Nutritional ergogenic aids and exercise performance

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Abstract

The use of nutritional supplements in sport is widespread and few serious athletes do not, at some stage in their career, succumb to the temptation to experiment with one or more nutritional supplements. Nutritional ergogenic aids are aimed primarily at enhancing performance (either by affecting energy metabolism or by an effect on the central nervous system), at increasing lean body mass or muscle mass by stimulation of protein synthesis and at reducing body fat content. Although not strictly ergogenic (i.e. capable of enhancing work performance), supplements aimed at increasing resistance to infection and improving general health are seen by athletes as important in reducing the interruptions to training that minor illness and infection can cause. Creatine is perhaps the most widely used supplement in sport at the moment. Supplementation can increase muscle creatine phosphate levels and, although not all published studies show positive results, there is much evidence that performance of short-term high-intensity exercise can be improved by supplementation. Ingestion of large doses of bicarbonate can enhance performance of exercise where metabolic acidosis may be a limiting factor, but there is a significant risk of adverse gastrointestinal side effects. Caffeine can also improve performance, in part by a stimulation of fatty acid mobilization and sparing of the body's limited carbohydrate stores, but also via direct effects on muscle and possibly by central nervous system effects on the perception of effort and fatigue. Carnitine plays an essential role in fatty acid oxidation in muscle but, although supplements are used by athletes, there is no good evidence of a beneficial effect of supplementation. None of these products contravenes the International Olympic Committee regulations on doping in sports, although caffeine is not permitted above a urine concentration of 12 mg/l. Supplementation is particularly prevalent among strength and power athletes, where an increase in muscle mass can benefit performance. Protein supplements have not been shown to be effective except in those rare cases where the dietary protein intake is otherwise inadequate. Individual amino acids, especially ornithine, arginine and glutamine, are also commonly used, but their benefit is not supported by documented evidence. Cr and hydroxymethylbutyrate are also used by strength athletes, but again there are no well-controlled studies to provide evidence of a beneficial effect. Athletes use a wide variety of supplements aimed at improving or maintaining general health and vitamin and mineral supplementation is widespread. There is a theoretical basis, and limited evidence, to support the use of antioxidant vitamins and glutamine during periods of intensive training, but further evidence is required before the use of these supplements can be recommended.

Ergogenic aids: Exercise: Nutritional supplements

Abbreviation: CP, creatine phosphate.

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Introduction

A number of physiological, biochemical, psychological and nutritional factors that may limit exercise performance have been identified. In the pursuit of success, athletes and their scientific and medical advisers seek to identify these factors and to identify ways to minimize their potential impact. This has led to the widespread use of nutritional strategies of varying degrees of efficacy. Foods and food components that can improve the capacity of an individual to perform an exercise task have been described as ergogenic aids (Williams, 1983). At one end of the spectrum of ergogenic aids are normal foods and at the other are substances that are clearly drugs: in between, however, are a number of compounds that are more difficult to classify. The term includes a number of foods, including for example those high in carbohydrate (Williams, 1998), and carbohydrate–electrolyte sports drinks (Maughan & Shirreffs, 1998), whose effectiveness in improving exercise capacity is beyond doubt. It is, however, usually a term applied to specific nutrients or compounds rather than to whole foods. It is on this latter category of supplements that this review will focus.

The athlete who uses nutritional supplements often consumes these in amounts far in excess of those normally ingested and is usually concerned primarily with the effectiveness of any supplement used: the amount and timing of supplementation and the specific exercise conditions under which its effects may be optimized must be considered. A second concern relates to whether there is a possibility of contravening the rules imposed by the governing bodies of sport, which might lead to suspension from competition. Third, and perhaps most important of all, the question of safety of supplementation must be considered. Although this should perhaps be the primary concern, the use by athletes of pharmaceutical agents with well-recognized harmful side effects shows that this is often not the case.

As a general principle it is safe to assume that most supplements that are effective are against the rules of sport; this category includes drugs and hormones. Most substances that are not banned are not effective; this includes most of the vitamin and mineral supplements as well as the herbal products sold in health-food shops. There are, however, some exceptions to these generalizations; substances in this category might include creatine, bicarbonate, and a number of individual amino acids as well as antioxidant nutrients. There are also grey areas, sometimes referred to as ‘nutraceuticals’, including compounds such as caffeine that are normal components of foods but which are consumed for their pharmacological action.

Supplement use is widespread in sport. A recent report of supplement use among 100 Norwegian national-level competitors from various sports revealed that 84 % of all the athletes surveyed used some form of micronutrient supplement (Ronsen *et al.* 1999). Most athletes took multiple supplements, although many had nutritional habits that were described as ‘unsatisfactory’, implying that attention to the normal diet might be a more beneficial approach for these athletes. Reviews of the published literature suggest that the use of supplements is more prevalent in athletes (46 %) than in the general population (35–40 %), while among elite athletes 59 % report supplement use (Sobal & Marquart, 1994). All these surveys find that the overall prevalence and the types of supplements used vary with the nature of the sport, the sex of the athletes, and the level of competition. In some surveys, 100 % of weightlifters use some form of nutritional supplementation (Burke & Read, 1993).

It is not possible to review all of the nutritional supplements used by athletes, nor to consider in any detail the evidence relating to more than a few. However, consideration of some specific examples will illustrate the general principles that determine usage, and the evaluation that ought to be applied to these supplements. The review will focus on three main categories of supplements: those that affect energy production and metabolism, those that may influence

muscle hypertrophy and lean body mass, and those that can influence general health. Issues relating to the use of creatine will be considered in some depth as these highlight the questions that relate to all supplement use.

Supplements that may influence energy metabolism

Creatine

Creatine has been used by many successful athletes, particularly in track and field athletics, but also now in many, if not most, other sports. Some indication of the extent of its use is gained from the fact that the estimated sales of creatine to athletes in the US alone in 1997 amounted to over 300 000 kg. This represents a remarkable growth, as its use first became popular in sport after the 1992 Olympic Games in Barcelona. What distinguishes creatine from other ergogenic aids is that it seems to be effective in improving performance. More significantly, perhaps, its use is not prohibited by the governing bodies of sport and there appear to be no harmful side effects even when very large doses are taken, at least in the quantities that are necessary to produce an ergogenic effect.

Metabolic role of creatine. The biochemistry of creatine metabolism is covered in standard textbooks of biochemistry and will not be discussed in detail here. The highest tissue concentrations of creatine are found in skeletal muscle, and approximately two-thirds of the total is in the form of creatine phosphate (CP) (Harris *et al.* 1974). CP is present in resting muscle in a concentration approximately 3–4 times that of ATP, the immediate energy source for muscle contraction. The amount of ATP in muscle cells is small and only a fraction of this can be viewed as an energy store; when the cellular ATP concentration falls too far, fatigue ensues. There have been suggestions that the ATP content of some individual fibres may be almost zero after very high-intensity exercise in the horse, but this has not been found to occur in man (Jansson *et al.* 1987). Whole muscle ATP content rarely falls by more than about 25–30 % at the point of fatigue in high-intensity exercise (Karlsson & Saltin, 1970).

Because muscle fatigue is associated with decreased intracellular ATP concentrations, regeneration of ATP at a rate close to that of ATP hydrolysis is essential if fatigue is to be delayed. Transfer of the phosphate group (Pi) from CP to ADP is catalysed by the enzyme creatine kinase (*EC* 2.7.3.2), resulting in the restoration of ATP and the release of free creatine (C). The situation during muscle contraction can be represented as follows:

$$\mathrm{ATP} \rightarrow \mathrm{ADP} + \mathrm{Pi},$$

and

$$\mathrm{CP} + \mathrm{ADP} \rightarrow \mathrm{ATP} + \mathrm{C}.$$

The rate of ATP hydrolysis is set by the power output of the muscle; in electrically-induced isometric contractions of the quadriceps muscle of 1·26 s duration, an ATP turnover rate of approximately 11 mmol/kg dry muscle per s has been reported (Hultman & Sjoholm, 1983). The resting ATP content of muscle is about 24 mmol/kg, but this cannot fall by more than about 30 %, so the need for rephosphorylation of the ADP formed during contraction is obvious. The creatine kinase reaction is extremely rapid, and since the muscle CP concentration can fall to almost zero (Karlsson & Saltin, 1970), it can make a significant contribution to the energy supply necessary for brief bursts of very high intensity exercise. The CP store is finite, however,

and increasing the CP content of muscle ought to allow a greater amount of work to be done using this energy source.

