The Clinical Pharmacology of Sport and Exercise
T. Reilly and M. Orme, editors

The Effect of Athletic Training and Dietary Factors on the Modulation of Muscle Glycogen*

F. Brouns[ab]

[a]Sandoz Nutrition Research Unit, P.O. Box 1350, 6201 BJ Maastricht**, [b]Nutrition Research Center, Dept of Human Biology, University of Maastricht, The Netherlands

Key words: Caffeine, carbohydrate, MCT, L-carnitine.

1. INTRODUCTION

Glycogen sparing practices have become common among athletes and coaches since early studies in the sixties showed a relation between muscle glycogen content and fatigue. Although the effect of carbohydrate (CHO) intake on muscle glycogen resynthesis at rest is well established, there are less data available on the effect of CHO intake during exercise on muscle and liver glycogen.This article reviews the factors which affect glycogen metabolism and summarizes measures that can be taken to "economize" glycogen use during exercise.

2. GLYCOGEN STORES

Assuming a muscle weight of about 40% of BW, the body's glycogen content amounts to about 480 g [1]. The amount of muscle glycogen is prone to variation according to daily CHO intake and activity. The liver contains about 100 g glycogen in the fed state. Liver glycogen declines during fasting due to a sustained glucose output to blood, while no input from food takes place. After refeeding, liver glycogen increases [2-4].

3. CHO AVAILABILITY AND FATIGUE

Many studies have shown a relation between the level of muscle and liver glycogen and performance capacity [5-13]. In cases of glycogen depletion the actual performance capacity of well-trained subjects may drop to about 40-50% of maximum [13,14]. A similar observation has been made in McArdle's patients who lack the ability to use glycogen for rapid delivery of energy [15,16], pointing to the fact that continued glucose supply from glycogen stores in muscle is a necessity for appropriate energy production and power development. The rate of

*This work was supported by grants of Sandoz Nutrition Ltd., Switzerland

**Address for correspondence.

glycogen depletion is closely related to the exercise intensity. Short-term, high intensity interval exercise causes a rapid depletion, whereas long-term submaximal endurance exercise depletes glycogen less rapidly. The depletion pattern in muscle fibre types depends on the intensity of exercise. Submaximal exercise depletes primarily type I (slow twitch) muscle fibres. With increasing intensity and/or increasing depletion of type I fibres, there is more involvement of type II fibres [11,17-20]. Long-term exercise may also deplete liver glycogen to such an extent that the glucose output to the circulation falls, causing blood glucose sometimes to fall to low levels. Central as well as local fatigue may then occur [2,21,22] which may be explained by a reduced production of pyruvate due to a lack of glucose. This reduces the rate of acetyl CoA production, which in turn reduces the capacity of the tricarboxile acid (TCA) cycle to oxidize substrates. The latter is assumed to cause a reduction in ATP resynthesis rate [10,23,24] and in the energy charge of the muscle cells, by reducing the high energy phosphate pool, under formation of ammonia [10,16,25]. Both a reduced glucose availability and increased ammonia production have been suggested to be involved in the aetiology of fatigue [26,27]. In accordance with these observations, the supply of carbohydrate orally or intra-venously leads to a reduced ammonia production, a lower IMP accumulation and improved performance [7,8,13,16,23,28].

This has led to the insight that augmenting muscle and liver glycogen content prior to exercise and delaying the depletion of endogenous CHO stores during exercise, will result in improved CHO availability and a delay in fatigue development. By evaluating the mechanisms which act on muscle and liver glycogen during exercise and as a result of diet, it may be possible to gain insight in how to economize glycogen metabolism in favour of optimizing physical performance capacity.

4. MECHANISMS FOR GLYCOGEN ECONOMIZATION

There are two potential sites at which it may be possible to influence the level of muscle and liver glycogen. The first is the site of synthesis, while the second is the site of breakdown. Both are regulated by a multi-enzymatic process: breakdown is achieved by the activities of phosphorylase, phosphorylase kinase and phosphatase, whereas synthesis is regulated by synthase, synthase kinase and synthase phosphatase.

The activity of the enzymes involved in glycogen degradation is enhanced by local factors such as AMP, IMP and cytosolic Ca++, which stimulate the conversion of the inactive phosphorylase b form into the active a form. Additionally, adrenaline stimulates the formation of cyclic AMP which in turn activates phosphorylase kinase, leading to increased phosphorylase a activity and subsequently enhanced glycolysis [29,30]. That adrenaline has a significant effect on the activation of phosphorylase a has further been shown in studies with adrenaline infusion in both humans [31,32] and animals [33]. Accordingly, exercise induced increases in adrenaline levels have been observed to enhance glycolysis in active and even in non-active muscles [34-37]. This may also explain the net lactate release observed in non-active arm muscle while performing leg exercise [38] or in non-active leg muscle while performing arm crank exercise [39]. However, a very recent study by Wendling *et al.* [40] failed to show an effect of adrenaline infusion in physiological doses in 8 subjects who exercised for 90 min at 65% VO_2max. Infusion resulted in a 2.5 fold increase in plasma adrenaline, increased blood glucose and lactate levels, but no change in muscle glycogen,

plasma FFA and glycerol. This study suggests that physiological increases in adrenaline may affect liver glycogen breakdown, but not that of muscle. ATP, G6P and insulin which signal an appropriate substrate and energy supply, stimulate the inactivation of the a form [41-43]. Since the concentrations of energy rich phosphates AMP, IMP, ATP, as well as G6P, are all involved in the activation/deactivation of phosphorylase, it is evident that phosphorylase activity is regulated indirectly by the rate at which these compounds are produced in glycolysis and TCA cycle.

4.1. Local glycogen effects

There is evidence that the local glycogen content of muscle itself may influence phosphorylase activity and the rate of glycolysis. This evidence is obtained from studies which showed a relation between the rate of glycolysis and initial glycogen content [4,44-48]. However, others failed to observe such an effect [13,49].The mechanism of this effect, if it exists, has not been elucidated, though the enzymatic machinery of CHO metabolism and of fat metabolism are respectively up- and down-regulated after CHO rich meals.

4.2. Plasma substrate effects

Apart from the above mentioned local regulatory factors, there is also an influence of circulating substrates on the rate of glycolysis and TCA cycle. The concentration of specific substrates such as glucose, lactate, free fatty acids (FFA) and lipoprotein, together with "accompanying hormonal patterns", influence the direct substrate supply from the circulation to the cell membranes and will influence substrate entry into the cell [50,51]. The intra-cellular substrate concentration influences glycogen phosphorylase and glycogen synthase activity indirectly. In this respect, it has been suggested that an enhanced plasma FFA level at rest, causing an increased FFA uptake, enhances the beta oxidation thereby increasing citrate formation. The latter leads to an inhibition of PFK and subsequent increase in cellular G6P, which in its turn will inhibit phosphorylase activity [3,42,52-54].

