Pathways for glucose disposal after meal ingestion in humans

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STUDIES OF GLUCOSE HOMEOSTASIS in humans have generally dealt with the postabsorptive state, i.e., 12–14 h after an overnight fast. However, people usually eat at least three times a day, and assimilation of ingested nutrients takes ~5–6 h (38). The majority of the day, therefore, is spent in the postprandial state. This consideration and data suggesting that postprandial hyperglycemia is an important risk factor for cardiovascular disease (24) have made the postprandial state a subject of considerable interest.

Most studies evaluating postprandial glucose homeostasis have used an oral glucose load (14). However, metabolic responses to oral glucose may differ from those of a meal (7, 15, 26, 58, 59). The few studies that have assessed the disposal of a meal (5, 6, 29, 38, 39, 45, 58, 59) have measured net organ glucose balances, net hepatic and muscle glycogen accumulation, whole body carbohydrate oxidation, and isotopically determined glucose uptake by splanchnic and peripheral tissues. None, however, has examined glycolysis, an important route for glucose disposal (19).

Because the pentose phosphate shunt is a minor pathway (25), glucose taken up by tissues postprandially can be considered either to be immediately stored or to undergo glycolysis (Fig. 1). Therefore, direct storage of glucose (e.g., glucose → glucose 6-phosphate → glyceron) can be calculated as the difference between whole body glucose uptake and whole body glycolysis. Virtually all of this storage should represent glycogen formation, since postprandial de novo lipogenesis and adipose tissue glucose storage are negligible in humans (21, 37). Of the glucose undergoing glycolysis, some will be oxidized; the remainder will undergo nonoxidative glycolysis leading to the formation of lactate, pyruvate, and alanine. These 3-carbon compounds will then be available to undergo gluconeogenesis and either be stored in glycogen via the indirect pathway or be released into plasma as glucose.

In studies reported to date (21, 22, 28, 38, 51), whole body glucose storage after ingestion of a meal or a glucose load has been calculated as the difference between plasma glucose disposal and whole body glucose oxidation rather than whole body glucose disposal minus whole body glycolysis. This could lead to an overestimation of postprandial glucose storage, because whole body glucose oxidation represents only a portion of whole body glycolysis. The magnitude of this is unclear, since the proportion of glucose undergoing oxidative and nonoxidative glycolysis has not as yet been determined. Moreover in previous studies (5, 6, 17, 18, 22, 29, 30, 38, 39, 42, 43, 45), whole body glucose disposal has been equated with the isotopically determined amount of glucose removed from the systemic circulation; the amount of glucose not reaching the systemic circulation because of disposal in splanchnic tissues has not been taken into consideration. Use of...

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plasma glucose disposal rather than whole body glucose disposal could lead to an underestimation of postprandial glucose storage.

Nearly 10 years ago, Rossetti and colleagues (52, 53) validated a method using generation of tritiated water from infused tritiated glucose to measure glycolysis of plasma glucose. Fery et al. (19) have used this approach to compare glycolysis of intraduodenally and intravenously infused glucose in normal volunteers and the effect of metformin on the disposal of an oral glucose load in patients with type 2 diabetes (20). In the present studies, we used the tritiated water technique to assess glycolysis after ingestion of a meal in normal human volunteers. Additionally, using indirect calorimetry and isotopic measurements of glucose taken up by splanchnic and peripheral tissues as well as glucose entering plasma via gluconeogenesis, we estimated postprandial whole body direct and indirect glucose storage and partitioned postprandial glycolysis into oxidative and nonoxidative components.