During the recovery process after exercise, the creatine kinase reaction is reversed, using energy made available by oxidative metabolism which occurs within the mitochondria:

$$C + ATP \rightarrow CP + ADP,$$

and

$$ADP + Pi + \text{metabolism} \rightarrow ATP.$$

In high-intensity exercise, glycolysis will result in the formation of pyruvate at a rate higher than that at which it can be removed by oxidative metabolism, leading to an accumulation of lactate within the muscle. The H^+ associated with anaerobic glycolysis cause muscle pH to fall, and this fall in pH has been implicated in the fatigue process (Sahlin, 1986). A number of buffers within the cell resist changes in pH, and the breakdown of CP is such a mechanism. The creatine kinase reaction can be rewritten to take account of the charges involved:

$$CP^{2-} + ADP^{3-} + H^+ \rightarrow ATP^{4-} + C.$$

An increased availability of CP for breakdown has the potential to increase the intramuscular buffering capacity, delaying the point at which pH reaches a critically low level.

CP has been reported to play another role within the muscle cell, which is to transfer ATP equivalents from within the mitochondria, where ATP is generated by oxidative phosphorylation, to the cytoplasm where it is required for cellular metabolism (Bessman & Geiger, 1981; Meyer *et al.* 1984). There is, however, no evidence that this process is limited by the availability of creatine, and it has been suggested that this may be less important in skeletal than in cardiac muscle (Meyer *et al.* 1986). The failure of creatine supplementation to influence the metabolic response to exercise of moderate intensities or performance in this type of exercise (Balsom *et al.* 1993*b*; Stroud *et al.* 1994) also argues against an important, or at least limiting, role for this shuttle.

Creatine supplementation and muscle creatine phosphate concentration. Creatine is an amino acid (methylguanidine-acetic acid) which occurs naturally in the diet, being present in meat; 1 kg fresh steak contains about 5 g creatine. The normal daily intake is less than 1 g (Heymsfield *et al.* 1983), but the estimated daily requirement for the average individual is about 2 g (Walker, 1979). The body has a limited capacity to synthesize creatine in the liver, kidney and pancreas and in other tissues, but the primary site of synthesis in man is the kidney. This supplies the amount required in excess of the dietary intake and is also the only way in which vegetarians can meet their requirement. Synthesis occurs from amino acid precursors (arginine and glycine) but the synthetic pathway is suppressed when the dietary creatine intake is high.

Studies of resting human skeletal muscle have shown the CP concentration to be about 75 mmol/kg dry weight and the free creatine concentration to be about 50 mmol/kg (Harris *et al.* 1974). There is, however, quite a large range of values reported in the literature, and it seems clear that there is considerable inter-individual variability. A number of factors may account for this, including differences in the composition of the preceding diet. The muscle fibre composition may also be of some importance; Rehunen & Harkonen (1980) showed a higher CP content in slow-twitch fibres than in fast-twitch fibres in women, although in men the difference was not statistically significant. There is some evidence that the muscle creatine content is higher in women than in men.

The first study to investigate systematically the effects of supplementation of large amounts of creatine was that of Harris *et al.* (1992). In a comprehensive study, they showed that ingestion of small amounts of creatine (1 g or less) had a negligible effect on the circulating creatine concentration, whereas feeding higher doses (5 g) resulted in an approximately 15-fold increase. Repeated feeding of 5 g doses every 2 h maintained the plasma concentration at about 1 mmol/l over an 8 h period. Repeated feeding of creatine (5 g four times per day) over a period of 4–5 d resulted in a marked increase in the total creatine content of the quadriceps femoris muscle. An increase in muscle creatine content was apparent within 2 d of starting this regimen, and the increase was greatest in those with a low initial level; in some cases an increase of 50 % was observed. Approximately 20 % of the increase in total muscle creatine content is accounted for by CP.

It seems clear that there is an upper limit to the creatine and CP levels that can be achieved in muscle, and this is not unexpected. There was some evidence, from a model where one leg was exercised during a period of creatine supplementation while the other leg was rested, that exercise enhanced the effect of creatine supplementation on the muscle creatine content. There was no effect of creatine supplementation on the ATP content of the muscle, and no adverse side effects were noted, even when 30 g/d were taken for 7 d. In contrast to these reported effects of creatine supplementation on muscle creatine and CP content of human skeletal muscle, there seems to be little effect in the rat (Oopik *et al.* 1994) and care may be necessary in the translation of data from animal models to the human situation.

Effects of creatine supplementation on exercise performance. Because of the newness of the concept, there are only a limited number of scientific studies which have reported the effects of dietary creatine supplementation on muscle function and exercise performance. The results of many of these investigations are available only in preliminary form at the present time. Most of the published studies appear to be well-controlled, but crossover designs are impractical because of the long washout period from the muscle. Where high doses are ingested over a period of 4–6 d, the muscle creatine content will remain elevated for several weeks. If athletes are used as subjects, the increased training loads that seem to be possible after creatine supplementation make it difficult to interpret results of crossover studies where placebo is administered as the second treatment. For these reasons, most of the reported studies have used matched groups of subjects. From these results, there appears to be no beneficial effect on the peak power output that can be achieved in a range of tests, but the balance of the available evidence suggests that performance is improved in high-intensity exercise tasks, especially where repeated exercise bouts are carried out.

A survey of the full papers (ignoring studies published in abstract form only) published in papers cited on the Medline database (R. Maughan, unpublished results) revealed a total of twenty-three published papers with results of twenty-four separate studies investigating effects of creatine supplementation on high-intensity exercise performance. These encompassed a variety of laboratory exercise models, including single and multiple sprints with varying exercise and rest periods as well as single exercise bouts. Also included are a number of field trials and simulated competitions. Slightly over half (thirteen out of twenty-four) of the studies found a positive effect on performance. Of those which found no significant effect, several found trends which, although not statistically significant, may be meaningful to the athlete. Some studies failed to include sufficient numbers of subjects to detect a difference and most did not contain information on the repeatability of the performance test. It is nonetheless difficult to see clear differences in design, experimental model used, type of subjects, creatine dosage or

other factors between those studies showing a positive effect on performance and those which found no effect.

Of the studies showing positive effects, Greenhaff *et al.* (1993) measured the ability of two groups of subjects to complete five bouts of thirty maximal voluntary contractions on an isokinetic dynamometer; half the group then received a placebo and the others received 24 g creatine/d for 5 d. Peak torque was not different after the placebo treatment compared with the initial measurements, but the creatine-supplemented group showed significantly improved peak torque production.

Harris *et al.* (1993) used a creatine dose of 30 g/d for 6 d and again compared parallel treatment and placebo groups. The subjects in this study were trained runners and two different exercise tests were carried out (on separate days). One test consisted of 4 × 300 m runs with a 4 min rest between runs, and the other test consisted of 4 × 1000 m with a 3 min rest between runs. The results showed a significant benefit of creatine supplementation: at the 300 m distance the improvement was only statistically significant for the last run of the set; at the 1000 m distance total time for all 4 runs improved by a mean of 13·0 s, with the improvement on the last run being 5·5 s.

Other studies (Balsom *et al.* 1993*a*; Soderlund *et al.* 1994) have confirmed the beneficial effect of creatine supplementation in high doses (20 g/d for 6 d) on high-intensity exercise performance, although these same authors have also reported one study that gave inconclusive results (Harridge *et al.* 1994).

Another placebo-controlled matched-pairs trial, published in abstract form only (Earnest *et al.* 1994), used a dose of 20 g/d for 4 d. The exercise test used consisted of three 30 s Wingate tests on a cycle ergometer with 5 min rest periods between tests: peak anaerobic power was measured as the highest power output in a 5 s period and anaerobic capacity as the total work done in the 30 s period. Peak power was not affected by treatment. Anaerobic capacity was higher in all three tests after creatine supplementation, but there was no difference with placebo treatment.

