GOT THE MOVES?
How your body fuels an active life
All living things move. Whether it’s a plant growing towards the sun, bacteria swimming away from a toxin or you walking home, anything alive must move to survive. For humans though, movement is more than just survival – we move for fun, to compete and to be healthy. In this issue we look at the biological systems that keep us moving and consider some of the psychological, social and ethical aspects of exercise and sport.

Moving figures
A numerical look at exercise, energy and movement

**WHAT IS ATP?**
ATP stands for adenosine triphosphate, a molecule involved in the transfer of energy in living cells.

**ATP MOLECULES PER SECOND**
9000000
0000000
0000000

The number of ATP molecules made per second in humans. Source: Nick Lane, Power, Sex and Sacro

**PERCENTAGE OF BODY FAT**
18–24%
25–31%

Percentage of body fat classed as ‘average’ for men (left) and women (right). Source: www.sheff.ac.uk/lsf/bi1s12/whats-the-guideline-for-percentage-of-body-fat

**DISCOUNTING FAT, THE BODY CONSISTS OF...**
Skin 8.5%
Bone 20.6%
Muscle 50%
Other* 20.9%

* Undifferentiated tissue, such as organs, spinal cord and gastrointestinal tract. Source: www.sfh.cz/~vard/Cadavre.pdf

**ATP TURNOVER, MARATHON RUNNER VS. SPRINTER**

A marathon runner needs about 10 g ATP/second. Muscles’ total ATP content is about 50 g, which is used up in a second by a sprinter. Source: Guy Brown, The Energy of Life

**ENERGY USED IN DIFFERENT ACTIVITIES**

The energy we use expressed as multiples of our resting metabolic rate – metabolic equivalent of task (MET). Source: sites.google.com/site/compendiumofphysicalactivities

**REACTION TIME BY AGE**

In milliseconds, averaged between sexes and rounded. Source: wellc.me/u8gWRR

**FINDING DATA**

Putting this diagram together, we found that different sources gave different numbers for the same thing. Why don’t they match?

Well, data can be interpreted in different ways, and estimates can be made using different methods and/or baseline data. Definitions matter, too – different sources might define ‘exercise’ or ‘adult’ differently.

Which should you choose? The source itself is important – is it reliable? Are the figures recent? How might an organisation’s ‘agenda’ affect how it calculates and presents data?

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Source: www.sfu.ca/~ward/Cadavre.pdf
Animals swim, creep, fly, walk or run to find food and shelter, to hunt and fight, and to escape from danger. Humans move for the same reasons, but there are peculiarities about our locomotion. The reasons for the way we move and how we developed our upright gait are still argued about by researchers.

BARE BONES
What are our skeletons for?
If your skeleton were taken away, your organs would be in an untidy heap on the floor. But your skeleton is much more than a simple support for your softer parts – it transmits force and providing leverage, it allows you to move. The centres of the long bones (such as those in the arms and legs) are hollow, which makes them strong yet light. The cavity inside the bone is filled with bone marrow, where blood cells are made. In childhood, the ends of the long bones in our arms and legs, which normally go on growing for 17 years or so, are made mainly of cartilage. This softer tissue gradually becomes calcified as it turns into the solid, but still spongy, tissue of mature bone. By then, cartilage is left only at the ends, where it eases joint movements. Even when calcified, bones are still living tissue. Bone – particularly the protein and mineral of the bone matrix – is continually remodelled and replaced in response to the stresses and strains of movement.

TWO LEGS GOOD?
Why did humans evolve to be bipedal?
Most animals get around fine on four, six or eight legs. So what made us bipedal, walking and running on just two? It is unlikely that we will ever know the real answer, but by studying our closest living relatives, the great apes, alongside fossil data, we can begin to build a picture of how our common ancestor may have moved. One prevailing current theory is that we evolved from an ancestor that moved around using quadrupedal knuckle-walking, much like our African ape relatives (chimpanzees, bonobos and gorillas) do today. Later, our ancestors stood up and began to move around on two legs. Various reasons for this have been proposed, including improved carrying ability or reaching food on low branches from the ground. Recent fossil evidence, however, suggests that we spent more time in the trees than previously thought. Orang-utans are the most arboreal (tree-dwelling) of the great apes, and recent studies show that they use a human-like form of straight-legged bipedalism to move around on the very thin branches in the trees to obtain food. So, we might even have been using some form of bipedalism before we came down to the ground.

CHANGE IS AFOOT
What changed when we began to walk on two legs?
The switch to modern human locomotion goes along with a set of changes in our skeleton, tendons, ligaments and muscles. We are adapted for walking, but we are also adapted for upright running. Compared to other running animals, humans are poor sprinters but outstanding long-distance runners. We stay cooler and tire less quickly than quite a few animals that are prey for hunter-gatherer tribes. Some tribes, including those in the Kalahari Desert, still catch their meat by running down animals such as deer and antelope.

One of our bipedal ancestors was Australopithecus afarensis, which lived between two and four million years ago. Modern humans’ anatomy has changed, making running easier for us than it would have been for Australopithecines. These modifications include changes to the head, shoulders and spine, a longer trunk and legs, shorter forearms and larger, more muscular buttocks. We also have a longer, more elastic Achilles tendon and have undergone changes to the heel bone and big toe. There was also a complex series of changes in the bones of the pelvis, including it becoming narrower, which probably gave increased running efficiency. Because babies pass through the pelvis, humans had to enter the world earlier and earlier in gestation as their brains increased in size. Otherwise, birth would have been too risky for mother and child. Our newborn helplessness, and long dependency as infants, may come from the shift to an upright stance.