Increased plasma glucose levels and associated high insulin and low glucagon levels will up-regulate glycogen synthase activity and down-regulate phosphorylase activity. A nice example in this respect is that of rebound hypoglycaemia after a glucose load on an empty stomach after an overnight fast. This is known to induce a rapid absorption and increase in blood glucose and may cause a rebound hypoglycaemia if exercise is performed subsequently. A high insulin concentration stimulates glucose entry into the cell, activates glycogen synthesis and inhibits phosphorylase. The latter also occurs in liver. The result is that the degradation of glycogen both in liver and muscle slows down, causing an increased reliance of the muscle on blood glucose. As a result, blood glucose will drop dramatically but the liver cannot respond with an adequate glucose output as glycogen degradation is inhibited [55,56]. This situation will persist until counter-regulatory mechanisms (glucagon, adrenaline, noradrenaline and cortisol increase, as well as a synchronically occurring insulin decrease) reactivate phosphorylase potently or until oral carbohydrate can compensate for the reduced liver glucose output [57]. If no oral CHO is supplied, the high levels of catecholamines induced by rebound hypoglycaemia will promote a rapid glycogen breakdown to compensate for the lack of glucose availability [58].

4.3. Exercise effects

Since exercise has effects on hormonal regulation, blood flow, local allosteric factors and energy charge of the cell, it is evident that the effects of exercise *per se* are difficult to separate from the circulating- and local substrate effects. During exercise there is a general increase in sympathetic activity, catecholamines, glucagon, growth hormone as well as a decrease in insulin. These changes are all known to stimulate lipolysis in adipose tissue [57,59-61] leading to an increased supply of glycerol and FFA to the blood. Generally, the supply of fatty acids to muscle during exercise exceeds by far the amount taken up by the cell. Although at rest there is a close relationship between plasma concentration and FFA uptake, this is not necessarily the case with higher blood FFA levels during exercise. Calculations of FFA uptake during exercise indicate a figure of only 10-20% of the amount supplied to the muscles by albumin bound FFA and triacylglycerol [62,63]. Thus, while elevated plasma FFA levels at rest may increase muscle fat uptake and oxidation in favour of a sparing of intra-muscular CHO stores, this may not necessarily be the case during exercise. In addition to the supply of FFA from plasma, muscle cells obtain FFA from adipocytes which are positioned between the muscle cells. Recent studies have indicated that the contribution on intra-muscular triglycerides (IMTG) to overall fat oxidation during exercise may be in the order of 30-70%, depending on exercise duration and intensity [64-67]. However, some authors have observed no significant contribution of IMTG in highly trained individuals [68,69].

The availability of FFA and its transportation into the mitochondria may therefore be important limiting factors during exercise. Two fatty acid transport-related processes are proposed to be involved in this limitation:

1) Fatty acids (FA) are to a large extent transported actively across the myocyte membrane by fatty acid binding protein (FABP). Once inside the cell the FA are further transported by cytoplasmic FABP to the mitochondria, where the FA will be liberated and activated to fatty acyl CoA.

2) Fatty acyl CoA will be converted to acyl-carnitine by carnitine acyl coA transferase I (CAT I). This complex will be translocated across the mitochondrial membrane after which reconversion to fatty acyl coA takes place, which will be channelled subsequently into the beta oxidation process.

When plasma FFA are high both the transport of FA to the mitochondria, involving FABP and the translocation by CAT I, are believed to be limiting steps in the regulation of fat oxidation and therefore indirectly for the possibility of sparing endogenous CHO stores during exercise [70-75]. When plasma FFA levels are low, the limitation is thought to be more on the level of FFA availability. This is especially the case in the early phase of exercise or after hyperinsulinaemia induced by CHO intake.

4.4. Training effects

Further evidence for limitations of fat uptake and combustion by muscle cells comes from the observation that lipoprotein lipase (LPL) activity of muscle, necessary for the removal of FA from triacylglycerol in blood, is hardly changed during the first hour of exercise, indicating that at least in the early phase of exercise fat uptake is limited by the activity of this enzyme [76,77]. In addition, the maximal activity of mitochondrial enzymes may pose a limitation. Training adaptation results in both an increased LPL activity [76,78] and

mitochondrial enzyme activity [65,79-81], pointing to an inappropriate activity of both enzyme complexes in the untrained state.

5. MANIPULATION OF GLYCOGEN USE

Several attempts have been made to use biochemical knowledge in order to manipulate fat and CHO uptake by the cell and subsequent metabolism, in order to improve performance. Some of these attempts will be described hereafter.

5.1. Caffeine

Caffeine (trimethylxanthine) is used widely to improve performance in endurance events. One of the theories put forward to explain the performance enhancing effects of caffeine is the stimulation of lipolysis. Caffeine has been observed to enhance plasma FFA in many studies in man and animals. However, in only a few of these studies was the respiratory exchange ratio (RER) reduced and glycogen spared [55,82-84]. In the study of Spriet [85] glycogen sparing only occurred during the initial phase of exercise when lipolysis is known to be low.

In contrast to these few studies, the majority of studies showing enhancement of, or no effect on lipolysis, did not show any effect on RER, hormones, overall substrate utilization and glycogen metabolism. This may indicate that although FFA was elevated in a number of studies, this elevation may have been in excess of the level needed to saturate the LPL and/or subsequent transport mechanism across the sarcolemma (no change in RER). Thus, although the existence of a glucose fatty acid cycle has been postulated to result in decreased CHO utilization when plasma FFA levels are high, this is certainly not always the case. The effects of caffeine on fat and CHO metabolism have been reviewed extensively in a number of recent papers. It appears that the performance enhancement due to caffeine is most likely related to effects on the central nervous system rather than to effects on fat mobilization and oxidation [86-89].

5.2. Medium chain triglycerides (MCT)

Medium chain triglycerides contain fatty acids with a chain length of 6,8 or 10 carbon atoms. Generally MCT are rapidly emptied from the stomach and taken up by the intestine.

After absorption by the enterocyte MCT are transported with blood to the liver, in contrast to LCT (long chain) which are transported by the lymphatic system. Medium chain triglycerides readily increase plasma FFA and TG levels. In muscle, MCT are rapidly taken up by the mitochondria and do not require the carnitine transport system. Several studies have been done to evaluate the effect of MCT ingestion on fat and CHO metabolism. These studies have shown that MCT are rapidly oxidized by muscle but do not lead to glycogen sparing. The fact that total fat oxidation remained the same after MCT ingestion, even in a glycogen depleted state, points to the fact that oral MCT does lead to a sparing of endogenous fat stores, most probably intramuscular fat, but not of glycogen. One of the limitations in boosting MCT to a level that would allow for glycogen sparing is that MCT ingestion of >30 grams in a short time leads to severe gastrointestinal discomfort. The latter will hinder athletic performance to such an extent that it would be unwise to do so. Thus, it has not been proven that MCT ingestion has any benefit for glycogen sparing [49,90-92].

