Blood Safety in the Age of AIDS

By Shauna S. Roberts

This series of essays was developed as part of FASEB's efforts to educate the general public and the legislators whom it elects about the benefits of fundamental biomedical research - particularly how investment in such research leads to scientific progress, improved health, and economic well-being.

"Blood Safety in the Age of AIDS" examines the effects of the AIDS epidemic on the safety of the blood supply. Just as a pebble tossed in a lake sends out ripples that last long after the pebble sinks, the discovery more than a decade ago that the AIDS virus was in the blood supply is still having repercussions on research and transfusion practices. New screening tests for blood and new ways of using one's own blood during surgery are among the steps that have made transfusions much safer. Meanwhile, researchers continue tracking down new threats and devising ways to circumvent them. (This is the second article in the series)

Risk, like beauty, is in the eye of the beholder. Today, having a blood transfusion is safer than it has ever been. It is far less risky, for example, than eating a poor diet or not exercising, which can cut years from a person's life. Yet people are more afraid of transfusions than ever before.

Ironically, the AIDS epidemic is responsible for both the current safety of blood and people's new fear of it. The epidemic revealed how vulnerable the blood supply is to new diseases. But it also served as a wake-up call. As a result, doctors are making better choices about when to transfuse. Scientists are working on better ways to test for diseases and inactivate viruses, and they are pursuing new viruses with great vigor. Blood banks are reorganizing to reduce mistakes in blood handling. The lessons of AIDS may help us avoid disasters in the future.

Of lambs and lives: mysteries of blood safety

Today we know that blood cells carry proteins and sugars on their surfaces. The proteins determine whether a person is Rh positive or Rh negative, whereas the sugars determine whether that person has type A, B, AB, or O blood. Because of these membrane components, transfusions between species usually don't work, and transfusions between people must consider their blood groups. Today we also know about bacteria and the importance of cleanliness. Not so in 1667. On June 25th of that year, French physician Jean-Baptiste Denys transfused lamb's blood into a teenage boy who had been feverish for two months. Denys chose animal blood in part for safety. Because animals don't engage in "debauchery," Denys believed their blood was purer.
<table>
<thead>
<tr>
<th>Types of blood products</th>
<th>Blood product</th>
<th>What is it?</th>
<th>Use in transfusion</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Whole blood</td>
<td>Blood as it exists in the body; it consists primarily of cells (red blood cells, white blood cells, and platelets) and plasma</td>
<td>Rarely used except in massive blood loss (loss of more than 25% of blood); usually is broken into components</td>
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<tr>
<td></td>
<td>Red blood cells</td>
<td>Blood cells that carry oxygen</td>
<td>Treat anemia; provide oxygen to tissues; replace blood lost during surgery</td>
</tr>
<tr>
<td></td>
<td>White blood cells</td>
<td>Several types of blood cells, all of which protect the body against infection</td>
<td>Fight infections; provide stem cells for transplantation</td>
</tr>
<tr>
<td></td>
<td>Platelets</td>
<td>Sticky cell fragments that help blood clot</td>
<td>Control bleeding caused by platelet deficiency, such as occurs in people who take certain medications or who have leukemia or cancer</td>
</tr>
<tr>
<td></td>
<td>Plasma</td>
<td>The fluid portion of blood, which carries proteins, salts, and nutrients</td>
<td>Control bleeding caused by low levels of clotting factors</td>
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<tr>
<td></td>
<td>Cryoprecipitate</td>
<td>A product derived from plasma</td>
<td>Control bleeding; treat hemophilia</td>
</tr>
<tr>
<td></td>
<td>Concentrated plasma proteins</td>
<td>Proteins derived from plasma</td>
<td>Treat genetic diseases (such as hemophilia), dissolve clots, treat Rh incompatibility disease, or protect against certain infectious diseases, depending on the protein</td>
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</table>

Although Denys' first patient recovered, later transfusion recipients weren't as lucky. France banned transfusions, and a papal proclamation ended transfusion experiments elsewhere.

