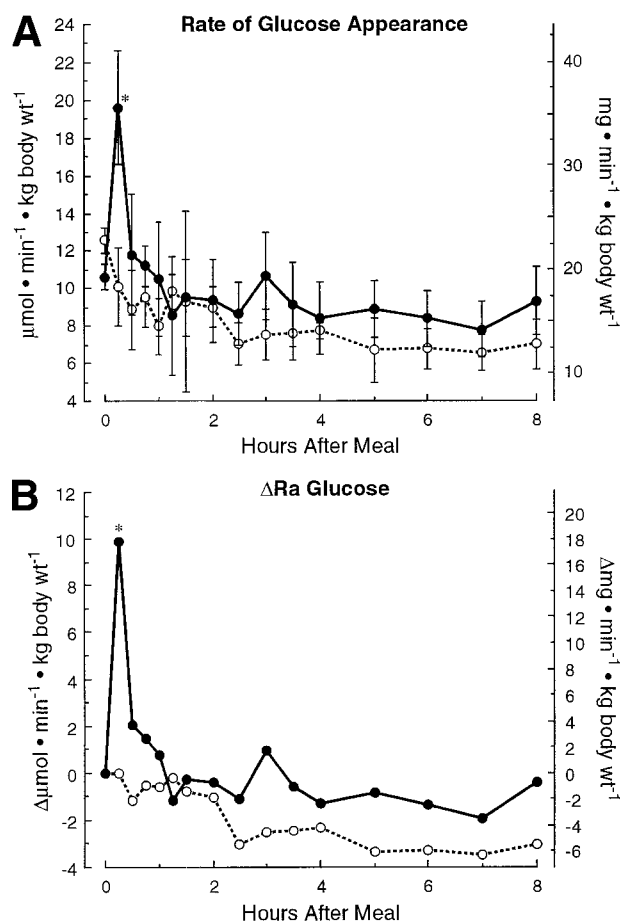

Fig 2. (A) Calculated R_a of glucose following ingestion of 50 g galactose (●) or water alone (control, ○) in 5 normal male subjects. Values are the mean ± SEM. (B) Change in R_a (B). The R_a was significantly elevated at the 15-minute time point only. *P < .05 v control (water).

Table 1. Galactose, C-Peptide, Glucagon, NEFA, C and Triglycerides for Control Versus Galactose Treatment

