The changing landscape of infective endocarditis (IE) in congenital heart disease (CHD)

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Chiang Mai University Hospital,
24th March 2018
Infective endocarditis (IE) and CHD

- CHD increases risk IE which increased morbidity & mortality
- Non-CHD population: $5-7/100,000$ patient-year (PY)

- Incidence of IE in CHD is $15-140$ times > general population
- Higher Incidence IE adult>children
  * Adult CHD $1-1.3/1,000$ PY
  # Children CHD $0.4-1/1,000$ PY

- IE @ CMU : in adult :underlying CHD : $10\%$, children : $80\%$

Incidence of CHD in children

70-75% Acyanotic heart dis.

25-30% Cyanotic heart dis

Hoffman et al. JACC2002
Lifetime risk IE for Unrepaired CHD

Highest; cyanotic CHD: \textbf{8.2} cases/1,000 PY (patients/year)
VSD: \textbf{2.4} cases/1000 PY

\uparrow \textit{VSD with AR / LV to RA shunt}

unrepaired VSD,

Lifetime risk for IE at age @ 30 years is \textbf{9.7%}
and by the end of life is \textbf{12%}

Mortality rate ↓

Simple lesions

VSD patch/ device closure

ASD patch or device closure
PDA device closure

Coarctation of aorta: stent

Prosthetic material increases the risk of associated infections & IE 6mo. Until complete epithelialization
TOF: surgery: palliative/corrective

Modified Blalock-Taussig shunt
Post-op TOF: chronic PR: 10-15 yr. after total correction need **pulmonic valve replacement (Bio prosthetic)**
Transcatheter Implanted PV: Bio prosthetic valve
Population of CHD in adult Adult CHD>18yr.(N=6970)

Verheugt, EHJ,2010,
Localized lesions IE in CHD

**Intracardiac:** 81%
- MV: 26%
- AV: 16%
- VSD: 5.2%, VSD & AR

**Extra cardiac:** 19%
- PDA: 2.7%,
- Shunt: 2.5% (*Blalock Taussig*)
- PA: 2.3%

### Microorganisms: IE in CHD

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptococci</strong></td>
<td></td>
</tr>
<tr>
<td>- α-hemolytic (viridans)</td>
<td>Most common</td>
</tr>
<tr>
<td>- β-hemolytic</td>
<td>Uncommon</td>
</tr>
<tr>
<td>- Enterococci</td>
<td>Rare</td>
</tr>
<tr>
<td>- Pneumococci</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Staphylococci</strong></td>
<td></td>
</tr>
<tr>
<td>- S. aureus</td>
<td>Second most common</td>
</tr>
<tr>
<td>- Coagulase-negative</td>
<td>Uncommon</td>
</tr>
<tr>
<td><strong>Gram-negative</strong></td>
<td></td>
</tr>
<tr>
<td>- Pseudomonas</td>
<td>Rare</td>
</tr>
<tr>
<td>- HACEK</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Fungi</strong></td>
<td></td>
</tr>
<tr>
<td>Candida</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>

- **Low-virulence organisms**
  - α-streptococci (viridans)
  - Enterococci
  - Coagulase-negative staph

- **High-virulence organisms**
  - Staph aureus
  - Strep pneumoniae
  - β-streptococci
## Risk factors for infective endocarditis in children with congenital heart diseases - A nationwide population-based case control study

Taiwan, 2017

<table>
<thead>
<tr>
<th>CHD lesions</th>
<th>No. of IE (%)</th>
<th>Person-year</th>
<th>Incidence rate$^a$ /10,000 PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanotic CHD</td>
<td>88 (37.13)</td>
<td>24,627.97</td>
<td>35.73</td>
</tr>
<tr>
<td>ECD</td>
<td>5 (2.11)</td>
<td>1835.21</td>
<td>27.24</td>
</tr>
<tr>
<td>Left-sided lesions</td>
<td>10 (4.22)</td>
<td>7012.84</td>
<td>14.26</td>
</tr>
<tr>
<td>VSD</td>
<td>74 (31.22)</td>
<td>73,221.58</td>
<td>10.11</td>
</tr>
<tr>
<td>Right-sided lesions</td>
<td>5 (2.11)</td>
<td>16,627.17</td>
<td>3.01</td>
</tr>
<tr>
<td>Other CHD</td>
<td>36 (15.19)</td>
<td>7067.1</td>
<td>50.94</td>
</tr>
<tr>
<td>PDA</td>
<td>5 (2.11)</td>
<td>32,953.83</td>
<td>1.52</td>
</tr>
<tr>
<td>ASD</td>
<td>14 (5.9)</td>
<td>49,681.47</td>
<td>2.82</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>237</strong></td>
<td><strong>213,027.17</strong></td>
<td><strong>11.13</strong></td>
</tr>
</tbody>
</table>

