



International Society for Heart & Lung Transplantation
www.isHLT.org

FOR IMMEDIATE RELEASE

Contact: Susan Speer
Phone: (210) 678-9248
E-mail: sspeer@masonpr.com

INFANTS NEEDING A HEART TRANSPLANT CAN ACCEPT ORGANS FROM DIFFERENT BLOOD TYPES

New Findings Give Infants a Greater Window of Opportunity, Better Survival Odds

ADDISON, Tex., April 4, 2005 — A study showing that infants under one year of age can accept heart transplants from donors of different blood groups without the risk of organ rejection means a better chance of survival for infant patients and more efficient use of donor organs overall.

Results will be presented at the International Society for Heart and Lung Transplantation (ISHLT) Annual Meeting and Scientific Session in Philadelphia this week.

The study, published in *Nature Medicine*, shows that a heart from a donor with Type A blood can successfully be transplanted into an infant with Type O blood. Unlike older children and adults, babies do not yet have the antibodies that would normally reject antigens from a different blood type.

“The baby’s body educates itself to accept the organ and become tolerant of the blood type,” says Lori West, MD, a pediatric cardiologist at the Hospital for Sick Children in Toronto and co-author of the study.

The body’s tolerance of a donor organ has always been one of the greatest challenges of transplant medicine. A cardinal rule is that a transplant from a mismatched donor results in the recipient rejecting the organ.

“The medical community has been trained that you just don’t cross that blood group barrier,” says West. “For the first time, we have shown that the immune systems of human infants can tolerate intentional induction of B-cells to T-independent A and B antigens,” says West. Other combinations have proved successful as well: “We have induced Type B to Type O, AB to O, A to B, etc., all with excellent results.”

Many babies who undergo heart transplantation require a second donor heart at some point. The results of the study show that because the immune cells that would normally respond and attack the donor organ were eliminated with the first transplant, the patient can again receive a donor heart from that same blood type.

Known as the Toronto Protocol, the study originally involved fetal and infant mice and later, human babies, whose progress has been tracked for more than eight years. The Protocol has now been adopted at 15 medical centers around the world with similar successes at each of the centers.

- more -

"We found that the acceptance in mice and in humans occurs through the same processes," says West. "This means that what happens in mice tends to be successful in humans as well."

"This knowledge will save lives," says West. "More babies will survive congenital heart defects and go on to live fulfilling lives with a donor heart. We can use this knowledge to decrease the amount of time a patient must wait for a new heart – we'll be able to use donor organs more efficiently and perform increasingly successful transplants."

About ISHLT

The International Society for Heart and Lung Transplantation (ISHLT) is a not-for-profit organization dedicated to the advancement of the science and treatment of end-stage heart and lung diseases. Created in 1981, the Society now includes more than 2,200 members from 45-plus countries, representing a variety of disciplines involved in the management and treatment of end-stage heart and lung disease.

ISHLT maintains two vital databases. The International Heart and Lung Transplant Registry is a one-of-a-kind registry that has been collecting data since 1983 from 223 hospitals from 18 countries. The ISHLT Mechanical Circulatory Device (MCSD) database has been collecting data since 2002 with the aim of identifying patient populations who may benefit from MCSD implantation; generating predictive models for outcomes; and assessing the mechanical and biological reliability of current and future devices. For more information, visit www.ishlt.org.

#



International Society for Heart & Lung Transplantation
www.isHLT.org

FOR IMMEDIATE RELEASE

Contact: Susan Speer
Phone: (210) 678-9248
E-mail: sspeer@masonpr.com

MOLECULAR TESTING IMPACT: HEART TRANSPLANT PATIENTS BENEFIT FROM NEW TECHNOLOGY, EASIER MONITORING

ADDISON, TEX., April 6, 2005 — New technology for cardiac transplant patients indicates a patient's risk of organ rejection with a simple blood test. News of this revolutionary testing method was presented today at the International Society for Heart and Lung Transplantation's (ISHLT) Annual Meeting and Scientific Session in Philadelphia.

This breakthrough in molecular testing is a non-invasive method that translates the complex signals of the immune system's multiple genes and pathways in to an objective, actionable score. Along with proactive monitoring of the patient's immune system, physicians can now use this test to identify rejection and tissue damage before it occurs.

The most common cause of death in the first year after transplantation is acute cardiac rejection; the patient's immune system attacks the heart as if it were a foreign object until the organ stops functioning properly. As a result of this risk, physicians continuously monitor transplant patients for rejection.