METHODS

Subjects. Informed written consent was obtained from 11 healthy volunteers after the protocol had been approved by the University of Rochester Institutional Review Board. The subjects (5 men and 6 women 47 ± 4 yr of age, body weight 87 ± 6 kg, %body fat 25 ± 2) had normal physical examination, routine laboratory tests, and glucose tolerance (World Health Organization criteria) (62), as well as no family history of diabetes mellitus. For 3 days before the study, all had been on a weight-maintaining diet containing 20% fat, and 20% protein, respectively as dextrose (Dextol; Baxter Healthcare, McGaw Park, IL), corn oil, and an amino acid mixture (Promod; Ross Laboratories, Columbus, OH). This consisted on average of 78 g of glucose, 10 g of fat, and 26 g of protein, including 3 g of [6,6-2H2]glucose to permit determination of the systemic appearance of ingested glucose. Subjects remained supine throughout the study, except while ingesting the meal.

Analytical procedures. Blood samples were collected for glucose, lactate, alanine, and glycerol levels, glucose specific activities, and tritiated water in oxalate-EDTA tubes for FFA, insulin, glucagon, lactate, glycerol, and alanine levels, glucose specific activities, and glucose enrichments. Breath samples for 14CO2 specific activities were collected at 30-min intervals beginning at 60 min.

At 10:00 AM, subjects ingested a meal over 5 min. The composition of this meal was designed to simulate a normal breakfast (omelet and flavored Glucola). The size of the meal was 6 kcal/kg, with a composition of 50% carbohydrate, 30% fat, and 20% protein, respectively as dextrose (Dextol; Baxter Healthcare, McGaw Park, IL), corn oil, and an amino acid mixture (Promod; Ross Laboratories, Columbus, OH). This consisted on average of 78 g of glucose, 10 g of fat, and 26 g of protein, including 3 g of [6,6-2H2]glucose to permit determination of the systemic appearance of ingested glucose. Subjects remained supine throughout the study, except while ingesting the meal.

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rate of appearance of the oral glucose in the systemic circulation was calculated from [6,6-2H₂]glucose data with the equation of Chiasson et al. (8; see also Ref. 28). The proportion of systemic glucose uptake attributable to glucose originating in the meal was calculated as the product of plasma glucose disappearance and the ratio of the rate of appearance of the ingested glucose in plasma to overall plasma glucose appearance (28). Endogenous glucose release was calculated as the difference between the overall rate of plasma glucose appearance and the rate of appearance of exogenous glucose (28, 42). Glucose entering plasma via gluconeogenesis was calculated from the incorporation of 14C into plasma glucose from [14C]NaHCO₃ by modifications of the aforementioned equations for the postabsorptive and postprandial states (16, 38). In the postabsorptive steady state, it was calculated as \( R_a \times S_A \times S_{ACO₂} \), where \( R_a \) is the overall rate of plasma glucose appearance, \( S_A \) is the 14C plasma glucose specific activity (dpm/μmol), and \( S_{ACO₂} \) is the 14C specific activity of CO₂ in exhaled breath (dpm/μmol). After meal ingestion, the non-steady-state equation was used

\[
(R_a + R_{dl})(0.5)(S_{Ap} + S_A)(0.5) + V_1(T_1 - T) - V_2(T_2 - T) \times (S_{Ap} + C_2 - (S_{Ap} + C_1)(0.5(S_{ACO₂} + S_{ACO₂^2}))
\]

where \( R_a, S_A, C_1, \) and \( CO \) are rates of plasma glucose disposal, 14C plasma glucose specific activities, plasma glucose concentrations, and breath 14CO₂ specific activities at times \( T_1 \) and \( T_2 \). In the equation above, glucose specific activities should be divided by 2, because two molecules of pyruvate are required to synthesize one molecule of glucose; however, this factor cancels out because, for each two molecules of 14CO₂ incorporated into oxalacetate, one is lost during randomization of oxaloacetate with fumarate (3, 16). Nevertheless, this equation still provides a minimal estimate of the incorporation of CO₂ into glucose. Because of the lack of complete equilibration between oxaloacetate and fumarate, the carbon incorporated into oxaloacetate during the pyruvate carboxylate reaction is eliminated by phosphoenolpyruvate carboxykinase during generation of phosphoenolpyruvate (3, 16).