5.3. Oral fat and fat infusions

Another attempt to improve fat oxidation with the goal of sparing glycogen stores, has been to enhance blood FFA levels by ingesting or infusing lipid emulsions.This procedure has resulted in a significant reduction of glycogen degradation in two studies [93-94]. In line with the observations that fat infusion spares muscle glycogen, a reduction of plasma FFA, induced by inhibiting lipolysis by nicotinic acid, resulted in an increased rate of glycogen degradation [95]. An appropriate level of circulating fat is thus a prerequisite for reducing the rate of utilizing endogenous CHO stores during exercise. However, for sports practice intravenous supply of nutrients seems to be impractical. Infusion during competition is not possible and even if it was possible, it would be forbidden by the doping regulations. Additionally, oral intake of fat emulsions reduces the rate of gastric emptying significantly and may lead to substantial gastrointestinal discomfort [96].

5.4. L-carnitine

Attempts to enhance mitochondrial FA transport and oxidation during exercise in healthy athletes, by oral L-carnitine intake, have failed because the L-carnitine content in muscle could not be increased (for extensive review see Wagenmakers [97]). Recent studies have indicated that the activity of CAT I is inhibited by malonyl CoA, a fatty acid synthesis intermediate which is produced in larger quantities when blood glucose and insulin are raised [98]. Thus, an increased malonyl CoA production after CHO intake, resulting in a downregulation of CAT I activity, may be one of the factors involved in the inhibitory action of CHO on fat metabolism and oxidation.

5.5. Oral CHO

Apart from the anti-lipolytic action after CHO intake, enhanced blood glucose levels *per se* will influence the rate of glucose uptake and glycolysis during exercise. The lipolytic effect of caffeine is counteracted by CHO ingestion. Several authors [85,99-101] observed that a high CHO diet or pregame meal countered the effects of caffeine on lipolysis. Bellet [43,102] observed a delay in the lipolytic response to caffeine and Giles and McLaren [81] observed a full counter-effect. Sasaki [103] did not observe inhibition due to CHO intake. The mechanism may be that lipolytic enhancing effects on the one hand (exercise+caffeine ----> catecholamines ↑↑ ---> lipolysis ↑↑) are counteracted by inhibiting effects (exercise+CHO --->insulin ↑ ---> lipolysis ↓).

Additionally, CHO intake during exercise may inhibit catecholamine and glucagon response and thereby reduce lipolysis. The balance of these two oppositely directed stimuli will therefore determine the final "metabolic direction". It can therefore be assumed that the quantity of CHO ingested as well as subsequent response of insulin, glucagon and catecholamine levels determine the final response. The reason that some studies did observe a strong effect of CHO and others less or no effect, may therefore be linked to the amount and timing of CHO intake.

5.5.1. Glucose uptake

Several factors affect the rate of glucose uptake by the muscle cell and therefore endogenous glycogen utilization during exercise. Contractile activity increases muscle cell glucose uptake, even in the absence of insulin [104-106]. One of the explanations given for this phenomenon is that contractile activity enhances the translocation of glucose transport

proteins GLUT 1 and GLUT 4 from an intracellular location to the cell membrane, thereby increasing the glucose transport capacity. Quantitatively GLUT 4 is most important [107-112]. This effect of contractile activity on glucose uptake seems to depend on the exercise intensity [113,114]. This may be partly explained by increased blood flow, which will enhance the absolute amount of glucose offered to muscle tissue per unit of time, but also an increased fractional glucose extraction as observed from arterio-venous concentration differences may play a role [38,113,115,116].

Insulin also enhances GLUT 4 translocation and the fact that a plasma insulin elevation in periods of muscular activity augments glucose transport further, points to the fact that contractile activity and insulin act synergistically [104,117-119]. As enhanced blood glucose and insulin always go hand in hand, even during exercise [6,8,120] when insulin release is known to be reduced by adrenergic influences [6], it will be difficult to differentiate the effects on glycogenolysis. In any case, elevated blood glucose levels reduce the rate of glycogen degradation both in animals [59,121,122] and humans [5,6,123-125]. At low exercise intensities even net synthesis of glycogen occurs [34,121,126-128]. The latter contrasts statements in many textbooks that exercise results in activation of phosphorylase and inactivation of glycogen synthase, disabling glycogen synthesis. Apart from stimulating blood glucose uptake, contractile activity has been shown to increase the activity of glycogen synthase I [129,130].

Most probably, at rest and low exercise intensities, the effect of contractile activity, glucose uptake and insulin on the interplay of glycogen degradation and synthesis depend on their absolute levels. What is suggested here is that when blood glucose and insulin are elevated, the counter-regulatory factors, glucagon, cortisol and catecholamines, will be low. In that situation glucose availability to the muscle cells may be high which, by enhanced GLUT 4 transport capacity may result in an accumulation of intracellular glucose and subsequent channelling into glycogen. Glycogen synthase activity may be upregulated more than glycogen phosphorylase in this situation. Price *et al.* [131], using NMR technique, recently showed that human gastrocnemius muscle can both degrade and synthesize glycogen simultaneously during prolonged low-intensity exercise, whereas net glycogen synthesis has also been observed during active post-exercise recovery [132]. In keeping with this, glycogen sparing and/or synthesis have been observed in situations of relative CHO overload. For example, infusion of glucose to high plasma levels of >15 mmol, reduced glycogen breakdown [5]. Infusion during low intensity exercise (50% VO_2max) combined with high intensity sprinting also reduced glycogen degradation [124]. Brouns [6] observed that cycling exercise at intensities ranging from 50-80% Wmax with a one-hour refeeding period at 50% Wmax, resulted in a highly significant reduction of glycogen degradation. Intake of CHO was higher than its utilization in this experiment. These studies indicate that glycogen synthesis occurred during periods of relatively low exercise intensity, finally resulting in the observed decreased quantitative glycogen utilization. In contrast, glucose infusion to a level of about 10 mmol during more intense continuous cycling did not result in muscle glycogen sparing, but did nevertheless result in improved performance [8,120,133]. Thus, to achieve reductions in muscle glycogen degradation, CHO supply must be quantitatively high, insulin levels must be substantially elevated and exercise intensity must be relatively low. The latter is important in this respect because the glucose flux into the glycolytic pathway is to a large extent regulated by the cellular energy charge (adenino nucleotides), ammonium ions, F6P level, citrate, hexokinase biphosphates, Pi and ATP turnover [24,41,134-136].

