Integration of Carbohydrate, Fat, and Protein Metabolism in Normal Daily Life

Figure 7.1 Relative constancy of blood glucose concentrations during a typical day, compared with the relative variability of plasma insulin concentrations. For a mechanical analogy, see Figure 7.2. Based on Reaven et al. (1988). From Diabetes by Reaven, G.M., Hollenbeck, C., Jeng, C.-Y., Wu, M.S., Chen, Y.-D. Copyright © 1988 by American Diabetes Association. Reproduced with permission of American Diabetes Association.
Figure 7.2  An analogy for metabolic regulation. The temperature in a thermostatically controlled water bath (the controlled variable) is relatively constant with only small variations around the set-point (the desired temperature), whereas the electrical current flowing through the heater (the controlling variable) varies between much wider extremes.

Figure 7.3  The pattern of glucose metabolism after an overnight fast. The numbers are approximations only, in mg per min, for a typical person of 65 kg body weight. Much of the glucose delivered to peripheral tissues (muscle, adipose tissue, blood cells, etc.) is "recycled" as lactate, which returns to the liver as a substrate for gluconeogenesis. However, a large proportion is oxidized, especially in the brain, and this constitutes an irreversible loss from the body's store of carbohydrate. Note that this picture shows only glucose metabolism: muscle and other tissues (e.g., renal cortex) will also be oxidizing non-esterified fatty acids from the plasma.
Figure 7.4 Concentrations of insulin, glucose, and lactate in blood after an overnight fast and following a single meal. The meal, shown by the arrow, contained 96 g carbohydrate and 33 g fat. Mean values for eight normal subjects are shown; based on data in Frayn et al. (1993).
Figure 7.5 Rates of glucose release from liver, from exogenous (dietary) and endogenous (gluconeogenesis + glycogenolysis) sources in normal subjects before and after drinking 75 g glucose in water. The rate of glucose disappearance from the circulation (i.e., utilization by all tissues) is also shown. All rates are in mg/min. The measurements were made by radioactive tracer techniques. Labeled [H³]-glucose was infused into the circulation at a constant rate; the extent to which it was “diluted” with unlabeled glucose was used to estimate the rate of entry of glucose into the circulation (“total glucose appearance”). In addition, the glucose drink was labeled with [¹⁴C]-glucose, so that the rate of entry of exogenous glucose into the circulation could be measured. The “endogenous” glucose production was then calculated by difference. Total glucose entry into the circulation (the sum of exogenous and endogenous appearance) increased after the glucose drink and, hence, the blood glucose concentration rose – top panel. Release of endogenous glucose from hepatocytes was markedly suppressed. The rate of disappearance of glucose from the circulation also increased, stimulated by the increased insulin concentration. Based on Fery et al. (1990). From American Journal of Physiology. Copyright © 1990 by American Physiological Society. Reproduced with permission of American Physiological Society.
Figure 7.6 Increases in liver and muscle glycogen after a single meal in normal subjects, studied by the technique of nuclear magnetic resonance. Liver glycogen was studied after ingestion of 98 g glucose; muscle glycogen after a meal that contained 290 g carbohydrate and 45 g fat (so they are not directly comparable). The units are mmol glucose equivalents per liter of tissue. They are both shown as change from fasting value. The initial liver glycogen concentration was 305 mmol/l, muscle 83 mmol/l. Redrawn from: (liver) Petersen et al. (2001); (muscle) Taylor et al. (1993).
Figure 7.7  **The pattern of glucose metabolism after a carbohydrate breakfast.** The direct pathway of glycogen storage is shown (glucose from small intestine going to liver glycogen), as is the indirect pathway (glucose forming lactate in the small intestine or in peripheral tissues, lactate then being used for liver glycogen synthesis); Section 5.1.2.1.

Figure 7.8  **Plasma non-esterified fatty acid (NEFA) concentrations after an overnight fast and following a meal.** The meal was the same as described in Figure 7.4. The plasma insulin concentration (expressed in nmol/l) is shown as a dotted line. Mean values for eight normal subjects are shown; data taken from Frayn et al. (1993).
Figure 7.9 The pattern of non-esterified fatty acid (NEFA) metabolism after an overnight fast. Fatty acids are released by lipolysis of the triacylglycerol (TAG) stores in adipose tissue. VLDL: very-low-density lipoprotein.
Figure 7.10 The milky appearance of blood plasma (right) after a fatty meal, compared with its clear appearance in the fasted state (left). The turbidity is caused by the presence of the large chylomicron particles.

Figure 7.11 Concentrations of triacylglycerol (TAG) in whole plasma (solid circles) and in chylomicrons (open circles) after overnight fast and after meals (shown by the arrows) containing either 33 g fat (a typical mixed meal) or 80 g fat (a high-fat meal) in groups of normal subjects. Data from Griffiths et al. (1994) and Coppack et al. (1990).
Figure 7.12 The pattern of plasma triacylglycerol metabolism after a breakfast containing both fat and carbohydrate. Triacylglycerol (TAG) enters the circulation in the form of chylomicron particles and is hydrolyzed by the enzyme lipoprotein lipase (LPL) in the capillaries of tissues (see Figure 5.17 for more details of this process).