No beneficial effect of creatine supplementation was reported by Odland *et al.* (1994). They used a crossover design involving control, placebo and creatine supplementation trials; creatine was administered for 3 d (20 g/d). The exercise test consisted of a single 30 s Wingate test. Muscle free-creatine content and the muscle total creatine:ATP ratio were enhanced by the treatment, but neither total creatine nor CP content were significantly altered. There were no differences between the three experimental conditions in any of the exercise test parameters. The clear difference between this study and the others reported earlier, apart from the fact that it failed to demonstrate enhancement of exercise performance after creatine supplementation, is that the experimental model consisted of a single exercise test rather than multiple exercise bouts. It is worth noting, however, that Earnest *et al.* (1994) did show an increased total work output in the first of the three 30 s tests used in their study. It is also the case, however, that the total creatine dose was smaller (60 g) in this study than in any of the others quoted, where the dose used was generally 80–180 g.

There is little information on the effects of creatine supplementation on the performance of more prolonged exercise. In an incremental treadmill running test there was no effect of creatine supplementation on the cardio-respiratory or metabolic response to submaximal exercise, but exercise performance was not measured in this study (Stroud *et al.* 1994). However, Balsom *et al.* (1993*b*) showed no beneficial effect of creatine supplementation on performance in an endurance running test.

Creatine and muscle strength. Although there have been numerous investigations into the effects of creatine supplementation on the ability to generate high levels of muscle power, few studies have looked for possible effects on muscle strength. This seems surprising in view of the importance of a high force generating capacity for the development of power. In an early study, Greenhaff *et al.* (1993) required subjects to perform five sets of thirty maximal voluntary isokinetic contractions before and after supplementation with creatine or placebo. No effect was seen in the placebo group, and an increase in muscle peak torque production was seen in the creatine group only in the later stages of some of the sets. No effect of creatine supplementation on peak torque was seen, but this experimental model might not allow subjects to generate maximum forces because of the large number of contractions to be performed.

More recently, Maganaris & Maughan (1998) showed that 5 d of creatine supplementation was effective in increasing maximum voluntary isometric strength of the knee-extensor muscles in individuals engaged in a strength training programme. This gain was maintained in a subsequent test after a period during which a placebo was administered. In a second group of subjects, the treatment order was reversed; no gain in strength was seen after the first period of placebo administration, but an increase was observed in the third test, after the creatine supplementation period. Isometric endurance capacity at various fractions of maximum voluntary force of contraction (MVC) was also increased after creatine supplementation but was not affected by the placebo treatment.

In a group of previously untrained young women, the effects of a 10-week programme of strength training were enhanced by daily supplementation with creatine relative to the effects observed with placebo treatment (Vandenberghe *et al.* 1997). Similarly, Volek *et al.* (1997) found that a 7 d supplementation period increased performance in strength-related tasks in young men undertaking a strength training programme.

More information is clearly required as none of these studies was able to provide a mechanism for the observed effects, though all three studies reported an increase in body mass with creatine supplementation. It does, however, appear that short-term supplementation with creatine can increase the force generating capacity of skeletal muscle.

Effects of creatine supplementation on the metabolic response to exercise. The mechanism by which creatine supplementation might improve performance is not entirely clear, although it seems clear that this effect is related to the increased muscle CP content. Recent results indicate that the rate of CP resynthesis after intense exercise is enhanced after high-dose creatine supplementation (Greenhaff *et al.* 1994). This allows faster recovery after sprints as well as allowing more work to be done during each subsequent high-intensity effort. These effects will allow a greater amount of work to be done in training and should therefore result in a greater training response. This may be particularly important in view of the fact that the muscle creatine content remains high for weeks or even months after only a few days of high-dose dietary creatine supplementation.

Greenhaff *et al.* (1993) showed that the post-exercise plasma NH_3 concentration was lower after creatine supplementation, although there was no difference in the blood lactate concentration, but interpretation of the results is complicated by the fact that the total work output was higher in this condition. Earnest *et al.* (1994) also showed no difference in blood lactate between the creatine-supplemented and placebo trials in spite of differences in power output, and they also found a suggestion of a lower blood NH_3 concentration after creatine supplementation. Green *et al.* (1993) reported no effect of creatine supplementation (20 g/d for 5 d) on O_2 consumption or on blood lactate concentration during an incremental treadmill running test at intensities of 50–80 % of maximum O_2 uptake; they did, however, show that this treatment

regimen was effective in improving the performance of these same subjects in a test consisting of repeated bouts of isometric exercise. In contrast to the lactate results obtained in these three studies, Soderlund *et al.* (1994) reported a lower muscle lactate, in spite of a higher total work output, after creatine supplementation; in this study, the exercise test consisted of a series of high intensity sprints of 6 s duration on a cycle ergometer.

There are many anecdotal reports of elite athletes successfully using creatine supplementation in preparation for competition, but as with all other ergogenic aids, there can be no certainty as to the truth of these reports. Many athletes also claim to have experimented with creatine supplementation but to have experienced no benefit. In this latter case, at least in the UK, most have been taking a creatine dose of about 4 g/d for prolonged periods, according to the recommendations of some suppliers. The scientific studies that have shown beneficial effects have generally involved the use of much higher doses (20–30 g/d) for short periods of time, and there is currently no evidence to support the idea that performance benefits will result from the dosage regimen recommended by the suppliers.

The use of any nutritional supplement which is effective in improving performance inevitably raises ethical issues. Ergogenic aids are banned by the governing bodies of sport for one of two reasons: on the grounds that they pose a threat to the health of the individual, or because they confer what is seen to be an 'unfair' advantage. Although there is no reason to suppose that there are any risks to health associated with long-term use of high doses of creatine, the studies quoted above which have used high doses, in the order of 20–30 g/d, have been of relatively short duration (5–14 d). The normal daily diet of non-vegetarians contains less than 1 g creatine (Heymsfield *et al.* 1983), but in populations with a high meat intake this will be substantially higher. There is, however, no reason to believe that those diseases, primarily cancer of the colon, which are more common in populations with a high meat intake are in any way associated with the dietary creatine intake. Studies are currently underway to investigate some of the effects of long-term creatine supplementation, and this information will become available in due course. This leaves the ethical question of whether the use of creatine should be disallowed on the grounds of its ergogenic effect, as is the case with other normal dietary components such as caffeine. There seems to be no logic to the argument for the acceptance of the use of creatine in any dose, but restriction of the amount of caffeine that may be used. There may, however, be an intuitive opposition to the use of substances which have an effect on the central nervous system, as caffeine does in high doses, which does not apply to substances whose effects are purely peripheral. As more information emerges, this issue will be resolved, and the governing bodies of sport will make a decision.

Creatine and body mass. Many studies and anecdotal reports support the suggestion that acute supplementation with creatine is associated with a prompt gain in body mass. This typically seems to amount to about 1–2 kg over a supplementation period of 4–5 d, but may be more than this. In reviewing those studies where changes in body mass were reported, Clarkson (1998) reported eleven studies where body-mass increases occurred and three where no change in mass was reported.

Because of the rapid increase in body mass, it must be assumed that this is mostly accounted for by water retention. Increasing the creatine content of muscle by 80–100 mmol/kg will increase intracellular osmolality, leading to water retention. Hultman *et al.* (1996) found a reduction in urinary output during supplementation, tending to confirm this suggestion. The increased intramuscular osmolality due to creatine itself, however, is not likely to be sufficient to account for all of this water retention. It has been suggested that co-ingestion of creatine and carbohydrate, which results in high circulating insulin levels (Green *et al.* 1996*a*,*b*), may sti-

mulate glycogen synthesis, which will further increase the water content of muscle. Evidence from an animal model, however, does not show an effect of creatine on glycogen resynthesis in muscle or liver after exercise-induced glycogen depletion (Oopik *et al.* 1996).