Overall splanchnic glucose disposal of the ingested glucose was calculated as the difference between the amount of glucose ingested and the total appearance of the ingested glucose in the systemic circulation during the 6-h postprandial period, assuming that absorption of the ingested glucose had been completed as has been reported by Radziuk et al. (49).

Rates of whole body glucose and lipid oxidation were calculated using indirect calorimetry, with protein oxidation estimated from measurement of urine urea nitrogen (23, 28, 56).

\[
gluconeogenesis in g/min = 4.55V_{CO₂} - 3.21V_{O₂} - 2.87N
\]

\[
fat oxidation in g/min = 1.67V_{O₂} - 1.67V_{CO₂} - 1.92N
\]

where \( V_{CO₂} \) is CO₂ production, \( V_{O₂} \) is oxygen consumption, and \( N \) is urinary nitrogen excretion in liters per minute, liters per minute, and grams per minute, respectively.

Glycolysis from plasma glucose was calculated from the production of tritiated water from [3-3H]glucose. The validation and limitations of this technique have been discussed elsewhere in detail (52). The increment per unit time in tritiated H₂O calculated as described by Rossetti et al. (53) times body water mass was divided by the plasma glucose 3-3H specific activity. Plasma water was assumed to be 93% of total plasma volume, and total body water was measured using bioelectrical impedance (33).

This approach measures glycolysis from the infused tracer. Whole body glycolysis was calculated as the sum of plasma and splanchnic glycolysis. Plasma glycolysis was directly measured as described above. Splanchnic glycolysis was calculated as the product of the percentage of plasma glucose disposal undergoing glycolysis and splanchnic glucose uptake. The rationale for this approach is the observations of Féry et al. (20) that virtually identical proportions of intravenously and intraduodenally infused tritiated glucose undergo glycolysis in normal volunteers (19). Whole body non-oxidative glycolysis was calculated as the difference between whole body glycolysis and whole body glucose oxidation as assessed by indirect calorimetry.

Whole body glucose disposal was calculated as the sum of plasma glucose disposal and splanchnic disposal of the ingested glucose (20). Whole body direct pathway glucose storage was taken as the difference between whole body glucose disposal and whole body glucose oxidation. Whole body indirect glucose storage was calculated as the difference between whole body nonoxidative glycolysis and the amount of glucose entering plasma via gluconeogenesis. Because the latter is underestimated by the [14C]NaHCO₃ technique (3, 16), this calculation might overestimate indirect storage.

Statistical analysis. Unless stated otherwise, data are expressed as means ± SE. Paired two-tailed Student’s t-tests were used to compare the mean baseline data with the mean data obtained after oral glucose ingestion. A P value <0.05 was considered statistically significant.

RESULTS

Substrate and hormone concentrations. As shown in Fig. 2, After meal ingestion, arterial glucose increased from 4.6 ± 0.1 mM to a maximum of 8.1 ± 0.4 mM at 60 min and returned to near basal values by 240 min. Plasma insulin followed a similar pattern. Plasma glucagon decreased to nadir at 90 min and subsequently increased to values that were greater than baseline values at the end of the experiment (P = 0.03). Plasma lactate increased transiently to maximum at 90 min and returned to basal values by 180 min. Plasma alanine followed a similar pattern to lactate (data not shown). Plasma FFA decreased to nadir at 120 min and thereafter progressively increased to values above baseline at the end of the experiment (P = 0.05). Plasma glycerol followed a similar pattern to FFA (data not shown).

Rates of total, meal, and endogenous plasma glucose appearance and gluconeogenesis. Plasma glucose and breath bicarbonate specific activities and plasma glucose enrichments are given in Table 1. After meal ingestion, total plasma glucose appearance (endogenous plus ingested) increased almost threefold to a maximum of 75.7 ± 6.5 g/min at 120 min and returned to near basal values by 240 min. The rationale for this approach is the observations of Féry et al. (20) that virtually identical proportions of intravenously and intraduodenally infused tritiated glucose undergo glycolysis in normal volunteers (19). Whole body non-oxidative glycolysis was calculated as the difference between whole body glycolysis and whole body glucose oxidation as assessed by indirect calorimetry.

