The key to understanding creatine supplementation is to appreciate that it only helps with certain activities. A basic review of what creatine is, and how it is used in the body will help you understand how supplementation might be beneficial. First, the basics. Muscle cells generate mechanical work from an energy liberating chemical reaction -- ATP is split into ADP and P (phosphate). ATP can be used by muscle cells very quickly, but there is only an extremely limited supply -- usually only enough for a few seconds of high intensity work. When the ATP is gone, work stops. Fortunately, the body has several ways to convert ADP back to ATP. The fastest method is to move the phosphate group off of phosphocreatine and onto ADP. This yields ATP -- which is immediately available for muscular work -- and creatine. There is enough phosphocreatine to keep ATP levels up for several more seconds. So at this point we’ve moved from 2 - 3 seconds of all-out work (ATP) to almost 10 seconds (ATP + creatine). The body can recharge creatine back to phosphocreatine, but this takes time (approximately 30 - 60 seconds). This ATP + creatine system makes up the fastest component of the anaerobic system, and is most used by power athletes.

If you haven’t yet heard of creatine supplementation you soon will. It is being promoted as a muscular performance enhancer, and there is scientific evidence to support this. Unfortunately, claims have escalated beyond science, and now athletes from a wide variety of sports have begun taking this substance. The pursuit of performance enhancing potions has historically been like the alchemists dreams turning lead into gold. Too often the latest fad turns out to do nothing or is harmful. Although creatine supplementation offers short-term limited benefits, whether or not it is harmful long term has yet to be fully determined.

**Physiology of creatine in exercise**

The key to understanding creatine supplementation is to appreciate that it only helps with certain activities. A basic review of what creatine is, and how it is used in the body will help you understand how supplementation might be beneficial. First, the basics. Muscle cells generate mechanical work from an energy liberating chemical reaction -- ATP is split into ADP and P (phosphate). ATP can be used by muscle cells very quickly, but there is only an extremely limited supply -- usually only enough for a few seconds of high intensity work. When the ATP is gone, work stops. Fortunately, the body has several ways to convert ADP back to ATP. The fastest method is to move the phosphate group off of phosphocreatine and onto ADP. This yields ATP -- which is immediately available for muscular work -- and creatine. There is enough phosphocreatine to keep ATP levels up for several more seconds. So at this point we’ve moved from 2 - 3 seconds of all-out work (ATP) to almost 10 seconds (ATP + creatine). The body can recharge creatine back to phosphocreatine, but this takes time (approximately 30 - 60 seconds). This ATP + creatine system makes up the fastest component of the anaerobic system, and is most used by power athletes.
Aerobic endurance athletes, such as distance runners and triathletes, represent a much different picture from power athletes. Their levels of ATP and phosphocreatine don’t change during exercise because ATP is generated at the same rate it is used -- a “pay as you go” mechanism. Aerobic generation of ATP, via oxidation of glucose (and fats), is slower than by anaerobic systems, but the fuel supply is enormous. Aerobic athletes train their muscles differently, and indeed the muscle tissue itself is different from power athletes. Type I muscle fibers are known as “slow-twitch” because they have a slower speed of contraction than type II fibers (“fast-twitch”). Slow twitch fibers have less glycolytic capacity, but increased mitochondria, myoglobin, and aerobic enzyme pathways.

Thus, “slow twitch” athletes cannot generate the speed and force of their “fast twitch” cousins, but they can do their thing for a long time. If an endurance athlete needs to dip into the anaerobic range, for a sprint or hill climb, the needed extra energy primarily comes from anaerobic glycolysis of glucose (yielding lactic acid, and that wonderful muscular “burning” sensation.). The ATP-creatine system is not important for endurance athletes.

Diagram 2 illustrates the energy pathways that are the most important for all-out exercise of differing times. This diagram represents somewhat of an oversimplification since, in reality, aerobic pathways are used even in very short duration, high intensity exercise (e.g., 10 seconds), but to a small degree. The longer that exercise goes on the greater the proportion of energy acquired from aerobic glycolysis.

Aerobic endurance athletes, such as distance runners and triathletes, represent a much different picture from power athletes. Their levels of ATP and phosphocreatine don’t change during exercise because ATP is generated at the same rate it is used -- a “pay as you go” mechanism. Aerobic generation of ATP, via oxidation of glucose (and fats), is slower than by anaerobic systems, but the fuel supply is enormous. Aerobic athletes train their muscles differently, and indeed the muscle tissue itself is different from power athletes. Type I muscle fibers are known as “slow-twitch” because they have a slower speed of contraction than type II fibers (“fast-twitch”). Slow twitch fibers have less glycolytic capacity, but increased mitochondria, myoglobin, and aerobic enzyme pathways.
Where does creatine come from?
The creatine that is normally present in human muscle may come from two potential sources, dietary (animal flesh), and/or internally manufactured. What isn’t present in the diet is easily made by the liver and kidneys from a few amino acids (glycine, arginine, and methionine). A 70kg adult has about 120g of creatine in the muscles, and the daily turnover is roughly 2g. About half of this is replaced by the diet and half synthesized endogenously. The exogenous intake of creatine appears to exert negative feedback on the endogenous production of creatine (i.e., more creatine present in the diet means less production by the body). Creatine is eliminated from the body by the kidneys either as creatine, or as creatinine, which is formed from the metabolism of creatine.

