



Classical and contemporary muscle forms as depicted by Michelangelo's biblical David (left) and actor Arnold Schwarzenegger (right)

Retaining Muscle Strength

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A new approach could prevent or delay loss of muscle strength and thereby decrease the frequency of broken bones in the elderly or muscular dystrophy in the young.

MUSCLES have played a prominent role in the evolution of human beings from primate ancestors and also idealization of the male human form. Even today, Michelangelo's sculpture of David epitomizes a classical picture of excellence of the youthful male human form. The strength and power of David's skeletal muscles shining through the marble leave us with a mental picture of his easy domination over the gigantic Goliath. In modern times, an example of the idealization of a male human form is the bodybuilding champion and actor Arnold Schwarzenegger. Classical and contemporary muscle forms have always testified the importance of muscles in images of male strength and power.

Individually articulated different groups of skeletal muscles much larger than those pictured in the statue of David are acquired by the likes of Schwarzenegger through specialized weight training and a tough regime of exercises. Many times, anabolic steroids (chemical muscle stimulants) are used in combination with weight lifting to increase muscle size and strength. Examples of such compounds include methandrostenolone (Dianabol), Boldenone (Equi-Pan), Stanozolol (Winstrol V) and Drostanolone (Masteron).

As information about the effects of steroids spread, they began to be increasingly used by professional and amateur athletes although use of many of these compounds is banned by anti-doping organizations. The most noteworthy example is the disqualification of Canadian sprinter Ben Johnson, who won the gold medal in the 100 m sprint event at the Seoul Olympics in 1988. The

title and the record were subsequently rescinded as he was disqualified for doping the banned muscle stimulating steroid stanozolol.

Muscles, therefore, are essential to human life in a variety of ways. They are central components of physical strength and speed, attributes that are admired in most human cultures. Mobility of an individual depends on the strength of his muscles; whether one uses them to walk, run, and put his foot on the pedals of bicycles or hands on the brakes. As a basic component of physical vigour they also play a role in human attractiveness. As such, muscle tone is a major contributor to the 'sense of self' developed by each person.

During childhood, physical and sports activities develop and strengthen the muscles while at puberty production of estrogen and testosterone hormones enhance these processes. The muscular development usually peaks between 20

Canadian sprinter Ben Johnson was stripped of his gold medal at the 1988 Seoul Olympics (right)

and 30 years of age. Subsequently, strength and size of muscles declines by one-third between the ages of 30 and 80. Although it is difficult to define the exact number of muscles in humans it is approximated to be 640-850 types. Almost every muscle is part of a pair of identical muscles found on both sides of the body resulting in approximately 400 pairs of muscles.

Muscles move body parts by contracting and then relaxing. They pull bones but on their own cannot push them back to their original position. Thus, they work in pairs of flexors and extensors. First, the flexor contracts to bend a limb at a joint, then the extensor contracts to extend or straighten the limb at the same joint. For example, the biceps muscle in the front of the upper arm is a flexor and the triceps at the back of the upper arm is an extensor.

One of the strongest muscles in the human body is the jaw muscle that is active during mastication, biting, speech, and swallowing. To execute this variety in tasks, they control the position of the mandible precisely by instantaneously changing the forces applied on it. They are able to meet these different requirements because of their complex architecture in combination with a heterogeneous composition of fibres capable of producing a variety of forces at different contraction speeds.

Muscles in isolation do not generate strength and speed. They need to be physically integrated with bones and function harmoniously through their attachments to nerves, tendons and ligaments. They pull on the joints and allow us to move. Even when we sit perfectly still, there are muscles throughout our body that are constantly moving. Muscles enable our heart to beat, chest to rise and fall during breathing, our blood vessels to help regulate the pressure and flow of blood throughout our body. Even when we smile

and talk, muscles are helping us to communicate. All these activities accomplished by movements of the muscles are coordinated and controlled by the brain and nervous system.

The human body contains three types of muscles such as the skeletal, smooth and cardiac muscles. Only skeletal muscles (40 percent of the body), responsible for shapely thighs and enviable pectorals, are controlled by the brain. These muscles are attached to the bone, mostly in the legs, arms, abdomen, chest, neck, and face. They are called striated muscles because they are made up of fibres that have horizontal stripes. These muscles hold the skeleton together, give the body shape and help it with everyday movements and are known as voluntary muscles because one can control their movement. They contract quickly and powerfully to produce burst of energy but tire very quickly.