For patients, molecular testing means less discomfort during the constant monitoring for rejection that is required for prolonged transplant success. Until recently, heart biopsy was the standard method of monitoring for transplant rejection. During this invasive procedure, a biptome – a wire with small clippers – is inserted into a vein in the patient's neck or groin and threaded through blood vessels into the heart. Small pieces of the heart muscle are clipped off and sent for laboratory evaluation for microscopic evidence of rejection.

Patients generally endure multiple cardiac biopsies, as many as 12 – sometimes more – in their first year after a transplant; periodic biopsies may continue for years. Unfortunately for many patients, biopsy procedures carry significant risk of adverse effects and they detect rejection only after damage to the heart has occurred. With 4,500 cardiac transplants performed worldwide each year, it is believed that the new molecular testing procedures will alleviate the need for tens of thousands of biopsies and the patient discomfort that accompanies the biopsy.

Mandeep Mehra, M.D., professor and head of the Division of Cardiology, the University of Maryland, Baltimore, praised the newest development in molecular testing in a symposium held during the ISHLT meeting.

continued...

"In the past decade, this is truly one of the most important breakthroughs in the field of heart transplantation," said Mehra. "Now that we have a test based on analysis of the human genome, we can begin to better understand why tissue and organ rejection occurs and use that knowledge to improve individual patient outcomes."

The symposium highlighted AlloMap™ molecular expression testing, which monitors the immune system with non-invasive technology and is currently being used in the management of heart transplant patients. In addition to detecting rejection, AlloMap™ identifies at-risk patients that biopsy misses, clarifies indeterminate biopsy results, and reduces the need for biopsies altogether.

The clinical value of AlloMap™ testing was demonstrated in a landmark multi-center, prospective study known as the Cardiac Allograft Rejection Gene Expression Observational (CARGO) study, which was presented at ISHLT's 2004 meeting.

Today, Howard Eisen, M.D., reviewed the results of the CARGO study and discussed the clinical implementation of molecular testing protocols at Drexel University College of Medicine (Hahnemann Medical Center) in Philadelphia. Hannah Valantine, M.D., reviewed clinical uses for AlloMap™ testing and discussed specific cases where the test has been used clinically at Stanford University Medical Center.

AlloMap™ is also undergoing clinical trials for lung transplant patients. Shaf Keshavjee, M.D., Toronto General Hospital, Canada, provided an update on LARGO, an international, multi-center clinical trial that studies the ability of AlloMap™ to improve clinical management of lung transplant recipients. He also discussed his work on molecular evaluations of donor lungs.

About ISHLT

The International Society for Heart and Lung Transplantation (ISHLT) is a not-for-profit organization dedicated to the advancement of the science and treatment of end-stage heart and lung diseases. Created in 1981 the Society now includes more than 2,200 members from 45-plus countries, representing a variety of disciplines involved in the management and treatment of end-stage heart and lung disease.

ISHLT maintains two vital databases. The International Heart and Lung Transplant Registry is a one-of-a-kind registry that has been collecting data since 1983 from 223 hospitals from 18 countries. The ISHLT Mechanical Circulatory Device (MCS) database has been collecting data since 2002 with the aim of identifying patient populations who may benefit from MCS implantation; generating predictive models for outcomes; and assessing the mechanical and biological reliability of current and future devices. For more information, visit www.ishlt.org.



International Society for Heart & Lung Transplantation
www.isHLT.org

FOR IMMEDIATE RELEASE

Contact: Susan Speer
Phone: (210) 678-9248
E-mail: sspeer@masonpr.com

ORGAN TOLERANCE FOR TRANSPLANT PATIENTS FOCUS OF NEW RESEARCH

Bone marrow transplants, immunosuppression therapies and greater infant survival are key topics

ADDISON, Tex., April 8, 2005 – The human body’s tolerance of a donor organ has traditionally been one of the greatest challenges of transplant medicine. Despite advances in transplant technology, tolerance and addressing complications, such as infection, from the use of immunosuppression drug therapy remain the leading causes of death in the initial years following an organ transplant.

Research focused on patients’ tolerance of a donor organ, exploring bone marrow transplants, drug therapies which target the immune system and infant survival, will be presented on Saturday at the International Society for Heart and Lung Transplantation (ISHLT) Annual Meeting and Scientific Session in Philadelphia.