MAKE OR BREAK
What factors affect bone strength?
What we eat and how much we move about affects how strong our bones are. Jumping strengthens the bones more than running, for example, because the bones are under a greater load. More than two-thirds of bone by weight is made of calcium phosphate crystals embedded in the matrix that bone cells build. High-calcium foods and drinks like cheese and milk help raise peak bone mass, a key factor in delaying the onset of osteoporosis. Vitamin D is important, too, because it helps calcium absorption. We make most of the vitamin D we need through exposure to sunlight. Darker skin takes more time in sunlight to make vitamin D than lighter skin, so some dark-skinned people living in temperate countries may need extra vitamin D in their diet to make up for the lack of strong sunlight.

WALK LIKE A MAN
What steps are involved in walking?
Walking may seem as simple as putting one foot in front of the other. Analyse the motion, though, and at any one time you are balanced on one leg as you move forward. That leg pushes around the planted foot and transmits force from the ground up to your hipbones, initially slowing you down. As you do so, you also push upwards, then you start to accelerate again. You might simply fall forwards, but you swing the other foot in front of you just in time to begin the next step. The degree to which bouncing, by flexing tendons in the leg and foot, is involved in walking (as it definitely is in running) is still being studied by biomechanics experts.

Watch a toddler taking their first steps, or someone recovering from a stroke learning how to walk again, and it’s clear that the co-ordination needed is tricky to master. Constant small adjustments are needed to keep a person upright and moving forward. The patellar, or knee-jerk, reflex is routed through the spinal nerves for speed so that it can contract the thigh muscles almost instantly when the foot is loaded. Without that contraction, you would stumble at every step. Walking also needs good proprioception, or a sense of exactly where your body is in relation to your surroundings. Losing this sense is why you lose your footing if there is one more – or one less – step in a flight of stairs than you thought. Robots that mimic human walking are now available. For one example, see www.andrew.cmu.edu/user/shc17/Robot/Collins_2005_Science.pdf

OUT OF THIS WORLD
Long-term low gravity can seriously affect us
When we move around in low or zero gravity, the mechanical strain applied to our skeleton is much lower than on Earth. This is why moving around in low-gravity environments, such as space, gradually depletes bone mass. Muscle atrophy (wasting) is also a problem and begins even on short missions (see more on muscles on pages 6 and 7). Crew on the International Space Station can spend six months in orbit and have to exercise for hours every day on special equipment to reduce muscle loss; they also have to follow an exercise programme when they return to Earth. A human mission to Mars would take almost a year, and mission planners will have to devise some high-tech gym kit on the craft to maintain the muscles and bones of those on board.

THINNING BONES
Age and diet can contribute to thinning bones
Bone strength is maintained if bone is replaced at the same rate as old bone is removed. When the laying down of new bone cells slackens, the bones become thinner. In our late teens, the mass and density of our bones reaches its peak, then slowly declines with age. Older people, therefore, have thinner bones, combined with a decrease in muscle mass, this leaves elderly people prone to injuries from falls. Some 75 000 broken hips are treated in the UK per year – mostly in older women. The depletion of bone is known as osteoporosis and is more common in women, probably because of hormonal changes linked to the menopause. Very strenuous exercise can also disturb the balance between bone removal and renewal. In athletes this puts them at risk of stress fractures, which leave hairline breaks in bones put under load. There is evidence that some fizzy drinks can speed up bone thinning. In one study, regular cola drinking was linked to lower bone density in women, for example, although the reasons for this are somewhat unclear. It could be because cola features in diets that are otherwise low in calcium or because such drinks contain phosphoric acid, which is known to bind to calcium and magnesium in the gut, reducing absorption of the minerals.

MORE ONLINE: Read about which bones humans break most often and why at www.wellcome.ac.uk/bigpicture/exercise.
**MUSCLES AND MOVEMENT**

**KNOW YOUR TYPE**

*Our bodies contain three main types of muscle*

We each have hundreds of muscles, and these specialised bundles of proteins are involved in all kinds of biological processes – from locomotion to pumping blood around our body and from squeezing food through the digestive tract to controlling how much light enters the eye. So what do muscles look like? How are they made? How do they work?

**MUSCLE TYPES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal muscle</td>
<td>Mainly found in our limbs, used for movement and strength, controlled by the nervous system.</td>
</tr>
<tr>
<td>Smooth muscle</td>
<td>Found in the walls of blood vessels and digestive organs, involuntary.</td>
</tr>
<tr>
<td>Cardiac muscle</td>
<td>Specialised for pumping blood, involuntary.</td>
</tr>
</tbody>
</table>

**SKELETAL MUSCLE**

Skeletal muscle is the most dominant type of muscle and is responsible for generating force to move our bodies. It is under voluntary control, meaning we can decide when and how much of it to use. Skeletal muscles make up about 40% of our body weight and consist of many individual muscle fibres, each of which is made up of muscle cells. When a muscle contracts, the ends of the muscle fibres come closer together, shortening the muscle. This is achieved through a process called muscle contraction, which involves the interaction of two proteins: actin and myosin. When myosin interacts with actin, it causes the muscle to contract, generating force.