When transfusion research resumed in the 1800s, the practice continued to be dangerous, with a third of transfusion recipients dying for unknown reasons. But in 1901, immunologist and pathologist Karl Landsteiner and his students discovered the first blood group, the ABO group. Their experiments solved the mystery of why some transfusions killed: Receiving incompatible blood can cause disastrous immune system reactions. The first transfusion of matched blood took place in 1907. Landsteiner later played important roles in the discoveries of three other blood groups, including the Rh group.

Another leap forward in the early 20th century was the discovery that sodium citrate could safely keep blood from clotting. Armed with this anti-coagulant, knowledge of blood groups, and a greater attentiveness to cleanliness, battlefield hospitals during World War I saved thousands of lives with transfusions. Techniques then improved so rapidly that by the 1960s, many people had stopped thinking of transfusion as carrying any risk—even though many people had allergic reactions or got hepatitis.
This complacency was shattered in the early 1980s. In 1981, the Centers for Disease Control (CDC, now called the Centers for Disease Control and Prevention) reported several cases of Kaposi's sarcoma (a kind of cancer) and of *Pneumocystis carinii* pneumonia in previously healthy homosexual men. These two conditions usually struck only people whose immune systems had broken down. After more cases came to light, scientists began to suspect that a new disease was afoot, one that shut down its victims’ immune systems, rendering them helpless against infections.

In July 1982, the disease received a name: acquired immunodeficiency syndrome (AIDS). That month, CDC reported the first cases of AIDS in people with hemophilia. Hemophilia is a disease in which the blood lacks one of the clotting proteins. At one time, even a tiny cut could lead to massive blood loss. However, in the 1960s, a method of replacing clotting proteins was developed. Plasma (the fluid portion of blood) from thousands of donors was combined and the blood-clotting factors extracted. Hemophiliacs could then infuse themselves with the antihemophilic factor (AHF) in this extract and prevent dangerous bleeding.

Because hemophiliacs were exposed to blood from millions of people, most—about 80%—eventually became infected with hepatitis. When hemophiliacs began to get AIDS, it was a red flag that the disease might be transmitted through blood products. By the end of 1982, more cases of AIDS in hemophiliacs had been discovered, and a baby who had had a transfusion also got the disease.

Like piranhas attacking a baby whale, HIV particles (tiny blue dots) gang up on a T cell (an immune system cell). Each virus particle measures 10 nanometers (4/10,000,000 inch) across, whereas the diameter of a T cell is roughly 1,000 times as large (3/10,000 to 5/10,000 inch). Despite its tiny size, the AIDS virus can be quite difficult to kill. A major challenge facing researchers is to learn how to destroy the virus in blood for transfusions without harming blood cells. Copyright Boehringer Ingelheim International GmbH.

If AIDS was in the blood, what should be done? One urgent need was to learn as much as possible, as quickly as possible, about this mysterious disease. Unfortunately, belts were being painfully tightened throughout the government. Even so, Congress, which had given the National Institutes of Health (NIH) some $3 million for AIDS research for fiscal year 1982, upped the amount to more than $21 million for 1983.
It was equally urgent to devise ways to weed out infected donors, but how to do so was unclear. In 1983, CDC scientists recommended asking blood donors about their sexual behavior and performing "surrogate tests." Such a test would detect something associated with AIDS. For example, one study had found that 88% of people with AIDS had antibodies to the so-called hepatitis B core antigen. (Antibodies are immune system proteins that attack specific foreign invaders—in this case, a particular protein of a hepatitis virus.) Some scientists proposed that testing for these antibodies would be a useful surrogate test to exclude some AIDS-infected donors.

But the Food and Drug Administration (FDA) and many blood banking organizations did not agree with the CDC recommendations. They believed that surrogate tests were not specific enough and would eliminate many uninfected blood donors. Also, it was unclear how to counsel the deferred donors. Thus, weaker recommendations were adopted. These included training personnel to recognize the symptoms of AIDS and educating the public that members of high-risk groups should not donate blood.

About this time, research on inactivating hepatitis viruses in AHF, which had started long before AIDS, finally bore fruit. The first treated factor VIII (the factor lacking in 85% of people with hemophilia) hit the market in 1983. Treatment of factor IX (missing in 14% of hemophiliacs) began in 1984.

