Contributions of the Texas Children’s Hospital Pediatric Cardiology Program to the Field of Pediatric Cardiology

The Texas Children’s Hospital (TCH) cardiac team has been involved with advances in the care of children with heart problems since the hospital opened in the early 1950s. The team’s surgical contributions have been discussed previously in this journal; the purpose of this paper is to highlight several areas of the cardiology program and discuss future possibilities in the field.

Fellowship Training

Numerous pediatric cardiologists who trained at TCH have had an impact upon pediatric cardiology, and some features of the fellowship training program have been incorporated into many other training programs. In addition, faculty from the TCH program have served on the Sub-board of Cardiology of the American Board of Pediatrics.

Electrophysiology

Many advances in understanding rhythm problems affecting children and progress in the treatment of children with cardiac rhythm abnormalities are attributable to work done at TCH, and pioneers in the field of electrophysiology include Kugler, Porter, Friedman, Van Hare, Beder, Smith, White, Perry, Fenrich, Bink-Boelkins, Denfield, Knilans, Paul, Fournier, Villane, Ross, Hesslein, Hamilton, Bryant, Johnsruede, Kertesz, Cecchin, and many others whose innovations have advanced the care of children with cardiac arrhythmias. Some of the earliest studies recording the intracardiac electrophotogram were done by Mullins and El-Said; El-Said’s research on rhythm problems after the Mustard operation led to changes in medical management, intraoperative management, and postoperative care—and ultimately the overall surgical strategy for babies with transposition. Mullins and Gillette provided surgically important descriptive information about the conduction system in complicated heart malformations. Gillette pioneered the use of artificial pacing in children. Gillette and Garson helped develop pediatric cardiac electrophysiology as a distinct subspecialty of pediatric cardiology. Innovative surgical treatments of refractory arrhythmias were a precursor to the use of radiofrequency ablation techniques in the catheterization lab. Garson’s work to understand the cause of sudden cardiac death following surgery for congenital heart defects led to a decrease in the incidence of late sudden death. Careful evaluation of the use of standard antiarrhythmics in children and the development of new drugs affected practice: the discoveries of cardiac tumors in infancy as a cause of chronic, incessant ventricular tachycardia and of chronic tachycardia as a reversible cause of cardiomyopathy were also notable TCH advances. Understanding the clinical features of long Q–T interval syndromes led to increased recognition of this cause of sudden cardiac death in young people. Friedman, Perry, and Fenrich ushered in the radiofrequency ablation era at TCH, and Fenrich and Friedman’s work with thermally modulated ablations provided a new standard for the field. Friedman’s expertise and innovation in pacing, work with lead removal, and development of laser applications for elec-
trophysiology at TCH have helped many adult patients as well as children.31

Cardiac Catheterization
Diagnostic precision in the cardiac catheterization laboratory was an essential part of the success of the congenital heart surgery program at Texas Heart Institute (THI) and TCH.32 Percutaneous techniques for venous access33,34 facilitated safe and expeditious procedures. Nihill developed specialized angiographic techniques,35 including pulmonary arterial wedge angiography for evaluation of the pulmonary microvasculature36 and venous wedge angiography for visualization of the pulmonary artery anatomy.37 Vargo38 provided several generations of trainees with the conceptual framework for laboratory calculations and specialized procedures. Of the many innovations from the diagnostic catheterization laboratory, the use of catheterization diagrams that provided anatomically descriptive information may have had the greatest impact on the care of children with heart disease. These diagrams, developed by Mullins, were disseminated widely by former TCH trainees and published by Mullins and Mayer as a text, which is now used in most pediatric heart catheterization laboratories. The Mullins transseptal sheath and technique for transseptal left atrial catheterization were developed in the TCH catheterization laboratory,39,40 as was the Mullins malleable deflector wire.41 The Mullins long transseptal sheath has a number of additional applications in the current practice of pediatric cardiac catheterization, including endomyocardial biopsy42 and interventional techniques.43,44 The Houston experience contributed to the early development of the Park atrial septostomy blade technique.45 Mullins worked with Rashkind on the development and refinement of the ductus occlusion device46 and subsequently taught cardiologists around the world how to close the ductus arteriosus without surgery. The TCH team was also instrumental in the development of the clampshell technique for atrial septal defect closure.47 The development of the Grifka-Gianturco Vascular Occlusion Device began as a research project during Grifka's fellowship under Mullins' supervision; this work progressed from initial animal lab studies in THI laboratories to the 1st studies in children and to Food and Drug Administration (FDA) approval for use in TCH catheterization laboratories.48

Innovations in balloon dilation of intracardiac, cardiac, and vascular structures at TCH have included critical evaluation of immediate and follow-up results.49-51 Mullins and coworkers have been leaders and innovators in the application of endovascular stents in pediatrics, and Ing developed a "break-away" expandable stent for use in babies.49,52 Early work with therapeutic laser cardiac procedures in the catheterization laboratory has also been promising.