There is some preliminary evidence for a stimulation of protein synthesis in response to creatine supplementation (Ziegenfuss *et al.* 1997), but further experimentation is required. It seems unlikely that major effects on muscle protein content can be achieved within 4–5 d. It must be conceded, however, that the reported gains in muscle strength within the same time scale are difficult to explain.

Health concerns of creatine supplementation. Many concerns have been raised that the effects of long-term use of large doses of creatine are unknown and that its use may pose a health risk. Concerns seem to focus primarily on the possible effects on renal function, in particular in individuals with impaired renal capacity. Studies on the response to long-term creatine use are in progress at this time, but results are not yet available. There have, however, been no reports of adverse effects in any of the studies published in the literature. One study that specifically examined renal function in individuals supplemented with creatine found no reason to believe that renal complications were likely (Poortmans *et al.* 1997). Anecdotal reports of an increased prevalence of muscle cramps in athletes taking creatine supplements have been circulating for some time, but there is no substance to these stories. It seems likely that any injury suffered by an athlete will be ascribed to an easily identifiable change in habit, such as the introduction of a new supplement.

Uninformed comment ascribed the deaths of three American collegiate wrestlers to creatine use, but this was not substantiated at the formal inquiries conducted. Given the increase in body mass that often accompanies supplementation, it does seem possible that athletes who must acutely reduce body mass to qualify for a particular weight category might face particular problems. It is not unusual in some sports for body mass to be reduced by as much as 10 % in the few days before competition. If the mass loss necessary to make the qualifying weight is 1–2 kg more than anticipated, the measures required to achieve the target mass will be unusually severe and may provoke serious, and potentially fatal, complications related to dehydration and hyperthermia.

It is usually recommended that athletes take 20 g creatine/d for 4–5 d (a loading dose) followed by 1–2 g/d (maintenance dose). The muscle may be saturated with creatine when a dose as small as 10 g/d is taken for 3–4 d if this is taken together with sufficient carbohydrate to stimulate a marked elevation of the circulating insulin concentration. Many athletes, however, work on the principle that more is better and may greatly exceed these amounts. Even with very large doses, however, the possibility of adverse effects seems remote. Creatine is a small water-soluble molecule easily cleared by the kidney and the additional N load resulting from supplementation is small. The same concerns over renal damage have been raised in the context of protein supplementation among strength athletes and bodybuilders; these athletes may consume up to 3–4 g protein/kg body mass per d over very long periods (Burke & Inge, 1994), but there is no evidence that the theoretical problems of clearance of the extra solute load are real.

In conclusion, it seems clear that ingestion of high doses (10–20 g/d) of creatine over a period of 4–5 d causes a marked elevation of the free creatine and CP content of skeletal muscle. This results in an improved capacity to maintain power output during high intensity exercise, especially where repeated exercise bouts with only short recovery periods are involved. The effects on muscle CP content and on performance are likely to be greatest in those individuals who normally have a low muscle CP content, perhaps as a result of a low dietary intake. Creatine is a normal dietary component and its use is not contrary to the rules of

any of the governing bodies of sport. There are no documented adverse effects resulting from the ingestion of creatine. A number of extensive reviews are available (Greenhaff, 1995; Maughan, 1995; Mujika & Padilla, 1997; Toler, 1997; Williams & Branch, 1998).

Carnitine

Depletion of the intramuscular glycogen stores is recognized as one of the primary factors involved in the fatigue that accompanies prolonged exercise. A recent review of published work in this area is provided by Coyle (1997). The importance of carbohydrate as a fuel for the working muscles is confirmed by the close relationship between the pre-exercise glycogen concentration and the time for which exercise can be sustained. Further evidence comes from studies which show that increasing the combustion of fat during prolonged exercise, and thus sparing the limited carbohydrate stores, can improve endurance capacity. Increasing fatty acid mobilization by heparin administration after ingestion of a high-fat meal or by caffeine ingestion has been shown to be effective in improving performance. The former method, however, is not acceptable in sport and the use of caffeine requires care to ensure that urinary caffeine levels do not exceed the permissible level.

Although the supply of plasma free-fatty acids to the exercising muscle is an important factor in determining the relative contributions of fat and carbohydrate to oxidative metabolism, a number of other steps are recognized as being involved in fat oxidation. Fatty acid uptake into the cell and translocation across the mitochondrial membrane are also key steps. Carnitine combines with fatty acyl-Coenzyme A (acyl-CoA) in the cytoplasm and allows that fatty acid to enter the mitochondrion. The first step is catalysed by carnitine palmitoyl transferase 1 (*EC* 2.3.1.21), and the trans-membrane transport is facilitated by acylcarnitine transferase (*EC* 2.3.1.7). Within the mitochondrion, the action of carnitine palmitoyl transferase 2 regenerates free carnitine and the fatty acyl-CoA is released for entry into the β-oxidation pathway.

Within the mitochondrion, carnitine also functions to regulate the acetyl-CoA concentration and the concentration of free CoA. Free CoA is involved in the pyruvate dehydrogenase (*EC* 1.2.4.1) reaction as well as in the process of β-oxidation and thus plays a key role in the integration of fat and carbohydrate oxidation. It has been proposed that an increased availability of carnitine within the mitochondrion might allow the cell to maintain a higher free CoA concentration, with a stimulatory effect on oxidative metabolism.

Because of the key role of carnitine in the oxidation of both fat and carbohydrate, it has been proposed that carnitine supplementation may improve exercise performance. On the basis of this logic, carnitine is widely sold in sports shops as a supplement for endurance athletes. There is, however, no good evidence that carnitine deficiency occurs in the general population or in athletes. Carnitine is present in the diet in red meat and dairy products, so it might be thought that individuals who follow a vegan lifestyle might be at increased risk of deficiency, but it can also be synthesized from lysine and methionine in liver and kidney. Measurement of the effects of exercise and diet on muscle carnitine levels in human subjects (muscle accounts for about 98 % of the total body carnitine content) has only been carried out relatively recently and there have been few attempts to measure the effects of supplementation on the muscle carnitine level. Barnett *et al.* (1994) and Vukovich *et al.* (1994) reported that short-term supplementation with carnitine (4–6 g/d for 7–14 d) had no effect on muscle carnitine levels or on the metabolic response to exercise. Even when fatty acid mobilization was stimulated by

high-fat meals or heparin, there was no effect of carnitine supplementation on fat oxidation (Vukovich *et al.* 1994).

In contrast to these negative findings, however, there are published reports suggesting that carnitine supplementation can increase the contribution of fatty acids to oxidative metabolism and thus may have a glycogen-sparing effect. In a comprehensive review of the literature, Spriet (1997) identified eight studies which examined the effects of supplementation on the metabolic response to endurance exercise and found that three of those studies reported an increased rate of fat oxidation. He also reviewed the studies which have examined the effects of carnitine supplementation on exercise performance and concluded that the findings were not generally in support of an ergogenic effect of carnitine. In one recent study, the muscle carnitine concentration was reduced by about 50 % by long-term administration of pivalic acid; somewhat paradoxically, this resulted in a decreased rate of glycogen utilization during submaximal exercise (Abrahamsson, 1996) and the results are not easily explained.

It must be concluded that, although there is a theoretical basis for an ergogenic effect of carnitine on performance of both high-intensity and prolonged exercise, this is not supported by the experimental evidence. Supplementation of the diet with carnitine is unlikely to be beneficial for athletes.

Bicarbonate

In exercise that causes fatigue within a few minutes, anaerobic glycolysis makes a major contribution to energy metabolism. Although glycolysis allows higher rates of ATP resynthesis than can be achieved by aerobic metabolism, the capacity of the system is limited and fatigue is inevitable when high rates of anaerobic glycolysis occur. The metabolic acidosis that accompanies glycolysis has been implicated in the fatigue process, either by inhibition of key glycolytic enzymes, by interfering with Ca transport and binding, or by a direct effect on the actin–myosin interaction. Because of these effects of acidosis on the muscle, it is intuitively attractive to believe that induction of alkalosis before exercise, an increase in the muscle-buffering capacity, or an increased rate of efflux of H^+ from the active muscles will all have the potential to delay fatigue and improve exercise performance (Hultman & Sahlin, 1980).