Total organ acceptance on the horizon

The future of donor organ tolerance is complete acceptance of the donor organ, without additional therapies to ensure acceptance.

A “Mixed Chimerism” protocol, involving a bone marrow transplant along with the organ – all from the same donor – is successful in inducing tolerance. It is so effective that patients can live without the years of follow-up therapies that have been the hallmark of post-transplant patient care.

“It’s the most advanced protocol out there,” says Dr. Joren Madsen, Massachusetts General Hospital. Madsen, who will participate in the session, “The Future of Tolerance,” says that the trials have produced “impressive results” in humans.

The protocol study, conducted by Drs. David Sachs and Megan Sykes, also of Massachusetts General Hospital, would mean an end to years of drug therapy to assure patient acceptance of the donor organ.

“Drugs are risky,” he says. “They suppress the immune system, but they also block the body’s resistance to infections, cancers and other attackers, putting patients at an even higher risk of illness or death.”

Drugs that target the immune system

Chris Larsen, M.D., a kidney transplant surgeon and immunologist at Emory University in Atlanta, agrees with Madsen’s assessment, but believes that while waiting for the Mixed Chimerism protocol to be put into widespread practice, the right combination of newer, safer drugs may be a beneficial alternative to patients. Drugs currently used to suppress the immune system and prevent the body’s rejection of the donor organ do not exclusively target the immune system. Some of the current medications transplant patients take today affect other areas of the body and cause side effects that require additional drugs to address these side effects, says Larsen.

“We want to change that by developing a more effective combination of new drugs that target the immune system without side effects such as kidney toxicity, high blood pressure, high cholesterol and Diabetes. We want patients to take fewer, not more, pills.” Larsen points to an emerging class of

Continued...

drugs – Costimulation blockers – that target the immune system while sparing other organs and unrelated functions, thus avoiding many of the side effects.

Factors like T-cell response – how the immune system identifies and responds to foreign or native antibodies – are of interest to the transplant community, and researchers have identified specific immune system pathways on which to focus their attention.

Larsen says the knowledge gained in his kidney transplant research is useful to those in the heart and lung transplant community. "There are commonalities in our respective disciplines – we're all working toward long-term survival and quality of life – we should share what we know with each other," says Larsen, who is scheduled to present, "Toward Clinical Tolerance" tomorrow at the ISHLT Meeting.

Infant transplant patients have better survival odds

According to a study published in *Nature Medicine*, infants under one year of age can tolerate heart transplants from donors of different blood groups without the risk of organ rejection, because unlike older children and adults, infants do not yet have the antibodies that would normally reject antigens from a different blood type.

"The baby's body educates itself to accept the organ and become tolerant of the blood type," says Dr. Lori West, a pediatric cardiologist at the Hospital for Sick Children in Toronto and co-author of the study. West will present her findings tomorrow in a lecture, "Clinical Neonatal Tolerance" at the ISHLT Meeting.

The tolerance of the donor organ has far-reaching results. Many babies who undergo heart transplantation require a second donor heart at some point. The results of the study show that because the immune cells that would normally respond and attack the donor organ were eliminated with the first transplant, the patient can again receive a donor heart from that same blood type.

The Toronto Protocol, as the study is known, has now been adopted at 15 medical centers around the world, with similar successes at each of the centers. "This knowledge will save lives," says West. "More babies will survive congenital heart defects and go on to live fulfilling lives with a donor heart. We can use this knowledge to decrease the amount of time a patient must wait for a new heart – we'll be able to use donor organs more efficiently and perform increasingly successful transplants."

About ISHLT

The International Society for Heart and Lung Transplantation (ISHLT) is a not-for-profit organization dedicated to the advancement of the science and treatment of end-stage heart and lung diseases. Created in 1981, the Society now includes more than 2,200 members from 45-plus countries, representing a variety of disciplines involved in the management and treatment of end-stage heart and lung disease.

ISHLT maintains two vital databases. The International Heart and Lung Transplant Registry is a one-of-a-kind registry that has been collecting data since 1983 from 223 hospitals from 18 countries. The ISHLT Mechanical Circulatory Device (MCS) database has been collecting data since 2002 with the aim of identifying patient populations who may benefit from MCS implantation; generating predictive models for outcomes; and assessing the mechanical and biological reliability of current and future devices. For more information, visit www.ishlt.org.