During intense exercise all these factors will enhance the channelling of glucose taken up by the cell into glycolyses, instead of into glycogen synthesis. It may be suggested therefore, that the amount of glucose entering the muscle cell must be larger than the amount channelled into glycolysis and the TCA cycle. In that case, intracellular glucose accumulation would favour "glycogen cycling": incorporation into glycogen before entering into glycolysis. In support of this suggestion is the observation that ^{14}C radio-labelled glucose is incorporated into glycogen in the case of excess glucose mobilization [137]. In most competitive situations where exercise intensities are on the upper limits and glycogen breakdown to supply glucose to the system is significantly enhanced, this may not be the case. In that condition the rate of glucose utilization may exceed the amount which can enter the myocyte. There are indications that glucose transport across the muscle cell membrane is a limiting factor for glucose uptake and deposition [138]. Some evidence comes from the fact that endurance training results in increased skeletal GLUT 4 content as observed in animals [139] and humans [140]. If glucose transport capacity exceeded the actual needs, most likely there would be no such adaptation. Other evidence comes from a study where human GLUT 4 has been over-expressed in transgenic mice resulting in a seven-fold increase in glucose transport and a ten-fold increase in glycogen. The latter occurred in the absence of any change in glycogen synthase and phosphorylase activity or G6P concentration [141]. Ivy and co-workers [142] recently showed that increased GLUT 4 content increases primarily glucose uptake in fast twitch but not in slow twitch fibres and does not necessarily enhance glucose metabolic capacity [143]. It seems that besides FFA transport, quantitative glucose transport capacity across the muscle cell membrane in relation to the rate of CHO oxidation, is an important limiting factor for endogenous CHO sparing and glycogen synthesis.

Various studies have been done on the rate of absorption of glucose as well as the rate of oxidation of glucose from different CHO sources. Generally, all soluble CHO sources are about equally well absorbed and oxidized. Non-soluble CHO sources and fructose have been observed to have lower absorption and oxidation rates [144-146].

6. CONCLUSIONS

Based on the mechanisms described and variables which determine the rate of glycogen synthesis and degradation, the following measures can be recommended to economize glycogen utilization and maximize exercise performance capacity:

1) Perform regular early morning endurance training at about 50-60% of VO_2max (heart rate 140-150 beats/min) on an empty stomach. This will maximize adaptations in fat metabolism.
2) Enhance glycogen prior to competition by ingesting a high CHO diet followed by a fat-rich dinner during the evening prior to competition. This may result in a favourable hormonal milieu and enzymatic activity for reducing CHO oxidation.
3) Ingest a light, well-digestible mixed pregame meal containing 40-50% CHO and 30-40% fat. With adequate CHO loading prior to exercise there is no need for a breakfast high in CHO.

4) Do not ingest CHO containing drinks during the last 2 hours preceding the competition. Take tea, beverages containing caffeine or plain water in order to maintain low insulin levels to enhance plasma FFA.
5) Perform an appropriate warm-up, in order to raise plasma FFA prior to the start to reduce glycolysis in the early phase of exercise.
6) During exercise one should ingest about 0.5-0.8 g CHO/min along with plenty of fluid (non-hypertonic solution) during the first 90 min of exercise and 0.8-1.2 g/min thereafter, to present a maximal supply of glucose to muscles and liver. During high intensity exercise this may lead to a sparing of liver and non-active muscle glycogen stores, whereas during low intensity exercise periods this may lead to sparing or resynthesis of glycogen in all tissues.
7) Immediately post-exercise CHO should be taken as liquid supplement or in a light digestible solid form in case that recovery between competitions is short.
8) In case of travelling to a hot or cold climate, significantly different from usual, the athlete should consider appropriate acclimatization in order to reduce catecholamine responses and related effects on glycogen degradation.

7. ACKNOWLEDGEMENT

I owe a word of thanks to my colleagues Prof. W.H.M. Saris, Dr. A.J.M. Wagenmakers and Drs. A. Jeukendrup for their continuous inputs during our various discussions.

REFERENCES

1. P.D. Gollnick, D.R. Lamb and R. Murray (eds.), Prolonged Exercise, Indianapolis, Benchmark Press (1988) 1.
2. E. Hultman and L.H. Nilsson. B. Pernow and B. Saltin (eds), Muscle metabolism during exercise, New York, Plenum (1981) 143.
3. E.A. Newsholme and A.R. Leech (eds), Biochemistry for the medical sciences, Chichester, John Wiley & Sons (1983) 336.
4. E.A. Richter and H. Galbo, J. Appl. Physiol., 61 (1986) 827.
5. J. Bergström, L. Hermansen and E. Hultman, Acta Physiol. Scand., 71 (1967) 140.
6. F. Brouns, W.H.M. Saris, E. Beckers, H. Adlercreutz, G.J. van der Vusse, H.A. Keizer, H. Kuipers, P. Menheere, A.J.M. Wagenmakers, and F. ten Hoor, Int. J. Sports Med., 10 (1989) S49.
7. A.R. Coggan and E.F. Coyle, J. Appl. Physiol., 63 (1987) 2388.
8. E.F. Coyle, A.R. Coggan, M.K. Hemmert and J.L. Ivy, J. Appl. Physiol., 61 (1986) 165.
9. L. Hermansen, E. Hultman and B. Saltin, Acta Physiol. Scand., 71 (1967) 129.
10. K. Sahlin, A. Katz and S. Broberg, Am. J. Physiol., 259 (1990) C834.
11. B. Saltin and J. Karlsson (Eds), Advances in experimental medicine and biology, New York, Plenum Press (1971) 289.
12. W. Sherman and D.L. Costill, Am. J. Sports Med., 12 (1984) 44.
13. A.J.M. Wagenmakers, E.J. Beckers, F. Brouns, H. Kuipers, P.B. Soeters, G.J. van der Vusse and W.H.M. Saris, Am. J. Physiol., 260 (1991) E883.
14. C.T.M. Davies and M.W. Thompson, Eur. J. Appl. Physiol., 41 (1979) 233.