<table>
<thead>
<tr>
<th>Name of test</th>
<th>what it determines</th>
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<tbody>
<tr>
<td>ABO Test</td>
<td>Whether the donors blood type is A,, B,, AB,, or O</td>
</tr>
<tr>
<td>Rh test</td>
<td>Whether the donor is Rh positive or Rh negative</td>
</tr>
<tr>
<td>Unexpected antibodies</td>
<td>Whether the donors blood contains unusual proteins that might cause a reaction in the recipient</td>
</tr>
<tr>
<td>Hepatitis B surface antigen (HbsAg)</td>
<td>Whether the donor has hepatitis B and is able to infect others</td>
</tr>
<tr>
<td>Antibody to hepatitis B core antigen (anti-HBc)</td>
<td>Whether the donor was exposed to hepatitis B in the past</td>
</tr>
<tr>
<td>Antibodies to human T-cell lymphotropic virus type I (anti-HTLV-I)</td>
<td>Whether the donor has HTLV-I,, which causes leukemia in about 1% of people infected with it; the test also catches some samples with a related virus named HTLV-II</td>
</tr>
<tr>
<td>Antibodies to HIV-1 (anti-HIV-1)</td>
<td>Whether the donor has HIV-1,, the virus that causes nearly all cases of AIDS in the United States</td>
</tr>
<tr>
<td>Antibodies to HIV-2</td>
<td>Whether the donor has HIV-2,, a rare virus closely related to HIV-1 (anti-HIV-2)</td>
</tr>
<tr>
<td>Antibodies to hepatitis C (anti-HCV)</td>
<td>Whether the donor has hepatitis C</td>
</tr>
<tr>
<td>Rapid plasma reagin</td>
<td>Whether the donor has syphilis</td>
</tr>
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</table>

The standards of the American Association of Blood Banks (Bethesda, MD) require these tests to be performed on donated blood.

Treatment involved heating AHF for many hours. It inactivated not only most hepatitis viruses, but also the viruses that cause AIDS. Even so, hemophiliacs continued to become infected with AIDS after 1984,
for three reasons: FDA did not require AHF manufacturers to recall untreated factor until 1989, the companies did not do so on their own, and some doctors did not encourage their patients to switch to heat-treated factor.

In April 1984, NIH researchers announced that they had found a virus that caused AIDS. This virus, similar to one isolated previously in France from an AIDS patient, was later named the human immunodeficiency virus–type 1 (HIV-1). The first detection test, called the enzyme-linked immunosorbent assay (ELISA), became available in March 1985. Because the ELISA sometimes gave a positive result when a person was uninfected, all positive results were double-checked by another procedure called western blotting.

Neither the ELISA nor the western blot could detect the virus itself. Rather, both detected antibodies to HIV-1. These antibodies occur in people who are infected with the virus. The tests were able to make such speedy progress to market because they did not need to be developed from scratch. Immunologists and biochemists had invented the ELISA in 1971 as a cheap, sensitive, and easy way to measure proteins in serum. Similarly, the western blot had been developed in 1979 and 1981 as a way to sensitively locate a specific protein in a complex mix of proteins.

After these basic research procedures had been adapted for use as AIDS tests, blood banks could finally test donated blood and discard donations with positive tests. What was the human cost of having had AIDS in the blood supply until then? CDC reported in 1987 that about 9500 people with hemophilia—more than half—were infected with HIV-1. It estimated that 12,000 people without hemophilia had also been infected with HIV-1 between 1978 and 1984 through blood transfusions.

20/20 hindsight

Looking back, we can see that many cases of AIDS could have been prevented. By 1983, there was evidence that the AIDS virus was transmitted through blood, yet many people continued to get HIV from blood products until HIV testing began in 1985. The reasons government agencies, researchers, and blood banks did not take stronger steps to prevent the spread of AIDS are complex and surprising.

Naïveté. In the 20th century, running water, better hygiene, and antibiotics had seemingly vanquished most infectious diseases. Many doctors believed that epidemics were a thing of the past.