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subsequently returned toward basal rates. During the 6-h postprandial period, endogenous glucose release was 20.9 ± 3.3 g. This represented 27.6 ± 2.1% of all glucose entering the systemic circulation and a 58.3 ± 4.2% suppression compared with the amount of glucose that would have entered the circulation if basal rates of endogenous glucose release had remained constant (P < 0.001) (Fig. 3).

Glucose release into plasma due to gluconeogenesis, as estimated from the incorporation of infused $^{14}$CO$_2$

| Table 1. Plasma $[^3]$H- and $[^14]$C]glucose and breath $^{14}$CO$_2$ SA, plasma glucose enrichments, $V_{O_2}$, and $V_{CO_2}$ |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | 553 ± 40                        | 24 ± 2                          | 93 ± 6                          | 0.25 ± 0.09                     | 0.20 ± 0.08                     |
|                                 | 627 ± 51                        | 28 ± 3                          | 108 ± 7                         | 0.26 ± 0.10                     | 0.20 ± 0.09                     |
|                                 | 643 ± 50                        | 29 ± 5                          | 113 ± 8                         | 0.26 ± 0.10                     | 0.21 ± 0.09                     |
|                                 | 364 ± 20                        | 17 ± 0                          | 115 ± 8                         | 0.27 ± 0.11                     | 0.23 ± 0.11                     |
|                                 | 335 ± 27                        | 14 ± 2                          | 116 ± 8                         | 0.27 ± 0.10                     | 0.22 ± 0.09                     |
|                                 | 339 ± 31                        | 13 ± 2                          | 116 ± 9                         | 0.27 ± 0.10                     | 0.24 ± 0.09                     |
|                                 | 365 ± 35                        | 9 ± 1                           | 115 ± 9                         | 0.27 ± 0.10                     | 0.22 ± 0.08                     |
|                                 | 374 ± 36                        | 7 ± 1                           | 114 ± 10                        | 0.27 ± 0.10                     | 0.22 ± 0.07                     |
|                                 | 408 ± 45                        | 8 ± 1                           | 111 ± 9                         | 0.27 ± 0.10                     | 0.21 ± 0.07                     |
|                                 | 436 ± 58                        | 8 ± 1                           | 107 ± 10                        | 0.26 ± 0.10                     |                                  |
|                                 | 463 ± 55                        | 7 ± 1                           | 109 ± 8                         | 0.26 ± 0.10                     |                                  |
|                                 | 518 ± 65                        | 6 ± 1                           | 109 ± 8                         | 0.26 ± 0.10                     |                                  |
|                                 | 503 ± 68                        | 7 ± 1                           | 108 ± 7                         | 0.27 ± 0.10                     |                                  |
|                                 | 544 ± 73                        | 7 ± 1                           | 107 ± 7                         | 0.27 ± 0.10                     |                                  |
|                                 | 582 ± 77                        | 7 ± 1                           |                                  |                                  |                                  |

Values are means ± SE. SA, special activities; $V_{O_2}$, oxygen consumption; $V_{CO_2}$, carbon dioxide production.
into plasma glucose, decreased to nadir at 180 min and returned to near baseline values by 270 min. During the 6-h postprandial period, plasma glucose from gluconeogenesis totaled 10.7 ± 1.1 g and accounted for 51.1 ± 6.9% of endogenous glucose release. This was significantly greater than the proportion accounted for in the postabsorptive state (27.6 ± 3.2%, \( P < 0.01 \)), indicating a relatively greater suppression of glycogenolysis than gluconeogenesis during the postprandial period.

