ABSTRACT

The Child Health and Development Studies are longitudinal studies of pregnancy and the normal and abnormal development of the offspring. Women who were members of the Kaiser Foundation Health Plan entered the study in early pregnancy, and their children were examined frequently until the youngest child in the study was 5 years old. This is a more intensive follow-up than hitherto reported. Of the 19,044 live-born children, 163 had definite and another 31 had possible congenital heart disease; the crude incidence rates per 1,000 live births were 8.8 for definite congenital heart disease and 10.4 for definite plus possible congenital heart disease. The incidence rate of congenital heart disease was 7.9 percent among all stillborn fetuses subjected to autopsy and 10.2 percent among those in this group with autopsies evaluated as being detailed enough to detect heart disease. The incidence rate of congenital heart disease was 7.9 percent among all stillborn fetuses subjected to autopsy and 10.2 percent among those in this group with autopsies evaluated as being detailed enough to detect heart disease. Among the live-born children with congenital heart disease, 21 died in the neonatal period and 22 died in later infancy and childhood; about half the deaths were judged to have been due to heart disease. About 30 percent of the children with congenital heart disease had associated severe anomalies of other systems. In the whole cohort, 50 children had diagnosed chromosomal abnormalities (2.63/1,000 live births) and about 30 percent of them had congenital heart disease. Among the group of 163 children with definite congenital heart disease, the diagnosis was made in 46 percent by age 1 week, in 88.3 percent by age 1 year and 98.8 percent by age 4 years.

INTRODUCTION

Fifty years ago when the American College of Cardiology was established, pediatric cardiology was coming to be recognized as a significant cardiovascular specialty. New cases of rheumatic fever were in rapid decline. Oral penicillin was being used widely for 10 days in children with acute sore throat due to beta hemolytic Streptococcus infection. Penicillin was also used as prophylaxis for children as well as adults at risk of bacterial endocarditis following dental procedures or invasive manipulation of the gastrointestinal or urinary tract. Clinical diagnosis of congenital cardiac malformations was made increasingly accurate by angiocardiography and for children, though not yet for infants and toddlers, by cardiac catheterization. Furthermore, accurate diagnosis had been made relevant by the
success of extracardiac surgery for patent ductus arteriosus, coarctation of the aorta, and vascular ring. Then came the dramatic success of the Blalock-Taussig operation (anastomosis of the subclavian artery to the pulmonary artery). This changed cyanotic children born with tetralogy of Fallot or similar malformations associated with diminished pulmonary blood flow. No longer blue and breathless, they became pink and active. That accomplishment caught worldwide interest and attention, topping the list of recent advances and leading to the next fifty years of ever more remarkable accomplishments in cardiovascular medicine and surgery that we celebrate as we honor the first half century of the American College of Cardiology.

THE MOST COMMON CONGENITAL CARDIAC ANOMALY

King of the many kinds of congenital cardiovascular malformations is ventricular septal defect. It heads the list of early and more recent studies on the incidence and prevalence of congenital heart disease. Not only is it the most common anomaly at birth but it is also the most variable in size, shape, number, behavior and effects. Fifty years ago it was identified as a common and benign condition, the maladie de Roger, and it was recognized with a high degree of accuracy by a holosystolic murmur (sometimes accompanied by a thrill) at the lower left sternal border. Also known at that time was an uncommon condition, the Eisenmenger syndrome, in adults and children who became cyanotic as they grew older and who at postmortem examination had as the only cardiac abnormality a large, high ventricular septal defect. The stepwise, inexorable progression of involvement of the pulmonary vascular bed was not yet fully appreciated in 1948. Nor was it then realized that such a defect could be the cause of cardiac failure and lead to death early in infancy. It came as a surprise when we learned that small defects could close spontaneously, though this had been suspected when the characteristic murmur disappeared. Such an event was documented when progress in cardiac catheterization permitted its use in infants and when it came to be regarded as sufficiently safe as to permit serial studies in asymptomatic children. At this time it was a real shock to find that even large defects, sufficient to cause cardiac failure in the first one or two months of infancy, could also decrease in size and even close completely. Correlations of clinical, diagnostic, and pathologic studies led to an appreciation of the varied presentations of ventricular septal defect, for example, when it was associated with double-outlet right ventricle or the Taussig Bing malformation. Increasingly sophisticated diagnostic procedures, such as echocardiography with Doppler studies and magnetic resonance imaging, enabled noninvasive, painless studies to be performed, serially if need be, thus further expanding knowledge of ventricular septal defects, for instance those in unusual locations, such as the low, muscular defect or multiple defects.

