New trends in pediatric endocarditis

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Objectives
To evaluate the epidemiology, etiology and evolution of a cohort of infants and children with endocarditis and to compare their main characteristics to that of our previously published experience.

Material and methods
Patients less than 18 years of age diagnosed with endocarditis at the CHU Sainte-Justine of Montréal, between January 1986 and December 2000. The recent case series was compared to our previous experience of 1960-1985.

Results
56 children with endocarditis were included; 35 children with congenital heart disease, 15 with serious systemic underlying disease and 6 healthy children. Mean age was 7 years and ten months. Male sex: 54% of the cases. The prevalence of endocarditis increased from 1.5 cases/year to 4 cases/year in the previous vs. recent case series, respectively. In the present series, 10 patients (17.9%) had a central venous catheter. Sixteen (28.6%) patients had a vascular prosthesis. Blood cultures were positive in 50 patients (89%) with Streptococci spp. in 48% and Staphylococci spp. in 34% of cases. Echocardiography was positive in 36 of 55 patients (65.4%). All children were treated with intravenous antibiotics for an average of 43 1/2 days. There were no recurrences. Significant complications developed in 26 patients (46%). Embolic phenomena were seen in 11 children (20%). Twelve patients (21%) needed surgery. Of the six healthy children, five developed complications. Overall, seven children (12.5%) died; all were older than six years of age. Comparing our experience of 1960-1985 to 1986-2000, morbidity and mortality has decreased from 85.7% to 46.4% and from 27% to 12.5%, respectively.

Conclusions
Pediatricians must recognize that children with underlying immunodeficiency and those with central venous catheters have an increased risk of endocarditis. Healthy children with endocarditis have a greater risk of complications. The morbidity and mortality of endocarditis has decreased considerably in recent years.

Keywords:

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INTRODUCTION
Infectious endocarditis is still a rare infection in pediatrics. Recently, changes have been reported in incidence, agents and risk factors for endocarditis. In the past, rheumatic fever was a very frequent cause of endocarditis and has been disappearing in western countries. Congenital heart disease (with or without surgery) has remained the major risk factor for endocarditis in children. Other risk factors for endocarditis include serious systemic underlying illness and congenital and acquired immunodeficiency. There has been a steady increase in the number of children with these problems who would also be at risk for endocarditis. In spite of progress in diagnostic techniques and treatment, infectious endocarditis continues to be difficult to diagnose in children.

The first objective of this study was to evaluate the etiology, epidemiology, pathogens and evolution of a cohort of pediatric patients with endocarditis. The second objective was to compare their main characteristics to our previously published experience.

MATERIAL AND METHODS
A retrospective cohort study was conducted. All children less than 18 years of age diagnosed with endocarditis at the CHU Sainte-Justine in Montreal, Canada, between January 1986 and December 2000 were included in the study. Seventy eligible patients with endocarditis were identified through medical records according to the codes of the 9th Revision of the International Classification of the Diagnosis. There were fourteen cases who did not fulfill the Durack’s criteria and were excluded. Patients who fulfilled Duke’s criteria for endocarditis at the time of discharge were included in the study.

Patient information was recorded retrospectively by a single investigator (GL) using a standardized case report form. Data collected included: demographic characteristics, symptoms, signs, previous medical condition, history of congenital heart disease, presence of a central venous catheter and diagnosis at the time of admission to the hospital. Other data included were: white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), blood cultures and echocardiography results. Antibiotic therapy, length of hospital stay, surgery and evolution of the disease were also noted.

When available, pathological and autopsy results were reviewed. In patients who underwent cardiac surgery or autopsy, diagnostic confirmation was done by direct observation of the cardiac injuries and vegetations. Material obtained was evaluated by anatomopathological, bacteriological study and culture.

Characteristics of the recent series of 1986-2000 were compared to our previous experience of 1960-1985.

Conclusiones
El médico debe reconocer que los niños con inmunodefenencia o con catéteres tienen un riesgo aumentado de endocarditis. Los niños sanos con endocarditis presentan mayor riesgo de complicaciones. Las complicaciones y la mortalidad han disminuido considerablemente en los últimos años.