**SKELETAL MUSCLE FIBRES**

Skeletal muscle fibres are classified into two main types based on the speed at which they can contract:

- **Fast-twitch fibres** are faster to contract but fatigue quickly and are used for short, explosive bursts of power.
- **Slow-twitch fibres** are slower to contract but can sustain activity for longer periods.

**INHERITED VARIATION**

Muscle fibre types can be inherited. For example, some families have a higher proportion of fast-twitch fibres, which gives them an athletic advantage in certain sports. However, this variation is not always beneficial. For instance, some people may suffer from muscle wasting, or sarcopenia, which can be caused by a variety of factors, including age, disease, and disuse.

**MAKING MUSCLES**

Regular exercise can increase the size of muscle fibres by stimulating muscle growth. This process is known as muscle hypertrophy. To achieve muscle hypertrophy, it is important to perform resistance training, which involves lifting weights or performing exercises that challenge the muscles. The muscular response to resistance training is complex, involving changes in the number of muscle fibres (hypertrophy) and the size of individual fibres (fasciculation).

**WEIGHT TRAINING**

When performing weight training, it is important to choose the right kind of exercise. For example, if you want to increase muscle size, you should perform exercises that target a specific muscle group, such as squats for the legs or bench presses for the chest. The type of exercise you choose will depend on your goals and the muscle groups you want to develop.

**WASTING AWAY**

Muscle wasting, or sarcopenia, can be caused by a variety of factors, including age, disease, and disuse. It is characterized by a reduction in muscle mass and strength. One of the main causes of sarcopenia is disuse, which occurs when muscles are not used regularly. For example, bed rest can lead to significant muscle loss, especially in older people. Other causes of muscle wasting include illness, injury, and certain diseases.

**PHYSICAL ACTIVITY**

Regular physical activity, particularly resistance training, can help prevent muscle wasting. It is important to include a variety of exercises in your routine, targeting different muscle groups to ensure balanced muscle development.

**MORE ONLINE**

- [Check out our free ‘In the Zone’ experiment kits](http://www.wellcome.ac.uk/bigpicture/) for ages 14–16, explore the strength of your muscles and discover how they are used during movement. See more at [www.getinthezone.org.uk](http://www.getinthezone.org.uk).

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**FAST FACT**

Trim is a key part of stratified muscle, which allows muscles to stretch. Containing up to 35–300 amino acids and named after the Greek ‘trim’ (three), trim is the largest known human protein. Source: [www.expasy.org](http://www.expasy.org).

**ATHLETIC HEART SYNDROME**

Skeletal muscles grow if they are worked harder, and so does the heart. Muscles that are made stronger, or thicker, grow with more power. The left ventricle is the main pumping chamber of the heart, and athletes who train for hours every day tend to have more powerful left ventricles, with more muscle, thicker walls and a larger blood-pumping chamber. This goes along with a slower resting heart rate, as each beat moves more blood. These changes have been called ‘athletic heart syndrome’ and are normally harmless; however, athletic heart syndrome looks similar to several standard heart tests to an inherited enlargement of the heart muscle, hypertrophic cardiomyopathy, which can lead to heart failure. A small number of sudden deaths during sports events in people who seemed fit and had no diagnosis of heart disease are caused by cardiomyopathy. Athletes with enlarged hearts may find their doctors want to examine them very closely because of the similarities in appearance between the trained and malformed heart. A definitive difference is that an athlete who takes a break from training will find their heart revert to normal size, whereas the heart of someone with cardiomyopathy will not.

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**MORE ONLINE**

- [Visit our website](http://www.wellcome.ac.uk/bigpicture/) for more information on how muscles work and how they are used in everyday life.

---

**KNOW YOUR TYPE**

*Our bodies contain three main types of muscle*

We move our bodies using skeletal (voluntary) muscles, the only ones that we have conscious control over. Cardiac muscle in the heart and smooth muscle, which lines organs like the stomach, bladder and uterus, are involuntary. These muscles, controlled by the autonomic nervous system, work without our needing to think about them. There are many skeletal muscles, large and small. They all pull on bones for leverage but are adapted for different uses. ‘Slow’ muscle fibres have a richer blood supply and use oxygen to help release energy. ‘Fast’ fibres contract more rapidly and can use energy from organic molecules stored in their cells.

Most muscles have a mixture of fibre types, and some specialise in one type more than the other. The muscles that move your eyes, for example, contain mostly fast-twitch fibres. Think of chicken meat: chicken wings, used for short efforts in flight, have mostly fast-twitch muscle fibres. The breast meat is white because the wing muscles require relatively little oxygen. Chicken legs, by contrast, are contracting all the time and are mainly slow-twitch. Their oxygen use is greater and the meat is redder because it contains a greater concentration of the pigment myoglobin, which carries oxygen.

Naturally, people have different proportions of muscle fibre types. Different sports make use of different types too; for example, sprinters, throwers and weightlifters rely on bursts of power from muscles with a high proportion of fast-twitch fibres. Someone with many slow-twitch fibres is unlikely to break records over 100 metres, and someone with a higher proportion of fast-twitch muscle fibres will have a harder time getting in shape for a marathon. In both cases, though, training will make the person better at what they’re working towards and will cause changes in the appropriate type of muscle fibre.