As these medical facts were being discovered, cardiac surgeons accomplished the dramatic feat of intracardiac surgery with extracorporeal circulation. Thereafter, a clinically significant ventricular septal defect could be closed with a patch. In children with a tetralogy of Fallot, the pulmonic stenosis could be repaired, the subaortic VSD could be closed with a patch, thereby correcting the overriding aorta. Both maneuvers then allowed the right ventricular hypertrophy to regress, thereby taking care of all four parts of the tetralogy.

This historical perspective used the most frequent form of congenital heart disease as an example of progress in the field of congenital heart disease over the past 50 years. Now let us consider all forms of birth defects of the heart and major vessels and the important question of their frequency in the general population. To document the incidence was the purpose of the study reviewed here (1).

PLAN OF STUDY

This report was the outcome of the Child Health and Development Study, a longitudinal study of pregnancy as well as the normal and abnormal development of the offspring. Women in the Kaiser Foundation Health Plan entered the study early in pregnancy and their offspring were followed frequently until the youngest child was five years old. The authors attempted to determine the true incidence of congenital heart disease at birth and in the next five years. The long period of follow-up distinguishes this study. It is a unique and important aspect not attempted previously and to the best of my knowledge, not since. The plan permitted identification of those cardiac anomalies that were clinically evident at birth, such as the common cyanotic anomaly, complete transposition of the great arteries. Additionally it allowed the counting of those anomalies which did not manifest themselves until several months or years had passed. A prime example of the latter is atrial septal defect, one of the most common congenital abnormalities. This condition is silent to signs and symptoms until the relaxation and opening up of the pulmonary arterial tree causes a drop in pulmonary vascular resistance and pulmonary arterial pressure. Then regression of the right ventricular hypertrophy, that is normal for a fetus, follows. The consequent increased compliance of the thinned out right ventricle and the distensibility of the right atrium set the stage for a left-to-right shunt to develop. When that shunt causes a sufficient increase in pulmonary blood flow, a middiastolic murmur appears in the second left interspace, accompanied by wide and then fixed splitting of the second heart sound, both of these being characteristic auscultatory signs of an atrial septal defect. The time span of five years of periodic examination also enabled the detection of changes that decreased the prevalence of specific malformations, such as when a ventricular septal defect spontaneously closed and the murmur was lost. Thus their study design was commendable and wise.
They set out to find the incidence of congenital heart disease not only in liveborn infants but also in stillborn children with gestational age of 20 weeks or more. Here the method of diagnosis was by autopsy. Unfortunately, they soon learned that the answers they sought could not always be found, for description of internal organs, including the heart, was sometimes lacking.

In the liveborn, confirmation of diagnosis when congenital heart disease was suspected by the pediatrician was accomplished through examination by a pediatric cardiologist (JIEH) or by autopsy, cardiac catheterization, or surgery. The extremely useful tool of echocardiography with Doppler measurements was not available to them for diagnosis and follow-up in the 1960s when the study took place.

**FINDINGS**

Of a total of 19,502 births, 19,044 were liveborn, and of the latter, 163 had definite congenital heart disease, an incidence rate of 8.8 per 1,000. This figure is in good agreement with many previous and subsequent studies throughout the world. If to that number were added another 31 considered possibly to have congenital heart disease, the incidence increased to 10.4 per 1,000. They commented that the true incidence is probably higher than this number since they had no way of recognizing the common situation of bicuspid aortic valve, which has been estimated to be present in about 2% of the population. I believe that it is fair to say that the incidence of congenital heart disease (CHD) in the population is about 1 in 100.

