



## **No Man's Blood**

A Television Series of 13 x 30 minutes episodes

Experienced physicians have called it an unnecessary health risk, a disease factor, and a medical product that may do more harm than good. Some have even compared it to a dangerous drug.

They're talking about allogeneic blood -- blood that's donated by one person and transfused into another.

After decades of common use in hospitals and clinics worldwide, allogeneic blood is gradually losing its luster in the medical community, and for good reason. Its reputation has been clouded by the spread of blood-borne diseases such as AIDS and hepatitis, ever-increasing costs for "clean" blood, changing public attitudes, greater respect in many countries for patient choice, and exciting new technology that, in the minds of some experts, may have already rendered transfusion medicine obsolete.

Slowly, but perhaps irreversibly, blood transfusions may be going the way of leech treatment, blood-letting and other laughably outdated medical practices which today can be found only in the pages of history books.

The risks associated with allogeneic blood are clearly understood. A "Circular of Information" prepared by the American Red Cross and other US blood agencies contains the following notice:

*"WARNING: Because whole blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents (such as) viruses.... Careful donor selection and available laboratory tests do not eliminate the hazard."*

The potential dangers are also well known among many physicians who now conclude that avoiding or limiting the use of blood transfusions is highly advantageous. For example, Dr. Aryeh Shander of Englewood Hospital and Medical Center in New Jersey, says: "The risk for transmitting a blood-borne disease is always a concern because, no matter how safe we believe our blood banks to be, risk can never be completely eliminated."

Specialists such as Dr. Bruce Spiess, a professor and chief of cardiothoracic anesthesia at Virginia Commonwealth University, have challenged the use of primary blood components in critical procedures, including heart surgery. "There are few if any (medical journal) articles that support transfusion actually improving patient outcome," Spiess said. Many transfusions "may do more harm than good in virtually every instance except trauma," he said, and actually increase "the risk of pneumonia, infections, heart attacks and strokes."

Views toward allogeneic blood are changing outside the United States as well. For example, the Network for Advancement of Transfusion Alternatives (NATA) based in France is a clearinghouse for medical practitioners, researchers and opinion leaders around the world. Austria is the headquarters of the Medical Society for Blood Management. And the senior officer at the International Federation of Red Cross and Red Crescent Societies, Peter Carolan, once expressed this opinion: "Absolute guarantees on blood supplies can never be given.... There will always be new infections for which, at that moment, there is no test."

In addition to the identifiable health risks, public attitudes are forcing the medical community to rethink its traditional reliance on blood transfusions. Many well-educated patients -- including doctors themselves -- are actively shopping for medical care that does not require what's perceived as the dangerous use of a stranger's blood. Patients and doctors are also influenced by numerous medical studies that have shown how transfusion alternatives reduce costs and shorten hospital stays. Moreover, religious groups such as Jehovah's Witnesses are winning respect for their

faith-based stand against transfusions. And well-grounded fears about AIDS and other diseases are influencing public views toward blood and even healthcare in general.

Hospitals, researchers, clinics, physicians, public health agencies and the healthcare industry are responding to these trends in a number of ways. Some have become open critics of transfusion medicine, and many are looking beyond transfusions to new techniques, equipment and procedures that limit or eliminate the use of allogeneic blood as well as major blood components.

One set of alternatives to transfused blood is based on techniques using so-called blood "fractions," blood dilution and special drugs. Another involves technologically advanced equipment, ranging from clean-cutting scalpels to "cell-saver" machines. These alternatives and their professional proponents support an emerging field of health care often known as "bloodless medicine."

How do fractions and drugs contribute to bloodless medicine? Pharmaceutical researchers have learned to separate fractions from human blood and create blood-related drugs for use in a variety of patient-care techniques. These techniques rely on the fact that blood can be divided into two, basic categories -- cellular materials (45 percent) and plasma (55 percent), which is 90 per cent water. The remaining 10 per cent consists of small amounts of various proteins, hormones, salts, vitamins and enzymes.

A fraction-based treatment option involves the use of albumin, one of many proteins found in plasma. For example, if a patient suffers trauma and shock from heavy blood loss, albumin can be administered to maintain or increase blood pressure and blood volume. This protein can also help manage an underlying medical condition. It's a safe alternative to transfusions because albumin is prepared for medical use by fractionating it from the plasma of healthy donors before heating it to inactivate any disease-causing agents.

One new and beneficial family of drugs called hemoglobin-based oxygen carriers (HBOCs). They have been used after traumatic injuries with heavy bleeding, during surgery, or in cases of life-threatening anemia. Although a body is capable of maintaining essential functions with a very low amount of oxygen-carrying red cells after blood loss, provided the body has enough fluids to circulate the cells, not enough oxygen can be transported. As a result, body organs cannot survive for long. To treat this dangerous condition, HBOCs can be infused. The drugs transport oxygen to buy time until the body can make up for blood loss by producing its own red cells.

Different kinds of HBOCs are produced differently. But they all stem from the breakdown of red blood cells into their components. The hemoglobin molecule is extracted from a cell for further processing and the remaining parts of the cell are discarded. The end product is a red fluid containing hemoglobin molecules, which is then sterilized.

Another alternative involves the use of a hormone that's naturally produced in the kidneys called erythropoietin, also called EPO. The kidneys produce EPO and this hormone is sent to the bone marrow, where most blood cells are made, and stimulates the marrow to make more cells, which in turn can be released to carry more oxygen throughout the body.

EPO is one of several synthetic, genetically engineered medications that can stimulate blood cell production. These so-called recombinant hematopoietic growth factors can replicate the body's natural stimulating factors. While EPO revs up the production of red blood cells, the "colony stimulating factors" GM-CSF and G-CSF drive the production of certain white blood cells. Newer products such as interleukin-11 and thrombopoietin (TPO) have been developed to stimulate platelet production.

