The fuels for exercise

John Hawley

Abstract Compared with the body's limited carbohydrate (CHO) stores, the reserves of fat in humans are plentiful: if fat was the sole source of energy, it could sustain skeletal muscle contraction for approximately 120 hours of continuous, moderate intensity (65% of maximal oxygen uptake [VO_2 max]) exercise. On the other hand, if CHO was the only fuel oxidised, it could provide energy for approximately 90 minutes of intense (85% of VO_2 max) activity. As the men's world record for the marathon (42.2 km) is approximately 125 minutes, this highlights the importance of fuel integration during exercise. In contrast to fatty acid metabolism, the rate of CHO oxidation during exercise is regulated tightly with glucose availability closely matching the requirements of the working muscles. Both the absolute (power output or speed) and relative (percentage of individual VO_2 max or maximal heart rate) intensity of exercise have important roles in the regulation of substrate metabolism: the absolute work rate or energy flux determines the total quantity of fuel required, while the relative intensity determines the fuel mix (i.e. the proportion of fat and CHO oxidised by the working muscles). During moderate exercise more than 50% of total energy is derived from fatty acid oxidation. However, during intense exercise, CHO fuels predominate with muscle glycogen and glucose utilisation scaling exponentially to the relative workrate. Although controversy exists with regard to the mechanism(s) that regulate substrate choice for oxidation by skeletal muscle during exercise, there is a growing body of evidence to suggest that CHO metabolism in general and muscle glycolytic flux in particular, regulate fatty acid oxidation by direct inhibition of long-chain fatty acid oxidation. CHO stores are limited and often substantially less than the requirements of the training and competition sessions undertaken by many athletes. Furthermore, muscle and liver glycogen depletion often coincide with fatigue during both endurance events and many team sports. Therefore, any nutritional strategy that promotes fatty acid oxidation and conserves endogenous CHO stores could, potentially, improve exercise capacity. **(Aust J Nutr Diet 2001;58 Suppl 1:S19–S22)**

Introduction

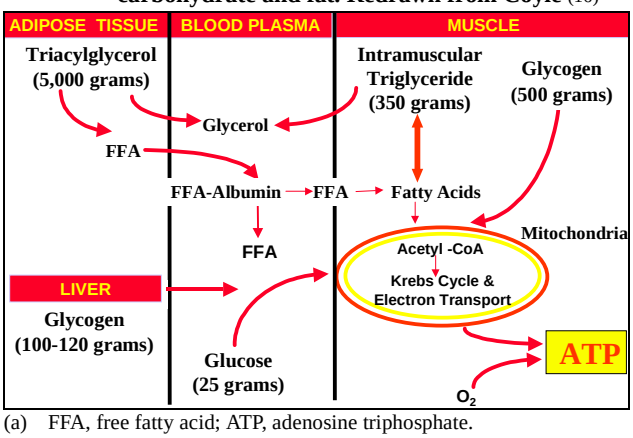
Fat and carbohydrate (CHO) provide the vast majority of fuel required for energy production in skeletal muscle during all intensities of aerobic exercise in humans. CHO also is consumed during 'anaerobic' (oxygen independent) exercise to sustain work rates performed above an individual's maximal aerobic power (VO_2 max). CHO is available within the muscle fibre (in the form of glycogen) and from blood glucose (from the breakdown of liver glycogen). Fat is available from triglyceride (TG) droplets within the muscle fibre (intramuscular triglyceride, IMTG) as well as from plasma free fatty acids (FFAs) from lipolysis.

The glycogen content of skeletal muscle of untrained individuals consuming a mixed diet is typically 80 mmol/kg of muscle wet weight (ww). For individuals involved in regular strenuous endurance training, muscle glycogen content is somewhat higher at approximately 125 mmol/kg ww (1). After several days of a high (8–10 g/kg body mass) CHO diet and a decrease in training, muscle glycogen content can be elevated to values greater than 200 mmol/kg ww. As 1 g of glycogen is stored in tissue with 2 to 3 g of water, an athlete may have a 2 to 3% increase in body mass after several days of CHO loading. In addition to skeletal muscle reserves, about 100 g of glycogen are stored in the liver: liver glycogen can be hydrolysed back to glucose and transported via the bloodstream to working muscle for oxidation.

