Pediatric Heart Transplant Society

PEDIATRIC HEART TRANSPLANTATION TODAY

PHTS NEWSLETTER

April 2022

Dr. Juan "Chuck" Alejos, Senior Editor
Dr. Neha Bansal, Junior Editor

PHTS GROWTH*

11,039	patients enrolled
11,442	total listings/ relistings entered
8,408	transplants/ retransplants entered
484	listings for 2021
382	transplants for 2021
51	listings for 2022
49	transplant for 2022

*as of April 1, 2022

A MESSAGE FROM THE EDITORS

Wishing the PHTS family a very happy 2022!

We would like to welcome you to the first edition of the PHTS quarterly newsletter of 2022. What an exciting start to the year with a pig-to-man heart xenotransplantation. We are in awe of collective scientific achievements! Pediatrics has a storied past with respect to xenotransplantation. In 1984, Baby Fae was the first infant to receive a xenotransplant heart from a baboon in an operation performed by Leonard Bailey. She survived 21 days, longer than anyone expected. Read more in this newsletter- an exciting, invited guest article by Dr. Kirklin. We are looking forward to resuming in person meetings. We hope you will join us at ISHLT scientific sessions in Boston this year and look forward to seeing each other face to face come April for the first time in 3 years!

Yours sincerely,
Chuck and Neha



PHTS President
Scott Auerbach, MD
Children's Hospital Colorado
Denver, Colorado



PHTS Vice President
Shriprasad Deshpande, MD
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The World's First Pig-to-human Heart Xenotransplant: Where is this Going?

Written by: James K. Kirklin, MD

The seminal genetically engineered pig-to-human heart xenotransplant by Dr. Bart Griffith on 7 January 2022, will be officially recognized not only as the first such heart transplant, but the first such genetically engineered transplant of any kind into a living human patient. This will rank up there with the Baby Fae neonatal heart transplant from a baboon to a baby with hypoplastic left heart syndrome (HLHS), performed by Dr. Leonard Bailey in October of 1984. Were he alive, Dr. Bailey would be thrilled that his early vision of xenotransplantation will now become a clinical reality. The immense scientific and industry investment in this xenotransplant construct will undoubtedly pave the way for large scale application of this model, and without the angry backlash of some groups against the Baby Fae experiment. After all, pigs are a routine source of food as well as biologic valves for human implants. Following this initial adventure, the clinical platform will likely rapidly turn toward a methodical clinical trial of pig-to-human kidney transplants using this same genetic model of approximately 10 modified genes.

So, what does this mean for the pediatric community? I must confess that I was stunned that the first human heart xenotransplant would be in an adult, since ventricular assist devices and the total artificial heart are readily available. At any rate, the FDA did approve this historic operation on a compassionate use basis, indicating that no other viable option was available for this patient. Going forward, perhaps the most likely patients will reside in the pediatric community. Although Bailey's amazing episode ignited the field of infant heart transplantation, the severe shortage of infant heart donors was rapidly appreciated, and infant heart transplantation settled into the realm of a highly successful but infrequently utilized therapy. Indeed, by 2000, almost no pediatric centers were routinely listing HLHS babies for primary heart transplantation; instead, the Norwood operation rapidly became standard therapy, despite the superior long-term outcomes with intial neonatal heart transplantation. [1]

From an immunologic perspective, the most important human antibodies against pig tissues bind to a galactose epitope on the surface of all pig endothelial surfaces, which is absent in humans, apes, and baboons. These "natural" anti-Gal antibodies in humans against this galactose epitope likely develop during the neonatal period when viruses and other microorganisms that express Gal enter through the gastrointestinal tract. Through genetic engineering, pigs can be bred in which the 3 known carbohydrate xeno-antigens are deleted (knock-out), thus avoiding immediate attack by the human immune complexes. In addition, up to 8 additional human complement-regulatory, coagulation-regulatory, and anti-inflammatory proteins have been incorporated into the pig genome. These genetic manipulations have effectively eliminated hyperacute rejection in the pig-to -primate models. Rejection is much more likely to manifest as antibody-mediated rather than cellular rejection, although t-cells are often seen in the grafts. [2]