Palabras clave: Endocarditis, Niños, Cardiopatía congénita.
others (5 cases = 9.8%). A patient underwent surgery for suspected appendicitis, another one was treated for several months with an erroneous diagnosis of rheumatoid arthritis. Forty-four patients were diagnosed using clinical signs and cardiac echocardiography. Ten cases diagnosed on clinical grounds were also confirmed with pathologic examination after surgery. Two cases who were not initially suspected, were subsequently diagnosed based on pathologic examination. Median duration of time to confirm the diagnosis of endocarditis was one day.

Thirty-five patients had congenital heart disease (62.5%) (fig. 1). Of those, 21 patients (60%) had undergone cardiac surgery. Three children with congenital heart disease developed endocarditis in the early postoperative period within two months of the surgery. One patient had undergone cardiac catheterization two months before the diagnosis of endocarditis was made. Ten patients had a central venous catheter. A total of 16 patients had vascular prostheses (coils, Hancock, Gore-Tex, Dacron, animal or homologous graft). Four patients had pre-existing cardiac disease that was not diagnosed until they presented with endocarditis: three had aortic valve anomalies and one an aortic coarctation. These four patients have been included in the group of children with heart disease (fig. 1). The diagnosis of endocarditis was made following varicella in two patients and dental manipulation in five.

**Hematology**

Increased WBC was present in only 28.5% of the patients. Anemia was documented in 67% and thrombocyto-

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**Figure 1. Risk factors and underlying diseases in 56 patients with infectious endocarditis. RV: right ventricle; LV: left ventricle. Patients with immunodeficiency: nephrotic syndrome, third degree burns, lupus, leukemia, HIV, lymphoma, neoplasia, juvenile rheumatoid arthritis. Patients with chronic disease: massive telangiectasia, encephalopathy. av: atrioventricular.**

**TABLE 1. Signs and symptoms of 56 children with endocarditis**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>47</td>
<td>84</td>
</tr>
<tr>
<td>Fatigue</td>
<td>27</td>
<td>48</td>
</tr>
<tr>
<td>Arteritis</td>
<td>25</td>
<td>44</td>
</tr>
<tr>
<td>Neurologic signs</td>
<td>23</td>
<td>38</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>18</td>
<td>32</td>
</tr>
<tr>
<td>Vomiting</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>14</td>
<td>25</td>
</tr>
<tr>
<td>Abnormal breathing</td>
<td>14</td>
<td>25</td>
</tr>
<tr>
<td>Cough</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Embolic signs</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Arthritis</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Chest pain</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Mycotic aneurism</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Roth spots</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

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topenia in 58% of patients. ESR was increased in 80% of
d patients.

**Microbiology**

Blood cultures were positive in 50 patients (89%). Cul-
tures were sterile in six children. Five of those six patients
were receiving antibiotics at the time the blood culture
was obtained. An average of 3 blood cultures were col-
lected from each patient (median of 2 and range: 0 to 13). The pathogens isolated in the patients are shown in
table 2. Staphylococcus aureus was found in 12 patients
(24% of all positive blood cultures). The patient hospitalized in
the neonatal intensive care unit with a history of necro-
tizing enterocolitis and ileostomy had a positive blood

culture for *Candida albicans*. Aspergillus was found on
pathological study of a valve in a single patient. This pa-
tient had congenital heart disease and had been treated
for osteomyelitis complicated with an endocarditis who did
not respond to medical treatment. *Enterococcus* spp.
alone was not responsible for any case of endocarditis in
our series, but was associated with another pathogen (*S
epidermidis*) in a patient with endocarditis in the inten-
sive care unit.