Adipose tissue TG constitutes by far the largest energy store in the body (Figure 1), sufficient to sustain skeletal muscle contraction for approximately 120 hours at marathon running pace! On the other hand, if only CHO were utilised as a fuel, it would deliver energy for approximately only 90 minutes of running. As the men's world record for the marathon is approximately 125 minutes, this highlights the importance of fuel integration during prolonged exercise. The size of the adipose tissue TG pool is difficult to estimate and obviously depends on the fat mass of each individual, but is likely to range from 50 000 to 100 000 kcal (approximately 200 000 to 420 000 kJ) in men and women with 10 to 30% body fat (Figure 1). In order for this TG to be used as a substrate for oxidative metabolism, it has to be exported from adipose tissue and transported by the blood to the active tissues where it will be utilised.

An important physiological store of fat is IMTG, stored adjacent to the mitochondria: the total active muscle mass may contain up to 300 g of IMTG within the myocyte as small lipid droplets, although this amount can vary substantially due to individual differences in fibre type (type I fibres contain a greater concentration of IMTG than type II fibres), endurance training status (2–4), and diet (5). Paradoxically, although regular endurance training elicits an increase in IMTG concentration in healthy individuals, an adaptation viewed as beneficial for

Figure 1. A schema of the major endogenous storage sites of carbohydrate and fat. Redrawn from Coyle (16)[(a)]



(a) FFA, free fatty acid; ATP, adenosine triphosphate.

Exercise Metabolism Group, Department of Human Biology and Movement Science, RMIT University, Melbourne
J. Hawley, PhD, FACSM, Professor
Correspondence: J. Hawley, Exercise Metabolism Group. School of Medical Sciences, RMIT University, Bundoora, VIC 3083. Email: john.hawley@rmit.edu.au

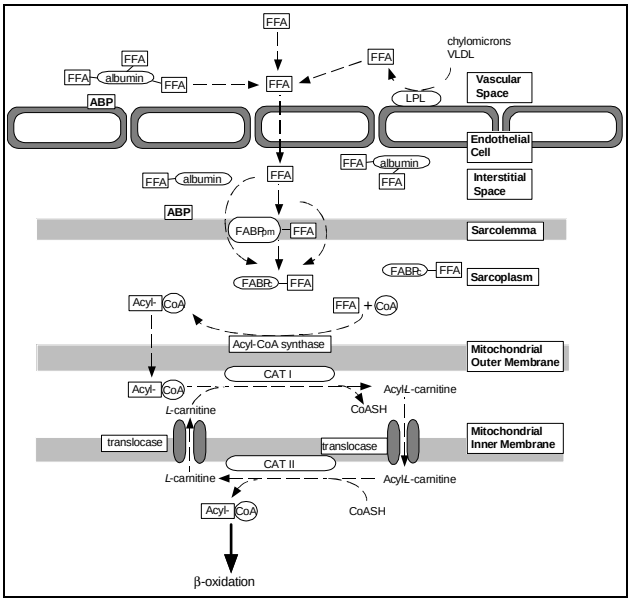
training and performance (2), IMTG stores are also increased in patients with type 1 diabetes mellitus (6). This latter condition is associated with the features of insulin resistance syndrome (7).

Finally, fatty acids also can be derived from circulating TG (chylomicrons) and very low density lipoproteins (VLDL) formed from dietary fat in the post-absorptive state. Recent evidence suggests that if all the circulating VLDL-TG were taken up and oxidised, VLDL-TG degradation could contribute up to 50% of the lipid oxidised during sub-maximal exercise (8).

As an energy source, fatty acids have several advantages over CHO: the energy density of lipid is higher (37.5 kJ/g for stearic acid versus 16.9 kJ/g for glucose), while the relative weight as stored energy is lower. Fatty acids also provide more adenosine triphosphate (ATP) per molecule than glucose (147 versus 38 ATP), although the complete oxidation of fatty acid requires more oxygen than the oxidation of CHO (6 versus 26 mol of oxygen per mole of substrate for glucose and stearic acid oxidation, respectively). However, despite the vast stores of endogenous TG (Figure 1), the capacity for fatty acid oxidation during exercise is limited. Unlike CHO oxidation, which is closely geared to the energy requirements of the working muscle, there are no mechanisms for matching the availability and utilisation of fatty acid to the rate of energy expenditure. As a result, the rate of fatty acid oxidation during aerobic exercise is largely determined by the availability of fatty acid, the rate of CHO utilisation and the exercise intensity.