Some differences in muscle type are inherited. In 2003, for example, one research group found that a variant in a gene affecting muscle fibres, known as ACTN3, was more common among a sample of elite athletes. The researchers then relaxed the muscle fibres slide past one another.

In skeletal muscle, the contraction is started by a rise in the concentration of calcium ions, triggered by the arrival of a neurotransmitter (a chemical signal) from the nerve ending that attaches to each muscle cell at the neuromuscular junction. The calcium ions, in turn, interact with two other proteins, actin and tropomyosin. These two proteins change shape to allow myosin to bind to actin. The myosin head binds to and hydrolyses the energy-rich chemical called adenosine triphosphate (ATP) in specialised muscle-wasting ‘slow’ protein diet is among its causes.

Just a few weeks’ bed rest during illness can cause long-lasting muscle loss, especially in older people. It is caused by the combination of a drop in manufacture of new protein and an accelerated breakdown of existing muscle fibres. The effects are worse in the legs and back, which still hold us up against gravity, and can quickly lead to immobility.

**INVOLUNTARY MOVEMENT**

Why do we sometimes move without meaning to?

The nerve impulses that make skeletal muscles move under conscious control, most of the time. Losing that control can be harmless, such as shivering in the cold, or more serious as a result of diseases that affect the nervous system. A well-known example is Parkinson’s disease, in which cells that make the neurotransmitter dopamine gradually disappear from one brain region, the substantia nigra. Early symptoms of Parkinson’s disease include too much movement (shaking) and too little (freezing or rigidity). In cases of Tourette syndrome, movement is normal most of the time, but people with this complex condition sometimes have involuntary, repetitive tics, often involving the facial muscles or shoulders.

**MAKING MUSCLES**

What can we do to build muscle?

Regular exercise makes skeletal muscles grow. If you work a muscle against a load that is harder than usual, it will get stronger, provided you are eating the right kind of food. You need a good supply of protein to build the building blocks of proteins after exercise. Without it, a heavily worked muscle can use up more protein, for part of its energy supply, than it is able to lay down. The growth is mainly specific to the muscle doing the work, so different training regimes produce different results. Formula 1 drivers are generally fit but lightly built; however, they have large neck muscles because they have to hold their heads against large g-forces on fast corners.

**Rhabdomyolysis** is the breakdown of muscle and can be caused by many factors, including crush injuries (for example, when part of the body is squeezed between two heavy objects), cocaine abuse and exercise. Muscle damage leads to the release of the pigmented protein myoglobin into the bloodstream and in severe cases can cause distinctive brown urine (see below) and even acute kidney failure. The link between kidney failure and crush injury was first made by Professor Eric Bywaters, who noticed brown urine in people hurt during the London Blitz in World War II.
**Fuel for life**

**Run as fast as you can for as long as you can. Why do you eventually stop? Probably not because of sore muscles or feeling tired. You get out of breath. As you stand there, bent over, sucking in air, you are showing that muscles need oxygen to move. But what do we use this oxygen for and how do we measure how much we can use?**

**TAKE A DEEP BREATH…**

How do we measure how much oxygen we can use?

Work your muscles hard, and you will need more oxygen. Your brain’s respiratory centre sends signals to the diaphragm and intercostal muscles to breathe more in and expel it faster, affecting how deeply and how fast you breathe. These aren’t the only factors affecting how much oxygen you can use. Also important is how fast and how much blood your heart can pump, how dense the red cells (which carry oxygen) are in your blood, how efficient the blood supply is to your muscles, and how efficiently your muscles can use the oxygen.

VO2 max is a measure of the maximum amount of oxygen (in millilitres) you can use per kilogram of body weight per minute. Men who do not train average around 45 ml/kg/min, and it is slightly lower in women, at 38 ml/kg/min (see table). Athletes commonly record values in the 70s, and a few exceptional people may reach into the 90s. The highest values have been seen in cross-country skiers. Fast animals also need higher VO2 max. Thoroughbred horses often reach 180 ml/kg/min, sled dogs, bred for strength and endurance, can register 240 ml/kg/min, and the pronghorn antelope (above right) beats them all with 320 ml/kg/min.

VO2 max is not the only thing that determines top speed. You have to dissipate heat from your muscles, for example. This is easier for a mouse, which has a high surface area relative to its mass, than a human. However, VO2 max is a good measure of general fitness.