Time	Galactose (mmol/L)		C-peptide (nmol/L)		Glucagon (ng/L)		NEFA (µEq/L)		Triglycerides (mmol/L)	
	Control	Galactose	Control	Galactose	Control	Galactose	Control	Galactose	Control	Galactose
8:00 AM	0.00 ± 0.00	0.00 ± 0.00	0.17 ± 0.02	0.13 ± 0.03	321 ± 85	240 ± 43	492 ± 60	463 ± 112	1.32 ± 0.34	1.41 ± 0.26
8:15	0.00 ± 0.03	0.49 ± 0.13*	0.18 ± 0.04	0.22 ± 0.02	362 ± 109	246 ± 38	481 ± 60	491 ± 113	1.32 ± 0.32	1.45 ± 0.29
8:30	0.00 ± 0.06	1.34 ± 0.37*	0.16 ± 0.03	0.25 ± 0.03	321 ± 73	245 ± 31	515 ± 82	365 ± 65	1.33 ± 0.33	1.45 ± 0.29
8:45	0.02 ± 0.08	2.52 ± 0.48*	0.17 ± 0.03	0.27 ± 0.05	268 ± 47	222 ± 40	481 ± 54	257 ± 46	1.39 ± 0.32	1.44 ± 0.30
9:00	0.00 ± 0.06	2.34 ± 0.50*	0.13 ± 0.03	0.28 ± 0.07	275 ± 52	195 ± 33	519 ± 53	184 ± 37*	1.39 ± 0.32	1.46 ± 0.28
9:15	0.00 ± 0.04	1.67 ± 0.18*	0.17 ± 0.03	0.24 ± 0.05	285 ± 56	198 ± 36	539 ± 53	165 ± 35*	1.44 ± 0.31	1.46 ± 0.29
9:30	0.00 ± 0.05	1.03 ± 0.20*	0.17 ± 0.03	0.24 ± 0.05	277 ± 50	204 ± 46	508 ± 56	169 ± 41*	1.38 ± 0.32	1.49 ± 0.29
10:00	0.05 ± 0.02	0.30 ± 0.07*	0.18 ± 0.03	0.22 ± 0.05	266 ± 66	226 ± 42	551 ± 53	186 ± 48*	1.38 ± 0.32	1.49 ± 0.28
10:30	0.03 ± 0.07	0.03 ± 0.03	0.16 ± 0.03	0.17 ± 0.04	274 ± 60	254 ± 50	529 ± 63	209 ± 39*	1.33 ± 0.28	1.44 ± 0.28
11:00	0.00 ± 0.03	0.07 ± 0.02	0.17 ± 0.03	0.14 ± 0.03	292 ± 60	262 ± 42	640 ± 107	361 ± 88	1.38 ± 0.30	1.51 ± 0.26
11:30	0.00 ± 0.06	0.04 ± 0.03	0.17 ± 0.03	0.13 ± 0.03	305 ± 67	236 ± 51	639 ± 111	401 ± 82	1.33 ± 0.30	1.51 ± 0.28
12:00 PM	0.00 ± 0.04	0.02 ± 0.01	0.15 ± 0.03	0.13 ± 0.03	325 ± 93	240 ± 49	599 ± 117	488 ± 111	1.27 ± 0.30	1.55 ± 0.25
1:00	0.01 ± 0.08	0.00 ± 0.02	0.15 ± 0.03	0.13 ± 0.02	294 ± 62	268 ± 83	699 ± 138	544 ± 103	1.28 ± 0.31	1.61 ± 0.23
2:00	0.00 ± 0.04	0.01 ± 0.02	0.15 ± 0.03	0.12 ± 0.02	300 ± 67	252 ± 70	592 ± 166	565 ± 134	1.36 ± 0.33	1.64 ± 0.22
3:00	0.00 ± 0.04	0.00 ± 0.03	0.15 ± 0.03	0.12 ± 0.02	285 ± 54	241 ± 71	1,118 ± 213	601 ± 89*	1.35 ± 0.33	1.75 ± 0.23
4:00	0.02 ± 0.08	0.00 ± 0.00	0.15 ± 0.03	0.12 ± 0.02	303 ± 59	256 ± 78	1,083 ± 183	668 ± 69*	1.44 ± 0.32	1.79 ± 0.25

NOTE. n = 6 except for galactose (n = 5) and C-peptide (n = 4).

*$P \leq .05$ *v* control (water).

grated glucose R_a was determined as the area above or below the mean of the fasting value. The area response was calculated by the trapezoid rule[20] using a program developed in our laboratory (©University of Minnesota, 1991, M.C.G.). The glucose disappearance rate (R_d) was calculated using the equation, $R_d = R_a -$ rate of change of the glucose pool.[21]

The amount of protein oxidized was determined by quantifying the urine urea nitrogen excretion over the 8 hours of the study, to which the change in the amount of urea nitrogen retained endogenously was added. The latter was calculated by determining the change in the plasma urea nitrogen concentration and correcting for plasma water by dividing by 0.94. The urea distribution volume was considered to be the same as total body water. The latter was calculated using the equation of Watson et al.[22] It is assumed that there is a relatively rapid and complete equilibration of urea in total body water, and that a change in the plasma urea concentration is indicative of a corresponding change in total body water urea concentration. The sum of total urea nitrogen in urine and body water was divided by 0.86 to account for 14% lost due to metabolism in the gut.[23]

The data are presented as the mean ± SEM. Statistical analysis was performed using Student's paired *t* test. A *P* value of .05 or less is the criterion for significance.