Influence of induced alkalosis on exercise performance. As early as 1932 an increased exercise capacity and an increased blood lactate concentration were observed when bicarbonate was administered before exercise (Dill, 1932). In view of the implications for athletic performance, it is hardly surprising that a large number of studies investigating the effects of metabolic alkalosis induced by ingestion of sodium bicarbonate or sodium citrate on the performance of high-intensity exercise have been carried out since that initial report was published. The results, however, are by no means consistent or conclusive (Heigenhauser & Jones, 1991).

Several investigators have reported a decrease in perceived exertion (Robertson *et al.* 1986; Swank & Robertson, 1989) or an increase in performance (Sutton *et al.* 1981; Costill *et al.* 1984; Maughan *et al.* 1986; Bouissou *et al.* 1988; Goldfinch *et al.* 1988) during high-intensity exercise after bicarbonate administration. Others, however, have shown no benefit of an induced metabolic alkalosis on perceived exertion (Poulus *et al.* 1974) or performance (Kindermann *et al.* 1977; Parry-Billings & MacLaren, 1986; Kelso *et al.* 1987; Horswill *et al.* 1988; Brien & McKenzie, 1989; Kowalchuk *et al.* 1989). In one study designed to simulate athletic competition, trained non-elite (best 800 m time about 2 min 5 s) middle-distance runners were used as subjects and the exercise consisted of a simulated 800 m race; in the

alkalotic condition, subjects ran almost 3 s faster than in the placebo or control trials (Wilkes *et al.* 1983). A more recent report indicates similar improvements (3–4 s) over a distance of 1500 m in runners who completed simulated races in about 4 min 15 s (Bird *et al.* 1995). Although these effects on performance might seem small, they are of considerable significance to the athlete; an improvement of even a fraction of a second in these events is considered to be a major achievement.

The reason for the conflicting effects reported in the published literature is not altogether clear, but some at least is probably due in part to variations in the intensity and duration of the exercise tests used, in the nature of the exercise task, in the dosage of sodium bicarbonate administered, and in the time delay between bicarbonate administration and the beginning of the exercise test (i.e. in the degree of metabolic alkalosis induced).

Performance has been monitored over exercise durations ranging from 30 s (Inbar *et al.* 1983) to 20 min (Jones *et al.* 1977), and during continuous (Kindermann *et al.* 1977; Goldfinch *et al.* 1988), incremental (Sutton *et al.* 1981; Kowalchuk *et al.* 1984) and intermittent (Costill *et al.* 1984; Parry-Billings & MacLaren, 1986) dynamic exercise as well as during isometric exercise (Maughan *et al.* 1986). There is no clear pattern of exercise duration between those studies where a positive effect was observed and those where no effect was seen. In most studies, a dose rate of 0·3 g sodium bicarbonate or citrate per kg body weight has been employed to induce alkalosis and this has usually been administered orally in solution or in capsule form. Such a dose rate has usually resulted in an increase of 4–5 mmol/l in the plasma buffer base 2–3 h after administration, although the time course of changes in acid–base status has not been carefully followed in most of these studies (Costill *et al.* 1984; Kowalchuk *et al.* 1984; McKenzie *et al.* 1986; Maughan *et al.* 1986). Horswill *et al.* (1988) examined the effects of doses of bicarbonate, in the range 0·1–0·2 g/kg, on performance of a cycle ergometer sprint lasting 2 min and found that none of these doses was effective in improving performance, even though they did elevate the blood bicarbonate concentration; on the basis of these results, they suggested that a dose-rate of less than 0·3 g/kg body weight might be ineffective in improving exercise performance. McKenzie *et al.* (1986), however, reported that a dose-rate of 0·3 g/kg was no more effective than 0·15 g/kg. From a recent study on racehorses it appears that, because of the more marked pre-exercise acid–base changes, an increased dose (0·6 g/kg) might be more effective than the dose of 0·3 g/kg normally employed in human studies (Greenhaff *et al.* 1990*b*); it also appeared from this study that bicarbonate administration might have a greater effect on performance if the exercise was not performed until at least 3 h after ingestion. This may partly explain the lack of an effect on performance noted by Kelso *et al.* (1987) who used a higher than normal dose of 0·4 g/kg, but allowed an interval of only 1 h between treatment ingestion and exercise; plasma bicarbonate was elevated by only 3 mmol/l before exercise.

There are, of course, potential problems associated with the use of increased doses of bicarbonate. Vomiting and diarrhoea are not infrequently reported as a result of ingestion of even relatively small doses of bicarbonate and this may limit any attempt to improve athletic performance by this method, certainly among those individuals susceptible to gastrointestinal problems. There have been reports of athletes using this intervention, which is not prohibited by the rules of sport, being unable to compete because of the severity of these symptoms. Although unpleasant and to some extent debilitating, these effects are not serious and there are no long-term adverse consequences of occasional use. Sodium citrate administration, which also results in an alkaline shift in the extracellular fluid, has also been reported to improve peak power and total work output in a 60 s exercise test, but without any adverse gastrointestinal symptoms (McNaughton, 1990).

Where an increase in performance after bicarbonate ingestion has been observed, it has been ascribed to an increased rate of H^+ efflux from the exercising muscles, reducing the rate of fall of intracellular pH and relieving the pH-mediated inhibition of phosphofructokinase (*EC* 2.7.1.11) (Sutton *et al.* 1981). The higher blood lactate levels after exercise associated with metabolic alkalosis, even when the exercise duration is the same, may therefore be indicative not only of a higher rate of lactate efflux, but also of an increased contribution of anaerobic glycolysis to energy production.

Associated with the development of fatigue during high-intensity exercise is a decline in the muscle adenine nucleotide content (Harris *et al.* 1987; Sahlin & Katz, 1988). The extent of the fall in muscle ATP concentration which occurs during maximal exercise in man has been shown to approach 40 % of the pre-exercise level (Hultman *et al.* 1967; Boobis *et al.* 1987); even greater losses of ATP (60 %) have been reported at exhaustion in the horse (Snow *et al.* 1985). There is evidence to suggest that an increase in H^+ efflux during near maximum intensity exercise after bicarbonate administration may decrease the extent of muscle adenine nucleotide loss during exercise (Greenhaff *et al.* 1990*a*). Whether this is due to a pH-mediated decrease in the activation of AMP deaminase or an increased rate of ADP rephosphorylation via glycolysis is not clear. Whatever the mechanism it seems reasonable to suggest that bicarbonate administration before high intensity exercise will only enhance performance when the intensity and duration of the exercise are sufficient to result in significant muscle acidosis and adenine nucleotide loss.

Caffeine

Caffeine is a drug which, because of its longstanding and widespread use, is considered socially acceptable. Caffeine and the related compounds theophylline and theobromine are naturally occurring food components (Table 1) and for many people these substances are part of the normal daily diet and caffeine is probably the most widely used stimulant drug in the world. The use of caffeine is not prohibited in sport, but there is a limit to the amount that may be taken by athletes in competition: any individual whose urine contains caffeine at a level of more than 12 mg/l is guilty of a doping offence and is liable to be banned from competition.

Actions of caffeine. Caffeine has effects on the central nervous system and on adipose tissue and skeletal muscle that give reason to believe that it may influence exercise performance. Early studies on the effects of caffeine on endurance performance focused on its role in

Table 1. Caffeine content of various foodstuffs

Foodstuff	Serving size	Caffeine content (mg/serving)
Coffee*	150 ml	50–120
Tea*	150 ml	15–20
Hot chocolate†	250 ml	10
Milk chocolate†	50 g	40
Soft drinks		
Coca Cola	330 ml	50
Pepsi	330 ml	40
Jolt	330 ml	100

* Caffeine content of tea and coffee varies widely depending on the source and method of preparation.
† In addition to its caffeine content chocolate contains appreciable amounts of the related compound theobromine. Although this is less pharmacologically active, the high content gives it an equivalent effect to that of caffeine.

the mobilization of free fatty acids from adipose tissue, increasing fat supply to the muscle, which in turn can increase fat oxidation, spare glycogen and thus extend exercise time. Caffeine ingestion before exercise to exhaustion at 80 % VO_{2max} increased exercise time from 75 min on the placebo trial to 96 min on the caffeine trial (Costill *et al.* 1978). A positive effect was also observed on the total amount of work achieved in a fixed 2 h exercise test. In this and other studies, caffeine was shown to increase circulating free fatty acid levels, increase fat oxidation and spare muscle glycogen during prolonged exercise (see Spriet (1995) for a review of these studies). The consistency and clarity of these findings led to the widespread popularity of caffeine consumption before marathon running, although caffeine in much higher doses had long been used, particularly in professional cycling.