Different physiological measures for average men and women versus elite cyclists

<table>
<thead>
<tr>
<th>Measure</th>
<th>Average man</th>
<th>Average woman</th>
<th>Elite cyclist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lung capacity (litres)</td>
<td>6.4</td>
<td>4.2</td>
<td>8.2</td>
</tr>
<tr>
<td>VO2 max (ml/kg/min)</td>
<td>45</td>
<td>38</td>
<td>88</td>
</tr>
<tr>
<td>Resting heart rate (beats/min)</td>
<td>64-72</td>
<td>72-80</td>
<td>32-144</td>
</tr>
</tbody>
</table>

1. Max endurance for racing
2. Miguel Indurain, who won five consecutive Tours de France
3. Lance Armstrong, who won seven consecutive Tours de France

Sources: news.bbc.co.uk/hi/i/6273202.stm
www.bbc.co.uk/science/humanbody/body/factfiles/heart/heart.shtml

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**STEP IN TIME**

**Feeling the rhythm might help you keep running**

Most animals show a breathing rhythm that is tied to their movements – a link known as entrainment. Humans can synchronise breathing with walking or running as well, but we do not have to. This may be because our bipedal gait puts fewer constraints on the muscles that work the lungs. The diaphragm is the most important muscle for breathing in. During quiet breathing (e.g. when we’re at rest), inspiration (breathing in) occurs when the diaphragm and other respiratory muscles contract. Expiration (breathing out) happens through relaxing the diaphragm and elastic rebound of the lungs themselves. The faster and more deeply you are breathing, the more the muscles of the abdomen and those between the ribs contribute to breathing in and out.

Letting your breathing rhythm fall in with your stride is not necessarily more efficient, but it seems to happen naturally for many runners. Part of the impact on running may be psychological. The rhythmic breathing can provide distraction from the discomfort of the exercise. Known as a ‘pseudo-mantra’, this can be a useful technique for someone trying to get into training.

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**SOMETHING TO SAY?**

Is our move to two legs linked to our ability to speak?

The way we talk depends on the way we breathe. Most primates breathe in constant rhythm, and their vocal sounds are limited to one per breath. Humans, however, can interrupt the rhythm when we choose and produce a whole string of syllables as we breathe out. This escape from tight, rhythmic control of breathing may have been important in the evolution of language. It may also be linked to the shift from involuntary to voluntary coupling of breathing and stride rhythm, which went along with our move to bipedal (two-legged) movement.

Some musicians take the long exhalations of speech a step further. Wind players such as trumpeters and saxophonists can learn ‘circular breathing’, a technique that demands breathing in through the nose while expelling air from the mouth using muscular pressure from the cheeks. This allows players to sustain a continuous stream of notes.

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**NO OXYGEN?**

**Energy can be released from food without oxygen**

Glycolysis is the initial breakdown of glucose, which happens in the cell’s cytoplasm and needs no oxygen – it is anaerobic. It is a complex process in which the six-carbon glucose molecule eventually yields products including two molecules of adenosine triphosphate (ATP) and two molecules of three-carbon pyruvate. From here, respiration can continue anaerobically or aerobically, using oxygen (see ‘aerobic workout’, right).

The process to extract energy from food anaerobically (without oxygen or mitochondria) evolved long before aerobic respiration, when there was no oxygen in Earth’s atmosphere. It remains in operation alongside aerobic respiration in organisms that are evolutionarily more recent. For more, see the poster accompanying this issue.

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**FEELING SORRY?**

Why might exercise leave us sore?

Your muscles may feel sore after energetic exercise if you are not used to it. Often this occurs a while after you stop and can last for two or three days. This delayed-onset soreness is more than mere stiffness but less than the major pain from a torn muscle. Although it used to be blamed on a build up of lactic acid from anaerobic energy supply, a more likely explanation is that uncustomised exercise produces a lot of small tears in muscle fibres, which lead to mild inflammation before they are repaired. Typically, this soreness occurs after lots of eccentric contractions, where the muscles lengthen under tension (e.g. lowering a weight in a biceps curl). This is why hillwalking makes your muscles more stiff than flat walking.

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**FAST FACT**

Rigor mortis (body stiffness a few hours after death) is caused by a lack of adenosine triphosphate (ATP). During muscle contraction, ATP releases myosin from actin. After death, when ATP sources become exhausted, the muscles cannot relax and rigor mortis sets in. The muscles relax only when the body begins to decompose. Source: www.jstor.org/pss/4450701

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**MORE ONLINE:** Check out our free ‘In The Zone’ experiment kits. For ages 16-19, explore how the cardiovascular system adapts during different activities. For ages 11-14, discover how exercise affects your breathing. See more at www.getinthezone.org.uk

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**AEROBIC WORKOUT**

The main way our bodies get energy needs oxygen

Aerobic respiration uses oxygen to break down glucose, amino acids and fatty acids and is the main way the body generates adenosine triphosphate (ATP), which supplies energy to the muscles. After glycolysis (the anaerobic breakdown of glucose into pyruvate), pyruvate is converted to acetyl CoA in the matrix of the energy-transfer mitochondria, in the link reaction. Next is the Krebs cycle, which occurs twice per glucose molecule, producing – among other chemicals that feed into the aerobic part of the process – more ATP molecules.

The aerobic part of the process depends on a series of enzymes that are organised along the folds of inner membranes ( cristae) of the mitochondria. The enzymes are arranged so that electrons pass from one reacting molecule to the next, in a series of steps known as the electron transfer chain. This process ends with ATP synthase, an enzyme that produces ATP from adenosine diphosphate (ADP) and inorganic phosphate – up to around 30 molecules of ATP per molecule of glucose, according to current thinking – and captures the final portion of the energy released by the whole complex of reactions in a form that the rest of the cell can use.