Swine flu. In 1918, 20 million people died from a particularly virulent flu virus, probably a close relative of swine flu. In 1976, CDC warned of a possible reoccurrence of this deadly flu strain. Fifty million Americans were vaccinated against swine flu. No epidemic occurred, and CDC lost credibility. When some CDC staffers predicted a possible AIDS epidemic, many scientists and blood bankers were not convinced.

Fear of blood shortages. If too few people donate blood, some people who need transfusions won't be able to get them and may die. In the early 1980s, blood banks had barely enough blood to meet demand. Blood bankers feared that bad publicity would discourage people from donating (which in fact it did—many Americans got the wrong idea that one could get HIV by donating blood). Blood bankers also worried that if they refused blood from people who belonged to risk groups, not enough donors would be left.

Political inaction. At a time when strong government action was needed to protect citizens from AIDS, prevailing political philosophies emphasized downsizing government and reducing regulation.
Desire not to offend donors. Blood bankers were appalled at the idea of asking men personal questions about their sex lives before accepting their blood. Blood bankers also believed that asking might not do any good because some men might be afraid to admit they were homosexual.

Homosexual groups' opposition to screening. Many homosexual groups vehemently opposed blood banks' asking men about their sexual history. If blood banks refused to accept blood from men who had had sex with men, prejudice against homosexuals might increase.

Using hepatitis as a model. In the early days of AIDS, researchers had to guess at its properties. The disease that seemed most similar was hepatitis B. Unfortunately, because hepatitis B infections kill few people and usually do not become chronic, many people assumed that AIDS was less deadly than it actually is.

The known risks of not using blood-clotting factors. In the 1960s, before AHF was available, the average person with hemophilia lived only 54 years and suffered crippling medical problems. Weighed against the very real threat of death from not using clotting factors, the unknown dangers of AIDS seemed small to some people.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Approximate risk</th>
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<tbody>
<tr>
<td>Infection with human immunodeficiency virus-type 1</td>
<td>1 case per 450,000 to 660,000 units transfused&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Infection with hepatitis C</td>
<td>1 case per 3,300 units transfused&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Infection with human T-cell lymphotropic virustype I</td>
<td>1 case per 70,000 units transfused&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Receipt of ABO-incompatible blood</td>
<td>1 case per 12,000 transfusion&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
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</table>


Poor organizational structure. Government agencies were not prepared to deal with a threat like AIDS. For example, FDA, which regulates blood products, preferred to make decisions based on consensus. This
collegial approach failed with AIDS. No one could agree on its dangers or what should be done to avert them, so little was done. In addition, no government agency had a mechanism in place for notifying the public about the risks. In 1993, the Department of Health and Human Services asked the Institute of Medicine to study how HIV spread through the blood supply in the early 1980s. With the benefit of hindsight, the study committee concluded in its 1995 report that "a failure of leadership and inadequate decision-making processes" were pivotal. In particular, donor screening was not very effective, regulatory action was weak, and hemophiliacs were not told enough about AIDS to make informed decisions.

The devastating effects of all these wrong-headed policies, ideas, and actions taught vital lessons. Everyone now accepts that new infectious diseases can appear. It's also now clear that the blood supply is vulnerable to unknown diseases and that a devastating epidemic can start slowly. Most people now acknowledge that keeping the blood supply safe is more important than not hurting people's feelings. Rose-colored glasses are no substitute for microscopes and computer models.

Zero chance of a zero-risk blood supply?

Ask 20 people what the safest car is. Then ask what car they drive. The two lists will probably not overlap much because people cannot always afford the car they think is safest. Just as people may trade off some safety to get a car they can afford, many people argue that society must trade off some safety to get a blood supply we can afford.

According to one estimate, the odds of getting HIV from a transfusion are now 1 in 450,000 or less. What would it take to reduce those odds to zero—that is, to make sure no one in America gets AIDS from a blood transfusion? There are many approaches to eliminating AIDS from the blood supply. Screening tests for donated blood are one strategy.