15. S.F. Lewis and R.G. Haller, J. Appl. Physiol., 61 (1986) 391.
16. A.J.M. Wagenmakers, J.H. Coakley and R.H.T. Edwards, Int. J. Sports Med., 11 (1990) S101.
17. P.D. Gollnick, R.B. Armstrong, C.W. Saubert, W.L. Sembrowich, R.E. Shepherd and B. Saltin, Pflügers Arch. 344 (1973) 1.
18. P.D. Gollnick, K. Piehl and B. Saltin, J. Physiol., 241 (1974) 45.
19. N.K. Vøllestad, O. Vaage and L. Hermansen, Acta Physiol. Scand., 122 (1984) 433.
20. N.K. Vøllestad and P.C.S. Blom, Acta Physiol. Scand., 125 (1985) 395.
21. P. Felig and J. Wahren, N. Eng. J. Med., 293 (1975) 1078.
22. P. Felig, M.S.A. Cherif, A. Minagawa and J. Wahren, N. Eng. J. Med., 306 (1982) 895.
23. M.K. Spencer, Z. Yan and A. Katz, Am. J. Physiol., 262 (1992) C975.
24. W.C. Stanley and R.J. Connett, FASEB J., 5 (1991) 2155.
25. K. Sahlin, N.H. Areskog, R.G. Haller, K.G. Henriksson, L. Jorfeldt and S.F. Lewis, J. Appl. Physiol., 69 (1990) 1231.
26. E.W. Banister and B.J. Cameron, Int. J. Sports Med., 11 (1990) S129.
27. A.J.M. Wagenmakers, Med. Sport Sci., 34 (1992) 69.
28. F. Brouns, E. Beckers, A.J.M. Wagenmakers and W.H.M. Saris, Int. J. Sports Med., 11 (1990) S78.
29. D. Chasiotis, K. Sahlin and E. Hultman, H. G. Knuttgen, J. Vogel and J. Poortmans, Biochemistry of Exercise, Champaign, Human Kinetics Publishers (1983) 723.
30. E.A. Richter, N.B. Ruderman, J. Gavras and E.R. Belur, Am. J. Physiol., 242 (1982) E25.
31. E. Jansson, P. Hjemdahl and L. Kaijser, J. Appl. Physiol., 60 (1986) 1466.
32. L.L. Spriet, J.M. Ren and E. Hultman, J. Appl. Physiol., 64 (1988) 1439.
33. B. Issekutz, Metabolism, 34 (1985) 457.
34. A. Bonen, G.W. Ness, A.N. Belcastro and R.L. Kirby, J. Appl. Physiol., 58 (1985) 1622.
35. R.S. Mazzeo and P. Marshall, J. Appl. Physiol., 67 (1989) 1319.
36. J.C. McDermott, G.C.B. Elder and A. Bonen, J. Appl. Physiol., 63 (1987) 1275.
37. J.C. McDermott, G.C.B. Elder and A. Bonen, Pflügers Arch, 418 (1991) 301.
38. G. Ahlborg and P. Felig, J. Clin Invest, 69 (1982) 45.
39. G. Ahlborg, J. Wahren and P. Felig, J. Clin. Invest., 77 (1986) 690.
40. P.S. Wendling, S.J. Peters, G.J.F. Heigenhauser and L.L. Spriet, Can. J. Appl. Physiol., 21 (1996) 271.
41. D. Chasiotis, K. Sahlin and E. Hultman, J. Appl. Physiol., 53 (1982) 708.
42. L.N. Johnson, FASEB J., 6 (1992) 2274.
43. S. Bellet, A. Kershbaum and E.M. Finck, Metabolism, 17 (1968) 702.
44. H. Galbo, J.J. Holst and N.J. Christensen, Acta Physiol. Scand., 107 (1979) 19.
45. P.D. Gollnick, K. Piehl, C.W. Saubert, R.B. Armstrong and B. Saltin, J. Appl. Physiol., 33 (1972) 421.
46. M. Hargreaves, G. Mcconell and J. Proietto, J. Appl. Physiol., 78 (1995) 288.
47. P. Hespel and E.A. Richter, J. Physiol, 427 (1990) 347.
48. P. Hespel and E.A. Richter, Biochem. J., 284 (1992) 777.
49. A.E. Jeukendrup, W.H.M. Saris, R. Diesen van, F. Brouns and A.J.M. Wagenmakers, J. Appl. Physiol., 80 (1996) 949.
50. P. Eaton and D. Steinberg, J. Lipid Res., 2 (1961) 376.
51. I.B. Fritz, D.G. Davis, R.H. Holtrop and H. Dunder, Am. J. Physiol, 194 (1957) 379.
52. P.J. Randle, E.A. Newsholme and P.B. Garland, Biochem. J., 93 (1964) 652.
53. M.J. Rennie, W.W. Winder and J.O. Hooloszy, Biochem. J., 156 (1976) 647.
54. M.J. Rennie and J.O. Holloszy, Biochem. J., 168 (1977) 161.

