

## ADVERSE EFFECTS OF BLOOD TRANSFUSIONS

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A blood transfusion can be used as a way of doping an athlete just before a competition by stimulating his organism with regenerated blood. This procedure carries a number of risks related to immunological reactions or due to the transmission of infections, among them the HTLV-III virus which causes AIDS, a terminal disease which is taking on pandemic proportions.

For these reasons, blood doping was prohibited by the IOC at its 90th Session in Berlin. Doctor H. Catlin, head of the clinical pharmacology department at the University of California, Los Angeles (UCLA), outlines the various blood components which can be used for transfusion purposes and the negative reactions a treatment of this kind can produce.

**A** blood transfusion refers to the intravenous administration to an individual of red blood cells (erythrocytes) or related blood products that contain erythrocytes. In the United States about three million individuals receive transfusions annually.

The red cells are obtained from a donor by removing approximately 250 ml of whole blood. The subsequent processing of the whole blood determines the nature and utility of the blood products. Currently, five different types of blood

products are available, each tailored to a specific clinical circumstance.

The blood products are considered *drugs*, and their use, collection, storage and processing are regulated by the US Food and Drug Administration (FDA). Blood products cannot be transported across state boundaries without a license. A blood bank is a facility which collects, stores, processes, and tests blood for transfusions. These facilities are licensed by the FDA and are periodically inspected to assure that they are adhering to all regulations.

The two most common indications for red blood transfusions in conventional medical practice are acute blood loss and anemia. Exchange transfusions may be used to remove toxic substances. Other components of blood, such as platelets, white cells (leukocytes), and plasma, are available but these products do not contain red blood cells.

## RED CELL PRODUCTS

The *five different red cell products* are :

- A. whole blood ;
- B. red cell concentrates ;
- C. frozen red cells ;
- D. washed red cells ;
- E. white cell poor blood.

A. Whole *blood* consists of all the components of blood, i.e. erythrocytes, leukocytes, platelets and plasma. It is stored in the liquid state at 4° C with an anticoagulant. Whole blood should only be used to treat acute massive hemorrhage such as occurs in patients with gastrointestinal bleeding, major surgery or trauma. The administration of whole blood results in the restoration of oxygen carrying capacity and intravascular volume.

B. *Red cell concentrates* are obtained by removing the plasma from whole blood. The resulting product consists of 80% red cells in a total volume of about 300 ml (one unit). Red cell concentrates are used to restore oxygen carrying capacity such as that which occurs in patients with chronic anemia.

C. *Frozen red cells* are a relatively new product made available by advanced techniques in the field of cryopreservation. The cells are stored at extremely low temperatures (—85°C) in the presence of preservatives. In this state, the cells may be stored for up to three years, whereas the shelf life of liquid red cell products is 35 days. Frozen red cells are used for patients with relapsing anemias and for patients that require rare types of blood with specific antigen patterns. The availability of frozen red cells has led to the practice of *autologous transfusions*. In this case individuals in effect donate blood to themselves. Blood is taken from a person, processed and stored. While the blood is stored, the normal processes of restoration take place and the individual's red cell mass returns to normal. It takes up to 70-90 days to replenish two units of blood. At a later time, when the blood product is

needed, the individual is transfused with his own blood product. The major use of autologous transfusions has been for patients undergoing elective surgery. The technique has also been applied to increase the aerobic work capacity of athletes<sup>1</sup>.

D. *Washed red cells* are prepared by removing the plasma from whole blood and washing the red cells several times with saline. This product is used for patients who experience allergic reactions due to components of plasma.

E. *Leukocyte poor red cells* are obtained by separating the white cells from the red cells. This product is used for patients with a history of a transfusion reaction that can be traced to a reaction to the leukocytes.

## RISKS OF TRANSFUSIONS

The following risks may be subdivided according to the mechanism mediating the adverse effect. *immunologically* mediated reactions involve the interaction of antigens with antibodies and a subsequent chain of immunochemical and clinical manifestations. Reactions mediated by *infectious* agents result in the recipient developing an infectious disease such as hepatitis or malaria. A miscellaneous group of reactions are mediated by a variety of non-immunological and non-infectious mechanisms.