In this close-up of the surface of a T cell, HIV particles (small bluish spheres) are escaping from the interior of the cell, ready to infect other T cells. Blood transfusion is one way HIV can be transmitted from person to person. Copyright Boehringer Ingelheim International GmbH.
Like the first generation of AIDS blood tests, current tests detect antibodies to the AIDS viruses. Unfortunately, for a brief time after infection, people make too few antibodies for these tests to detect. As a result, their blood passes all the screening tests, even though it can transmit HIV. The "window period" for HIV-1 lasts about 22 days.

The FDA recommended in August 1995 that blood banks begin using the new p24 antigen test for HIV-1 when it became available. This test might cut 6 to 12 days from the window period—at an added cost of perhaps $60 million each year.

Future tests may be based on the polymerase chain reaction (PCR), which can detect HIV directly by detecting its genetic material.

PCR is sensitive enough to detect HIV in blood several days earlier than the p24 antigen test. PCR was invented in the mid-1980s, and it gave scientists a way to quickly and simply make millions of copies of genes for their experiments. Molecular biologists could probe the gene defects underlying cystic fibrosis, muscular dystrophy, and many other diseases. Virologists could study the myriad variants of HIV-1 to determine how the virus changes over time. Pharmacologists could measure the effects of potential drugs on viruses. Archaeologists could track ancient human migrations.

Once refined by experimental scientists, PCR was eagerly adapted by clinicians. Its sensitivity made it seem a natural for testing donated blood for diseases. But so far, PCR has proved difficult to automate, a necessity for processing the 14 million units of blood donated each year. Also, PCR is expensive and, as viewers of the O.J. Simpson trial learned, demands pristine handling conditions and meticulous technique. More research is needed before blood banks can take advantage of PCR's power.

But protecting the blood supply from HIV-1 is not enough. Scientists continue to discover other diseases that can be transmitted in blood. Also, mistakes can occur. Blood can be mislabeled. Blood bank volunteers can neglect to ask prospective donors all the required questions. Lab workers can be sloppy in testing blood, or a test kit can be defective. Thousands of errors and accidents are reported to FDA each year.

And even if cheap, reliable, error-proof screening tests were available for every transmittable disease, transfusion would still not be 100% safe. No medical procedure is. Transfusions cause some kind of problem in about 10% of recipients. These problems range from fever and hives to iron overload and congestive heart failure.

Scientists estimate that smoking kills 150,000 Americans each year. Car accidents kill another 50,000. Infections picked up while staying in the hospital kill about 20,000. Surgery is responsible for another 2800 deaths. As a result of blood transfusions, each year perhaps 10 Americans become infected with HIV and perhaps 2000 with hepatitis.

Choosing to accept a blood transfusion is thus safer than choosing to have surgery or ride in cars or smoke. But are transfusions safe enough? Some people argue that even one person a year infected with a deadly disease is one person too many. Yet the alternatives themselves carry dangers. Expensive new screening tests could make blood transfusions too costly for most people. Tighter screening would result in fewer donors, possibly leading to blood shortages. Finding replacement donors and counseling rejected donors would add to the cost of a transfusion.
In addition, in a time of tight budgets, is developing costly blood-screening tests the best use of health-care dollars? Immunization programs for children, for example, would save many more lives than new tests at blood banks. These are among the difficult trade-offs that society must weigh.

**Lurking on the horizon**

As people travel, so do their diseases. This problem is not new. In 1346, caravans laden with trade goods bore some dangerous stowaways to Europe: plague-infected rats. In the next few years, the Black Death wiped out a quarter of the inhabitants of western Europe.

Today, cars, motorcycles, and airplanes make long-distance travel easy and common. Urbanization creates dense pockets of potential hosts. Because of these factors, a disease that might once have ravaged only a tiny village before running out of victims can today become a worldwide epidemic.

New diseases can arise as well. Sometimes an agent that infects animals but causes little or no disease in them can infect humans and cause severe disease. For example, forested lands in the Eastern United States that had been turned into farms are reverting to forest. Deer multiply rapidly in these young woods, leading to tick population explosions. When suburbs began encroaching on the new forests, the ticks found a new host. Since the first recognized cases in Connecticut in 1975, Lyme disease (caused by a microorganism that lives in ticks) has spread to nearly every state. Similarly, HIV probably arose first in monkeys and then spread to humans.