The authors detected increasing numbers of affected children as they followed the cohort. At birth, among 19,044 children the incidence was 3.3/1,000. By one month, it was 5.2; by six months it was 7.3; and by 12 months, 7.8. At last follow-up at the age of 60–71 months, among the 12,926 children available for assessment, the incidence had increased to 9.1/1,000. Thus, when considering prevalence, it is important to know the age of the subjects.

The authors expressed their findings in a different way, but to the same effect when they stated that the diagnosis of CHD was made at birth in 38.7%, by one week in 45%, by one month in 59.5%, and by the first birthday in 88.3%. This emphasizes the importance of frequent examinations of the baby during the first year of life.

Deaths among the 163 children with definite CHD occurred in 43, and about half of those (21 children) were in the neonatal period. Importantly, in only six was the death related to the heart disease. In contrast, among the 22 older infants and children who died, most deaths (16 children) were due to the CHD.

Calculation of the incidence of congenital heart disease in stillborns was limited to those with autopsies that included examination of the heart. The incidence figure of 10.2/1,000 was higher than the overall figure for liveborn children: 8.8.

The specific cardiac conditions found in the liveborn and stillborn infants were similar, with the exception that in the stillborn, complex lesions were more numerous. In both groups, common anomalies included ventricular septal defect (first as expected) together with other malformations such as coarctation of the aorta, complete transposition of the great arteries, tetralogy of Fallot, pulmonic stenosis, aortic stenosis, patent ductus arteriosus and atrial septal defect as well as more unusual conditions such as single ventricle and truncus arteriosus.

Surprising to me, and not consistent with my experience, was the high incidence among the 163 liveborn children with congenital heart disease of associated anomalies:

- severe anomalies in 30.1% and non-severe in another 12.1%.
- Incidence of Down’s syndrome in the entire cohort was 1.94/1,000 live births. Nine of the 37 children with this syndrome had a cardiac condition, most often a ventricular septal defect or atroventricular canal. In all, 50 children had a chromosomal abnormality (2.63/1,000 live births) and of these, 30% had congenital heart disease.

**ETIOLOGY AND PREVENTION?**

In the study design from which these data were derived was the registration of information that might possibly be related to malformation in the offspring. This information was obtained for the six months prior to conception and throughout pregnancy. Questions concerned all illnesses and conditions as well as all drugs prescribed during the period. No results were provided and no note was taken of any unusual environmental events during the course of the study, which terminated in 1966.

The extensive and thorough Baltimore-Washington Infant Study 1981–1989 by Charlotte Ferencz et al. (2) was designed to study genetic and environmental risk factors of major cardiovascular malformations. In its 463 pages there is a great wealth of information, carefully analyzed. The cases of congenital heart disease totaled 4,390 among 906,626 area births. A control group numbered 3,572. Median length of follow-up was 10 months. Findings of prevalence of the cardiac malformations was similar to those in this report by Hoffman and Christianson. Dr. Ferencz concluded that while the Baltimore-Washington Study answered many questions that have long been asked about cardiovascular malformations, nonetheless the etiology of congenital heart disease remains elusive. She concluded with the confident hope “that a new generation of researchers will make use of these findings and open the remaining doors that lead to prevention of congenital heart disease and other malformations.”

**CONCLUSIONS**

Congenital heart disease is not uncommon. It was found in definite form in 8.8/1,000 live births, or in 10.4% if some cases of possible heart disease were also included. Since these numbers did not include people with bicuspid aortic
valve, a common anomaly, the incidence is probably higher still. The most common congenital cardiac lesion is ventricular septal defect. The reasons for these congenital defects is unknown; so at this time prevention is not possible. We pediatric cardiologists and the adult cardiologists who are now inheriting our grown-up patients, as well as the skilfull cardiovascular surgeons who have been our allies, can all be grateful for the progress that has been made in this field since 1949 when the American College of Cardiology came into existence. The fellows of the College helped to set the high standards for diagnosis and successful management of people of all ages who were born with a malformed heart.