RESULTS

When the subjects ingested only water, there was a gradual small decrease in the glucose concentration over the 8-hour period of study. When the same subjects ingested 50 g galactose, there was a rapid increase in glucose from a mean of 4.9 mmol/L (88 mg/dL) to 5.7 mmol/L (103 mg/dL) at 30 minutes. It then decreased to the initial 8 AM value by 2.5 hours and remained stable at this concentration for the remainder of the study, ie, it remained higher than the value obtained when only water was ingested (Fig 1).

The initial glucose R_a was modestly but not statistically different on the two occasions when the subjects were studied (Fig 2). To more easily distinguish the differences in the R_a when subjects ingested water or galactose, the data are plotted as the change from the initial mean value for each (Fig 2). As with the glucose concentration, the mean glucose R_a decreased when subjects ingested only water, ie, 8 hours of starvation. When galactose was ingested, there was a rapid approximately 80% increase in the glucose R_a. It then returned to the initial R_a by about 1 hour. The R_a then remained stable over the subsequent 7 hours. Thus, the glucose R_a returned to the initial value considerably faster than the glucose concentration, but both remained relatively higher versus the values obtained when the subjects ingested only water for the remainder of the study (Figs 1 and 2).

The glucose rate of removal (R_d) from the circulation slowly decreased after both water and galactose ingestion (from 10.4 ± 1.4 to 6.6 ± 1.2 µmol/min/kg for water and 9.5 ± 1.7 to 8.0 ± 1.9 µmol/min/kg for galactose, respectively; data not shown).

The amount of glucose appearing in the circulation as a result of galactose ingestion was calculated to be 9.8 g; the amount disappearing was 9.9 g.

Plasma galactose was undetectable following ingestion of water. Following ingestion of 50 g galactose, the plasma galactose concentration increased rapidly, reached a peak at 1 hour, and subsequently returned to the basal level by 2.5 hours (Table 1).

The insulin concentration decreased slightly when the subjects ingested water only. Following galactose ingestion, there was a rapid increase in insulin that paralleled the increase in glucose. After 3 hours, it had returned to a concentration not different from that obtained when only water was ingested (Fig 3). This occurred even in the presence of a galactose-induced, persistently higher glucose concentration. The C-peptide response was similar to the insulin response (Table 1).

The mean glucagon concentration decreased modestly when the subjects ingested water only (Table 1). After galactose ingestion, it decreased modestly and transiently. It then re-
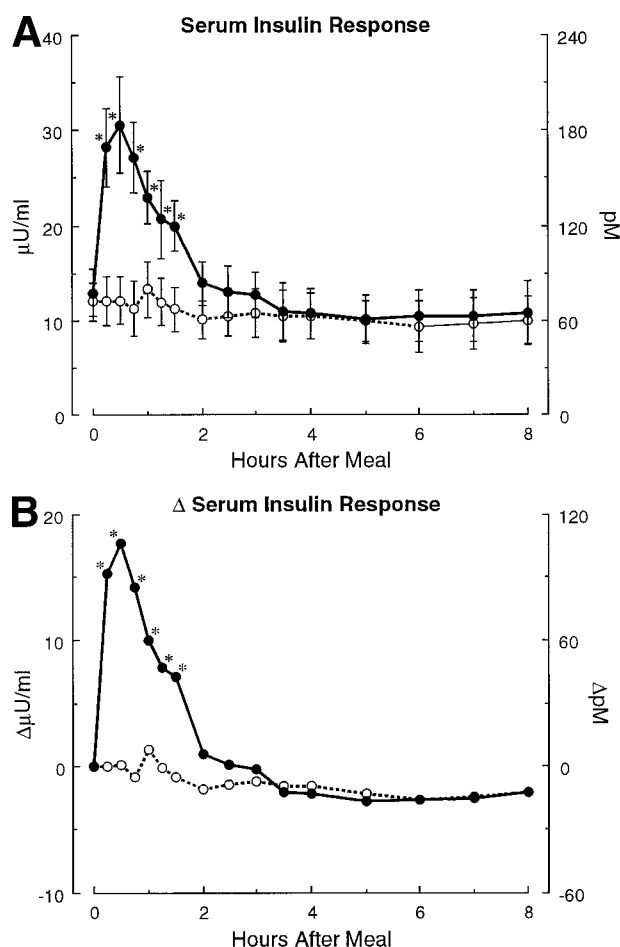
Fig 3. Mean arterialized serum insulin (A) or change in insulin concentration (B) following ingestion of 50 g galactose (●) or water alone (control, ○) in 6 normal male subjects. The mean baseline insulin concentration was 2.0 ± 0.5 and 2.2 ± 0.5 pmol/L (12 ± 3 and 13 ± 3 μU/mL) for water and galactose, respectively. *P < .05 v control (water).