Invasive procedure 6 mo. before index case (OR; 95% CI)

- **Central venous catheter (CVC) insertion** 3.17; (2.36–4.27)
- **Cardiac catheterization** 3.74; (2.67–5.22)
- **Open-heart surgery** 2.47; (1.61–3.77)
- **Valve surgery** 3.20; (1.70–6.02)
- **Shunt surgery** 7.43; (2.36–23.41)

Dental procedures did not increase the risk of IE

*L-C. Sun et al. / International Journal of Cardiology 248 (2017) 126–130*
Quebec, Canada

- 1 case per 1000 PY

• 1991-2016 (25 yr.) : 74 episode in 62 pts

• Incidence ACHD: 0.9 cases/1000 PY
  Complex CHD 1.4 cases/1000 PY
  VSD 1.9 cases/1000 PY
  Bicuspid AV post AVR 1.8 cases/1000 PY

• Prosthetic material was involved in 47%*

  left-sided infection predominated (66%)

Blood culture positive 91% the most common organism:

- Streptococcus (37%)
- Staphylococcus aureus (28%).

Unusual organisms such as *Brucella* (goat milk), *Bartonella* (cat)
• Emboli: 34% of cases with cerebral.
• 46% pts. required surgery: replace severe regurgitant bicuspid AV
• Early IE mortality 15%: cerebral emboli & acute renal failure.

<table>
<thead>
<tr>
<th>Congenital condition</th>
<th>Organism</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mustard for d-TGA</td>
<td>Recurrent <em>Streptococcus</em> (blood),</td>
<td>AICD lead, sub-pulmonary AV valve (large vegetation)</td>
</tr>
<tr>
<td></td>
<td>Candida on AICD lead</td>
<td></td>
</tr>
<tr>
<td>Palliative Mustard for d-TGA/VSD/PS</td>
<td>CNS</td>
<td>Systemic venous baffle</td>
</tr>
<tr>
<td>Rastelli for d-TGA/VSD/PA</td>
<td>Recurrent CNS</td>
<td>LV-PA conduit</td>
</tr>
<tr>
<td>AVSD (cyanotic)</td>
<td>Staphylococcus aureus</td>
<td>Undefined</td>
</tr>
<tr>
<td>Repaired VSD/tricuspid valve replacement</td>
<td>Recurrent <em>staphylococcus aureus</em></td>
<td>VSD patch, prosthetic tricuspid valve</td>
</tr>
<tr>
<td></td>
<td>(IVDU)</td>
<td></td>
</tr>
<tr>
<td>Repaired VSD/unoperated BAV</td>
<td>Staphylococcus aureus</td>
<td>Aortic valve, aortic root abscess, mitral valve</td>
</tr>
<tr>
<td>Mechanical AVR for BAV</td>
<td>Recurrent bartonella</td>
<td>Mechanical AVR</td>
</tr>
<tr>
<td>Mechanical AVR for BAV</td>
<td>Staphylococcus aureus</td>
<td>Aortic root abscess</td>
</tr>
<tr>
<td>BAV</td>
<td>Staphylococcus aureus</td>
<td>Aortic root abscess</td>
</tr>
<tr>
<td>BAV</td>
<td><em>Corynebacterium</em></td>
<td>Undefined</td>
</tr>
<tr>
<td>BAV</td>
<td>Culture negative</td>
<td>Aortic valve</td>
</tr>
</tbody>
</table>

Guidelines for Management of IE

AHA Scientific Statement

Infective Endocarditis in Childhood: 2015 Update
A Scientific Statement From the American Heart Association