As a result, keeping the blood supply safe requires consideration of the spread of diseases from other places, the jumping of diseases from animals to people, and the emergence of new diseases.

**New kinds of hepatitis.** Doctors during World War II recognized two kinds of hepatitis, one that developed right away and rarely was associated with blood transfusion, and one that could lie dormant for a long time and was often associated with transfusion. But even after tests were developed for hepatitis A (a short-acting form) and hepatitis B (a chronic form) in the 1970s, about 20% of transfusion recipients still got hepatitis. Since then, scientists have discovered five more kinds of hepatitis viruses, at least three of which can be transmitted through blood: C, which, like hepatitis B, can also cause chronic liver disease and liver cancer; D, which worsens the consequences of hepatitis B infection but does not make people sick by itself; and G, which is similar to hepatitis C but appears to cause a milder chronic disease. In addition, a mutant form of hepatitis B virus has been discovered that evades some hepatitis B blood tests.
Creutzfeldt-Jakob disease. Creutzfeldt-Jakob disease is a fatal brain disease probably caused by a strange protein called a prion. The disease can be transmitted through some tissue transplants. Although no cases transmitted through blood transfusion have been reported, finding out whether such transmission is possible could take years. Since August 1995, FDA has required blood banks to recall blood donated by people who later are discovered either to have Creutzfeldt-Jakob disease or to have a blood relative with it.

Cytomegalovirus. Cytomegalovirus (CMV) is a herpes virus that can be transmitted in blood and that infects 80% of Americans. CMV is harmless to healthy people. But in people with weak immune systems, CMV can cause severe—sometimes deadly—infections.

Chagas' disease. Chagas' disease is a slow-developing parasitic disease for which there is no cure. The parasite is usually spread by bites from bugs that live in Mexico and Central and South America, but can also be transmitted in blood transfusions. People who travel to these areas or emigrate from there can bring the parasite here. Perhaps 50,000 to 100,000 Americans are infected. Some blood banks are now testing for the parasite.

Fighting back

To deal better with threats to the blood supply, government agencies and blood banks have been struggling to restructure. FDA, for example, has made many changes, such as adding people outside the blood industry to its advisory committee. Blood banks are adopting the rigorous quality assurance and standardization procedures that manufacturers use to prevent mistakes.
Research is also playing a vital role in making blood safer. Researchers have made blood far safer through technological improvements, and continue to do so.

**Virus inactivation.** Today, some manufacturers still inactivate AHF with heat, but others treat plasma products with a detergent that dissolves the fatty walls of most viruses. Both heat and detergents harm the walls of blood cells, so these methods are not suitable for treating red blood cells and platelets. Many immunologists, pathologists, and other scientists are working on new ways to inactivate viruses without harming blood cells. Several methods are based on adding a dye to the blood and then exposing the blood to light. The light triggers a reaction that either destroys the walls of the viruses or prevents them from reproducing.

**Blood substitutes.** Many researchers are trying to create artificial substances that can carry oxygen to tissues, which is normally the job of the hemoglobin molecules inside red blood cells. Research groups are exploring a variety of blood substitutes including a liquid Teflon-like chemical, genetically engineered hemoglobin, and purified hemoglobin from animals. Several are now going through clinical testing. In addition, some researchers are in the beginning stages of developing artificial platelets.

**Growth factors.** Some people must get transfusions because they have anemia caused by a disease or a medical treatment. Researchers are studying ways to reduce these people's need for transfusions by giving them proteins called growth factors that boost the body's production of one or another blood cell. These factors were first discovered in the 1960s by cell biologists struggling to entice cells to grow in colonies outside the body. They learned that cells needed various proteins found in blood, including growth factors, to grow and flourish. Later research proved these proteins were just as vital to cells in the body, and so the search began for ways to use growth factors clinically.

The most useful growth factors so far for blood transfusion are erythropoietin, which increases red blood cell production in premature infants and people with kidney failure, and granulocyte colony-stimulating factor and granulocyte-monocyte colony-stimulating factor, which increase white blood cells in people who have had bone marrow transplants or cancer chemotherapy. The recently discovered thrombopoietin, which may increase platelets in people who have AIDS or have had bone marrow transplants or cancer chemotherapy, has entered clinical trials, but its safety and effectiveness are not yet known.

