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Biology

Advanced
Unit 5: Energy, Exercise and Coordination

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Scientific Article for use with Question 7

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Scientific article for use with Question 7

Superhuman: what gives elite athletes the edge?

1. Even if you're not a cycling fan, it's hard not to marvel at the amazing physical prowess of the Tour de France finalists. They will cross the finishing line having cycled 3553 kilometres in just 23 days. They will have climbed mountain passes more than 2000 metres high and averaged a speed of around 40 kilometres per hour.

2. Tour de France cyclists aren't the only people to have performed feats that seem superhuman to the rest of us. For example, Dean Karnazes, a 44-year-old ultramarathon runner from San Francisco, ran 50 marathons in 50 US states in 50 consecutive days, before running half the way home, from New York to St Louis, Missouri.

3. Some say many extreme endurance athletes are drugged up to their eyeballs. Tour de France winner, Floyd Landis was stripped of his title because he failed a drug test. His predecessor, Lance Armstrong, was also accused of drug abuse, though he has always denied the allegation and has never failed a drugs test. Armstrong famously won the title seven times in a row, and all this after being diagnosed with testicular cancer nine years earlier and having extensive chemotherapy and surgery. Yes, the spectre of performance-enhancing drugs looms large over extreme competitive sports, but could there be a more natural explanation for some athletes' incredible abilities?

Double-edged sword

4. One possibility is that some people are simply natural born superhumans. Sure, training and mental drive play major roles, but – all other things being equal – the key to gaining the ultimate competitive advantage might be hidden in our genes. It's not just a matter of long legs and large muscles: it seems the one thing many elite endurance athletes appear to share is incredibly efficient cellular mechanisms for producing energy.

5. That head start may come at a price. The genes that bless you with superhuman powers of endurance can also be a curse. Researchers have found that individuals with these genes who don't engage in regular exercise could be increasing their chances of suffering from obesity, diabetes and cancer. If you enjoy sports, on the other hand, but don't have the genes to be superhuman, all is not lost. Some researchers are developing supplements and gadgets (see "Cool it") that can enable you to temporarily become almost as good.

6. The Tour de France is one of the toughest physical endurance challenges in the world, so its cyclists are good subjects for studying the biology of extreme endurance athletes. At the top of the pack is Armstrong, one of the world's most successful extreme sportsmen. His innate physiology already sets him apart from the norm. Armstrong was born with a larger than average heart and lungs – a characteristic common among top competitive cyclists, marathon runners and freedivers. This means the rate at which oxygen is pumped around his body is greater than that of ordinary people.

7. To be an extreme endurance athlete, your body needs to be super-efficient at making energy, and blood oxygen levels are the key to that. Cells make energy in one of two ways. For quick bursts of power, they can burn carbohydrates without oxygen – known as anaerobic respiration. This is an inefficient process that generates lactic acid, which contributes to muscle tiredness but this respiration is a key source of energy for sprinters and weightlifters. Cells normally use aerobic respiration – a slower process using oxygen and glucose or fats. Endurance athletes generate most of their energy this way.

8. The maximum rate at which your body can transport oxygen to your muscles and then use it to convert fuel into energy is called the VO_2max, and is a measure of the volume of oxygen per kilogram of body weight per minute. The average healthy male has a VO_2max of between 40 and 50 ml/kg/min, which may climb to around 60 to 65 after prolonged training. When fully trained, Armstrong had a VO_2max of 83.8, and other top athletes have similar scores. Bjorn Daehlie, a Norwegian cross-country skier who holds the record for the most medals won at the Winter Olympics as well as the greatest number of golds, reportedly had a VO_2max of 96 – the highest ever recorded – and the earlier Tour de France record-holder, Miguel Indurain, came in at 88.

9. Edward Coyle of the Human Performance Laboratory at the University of Texas at Austin predicts that even if Armstrong was a couch potato, his VO_2max would not drop below 60. It's not just training, Coyle says. Armstrong is genetically predisposed to be above average.

10. So what other physiological advantages do these elite athletes have? Craig Atwood, an endocrinologist at the University of Wisconsin-Madison, thinks that in Armstrong's case there are some special circumstances. He has a controversial hypothesis: it's all down to the loss of his right testicle. "One of the interesting things about Lance Armstrong is that he went from being an exceptional one-day athlete before his surgery for cancer, to becoming a three-week endurance champion afterwards. The removal of his testicle may have produced changes in the levels of his hormones, which may have affected his metabolism."