The smooth or involuntary muscle is also made of fibres but this type of muscle looks smooth and not striated. Smooth muscles are controlled by the nervous system automatically and are also called involuntary muscles. Examples of smooth muscles are the walls of the stomach and intestines, which help break up food and move it through the digestive system. They are also found in the walls of blood vessels, where they function to squeeze out blood flowing through the vessels to maintain blood pressure. They take a longer time to contract than skeletal muscles but can stay contracted for a long time and don't tire easily.

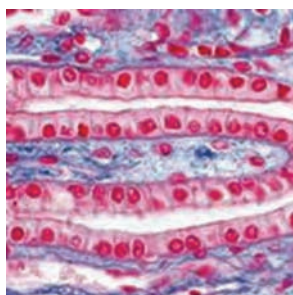
Cardiac muscle is a unique type, found only in the heart. The walls of the heart's chambers are composed almost entirely of these muscle fibres. These are also involuntary type of muscle. These are rhythmic, powerful in contraction and force blood out of the heart to supply



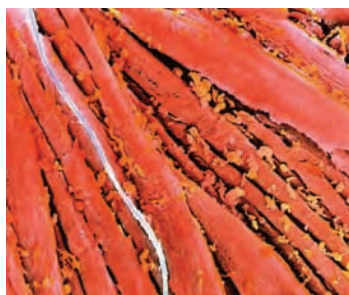
oxygen to different parts of body. These muscles never tire and when they stop working, the individual dies of cardiac/heart failure.

Although, the muscles perform tapestries of work in human body their origin is much simpler. All types of muscles arise from a particular type of stem cell called "satellite cells". Multiplication and differentiation of mono-nucleate satellite cells leads to formation of myoblasts. Fusion of myoblast cells with each other and with pre-existing myotubes leads to formation of multinucleate myotubes and higher order muscle fibres. Thus, muscle is the only tissue in the body that is formed by fusion of cells in a predetermined and precise manner. A particular numbers of cells fuse to form a particular muscle at a predetermined neuromuscular connection, each with its own individual identity.

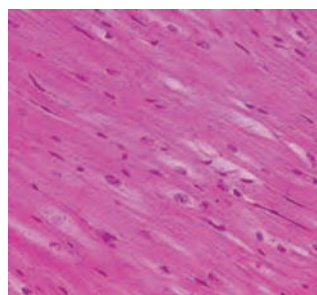
The entire process is coordinated and regulated by specific growth factors such as insulin-like growth factor 1 (IGF-1), hepatocyte growth factor and growth hormones such as testosterone and estrogen. IGF-1 stimulates multiplication of satellite cells to produce more satellite



A. Skeletal muscle



B. Smooth muscle



C. Cardiac muscle

Different types of muscles in human beings



This loss of muscle size and strength that accompanies ageing is known as sarcopenia, which is a significant problem for older persons.

cells and further differentiates these cells into myoblasts. In addition to well characterized IGF-1, MAP kinases, RAC/ RHO pathway and a novel family of proteins known as Ras GTPase are found to be involved in terminal muscle differentiation.

When working at its optimal best, the muscle system produces the fastest animals like cheetah to the greatest athletes like Jackie Joyner-Kersey, Carl Lewis, Pele, Maradona and Messi. But when there is a problem, the same helpful and powerful muscles shrivel, twist, and degenerate making the individual sedentary. Many times the problem arises due to lack of the protein 'Dystrophin' in muscles or mutations in the genes associated in differentiation of muscles.

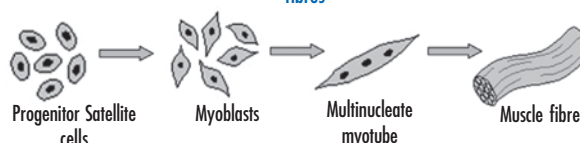
With ageing, production of IGF-1 decreases and muscles shrink, become smaller, weaker and less responsive to the action of IGF-1 so that the impact of exercise on muscle size and strength diminishes. This loss of muscle size and strength that accompanies ageing is known as sarcopenia, which is a significant problem for older persons. While not painful or directly debilitating, sarcopenia is associated with an increased tendency to fall and break bones. Such falls and broken bones are major causes of morbidity among the elderly persons.