Growing evidence of a positive effect of caffeine on performance in the absence of any glycogen-sparing effect, and of effects on high intensity exercise, where glycogen availability is not a limiting factor, has stimulated the search for alternative mechanisms of action. There is evidence for a number of effects of caffeine directly on skeletal muscle. It may affect the activity of the Na^+, K^+-ATPase (*EC* 3.6.1.37) and the intracellular localization and binding of Ca, it can cause an elevation of the intracellular cyclic AMP level as a result of inhibition of the action of phosphodiesterase, and it may have direct effects on a number of enzymes, including glycogen phosphorylase (*EC* 2.4.1.1) (Spriet, 1997). Whether all these effects can take place at the tissue concentrations of caffeine that occur after ingestion of moderate doses of caffeine remains unclear. Effects on the central nervous system, either to modify the perception of effort or on the higher motor centres, have been proposed, but in the absence of evidence, this remains speculation.

Effects of caffeine on performance. There are several recent and comprehensive reviews of the effects of caffeine on exercise performance and a detailed review of the literature will not be attempted here (Dodd *et al.* 1993; Graham *et al.* 1994; Spriet, 1997). There are a number of studies showing beneficial effects of caffeine ingestion on a variety of laboratory tests of endurance performance. An increased time to exhaustion has been observed in a number of tests, but performance in simulated race situations, where a fixed amount of work has to be done in the shortest possible time, is also improved. More recent studies have focused on exercise of shorter duration and a number of studies have shown beneficial effects on performances lasting only a few (about 4–6 min) (Collomp *et al.* 1991; Wiles *et al.* 1992; Jackman *et al.* 1996). There is little information on performance in sprint tasks, and what is reported is conflicting (Spriet, 1997).

It is clear from the published studies that positive effects of caffeine can be obtained in a variety of exercise situations with caffeine doses that are far below those necessary to produce a positive test. Doses of as little as 3 mg/kg body mass can produce ergogenic effects, but there appears to be a wide inter-individual variability in the sensitivity to caffeine. The reasons for this variability are not altogether clear but, perhaps surprisingly, they do not appear to be related to the habitual level of caffeine consumption.

Other effects of caffeine. Caffeine has a number of unwanted side effects that may limit its use in some sports or by sensitive individuals: these effects include insomnia, headache, gastrointestinal irritation and bleeding, and a stimulation of diuresis. There are also some suggestions that high levels of caffeine intake may be a risk factor for bladder cancer. This is unlikely to be modified by occasional use of modest doses before competition, but the athlete who may contemplate using high doses of caffeine before training on a daily basis should

consider this. In the very high doses that were sometimes used by athletes, noticeable muscle tremor and impairment of coordination have been noted (Spriet, 1995).

The diuretic action of caffeine is often stressed, particularly in situations where dehydration is a major issue. This particularly affects competitions held in hot, humid climates where the risk of dehydration is high and is more important for endurance athletes where dehydration has a greater negative effect on performance. Athletes competing in these conditions are advised to increase their intake of fluid, but are usually also advised to avoid tea and coffee because of their diuretic effect. It seems likely, however, that this effect is small for those habituated to caffeine use (Wemple *et al.* 1997) and the negative effects caused by the symptoms of caffeine withdrawal may be more damaging.

Ethical issues in caffeine use. An athlete found to have a urine caffeine concentration of more than 12 mg/l is deemed to be guilty of a doping offence and is liable to suspension from competition. It is clear from this that caffeine is considered by the International Olympic Committee to be a drug, but an outright ban on its use is impractical and manifestly unfair to those who normally drink tea and coffee. It is equally clear, however, that the amount of coffee that must be drunk to exceed the permitted limit (about 6 cups of strong coffee consumed within a period of about 1 h) is such that it is unlikely that this would normally be achieved. In addition, in endurance events, a urine sample taken after the end of the event would probably not register a positive test even if large amounts had been consumed before the start.

It is also clear, however, that beneficial effects on performance can be achieved with caffeine doses that are less than those that constitute a positive drug test, so athletes may feel justified in their view that use in these amounts is acceptable. It is difficult, but not impossible, to achieve an effective intake from drinks such as tea or coffee, but there are various products on the market that contain significant amounts of caffeine (Table 1). Caffeine tablets, commonly used by overworked students studying for examinations, are also commonly used and these can easily lead to an intake that exceeds the permissible limit. Athletes may feel justified in establishing their own dose–response relationship to establish the amount that is safe to take and in going as close as possible to the limit. Some may feel this is entirely acceptable; others take the view that this approach encourages the drug culture.

Supplements that may increase muscle mass

In sports that require strength and power a high lean body mass, and especially a high muscle mass, confers a definite advantage. Supplement use is widespread among athletes in strength sports, and a wide variety of supplements are used. A few of the supplements that are more commonly used by athletes are described briefly below, but this list is by no means exhaustive.

Protein and amino acids

The idea that athletes need a high-protein diet is intuitively attractive, and indeed there is evidence that the requirement for protein is increased by physical activity (Lemon, 1995). Muscles consist largely of protein and their involvement is fundamental to performance in all sports. It is also readily apparent that regular exercise has a number of highly specific effects on the body's protein metabolism. Strength training results in increases in muscle mass, indicating an increased formation of actin and myosin, and it is tempting to assume that this process is

dependent on protein availability. Endurance training has little effect on muscle mass, but does increase the muscle content of mitochondrial proteins, especially those involved in oxidative metabolism. Hard exercise also results in an increased level of muscle damage, usually at the microscopic level, and there is clearly a role for protein in the repair and recovery processes.

The changes comprising this adaptive response are selective and are specific to the training stimulus; they are also dependent on the availability of an adequate intake of protein in the diet. The case for a high-protein diet for athletes thus seems to be well founded and is widely believed to be true. In a survey of American college athletes, 98 % believed that a high-protein diet would improve performance. There is, however, compelling evidence that protein supplementation is not necessary for the athlete. The dietary protein requirements of the general population have been the subject of extensive investigation. It is now generally accepted that a daily requirement of about 0·6 g protein/kg body weight per d will meet the needs of most of the population, provided that a variety of different protein sources make up the diet, and provided also that the energy intake of the diet is adequate to meet the energy expenditure (Lemon, 1991). To allow for individual variability and variations in the quality of ingested proteins, the recommended daily allowance for protein is set at about 0·8 g/kg in most countries.

The contribution of protein oxidation to energy production during exercise decreases to about 5 % of the total energy requirement, compared with about 10–15 % (i.e. the normal fraction of protein in the diet) at rest, but the absolute rate of protein degradation is increased during exercise because of the high energy turnover (Dohm, 1986). This leads to an increase in the minimum daily protein requirement, but this will be met if a normal mixed diet adequate to meet the increased energy expenditure is consumed. Deficiencies in protein intake are more likely in the sedentary individual, especially when energy intake is restricted in order to control body weight, than in the athlete training hard who consumes sufficient energy to meet the demand. In spite of this clear relationship between total energy intake and the adequacy of dietary protein intake, many athletes ingest large quantities of protein-containing foods and expensive protein supplements. Daily protein intakes of up to 400 g are not unknown in some sports and in the diet of bodybuilders protein typically accounts for more than 20 % of total energy intake and occasionally as much as 40 % (Burke & Inge, 1994). Disposal of the excess N is theoretically a problem if renal function is compromised, but there does not appear to be any evidence that excessive protein intake among athletes is in any way damaging to health (Lemon, 1991).