**Plasma glucose disposal, glycolysis and direct storage.** After meal ingestion, plasma glucose disposal increased to maximum at 120 min and returned to values not significantly different from baseline at 270 min (\( P = 0.26 \)). During the 6-h postprandial period, 75.4 ± 7.5 g of glucose were removed from the systemic circulation. Of these, 54.8 ± 5.1 g represented glucose from the meal and 20.8 ± 3.3 g from residual endogenous glucose release.

As shown in Fig. 4, the tritiated water content of plasma increased progressively during the entire experimental period as expected (19, 27). Glycolysis from plasma glucose (Fig. 5), calculated from the increases in plasma tritiated water, followed a pattern similar to that of disposal, returning to baseline values at 6 h. During the 6-h postprandial period, a total of 50.2 ± 3.9 g of plasma glucose underwent glycolysis, accounting for 66.5 ± 3.5% of plasma glucose disposal.

Plasma glucose undergoing direct storage, calculated as the difference between plasma glucose disposal and plasma glucose glycolysis, followed a pattern closely paralleling plasma glucose disposal, increasing to maximum values in individual subjects between 90 and 270 min and subsequently decreasing to basal values after 270 min (\( P = 0.45 \)). During the entire 6-h postprandial period, 24.4 ± 4.6 g of plasma glucose were directly stored. This accounted for 32.4 ± 3.5% of plasma glucose disposal, significantly less than the proportion accounted for by plasma glucose glycolysis (\( P = 0.02 \)).

**Whole body glucose disposal, glycolysis, oxidation and storage.** The meal that our subjects consumed contained an average of 77.8 ± 5.0 g of glucose. Of these, only 54.8 ± 5.1 g entered the systemic circulation. Because all of the glucose in the meal should have been absorbed from or metabolized by the gastrointestinal tract by the end of the 6-h postprandial period,
(49), the 22.9 ± 2.6 g of the glucose in the meal that did not enter the systemic circulation must have been disposed of by splanchnic tissues. Accordingly, total body glucose disposal, the sum of plasma glucose disposal (75.4 ± 7.5 g) and splanchnic glucose disposal (22.9 ± 2.6 g), was 98.3 ± 6.9 g.

Whole body glycolysis, calculated similarly as the sum of splanchnic glycolysis (16.0 ± 2.1 g) and plasma glycolysis (50.2 ± 3.9 g), totaled 66.2 ± 2.9 g over the 6-h postprandial period. Whole body glucose storage, calculated as the difference between whole body disposal and whole body glycolysis totaled 32.1 ± 5.8 g over the 6-h postprandial period. \( \bar{V}O_2 \) and \( \bar{V}CO_2 \) data used for indirect calorimetry are given in Table 1. Whole body glucose oxidation increased to maximum at 180 min and subsequently decreased to baseline at 240 min. Over the 6-h postprandial period, 43.1 ± 2.8 g of glucose were oxidized. Whole body nonoxidative glycolysis, calculated as the difference between whole body glycolysis and whole body glucose oxidation totaled 23.1 ± 2.9 g over the 6-h postprandial period. This would represent the maximal carbon derived from glycolysis available for conversion to plasma glucose or glycogen via gluconeogenesis. Because 10.7 ± 1.1 g of glucose entered plasma via gluconeogenesis, 12.4 ± 2.6 g would be left for whole body indirect glucose storage. Adding this amount to the glucose initially undergoing direct storage yields a value of 44.5 ± 6.8 g for total body glucose storage (Figs. 4 and 5).
DISCUSSION

The present studies were undertaken to characterize postprandial glucose homeostasis more completely. For this purpose, we used a combination of isotopic techniques and indirect calorimetry to assess routes of glucose disposal after ingestion of a meal by healthy volunteers. Included among these routes was the proportion of postprandial glucose disposal attributable to glycolysis that had not been hitherto examined and that would allow one to calculate postprandial glucose storage more accurately.

