Special Reports

Report of the Task Force on Research in Pediatric Cardiovascular Disease
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Since the 1940s, when major breakthroughs occurred in the surgical treatment of congenital malformations, great strides have been made in the treatment of cardiovascular disease in infants and children. Nonetheless, significant difficulties remain that hinder our ability to treat the very youngest and smallest patients with cardiovascular disease, including those still in utero. Heart disease in infants, children, and adolescents is still a large problem, with substantial burden and cost for both families and society.

Although surgical and technological innovations have greatly advanced treatment of cardiovascular disease in adult patients, treatment of infants, children, and adolescents has not kept pace. The most obvious reason for this situation is that children are not simply smaller adults. If they were, the appropriate miniaturization of instruments and equipment, scaling down from adults to children, would be sufficient. However, when considering interventions for neonates, or even fetuses, one must remember that they exhibit marked physiological characteristics that distinguish them from adults, such as increased heart rate and immature tissue development.

To stimulate clinical research and thereby enhance our ability to treat infants, children, and adolescents, the National Heart, Lung, and Blood Institute (NHLBI) has launched 2 major initiatives. First, in May of 2000, we issued a solicitation for the establishment of a Pediatric Heart Disease Clinical Research Network of interactive pediatric clinical research centers (http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-00-013.html). Its purpose is to promote efficient evaluation of innovative treatment methods and management strategies for children with structural congenital heart disease, inflammatory heart disease, heart muscle disease, and arrhythmias. We anticipate that one outcome of the Network will be to promote rapid dissemination of the findings from these clinical studies to the medical community. Seven clinical centers and a data-coordinating center were funded in September 2001, and it is expected that 2 protocols will be under way by the end of this calendar year.

Second, in March of 2002, the NHLBI released a solicitation for Specialized Centers of Clinically Oriented Research (SCCOR) in Pediatric Heart Development and Disease, with the broad goal of fostering multidisciplinary research on clinically relevant questions, thereby enabling basic science findings to be more rapidly applied to clinical problems (http://grants1.nih.gov/grants/guide/rfa-files/RFA-HL-02-027.html). It is worth noting that this new centers program builds on long-standing Institute efforts to address pediatric cardiovascular disease. A Specialized Center of Research (SCOR) in congenital heart disease was funded in 1990 as part of the NHLBI Ischemic Heart Disease SCOR Program. A SCOR solicitation dedicated to pediatric heart disease resulted in three 5-year awards in 1992, and the SCOR program was expanded to comprise 5 programs in 1997.

As these activities were being planned and implemented, the NHLBI convened the Task Force on Research in Pediatric Cardiovascular Disease in January of 2001 to identify the most important research priorities and scientific opportunities over the next 5 years in basic science, clinical medicine, and epidemiology associated with pediatric cardiovascular disease. Its findings and recommendations are summarized below, and the full report can be found at http://www.nhlbi.nih.gov/resources/docs/pediatric_cvd.htm.

The Institute is pleased to have this report to help guide its efforts in the fight against pediatric cardiovascular disease. We hope the community will give it full and thoughtful attention.

Overview of the Task Force Report

In the United States, congenital cardiovascular malformations (CCVMs) are the most common birth defect, affecting 1 in 100 infants born each year. Many of these infants need intervention, by catheter or surgically, during their first weeks of life, but most of the procedures are palliative rather than curative. As many as one third of children with CCVMs also have congenital or acquired conditions affecting their kidneys, brain, digestive system, lungs, bones, immune system, and other organs. For those children with disorders specifically involving the myocardium, these cardiomyopathies may be primary or secondary disorders. Researchers continue to identify an increasing number of specific gene defects for primary cardiomyopathies, whereas the various causes of secondary cardiomyopathies include toxic medications, chronic overload of left ventricular volume, and myocarditis.

Because of the remarkable innovations made in medical and surgical therapy, many pediatric patients with cardiovascular disease now survive into adulthood. Unfortunately, the incidence of residual disease is relatively high, and these
Development of the Normal and Abnormal Heart and Vascular System

The task force highlights scientific opportunities in 4 topics: development of the heart, development of the vascular system, laboratory cores for the study of animal models, and risk factors for CCVMs.

Development of the Heart

Recommendations: Investigate cardiomyocyte lineages and the molecular mechanisms underlying differentiation and proliferation of cardiomyocytes; further characterize molecular and cellular mechanisms involved in cardiac morphogenesis.

