Meeting Highlights Summary of the 1st conference on the Scientific Basis of Heart Failure in Children

Basic Mechanisms in Pediatric Heart Failure

Basic research from 5 leaders in the fields of cardiac metabolism (Fabio Recchia and Jennifer Duncan), contractile proteins (Anne Murphy), syndromic congenital heart disease (Jeff Robbins) and receptor signaling (Dan Bernstein) were presented during the initial session. In addition, 4 abstracts were selected for oral presentation from trainees. It is clear that metabolism of the failing heart is an important contributor to heart failure and is an area that needs greater basic and translational research. In particular, there is strong interaction between metabolism and revascularization of the heart and better understanding may lead to novel diagnostic and therapeutic interventions. A particularly interesting presentation was on Noonan’s Syndrome and illustrated current concepts on how a current investigation of a congenital heart disease might be carried out using transgenic animal models to understand basic mechanisms of human disease.

Novel Tools for Quantifying Heart Failure

This exciting session presented talks and one oral abstract on novel and advanced approaches to quantifying cardiac function. Advances in 3D echocardiography was presented by Girish Shirali and included new applications of this technology to heart failure, such as its’ potential use in cardiac resynchronization therapy and quantification of diastolic function. Novel and basic investigational use of MRI (Sam Wickline) to evaluate myocardial scarring in cardiomyopathy suggests that new imaging modalities may allow better clinical understanding and follow up of cardiac dysfunction. Finally, an excellent overview of the complexities and considerations underlying the discovery of proteomic biomarkers of cardiac disease in children was presented by Jenny Van Eyk. These three talks emphasized how rapidly the field is changing for evaluation of cardiac function and how future tests may analyze not just the performance of the heart, but how other organ systems are impacted as well.

Novel Therapies for Heart Failure

Multiple new approaches for intervening in heart failure in children were presented, many of which are still under development or basic investigation. For example, Betsy Blume discussed the use of ventricular assist devices for mechanical support of the failing heart in children. The Berlin Heart is a significant improvement in size and efficiency for this population, but anticoagulation remains the biggest risk. This intervention is in clinical use and trials now. Cardiac resynchronization therapy (David Rosenthal), and the molecular and hemodynamic determinants of RV failure (Hunter Champion) were also concepts that are in current clinical use but require better clinical trials in children to determine appropriate use. Recent and rapid advances in applying basic research to human disease included presentations of viral (Wally Koch) and non-viral (Mark Payne) approaches to gene therapy for heart failure in children. In a similar manner, the use of endothelial stem cells (Dave Ingram) and human embryonic stem cells (Harold Bernstein) in cardiovascular disease was presented, along with the current limitations of these technologies.

Clinical Science of Pediatric Heart Failure: Evidence-Based Treatment of Chronic and Acute Heart Failure

This interactive session was broken into three talks and one oral abstract on chronic heart failure, and the same format for acute heart failure. Carolyn Ho presented the data and rationale behind using genetic testing in hypertrophic cardiomyopathy to guide the use of calcium channel blockers. This concept is certain to grow as a greater understanding of the
molecular defect guides the use of the therapeutic intervention in heart disease. Charlie Canter presented data on failure of the single ventricle in young adults and the difficulties in transplanting these patients years after a Fontan operation. Fontan failure is all too common in this population and therapies to improve cardiac function are very limited at this point. Bob Shaddy discussed the Carvedilol trial in children with heart failure. A key point from his presentation was the difficulty in defining (and quantifying) heart failure and how this impacts management of this disease. In particular, development and use of clear end points for a clinical trial is important for FDA approval.

The acute heart failure session included data from Lynn Jeffries on myocarditis. He emphasized that there is a significant need for prospective trials in this disease, and that diagnosis and treatment needs to be based on evidence and not associations. Problems and opportunities for conducting clinical trials in the ICU were presented by Sarah Tabbutt. She noted that a key problem is the number of studies being conducted simultaneously in ICU’s, which impacts parent’s decisions to participate. Finally, Steve Lipshultz gave an excellent presentation of the long term outcome of children after chemotherapy. A significant number of these children develop dilated cardiomyopathy many years later as young adults, and progress to heart failure. Since they are often discharged from cardiac follow up after a few years because of normal heart function, it is worth re-considering the long term follow up protocols for these patients to avoid missing the onset of their heart disease. He noted that the lack of support for long term registries of these patients has significantly hampered our understanding of the outcomes of heart disease in these children.

Tools for Building a Pediatric Heart Failure Research Program

The final session presented the rationale and methods for developing a heart failure research program both locally, as well as engaging in national programs. Lynn Mahony gave an excellent overview of the Pediatric Heart Network (PHN) results to date. She noted that clinical trials in pediatric cardiology are often limited by the low numbers of patients, lack of money, and lack of infrastructure. These trials are especially hard when conducted across the multiple institutions needed to generate adequate numbers for a meaningful trial. The PHN may move towards considering more pilot studies in an effort to generate preliminary data to power larger studies. Again, the lack of a national registry for heart disease in children was noted as a large impediment to understanding the mechanisms and outcomes of heart failure in this population. The social and financial cost of heart failure in children was presented by Bill Mahle, who calculated that the direct costs of this disease are significantly greater than previous estimates and may be in the range of $6 – 9B / year. Allen Everett presented the MAGIC Consortium as a model of data sharing on an international basis. This is a largely automated system for reporting cardiac cath data in an anonymous fashion, and patient data is maintained in a registry. Andrew Redington discussed the failure of the RV with and without LV failure, and posed the question of long standing pulmonary regurgitation as a source for isolated RV failure. His presentation also raised the question of who will benefit from resynchronization therapy and how to predict the outcome. This is an important and poorly addressed problem at this time. Steve Webber discussed heart failure after transplant and noted that this is a particularly aggressive form of failure that is very difficult to treat. Finally, Larry Markham presented data on the Duchenne Cardiomyopathy population. He noted that survival has increased significantly, but the quality of life has not increased over time. Understanding the genotype in this disease does matter in predicting the clinical course.

In Summary, this 2.5 day conference was judged by the attendees to be an exciting and excellent format for a focused discussion of heart failure in children. Multiple new collaborations were noted to come out of this meeting, and there was very good interaction between trainees, junior and senior faculty. The conference highlighted the progress and problems in this field,
which include a lack of support for a national registry for heart disease in children, difficulty in conducting multi-center prospective clinical trials, and the lack of movement in some fields of heart research beyond observational, or anecdotal, studies into hypothesis driven translational and clinical research. Many of these issues will require support at a national level to address, yet there is also significant progress in heart failure research being made at local institutions and programs by informal means. This conference was judged to help in this regard, and the organizers were asked to plan a second conference to follow in 2 years because of this success.