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**FAST FACT**

Tissues with large but variable energy demands, such as skeletal muscle, spermatozoa and the brain, store energy for instant availability as phosphocreatine. This reversibly transfers a phosphate group to adenosine diphosphate (ADP) to make adenosine triphosphate (ATP).

www.uniprot.org/uniprot/P06752

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**BIG PICTURE**: Exercise, energy and movement
**Fit in mind and body?**

Being fit sounds good, but what do we mean by it? In everyday language, things can be fit for use or simply a good fit, like a pair of jeans. Physical fitness is hard to define by itself. It might mean some combination of power, speed, endurance and flexibility. We tend to associate physical fitness with feeling healthy, so there is a mental component as well.

**EVERYTHING IN MODERATION?**

What do we need to do to be healthy?

It’s easy to say that moderate exercise must be good for everybody, but the emerging idea is that the best way to keep healthy is to lead an active lifestyle (using the stairs, walking more, and so on) and top this up with short bursts of intense exercise. A completely sedentary lifestyle is dangerous but not necessarily the same as a life lacking a formal exercise regime.

If the most simple definition of fitness is exercising enough to stay healthy, then the benefits of active stays are pretty clear. An active lifestyle cuts the risks of heart disease, stroke, and Alzheimer’s disease and dementia. It can also help you combat obesity if you don’t eat more calories than you burn off. Reducing obesity, in turn, reduces your risk of cancer and diabetes and results in stronger bones.

How do we know what we should do to be healthy? Often, guidelines are based on epidemiological data, gained by observing large populations. Some researchers argue that conventional studies – where specific treatments or behaviours are applied and tested – will give us a firmer idea of what really works to keep us healthy.

**WEARING OUT**

*Is the future grow-your-own?*

Many people now have their worn joints fixed with metal and plastic substitutes – operations that could be avoided if we were able to regrow bone and cartilage to replace worn-out parts. That is one possible application for stem cells, versatile cells that can be nurtured to develop into different types of tissue. If they are grown in the lab on the right kind of scaffold, bone stem cells can, in theory, generate new bone. At the moment, the cells are grown on donated bone from earlier operations, but the search is on for artificial materials that will do the job.

The aim is to make scaffolds that are as similar to natural bone matrix as possible (i.e. that are biomimetic). They need to be made of material that will degrade once new tissue has formed and that has the right mechanical and chemical properties. This is a very demanding specification, but the formulation of such materials is gradually improving. Naturally occurring materials can also help: a British company is developing replacements for damaged cartilage, especially in knee joints, using a new material based on spider silks. For more, see wellcome.ac.uk/ot2icu.

**MENTALLY STRONG**

Exercise can change our mental state

Doing exercise affects our mental state, and vice versa. Just going for a stroll can improve your mood, and making yourself get out and be active is important when you are depressed or anxious. Trials show that exercise can be as good for people with depression as drugs, and animal studies have found changes both in neurotransmitters and in the number of some types of neurons when mice and rats are allowed to exercise freely.

Feeling confident may also be linked to a lower risk of injury during heavy exercise. In one study in which former athletes were training the skills needed by their new employer, the Cirque du Soleil, more than half the trainees hurt themselves badly enough to seek help from the resident physical trainer. Those who had a low self-confidence score on a standard questionnaire were more than twice as likely to hurt themselves as those with a high rating (see more at www.ncbi.nlm.nih.gov/published/21350616).

**UNDER STRAIN**

 Extreme exercise can be harmful

Doing an exercise programme on top of an active lifestyle can have costs – it can make you tired or cause injuries. Injuries can occur when people exercise inappropriately (e.g. when lifting weights the wrong way), so it might be wise to get in instruction and coaching and to allow your body to adapt slowly to new forms of exercise. Muscle strain and stress fractures in bones often affect athletes whose sport requires continued repetitive effort, such as tennis players.

Simple wear and tear is a risk for joints, which bear a lot of the strain of different forms of exercise. Habitual runners work their knees hard, and running has previously been linked to arthritis in later life. More recent reviews, however, suggest that it is harmless at worst and might even be good for the joints in the majority of people. Running after a knee injury or which you weight does appear to be harmful, though, and weightlifters and football players have both been found to suffer from arthritic knees in later life. Football can be particularly damaging because of the twisting and turning on the knee involved.

Another general effect of very frequent and intense exercise shows up in the immune system: doing exercise seems to boost the immune response, but overdoing it can have the opposite effect. Intense exercise – for example, a marathon – appears to make athletes more susceptible to infections like colds and sore throats. Part of the reason is release of the hormone cortisol, which helps us cope with stress by boosting glucose use but also damps down immune reactions and reduces inflammation.

There is also evidence that long-term endurance exercise can do harm to the heart. A study of men who had earned admission to the 100 Marathon Club found that the older among them had some heart muscle scarring. More research is needed to understand the implications of this finding (www.ncbi.nlm.nih.gov/published/21350616).

**FAST FACT**

Extrapolating from current data, women will be finishing men in the 100 m sprint at the 2016 Olympics. However, this ignores many factors that make this very unlikely, including that men and women may each have a physiological limit regarding sprint speed. Source: Tatam et al. Science 2004;304:535

**LOCATION, LOCATION, LOCATION**

Does it matter where you exercise?

What effect does where you exercise have on you? This is tricky to investigate because just being in natural surroundings can have positive effects on people’s mood. Still, there is some evidence that being outdoors boosts the good mood induced by a walk or a run, compared with the same amount of effort in the gym. Green landscapes and water also seem to make people feel better about themselves and more inclined to go out for another session.