**Echocardiography**

One patient with trisomy 18 and congenital heart dis-
ease, died before echocardiography was performed. Echocardiography was positive in 36 of the 55 patients
who underwent this examination (65.4%). During the
time tranesophageal echocardiography has been used, there were 28 cases of endocarditis and this technique
was used in 46.4% of the patients. At the time of the di-
agnosis of endocarditis, echocardiographic anomalies
were located on the right side of the heart in 11 patients
and on the left side in 18. In several cases, the vegeta-
tions were not present at the initial examination, but
were seen on follow-up examinations. Thirty-one pa-
tients had obvious vegetation present on ultrasound. Three patients had vegetations in two valves. The mitral
valve (fig. 2) was more frequently involved (15 patients).
Anomalies in other structures were: tricuspid valve (5 pa-
tients), aortic valve (5 patients) (fig. 3), right atrium
(4 patients), coronary sinus (1 patient) and pulmonary
valve (1 patient). In four patients, anomalies were locat-
ed in the ventricular septal defect. The six healthy chil-

![Figure 2. Vegetation on mitral valve. RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle.](image-url)

**Table 2. Pathogens isolated in our 56 patients with endocarditis**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococci spp.</td>
<td>24 (48%)</td>
</tr>
<tr>
<td><em>S. epidermidis</em></td>
<td>5</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>12</td>
</tr>
<tr>
<td><em>S. epidermidis</em></td>
<td>5</td>
</tr>
<tr>
<td>Other bacteria</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Corynebacterium striatum</td>
<td>1</td>
</tr>
<tr>
<td>Gemella haemolymnae</td>
<td>1</td>
</tr>
<tr>
<td>Thermophiles</td>
<td>1</td>
</tr>
<tr>
<td>Kingella kingae</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>2</td>
</tr>
<tr>
<td>Fungi</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><em>Candida</em> spp.</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>1</td>
</tr>
<tr>
<td>Multiple pathogens</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Sterile blood cultures</td>
<td>6 (11%)</td>
</tr>
</tbody>
</table>

*Other streptococci included: group A streptococci, group C streptococci, nutritionally deficient group G streptococci.
One patient had a blood culture positive for gram positive cocci on Gram stain, but no pathogen was isolated in culture, the pathogen was suspected to be *S. epidermidis*
Multiple pathogens: *Enterococcus faecalis* and *Staphylococcus haemolymnae.*
Children presented with anomalies located only in the left side of the heart.

Treatment and evolution

All patients were treated with intravenous antibiotics for an average of 43 days ± 15 (median of 42 days and range: 1 to 84 days). Thirteen patients completed antibiotic therapy at home after their medical condition had been stabilized. There were no recurrences.

Evolution was favorable in 30 patients who responded to medical treatment. Significant complications occurred in 26 patients (46%) (table 3). Children who had risk factors either central venous catheters or valvular prostheses (20/26) preceding the diagnosis of endocarditis, developed more complications (p < 0.05) than those who did not. Complications secondary to endocarditis decreased significantly: from 85.7% in 1960-1985 to 46.4% in 1986-2000 (p < 0.001). Embolic phenomena were seen in 11 children (20%). One child developed a central nervous system complication (cerebro-vascular accident) secondary to a mycotic aneurism. Three patients developed respectively, cardiac tamponnade, acute tubular necrosis, and nodules in the lungs and liver. Twelve patients (21%) needed surgery during the initial hospitalization, including valvular surgery in six children, removal of vegetation in four, and replacement of vascular patch or fistula in two. Of the six healthy children without pre-existing heart disease, five developed complications: three had a mycotic aneurism and two cerebral emboli. Three of these patients needed surgery.

Mortality secondary to endocarditis decreased significantly: from 27.0% in 1960-1985 to 12.5% in 1986-2000. Seven children died; all were older than six years of age (table 3). Four patients died of early complications of their endocarditis. Two children died in the pediatric intensive care unit with multiple organ failure. One patient died with trisomy 18 and congenital heart disease. Three of the patients who died had congenital heart disease (3/35, 8.5% mortality rate), three had another systemic underlying disease other than cardiac pathology and only one patient was healthy with normal cardiac anatomy.

According to Duke’s criteria, the cases of infectious endocarditis were considered either definitive (24 patients) or possible (24 patients). According to the modified criteria by Li, the patients would have been classified as definitive endocarditis (24 patients), possible (29 patients) and three cases would have been rejected. These three patients had complex congenital heart disease. Two of them had had previous cardiac surgery and one had undergone cardiac catheterization. These three patients presented with only two minor criteria: heart disease and prolonged fever; they were treated as possible endocarditis.

