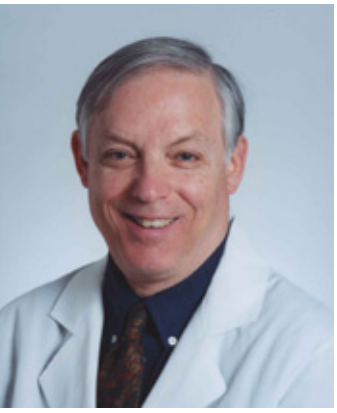
What Happens WHEN DOPERS DOPE?

Jerry L. Spivak, MD and Richard T. Silver, MD



The news and disappointment about Lance Armstrong's confession and revelation about blood doping and the use of transfusions for increasing athletic importance has raised enormous public interest. A number of CR&T newsletter readers have asked about this. We thought it would be of interest to tell our readers about our understanding of the issue.

Although there is a long history of blood transfusion between animals and animals to humans over the past several hundred years, the results, needless to say, were catastrophic. At the beginning of the 20th century, blood transfusion between human subjects became possible and at its end, purification and manufacture of the hormone known as erythropoietin through recombinant DNA technology made it possible to obtain many of the benefits of blood transfusion without actually transfusing blood. As is always the case, and without waxing philosophical, good brings evil and life saving practices such as the administration of EPO resulted in sinister alternatives. The basic intent of blood transfusion or hormonal stimulation of the bone marrow is to obtain the necessary number of red cells to meet the body's oxygen demands. Of course, the greater the number of red cells available means the greater the amount of oxygen available for consumption and this was quickly appropriated by world class athletes to improve their performance in many sports. This is not only unethical and illegal as our readers know, but as we will stress, it is also very dangerous.

Under normal circumstances, the number of red blood cells in a given individual available to transport oxygen from the lungs to the tissues is held relatively constant, although that number varies within limits among different individuals of the same sex. Red blood cells production is tightly regulated by the hormone erythropoietin (EPO), which is commercially manufactured by Amgen and Johnson and Johnson. Under normal circumstances, the concentration of EPO in the blood is held constant and its principal function is to regulate red cell production to meet long-term oxygen requirements. Surprisingly, it is not manufactured in the bone marrow in adults, but primarily in the kidneys. In the body, low oxygen levels are the principal stimulus for increasing EPO production which leads to greater red blood cell production. Conversely, an increase in oxygen in the tissues decreases EPO production. When an individual is administered oxygen or blood transfusions, EPO production is reduced.

There are significant adverse effects and risks to inappropriate EPO use because increasing the number of red blood cells in the circulation is associated with a decrease in the amount of plasma, the fluid part of the blood. This increases blood viscosity and can lead to hypertension, cardiac overload, and thrombosis in the brain, heart, lungs and extremities, and sudden death. In fact, there are strict Food and Drug Administration (FDA) regulations for the use of EPO in patients to prevent these complications that have been endorsed by the American Society of Hematology and the American Society of Clinical Oncology.

What about the use of excess blood transfusion to increase athletic performance?

For more than half a century, it has been known that increasing the number of red blood cells increases oxygen transport and the maximum ability for muscle function (aerobic capacity and/or increased work endurance). Increasing the number of red cells is similar to a conditioning benefit. In carefully conducted experiments, increasing the number of red blood cells by one transfusion in highly trained runners and cross country skiers improved their performance in a ten kilometer race by approximately one minute and remarkably, but for unknown reasons, this improvement

in performance was sustained for thirteen days. However, the effects of such an increase in red blood cells number is directly related to the fitness of an individual and the benefit is only likely to be of measurable significance in world class athletes

Of course, there are hazards to the transfusion of stored blood. Under the usual hospital circumstances, blood banks are very careful to monitor blood compatibility as well as the temperature and other factors used to insure safe blood storage. Armstrong and others who used this approach were clearly aided and abetted by others with a medical background.

For the above reasons, the use of EPO for blood doping is easier than blood transfusion. The availability of recombinant EPO also led to the development of sensitive, specific and easily measured tests for this hormone in body fluids such as blood and urine. If you listened to the Oprah Winfrey show, Lance Armstrong announced that when he was tested during his races, he was never proven to have administered EPO. This is because of the fact that when

EPO is given intravenously, it can only be detected in the plasma in the first 48 hours after its administration, so that by timing the testing or its administration, the demonstration of positivity can be avoided.

In contrast to blood transfusion, the EPO use can lead to an increased blood pressure with exercise. Interestingly, despite the belief of dopers that doping results in increased performance, there are no controlled studies of the impact of the EPO administration on performance or endurance, but, since many of the athletes who have been caught have been medal winners, there appears to the dopers to be a risk-benefit advantage. That there are many reports of fatal consequences because EPO use was so rapidly embraced, says much about the assumed effectiveness and convenience of blood doping. It also reflects, however, a lack of the understanding of EPO physiology.

All conditioned athletes differ from their unconditioned counterparts with respect to blood volume size, how much blood each heart beat ejects and heart rate during exercise. Conditioning leads to an increase in the amount of fluid in the body (plasma volume). Usually, there is a small increase in red blood cell number also. An enlarged heart and a decreased number of beats are a consequence of effective conditioning. (We are told that Lance Armstrong has a resting pulse rate of 38, which is well below normal) The net result is a decrease in blood vessel resistance while systemic oxygen transport is increased. However, like EPO exposure, following blood transfusion there is also a reduction in plasma volume so that unless Lance drank a lot of fluids, he may have defeated his purpose.

In summary, increasing the number of red blood cells improves athletic performance but its value is only for the most fit athlete. On the other hand, the adverse consequences of this practice is unequivocal since increasing the number of red blood cells can lead to effects which are the opposite of exercise- induced conditioning. This presents an ironic twist to those athletes who attempted to increase their red blood cell counts and it adds to the irony of the tragic consequence of the story of Lance Armstrong.

Based on a chapter written by Jerry Spivak, MD entitled "Erythropoietin use and abuse: When physiology and pharmacology collide" (Adv Exp Med Biol. 2001;502:207-24).