A number of trainees from TCH became contributors to the field of cardiac catheterization following training. Latson, Grifka, Ing, Vincent, Recto, Ward, Moore, McMahon, Morrow, and O'Laughlin are among those trained in the TCH catheterization laboratory who have had important impact on the field.

Cardiac Imaging
Gutgesell directed the echocardiography laboratory from the purchase of the 1st echocardiography machine in the early 1970s to the beginning of the era of surgery without catheterization in the mid-1980s and thus played a key role in the development of noninvasive pediatric cardiac diagnostic capabilities at TCH and THI. Descriptions of echocardiographic features of a number of cardiac conditions were provided by the TCH team, and Gutgesell's Atlas of Pediatric Echocardiography was widely used by trainees. Advances in 2-dimensional imaging included the segmental approach to cardiac imaging, imaging of the aortic arch, and imaging of the ductus arteriosus by Gutgesell, Huhta, and coworkers.53,54 Huhta pushed and thus advanced the ability of echocardiographers to provide the anatomic and physiologic details needed by surgeons and also began the fetal imaging program in the early 1980s. Ludomirsky did early work on color Doppler echocardiography in congenital heart disease and published the 1st atlas on this topic. Murphy's studies provided information about a number of cardiac functional disorders in neonates, including Kawasaki disease, and his organization of the echocardiography laboratory for efficient and thorough studies and high-quality teaching was extremely valuable to the institution. Ayres has advanced the practice of perinatal cardiology and directed an overall improvement in the quality of diagnostic imaging as new techniques have been added under her leadership.55,56 She has also contributed data on infant sedation for echocardiography.57 Echocardiographic research data on a large cohort of children with perinatally acquired AIDS,58 and longitudinal echocardiographic measurements on a large cohort of children throughout adolescent maturation.59

Geva published anatomic-echocardiographic correlations with functional and physiologic analysis of a number of cardiac conditions.60,61 Ludomirsky, Geva, Feltes, Ayres, Bezold, and others introduced transesophageal echocardiography to TCH for use in a number of operative and catheterization procedures.62 Pignatelli, Vick, and others have provided innovation and expertise in telemedicine applications for pediatric echocardiographic services, and Vick's work in magnetic resonance imaging has directly affected TCH's day-to-day management of
children with heart disease. Gajarski, Bezold, Kovalchin, Altman, Shirali, Sklansky, Marcus, Pagotto, and Tani are some of the echocardiography laboratory trainees who have distinguished themselves in the field of pediatric cardiac imaging.

Postoperative Care
Postoperative cardiac care at TCH has long been an interest and priority of the Department of Cardiology. Under the leadership of Feltes, this discipline has become an additional area for advanced academic training during a 4th year of cardiology fellowship. Initial animal laboratory, hemodynamic laboratory, and intensive care unit (ICU) investigations of vasopressors were done by Driscoll and other members of the TCH cardiac team. Strategies for management of postoperative arrhythmias approaches for biochemical evaluation and hemodynamic assessment of functional status, and innovations in the use of mechanical support have all been developed in the TCH cardiovascular recovery room. Feltes and coworkers have research in progress related to the hemodynamics of milrinone, the use of nitric oxide, and steroid prophylaxis of postpericardiomyopathy syndrome. Vargo developed an “alphabetical approach to being orderly” for use in the ICU. Dreyer, Entman, and coworkers have investigated inflammatory mediators at the basic and clinical levels with important implications for operative and perioperative management.

Transplantation
Texas Children's Hospital and THI have a very successful pediatric heart transplantation program developed by Bricker and Towbin and now directed by Gajarski. Work by Nihill and Somerville at TCH in the late 1960s with antithymocyte globulin was quite promising, but transplantation was not routine until after the availability of cyclosporine in the 1980s. Neonatal biopsies, work to understand neurologic complications, progress in pediatric left ventricular assist, studies related to pulmonary resistance and suitability for transplantation, and electrophysiologic assessment of transplantation candidates were done at TCH. A cardiomyopathy clinic with strong links to the cardiomyopathy basic science research programs has also been developed.