In animal models, researchers have identified genes that control development of the heart, which can now be investigated as possible culprits in the development of CCVMs in humans. Equally important is the mapping and identification of genes responsible for CCVMs in humans. A single clinical entity, such as tetralogy of Fallot, can be associated with defects in several different genes. Alternatively, defects in a single gene can cause multiple abnormalities.

Examples of research in the above areas include: studies to increase understanding of the role of the endocardium in development of the heart; studies of the ontogeny of specialized conduction tissues to help clarify the genesis of arrhythmias; construction of a repository of developmentally staged samples of cardiovascular genes and proteins from model organisms, to help characterize the expression of genes and proteins during development; correlation of particular amino acid substitutions with specific cardiac malformations to gain insight into the structure-function relationships of encoded proteins in vivo; use of large-scale approaches to mutagenesis and gene modification in animal models to discover additional genes responsible for CCVMs; and development of new animal models that have mutations which are not lethal during embryogenesis and thus mimic the human condition more closely.

Development of the Vascular System

Recommendation: Encourage investigations of angiogenesis and vasculogenesis, especially in relation to the development of the pulmonary vasculature and coronary arteries.

Many investigators have focused on factors that regulate the differentiation and organization of the myocardium during cardiac morphogenesis, but fewer have explored the development of the associated systemic and pulmonary vasculature. At the earliest stages of differentiation, the endothelium of veins and arteries is molecularly distinct from the mesoderm that gives rise to most heart structures.

The pulmonary circulation is a potential target for therapeutic intervention because it is one of the few vascular beds in which the most expansive growth occurs during the perinatal and postnatal periods. However, before researchers can design rationally based therapies, they need to further study the mechanisms that regulate development and remodeling of the pulmonary vasculature.

Examples of research in the above areas include: characterization of the specification and proliferation of endothelial and vascular smooth muscle cells, investigation of the mechanisms that regulate development of the pulmonary vasculature in CCVMs, and characterization of the development of the coronary vasculature.

Laboratory Cores for Studying Animal Models

Recommendation: Develop core facilities for imaging and studying the physiology of the cardiovascular system in small animals to serve as national resources for research on CCVMs.

Characterization of the physiological phenotype of diseases in animal models is essential for understanding the pathophysiology of these diseases and their relevance to human conditions. For research in mice and other small animals, such as zebra fish, sophisticated techniques and specialized equipment are needed to enable investigators to characterize cardiac function, regulation of circulation, and cardiovascular responses to pharmacological and physiological interventions. To evaluate the efficacy of pharmacological and gene therapies in these animal models, researchers also need to be able to characterize the animals’ functional physiological responses to specific interventions.

Most of the imaging techniques currently used to diagnose cellular, molecular, and metabolic processes have limitations. The new techniques of MRI, MRA, MR spectroscopy, PET, and single-photon-emission computed tomography (SPECT), as well as other emerging imaging modalities, have the potential to define structural, physiological, and metabolic processes at molecular and cellular levels.

Any plans to develop core physiology laboratory facilities must include sophisticated imaging facilities to correlate function and structure of the cardiovascular system. Support for a single comprehensive laboratory that serves as a national resource center could help to ensure uniform analyses and the use of appropriate experimental approaches for specific animal models and research questions.

Risk Factors for CCVMs

Recommendations: Evaluate the role of genetic and environmental risk factors and gene-environment interactions in the development of CCVMs; establish a centralized core resource that includes a comprehensive DNA database for analysis of CCVMs in humans and experimental models (mouse and zebra fish).
Improved understanding of the causes and prevention of CCVMs depends on studies in large populations. Yet, these studies are complicated because CCVMs encompass different anatomic lesions and clinical manifestations and have various causes, and because children with CCVMs are difficult to ascertain, diagnose, and classify within a population. Also, although researchers can identify and diagnose most children with serious heart defects in population-based studies, children with milder or asymptomatic heart defects tend to be missed. To facilitate research on the causes of CCVMs, researchers must have a core resource with microarray technology and a comprehensive DNA database to enable identification of a large number of genes with altered expression, as well as their multiple downstream targets.