**NHS GUIDELINES FOR PHYSICAL ACTIVITIES**

<table>
<thead>
<tr>
<th>Under 5s</th>
<th>Ages 5–18</th>
<th>19 and over</th>
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<tr>
<td><strong>Under 5</strong></td>
<td><strong>Ages 5–18</strong></td>
<td><strong>19 and over</strong></td>
</tr>
<tr>
<td>Children who can walk alone should be physically active for at least 30 minutes every day.</td>
<td>At least 60 minutes of mixed moderate-intensity and vigorous-intensity aerobic activity and muscle- and bone-strengthening activities, every day.</td>
<td>At least 150 minutes of moderate-intensity aerobic activity every week and muscle-strengthening activities on two or more days a week that work all major muscle groups or 75 minutes of vigorous-intensity aerobic activity every week and muscle-strengthening activities on two or more days a week or a mixture of both.</td>
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**CLASSIFICATION OF ACTIVITIES**

- Moderate-intensity aerobic: cycling, fast walking, skating, mowing the lawn
- Vigorous-intensity aerobic: running, football, hockey, skipping, martial arts
- Muscle-strengthening: press-ups, weightlifting using all major muscle groups
- **www.nhs.uk/LiveWell/Fitness/Pages/Fitnesshome.aspx**
Peak performance

Here, we explore some current and potential future scenarios around the ethical, legal and social issues of sport and exercise.

DRUGS

Now: Erythropoietin (EPO)

Some competitive cyclists have abused the hormone erythropoietin (EPO), which increases the production of red blood cells and allows them to transport oxygen more easily. The effect is similar to the adaptation seen in people who live at high altitudes, with reduced air pressure. Indeed, some athletes train at altitude for this reason, a practice that is not banned. The use of EPO in endurance sports is banned, but manufactured forms of the hormone are very similar to the naturally occurring manufactured forms of the hormone are identical to normal EPO. Gene doping is the non-therapeutic manipulation of genes to improve athletic performance, and the first documented case of gene doping was in 2008. It involved a product called Repoxygen, which boosted EPo levels. If muscles can be tweaked genetically so that more EPo is produced, the product might be acceptable because it is identical to normal EPo. Gene doping is a growing challenge to sports, and the World Anti-Doping Association (www.wada-ama.org) is devoting “significant resources and attention” to the detection of gene doping.

PROSTHETICS

Now: Oscar Pistorius

Oscar Pistorius was born with no lower leg bones and underwent a double amputation as a child. He runs with carbon-fibre prosthetic legs; each has a sprung ‘blade’ on the foot (see an example of this kind of blade above). In 2011, he became the first amputee to ever compete in the World Athletics Championships, and he is hoping to qualify for the 2012 Olympics. His times are comparable with others, but there has been a lot of discussion about whether his prosthetics give him an unfair advantage over ‘able-bodied’ athletes. For more, see jrne.bmj.com/content/34/9/639.full.pdf.

Future: Hand-built shoes

Elite athletes commonly wear hand-built shoes. New rapid manufacturing technologies will make it possible to make shoes optimized for an individual’s physique and running style through precision measurement and engineering (e.g., www.lboro.ac.uk/service/publicity/news-releases/2008/116_spikes.html). Adidas has also been working on undergarments containing plastic strips that act like springs, which help wearers jump further and run faster (www.popsci.com/entertainment-amp-gaming/article/2009-02/super-undergarments-01).

NUTRITION

Now: Sports supplements

There are lots of specially formulated foods and drinks that are sold to nourish people who are training or to help recovery after exercise. A normal, balanced diet, with plenty of protein and carbohydrate, supplies all that athletes really need, though – they just need more of it.

If you get thirsty during or after exercise, you need to drink water. Sports drinks supply that but also contain a mix of other chemicals. Isotonic drinks have a similar salt content to body fluids and often provide a sugar boost (see sucrose, above) as well. They can aid rehydration and boost energy levels, and they may increase water intake because a nice taste encourages people to drink more. Their high energy content can undo the weight-loss benefits of moderate exercise, however. These are not to be confused with ‘energy drinks’, which mainly rely on caffeine for their effects.

Future: Antioxidants

There are varied claims about the benefits of particular substances in reducing the stress-related effects of heavy exercise. For example, some antioxidants in plants may help protect the liver of some of the metabolic by-products of their training regimes, and other natural products have anti-inflammatory properties, which can counteract immune reactions to extreme exercise. However, the real benefits of consuming foods or supplements containing these substances need more research.

LIMITED KNOWLEDGE

Improvement in sports records tends to level off, although astounding athletes like sprinter Usain Bolt can still sometimes leap ahead of everyone else. Can we predict an ultimate limit to human performance? Mathematically, the technique to use here is called extreme value theory (see left). This allows statisticians to estimate how far the extreme of a probability distribution extends, even if we have not sampled it in reality. Applying this technique to the existing records of times over 100 metres indicates an ultimate limit of between 9.3 and 9.5 seconds. Bolt’s current record stands at 9.58, and he beat the previous record holder by 0.16 seconds. Athletes improve through competition, but animals can be bred for high performance. Even so, records tend to level off. Timings from events run over the same course for many years typically show only slow improvement. So any species, unaided, has performance limits that are unlikely to change. Humans, though, have technology, which can be a game-changer.