Another chronic muscular disorder with excruciating pain that affects younger people is muscular dystrophy (MD) in which all types of muscles are affected. It is a group of muscle diseases that weaken the musculoskeletal system with progressive muscle weakness, deficient in muscle protein dystrophin, and is inherited through generations. It may occur in childhood or adulthood but more severe forms tend to occur in early childhood.

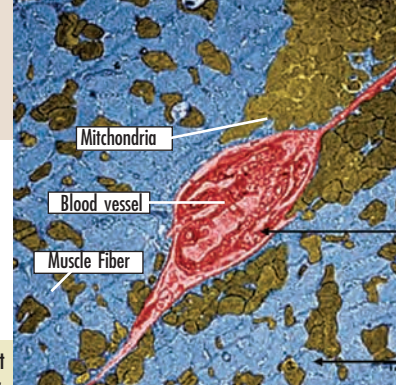
Most of the victims of the severe form of dystrophies, known as Duchenne's Muscular Dystrophy, die from heart failure. Those who have a milder form, known as Becker's Muscular



Process of muscle formation in humans from progenitor satellite cells to muscle fibres



Dramatically enhanced muscle tissue in a high performing mouse with abundant mitochondria (brown), blood vessel (red cross section) and muscle fibres (blue) Right.



Dystrophy, can survive to middle age. It is possible that they have a defective gene that makes muscles but the muscles slowly degenerate. In humans the gene responsible for muscular dystrophy disease has been located on the X chromosome and therefore almost always affects males while females act as carriers as they have two X chromosomes and can compensate if one is defective.

The commercial and competitive pressures to use genetic muscle treatments to build up, maintain and repair muscles of diseased, old aged as well as professional athletes has been very strong. Thus, there have been efforts to ameliorate the muscle problem by gene therapy using appropriately regulated efficient delivery of human mIGF-1 to muscle cells. However, this approach, instead, led to pathological enlargement of the heart muscle and thus a cure for the disease remained elusive for a long time.

Recently, growing understanding of muscle physiology at the molecular level coupled with sophisticated genetic engineering has made it possible to enlarge skeletal muscles selectively, without damaging heart muscles in the process. An international team of scientists has created super-strong, high-endurance muscles by tweaking a gene called *NCoR1*. This creates a new avenue for treating muscle degeneration in people who are unable to exercise due to obesity or other health complications, such as diabetes, immobility and frailty or injured young athletes.

Contrary to known dogma, scientists found that *NCoR1*, a natural muscle-growth inhibitor, is responsible for determining the strength of our muscles. *NCoR1* are molecular brakes that decrease the activity of genes. Releasing the brake by mutation or with chemicals reactivates gene circuits to provide more energy to the muscle and enhances its activity. By modulating the activity of this gene they were able to create a mighty mouse

whose muscles are twice as strong as those of normal mice. The muscles of engineered mouse have more blood vessel, muscle fibres and more numbers of mitochondria to provide more energy to the muscles. The mice with the mutation became true marathoners, capable of running faster and longer before showing any signs of fatigue. They were able to cover almost twice the distance run by mice that had not received the treatment and exhibited better cold tolerance.

Unlike previous experiments that focused on genetic accelerators such as IGF1, this discovery shows that suppressing an inhibitor is a new way to build muscle. Examination under a microscope confirmed that the muscle fibres of the modified mice are denser and massive. Interestingly, no harmful side effects were detected by elimination of *NCoR1* from muscle and fat tissues. While the IGF1 approach had advantages and disadvantages, the mouse experiment suggests treatments for age-related or genetics-related muscle degeneration are within reach. However, developing any one of them would take some time and drug administration would require demonstrations that the proposed treatment is safe, effective and free of undesirable side effects.

Current finding gives us a glimpse of possible long-term therapeutic applications for humans. If the results are confirmed in humans, the new approach will prevent or delay such loss of muscle strength and thereby decrease the frequency of broken bones in the elderly or muscular dystrophy in young people.

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