Now, after more than 2 decades of orderly scientific investigations using genetically engineered pigs, the experience with so-called triple knock-out (TKO) pig to primate heart transplants suggest a high likelihood of short to mid-term survival in humans. Although essentially non-working heterotopic models with abdominal implants have been extensively studied to understand the immunologic response by primates to TKO pig hearts, the real test of clinical utility is complete replacement of the recipient heart with the pig heart (orthotopic heart transplant). The early success of McGregor at the Mayo Clinic and more recently the Munich group with pig-to-primate orthotopic heart transplantation has produced survivors out to 6 months or more . Of considerable importance is the unique susceptibility of the pig heart to ischemic/reperfusion injury following transplantation,[3] *resulting in transient myocardial edema and reversible depressed cardiac function4. This led investigators to propose unorthodox solutions for myocardial preservation that continue to pose important barriers to achieving prompt excellent graft function* [4]*. Investigators at the University of Alabama at Birmingham have reported success with standard Del Nido cardioplegia solution as used in standard cardiac surgery (personal communication, David Cleveland, September, 2021), and Griffith's team used continuous ex-vivo perfusion of the explanted pig heart in their human case.*

The World's First Pig-to-human Heart Xenotransplant: Where is this Going?

Written by: James K. Kirklin, MD

When clinical trials are considered for heart xenotransplants, pediatric patients are a likely target, since durable mechanical circulatory support devices as a bridge to transplantation are much less effective in infants and small children compared to adolescents and adults. The pediatric patient groups most likely to be considered are those with difficult anatomy for ventricular assist device implant, highly sensitized patients unlikely to get a suitable donor match, and small patients who are unlikely to survive the extended period needed to find a suitable donor. In this context, pediatric xenotransplantation might be considered in a "bridge-to-transplant" trial. The following are possible examples of patient groups for such a hypothetical trial:[5]

1. *Primary therapy for HLHS with contraindications for the Norwood procedure, particularly with unstable hemodynamics.*
2. *Early post-transplant graft failure in infants and children and potentially older pediatric patients.*
3. *Conditions with high waitlist mortality, such as infants with Ebstein's malformation and hemodynamic compromise and single ventricle palliation with poor ventricular function or severe AV valve insufficiency.*
4. *Congenital heart disease with prior cardiac surgery, poor hemodynamics, and sensitization with high titers of pre-formed antibodies*
5. *Patient groups at high risk with standard mechanical circulatory support, such as those with single ventricle physiology*

Whatever the specific trial design, the path is now much clearer for real, large scale application of pediatric heart xenotransplantation. Once babies and children can be thoroughly studied for their immune response to the pig heart, the hemodynamic response related to growth and possible restrictive physiology, and possible susceptibility to side effects of potentially new immunosuppressive regimens, the role of this incredible therapy as a bridge to a human heart or long term therapy will become much clearer. So, buckle up and enjoy what will certainly be an amazing era in pediatric heart transplantation.

REFERENCES

1. *Stackhouse KA, McCrindle BW, Blackstone EH, Rajeswaran J, Kirklin JK, Bailey LL, Jacobs ML, Tchervenkov CI, Jacobs JP, Pettersson GB, Congenital Heart Surgeons' Society. Surgical Palliation or Primary Transplantation for Aortic Valve Atresia. J Thorac Cardiovasc Surg. 2020; 159 (4), 1451-1461,e7 PMID 31740116.*
2. *Cooper DK, Ezzelarab MB, Hara H, Iwase H, Lee W, Wijkstrom M, Bottino R. The Pathobiology of Prg-to-Primate Xeno: A Historical Review. In Clinical Xenotransplantation, editors Cooper DK, Byrne G. Springer Nature Switzerland Publications, 2020.*
3. *Mohiuddin MM, Reichart B, Byrne GW, McGregor CGA. Current status of pig heart xenotransplantation. Int J Surg. 2015: 23 (Pt B): 234-9.*
4. *Byrne GW, McGregor CGA. Cardiac xenotransplantation: progress and challenges, Curr Opin Organ Transplant. 2012: 17: 148-54*
5. *Kirklin JK, Cleveland DC. Selection of pediatric patients for the initial clinical trials of cardiac xenotransplantation. In Clinical Xenotransplantation, editors Cooper DK, Byrne G. Springer Nature Switzerland Publications, 2020.*

Join us this April!