Robert S. Baltimore, MD, Chair; Michael Gewitz, MD, FAHA, Vice Chair;
Larry M. Baddour, MD, FAHA; Lee B. Beerman, MD; Mary Anne Jackson, MD;
Peter B. Lockhart, DDS; Elfriede Pahl, MD, FAHA; Gordon E. Schutze, MD;
Stanford T. Shulman, MD; Rodney Willoughby, Jr, MD; on behalf of the American Heart Association
Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular
Disease in the Young and the Council on Cardiovascular and Stroke Nursing


2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

Authors/Task Force Members: Gilbert Habib* (Chairperson) (France),
Patrizio Lancellotti* (co-Chairperson) (Belgium), Manuel J. Antunes (Portugal),
Maria Grazia Bongiorni (Italy), Jean-Paul Casalta (France), Francesco Del Zotti (Italy),
Raluca Dulgheru (Belgium), Gebrine El Khoury (Belgium), Paola Anna Erba* (Italy),
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(The Netherlands), Ulrika Snygg-Martin (Sweden), Franck Thuny (France),
Pilar Tornos Mas (Spain), Isidre Vilacosta (Spain), and Jose Luis Zamorano (Spain)

Eur Heart J 2015;36:3075-128.
# Clinical and Laboratory Findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
</tr>
<tr>
<td>- Fever</td>
<td>++++</td>
</tr>
<tr>
<td>- Myalgia, malaise, headache</td>
<td>+++</td>
</tr>
<tr>
<td>- Heart murmur (new or changing)</td>
<td>++</td>
</tr>
<tr>
<td>- Heart failure</td>
<td>++</td>
</tr>
<tr>
<td>- Embolic phenomena</td>
<td>++</td>
</tr>
<tr>
<td>- Splenomegaly</td>
<td>++</td>
</tr>
<tr>
<td>- Neurologic findings</td>
<td>++</td>
</tr>
<tr>
<td>- Osler nodes, Janeway lesions, Roth spots, splinter hemorrhages</td>
<td>+</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td></td>
</tr>
<tr>
<td>- Positive blood culture</td>
<td>++++</td>
</tr>
<tr>
<td>- Elevated ESR or CRP</td>
<td>++++</td>
</tr>
<tr>
<td>- Anemia</td>
<td>+++</td>
</tr>
<tr>
<td>- Hematuria</td>
<td>+++</td>
</tr>
<tr>
<td>- Leukocytosis</td>
<td>++</td>
</tr>
</tbody>
</table>
Echocardiography: TTE & TEE

- Native valve IE: TTE: sensitivity 75%, TEE: 90%
- Prosthetic valve /cardiac complications/ device infection: TEE
Boy, 13 yrs, Cyanotic heart disease, CC: Low graded fever with hemoptysis PE: Oxygen Sat 75%, SEM 3/6 LMSB
ESC 2015 Modified Criteria for the Diagnosis of IE

Clinical Suspicion of IE

Modified Duke Criteria

Definite IE

Possible IE

Rejected IE

Native valve

1. TEE
2. Cardiac CT
3. Microbiology

Prosthetic valve

1. TEE
2. Cardiac CT
3. $^{18}$F-FDG PET/CT
4. Microbiology

ESC 2015 Modified Diagnostic Criteria

Eur Heart J 2015;36:3075-128.
# ESC 2015 Modified Criteria for the Diagnosis of IE

## Major Criteria

<table>
<thead>
<tr>
<th>Major Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Blood culture positive @ CMU positive 30-50%</strong></td>
</tr>
<tr>
<td>A. Typical microorganisms: <em>Viridans streptococci, Streptococcus bovis, HACEK group, S. aureus, or enterococci</em></td>
</tr>
<tr>
<td>B. Microorganisms persistently positive H/C</td>
</tr>
<tr>
<td>i. At least two positive H/C drawn &gt;12 hrs apart</td>
</tr>
<tr>
<td>ii. All of three or a majority of ≥four separate H/C (with first and last sample drawn ≥1 hr apart)</td>
</tr>
<tr>
<td>C. Single positive H/C for Coxiella burnetii or anti–phase-1 IgG antibody titer &gt;1:800</td>
</tr>
<tr>
<td><strong>2. Imaging positive for IE</strong></td>
</tr>
<tr>
<td>A. Echocardiogram positive: vegetation, abscess, pseudoaneurysm, fistula, valvular perforation, new partial dehiscence of prosthetic valve</td>
</tr>
<tr>
<td>B. Abnormal activity around the site of prosthetic valve implantation detected by $^{18F}$FDG PET/CT</td>
</tr>
<tr>
<td>C. Definite paravalvular lesions by cardiac CT</td>
</tr>
</tbody>
</table>
Microbiology in Culture-positive and Culture-negative IE