Examples of research in the above areas include: studies to ascertain current trends over time in the incidence of CCVMs; evaluation of the role of metabolic and nutritional factors in causing CCVMs; collaboration with the National Birth Defects Prevention Study of the Centers for Disease Control and Prevention to foster further studies of the epidemiology of CCVMs; evaluation of the heterogeneity of CCVMs in relation to genetic and environmental risk factors; expansion of the DNA database to include samples suitable for nonparametric linkage approaches, such as the transmission disequilibrium test and the affected relative pair approach, to identify the genetic loci for susceptibility to CCVMs and modifying factors; and facilitation of connections between microarray analyses and human DNA databases so that researchers can consider human candidate genes for study when new gene cohorts are identified from microarray analyses of model systems (mice and zebra fish).

**Imaging**

In this priority area, the task force highlights 4 general scientific opportunities: development and modification of imaging technologies for patients with CCVMs, development of fetal diagnostic imaging technologies, use of imaging to guide transcatheter and minimally invasive surgery, and integration of multimodal imaging display and bioinformatics.

**Development and Modification of Imaging Technologies for Patients With CCVMs**

**Recommendations:** Assess the anatomy and function of the cardiovascular system in infants and children who have congenital and acquired heart diseases, with the use of improved techniques such as MRI, MRA, MR spectroscopy, ultrafast and electron-beam CT, and real-time, three-dimensional and miniature echocardiography; develop, validate, and integrate innovative imaging tools for noninvasive assessment of myocardial mechanics, flow dynamics, and metabolic and molecular processes in patients with congenital and acquired pediatric heart diseases; stimulate development of new multidimensional imaging technologies; and design and implement prospective clinical studies to develop diagnostic algorithms with optimal cost-effectiveness and risk-benefit profiles for specific clinical circumstances in pediatric cardiovascular medicine.

Diagnostic imaging of cardiovascular structures in a fetus, infant, or child is especially challenging compared with that of an adult because the cardiovascular structures are much smaller, the heart rates are faster, young patients are less able to remain still during procedures, the spectrum of congenital anomalies is much wider, and most disease processes are dynamic.

Researchers in only a few heart centers for children are studying the use of MRI for pediatric patients, and they use equipment and diagnostic techniques for infants and children that are adapted from medical procedures for adults. Because, as noted above, infants and children are not simply “small adults,” researchers should concentrate on developing MRI hardware and software designed specifically for fetuses, neonates, and children with congenital heart disease.

Investigators also need to improve echocardiography, to move it from two-dimensional imaging to a high-resolution, real-time, three-dimensional imaging modality.

Examples of research in the above areas include: development of innovative sequences and methods of analysis, including high-resolution, interactive, real-time MRI; online quantification of blood flow; automated myocardial strain analysis; and structure-specific tracking methods; provision of accurate quantitative data on specific domains, including global pump function, regional myocardial mechanics, perfusion, and cardiovascular metabolism; noninvasive quantification of blood flow pressure, energy, and shear stress; development of four-dimensional anatomic imaging (and three-dimensional spatial imaging over time); and determination of the safety, accuracy, and reproducibility of new imaging modalities in infants and children.

**Development of Fetal Diagnostic Imaging Technologies**

**Recommendations:** Develop noninvasive tools and technologies to assess cardiovascular function in fetuses; design a multicenter collaborative study of the natural history of prenatal congenital heart disease; develop noninvasive imaging tools to guide cardiovascular therapy in fetuses.

The development of high-frequency ultrasound transducers and digital image processing has greatly improved diagnostic imaging of congenital heart disease in utero. Currently, clinicians can diagnose most structural congenital heart defects reliably after 16 weeks of pregnancy. However, their ability to assess the functioning of the cardiovascular system of fetuses is more primitive, limited to estimating global ventricular function, determining variations in the velocity of blood flow with the use of the Doppler technique, and assessing heart rate. Development and use of new noninvasive tools and techniques will help to improve assessments of cardiovascular function in the fetus.

Examples of research in these areas include: development of methods to accurately quantify global ventricular function, myocardial mechanics, and the dynamics of blood flow in the fetus; and definition of the natural history of congenital heart disease in utero, through a multicenter collaborative study.

**Use of Imaging to Guide Transcatheter and Minimally Invasive Surgery**

**Recommendation:** Develop and integrate new tools, such as real-time MRI and three-dimensional echocardiography, for
image guidance of transcatheter, minimally invasive, and robotic surgery for CCVMs.

As therapy for congenital heart disease advances, cardiologists and surgeons need accurate noninvasive imaging tools to guide their therapeutic interventions in children. Researchers could adapt real-time MRI, ultrafast CT, and ultrasound to guide minimally invasive and robotic surgery and transcatheter interventions to deliver drugs, genes, energy (eg, radio-frequency, laser, electric, or focused ultrasound), instruments, and devices to targeted areas in the cardiovascular system. With the use of image guidance during cardiac therapy, physicians also will be able to evaluate, in real time, the effects of interventions, the prognoses, and the need for further treatment.