FAST FACT

A ban on performance-enhancing polyurethane swimming suits was implemented by FINA (the international governing body for swimming) on 1 January 2010, after 29 world records were set in the first five days of the FINA World Championships in Rome 2009. Source: news.bbc.co.uk/1/hi/olympic_spport/sports/5161865.stm.

THE PLACEBO IN PERFORMANCE

Give an athlete the latest equipment, and he or she may well break records. But it can be hard to tell whether the equipment itself is directly responsible: competitors who believe they can go faster, or lift heavier weights, may do just that. The placebo effect is well known in medicine – an inert substance can show results comparable to an active compound. This does not mean the effect is not real. Beliefs are seated in the brain, which can affect metabolism, the immune system and other body functions. In one study, runners were told they were taking part in a trial of the effects of super-oxygenated water, which contains more than the usual amount of dissolved oxygen. Research indicates this has no measurable physiological effects, but the runners were given tap water to make sure. Even so, they improved on their normal times during the experiment, and the slower ones improved the most.

MORE ONLINE: From hula-hooping to pilates, there’s always a different exercise ‘craze’ sweeping the nation. Read about the history of fitness fads at www.wellcome.ac.uk/bigpicture/exercise
Who are you?
I’m a 17-year-old British Paralympic swimmer. I was born with achondroplasia, a bone growth disorder that causes dwarfism.

How did you first get into swimming?
When I was really young, I went to swim classes. The club had a competitive side, so I was invited into the squad swimming when I was about seven and a half years old. It was then I discovered I really loved it.

What's your training regimen?
I love sport as a child. I was quite a good cricketer as a youngster, but when I got to 16 I was affected by something called the yips, which meant that when I ran into bowl I just couldn't let go of the ball. I had training soon after and spoke to the coach. He said ‘I’ve got a little piece of advice for you – start batting, because you’ll never get rid of the problem.’ From that moment, my cricket career was gone.

What do you do at university?
I spend half my time working with the English Institute of Sport as Head of Sports Psychology: we have 30 psychologists working with various sports and preparing for London 2012. For seven years, I worked on a winter sport called short-track speed skating.

Have you always been sporty?
I loved sport as a child. I was quite a good cricketer as a youngster, but when I got to 16 I was affected by something called the yips, which meant that when I ran into bowl I just couldn’t let go of the ball. I had training soon after and spoke to the coach. He said ‘I’ve got a little piece of advice for you – start batting, because you’ll never get rid of the problem.’ From that moment, my cricket career was gone.

What do you do now?
I'm a sports psychologist. I spend half my time working with the English Institute of Sport and the other half working with the English Institute of Sport as Head of Sports Psychology: we have 30 psychologists working with various sports and preparing for London 2012. For seven years, I worked on a winter sport called short-track speed skating.

What's the main aim of your job?
The art of sport psychology is to simplify people's thinking to its absolute minimum. We're not thinking about very much except the one thing you need to do. In cricket, if you're batting for a long period of time, then one thing you have to do is watch the ball and ignore everything else – like the bowler's doing, the crowd and the cameras.

What is muscular dystrophy?
Muscular dystrophies are defined as hereditary, progressive conditions that lead to deterioration of muscle mass and function. The most common muscular dystrophy is Duchenne muscular dystrophy, an X-linked condition that leads to the absence of the protein dystrophin in muscle fibres.

What cells do you study?
Our skeletal muscle consists of lots of long muscle fibres, which have got lots of nuclei, and they contain the contractile elements of the muscle. On the edge of these fibres are ‘satellite cells’, which become activated in young muscle that is growing or muscle that’s been injured. They can proliferate and make a pool of precursor cells, which can either repair the muscle fibres or replace them by making completely new fibres. They can also give rise to more satellite cells, and so are, by definition, a muscle-specific stem cell.

How might these be useful?
You can inject satellite cells into dystrophic muscle and they can regenerate muscle fibres. However, the main problem of this treatment is that satellite cells can act only very locally. In Duchenne muscular dystrophy all the muscles of the body are affected, so ideally you'd like a stem cell you could inject and get to all muscles via the blood system. So we're also exploring other sorts of stem cells, which other groups have shown can spread throughout the body.

How do you study muscular regeneration?
We've got some mouse models of muscular dystrophy, and we transplant cells from normal donors into these models. The donors are usually genetically modified to express a marker gene so that we can follow the fate of transplanted cells to see if they make muscle and reconstitute the muscle stem-cell pool.

Why did you choose this career?
I think it was just by chance initially! When I graduated many years ago I wasn't quite sure what to do. I saw a one-year post advertised on Duchenne muscular dystrophy, so I thought it would be a good thing to do without committing myself to anything more. I really enjoyed it, so I stayed in the same group and did a PhD. The most rewarding aspect of this job is when you find something new and interesting that's unexpected – for example, an unusual type of cell making lots of muscle. I also supervise a number of PhD students, so encouraging them to see if they make something interesting really is good.

For more information about this work, visit www.ucl.ac.uk/ich/research/duch/dubowitz, and for more about Duchenne muscular dystrophy, see www.muscular-dystrophy.org/.
Sign up to receive free regular copies of Big Picture at www.wellcome.ac.uk/bigpicture/order

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