Discussion

Despite being a rare infection, our recent experience shows an increased prevalence of endocarditis; this is in agreement with other authors. In addition to an increased survival following cardiac surgery, there are other risk factors considered as predisposing conditions for infective endocarditis. Improvement of resuscitation methods and newer technologies introduced in intensive care units for newborns and very ill children, have created a new group of patients with an increased risk of endocarditis. Twenty-five percent of the patients had a serious systemic underlying disease or underlying malignancy. Patients with immunodeficiency can present without fever. Central venous catheters increase the risk of endocarditis and are a frequent cause of nosocomial infections. Healthy children, without pre-existing heart disease or other risk factor, constitute 8-10% of the cases of endocarditis in the literature; in our series, it was 10.7%. Frequently, in these cases, the endocarditis is secondary to bacteremia with S. aureus and has a worse...
prognosis. Dental alterations or manipulations were im-
portant risk factors in our first series (17 cases = 46%), as
compared to the present study (5 cases = 9%), probably
secondary to better dental follow-up.

In our recent study, congenital heart disease continues
to be the most common risk factor for endocarditis (be-
fore or after surgery) when tissues weaves or prosthesis
have been implanted. As in the literature, tetralogy of
Fallot and transposition of the great vessels continue to
be the most frequent cyanotic heart disease involved in
endocarditis. In the non cyanotic heart diseases, ventric-
ular septal defect and left ventricular outflow tract ob-
struction are the most important underlying conditions.

The clinical presentation continues to be non-specific
and the diagnosis is difficult. The extra-cardiac manifes-
tations that are frequent in adults are rare in children,
with the exception of embolic, neurologic and cutaneous
phenomena. The pediatrician must have a great index of
suspicion for endocarditis in children with fever and un-
derlying cardiac abnormalities. The presence of a patho-
logic heart murmur in a child who presents to the emer-
gency room with fever should raise the possibility of
endocarditis; however, absence of an heart murmur does
not rule out this diagnosis.

The WBC is non specific for the diagnosis of endo-
carditis. In our experience, 71% and 53% of our patients
had a normal WBC and hemoglobin, respectively. The
erythrocyte sedimentation rate was elevated in a signifi-
cant proportion of patients with endocarditis; neverthe-
less, it can be normal at the time of the initial visit or ad-
mision to the hospital. In our center, we obtained an
average of three blood cultures, in concordance with the
recommendations of the literature. In 89% of patients,
the blood cultures were positive, a similar rate has been
reported in the literature. Some authors report that S.
aureus causes 12% of endocarditis cases, with a mortal-
ity of 40%.

Recently, Fowler and colleagues published a study of 1800 adult
patients from 16 different countries, reporting that S. aureus was the pathogen in 51.4% of their cases of endocarditis. In our series, twelve children were infected with S. aureus (24.3%) and only one of these patients died. In our study, Streptococcus viridans con-
tinues to be the most frequent pathogen (30%). Another
recent study reports that S. viridans is the most frequent
pathogen of endocarditis in adults.

Echocardiography was positive in 64% of our patients, similar
to what has been reported in the literature. Sensi-
tivity of transthoracic echocardiography in pediatric pa-
tients is 96% for general cardiac examination and 95% to
identify vegetation. The heart ultrasound must be re-
peated to demonstrate vegetation; sometimes on the first
examination an echogenic mass is seen, and in a later ex-
amination, the vegetation is evident. A transoe-
sophageal echocardiography must be considered in pedi-
atric patients with sub optimal transthoracic window or
when vegetation is not detected by conventional ultra-
sound.