During the 6-h interval following ingestion of a meal that contained on average ~78 g of glucose, a total of ~98 g was disposed of (~75 g of glucose that had entered the systemic circulation plus ~23 g of glucose disposed of by splanchnic tissues; Fig. 6). The reason that total glucose disposal was greater than the amount of glucose ingested can be readily attributed to the fact that endogenous glucose release was found to be suppressed only ~60%, as has been previously observed (14). Indeed, the sum of the ingested glucose and the endogenous glucose disposed of (98 g) equaled the sum of splanchnic glucose and plasma glucose disposal (98 g).

Using the generation of tritiated water to estimate glycolysis from plasma glucose, we found that ~66% of plasma glucose disposal was initially attributable to glycolysis. As indicated above, however, plasma glucose disposal represents only ~80% of total body postprandial glucose disposal. Nevertheless, even if no glycolysis had occurred in splanchnic tissues, glycolysis from plasma glucose would still initially account for ~50% of whole body postprandial glucose disposal. This must, however, be considered a minimal estimate, since there is evidence for appreciable postprandial glycolysis in splanchnic tissues (2, 41, 44).

Féry et al. (19) found that virtually identical proportions of intravenously and intraduodenally infused tritiated glucose underwent glycolysis during 180-min experiments in normal volunteers. Therefore, to obtain an estimate of total body glycolysis, we multiplied splanchnic glucose disposal by the fraction of plasma glucose disposal undergoing glycolysis (~66%). The applicability of this approach is further supported by the studies of Radziuk (48), indicating that ~60% of splanchnic glucose uptake is not directly converted to glycogen, i.e., must undergo glycolysis. This approach yielded an estimate of 16.0 ± 2.1 g for postprandial splanchnic glycolysis. Adding this to the amount of plasma glucose undergoing glycolysis (50.2 ± 3.9 g) gives 66.2 ± 2.9 g for whole body glycolysis (Fig. 6).

This amount of glycolysis seems physiologically reasonable when one considers the 3-carbon precursors produced via nonoxidative glycolysis that would be needed for ongoing postprandial gluconeogenesis (see below) and that would be needed to satisfy tissue energy requirements via oxidative glycolysis during postprandial reduction in the availability of FFAs. Oxidative glycolysis, measured independently by indirect calorimetry in the present study, alone accounted for ~65% of whole body glycolysis.

Having an estimate of whole body glycolysis permitted the calculation of whole body direct glucose storage and partition of glycolysis into oxidative and nonoxidative pathways. Subtracting whole body glycolysis from total body glucose disposal (~98 g) yields a value of ~32 g for postprandial whole body direct glucose storage (Fig. 6).

Whole body nonoxidative glycolysis, calculated by subtracting whole body glucose oxidation from whole body glycolysis, amounted to ~23 g and accounted for ~35% of overall glycolysis and ~23% of total body glucose disposal. On the basis of euglycemic hyperinsulinemic clamp experiments, it has been thought that nonoxidative glycolysis accounts for only ~10% of insulin-mediated glucose disposal (12). Although the magnitude of nonoxidative glycolysis found to occur postprandially in the present study is substantially greater than that found in euglycemic clamp experiments (13, 53), it is consistent with the results of previous postprandial studies (9, 19). For example, Consoli et al. (9) found that ~15 g of lactate entered the systemic circulation during a 3-h period following ingestion of 75 g of glucose by normal volunteers. Féry et al. (19) found that, during a 3-h intraduodenal infusion of 92 g of glucose in normal volunteers, ~26 g of glucose were disposed of via nonoxidative glycolysis.