55. D.L. Costill, E. Coyle, G. Dalsky, W. Evans, W. Finkand and D. Hoopes, J. Appl. Physiol., 43 (1977) 695.
56. M. Hargreaves, D.L. Costill, A. Katzand and W.J. Fink, Med. Sci. Sports Exerc., 17 (1985) 360.
57. F. Brouns, N.J. Rehrer, W.H.M. Saris, E. Beckers, P. Menheere and F. ten Hoor, Int. J. Sports Med., 10 (1989) S68.
58. A. Bonen, J.C. McDermott and C.A. Hutber, Int. J.Sports Med., 10 (1989) 385.
59. G.J. Bagby, H.J. Green, S. Katsutaand and P.D. Gollnick, J. Appl. Physiol., 45 (1978) 425.
60. A.E. Boyd, S.R. Giamber and M. Mager, Metabolism, 23 (1974) 531.
61. J. Issekutz, W.A.S. Shaw and F.B. Issekutz, J. Appl. Physiol., 39 (1975) 349.
62. L. Hagenfeldt and J. Wahren (Eds). Muscle metabolism during exercise. New York, Plenum Press (1971) 153.
63. L. Hagenfeldt and J. Wahren, Scand. J. Clin. Lab. Invest., 30 (1972) 429.
64. B.F. Hurley, P.M. Nemeth, W.H. Martin III, J.M. Hagberg, G.P. Dalsky and J.O. Holloszy, J. Appl. Physiol., 60 (1986) 562.
65. E. Jansson and L. Kaijser, J. Appl. Physiol., 62 (1987) 999.
66. W.H. Martin III, G.P. Dalsky, B.F. Hurley, D.E. Matthews, D.M. Bier, J.M. Hagberg, M.A. Rogers, D.S. King and J.O. Holloszy, Am. J. Physiol., 265 (1993) E708.
67. J.A. Romijn, E.F. Coyle, L.S. Sidossis, A. Gastaldelli, J.F. Horowitz, E. Endert and R.R. Wolfe, Am. J. Physiol., 265 (1993) E380.
68. L.A. Carlsson, L. Ekelund and S. Fröberg, Eur J. Clin. Invest., 1 (1971) 248.
69. B. Kiens, B. Éssen-Gustavsson, N.J. Christensen, B. Saltin, J. Physiol., 469 (1993) 459.
70. E.F. Coyle, A.E. Jeukendrup, A.J.M. Wagenmakers, W.H.M. Saris, Am. J. Physiol., submitted (1996).
71. J.D. McGarry, S.E. Mills, C.S. Long and D.W. Foster, Biochem. J., 214 (1983) 21.
72. E.A. Newsholme, Principles of Exercise Biochemistry. Med. Sport Sci., Basel, Karger (1988) 40.
73. M.M. Vork, J.F.C. Glatz and G.J. Vusse van der, J. Theor. Biol., 160 (1993) 207.
74. W.W. Winder, J. Arogyasami, R.J. Barton, I.M. Elayan and P.R. Vehrs, J. Appl. Physiol., 67 (1989) 2230.
75. W.W. Winder, R.W. Braiden, D.C. Cartmill, C.A. Hutber and J.P. Jones, J. Appl. Physiol., 74 (1993) 2548.
76. B. Kiens and H. Lithell, J. Clin. Invest., 83 (1989) 558.
77. H. Lithell and J. Boberg, Biochim. Biophys. Acta, 528 (1978) 55.
78. E.A. Nikkilä, R. Taskinen, S. Rehunen, M. Härkönen, Metabolism, 27 (1978) 1661.
79. K.M. Baldwin, G.H. Klinkerfuss, R.L. Terjung, P.A. Molé and J.O. Holloszy, Am. J. Physiol., 222 (1972) 373.
80. K.J.A. Davies, L. Packer and G.A. Brooks, Arch. Biochem. Biophys., 209 (1981) 539.
81. P.D. Gollnick, Fed. Proc., 44 (1985) 353.
81. D. Giles and D. MacLaren, J. Sports Sci., 2 (1984) 35.
82. D.L. Costill, G.P. Dalsky and W.J. Fink, Med. Sci. Sports, 10 (1978) 155.
83. D. Essig, D.L. Costill and P.J. Handel van, Int. J. Sports Med., 1 (1980) 86.
84. J.L. Ivy, D.L. Costill, W.J. Fink and R.W. Lower, Med. Sci. Sports, 11 (1979) 6.
85. L.L. Spriet, D.A. MacLean, D.J. Dyck, E. Hultman, G. Cederblad and T.E. Graham, Am. J. Physiol., 262 (1992) E891.
86. J.W. Daly, S. Garattini (Eds), Coffee, caffeine and health, New York, Raven Press (1993) 97.
87. S.L. Dodd, R.A. Herb and S.K. Powers, Sports Med., 15 (1993) 14.
88. A. Nehlig, J.L. Daval and G. Debry, Brain Res. Rev., 17 (1992) 139.

89. L.L. Spriet, Int. J. Sport Nutr., 5 (1995) 584.
90. E.J. Beckers, A.E. Jeukendrup, F. Brouns, A.J.M. Wagenmakers and W.H.M. Saris, Int. J. Sports Med., 13 (1992) 581.
91. A.E. Jeukendrup, W.H.M. Saris, P. Schrauwen, F. Brouns and A.J.M. Wagenmakers, J. Appl. Physiol., 79 (1995) 756.
92. A. Jeukendrup, W. Saris, F. Brouns, D. Halliday and A.J.M. Wagenmakers, Metabolism, 45 (1996) 915.
93. E. Jansson and L. Kaijser, Acta Physiol. Scand., 122 (1984) 145.
94. M.D. Vukovich, D.L. Costill, M.S. Hickey, S.W. Trappe, K.J. Cole and W.J. Vink, J. Appl. Physiol., 75 (1993) 1513.
95. J. Bergström, E. Hultman, L. Jorfeldt, B. Pernow and J. Wahren, J. Appl. Physiol., 26 (1969) 170.
96. F. Brouns, W. H. M. Saris and E. A. Newsholme (Eds), Advances in Nutrition and Top Sport, Basel, Karger (1991) 166.
97. A.J.M. Wagenmakers, F. Brouns, Advances in Nutrition and Top Sport, Basel, S. Karger (1991) 110.
98. A.K. Saha, T G. Kurowski and N.B. Ruderman, Am. J. Physiol., 269 (1995) E283.
99. T.E. Graham and L.L. Spriet, J. Appl. Physiol., 71 (1991) 2292.
100. T.E. Graham and L.L. Spriet, J. Appl. Physiol., 78 (1995) 867.
101. J. Weir, T.D. Noakes, K. Myburgh and B. Adams, Med. Sci. Sports Exerc, 19 (1987) 100.
102. S. Bellet, A. Kershbaum and J. Aspe, Arch Intern Med., 116 (1965) 750.
103. H. Sasaki, J. Maeda, S. Usui and T. Ishiko, Int. J.Sports Med., 8 (1987) 261.
104. S.H. Constable, R.J. Favier, G.D. Cartee, D.A. Young and J.O. Holloszy, J. Appl. Physiol., 64 (1988) 2329.
105. T. Ploug, H. Galbo and E.A. Richter, Am. J. Physiol., 247 (1984) E726.
106. H. Wallberg-Henriksson and J.O. Holloszy, Am. J. Physiol., 249 (1985) C233.
107. J.T. Brozinick, G.J. Etgen, B.B. Yaspelkis and J.L. Ivy, Biochem. J., 297 (1994) 539.
108. A.G. Douen, T. Ramlal, G.D. Cartee and A. Klip, FEBS Letters, 261 (1990) 256.
109. L.J. Goodyear, M.F. Hirshman and E.S. Horton, Am. J. Physiol., 261 (1991) E795.
110. M.F. Hirshman, H. Wallberg-Henriksson, L.J. Wardzala, E.D. Horton and E.S. Horton, FEBS Letters, 238 (1988) 235.
111. T. Ploug, J. Wojtaszewski, S. Kristiansen, P. Hespel, H. Galbo and E.A. Richter, Am. J. Physiol., 264 (1993) E270.
112. B.A. Zinker, D.B. Lacy, D.P. Bracy and D.H. Wasserman, J. Appl. Physiol., 74 (1993) 2915.
113. A. Katz, S. Broberg, K. Sahlin and J. Wahren, Am. J. Physiol., 251 (1986) E65.
114. J. Wahren, P. Felig, G. Ahlborg and L. Jorfeldt, J. Clin. Invest, 50 (1971) 2715.
115. G. Ahlborg, P. Felig, L. Hagenfeldt, R. Hendler and J. Wahren, J. Clin. Invest, 53 (1974) 1080.
116. M. Hargreaves, I. Meredith and G.L. Jennings, Exp. Physiol., 77 (1992) 641.
117. T. Ploug, H. Galbo, J. Vinten, M. Jørgensen and E.A. Richter, Am. J. Physiol., 253 (1987) E12.
118. H. Wallberg-Henriksson, S.H. Constable, D.A. Young and J.O. Holloszy, J. Appl. Physiol., 65 (1988) 909.
119. D.H. Wasserman, R.J. Geer, D.E. Rice, D.E. Rice, D. Bracy, P.J. Flakoll, L.L. Brown, J.O. Hill and N.N. Abumrad, Am. J. Physiol., 260 (1991) E37.
120. E.F. Coyle, M.T. Hamilton, J. González-Alonso, S.J. Montain and J.L. Ivy, J. Appl. Physiol., 70 (1991) 834.