Examples of research in this area include: development of new MRI sequences for tracking catheters and instruments; high-performance gradient systems; and new hardware to optimize access to a patient during interventional procedures; development of a new generation of MRI-compatible instruments; integration of several imaging modalities (eg, MRI, three-dimensional echocardiography, x-ray fluoroscopy) into one platform to achieve a more flexible and capable imaging system that can be used to guide various interventions and assess their effects; and use of focused ultrasound energy to release bioactive substances, such as drugs or genes, in specific areas within the heart or to open up restrictive septa or valves.

Integration of Multimodal Image Display and Bioinformatics

Recommendations: Develop, validate, and implement new bioinformatics systems that combine input from multiple diagnostic and imaging modalities to derive anatomic and functional information; design and implement studies to determine the optimal use of imaging technologies on the basis of analyses of cost-effectiveness and risk-benefit.

From the exploration of new methods for bringing biomedical imaging data to the desktops of clinicians and researchers to the promotion of rational, science-based use of imaging technologies, research in bioinformatics can greatly enhance communication in clinical research and access to biomedical data and, in turn, will stimulate new opportunities for research collaboration and greater efficiency in clinical practice.

An example of research in this area is the combining of biochemical data obtained by MR spectroscopy or SPECT (which have poor spatial resolution) with high-resolution MRI, MRA, CT, or echocardiographic images to pinpoint metabolic processes within the myocardium or walls of blood vessels.

Minimally Invasive Surgery and Transcatheter Therapy

Recommendations: Use bioengineering and material science approaches to improve robotic technologies, endoscopic instruments, and minimally invasive and transcatheter techniques; develop large-animal models to test various minimally invasive approaches to surgery for specific CCVMs; and develop left ventricular assist devices and extracorporeal membrane oxygenation systems that are appropriate for pediatric patients.

Minimally invasive surgery can improve the treatment of patients with CCVMs by speeding recovery times, improving cosmetic results, and reducing wound complications. Furthermore, robotic technology has great potential for expanding the role of endoscopic surgery in procedures that are becoming increasingly complex. But first, endoscopic instruments need to be miniaturized for use in small patients and researchers need to develop other equipment, such as suction devices, retractors, stabilizers, and catheters, for pediatric surgery. Additionally, investigators need to adapt and refine current techniques of left ventricular assist and extracorporeal membrane oxygenation for use in infants and small children.

Examples of research in the above areas include: application of robotic technologies in surgeries to create palliative shunts (eg, the Blalock-Taussig shunt) or assist with percutaneous procedures and, in selected cases, cardiopulmonary bypass; development of new surgical techniques and instruments for treating CCVMs with the use of minimally invasive approaches; adaptation of extracorporeal membrane oxygenation and left ventricular assist technology as adjuncts to care for infants and small children; development of tools for suturing heart tissues with the use of transcatheter approaches; and development of new materials that can be implanted safely in the circulation of growing children.

Intervention During Fetal Life

Recommendation: Refine techniques for interventions in the fetus, including improved technology for cardiopulmonary bypass and myocardial protection, reconstructive techniques, and transcatheter interventions.

Surgical and transcatheter interventions in the fetus to repair primary defects and to normalize blood flow patterns could improve function and minimize structural deformation. Currently, a disproportionate share of the resources available for treating congenital heart disease is extended to patients with selected defects, such as hypoplastic left heart syndrome, because these conditions are complex and the options for treatment are only partially effective. Interventions during fetal life have special promise for these patients and could help to contain the costs of continued care.

Examples of research in these areas include: studies to optimize extracorporeal circulation and myocardial protection in the fetus; development of biological glue and laser tissue-welding techniques for reconstructing fragile fetal tissues; modification and development of surgical instruments specifically for use in fetuses; development of miniaturized and semi-robotic catheter tools specifically for interventions in fetuses; and testing of newer imaging techniques, such as three-dimensional echocardiography and three-dimensional MRI, as necessary adjuncts to successful transcatheter procedures in fetuses.

Development of Cardiovascular Cell Therapies

Recommendation: Define the differentiation, proliferation, and interactions of stem cells during development as a basis for using them as potential sources of cardiomyocytes,
endothelial cells, and vascular smooth muscle cells for treating cardiovascular disease during childhood.