11. Fat and glucose are what our bodies use for fuel. Small amounts of glucose are stored in the muscle in the form of glycogen, which is a more accessible fuel than the fat stored around the body and produces more energy per molecule of oxygen. However, it is in limited supply. This means that unless endurance athletes keep their nutrient intake up, they can use up their stores of glycogen during the race, resulting in extreme fatigue – known as "hitting the wall".

12. Atwood thinks the hormonal changes Armstrong underwent when he had a testicle removed may have enabled him to use more fats than he would otherwise have been able to. Studies of non-athletes who have had a testicle removed suggest that after surgery there is an increase in the levels of certain hormones called gonadotropins, which are known to boost fat metabolism. Levels of testosterone, a muscle-building hormone, remain about the same (*Medical Hypotheses*, vol 68, p 735).

13. A similar thing happens as men age: the rate at which their testicles produce hormones that would normally limit gonadotropin production, including testosterone, slows down. "In a sedentary individual, these changes will allow for the mobilisation and laying down of fat in different areas of the body, typically around the waist, as seen in older men and women," says Atwood. "However, if these changes occur in a young and active person, a lot of the free fatty acids can be taken up by the muscle and used as a source of energy."

14. Atwood thinks this may have helped Armstrong race harder on successive days, because his muscles would use the excess free fatty acids instead of the glycogen stores in his muscles, meaning he would have less glycogen to replenish at the end of each day. "Winning a Tour de France is all about recovery," says Atwood. "These guys have 18 hours in which to replenish their glycogen stores between stages. If you can't fully recover in that 18-hour window then you're obviously not going to do as well."

15. These hormone changes could also help explain why endurance capacity reaches its peak in most men at around 26 years old, when gonadotropin levels naturally start to increase, Atwood says. This peak is maintained for around five years. It may be no coincidence that the vast majority of Tour de France winners have been aged between 27 and 32.

16. Though direct evidence is lacking, Atwood's hypothesis does have a scientific basis. For example, a study in which an emulsion containing fatty acids was injected intravenously into athletes' bloodstreams before exercise showed an increased use of fatty acids and a decreased use of glycogen as a fuel, according to Trent Stellingwerff, formerly of the Department of Movement Sciences at Maastricht University in the Netherlands and now at Nestlé's Physical Performance and Mobility group in Lausanne, Switzerland. "However, despite strong evidence for glycogen sparing, there appears to be no consistent effect on exercise performance, with evidence actually showing a decrease in sprint performance," he says.

17. The biggest question is whether the hormone changes would affect how fast fat burns during exercise, says Lawrence Spriet at the University of Guelph in Ontario, Canada. It is possible that the loss of a testicle produces hormonal changes that alter metabolism at rest, but during exercise the "fight-or-flight" hormones – adrenalin and noradrenalin – become dominant in controlling the release of fatty acids, he says. "All other influences appear to be overridden."

18. There is also no guarantee, he adds, that increasing fat supply to the muscles would increase the uptake of fatty acids in the mitochondria – the cell's energy generators. Although some researchers are looking for other ways to increase the amounts and types of fuel that muscles can use (see "Energy bar"), for now the easiest way to improve your energy-producing capacity is to make more mitochondria and/or increase the size of the existing mitochondria, Spriet says. This is precisely what happens over the course of an intensive training regime.

19. Coyle agrees. Armstrong certainly has genetic potential, as his unusually high VO_2max shows, he says, but it's the years of training that have stimulated changes in his muscles, not the surgery. Between the ages of 21 and 28, when Armstrong won his first Tour de France, Coyle recorded an 8 per cent improvement in the power of his muscles. He also lost a relatively large amount of body fat, so his muscles had less weight to carry, resulting in even more effective power (*Journal of Applied Physiology*, vol 98, p 2191).

20. Coyle suggests greater muscle efficiency may also be linked to an increase in the percentage of "slow" muscle fibres, which tire less quickly than their "fast" counterparts and are therefore good for endurance activity. Such changes have been seen in rats during periods of extreme endurance training.