There are many potential sites at which the ultimate control of fatty acid oxidation may reside (Figure 2), with the relative importance of each site depending on a myriad of external factors such as the aerobic training status of the individual, habitual dietary intake, ingestion of substrates (CHO and fat) before and during exercise, gender, and the relative and absolute exercise intensity (for reviews see 9–12).

Figure 2. A schema of the transport of fatty acids from the vascular space to the inner mitochondria of the skeletal muscle where ß-oxidations occurs. Reproduced from Jeukendrup (12)[(a)]



(a) CATI, carnitine acyl transferase I; CAT II, carnitine acyl transferase II; FABPc, fatty acid binding protein; FABPpm, plasma membrane bound fatty acid binding protein; FFA, free fatty acid; VLDL, very low density lipoprotein. The various processes are described in detail in the text.
Reproduced from Jeukendrup (12) with permission from the author.

The effects of exercise intensity on fuel selection by skeletal muscle

Both the absolute and relative (i.e. the percentage of VO_2 max) exercise intensities play a role in regulating the fuel mix: the absolute work rate determines the total quantity of fuel required, while the relative intensity determines the proportions of CHO and fat oxidised by the working muscles vz (13). In the post-absorptive state, fatty acid oxidation provides a major portion of the energy requirements for skeletal muscle: at rest, the rate of total fatty acid oxidation is approximately 4 µmol/kg/minute, which represents about 50% of oxygen consumption. The rate of lipolysis at rest is usually in excess of that required to provide resting energy requirements such that at the onset of low to moderate intensity exercise, a significant increase in fatty acid oxidation could occur even if there was no instant increase in lipolysis. During low intensity exercise (25% of VO_2 max), an intensity comparable to walking, most of the energy requirements can be met from plasma fatty acid oxidation, with a small contribution from the oxidation of plasma glucose. At exercise of low intensity the rate of appearance of fatty acid in plasma matches closely the rate of fatty acid oxidation. Even when low intensity exercise is sustained for one to two hours, the pattern of fuel utilisation does not change considerably. Presumably this is because the muscle energy requirements can be met almost exclusively from the oxidation of the fatty acid mobilised from the large adipose TG stores, and lipolysis is not limited by blood flow.

With an increase in exercise intensity from 25% to 65% of VO_2 max (the pace that could be sustained by a trained person for up to eight hours), total fat oxidation reaches its peak, despite a slight decline in the rate of appearance of plasma fatty acid. The higher rate of total fatty acid oxidation at 65% compared to 25% of VO_2 max reflects a substantial increase in the oxidation of IMTG. Of interest is that even when the absolute rate of fatty acid oxidation is at a peak (i.e. 42.8 µmol/kg/minute), fat contributes only about 50% to the total fuel requirements of exercise, with the remainder of the energy coming from CHO.

During high intensity exercise at 85% of VO_2 max (race pace for endurance events lasting approximately one hour) there is a decline in total fatty acid oxidation (from 42.8 to 29.6 µmol/kg/minute) compared to moderate intensity exercise (Figure 3). This is largely due to a marked reduction in the rate of appearance of plasma fatty acid. It is likely the rate of appearance for plasma fatty acid decreases with increasing exercise intensity because of an insufficient blood flow and albumin delivery to transport fatty acid from adipose tissue into the blood stream. On the other hand, glycerol is water-soluble and so its appearance in the plasma is not blood flow dependent: consequently the rate of appearance for glycerol is not affected. In addition, continuous high intensity exercise is associated with high rates of glycogenolysis (Figure 3) and the concomitant production of lactic acid which accu-

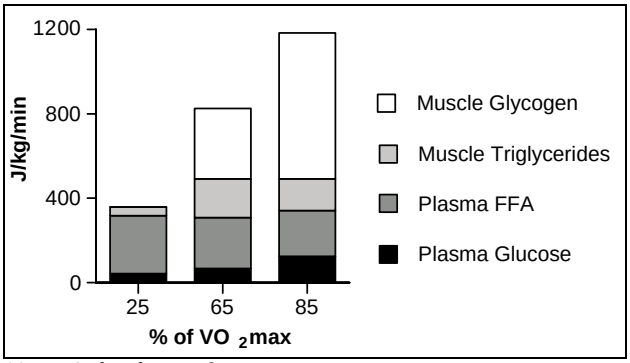
mulates in muscle and blood. This increased glycolytic flux also acts to inhibit fatty acid oxidation by skeletal muscle (see below).