Join us for the month of April for the PHTS Virtual Run, Mending Hearts and Saving Lives - 5k and 1 Mile Fun Run

PHTS at ISHLT 2022



Oral Presentation

Session SESS 41

Thursday, April 28, 2022 4:30 PM - 4:45 PM ET

Use of Donor Hearts with Low Ejection Fraction in Pediatric Heart Transplantation: A PHTS Analysis

Dipankar Gupta, MD
University of Florida College of Medicine

Mini Oral Presentation

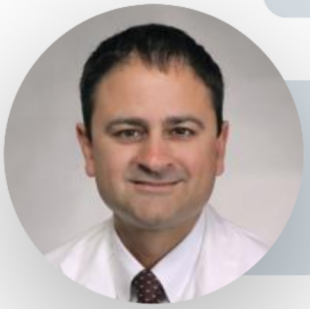


Session MINI ORAL 11

Thursday, April 28, 2022 6:09 PM - 6:15 PM ET

Long-Term Survivors Following Pediatric Heart Transplantation: A PHTS Database Analysis

Emily Anne Hayes, MD
Nationwide Children's Hospital



Oral Presentation

Session SESS 63

Friday, April 29, 2022 2:30 PM - 2:45 PM ET

Racial and Socioeconomic Disparities in Pediatric Heart Transplant Outcomes in the Era of Anti-Thymocyte Globulin Induction

Waldemar F. Carlo, MD
University of Alabama Birmingham

Poster Presentation



Session POSTER SESSION 3

Friday, April 29, 2022 5:00 PM - 6:00 PM ET

Reducing Donor Acceptance Practice Variation - Learnings from a Discussion Forum

Neha Bansal, MD
Children's Hospital at Montefiore

Registration Now Open!

Wednesday, April 27, 2022
7:15pm - 9:15pm ET
Sheraton Boston Hotel

Register by Friday, April 22nd: $90
Register after Friday, April 22nd: $100

7:15 - 8:00pm Republic Foyer, 2nd Floor	On site Registration & Reception for 2021 PHTS Lifetime Achievement Award Recipient – *Sponsored by Boston Children's Hospital*
8:00 - 9:15pm Republic Ballroom, 2nd Floor	May Wang, PhD – Associate Professor and Georgia Research Alliance Distinguished Cancer Scholar, Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University – *Sponsored by CareDx, Inc*

Register at www.PHTSociety.org

CareDx®
Your Partner in Transplant Care™

This is an independent Non-CME event and is not an official part of the ISHLT Annual Meeting & Scientific Sessions.

Research Updates

PHTS now has a Data Request Form

The data request form is to be used for minor data request (basic frequencies and request requiring less than 4 hours of analytic time) for research proposal submissions, quality assurance requests for site specific data, or other minor data request.

When requesting data frequencies, please provide the question number and the specific variable names listed on the current version of annotated forms found on the PHTS website.

The PHTS Data Request Form can be found on the PHTS wesbite at https://pediatricheartransplantsociety.org/data-request-form/

Published Papers



Obesity and dyslipidemia predict cardiac allograft vasculopathy and graft loss in children and adolescents post-heart transplant: A PHTS multi-institutional analysisplaceholder

Carmel Bogle, Ryan Cantor, Devin Koehl, Jillien Lochridge, James K Kirklin, Aliessa Barnes, Gonzalo Wallis, Shahnawaz Amdani, Rebecca Ameduri, Elfriede Pahl, Kathleen E Simpson, Elizabeth D Blume



Cardiac allograft vasculopathy in pediatric heart transplant recipients does early-onset portend a worse prognosis?

Michael Khoury, Jennifer Conway, Jeffrey G Gossett, Erik Edens, Stephanie Soto, Ryan Cantor, Devin Koehl, Aliessa Barnes, Vernat Exil, Lauren Glass, James K Kirklin, Warren A Zuckerman

New PHTS Committee

QI Committee

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Neha Bansal
Adam Morrison
Irene D. Lytrivi
Kim Beddows
Maria Bano
Dipankar Gupta
Riki Graves
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Melanie Everitt
Matt Bock
Natalie Shwaish
Jennifer Carapellucci
Marc Richmond
Bethany Wisotzkey
Lydia Wright
Irene (Rena) Lytrivi

Information Corner

Job Postings

Pediatric Transplant Child Psychologist

We at UW-Madison/American Family Children's Hospital are underway at building and growing our pediatric heart transplant and solid organ transplant programs (kidney and liver as well). We are looking to recruit a general pediatric and pediatric transplant psychologist.