21. There is one other factor that singles Armstrong out from most of his contemporaries. When Coyle measured the level of lactic acid – a by-product of glycogen metabolism – in Armstrong's muscles after exercise, he found it was much lower than in any other competitive cyclists he had tested.

22. Until recently, it has been assumed that lactic acid, or lactate, is a bad thing, causing muscle fatigue and cramps. However, there is growing evidence that it can also act as an extra source of fuel – if your body has learned how to use it. Last year, George Brooks at the University of California, Berkeley, and his colleagues showed that muscle cells can reuse lactate by transporting it from the cytoplasm – the gelatinous fluid that fills cells – into the mitochondria, which use it to produce energy. Endurance training seems to increase the amount of lactate that is taken up by mitochondria, though it is probably also the case that some people's mitochondria are just naturally better at doing it, says Brooks. Efficient lactate use would be indicated by low levels of it in the muscles after exercise – as seen in Armstrong. "I would guess that Armstrong is a master of lactate clearance, both innate and acquired," says Brooks.

23. Lactic acid isn't the only cause of muscle fatigue. Andrew Marks at Columbia University in New York and his colleagues have discovered that a key factor in both muscle fatigue and how heart muscle responds after a heart attack is the development of a leak in a specific class of calcium channel in muscle cells. In both cardiac and skeletal muscle, contraction depends on the release of calcium stores from inside muscle cells. With muscle fatigue, one of the proteins that controls the channel gets used up, "so you end up getting a constant leak of calcium out of the channel, meaning the muscle no longer contracts properly", says Brett Giroir of the US Defense Advanced Research Projects Agency's Peak Soldier Performance programme, which part funds Marks's work. Marks has now developed a drug that stops this leakiness in heart muscle and is testing it to see if it can stop skeletal muscle from fatiguing so quickly.

The endurance gene

24. Researchers have yet to identify gene variants that predispose an individual to more efficient lactate use or less leaky muscles. However, the search for other genes that might influence athletic performance is well under way and there seem to be a number of likely candidates.

25. One of the best studied of these genes is *ACE*, which codes for the production of angiotensin converting enzyme, which helps to regulate blood pressure. It is also thought to influence how efficiently cells use oxygen, although exactly how is not fully understood. Nevertheless, there is evidence that one variant, labelled II, is more common in endurance athletes, while another variant, labelled DD, is associated with good performance in sports in which bursts of speed are needed, like football or sprinting.

26. The II variant also appears to be more prevalent in mountaineers, suggesting that it may help people adapt to low oxygen.

27. A better understanding of the factors that enable mountaineers to cope with low oxygen could help people in critical care. Clarifying the links between genetic disease and exercise could also enable genetic screening of individuals whose health may be put at risk by engaging in a particular sport. For example, one variant of the *APOE* gene, which is thought to be important for brain-cell repair, is associated with a neurological disorder called chronic traumatic encephalopathy – or "punch-drunk" syndrome – and Parkinson's syndrome, both of which can develop if you suffer repeated blows to the head (*The Journal of the American Medical Association*, vol 278, p 136). People with this variant should therefore avoid contact sports such as boxing and rugby, says Kathryn North of the University of Sydney, Australia.

28. Eventually drugs could be developed that would reduce these risks – a kind of tailored medicine for sportspeople, says Mike Grocott of the UCL "Extreme Everest" team. "If you were going to play rugby and you knew that you were at high risk of injury, you might take a medicine beforehand to compensate for your particular weakness."

29. Whether genetic screening could be used to identify children with the potential to become world-class athletes remains to be seen. Its success would depend on the relative importance of individual genes to elite athletic performance. "If there were a small number of genes with large effects, then tests could be quite valuable," says Claude Bouchard of Pennington Biomedical Research Center in Baton Rouge, Louisiana. "However, so far it seems that we are dealing with a large number of genes, each of which contributes 3 to 4 per cent, if that." North agrees: "Ultimately, there are likely to be around 50 genes that influence the elite athletic phenotype."

30. Genes may also influence factors such as how much your body responds to fitness training. Two genes in particular seem to influence a person's ability to increase the amount of blood they pump per minute through training – *titin*, which is involved in muscle contraction, and *kinesin 5B*, which transports large molecules around the cell.