In our series, the diagnosis and treatment were estab-
lished for most patients within the first 24 hours after ad-
mision, as mentioned in the literature. There were
some patients who had a delayed diagnosis, up to two
months demonstrating that endocarditis diagnosis can still
be difficult. Risk factors for complications mentioned in
the literature include type of infectious pathogen, location
and size of the vegetation, previous cardiac conditions,
heart with a pre-existing normal anatomy, and children
less than 2 years of age. The complications were statisti-
cally more frequent only in patients with risk factors pre-
TABLE 1. Endocarditis: 40 year’s experience (1960-2000)

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n=37</td>
<td>n=56</td>
</tr>
<tr>
<td><strong>Epidemiological data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>49%</td>
<td>54%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Age range</td>
<td>3 days-21 years</td>
<td>19 days-18 years</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal children</td>
<td>28 (75.7%)</td>
<td>35 (62.5%)</td>
</tr>
<tr>
<td>Other systemic underlying disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal children</td>
<td>9 (24.5%)</td>
<td>6 (10.7%)</td>
</tr>
<tr>
<td>Other pathogens</td>
<td>8 (25.5%)</td>
<td>6 (12.0%)</td>
</tr>
<tr>
<td>Fungus</td>
<td>2 (5.9%)</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td>Multiple pathogens</td>
<td>5 (13.5%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>Sterile blood cultures</td>
<td>5 (13.5%)</td>
<td>6 (10.7%)</td>
</tr>
<tr>
<td><strong>Microbiological data</strong></td>
<td></td>
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</tr>
<tr>
<td>Positive blood cultures</td>
<td>34 (91.9%)</td>
<td>50 (90.9%)</td>
</tr>
<tr>
<td>S. viridans spp.</td>
<td>17 (50.0%)</td>
<td>24 (46.0%)</td>
</tr>
<tr>
<td>Other pathogens</td>
<td>8 (25.5%)</td>
<td>6 (12.0%)</td>
</tr>
<tr>
<td>Fungus</td>
<td>2 (5.9%)</td>
<td>2 (4.0%)</td>
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<td>Multiple pathogens</td>
<td>0 (0.0%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>Sterile blood cultures</td>
<td>5 (13.5%)</td>
<td>6 (10.7%)</td>
</tr>
<tr>
<td><strong>Cardiac ultrasound</strong></td>
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<tr>
<td>Abnormal findings:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left side: Mitral or aortic valves</td>
<td>15 + 5 = 18 (52.7%)</td>
<td></td>
</tr>
<tr>
<td>Right side</td>
<td>11 (20.0%)</td>
<td>4 (7.5%)</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>5 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>Multiple sites</td>
<td>5 (9.5%)</td>
<td>5 (9.5%)</td>
</tr>
<tr>
<td>Without localization</td>
<td>17 (30.9%)</td>
<td></td>
</tr>
<tr>
<td><strong>Evolution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>30/35 (85.7%)</td>
<td>26/56 (46.4%)</td>
</tr>
<tr>
<td>Death</td>
<td>10/35 (29.0%)</td>
<td>10/56 (17.9%)</td>
</tr>
<tr>
<td>Mortality of children without underlying disease</td>
<td>5/35 (50.0%)</td>
<td>1.0 (18.7%)</td>
</tr>
</tbody>
</table>
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En nuestra experiencia (tabla 3), complicaciones relacionadas con el endocarditis han disminuido más de la mitad: de 85.7% en 1960-1985 a 46.4% en 1986-2000.

Thejeh et al. reportaron un estudio de 30 años en el cual la incidencia de endocarditis y mortalidad ha disminuido considerablemente debido a la mejoría en el manejo antibiótico y medidas de soporte durante el curso de la infección.

Según Coward et al., la mortalidad en niños sanos ha disminuido de 12.5% en 1986-2000.

Mortalidad en niños sanos con endocarditis se ha descrito una vez entre 27% en 1960-1985 al 12.5% en 1986-2000. Según Coward et al., la mortalidad en niños con cardiopatía congénita es ahora 12.5%.

En conclusion: Endocarditis es una infección rara. El pediatra debe conocer que los niños con inmunodeficiencia o con catéteres venosos centrales tienen un riesgo aumentado de desarrollar endocarditis. Los niños sanos pueden tener complicaciones significativas. En los casos recientes, complicaciones y mortalidad han disminuido considerablemente debido a la mejora en técnicas ecocardiográficas, el uso eficaz de antibióticos y las medidas de soporte mejoradas durante el curso de la infección.

Bibliografía