Although the recommended protein intake for athletes has been set at about 1·2–1·7 g/kg per d (Lemon, 1991), protein may account for a lower than normal percentage of total energy intake on account of the increased total energy intake. In endurance athletes, and especially in marathon runners, it is not uncommon to find that protein accounts for less than 10 %, and sometimes even less than 8 %, of total energy intake. Even lower values, perhaps even less than 5 % of total energy intake, may be able to provide sufficient protein when the total intake is very high. It seems clear, therefore, that supplementation with protein is not necessary for athletes, except perhaps in the rare situations where energy intake is restricted. Even then, restriction of energy intake will severely limit the duration and intensity of exercise that can be performed and there is unlikely to be a need for a higher intake of protein than will be supplied by the diet.

Sales of whole-protein powders account for a major part of the nutritional supplement sales to athletes, but a number of individual amino acids are also popular. Arginine and ornithine are reported to stimulate growth hormone release and to promote growth of lean tissue when taken during a period of strength training (see Clarkson (1998) for a review of these studies). There is some published evidence to support this, but any increase in growth hormone secretion is small

compared with that which results from a bout of high intensity exercise. A number of other amino acids, including histidine, lysine, methionine and phenyalanine, are sold as 'anabolic agents', but Clarkson (1998) concluded after a review of the literature that 'there is little reason to believe that amino-acid supplements will promote gains in muscle mass'.

Notwithstanding the lack of experimental data to support their beliefs, most strength trained athletes believe that a high-protein diet can improve the rate of gain of muscle mass. Science ignores the accumulated wisdom at its peril and it is possible that there are effects that remain to be identified. It is clear that a prolonged period of training will cause substantial changes in the structural and functional characteristics of skeletal muscle and other tissues. Although major changes in muscle function are not apparent in response to single exercise bouts, small cumulative changes must take place between training sessions. There is good evidence of adaptive changes in muscle structure and function taking place in response to only a few exercise sessions (Green *et al.* 1991). These changes are different from those that are commonly observed to occur after a single exercise bout, when the observed responses are largely catabolic in nature and evidence themselves as muscle damage and soreness (Clarkson, 1997). Nonetheless, there must be adaptive changes involving synthesis of new proteins in response to each training stimulus. It is likely that the methods currently available are simply inadequate to measure these changes with any degree of reliability.

In the recovery period muscle glycogen synthesis is a priority, but synthesis of new proteins should perhaps be seen as being of equal or even greater importance. Because little attention has been paid to this area, it is not at present apparent what factors may be manipulated to influence these processes. The hormonal environment is one obvious factor that may be important and nutritional status can influence the circulating concentration of a number of hormones that have anabolic properties, the most obvious example being insulin. It is, however, increasingly recognized that cell volume is an important regulator of metabolic processes (Waldegger & Lang, 1997; Lang *et al.* 1998) and there may be opportunities to manipulate this to promote tissue synthesis. During and after exercise there may be large changes in cell volume, secondary to osmotic pressure changes caused by metabolic activity, hydrostatic pressure changes, or by sweat loss.

Alterations in cell volume induced by changes in osmolality are well known to alter the rate of glycogen synthesis in skeletal muscle (Low *et al.* 1996). Amino acid transport into muscles is also affected by changes in cell volume induced by manipulation of the transmembrane osmotic gradient; skeletal muscle uptake of glutamine is stimulated by cell swelling and inhibited by cell shrinkage (Low *et al.* 1997). The intracellular glutamine concentration appears to play an important role in a number of processes, including protein and glycogen synthesis (Rennie *et al.* 1998), but the effect of ingestion of glutamine on these aspects of post-exercise recovery is not known at this time.

The full significance of these findings for the post-exercise recovery process and the roles they play in adaptation to a training programme remain to be established (Lang *et al.* 1998). Manipulation of fluid and electrolyte balance and the ingestion of a variety of osmotically active substances or their precursors offers potential for optimizing the effectiveness of a training regimen.

Chromium picolinate

Cr is an essential trace element which has a number of functions in the body and has been reported to potentiate the effects of insulin (Mertz, 1992). Because of the anabolic effects of insulin, it might be expected that amino acid incorporation into muscle protein would be

stimulated, enhancing the adaptive response to training. There is also some evidence to suggest an increased urine Cr loss after exercise, further supporting the idea that athletes in training may have higher requirements than sedentary individuals. Cr is widely used as a supplement by strength athletes and is usually sold as a conjugate of picolinic acid; this form is reported to enhance Cr uptake (Evans, 1989).

Supplementation of the diet with chromium picolinate was reported to enhance the adaptive response to a strength training programme, with an increase in lean body mass (Evans, 1989). No direct measures of muscle mass were made, however, and the results of this study must be viewed with caution. A number of subsequent studies, mostly using more appropriate methodology, have failed to reproduce these results, with no effect on lean tissue accretion or on muscle performance being seen (Clarkson, 1998; Walker *et al.* 1998). Nonetheless, Cr supplementation remains popular.

β-Hydroxy β-methylbutyrate

β-Hydroxy *β*-methylbutryrate (HMB) is a metabolite of leucine and is also present in small amounts in some foods. There appears to be only one study published in a peer-reviewed journal in which the effects of HMB administration to human subjects has been investigated (Nissen *et al.* 1996). This paper presented the results of two supplementation studies which showed that subjects ingesting 1·5 or 3 g HMB/d for 3–7 weeks experienced greater gains in strength and in lean body mass compared with control groups. Although it is not easy to find any fault with this study, it would be premature to conclude on the basis of this report that there is an advantage to be gained from HMB supplementation. Nonetheless, it is sold in large amounts in sports nutrition stores.

No mention has been made of supplements such as Fe or Ca or of the varied vitamin preparations which are widely used by the general public. The evidence suggests that the use of these supplements is perhaps more prevalent in athletes than in the general population, but the perceived benefits are similar. Fe, of course, is important to the athlete because of the importance of haemoglobin in O_2 transport and, while anaemia is not more prevalent in athletes than in the general population, the consequences may be more apparent. Nonetheless, the same principles apply and supplementation is not warranted unless a specific deficiency is known to exist.

Supplements that may improve general health

Glutamine

Modest levels of regular exercise are associated with an increased sensation of physical well-being and a decreased risk of upper respiratory tract infections (Nieman *et al.* 1993, 1998). The consequences of minor upper respiratory tract infection symptoms are usually minimal, but for the athlete in hard training or preparing for a major competition, any injury or illness can have a devastating effect. Although there is good evidence that an active lifestyle is associated with improved health, a number of recent epidemiological surveys have suggested that the athlete in intensive training or completing an extreme endurance event is more susceptible to minor opportunistic infections than is the sedentary individual (Nieman, 1997; Peters-Futre *et al.* 1997; Shephard & Shek, 1997).

It has been suggested that severe exercise results in a temporary reduction in the body's ability to respond to a challenge to its immune system and that an inflammatory response similar to that occurring with sepsis and trauma is invoked (Nieman, 1997). It is not clear, however, whether the various changes in parameters of the immune system that have been reported will result in a reduced ability to deal with opportunistic infective agents. Several studies have shown a reduced circulating glutamine level in the hours after hard exercise (see Rowbottom *et al.* (1996) for a review of these studies). In view of the role of glutamine as a fuel for the cells of the immune system, this has been proposed as a mechanism that would compromise the ability to respond to infection (Newsholme, 1994). Other studies have shown that athletes suffering from chronic fatigue symptoms attributed to overtraining also have low circulating glutamine concentrations (Rowbottom *et al.* 1995).

At present, the limited information on the influence of glutamine supplementation that is available provides no clear pattern of results. Studies by Newsholme and colleagues suggest a beneficial effect of glutamine supplementation on resistance to infection after endurance exercise (Castell *et al.* 1996; Castell & Newsholme, 1997) although a positive effect was not always seen (Castell *et al.* 1997). In the rat, prolonged treadmill running has been shown to reduce the plasma glutamine concentration in the post-exercise period and to reduce the proliferative response of leucocytes to a mitogen challenge (Moriguchi *et al.* 1995); in contrast, animals fed on a glutamine-supplemented diet for 3 weeks before exercise maintained their plasma glutamine levels and showed a higher response to mitogens than the control group. A similar study carried out with human subjects did not support these results and found no beneficial effect of acute glutamine supplementation on these same parameters (Rohde *et al.* 1998).