121. H. Kuipers, D.L. Costill, D.A. Porter, W.J. Fink and W.M. Morse, J. Appl. Physiol., 61 (1986) 859.
122. W.W. Winder, J. Arogyasami, H.T. Yang, K.G. Thompson, L.A. Nelson, K.P. Kelly and D.H. Han, J. Appl. Physiol., 64 (1988) 2300.
123. O. Björkman, K. Sahlin, L. Hagenfeldt and J. Wahren, Clin. Physiol., 4 (1984) 483.
124. M. Hargreaves, D.L. Costill, A. Coggan, W.J. Fink and I. Nishibata, Med. Sci. Sports Exerc., 16 (1984) 219.
125. O.K. Tsintzas, C. Williams, L. Boobis and P. Greenhaff, J. Physiol., 489 (1995) 243.
126. S.H. Constable, J.C. Young, M. Higuchi and J.O. Holloszy, Am. J. Physiol., 247 (1984) R880.
127. H. Kuipers, H.A. Keizer, F. Brouns and W.H.M. Saris, Pflügers Arch, 410 (1987) 652.
128. H. Kuipers, W.H.M. Saris, F. Brouns, H.A. Keizer and C. ten Bosch, Int. J. Sports Med., 10 (1989) S63.
129. A.T. Hostmark, O. Gronnerod and R.S. Horns, Horm. Metab. Res., 10 (1978) 81.
130. C. Lavoie, L. Coderre, F. Peronnet, Can. J. Spt. Sci., 12 (1987) 13.
131. T.B. Price, R. Taylor, G.F. Mason, D.L. Rothman, G.I. Shulman and R.G. Shulman, Med., Sci. Sports Exerc., 26 (1994) 983.
132. E.M. Peters Futre, T.M. Noakes, R.I. Raine and S.E. Terblanche, Am. J. Physiol., 253 (1987) E305.
133. M. Hargreaves and C.A. Briggs, J. Appl. Physiol., 65 (1988) 1553.
134. C. Picton, C.B. Klee and P. Cohen, Cell Calcium, 2 (1981) 281.
135. J.M. Ren and E. Hultman, J. Appl. Physiol., 67 (1989) 2243.
136. J.M. Ren and E. Hultman, J. Appl. Physiol., 69 (1990) 919.
137. B. Sonne and H. Galbo, J. Appl. Physiol., 59 (1985) 1627.
138. J.O. Holloszy, S.H. Constable and D.A. Young, Diabetes/Metabolism Reviews, 1 (1986) 409.
139. P.D. Neufer, M.H. Shinebarger and G.L. Dohm, Can. J.Physiol Pharmacol, 70 (1992) 1286.
140. J.A. Houmard, P.C. Egan, P.D. Neufer, J.E. Friedman, W.S. Wheeler, R.G. Israel and G.L. Dohm, Am. J.Physiol., 261 (1991) E437.
141. J.M. Ren, B.A. Marshall, E.A. Gulve, J. Biol Chem, 268 (1993) 16113.
142. C.E. Torgan, G.J. Etgen, H.Y. Kang and J.L. Ivy, J. Appl. Physiol., 79 (1995) 163.
143. J.T. Brozinick, B.B. Yaspelkis, C.M. Wilson, Biochem. J., 313 (1996) 133.
144. W.H.M. Saris, B.H. Goodpaster, A.E. Jeukendrup, F. Brouns, D. Halliday and A.J.M. Wagenmakers, J. Appl. Physiol., 75 (1993) 2168.
145. A.J.M. Wagenmakers, F. Brouns, W.H.M. Saris and D. Halliday, J. Appl. Physiol., 75 (1993) 2774.
146. J.A. Hawley, S.C. Dennis and T.D. Noakes, Sports Med., 14 (1992) 27.

Discussion: The Effect of Athletic Training and Dietary Factors on the Modulation of Muscle Glycogen

T. Reilly:

You recommended early morning training on an empty stomach. Now, many marathons, for example, take place early in the morning. What is your view in terms of advising feeding for early-morning marathon starts?

F. Brouns:

It is difficult because you deal with the circadian rhythm which also affects the dietary pattern. What we normally recommend is: increase carbohydrate intake during the days prior to exercise while tapering the training load. This will build up glycogen in muscle and liver. The day before: go on a normal diet with more fat. This will preserve further the glycogen content and will up-regulate the lipolysis system and the fat-handling enzymes. Prior to exercise, if the marathon is early in the morning, the athlete will not have much appetite to eat a breakfast generally, due to pre-competition stress. Normally we advise to take a small and light digestible breakfast. In this respect I think that it is very individual what athletes can tolerate. I know some athletes who start on an empty stomach and then take carbohydrate drinks during exercise. Others prefer to take a light breakfast as early as 5-6 o'clock in the morning. But you can imagine that eating so early is not very comfortable if your daily schedule is to get up at 7.00 AM. Shifting meal and activity times towards those which will be actual during the competition day may be one measure to get more adapted. If so, this should be practised for 7-10 days before the major competition.

D.P.M. MacLaren:

Do you agree with the concept of the glucose-fatty acid cycle? If your answer is "yes", then how do you justify muscle glycogen sparing with carbohydrate ingestion?

F. Brouns:

There is currently a debate on the existence of the glucose-fatty acid cycle. Personally, I think that the glucose-fatty acid cycle may work in the resting condition and during low-to-moderate exercise intensities. In those conditions you can really see the effects of increased fatty acid availability on endogenous carbohydrate sparing. During highly intense exercise, it is thought that the glucose-fatty acid cycle may not work. There you do not see the effects of increased FA availability on glycogen sparing. However, if you overload the system with carbohydrates during periods of low intensity exercise, you suppress the FA oxidation on the one hand, but, on the other hand this results in a high glucose uptake while at the same time the rate of glycogen breakdown is low. This simultaneous effect influences the intracellular free glucose level, which will affect the balance between glycogen synthesis and breakdown. But there is not much data other than the obtained by muscle biopsy analysis. I think the best would be to do studies with NMR, because it is known that there are considerable differences when one compares biopsies from different sites taken at the same time.

P.M. Clarkson:

In the States there has been much attention on the high fat diet instead of a high carbohydrate diet. Could you comment on high fat diets and the criticisms behind the research theorizing that fat loading causes a beneficial effect?