What about creatine supplements and performance?
In the early 1900’s it was discovered that increased dietary creatine resulted in increased muscular stores of creatine and phosphocreatine. A study published in 1992, demonstrated approximately a 20% increase in total creatine stores in subjects fed 20 g of creatine per day for several days (1). This increase appears to be the upper limit and it has been shown that, even over a few days, a progressively increasing percentage of supplemented creatine ends up in the urine (1).

Since creatine supplementation increases muscular creatine levels, the next logical step would be to see if this helped athletic performance. From the brief discussion so far, one might expect that power athletes would benefit, and endurance athletes, not. Indeed, the exercise studies to date have confirmed that supposition.

Brief, intermittent high-intensity exercise.
A variety of protocols have been used to study the effect of creatine supplementation of brief, intermittent, high intensity exercise. Some of the exercise protocols which have shown improvements in performance are listed below, with indexed references. The most common method of supplementation used a 5 or 6 day loading period, consisting of approximately 20 grams of creatine per day.

1. Five sets of 30 maximum voluntary knee extensions, with 60 seconds rest between sets. (2)
2. Ten x 6 second bouts with 30 seconds rest. High intensity work on a bicycle ergometer. Placebo controlled, double-blind study design.(3)
3. Bench press; 5 sets to failure (predetermined 10 rep maximum), with 2 minute rest periods. Jump squats; 5 sets of ten, with 2 minute rest periods, using 30% of each subjects predetermined 1 rep. maximum. Placebo controlled, double-blind study design. (4)
4. Maximum continuous jumping exercise; 45 seconds. All-out treadmill running (approx. 60 seconds), at 20 km/hr, 5 degree incline. Placebo controlled, double-blind study design. (5)
5. Cycling to exhaustion at 150% peak VO2 at several different protocols; non-stop (a), 60 seconds work / 120 seconds rest (b), 20 seconds work / 40 seconds rest (c), and 10 seconds work / 20 seconds rest (d). Group D showed the greatest improvement with creatine supplementation. Placebo controlled, double-blind study design. (6)

It is interesting to note that one study, which looked at intermittent, high intensity work, found that caffeine completely abolished the ergogenic effect of creatine supplementation (7). Despite this, some of the commonly available supplements, such as powdered drink mixes possessing many ingredients, contain both creatine and caffeine!
Endurance exercise and creatine supplementation

As expected, the studies which looked at endurance exercise failed to show any benefit of creatine compared to placebo. In fact one study, which measured running performance over a 6 km course, found slower times in the creatine supplemented group (8). This effect is possibly related to the weight gain (mean 1 kg) associated with creatine use. Since the creatine-ATP system is not used by endurance athletes, the weight gain is “dead weight” -- it adds nothing to moving the athlete forward. Instead, the extra weight makes the athlete less efficient.

Side effects and adverse reactions to creatine supplementation

Short term (less than 2 weeks) exercise studies have not reported any adverse events associated with creatine supplementation. There have been no long term studies done to evaluate the safety of prolonged administration. This is unfortunate because increasingly more and more athletes are taking creatine supplements for longer periods. Anecdotal reports have begun to emerge and have noted increased muscle cramping (especially during exercise in the heat), nausea and other gastrointestinal disturbances, elevated liver transaminases, and acute renal injury.

Creatine supplementation, in the dosages commonly used, results in urinary concentrations that are 90 times greater than normal. The long term effects of this have not been investigated, but there is possibility for a variety of nephrotoxic, i.e., kidney damaging, events. There is potential for direct toxicity on renal tubules where urine is formed, and for acceleration of kidney stone formation. Recently, a baseball player for the Houston Astros was determined to have suffered from dehydration, kidney stones, and transient kidney damage as the result of creatine supplementation. Additionally, the recent deaths of 3 collegiate wrestlers, during deliberate dehydration to make weight cutoffs, are being investigated to determine what role, if any, creatine supplementation may have played.

Impurities are present in virtually every manufactured product, and in some cases, even though the product may be considered harmless, the impurity is not. Such was the case in the late 1980’s when an epidemic of cases of eosinophilia-myalgia syndrome, including over 30 deaths, were blamed on a contaminant present in L-tryptophan (9), an amino acid supplement widely taken as a sleep aid. Creatine, and other such supplements, are not regulated by the FDA. No published investigation has been conducted on creatine to determine what impurities might be present in creatine supplements, and what their long term effect might be.

Currently, there are 2 studies, due to be completed in 1999, specifically designed to determine longer term toxicity of creatine. The bottom line is that, at this time, no one can confidently state that prolonged creatine supplementation is safe. Its use would best be avoided until more data can be compiled. Prolonged administration is, in essence, an uncontrolled toxicity study -- and one which might yield harmful results. Is it worth the risk? Remember, it’s your body!
References


Text references used in this review