Figure 7.13 Overview of protein and amino acid turnover in the body. We eat (very approximately) 100 g protein per day and therefore (unless we are growing) must dispose of an equal amount, mainly by oxidation of amino acids with generation of CO₂, H₂O, urea, and some NH₃. Of the (approximately) 10 kg of protein in the body, there is continuous synthesis and breakdown of (about) 300 g/day (i.e., a 3% “turnover”), although this varies greatly from tissue to tissue (Table 7.1). Some of the amino acid pool is used for synthesis of purines, pyrimidines, and hormones. This may also be put in terms of nitrogen balance. Each 6.25 g protein contains about 1 g nitrogen. Therefore, (in round figures) we take in about 16 g N per day. Each day, around 2 g is lost in feces, 0.5 g in shed skin cells, and so on, and the remainder of the 16 g as urea and NH₃ in urine. Reproduced from Frayn (2003), from Oxford Textbook of Medicine edited by Warrell, Cox, Firth, and Benz (1995) with permission from Oxford University Press. www.oup.com.
Figure 7.2.1  A representative transamination reaction.

Figure 7.14  The typical pattern of amino acid metabolism in different tissues. The diagram shows the difference in concentration between arterial blood and (1) the blood in a hepatic vein, carrying the venous blood from the liver, or (2) a femoral vein, which carries the venous blood mainly from the skeletal muscles of the leg. Thus, the solid bars represent the extent to which different amino acids are taken up across the small intestine and liver (the splanchnic bed), while the open bars show the release of amino acids from muscle into the bloodstream. These observations led to the idea that alanine (Ala) and glutamine (Gln) predominated in transferring both amino groups and carbon atoms from muscle proteolysis, to be taken up by the liver for urea synthesis and gluconeogenesis. The studies were carried out in normal subjects after an overnight fast. AIB: α-amino-isobutyric acid (a minor amino acid, not incorporated into protein). Based on Felig (1975). Reprinted, with permission, from the Annual Review of Biochemistry, 44. © 1975 by Annual Reviews. www.annualreviews.org.
Figure 7.15  The reactions that synthesize (glutamine synthetase) and break down (glutaminase) glutamine. (Note that, for simplicity, ionization states are not shown correctly; for example, NH₃ would be in the form of NH₄⁺ at physiological pH.)
Figure 7.16 Major amino acids interconversions in muscle. (Adipose tissue and brain may be similar.) 1, alanine aminotransferase (also called glutamate-pyruvate transaminase); 2, leucine, valine or other aminotransferase; 3, glutamine synthetase; 4, glutamate dehydrogenase; 5, branched-chain 2-oxoacid dehydrogenase and further catabolism; 6, muscle protein synthesis; 7, muscle protein breakdown (proteolysis). For simplicity, ionization states are not shown (e.g., NH$_3$ would be in the form of NH$_4^+$ at physiological pH).
Figure 7.17 Major pathways for amino acid flow between tissues. The pathways are discussed in the text, with the exception of serine release by the kidney. The precursor for this is probably glycine (released from peripheral tissues). In the liver, serine may be converted to D-2-phosphoglycerate (or pyruvate in some species) and, thus, enter the hepatic pool of gluconeogenic precursors. Based loosely on Felig (1975) and Christensen (1982); for discussion of serine metabolism see Snell (1986), Snell and Fell (1990).
Figure 7.18  **Overall control of protein synthesis and breakdown in muscle (and other tissues).** Some of the stimuli here are tissue specific (especially physical activity, testosterone, and β-adrenergic stimulation); more details are given in the text. IGFs are the insulin-like growth factors (IGF-1 and -2), generated in the liver in response to growth hormone (GH). β-adrenergic represents activation of β-adrenergic receptors, either by noradrenaline released at sympathetic nerve terminals or by adrenaline in the plasma.

Figure 7.4.1
Figure 7.19 The glucose–alanine cycle operates in parallel with the Cori (glucose–lactate) cycle. Muscle is shown, but adipose tissue also participates, and a number of tissues – for example, red blood cells – take part in the glucose–lactate cycle.

Figure 7.20 Blood flow through adipose tissue and forearm muscle during a typical day with three meals. The volunteers received three meals of equal energy content, at the times shown by the dashed lines. Note how adipose tissue blood flow (solid points) increases rapidly after each meal. Blood flow through the muscles of the forearm (open points) also increases but much less (the real stimulus for increased muscle blood flow is exercise; see Chapter 9). Data from seven of the volunteers reported by, and figure adapted from, Ruge et al. (2009).
Figure 7.21 Increasing fat storage with successive meals during a typical day with three meals. The volunteers received three meals of equal energy content, at the times shown by the dashed lines, as shown also in Figure 7.20. The graph shows the movement of fatty acids between adipose tissue and bloodstream. A negative value means that fatty acids are flowing from adipose tissue into the bloodstream (fat mobilization). A positive value means that fatty acids are flowing into the tissue from the action of lipoprotein lipase on triacylglycerol-containing lipoproteins (especially chylomicrons, after each meal) in the capillaries. Note how fat deposition in adipose tissue ("positive" area of the graph) increases successively with three meals. The volunteers were sedentary, akin to the "Lazy Day" described in the text. Data from seven of the volunteers described by, and figure adapted from, Ruge et al. (2009).