An improved understanding of stem cell biology is critical to the development of tissue-engineered implants. The lack of methods to deliver cells to affected tissues or organs hampers the development of cell therapies for diseases involving solid organs such as the heart.

Examples of research in this area include: development of improved techniques for isolating and culturing human stem cells; studies to improve understanding of the mechanisms that regulate the survival and differentiation of stem cells in vitro and in vivo; and development of methods to ensure proliferation of only desired cell types.

**Creation of Materials for Cardiovascular Bioprostheses**

**Recommendation:** Develop tissue-engineered structures for blood vessels, heart valve components, and materials for surgical repairs within the heart and for use in devices placed in the heart during surgery or cardiac catheterization.

The placement of artificial valves and conduits is an important facet of therapy for patients with CCVMs. However, artificial valves and conduits tend to deteriorate because of calcification and degradation of the extracellular matrix, and they do not grow with the patient. Pediatric patients who receive replacement heart valves or blood vessels have to undergo subsequent operations to replace these bioprostheses. Some of these patients are always at risk of serious bleeding because they must take anticoagulant medication to avoid life-threatening thromboses associated with certain artificial valves. Development and use of improved substitutes for cardiovascular tissue will reduce the need for multiple surgeries for children with CCVMs.

Examples of research in this area include: identification of polymers that function as workable scaffolds, but resorb after cellular and matrix remodeling has bioengineered a stable valve or vessel; investigation of the correct balance of endothelial cells, vascular smooth muscle cells, and fibroblasts needed to elaborate the appropriate extracellular matrix for bioprostheses; development of prosthetic, electrophysiologically active tissue implants to restore nodal function in patients with atrioventricular node block or sinus node dysfunction; and testing of developed biomaterials in animal systems.

**Translating Research Advances to Clinical Care**

In this priority area for research on pediatric cardiovascular disease, the task force highlights 5 general scientific opportunities: clinical trials, surrogate outcome measures, patient research registries, clinical effectiveness, and measuring general health status.

**Clinical Trials**

**Recommendations:** Support integrated networks and infrastructures for clinical trials; conduct multicenter, randomized trials to test and assess new therapies for pediatric cardiovascular disease.

Multicenter studies enable investigators to accrue the sample sizes needed in a reasonable amount of time and to generalize results because they involve a broader range of clinical settings than is possible with single centers. Even the largest clinical centers can individually enroll only small numbers of patients with rare CCVMs, and the findings are not as readily generalizable as in multicenter trials.

Examples of research in this area include prospective, randomized trials of the following: new biomechanical methods and drugs for better preservation of vital organs, including the brain and heart, during cardiopulmonary bypass and the early postoperative period; new drugs for nonstructural pediatric cardiovascular diseases, such as myocarditis, Kawasaki disease, and heart failure; and resynchronization therapy for dilated cardiomyopathy in infants and children.

**Surrogate Outcome Measures**

**Recommendation:** Conduct short-term and long-term studies to delineate validated and sensitive surrogate markers for clinical outcomes.

The proper conduct of prospective, randomized trials in children depends on delineation of appropriate outcome measures. Because the outcome of greatest interest may take a long time to develop and be difficult to measure, investigators often use surrogate markers as outcome measures in prospective studies of children and adults.

Examples of research in this area include: the defining of valid surrogate outcome measures for development of the following: arrhythmia or sudden death as a late consequence of CCVMs; complications in patients who have undergone a modified Fontan procedure, including those who are now adults; and neurocognitive dysfunction in school-age children who undergo surgery for CCVMs by use of cardiopulmonary bypass.

**Patient Research Registries**

**Recommendation:** Develop prospective, longitudinal databases and registries of patients with pediatric cardiovascular disease, including patients who are now adults.

Prospective, longitudinal registries of patients with pediatric cardiovascular disease contain valuable information about the epidemiology and outcomes of these diseases that investigators use to improve the clinical care of children. With the decline in deaths from surgery for CCVMs and the documentation of adverse, long-term cardiac and neurological sequelae in some survivors of CCVMs, investigators have shifted their research emphasis from ensuring survival to optimizing long-term outcomes.

Examples of research in this area include: the establishment of registries of patients who have the following conditions: high-risk arrhythmias and implanted cardioverter defibrillators; myocarditis; Kawasaki disease with coronary artery disease; univentricular heart palliated with a modified Fontan procedure; and transposition of the great arteries treated during infancy with Mustard or Senning atrial switch procedures.