*Normally, red blood cells move through the body evenly dispersed. But when red blood cells are exposed to an antibody to a protein or sugar on their membranes, the cells clump together (agglutinate). Blood banks take advantage of this property to test donated blood for ABO and Rh type and for unexpected antibodies. By exposing the blood to certain antibodies, the blood...*
bank can determine whether the red blood cells carry or lack a certain marker by seeing whether the cells agglutinate (left) or remain dispersed (right). (Courtesy Ortho Diagnostic Systems Inc., a Johnson & Johnson Company, Raritan, N.J.)

**Autologous (self) donations.** When surgery can be planned in advance and a transfusion is likely to be needed, healthy people can store their own blood. Red blood cells can be stored for 35 or 42 days, depending on the preservative used. Autologous donation prevents most transfusion-associated problems, but has some disadvantages. The special handling required makes autologous blood expensive, and some scientists believe that the longer-than-average storage time increases the chance for growth of bacteria.

**Intraoperative hemodilution.** Intraoperative hemodilution is a form of autologous donation. Blood is removed before surgery and restored at the end. Another liquid is infused to keep the volume high. This procedure lowers red blood cell loss during surgery and may increase the amount of oxygen tissues get.

**Blood recycling.** In intraoperative blood collection, the blood a person loses during surgery is saved. A machine concentrates and washes the red blood cells, which are then reinfused after surgery.

**Directed donations.** In directed donations, blood donors specify who should receive their blood. This practice is not necessarily safer because people who know they shouldn't donate blood sometimes feel pressured to do so when a friend or relative needs a transfusion.

**Surgeon and anesthesiologist education.** Sometimes, doctors order transfusions when they aren't required, just to be safe. Preliminary research suggests that after a brief session that teaches current guidelines for blood transfusion, most surgeons use blood more judiciously.

**Leukoreduction.** Filtering white blood cells from blood (leukoreduction) may reduce fevers and allergic reactions after transfusions. Depending on how many white blood cells are removed, the procedure may also eliminate some viruses, such as CMV. People who need transfusions and are susceptible to such viruses already get leukoreduced blood or blood that has tested negative for CMV. Whether healthy people should also get leukoreduced blood is controversial because of the added cost, the accidental but unavoidable loss of desirable cells, and the procedure's unproven efficacy and efficiency. An FDA expert panel concluded in March 1995 that more research was needed.

**Other research paths.** Some researchers are looking for ways to strip the proteins from the membranes of blood cells so that blood type matching won't be necessary. Other research is studying the errors that occur at blood banks as a step toward preventing them.

The AIDS epidemic exposed holes in the blood supply's safety net. Researchers have already patched some of these by devising new and better screening tests, hunting down unknown viruses, and improving our knowledge of how diseases develop and spread. The fruits of current research should make blood even safer.

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**RESOURCES**

National Academy Press, Washington, D. C. A 1995 Institute of Medicine report evaluates the events leading up to the transmission of HIV to people with hemophilia. But it also demonstrates how difficult it is to reconstruct events of even just 10 years past. To learn how a tangle of cultural, ethical, political, and scientific factors led to bad decisions that caused many extra people to become infected with HIV, read: Committee to Study HIV Transmission Through Blood and Blood Products (1995) *HIV and the Blood Supply: An Analysis of Crisis Decisionmaking*, National Academy Press, Washington, D. C.

In contrast to the Institute of Medicine report, which takes a broad view and examines AIDS in the 1980s from a multitude of perspectives, another report focuses on how one single blood center, the Stanford University Blood Center, evaluated the evidence and responded. By instituting a surrogate test, the center prevented an estimated 33 cases of HIV-1 transmission. The report, which also explores current threats to the blood supply, is: Galel, S. A., Lifson, J. D., and Engleman, E. G. (1995) Prevention of AIDS transmission through screening of the blood supply, *Annu. Rev. Immunol.* 13, 201–207.


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