turned to the initial value and remained unchanged for the duration of the study, ie, it remained relatively higher versus ingestion of water only. However, none of these differences were statistically significant.

Galactose ingestion resulted in a decrease in NEFAs and a late increase in triglycerides (Table 1).

The plasma α-amino nitrogen and uric acid concentration changed little following water or galactose ingestion. Plasma urea nitrogen decreased modestly after both, but was greater following galactose ingestion (Table 2).

The plasma lactate concentration was stable following water ingestion (Table 2). Following galactose ingestion, there was a rapid and large increase in the lactate concentration (~4-fold). By 4 hours after galactose ingestion, the lactate concentration returned to the baseline value.

Urinary excretion of creatinine, urea, and uric acid was similar following ingestion of water or galactose. However, 2.1 g galactose was excreted in the urine following galactose ingestion (Table 3).

DISCUSSION

As in previous studies,[1,8-11] the ingestion of a large amount of galactose resulted in a transient increase in glucose that was less than 1 mmol/L (18 mg/dL) compared with the initial glucose concentration. However, when compared with the glucose value obtained when the same subjects ingested water only, the ingested galactose clearly resulted in a persistently higher glucose concentration. This lasted for at least the 8 hours of the study. It is highly likely that essentially all of the galactose was absorbed by 3 to 4 hours, although this was not measured. Galactose and glucose are absorbed using the same transporter, and the absorption is very fast.[21]

The total amount of new glucose appearing in the extracellular fluid integrated over the 8 hours of the study was calculated to be about 51 g (283 mmol) when water was ingested and about 61 g (386 mmol) when galactose was ingested. When

Table 2. α-Amino Nitrogen, Urea Nitrogen, Uric Acid, and Lactate for Control Versus Galactose Treatment

