Endocarditis in Congenital Heart Disease
Who Is at Highest Risk?

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The risk of infective endocarditis (IE) remains a major concern in patients with congenital heart disease (CHD), whether unrepaired, palliated, or corrected. The overall incidence of endocarditis in adults with CHD has been reported to be 11 per 100,000 person-years, which is a considerable increase compared with the general population, in which a rate of 1.5 to 6.0 per 100,000 patient-years has been reported. In children, the incidence of IE in the general population is ≈3 times lower.

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CHD is the most prevalent underlying cardiac condition in patients with IE. Despite recommendations for antibiotic prophylaxis of IE, increased survival of children with CHD and the use of conduits and prostheses in corrective surgery may have contributed to an increasing incidence of IE. However, CHD-associated IE mortality has decreased substantially to 10% because of improvements in the diagnosis of IE, antimicrobial treatment, cardiac surgery, and interventional therapy. Given the prognosis, morbidity, and high cost of management of IE, IE prophylaxis has long been recommended in an attempt to minimize the incidence of IE.

However, no randomized study has been conducted yet to elucidate the efficacy and usefulness of IE prophylaxis. Based on case-control studies, expert opinions, and daily practice, guidelines on IE prophylaxis from international cardiology societies in 2008/2009 were greatly simplified and resulted from routine daily activities in causing IE, antibiotic prophylaxis was deemed reasonable in only a select group of high-risk patients. However, changes in the preexisting guidelines were based on limited data. Owing to a lack of evidence, all recent recommendations are Class IIa and Level of Evidence B or C, similar to the level of evidence of the previous recommendations.

At this time, surveillance with administrative databases and more detailed record review may be useful in ascertaining whether the adoption of the revised IE prophylaxis guidelines has changed the prevalence of IE. In addition, for improvement in future IE prevention guidelines, further studies are needed to gain insight into cardiac lesions and procedures at highest risk of developing IE.

Against this background, Rushani et al provide important new information. Using a population-based analysis, the authors report the cumulative incidence and predictors of IE in children (0–18 years of age) with CHD using the Quebec CHD Database from 1988 to 2010. Of 34,279 children who were followed up since birth and contributed 328,185 person-years up to 18 years of age, 136 cases of IE were observed. The cumulative incidence of IE from birth to 18 years of age in all CHD lesions combined was 6.1 first cases per 1000 children, corresponding to an incidence rate of 4.1 per 10,000 person-years. Analysis of the predictors of IE involved a comparison of 185 patients with IE and their 3700 calendar time–matched controls from the full population of 47,518 children with CHD. Cyanotic CHD lesions, left-sided lesions, and endocardial cushion defects were associated with an increased risk of IE acquisition in childhood. The relative risk of developing IE was substantially elevated during the 6-month postoperative period of cardiac surgery and in children <3 years of age.

The data are unique in this population-based approach but are limited by the validity and scope of the data used. Although the data sources ensured province-wide inclusion of children with CHD in the cohort, they are prone to misclassification error and lack clinical information, which can limit the validity and generalizability of the data.

How can these data improve our insight into cardiac lesions and procedures at highest risk of developing IE? How will the presented results of this Quebec study be relevant for future revision of guidelines? The population-based approach and the large number of patients allowed an estimation of the cumulative incidence of IE in children with CHD. The overall rate of IE was ≈3 times lower than the published estimate in adults with CHD. The reduced frequency of IE in children compared with adults with CHD parallels the trend in the general population. In future revisions of guidelines, these data on the incidence of IE in children with CHD may be important.

In line with the current guidelines for antibiotic prophylaxis, cyanotic CHD lesions and cardiac surgery in the previous 6 months were found to be strongly associated with the development of IE. The risk of IE, however, was also elevated among patients with left-sided lesions and endocardial cushion defects, even in children with no previous valve surgery.
or history of IE, 2 conditions currently included in the high-risk category for IE. Should patients with left-sided lesions and endocardial cushion defects therefore be considered eligible for IE prophylaxis in future revisions of IE guidelines? The results should be interpreted with caution because a lack of clinical information, inherent to the study design, makes accurate risk assessment somewhat delicate in several aspects. Importantly, as expected, the risk of IE varied markedly across the CHD lesions in the study by Rushani et al. However, the infrequency of IE prevented investigation of CHD lesions individually. CHD lesions were grouped into categories of comparable IE risk, but not all constituent lesions of the group shared identical IE susceptibility. Although, for example, 3 important subgroups of left-sided lesions—aortic coarctation, aortic valve disease, and mitral valve disease—showed a comparable IE risk, this finer breakdown led to fewer IE events per lesion and prohibited any statistical analysis. Because in most studies the incidence of IE has been reported to be substantially higher for aortic valve stenosis than for aortic coarctation, left-sided lesions as an overall group should not be considered eligible for IE prophylaxis in future guideline revisions. A further refining of the data is needed for an accurate estimation of patients at highest risk of IE. Similarly, within the cyanotic CHD group, the data did not permit a distinction between cyanosis in infancy (associated with the native anatomy) and chronic cyanosis. Moreover, the impact of spontaneous closures of ventricular septal defects could not be assessed, which might explain the remarkably low incidence of IE in ventricular septal defect patients. Ventricular septal defect is usually considered a high-risk defect in both children and adults. On the other hand, it has been suggested that IE is related primarily to associated valve disease rather than the septal defect itself. These limitations are obviously inherent to such a large population-based study. The present findings have to be extended with more clinical studies in which more subtle clinical data are available to discriminate the risk of IE between cardiac defects within combined subgroups.

Sex has been recognized to be an important risk factor for IE in adults. Men are affected at least twice as often as women. In children, the male-to-female ratio seems lower at 1.2:1, and in the Quebec study, a comparable IE frequency in males and females was observed. It is possible that high-risk behaviors and other lifestyle factors may be less likely to differ between males and females during childhood.

In summary, it has to be emphasized that our insight in CHD patients at high risk for IE is still limited. The question of who is at highest risk for the development of endocarditis within the CHD population remains largely unanswered. Still, the authors of the present study have taken a significant step to fill the gap of knowledge. The population-based cohort study design importantly allowed assessment of overall IE incidence in children with CHD. The authors compared combined groups of cardiac defects and estimated both relative and absolute risks in this population. This approach may form the basis for further studies comparing individual lesions within combined patient groups. Whether the use of antibiotic prophylaxis should be extended to patient groups and procedures not included in the current recommendations requires further research. These studies are required for future revision of IE prevention guidelines. Other crucial studies should include an evaluation of the protective efficacy and cost-effectiveness of prophylaxis and an evaluation of the relative importance of bacteremias from routine daily activities versus invasive procedures in causing IE. On the basis of studies such as that reported by the Quebec investigators, a future revision of IE prevention guidelines might lead to future recommendations that are based on much more robust data and substantial evidence.

Disclosures
None.

References
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