In spite of the attractiveness of this hypothesis, it has not yet been established that there is a clear link between hard exercise, compromised immune function and susceptibility to infection. Nonetheless, glutamine supplementation for athletes is being promoted and supplements are on widespread sale in sports nutrition outlets. The evidence that glutamine supplementation is beneficial is far from clear, but this is an active area of research, and the picture will undoubtedly be clarified in the near future.

Antioxidant nutrients

It has long been common practice for athletes to take vitamin supplements, usually without any thought as to the vitamin status of the individual concerned. There has been much interest recently among athletes in vitamins C and E which have been shown to have antioxidant properties, and which may be involved in protecting cells, especially muscle cells, from the harmful effects of the highly reactive free radicals that are produced when the rate of O_2 consumption is increased during exercise (Kanter, 1995). Many studies have shown that unaccustomed exercise, particularly if it involves eccentric exercise in which the muscle is forcibly lengthened as it is activated, results in damage to the muscle structure and post-exercise soreness. Because it normally peaks 1–3 d after exercise, this is often referred to as delayed-onset muscle soreness. It is believed that free radicals, highly reactive chemical species, may be involved in the damage that occurs to muscle membranes. Alleviating or avoiding these symptoms would allow a greater training load to be sustained. An increased generation of free radicals is also associated with damage to cellular DNA, and to a variety of lipids and proteins. If the post-exercise damage can be reduced by an increased intake of antioxidants, then recovery after training and competition may be more rapid and more complete. The

evidence for this at present suggests a possible role but is not conclusive. Even the suggestion, however, is enough to convince many athletes to take supplements of these vitamins 'just in case'.

The source of the free radicals generated during exercise seems to be primarily related to the increased O_2 use within the mitochondria (McCord, 1979). This suggests that the extent of free radical generation will be directly proportional to the intensity and duration of exercise. Infiltration of damaged muscle by leucocytes may also account for some of the elevation in free radicals that is observed after exercise as these cells generate free radicals as part of their cytotoxic defence mechanisms (Smith *et al.* 1989). A variety of other mechanisms that may promote free radical generation have been described (Kanter, 1995).

Free radicals have been implicated in a number of disease processes, including cardiovascular disease, diabetes and some forms of cancer, as well as in the ageing process. The body has a number of endogenous defence mechanisms which effectively neutralize free radicals before they cause tissue damage; important enzymes are superoxide dismutase (*EC* 1.15.1.1), glutathione peroxidase (*EC* 1.11.1.9) and catalase (*EC* 1.11.1.6). Several nutritional antioxidants also play important roles. Nutritional antioxidants include vitamins A, C and E. Other dietary components, including Se which has a structural role in glutathione peroxidase, and ubiquinone (or coenzyme Q_{10}) may also play important roles but are less well researched. Cu, Zn and Mn are structural components of superoxide dismutase, and Fe is a co-factor for catalase.

A number of studies have investigated the effects of antioxidant supplementation on indices of free radical-induced muscle damage in exercise and there is some evidence of a protective effect of supplementation. For a review of these studies, see Kanter (1995), Dekkers *et al.* (1996) and Packer (1997). The evidence seems to suggest that there may be a reduction in the signs of muscle damage after supplementation, but there is no evidence for any beneficial effect on performance. There are concerns about possible adverse effects of supplementation as several of these nutrients can also function as pro-oxidants. Toxic effects of megadose supplementation are unlikely, but there are concerns about the possible consequences of long-term use of megadoses of single antioxidants. A recent study has reported increased levels of muscle damage in exercise after supplementation with ubiquinone (Malm *et al.* 1996).

Regular training increases the effectiveness of the endogenous antioxidant mechanisms so that even extreme exercise (long-distance triathlon) may not cause any indications of oxidative damage in well-trained athletes (Margaritis *et al.* 1997). In contrast, short periods of modest exercise (8 weeks of training: 3 sessions of 35 min/week) do not result in any signs of increased capacity to neutralize free radicals (Tiidus *et al.* 1996). It is not clear from this whether individuals engaged in regular exercise have an increased requirement for exogenous antioxidants.

In conclusion, there is little evidence to support the suggestion that supplementation with antioxidant nutrients can improve exercise performance, but there is a growing body of evidence to suggest that supplementation may reduce the extent of exercise-induced oxidative damage to tissues. If this is indeed the case, it may be that the athlete undertaking a strenuous training programme may benefit in the long-term by being able to sustain a higher training load. There is also evidence, however, that prolonged exposure to training increases the effectiveness of the endogenous antioxidant mechanisms and it may be that supplementation is unnecessary (Margaritis *et al.* 1997).

Other compounds

Athletes use a wide range of nutritional supplements in their quest for improved performance. Even a cursory inspection of sports shops and magazines reveals the scale and diversity of

supplement use. Most of the exotic supplements make extravagant claims and are sold at inflated prices. The market is, however, largely unregulated and few of the claims made for these products are supported by any evidence; instead they rely on endorsement by top athletes (who are paid handsomely for doing so) and on the gullibility of the consumer.

Sales figures for exotic supplements such as ginseng, bee pollen, royal jelly and pangamic acid, together with a wide range of vitamins and minerals (including B, V, Zn, Mg and Mn), demonstrate that many athletes remain convinced of their effectiveness. In spite of the limited and conflicting evidence, however, the balance of the available information suggests that there is no benefit of these substances for healthy individuals consuming a normal diet. Examination of the information in the body-building world gives an idea of the range of products used and of the claims made for them (Phillips, 1996). Some supplements are potentially harmful in large doses and their use should be actively discouraged. Many studies that purport to show beneficial effects are poorly designed, often with inadequate subject numbers and no control group, and few are published in reputable journals. The power of the placebo effect is well-recognized and athletes seem to be particularly susceptible. Where a beneficial effect is obtained, this is often due to the presence of illegal substances; for example, ephedrine and related compounds are common ingredients of many herbal remedies and the use of these products renders the athlete liable to disqualification. Similarly, many products described as giving a feeling of 'increased energy' contain levels of caffeine that would cause the athlete to fail a drugs test.

Conclusions

Athletes are forever searching for nutritional supplements that will give them a significant advantage over their competitors, and are prepared to go to enormous lengths to find effective nutritional aids (Table 2). This accounts in part for the reports of widespread use of illegal drugs in sport, but the difficulty lies in finding something that is effective in improving performance, but is not against the rules. It is also important that any chemical substance to be used in this way should not have harmful side-effects.

There are many effective dietary ergogenic aids; the most obvious examples are carbohydrate supplements and sports drinks. All essential dietary components, including protein, essential fatty acids, vitamins and minerals, might be considered to come into this category. These components, however, are essential for the maintenance of health and normal physiological function, and supplementation above the level required for maintenance of health is not likely to improve exercise performance. The ergogenic aids discussed here are only a few of those used by athletes, but represent those for which there is evidence of efficacy, or where there is much topical interest.

Table 2. Ergogenic aids: do they work?

Ergogenic aid	Benefit
Antioxidants	Perhaps
Bicarbonate	Yes, in some cases
Branched-chain amino acids	Probably not
Caffeine	Sometimes
Carnitine	No
Creatine	Yes
Glutamine	Possibly
All sorts of other things	Probably not

In conclusion, it should be noted that there is not universal agreement on the acceptability of some of the nutritional supplements used in sport. Creatine is a normal component of foods and is not banned by any of the international sports organizations, but its use has been prohibited by the French Football Federation. The International Olympic Committee has a carefully defined list of drugs, categories of drugs and physical manipulations that are deemed unacceptable. The issue has not, however, been helped by the recent (4 February, 1999) *Lausanne Declaration on Doping in Sport* published by the International Olympic Committee. This includes the following definition: '... doping, which is defined as the use of an artifice, whether substance or method, potentially dangerous to athletes' health and/or capable of enhancing their performance'. This all-embracing definition includes not only all of the supplements discussed above, but all foods. As well as substances and methods that are clearly dangerous, it also includes training!

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