	α-Amino Nitrogen (mmol/L)		Urea Nitrogen (mmol/L)		Uric Acid (mmol/L)		Lactate (mmol/L)	
Time	Control	Galactose	Control	Galactose	Control	Galactose	Control	Galactose
8:00 AM	2.84 ± 0.14	2.63 ± 0.14	4.39 ± 0.25	5.14 ± 0.43	0.35 ± 0.03	0.38 ± 0.04	0.83 ± 0.14	0.73 ± 0.17
8:15	2.84 ± 0.07	2.56 ± 0.14	4.21 ± 0.14	4.78 ± 0.43			0.84 ± 0.15	1.50 ± 0.33*
8:30	2.77 ± 0.07	2.56 ± 0.14	4.07 ± 0.25	4.86 ± 0.39			0.79 ± 0.12	1.99 ± 0.32*
8:45	2.70 ± 0.07	2.56 ± 0.07	4.07 ± 0.14	4.57 ± 0.43			0.77 ± 0.13	2.76 ± 0.15*
9:00	2.70 ± 0.07	2.49 ± 0.07	4.21 ± 0.25	4.28 ± 0.50	0.35 ± 0.04	0.34 ± 0.02	0.88 ± 0.19	3.13 ± 0.15*
9:15	2.77 ± 0.07	2.49 ± 0.07	4.28 ± 0.25	4.50 ± 0.32			0.88 ± 0.19	3.06 ± 0.40*
9:30	2.70 ± 0.07	2.56 ± 0.07	4.14 ± 0.18	4.57 ± 0.32			0.81 ± 0.19	2.85 ± 0.30*
10:00	2.70 ± 0.07	2.49 ± 0.07	4.07 ± 0.29	4.64 ± 0.50	0.35 ± 0.05	0.40 ± 0.06	0.74 ± 0.18	1.81 ± 0.44*
10:30	2.77 ± 0.07	2.49 ± 0.07	4.07 ± 0.25	4.36 ± 0.39			0.76 ± 0.15	1.18 ± 0.29
11:00	2.77 ± 0.07	2.49 ± 0.07	4.14 ± 0.29	4.43 ± 0.32	0.36 ± 0.04	0.37 ± 0.03	0.71 ± 0.12	0.88 ± 0.08
11:30	2.70 ± 0.07	2.49 ± 0.07	4.21 ± 0.25	4.43 ± 0.32			0.62 ± 0.11	0.69 ± 0.08
12:00 PM	2.63 ± 0.07	2.34 ± 0.14	3.78 ± 0.18	4.43 ± 0.32	0.35 ± 0.02	0.39 ± 0.04	0.71 ± 0.18	0.61 ± 0.03
1:00	2.63 ± 0.07	2.41 ± 0.14	3.78 ± 0.18	4.43 ± 0.32	0.35 ± 0.02	0.39 ± 0.04	0.57 ± 0.09	0.61 ± 0.02
2:00	2.63 ± 0.07	2.49 ± 0.14	3.78 ± 0.18	4.28 ± 0.29	0.36 ± 0.03	0.39 ± 0.03	0.59 ± 0.12	0.77 ± 0.14
3:00	2.63 ± 0.14	2.41 ± 0.14	3.78 ± 0.25	4.50 ± 0.54	0.33 ± 0.03	0.39 ± 0.03	0.65 ± 0.13	0.94 ± 0.31
4:00	2.70 ± 0.14	2.49 ± 0.14	3.93 ± 0.36	4.28 ± 0.43	0.35 ± 0.03	0.38 ± 0.03	0.65 ± 0.09	0.71 ± 0.06

NOTE. n = 6.

*P ≤ .05 v control (water).

Table 3. Urine Data for Control Versus Galactose Treatment

Parameter	Time	Control	Galactose	Excretion/mg Creatinine Control	Excretion/mg Creatinine Galactose
Creatinine (mg)	8:00-12:00	272 ± 22	325 ± 25		
	12:00-4:00	273 ± 11	280 ± 12		
Urea (mg)	8:00-12:00	1,900 ± 237	2,303 ± 434	7.0	7.1
	12:00-4:00	1,842 ± 165	1,844 ± 125	6.7	6.6
Uric acid (mg)	8:00-12:00	125 ± 21	148 ± 19	0.5	0.5
	12:00-4:00	78 ± 16	98 ± 10	0.3	0.4
Galactose (g)	8:00-12:00	0	2.1 ± 0.8*	0	6.5
	12:00-4:00	0	0.04 ± 0.02	0	0.1

NOTE. n = 6.

*$P \leq .05$ *v* control (water).

corrected for the baseline difference, the glucose R_a due to the ingestion of galactose can account for 9.8 g, or 20%, of the 48 g of galactose ingested and metabolized. (Two grams of galactose were lost in the urine.) An increased glucose R_a also was associated with a persistent and modestly higher glucose concentration throughout the last 6 hours of the study. These data are similar to those obtained in our laboratory previously when normal subjects ingested 50 g fructose. Following fructose ingestion, the glucose concentration and glucose R_a also remained higher than the values obtained when the subjects were starving over the same period.[24] Thus, a continuation of an increased R_a can largely explain the persistently higher glucose concentrations.