You made the comment about not ingesting a sport drink prior to exercise because of the insulin response, and I wonder whether a sport drink of only six percent carbohydrate would be sufficient to cause an insulin response leading to a negative effect.

F. Brouns:

In my presentation I have discussed that a hight fat diet, medium chain triglyceride ingestion and other factors, may affect FA availability during exercise. Generally, the observations on the effects of high fat diets mainly come from animal studies, notably rats and dogs. It was shown that if you put these animals on a high fat diet and you let them do an endurance performance test, after some time they can perform longer at a certain exercise intensity than prior to the high fat diet. This is comparable to performance effects which we see with high carbohydrate diets in athletes. This has led to the current growth in popularity of high fat diets. Attempts have been made to do the same type of studies in humans but there are only a few studies available and I think the evidence is not good. There is one particular study which showed a significant increase in performance time after a high fat diet, but if you look critically at this study, it was done on five subjects. There was one subject who improved performance by 57% after the high fat diet. This single 57% increase caused the mean of the group to be improved and also influenced the statistics. So far, if you look critically to human studies, there is no evidence that a high fat diet improves performance. Additionally, there are effects of a high fat diet which are never discussed under the heading performance, but which may be very detrimental to the athlete on the long term! High fat diets are known to enhance cardiovascular disease, to cause insulin resistance and to suppress growth hormone secretion.

With respect to the insulin response, I think that the ingestion of a drink at rest, which contains 4-6 grams of carbohydrate per 100 ml, may lead to a significantly enhanced blood glucose and insulin level. An increased insulin level at the onset of exercise will automatically block lipolysis. This may result in enhanced glycogen breakdown. Therefore, we conclude that when an athlete has loaded carbohydrate prior to an important event and has done no exercise, there is no reason to believe that there is a suboptimal amount of carbohydrates in the body. Therefore, we discourage to consume carbohydrate drinks during the last 2-3 hrs prior to exercise. We aim at maintaining a high degree of lipolysis and start carbohydrate ingestion just prior to the start (3-5 min.) or during exercise, when insulin response in blunted.

M. Williams:

I wonder if you could give us some recommendations on glycogen resynthesis on a day to day basis for athletes who might want to synthesize glycogen very rapidly, maybe eating high glycemic index foods, and possibly also by the inclusion of protein along with carbohydrate.

F. Brouns:

A substantial amount of evidence shows that high glycemic index foods lead to a more rapid supply of carbohydrate to the system. Other evidence shows that the activity of glycogen synthase is most pronounced shortly after exercise, and you could benefit from that by making available carbohydrates quite rapidly after exercise. If you take high glycemic index foods,

you promote this situation. We recommend athletes that once they have finished either a hard training session or a competition and there will be a next one in a short time, they should ingest carbohydrate drinks or high glycemic index foods which are easily digestible immediately after exercise. Rice cakes, for example, are a favourite in the Tour of France, but also sweat corn, mashed potato or ripe bananas are good sources.

D.P.M. MacLaren:

With regard to the fat loading, we have performed two experiments which used elite performers. One was a group of elite cyclists and one was an elite group of runners. In the cycling study, we presented the athletes with a high fat, but reasonable carbohydrate, or a high carbohydrate breakfast in the morning and then we exercised them for a period of 90 minutes followed by a 10 Km time trial. The improved performances were on the high fat breakfast. In the study on runners, they were put on isocaloric diets (for three days). These were high fat, normal or high carbohydrate and, again, these are elite runners in a ten mile time trial performed better on the high fat diet.

M. Gleeson:

Dr. Brouns, you recommend to athletes that they should consume a relatively high fat diet the day before the event. What evidence is that based on?

F. Brouns:

It is not based on evidence. It is based on finger feeling of how physiology might fit best for the endurance athletes. In fact what Don MacLaren just said about a high fat breakfast is in line with this. What normally happens, is that athletes go on a high carbohydrate diet and they maintain that until competition. As a result, they have continuously high blood glucose levels and raised insulin levels. In this situation, the fat handling metabolic pathways are down-regulated. If then the athlete performs intense exercise, the lipolysis is inhibited and there will be an increased rate of glycogen breakdown. My opinion is that if you are on a high carbohydrate diet and once you have filled up your glycogen stores, you should shift again for a short term (the last two or three pre-competition meals) to more fat in the diet. By doing this, you depress insulin secretion, you enhance free fatty acid availability, delivery and oxidation. Thus, you up-regulate the fat handling system. The latter may be a benefit in the first half hour to 45 minutes of exercise by leading to enhanced FA oxidation and a reduced rate of glycogen utilization. The latter may finally lead to improved performance.

M. Gleeson:

Do you not at the same time effectively deplete the liver glycogen store?

F. Brouns:

It depends upon how much fat and carbohydrate you ingest. If you would go only for fat, of course you would do that, but a complete fat meal would be impossible. When we talk about high fat content, we mean 45-50% of the energy derived from fat. During an overnight fast the liver glycogen depletes only partly and I think that 30-40 grams of carbohydrate in the last pre-competition meal are sufficient to fill up that store again. Fructose containing CHO sources are optimal for that purpose.

B. Ekblom:

As it has been mentioned, protein can enhance the synthesis of glycogen after exercise. What amino acids would cause that? What is the reason?

F. Brouns:

There have been only a few studies on this subject. The mechanism offered as explanation is the following: ingestion of carbohydrate induces an insulin response which favours glycogen synthesis. Ingestion of protein also induces an insulin response. But if you ingest the two together, you get the synergistic effect, which means that the insulin response is stronger than with carbohydrate or protein alone. I do not know whether whithin whole protein there are specific amino acids being primarily responsible for this effect.

A.J.M. Wagenmakers:

Leucine, lysine and arginine have a strong insulinotropic effect, much stronger than any of the other amino acids. That is well-known old literature. It is not known though whether they can replace protein to increase the synthesis rate of glycogen after exercise.

Y. Hellsten:

It appears that some cyclists receive intravenous infusions of glucose during the night and I want to ask you if you think it is necessary for optimal performance and if you think it is ethically correct or incorrect?

F. Brouns:

This is an artificial measure to boost performance on the next day, so in fact it falls under the doping regulation, though nobody can control it. The question is whether it is necessary. I do not think it is. The amount you can infuse overnight is limited. I think you can do it orally by ingesting CHO solutions before sleeping, without having the risk of getting infections or whatever complications during the night.

D.P.M. MacLaren:

We have performed glucose infusion studies during exercise and at rest using a hyperglycaemic clamp, and have found that the maximum rates of glucose utilization are in the region of about 2 grams per minute. I think that you can get that from drinking, so it does support your point of view.