Why can't fatty acid oxidation sustain intense exercise?

At rest, the rate of appearance fatty acid (i.e. lipolysis) normally exceeds energy requirements of skeletal muscle. During low intensity exercise, when lipolysis increases further, there is still a sufficient supply of fatty acid to meet the muscles' energy demand. However, there is little further increase in lipolysis (i.e. the rate of appearance fatty acid) when exercise intensity increases to 65% of VO_2 max: at such work rates the rate of appearance fatty acid closely matches fatty acid oxidation. During high intensity exercise, lipolysis is suppressed markedly and the contribution of fatty acid oxidation to the total energy requirements of exercise is diminished. These observations would support the notion that the reduced availability of fatty acid (i.e. a reduction in lipolysis) may contribute to a part of the decline in fatty acid oxidation during intense exercise.

To evaluate the extent to which decreased fatty acid availability contributes to the lower rates of fatty acid oxidation during intense exercise, Romijn (14) studied well trained endurance subjects during 30 minutes of intense (85% of VO_2 max) cycling once during a 'control' trial when plasma FFA concentration was normal (i.e. 0.3 mM) and again when plasma FFA concentration was elevated to approximately 2 mM by an infusion of lipid (Intralipid) and heparin. Total fatty acid oxidation was increased 27% (from 26.7 to 34.0 µmol/kg/minute) with the lipid infusion compared to control. However, the elevation of plasma FFA concentration (i.e. increased availability) during intense exercise only resulted in a partial restoration of fatty acid oxidation as the rates of total fat oxidation at 85% of VO_2 max were still lower than those observed in normal conditions at 65% of VO_2 max. These findings indicate that fatty acid oxidation is impaired during intense exercise because of a failure of lipolysis to meet the energy demands of the muscle. Therefore, in theory, TG lipolysis establishes the upper limit to fatty acid oxidation during high intensity exercise. However, even when lipid is infused well in excess of the muscle requirements during high intensity exercise, less than half of the total energy requirements are met by fatty acid oxidation. This is because the muscle is also a major site of control of the rate of fatty acid oxidation during such exercise. Specifically, the increased rate of glycogenolysis during intense exercise appears to inhibit the entry of long-chain fatty acid (LCFA) into the mitochondria. Sidossis (15) reported that during cycling at 80% of VO_2 max, the accelerated glycolytic flux associated with the high work rates resulted in high rates of pyruvate and acetyl-CoA formation which inhibited Carntine palmitoyl transerase-1 activity and, in turn, fatty acid entry into the mitochondria. Coyle (16) also showed that CHO metabolism (i.e. glycolytic flux) regulates fatty acid oxidation during exercise. These workers had subjects ingest CHO before exercise (in order to produce high concentrations of plasma glucose and insulin) and subsequently determined the rates of oxidation of an LCFA (palmitate) and a medium-chain fatty acid (MCFA, octanoate). Unlike palmitate which requires CPT-I for transport into skeletal muscle mitochondria, octanoate is not limited by mitochondrial transport. The increased glycolytic flux from pre-exercise glucose ingestion significantly reduced palmitate oxidation, but had no effect on octanoate oxidation. Even when fatty acid availability is maintained by an infusion of lipid, CHO ingestion still inhibits LCFA oxidation (17), presumably because of the anti-lipolytic effects of elevated insulin concentrations. Taken collectively, these findings suggest that although the rate of lipolysis is important, the primary site of control of fatty acid oxidation during moderate to intense exercise resides at the muscle tissue level (18). Furthermore, increased glycolytic flux resulting from either CHO ingestion (19–21) and the concomitant rise in plasma insulin, or an increase in exercise intensity (14,15) directly inhibits LCFA oxidation.

Figure 3. The effect of exercise intensity on the contribution from the four major substrates to energy expenditure. Redrawn from Romijn (29)[a]



(a) FFA, free fatty acid
Reproduced with permission from the American Physiological Society from Romijn JA, Coyle EF, Sidossis LS, Gastaldelli A, Horowitz JF, Endert E, et al. Regulation of endogenous fat and carbohydrate in relation to exercise intensity. Am J Physiol 1993;E380–E391.