### A. *Immunologically mediated reactions*

When red blood cell products are administered according to present day standards the risk of an immune reaction is about 3 percent. There are several different types of immunological reactions each associated with a different immunochemical mechanism, clinical course and treatment. Many of these reactions are mild and self-limited. An urticarial reaction refers to the development of a characteristic rash during the transfusion. It is probably due to antibodies in the recipient that are directed to antigens in the donor plasma. *Febrile nonhemolytic* reactions consist of the development of fever, but not red cell destruction (hemolysis) during the transfusion. These reactions occur in recipients who 'have been transfused in the past or who have been pregnant. They result from the recipients' sensitivity to cellular components of blood. The sensitivity develops from a previous exposure to blood products. In the context of "blood doping" an athlete recipient is at greater risk to experience a

febrile nonhemolytic reaction than a person who has never received a transfusion.

An acute hemolytic reaction is a serious but relatively rare event. The current frequency in the US is about one per 6000 transfusions<sup>2</sup>. It usually occurs because incompatible blood is mistakenly transfused, thus it can be avoided if the blood banking procedures of typing and cross-matching are scrupulously adhered to, and if the correct unit of blood is administered to the correct recipient. The reaction is due to red cell antigens on the transfused red cells reacting with previously existing recipient antibodies. This triggers a complex chain of immunological events that result in intravascular hemolysis of the transfused cells. In addition, these reactions commonly result in acute renal failure and serious disruption of the coagulation mechanism (disseminated intravascular coagulation). At the first signs of acute hemolysis (fever and chills), the transfusion is discontinued and treatment is initiated. Most patients survive the acute hemolytic reaction but deaths have been reported<sup>3</sup>.

The delayed *transfusion* reaction differs from the acute hemolytic reaction in that it takes place several days after the transfusion and the destruction of the red cells occurs in the extravascular space. The mechanism involves the rapid development of antibodies to the transfused red cells. This type of reaction occurs in persons who were transfused months to years before the transfusion which triggered a delayed reaction. The previous transfusion invoked an antibody response to the red cells, but over time the level of circulating antibodies declined to undetectable levels. If the second transfusion contains red cells with antigens similar to the earlier transfusion(s), the immune system rapidly develops antibodies which destroy the newly transfused cells. The clinical consequences of the delayed reaction are fever, a fall in the concentration of hemoglobin, jaundice and the requirement that all future transfusions not contain the antigen which incites the antibody response. The latter problem can seriously jeopardize and complicate the subsequent management of a patient with continuing transfusion requirements.

*Anaphylactic* transfusion reactions are both serious and rare. They occur in patients who have a deficiency of immunoglobulin A (1gA) and have developed antibodies to 1gA. This reaction

must be treated acutely and skillfully, and may be prevented by administering washed red cells.

#### *B. Reactions due to transmission of infectious agents*

A wide variety of infectious diseases have been transmitted by blood transfusions. Some of these include malaria, cytomegalovirus, syphilis, and toxoplasmosis. Some of these can be avoided by practices such as testing the donor (e.g. syphilis), or eliminating donors who have had the disease or recently travelled in an area where the disease is endemic (e.g. malaria).



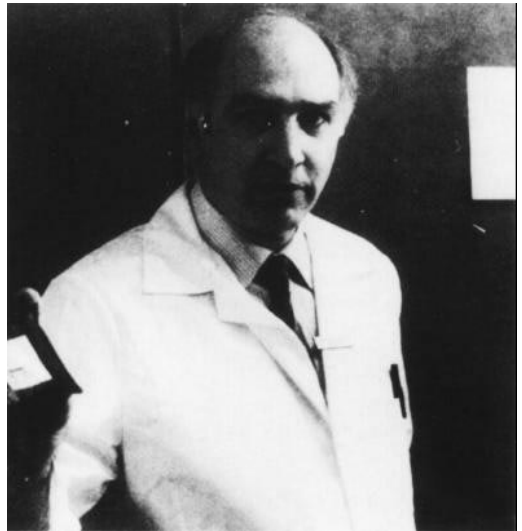
*Viral* hepatitis is the most common post-transfusion complication. The frequency of post-transfusion hepatitis is about 10% in the United States, despite the practice of eliminating paid blood donors and screening all units for type B hepatitis. Most cases of post-transfusion hepatitis are due to non-A, non-B hepatitis, which is caused by an agent for which there is no effective serological screen. The most serious sequelae of hepatitis is the development of chronic hepatitis and cirrhosis, that is chronic liver disease. The true incidence of transfusion related chronic liver disease and its associated morbidity and mortality is not known but may be quite high<sup>4</sup>.