31. So could coaches test for trainability and so tailor people's training programmes depending on their genetic make-up? "We just don't know at this stage," says Bouchard. North suspects it is possible. For example, erythropoietin (EPO) is a protein that increases the number of red blood cells in the body and therefore the amount of oxygen that can be carried in the blood. It can be increased artificially, which in professional sport is illegal, or naturally, through training at high altitude. If some individuals are genetically predisposed to produce more, or less, EPO than others they may respond differently to training in low oxygen – such as in a hypobaric oxygen chamber. Such simulated altitude training has been shown to improve speed, strength, endurance and recovery, and is practised by some athletes to improve their endurance ahead of competitions. How long the effects last is uncertain, however.

32. Unfortunately, having the right gene variants to be a superhuman endurance athlete is not necessarily all it's cracked up to be. Take energy efficiency. Some people's mitochondria are very efficient energy providers, while in other people they use more of the fuel to produce heat. Heat production is a natural function of these cell structures and is one of the main ways we keep warm in cold climates. Mitochondrial efficiency is very tightly linked to where in the world you come from: they are more efficient in people from warmer climates, and tend to produce more heat in people from cold climates, making them better able to tolerate the cold (see "Cool it"). That's not the case for everyone in cold countries, though. A study of elite Finnish athletes showed that all who excelled at endurance events had efficient mitochondria, (*European Journal of Human Genetics*, vol 13, p 965).

33. But these same highly efficient mitochondria may have a downside. They produce more reactive oxygen species – damaging free radicals – particularly if the energy they produce is not used up. So a person who eats a lot of chocolate and works at a desk, and yet has highly efficient mitochondria, is going to produce a lot of reactive oxygen species. This would make them more susceptible to a variety of degenerative diseases, cancer and premature ageing, says Douglas Wallace of the Center for Molecular and Mitochondrial Medicine and Genetics at the University of California, Irvine. It seems that if you're born with the genes for super-efficiency, you've got little choice but to exercise frequently to minimise the production of free radicals to stay healthy. Exercise hard, and you're more likely than the rest of us to reach the front of the pack.

34. "If Lance Armstrong never trained, an average young person would only be able to beat him if they trained as hard as they could," says Coyle. Even without practice, Armstrong could probably beat someone who had trained moderately. Of course, to train hard you obviously need the mental drive and a commitment to winning, something that is certainly true of Armstrong. "Again and again there are reports of Lance's incredible attention to every minute detail of his life leading towards getting himself ready for optimal performance," says Stellingwerff.

35. Whether the crowds at the Champs Elysées are about to see the next Lance Armstrong cross the finish line remains to be seen, because even if that person has the right physiology and is backed up by a crack team of coaches, nutritionists and sports scientists, it still might not be enough in the long run. "The best gene that you could find would be the mongrel gene that gives you the will to win," says North. "That is probably the most important factor of all."

Energy bar

The superfood that feeds both your muscles and your brain.

36. There are three main food groups: proteins, carbohydrates and fat. Now the US Defense Advanced Research Projects Agency (DARPA) is trying to create a fourth group. In doing so it hopes to provide soldiers, mountaineers and athletes with an extra source of energy and a means of maintaining their peak physical performance for longer.

37. During exercise, your muscles get most of their energy by burning a mixture of carbohydrates and fat. But if you are starving, the body begins to get extra energy from ketone bodies, acidic chemicals produced when the liver breaks down fatty acids. These are particularly important for the brain, as they can cross the blood-brain barrier and keep it supplied with energy.

38. Ketone bodies are not usually produced in large amounts, and they are not easy to get from food. But they are a more efficient source of fuel than fatty acids.

39. "The question we asked ourselves was 'can we fundamentally modify a person's diet to maintain their peak performance for longer?'" says Brett Giroir, manager of DARPA's Peak Soldier Performance programme. For the past few years, Kieran Clarke and her colleagues at the University of Oxford have been collaborating with DARPA to find forms of ketone bodies that could be taken up by the gut and used as a fuel.

40. "You can't give pure ketones, because they are too acid, and they would get used up very quickly," says Clarke. Instead, her team has created "ketone polymers" – chains of ketone bodies that can be broken down over time to create a sustained release of ketones.