Whether this persistently increased glucose R_a was due to a higher rate of direct conversion to glucose or indirectly due to galactose previously stored as glycogen and subsequently released by glycogenolysis or both cannot be determined from the present data. However, after 2.5 hours, when the galactose value had returned to an essentially undetectable concentration, it is likely to have originated from galactose stored in the liver as glycogen. Galactose is readily phosphorylated to Gal 1-phosphate and converted to UDP-Gal by uridyltransferase. UDP-Gal is epimerized to UDP-glucose. The latter is the immediate precursor that provides the glucose moiety for glycogen synthesis. Indeed, it has been known from the early studies by Deuel et al[25] that galactose administration results in glycogen deposition.

Following an intravenous bolus injection of 36.6 g galactose in humans[7] and oral administration of galactose 1.0 g/kg body weight in rats,[6] after a short delay, there is a rapid synthesis of glycogen. Formation of glycogen also can account for the great majority of galactose taken up by the liver, at least in rats.[5] Presumably, after the galactose is absorbed, it is followed by a slow rate of glycogen degradation, although this has not been studied, to our knowledge. Whether galactose ingestion initially results in an increased direct conversion to glucose with release into the circulation also is unknown, but with the rapid elevation in glucose, this is likely the case.

In the present study, the increase in the insulin concentration was relatively modest and similar to that reported previously in normal subjects ingesting 0.5 g galactose/kg body weight[11] and by our laboratory in subjects with untreated type 2 diabetes who ingested only 25 g galactose.[1] The increase paralleled an increase in the glucose concentration, and the latter may explain the insulin elevation. Galactose injected intravenously did not stimulate an increase in insulin.[10]

With an increase in the insulin and glucose concentration, a decrease in glucagon would be expected. This did not occur. Therefore, as noted in subjects with type 2 diabetes, galactose ingestion may attenuate the expected decrease in the glucagon concentration.[1] The modest but persistently high glucagon concentration as compared with the same period of starvation may also help to explain the modestly higher glucose concentration and higher glucose R_a later in the course of the study (Figs 1 and 2). A modest but persistently elevated glucagon concentration also was noted in normal subjects after ingestion of fructose.[24] In both studies, the insulin concentration had returned to the value found when only water was ingested. Thus, the glucagon to insulin ratio remained elevated compared with the ingestion of water only.

The increased insulin concentration did not result in a significant increase in the glucose removal rate.

In the present study, the NEFA concentration decreased and mirrored the increase in insulin, as expected (Table 1). The increase in triglycerides after galactose ingestion was surprising and remains unexplained. However, an increase following fructose[24] or protein ingestion also has been observed.[26] Thus, this may be a general response to ingestion of gluconeogenic substrates.

We have recently demonstrated that ingestion of fructose resulted in an increase in the lactate and alanine concentration, and speculated that this may be due to a reduced utilization of these substrates for glucose production in the presence of an increased utilization of fructose in the gluconeogenic pathway. In the present study, galactose ingestion resulted in a striking increase in the lactate concentration. Unfortunately, the alanine concentration was not determined. Whether the increase in lactate is the result of a decreased utilization of lactate, an increased production, or both remains to be determined.

In the present study, galactose modestly decreased the amount of protein metabolized to urea. Following the ingestion of water, 23.9 g protein were metabolized, based on the calculated amount of urea present in body plasma water and that excreted in the urine. Following galactose ingestion, 20.3 g protein was metabolized. A nitrogen-sparing effect of galactose was reported many years ago.[27] Interestingly, fructose ingestion did not affect overall protein metabolism.[24]

REFERENCES

1. Ercan N, Nuttall FQ, Gannon MC, et al: Effects of glucose, galactose and lactose on the plasma glucose and insulin response in persons with non–insulin-dependent diabetes mellitus. Metabolism 42: 1560-1567, 1993

2. Suarez FL, Savaiano DA, Levitt MD: A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. N Engl J Med 333:1-4, 1995

3. Goresky CA, Bach GG, Nadeau BE: On the uptake of materials by the intact liver: The transport and net removal of galactose. J Clin Invest 52:991-1009, 1973

4. Tygstrup N: Determination of the hepatic elimination capacity (Lm) of galactose by a single injection. Scand J Lab Clin Invest 18:118-128, 1966