Nutritional strategies to alter fuel selection during exercise

As endogenous CHO reserves are limited, and as muscle and liver glycogen depletion often coincide with fatigue during both endurance events and many team sports, there has been a recent surge of interest by athletes, coaches and sports practitioners in several nutritional practices which, in theory at least, could promote fatty acid oxidation, attenuate the normal rate of CHO utilisation, and improve exercise capacity (i.e. fat adaptation, fat feedings). The reader is referred to several recent reviews for further information on these topics (22–26).

Conclusion

Fat and carbohydrate provide the vast majority of fuel required for energy production in skeletal muscle during all intensities of aerobic exercise in humans. CHO is also consumed during 'anaerobic' (oxygen independent) exercise to sustain work rates performed above an individuals maximal aerobic power (VO_2 max). CHO is available within the muscle fibre (in the form of glycogen) and from blood glucose (from the breakdown of liver glycogen). Fat is available from triglyceride droplets within the muscle fibre as well as from plasma FFAs from lipolysis. The

rate of carbohydrate oxidation is closely geared to the energy needs of the working muscles. In contrast, fat utilisation during exercise is not regulated tightly, as no mechanisms exist for matching availability and metabolism of fatty acids to the prevailing rate of energy expenditure. As a result, the rate of fatty acid oxidation during aerobic exercise is determined largely by the availability of fatty acid, the rate of CHO utilisation and the exercise intensity. Both the absolute and relative (i.e. the percentage of VO_2 max) exercise intensities play a role in regulating the fuel mix: the absolute work rate determines the total quantity of fuel required, while the relative intensity determines the proportions of CHO and fat oxidised by the working muscles. With an increase in exercise intensity there is a concomitant drop in exercise duration. Probably the most potent intervention that alters the contributions of CHO and fatty acid to total energy utilisation is diet. Eating a high fat diet in the days before an exercise bout (27), or increasing the availability of fatty acid immediately before exercise by ingestion of a high fat meal (28) can markedly increase the contribution of fat to oxidative metabolism.