*AIDS* —The Acquired Immunodeficiency Syndrome (AIDS) is a serious disease characterized by a reduced ability of the body to resist infection. Some of the clinical manifestation of AIDS include lymphadenopathy, opportunistic infections, fever and Kaposis' sarcoma. The etiologic agent of AIDS is a virus from the retrovirus family called human T-cell lymphotropic virus type III (HTLV-III). HTLV-III has been isolated from the blood, semen, and saliva of patients with AIDS. Risk factors for AIDS include male homosexuals, intravenous drug abusers, Haitians who entered the United States after 1977, hemophiliacs, and sexual partners of persons in these groups.

AIDS is transmitted through intimate sexual contact, sharing contaminated needles, and transfusion of whole blood, the cellular components of blood, plasma, or clotting factors. The number of cases of AIDS reported in the United States as of August 1985 is 12,932. Of these cases, 195 (1.5 percent) were reported in persons with no known risk factors who had received blood transfusions within five years of diagnosis, and in 86 cases AIDS was detected in persons with hemophilia who had received antihemophilic concentrates<sup>5</sup>.

Determining the risk of developing AIDS through transfusions is difficult because of the complexity and nature of the pertinent variables. These include the type of blood product, the number of units, whether the units were from single donors or pooled from a large number of donors and the length of time between transfusion and diagnosis. Despite these problems, the risk is small and may decrease with the adoption of measures to eliminate donations from high-risk donors and widespread utilization of a laboratory test for antibodies to HTLV-III virus.

The risk of developing AIDS for a person with hemophilia who receives antihemophilic concentrates has been estimated at 1 case per 1000<sup>5</sup>. This relatively high risk is probably due to the fact that antihemophilic concentrates are prepared from plasma pooled from thousands of donors. In contrast a rough estimate of the annual rate of reported cases of AIDS in the United States among transfusion recipients is 1 case per 100,000<sup>6</sup>. Furthermore, these cases of AIDS that were associated with transfusions, differed from the average recipient because they received blood from an average of 15.9 donors (range 2-48) which is almost five times the



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national average<sup>6,7</sup>. One case report<sup>8</sup> has raised a concern about the possible transmission of AIDS from blood products obtained from a single donor. This brief summary suggests that the risk for a young healthy person in the US, who has no risk factors for AIDS, and who receives one or two units of red cell products on one occasion from a single donor will have an exceedingly low risk for developing AIDS.

Because AIDS may be transmitted by transfusions there has been an intense effort to develop a test that might identify blood products that contain HTLV-III. Recently a commercial test for antibodies to the HTLV-III has been developed and marketed. The antibody test is not a test for AIDS because not all individuals with AIDS have a positive antibody test, and a few individuals who do not have the clinical syndrome of AIDS may have a positive test. The test is used to screen blood and plasma prior to administration ; units that are positive for antibodies are discarded.

### *C. Miscellaneous Reactions*

Blood products are collected, processed, stored and transfused according to carefully designed and executed protocols that are designed to minimize the opportunity for infection, mislabelling

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or other mistakes. Nevertheless, mistakes do occur thus even autologous transfusions carry risks.

Infrequent complications of transfusions include overload of the circulation, metabolic shock, air and fat embolism, and hyperkalemia. The latter occurs with massive blood transfusions over short periods of time.

*D. H. C.*

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