5. Niewoehner CB, Neil B, Martin T: Hepatic uptake and metabolism of oral galactose in adult fasted rats. Am J Physiol 259:E804-E813, 1990

6. Niewoehner C, Neil B: Mechanism of delayed hepatic glycogen synthesis after an oral galactose load v an oral glucose load in adult rats. Am J Physiol 263:E42-E49, 1992

7. Fried R, Beckmann N, Keller U, et al: Early glycogenolysis and late glycogenesis in human liver after intravenous administration of galactose. Am J Physiol 270:G14-G19, 1996

8. Roe JH, Schwartzman AS: Galactose tolerance of normal and diabetic subjects, and the effect of insulin upon galactose metabolism. J Biol Chem 96:717-735, 1932

9. Stenstam T: Peroral and intravenous galactose tests: A comparative study of their significance in different conditions. Acta Med Scand 177:1-120, 1946

10. Ganda OP, Soeldner JS, Gleason RE, et al: Metabolic effects of glucose, mannose, galactose and fructose in man. J Clin Endocrinol Metab 49:616-622, 1979

11. Williams CA, Phillips T, Macdonald I: The influence of glucose on serum galactose levels in man. Metabolism 32:250-256, 1983

12. Metropolitan Life Insurance Company: New weight standards for men and women. Stat Bull Metrop Insur Co 40:1-4, 1959

13. Duncombe WC: The colorimetric micro-determination of non-esterified fatty acids in plasma. Clin Chim Acta 9:122-125, 1964

14. Hohorst HJ: L-(+)-lactate. Determination with lactic dehydrogenase and DPN, in Bergmeyer HU (ed): Methods of Enzymatic Analysis. New York, NY, Academic, 1965, pp 266-270

15. Goodwin JF: The colorimetric estimation of plasma amino nitrogen with DFNB. Clin Chem 14:1080-1090, 1968

16. Kurz G, Wallenfels K: D-galactose. UV-assay with galactose dehydrogenase, in Bergmeyer HU (ed): Methods of Enzymatic Analysis. Deerfield Beach, FL, Verlag Chemie International, 1974, pp 1279-1282

17. Steele R, Wall J, deBodo JR, et al: Measurement of size and turn-over rate of body glucose pool by the isotope dilution method. Am J Physiol 187:15-24, 1956

18. deBodo RC, Steele R, Altszuler N, et al: On the hormonal regulation of carbohydrate metabolism: Studies with ^{14}C-glucose. Recent Prog Horm Res 19:445-488, 1963

19. Hetenyi G, Norwich KH: Validity of the rates of production and utilization of metabolites as determined by tracer methods in intact animals. Fed Proc 33:1841-1848, 1974

20. Fuller G, Parker RM: Approximate integration. Applications 13-16, in Analytical Geometry and Calculus. Princeton, NJ, Von Nostrand, 1964, pp 367-368

21. Bugianesi E, Kalhan S, Burkett E, et al: Quantification of gluconeogenesis in cirrhosis: Response to glucagon. Gastroenterology 115:1530-1540, 1998

22. Watson PE, Watson ID, Batt RD: Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 33:27-39, 1980

23. Hamberg O, Vilstrup H: Effects of insulin and glucose on urea synthesis in normal man, independent of pancreatic hormone secretion. J Hepatol 21:381-387, 1994

24. Nuttall FQ, Khan MA, Gannon MC: Peripheral glucose appearance rate following fructose ingestion in normal subjects. Metabolism (in press)

25. Deuel HJ, MacKay EM, Gulick M: Glycogen formation in rats after administration of diets high in galactose, glucose and lactose. Proc Soc Exp Biol Med 30:24-25, 1932

26. Gannon MC, Nuttall JA, Damberg G, et al: Effect of protein ingestion on the glucose appearance rate in subjects with type 2 diabetes. (submitted)

27. Deuel HJ, Gulick M, Butts JS: The relative antiketogenic value of glucose and galactose. J Biol Chem 92:23-24, 1931