Cardiac Molecular Biology
A number of discoveries in cardiac molecular biology at TCH have had implications for optimal cardiac care of children. Towbin developed a research program to enhance basic understanding of the pathogenesis of cardiomyopathy in childhood, which led to discoveries related to the gene for X-linked dilated cardiomyopathy. Research on other forms of dilated, hypertrophic, and restrictive cardiomyopathy has been rewarding as well. The use of a polymerase chain reaction to amplify the viral genome led to discoveries about the specific viruses causing acute viral myocarditis and causes of chronic cardiac dysfunction developing later in life, including the importance of the adenovirus in pediatric heart disease and evidence that a mumps virus infection had been the cause of most cases of endocardial fibroelastosis in previous years. Molecular viral diagnostic work has also had great clinical impact on transplantation and perinatal cardiology. Investigations into the cellular cause of long Q–T interval syndrome have yielded new genetic information, and the use of fluorescent in situ hybridization techniques has provided very high resolution analysis of abnormal chromosomes. A Cardiovascular Genetics Clinic was recently developed at TCH by Towbin and Bricker within the genetics department; in addition to enhancing teaching and patient care, this clinic has facilitated and furthered cardiac genetic research projects. Understanding early cardiac development at the cellular and molecular level has been the aim of the Early Heart Development Program Project supervised by Schwartz.

Epidemiology of Pediatric Cardiovascular Disease
Estimates of occurrence of cardiac disease in the population and risks of recurrence in families with cases of congenital heart disease were provided by Nora. Research related to pediatric risk precursors for adult-onset heart disease has also been done by the TCH cardiology department in conjunction with the epidemiology faculty at The University of Texas School of Public Health. Longitudinal multicenter studies on the relation of perinatal human immunodeficiency virus (HIV) infection to the development of cardiac dysfunction have enhanced our understanding of this problem, and TCH/THI pediatric cardiology investigators are very involved with data analysis for the Texas Birth Defects Registry sponsored by the Centers for Disease Control.

General Cardiology
Gutgesell 1st identified the relationship between maternal diabetes and neonatal hypertrophic cardiomyopathy. Community educational programs started by McNamara decreased the age of referral of sick cardiac babies in Houston, and McNamara and Danford applied decision analysis to referral of babies with suspected cardiac problems. Fisher and associates developed a single-ventricle protocol in the early 1990s that was one of the earliest practice guidelines for optimal referral and evaluation of children with suspected cardiac disease, and studies on this complicated problem continue to be done in the TCH cardiac clinic.
Future Emphasis for TCH Cardiology

Descriptions of congenital cardiac abnormalities led to the 1st simple mechanical solutions for cardiac problems in childhood. Fine-tuning of anatomic descriptions and improvement in strategies for operative and catheterization therapy must continue. Incremental advances in cardiac surgery, perfusion, pacing, pharmacology, diagnosis, and interventional procedures will substantially benefit children with congenital heart defects. Work to understand cardiac pathophysiology and pharmacology has progressed to investigations designed to address mechanisms at the cellular and molecular level, which will allow better understanding of the functional, structural, and developmental aspects of pediatric disease. Future TCH cardiologists can anticipate the advent of gene therapy for storage disease affecting the heart, for ion-channel-related diseases, for familial abnormalities of lipid metabolism, and for some cardiomyopathies. Immunizations or specific antiviral therapy for the respiratory syncytial virus, adenoviruses, enteroviruses, and HIV, as well as new immune therapies for myocarditis, are expected to benefit the pediatric heart team and its patients. Selective and focused immunosuppression should make cardiac and cardiopulmonary transplantation more successful, and advances in xenotransplantation (including genetic engineering of donor species’ immunogenicity) should make transplantation more available and affordable. Work in mechanical support strategies will improve perioperative survival and provide a better bridge to transplantation.

Imaging will be done increasingly on a digital platform, which not only enhances image quality but also makes remote diagnosis more feasible. Telemedicine applications currently used on a daily basis in nurseries around Houston by the TCH team will have even more remote applications. Digital consultation via the Internet will become a routine means for TCH cardiologists to provide help to patients around the world. Advances in fetal diagnosis, pharmacotherapy, and interventions are expected.

Government regulations, changes in health care funding, and market forces in health care are having an adverse impact on research and on teaching hospitals around the country. However, these are all systems that require hypothesis-driven investigation and raise a whole new set of research questions for pediatric cardiologists. Improved training for scientists and clinicians who study and treat children with heart disease is anticipated. The cardiac team at TCH will be a contributor to progress in all of these areas in the future.

A commitment to providing the best patient care and teaching is linked to a departmental and institutional commitment to research. We owe this to our patients and their families. We are greatly indebted to our legacy at TCH and THI. Those who have provided the advances that have lessened suffering and death from childhood heart disease are the inspiration for us to push forward with enthusiasm.

References