Contact: Sonya Kirmani, MD - kirmani2@wisc.edu

Pediatric RN VAD/Transplant Coordinator

We are looking for a highly motivated individual to join our team as a pediatric RN VAD/Transplant coordinator!

Contact: Sonya Kirmani, MD - kirmani2@wisc.edu

Stanford Children's Hospital - RN VAD Coordinator

The Ventricular Assist Device (VAD) Nurse Coordinators are specialized registered nurses, in an ambulatory and inpatient care setting, that facilitate the care and education of ventricular assist device patients and their families. From initial contact, through the evaluation for VAD implant, during the pre-operative, peri-operative, and post-operative periods as well as continual outpatient follow-up. The VAD Nurse Coordinator ensure continuity of care across the VAD/Heart Transplant continuum.

Contact: Caron Burch MSN, FNP, CCTC - cburch@stanfordchildrens.org

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Pediatric Heart Failure/Transplant Position at Ochsner Hospital for Children

Ochsner Health in New Orleans is recruiting a pediatric heart failure/heart transplant cardiologist to join our rapidly growing program. This position includes care of patients with cardiomyopathies, heart failure, transplant, congenital heart disease, and ventricular assist devices. Candidates would be joining two heart failure/heart transplant cardiologists in the only pediatric heart transplant center in Louisiana.

Contact: Thomas Young MD - thyoung@ochsner.org

Pediatric Tx/HF Position - SickKids, Toronto

Effective July 1, 2022, a full-time permanent position is available as a Staff Cardiologist with a subspecialty interest in Heart Function and Cardiac Transplantation in the Labatt Family Heart Centre - Cardiology Division, The Department of Paediatrics at the Hospital for Sick Children (SickKids) 555 University Ave., Toronto, ON which is an academic health science centre dedicated to the care of children: a fully affiliated hospital with the University of Toronto.

Contact: Meagan Cameira - meagan.cameira@sickkids.ca

More job postings can be found on PHTS Basecamp under Resources for Job Opportunities
If you are interested in advertising with us,
Please email DeAnna Archer (deannabeckham@uabmc.edu) with your job postings.

Information Corner

Job Postings

CHOA- VAD RN Clinical Coordinator

Children's Healthcare of Atlanta is looking for a VAD RN Nurse Coordinator. This full time position will work with our physicians, APPs, and Transplant RN Coordinator focusing on our VAD population.

Contact: Visit choa.org to apply

Medical Director Pediatric Heart Failure and Transplant for Johns Hopkins Hospital, Baltimore, MD

The Johns Hopkins Medicine is seeking a **Medical Director for Pediatric Heart Failure and Transplant.**

Contact: Shelby Kutty at skutty1@jhmi.edu

Medical Director of Pediatric Heart Failure and Transplant at UT Health San Antonio

The Pediatric Heart Center of UT Health San Antonio, Joe R. and Teresa Lozano Long School of Medicine, is seeking a full-time medical director of pediatric heart failure, transplant and mechanical circulatory support to develop a pediatric heart failure and heart transplant program.

Contact: Ginnie Abarbanell, MD - abarbanell@uthscsa.edu

Pediatric Transplant Cardiologist Position at Cincinnati Children's Hospital Medical Center

We are seeking a Board Eligible/Board Certified Pediatric Cardiologist with formal 4th year training in Cardiomyopathy, Ventricular Assist Device, and Cardiac Transplantation for a faculty position at the Cincinnati Children's Hospital Medical Center.

Contact: Clifford Chin, MD in care of Deborah.Mancini@cchmc.org

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Pediatric Heart Failure/Transplant Cardiologist Position at Hassenfeld Children's Hospital - NYU (New York, NY)

We are seeking a pediatric heart failure/transplant cardiologist for a full-time academic faculty position in the Department of Pediatrics at NYU Grossman School of Medicine and Hassenfeld Children's Hospital at NYU Langone Health.

Contact: Rakesh Singh, MD, MS - rakesh.singh@nyulangone.org

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