A bloodless medicine technique for scheduled surgeries is called "normovolemic hemodilution." This process significantly reduces the amount of blood cells lost during surgery. It begins with the drafting of a blood-management plan by a chief surgeon and an anesthesiologist. Just before surgery begins, the anesthesiologist starts an IV in a vein to slowly drain blood inside a closed system. The blood is simultaneously replaced with fluid (a combination of water and minerals), so that the amount of liquid in the blood vessels remains constant. This consistency in volume stabilizes the patient, allowing surgery while the process continues.

Inevitably, some blood is lost during any surgery. However, hemodilution involves "thinned" blood that contains fewer cells and more liquid. The anesthesiologist returns to the patient blood that was removed in its original form, whole

and rich with cells. The blood is never stored, and never leaves a closed system that's in constant contact with the patient's circulatory system.

A variety of medical devices have also advanced the field of bloodless medicine. One standard is the "cell-saver," or intra-operative cell salvage machine. It recovers blood lost from a patient during operations such as hip replacements, prostate surgery or gynecological procedures. The cell-saver spins, washes, filters and returns the red blood cells to a patient's body.

Cell-saver supporters say it has several advantages over transfused blood. For example, they note that recycled blood is fresh, not stored. In addition, salvaged blood does not pose the kind of disease risk that comes with allogeneic blood. The cell-saver can be used for planned as well as emergency operations. And any amount of blood can be returned to a patient.

Medical equipment manufacturers have also developed products that fall under a category of bloodless alternatives called post-operative blood salvage and re-infusion. Basically, these allow the re-use of blood that is lost during the natural bleeding period, which can last for hours after a major surgery such as knee replacement. In many hospitals, post-operative blood is discarded. However, new technology allows this clean, uncontaminated blood to be collected and returned without transfusion.

Post-operative blood salvage begins before the end of an operation, when a surgeon places in the operative area a tube through which blood flows by suction or gravity into a filtering device. Then, through a system that is at all times connected to and in contact with a patient's circulatory system, the blood is returned through an intravenous line. This enables a patient to receive back his own non-stored blood.

In recent years many other medical devices have appeared and contributed to the shift toward bloodless medicine. They include the hyperbaric chamber, which distributes high concentrations of oxygen into blood before surgery to help patients withstand surgical procedures, and the argon beam coagulator, which coagulates or clots blood during surgery to minimize blood loss. Doctors also can use high-tech surgical tools such as the harmonic scalpel, which cuts with vibration and friction in a way that simultaneously causes blood clotting.

Interest in these and other bloodless medicine techniques is growing. Physicians are recognizing their benefits over transfusion and showing more sensitivity toward patients who, after educating themselves about the danger of allogeneic blood, are demanding non-transfusion options. In some communities around the world, entire hospitals have switched to bloodless medicine. Government agencies and insurance companies have recognized the value of transfusion alternatives as well. And the pharmaceutical and medical-equipment industries have responded by researching, developing and marketing new products that help meet the rising demand for alternative blood treatment.

What does the future hold? Certainly, the trend toward bloodless techniques is already stimulating advances in science and medicine. Among the synthetic drug innovations in the pipeline is "stem cell factor," or SCF, which stimulates the production of stem cells and is presently undergoing clinical trials. Moreover, the weekly journal *Science News* noted that "scientists have identified only several hundred of the estimated thousands of proteins typically coursing through a person's bloodstream." Perhaps new methods and products will emerge as researchers find and understand more blood proteins.

Bloodless medicine is also winning support in the face of new risks associated with allogeneic blood. For example, since the 1990s, blood transfusions have been linked to transfusion-related acute lung injury (TRALI), a life-threatening immune reaction. TRALI kills hundreds of patients annually, although experts fear the death toll may be much higher because the symptoms are not always recognized. Although it is not clear what causes the reaction, *New Scientist* says the blood that causes it "appears to come primarily from people who have been exposed to a variety of blood groups in the past, such as... people who have had multiple transfusions." One report says TRALI is near the top of the list for causes of transfusion-related deaths in the United States and Britain, making it "a bigger problem for blood banks than high-profile diseases like HIV."

Meanwhile, awareness of the risks has affected attitudes toward bloodless medicine within the medical community. Brian McClelland, director of the Edinburgh and Scotland Blood Transfusion Service, asks doctors to "remember that a

transfusion is a transplant and therefore not a trivial decision." He also advises doctors to ponder the question, "If this was myself or my child, would I agree to the transfusion?"

Although transfusion medicine is still widely practiced -- and defended -- advocates of alternative treatments are making headway. Many are busy persuading their professional colleagues to at least consider new perspectives. Since 1998 the NATA group, for example, has been promoting better use of blood products and transfusion alternatives through education and international conferences. The US-based Society for the Advancement of Blood Management is also actively pursuing its stated goal "to improve patient outcomes through optimal blood management, which includes the appropriate provision and use of blood and blood products, and strategies to reduce or avoid transfusion."

These and other initiatives, launched in reaction to increasing risk factors linked to allogeneic blood and advancements in medical technology, have opened a new chapter in the history of medicine. The changes under way are profoundly affecting patient-care quality, medical procedures, physician viewpoints, and overall healthcare costs by tipping the scales toward bloodless treatment. In many parts of the world, transfusion medicine is on the wane as its alternatives take hold.

"It's all about a mindset that sees challenges instead of obstacles," explains Dr. Francis Forte, an oncologist and hematologist at The New Jersey Institute for the Advancement of Bloodless Medicine and Surgery. "In our experience, we find bloodless techniques among the best and safest currently available."