**Clinical Effectiveness**

**Recommendations:** Develop and validate adjustment tools that are specific to procedures, conditions, and patients’ risks, to facilitate clinical research on determinants of outcome across the many rare and diverse congenital heart lesions;
identify processes and structures of care that predict outcomes for children with heart disease.

Even when clinical research demonstrates that a particular treatment is clearly advantageous, instigating changes in medical practice is difficult because physicians are often unaware about the best practices, healthcare systems may be inadequate, and outcomes depend on the skills of the individuals performing procedures, such as surgery.

Examples of research in this area include: elucidation of variables that underlie the relationship between institutions’ volume of cases and patients’ outcomes in pediatric heart surgery; identification of the effects of patients’ characteristics and the processes and structures of care (eg, age and ethnicity, insurance status, institutional characteristics) on morbidity and mortality; and exploration of the effects of factors (eg, an institution’s volume of cases, patients’ insurance status or race) on related outcomes, such as functional status, quality of life, and long-term cardiac and neurodevelopmental status.

**Measuring General Health Status**

**Recommendation:** Develop and validate instruments for assessing the functional status and quality of life of children with heart disease, to compare outcomes and practices across clinical centers and medical diagnoses.

Studies of clinical outcomes after heart surgery on infants document mortality and morbidity, but provide limited information on subsequent general health status or health-related quality of life. Investigators need to develop and refine instruments for assessing the general health status or quality of life of these children. Measures of functional status and quality of life that are validated in children with heart disease will be important when assessing the success of new therapies.

Examples of research in this area include: validation of the current generic instruments for measuring general health status and quality of life in children with heart disease; development of an assessment module for measuring general health status and quality of life specifically for pediatric cardiovascular disease; study of ways to track general health status over time in children with heart disease; and exploration of the relationship between assessments by parents, or their proxies, and children.

**Childhood Antecedents of Atherosclerotic Vascular Disease in Adults**

**Recommendations:** Increase understanding of the origins of atherosclerotic vascular disease (ASVD) during fetal life and childhood; develop strategies to identify children at high risk for ASVD and to develop effective therapeutic and preventive regimens.

Atherosclerotic vascular disease, particularly coronary artery disease, is the leading cause of death among adults in the United States. However, this disease process begins much earlier and perhaps even during fetal life. Further studies are needed to determine whether genotyping at young ages augments information on known risk factors to help physicians identify young patients who could benefit from preventive measures for early atherosclerotic disease.

Examples of additional research in the above areas include: investigations of the effects of socioeconomic status, gender, and ethnicity on childhood risk factors for ASVD; investigation of the effects of malnutrition during fetal development on physiology and metabolism; characterization of the relationship among specific genotypes, risk of ASVD, and response to therapy; examination of the mechanisms in childhood obesity that increase the risk for ASVD; development of effective strategies for reducing risk factors in families and through school-based and community-based programs; evaluation of the efficacy and safety of therapies to reduce various risk factors, to include use of noninvasive measures to assess the burden of disease; development of effective strategies to integrate the results of clinical trials into community and clinical practice; and determination of whether the genotyping of progeny of parents with early-onset atherosclerotic disease improves identification of children and adolescents who are at high risk for early development of atherosclerosis.

**Work Force for Academic Pediatric Cardiology**

**Recommendation:** Continue to develop successive generations of scientists to study pediatric cardiovascular disease.

The research work force is aging, and the number of practitioners is probably inadequate to meet the need for evolving models of clinical care and for increased levels of service for a growing population of survivors of pediatric cardiovascular disease. In addition, the future availability of well-trained clinical researchers and practitioners is uncertain.

Examples of approaches to address the issues in this area include: evaluation of strategies (eg, the NIH Loan Repayment Program) to encourage and support clinicians interested in becoming independent investigators; and optimization of strategies to develop centers for training scientists in developmental biology, genetics, population science, and information technology.

**Conclusion**

We are entering an exciting era in medicine characterized by human genomics, cell engineering, and the promise of increasingly sophisticated technology. Predicting the future is always hazardous. Contemplating opportunities, however, provides a framework for allocating resources and preparing the next generation of scientists and clinicians. The goal of the task force was to identify the high-potential areas for basic science, clinical investigation, and population-based studies. The issues and recommendations discussed by the task force are central to understanding the causes of pediatric cardiovascular diseases, improving clinical care for them, and eventually preventing them and their complications. The utility of our efforts will only become apparent with time.

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