References

1. Hawley JA, Schabort EJ, Noakes TD, Dennis SC. Carbohydrate-loading and exercise performance. An update. Sports Med 1997;24:73–81.
2. Kiens B, Essen-Gustavsson B, Christensen NJ, Saltin B. Skeletal muscle substrate utilization during submaximal exercise in man: effect of endurance training. J Physiol 1993;469:459–78.
3. Martin WH. Effects of acute and chronic exercise on fat metabolism. In: Holloszy JO, editor. Exercise and sport sciences reviews. Volume 24. Baltimore: Williams and Wilkins; 1996. p. 203–31.
4. Martin WH, Dalsky GP, Hurley BF, Matthews DE, Bier DM, Hagberg JM, et al. Effect of endurance training on plasma free fatty acid turnover and oxidation during exercise. Am J Phsyiol 1993;265:E708–E714.
5. Starling RD, Trappe TA, Parcell AC, Kerr CG, Fink WJ, Costill DL. Effects of diet on muscle triglyceride and endurance performance. J Appl Physiol 1997;82:1185–9.
6. Ebeling P, Essen-Gustavsson B, Tuominen JA, Koivisto VA. Intramuscular triglyceride content is increased in IDMM. Diabetologica 1998;41:111–5.
7. Phillips DIW, Caddy S, Illic V, Fielding BA, Frayn KN, Borthwick AC et al. Intramuscular triglyceride and muscle insulin sensitivity: evidence for a relationship in nondiabetic subjects. Metabolism 1996;45:947–50.
8. Kiens B, Helge JW. Adaptations to a high fat diet. In: Maughan RJ, editor. Nutrition in sport. Oxford: Blackwell Science; 2000. p. 184–91.
9. Brouns F, van der Vusse D. Utilization of lipids during exercise in human subjects: metabolic and dietary constraints. Br J Nutr 1998;79:117–28.
10. Spriet LL. Biochemical regulation of carbohydrate-lipid interaction in skeletal muscle during low and moderate intensity exercise. In: Hargreaves M, Thompson M, editors. Biochemistry of exercise X. Champaign, Illinios: Human Kinetics; 1999. p. 241–61.
11. Vusse van D, Reneman RS. Lipid metabolism in muscle. In: Rowell LB, Shepherd JT, editors. Handbook of physiology. Exercise: regulation and integration of multiple systems. New York: American Physiological Society, Oxford Press; 1996. p. 952–94.
12. Jeukendrup AE. Aspects of carbohydrate and fat metabolism. Haarlem: De Vrieseborch; 1997.
13. Brooks GA, Mercier J. Balance of carbohydrate and lipid utilization during exercise: the 'crossover' concept. J Appl Physiol 1994;76:2253–61.
14. Romijn JA, Coyle EF, Sidossis LS, Zhang XJ, Wolfe RR. Relationship between fatty acid delivery and fatty acid oxidation during strenuous exercise. J Appl Physiol 1995;79:1939–45.
15. Sidossis LS, Gastaldelli A, Klein S, Wolfe RR. Regulation of plasma fatty acid oxidation during low- and high-intensity exercise. Am J Physiol 1997;272:E1065–E1070.
16. Coyle EF. Fuels for sports performance. In: Lamb DR, Murray R, editors. Perspectives in exercise science and sports medicine. Volume 10. Optimising sport performance. Indiana: Cooper Publishing Group; 1997. p. 95–129.
17. Sidossis LS, Stuart CA, Schulman GI, Lopaschuk GD, Wolfe RR. Glucose plus insulin regulate fat oxidation by controlling the rate of fatty acid entry into the mitochondria. J Clin Invest 1996;98:2244–50.
18. Wolfe RR. Fat metabolism in exercise. In: Richter EA, Kiens B, Galbo H, Saltin B, editors. Advances in experimental medicine and biology. Volume 441. Skeletal muscle metabolism in exercise and diabetes.New York: Plenum Press; 1998. p. 147–56.
19. Coyle EF, Jeukendrup AE, Wagenmakers AJM, Saris WHM. Fatty acid oxidation is directly regulated by carbohydrate metabolism during exercise. Am J Physiol 1997;273:E268–E275.
20. Horowitz JF, Mora-Rodriguez R, Byerley LO, Coyle EF. Lipolytic suppression following carbohydrate ingestion limits fat oxidation during exercise. Am J Physiol 1997;273:E768–E775.
21. Horowitz JF, Mora-Rodriguez R, Byerley LO, Coyle EF. Substrate metabolism when subjects are fed carbohydrate during exercise. Am J Phsyiol 1999;E828–E835.
22. Coyle EF, Hodgkinson BJ. Influence of dietary fat and carbohydrate on exercise metabolism and performance. In: Lamb DR, Murray R, editors. Perspective in exercise science and sports medicine. Volume 12. The metabolic basis of performance in exercise and sport. Indiana: Cooper Publishing Group; 1999. p. 165–98.
23. Hawley JA. Nutritional strategies to enhance fat oxidation during aerobic exercise. In: Burke LM, Deakin V, editors. Textbook of clinical sports nutrition. Sydney: McGraw Hill; 2000. p. 428–54.
24. Hawley JA. Fat burning during exercise: can ergogenics change the balance? Phys Sportsmed 1998;26:56–68.
25. Hawley JA, Brouns F, Jeukendrup AE. Strategies to enhance fat utilisation during exercise. Sports Med 1998;25(4);241–57.
26. Hawley JA, Jeukendrup AE, Brouns F. Fat metabolism during exercise. In: Maughan RJ, editor. Nutrition in sport. Oxford: Blackwell Science; 2000. p. 192–7.
27. Burke LM, Angus DJ, Cox GR, Cummings NK, Febbraio MA, Gawthorn K, et al. Effect of fat adaptation and carbohydrate restoration on metabolism and performance during prolonged cycling. J Appl Physiol 2000;89:2413–21.
28. Hawley JA, Burke LM, Angus DJ, Martin DT, Fallon KE, Febbraio MA. Effect of altering fat availability on metabolism and performance during intense exercise in highly trained men. Br J Nutr. 2000;84:1–10.
29. Romijn JA, Coyle EF, Sidossis LS, Gastaldelli A, Horowitz JF, Endert E, et al. Regulation of endogenous fat and carbohydrate in relation to exercise intensity. Am J Physiol 1993;E380–E391.