41. Rats fed with ketone polymers ran 30 per cent faster and 30 per cent further on a treadmill on five consecutive days than those fed carbohydrates or fat. They also showed enhanced cognitive abilities. Human trials of the polymers are expected to start this year.

Cool it

Smart gloves keep exhaustion at bay

42. Working in the desert is tough. Temperatures can reach 50 °C in the daytime and drop to freezing at night. Troops deployed there often suffer from heatstroke, and sometimes even hypothermia. Craig Heller and his colleagues at Stanford University wanted to find a way of rapidly heating or cooling people to tackle bouts of both conditions. In doing so they discovered that cooling people down also increased their athletic endurance.

43. You can divide the human body into an inner core of the internal organs and an outer shell consisting of the skin and peripheral limbs. If you want to heat someone up by applying an external heat source, you usually have to heat up the entire shell. There is an exception, though. Specialised blood vessels exist in the palms of the hand that act as radiators, enabling the body to shed large amounts of heat very quickly. Using suction on the hand to open up these vessels seems to intensify the effect, while heating or cooling it at the same time provides a rapid way of directly controlling the body's core temperature. Heller's team has now developed a glove that does just that. Tests indicate that it could be useful for warming patients with hypothermia.

44. Conversely, cooling people's hands as they exercise increases their endurance. In treadmill tests, people who were exercised to exhaustion were able to last between 50 and 100 per cent longer if one hand was cooled at the same time. "We've done this time and time again and what it all points to is that the work capacity of an individual is limited by the heat of the muscle," he says.

45. Heller is now being funded by the US military to see if the glove could be used to improve the endurance of troops in the heat. He is also working on reducing its size, as at the moment it is about the size of a large coffee pot.

46. Heller's glove may also have important medical uses. "People with multiple sclerosis are incredibly sensitive to temperature," he says. "For them, walking down the block can be like climbing Mount Everest – if it's hot they just can't do it." In a recent study on 12 people with MS, Heller recorded a 35 per cent increase in their times on a treadmill test of endurance.

Superhuman: The secrets of the ice man

47. Perched on the edge of an Antarctic ice sheet, Lewis Gordon Pugh surveys the waves. At 0 °C, water does not get much colder than the sea beneath him. Undeterred, Pugh unzips his jacket, strips down to his swimming trunks and dives in.

48. Most of us would start to hyperventilate uncontrollably if we dived into such cold water. Pugh doesn't even gasp in pain but instead starts swimming. In December 2005, when Pugh took this plunge (pictured above), he went on to swim a kilometre in just over 18 minutes. Many ordinary people would drown after just a few minutes in such cold water. Pugh, however, not only survived but went on to make several more long-distance swims in extremely cold water. So what makes him able to keep swimming in such extreme cold?

49. A study of Pugh has confirmed that his response to cold water is anything but normal. Remarkably, though, while Pugh may have some innate advantages, it seems his near-superhuman ability is largely down to training – so perhaps it could be something we are all able to learn.

High metabolism

50. Pugh is far from the first to swim in icy water. There is a long tradition in Russia, China and many northern European countries of carving holes in frozen lakes, rivers or sea ice and diving in, often as part of a cultural or religious ritual. These are normally just quick dips, though: rarely do they involve distance swimming. Japanese and Korean pearl divers used to swim without wetsuits in temperatures of around 10 °C for up to 30 minutes. Part of their secret is their metabolism: the colder the water that Japanese Ama divers swim in during winter months, the higher their resting metabolic rate.

51. Even so, studies of Japanese Ama divers who have been diving for many years show that their response is not that different from the rest of us. Their core body temperature drops to 35 °C after 30 minutes in cold water – just above hypothermia, the point beyond which the body cannot warm up again without help. In contrast, Pugh can keep his core temperature as high as 36 °C even after swimming for 30 minutes in much colder water. How does he do it?

52. His background seems ordinary enough. Born in 1970 near Plymouth, in south-west England, he went to boarding school at the age of six. It wasn't until later, when he moved to South Africa, that he fell in love with swimming. At the age of 17, one month after his first proper swimming lesson, Pugh took part in an organised 7-kilometre swim from Robben Island – where Nelson Mandela was held for 18 years and the water is a chilly 12 °C. Back then he wore a wetsuit, but he says the swim planted the seeds of a passion for long-distance swimming and a desire to set new records.