Our value for postprandial nonoxidative glycolysis (~23 g) provides a maximal estimate of carbons derived from glucose that would be available for gluconeogenesis and, hence, for indirect pathway glycogen synthesis. In the present study, ~11 g of glucose appeared in plasma as a result of gluconeogenesis, a value comparable to those found in previous studies using the same 14CO2 technique (5, 22, 38, 39). If all of the carbons used for this gluconeogenetically derived plasma glucose were the result of nonoxidative glycolysis and if all of the remaining carbons generated by nonoxidative glycolysis were used for indirect pathway glycogen formation, this would provide a maximum of...
Assuming 60% glycogen cycling as reported by Magnus et al. (34, 35, 46–48, 50, 54, 58), our data are compatible with those of Pimenta et al. (47), Peterson et al. (46), and Magnusson et al. (34, 35), who found the indirect pathway to account for 33, 37, 23, and 35%, respectively, of overall glycogen formation.

Parenthetically, had we used only plasma glycolysis (~50 g) and not included estimates of splanchnic glycology, this would have left no carbon for indirect pathway glycogen formation after subtracting glucose oxidation (~43 g) and glucose entering plasma via gluconeogenesis (~11 g). This consideration supports our including an estimate for splanchnic glycology, since without it an unrealistic estimate for indirect pathway glycogen formation is obtained (34, 35, 46–48, 50, 54, 58).

It is possible, however, that our estimate for splanchnic glycology is too low. This would result in an overestimation of direct glucose storage and an underestimation of indirect glucose storage. If glycology accounted for all of splanchnic glucose disposal, which is unlikely (48), total body glycology would have been ~73 instead of ~66 g, direct glucose storage would have been ~25 instead ~32 g, and indirect pathway glucose storage would have been 19 instead of ~12 g, a value still representing only ~43% of total glucose storage. It is of note that total glucose storage would not have been altered; i.e., it is independent of estimations of splanchnic glycology. Had we calculated whole body glucose storage as the difference between plasma glucose disposal and whole body glucose oxidation, as was done in previous studies, whole body glucose storage would have been only 32 g in contrast to the 44 g found in the present study.

The amount of glucose calculated to have been stored postprandially in the present study (~44 g) should represent ~40 g of glycogen, since only 3–5 g would be expected to have been incorporated into adipocyte triglycerides (37). There is evidence that glycogen cycling occurs in humans postprandially (i.e., simultaneous glycogen formation and degradation) (31, 36). Our method mostly measures net storage, i.e., the difference between glycogen formation and degradation, since glycogen broken down and oxidized would have been measured as glucose oxidation by indirect calorimetry. Labeled glycogen that was broken down and underwent glycolysis would have been measured as glycolysis by the initiated water technique. On the other hand, our method would overestimate net glyco- gen storage to the extent that either unlabeled ingested glucose that had been directly stored or glyco- gen formed via the indirect pathway underwent nonoxidative glycolysis. An approximation of this overestimation can be calculated from our data to be ~8 g, assuming 60% glycogen cycling as reported by Magnusson et al. (36) (see APPENDIX). Subtracting these 8 g would yield a value for maximal net glycogen accumulation of ~32 g, ~41% of the ingested glucose. This value is in good agreement with results of studies directly measuring postprandial net glycogen accumulation in liver and muscle (1, 37, 46, 58, 59). These studies indicate that a total of ~40% of ingested glucose maximally accumulates in liver and muscle as glycogen.

In summary, our results indicate that glycolysis is the main initial postprandial fate of glucose after ingestion of a meal, accounting for ~66% of overall glucose disposal; somewhat less is accounted for by oxidation (~44%) and glycogen formation (~45%), of which the majority is via the direct pathway (~73%).

APPENDIX

The amount of glycogen formed via the indirect pathway (12 g) that could undergo nonoxidative glycolysis due to cycling is calculated as 12 g × the rate of cycling (0.6) × the proportion of overall glycolysis that is nonoxidative (0.35) = 2.5 g. Similarly, the amount of glycogen formed by the direct pathway (32 g) from unlabeled glucose that would undergo nonoxidative glycolysis is calculated as 32 g × the rate of cycling (0.6) × the proportion of overall glycolysis that is nonoxidative (0.35) × the proportion of direct storage from the unlabeled glucose (0.8) (the glucose load divided by total glucose disposal) = 5.4 g.

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