Mental preparation

53. Over the past 20 years he has taken part in 17 long-distance swims, including across the English Channel, along the whole of the river Thames from Kemble to London, and a 204-kilometre, 21-day swim along Sognefjord in Norway. During his travels he began noticing the effects of climate change such as melting ice caps and retreating glaciers, and decided to use his ever more extreme swims to raise awareness of the state of the planet – culminating in two long swims in the Antarctic and the Arctic.

54. It takes more than ideological conviction to survive icy waters, though. Pugh attributes his success to intense mental preparation. In the weeks building up to a swim he will spend up to 4 hours a day with a coach, going through mental exercises to calm him and focus his mind on the task. These include concentrating on emotionally challenging periods of his life to build up a sense of determination that will help him succeed. "I think about every part of the swim, how it will occur from beginning to end. I hear the sound of my stroke in the water and I feel ice on my skin," he adds.

55. As the swim gets closer, he psychs himself up by listening to music by the likes of Eminem and P. Diddy. In the minutes before entering the water, Pugh recalls these emotions and is able to raise his core temperature, without doing any physical exercise, to 38.4 °C. That's an extraordinary 1.4 °C above his normal body temperature. Such "anticipatory thermogenesis" has been observed before, but not to such a high degree, says Timothy Noakes, a sports scientist at the University of Cape Town, South Africa, who has been studying Pugh as he swims.

Adrenalin

56. Other experiments found that injections of adrenalin (epinephrine) can induce this effect in Russian cold-water swimmers. Noakes speculates that Pugh may somehow be tapping into this mechanism during his pre-swim preparations.

57. Pugh has a number of other surprising skills. For example, instead of gradually lowering himself into the cold water, he dives straight in, which in most people would induce a cold shock response, the most common cause of death in icy waters, says Michael Tipton, a physiology researcher at the University of Portsmouth, UK.

58. Usually when nerves on the surface of the skin sense a sudden and massive drop in temperature, they trigger uncontrollable and involuntary hyperventilation. Swallow water during this stage and you can quickly drown. The blood vessels to extremities also narrow to reduce the flow of blood – and heat – away from vital organs. The sudden rise in blood pressure can trigger a heart attack.

Cold shock response

59. It is possible to become habituated to the cold so the initial cold shock response doesn't kick in quite so dramatically. But Pugh seems remarkably resistant, although even he does find breathing difficult for the first few minutes. "I certainly feel the cold," he says, "It's excruciatingly painful."

60. People who survive the initial shock of entering very cold water face another problem: as your limbs and muscles cool, the nerves are affected, which makes coordinated movements such as swimming harder and harder. Pugh, however, seems able to cut the supply of blood to superficial muscles while keeping the deeper ones warm, an ability also seen in the Ama divers.

61. Pugh does have one skill that has so far defied scientific explanation: when swimming he can stop himself shivering. Normally, shivering is an involuntary response to cold that kicks in once core body temperature drops below 36.6 °C or when skin temperature falls below 28 °C. This is usually beneficial, as the muscle contractions generate heat, but in cold water it only serves to increase the rate at which the body cools, Noakes says. That's because the increased blood flow transfers more heat from the core to the body's extremities. Somehow Pugh manages to avoid shivering even when his core temperature is below 36.6 °C and his skin temperature is around 5 °C.

Close to disaster

62. Even Pugh has his limits, though. He came close to disaster during a swim across Whaler's Bay off Deception Island in Antarctica. Thirty minutes into the swim, his core temperature started to drop rapidly. By the time he left the water a few minutes later it had plunged to a dangerous 33.6 °C. "If he swam for another 2 or 3 minutes his temperature would have dropped much further and he would have probably lost consciousness," Noakes says.

63. Undeterred Pugh went on to complete several more ice swims. In 2007 he swam 1 kilometre in the coldest water yet – a glacial -1.7 °C – at the geographic North Pole.

64. "When I went below 0 °C the cells in my fingers started to freeze. It took another four months before I could feel my hands again," he says. After reaching his goal of swimming both in the Arctic and in Antarctica, Pugh has for now hung up his towel.

Acknowledgements

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