Suspected IE

Blood Culture

Mass spectrometry

Agar culture

Susceptibility testing

Serology

Blood PCR

Specific PCR

Susceptibility testing

Eur Heart J 2015;36:3075-128.
# Echocardiographic Features Suggesting Potential Need for Surgical Intervention

<table>
<thead>
<tr>
<th>Vegetation (prevention of emboli)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Persistent vegetation after systemic embolization</td>
<td></td>
</tr>
<tr>
<td>A. Anterior mitral leaflet &gt;10 mm</td>
<td></td>
</tr>
<tr>
<td>B. ≥1 embolic event during first 2 wk of ABO</td>
<td></td>
</tr>
<tr>
<td>C. ≥2 embolic events during or after ABO</td>
<td></td>
</tr>
<tr>
<td>2. Increase in vegetation size after 4 wk of ABO</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Valvular dysfunction (heart failure)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute aortic or mitral insufficiency with CHF</td>
<td></td>
</tr>
<tr>
<td>2. Heart failure unresponsive to medical therapy</td>
<td></td>
</tr>
<tr>
<td>3. Valve perforation or rupture</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perivalvular extension (uncontrolled infection)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Valvular dehiscence, rupture, or fistula</td>
<td></td>
</tr>
<tr>
<td>2. New heart block</td>
<td></td>
</tr>
<tr>
<td>3. Large abscess or extension of abscess</td>
<td></td>
</tr>
</tbody>
</table>
Complicated IE: refer to endocarditis team:

Clinician/Cardiologist:
- Patient History
- Fulfilment of Duke Criteria
- Overall responsibility for in-patient & out-patient management

Microbiologist:
- Identification of aetiological agent
- Guidance on antimicrobial therapy

Histopathologist:
- Microscopy of excised valve tissue/emboli/vegetation

Cardiac imaging Specialist:
- TTE
- TEE

Primary care physician:
- Patient History
- Symptoms
- Referral

Specialists:
- Infectious disease specialist
- Renal physician
- Haematologist
- Rheumatologist
- Orthopaedic surgeons

Cardiac Surgeon:
- Removal/replacement of valves and ICED
- Cardiac repair

Nuclear Physician (PET/CT):
- Echo inconclusive
- Surgical intervention (ICED)
- Monitoring embolic events & metastatic infection

CT/MRI specialists:
- Monitoring embolic events & metastatic infection in cases of secondary complications

Millar BC, Heart, 2016
Performance IE team CMU start 2557

Operative mortality — 1 yr mortality

IE Team

- Bench Mark
- Operative mortality ~ 12%
- Late mortality ~ 23%
**IE prophylaxis Guidelines**

- **1995**
  - *Moderate risk*
  - VSD, PDA, Stenosis: AS/MS/PS/TS
  - Regur.: AR/MR/PR/TR
  - *High risk*

- **2007**
  - Moderate risk
  - *High Risk*

- **2015**
  - **High Risk+**
  - *Transcatheter / bioprosthetic valve/Homograft*
Antibiotic prophylaxis should be considered for patients at highest risk for IE:

1. Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair.
2. Patients with a previous episode of IE.
3. Patients with CHD:
   a. Any type of cyanotic CHD.
   b. Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.

Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.
PO.cyanotic CHD: RV to PA: Bio prosthetic valve conduit

PO.Truncus arteriosus

PO.TOF/PA
# IE CHD associated bio prosthesis @cmu 2017

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Onset – fever to IE diagnosis</th>
<th>IV antibiotic @local hospital before refer</th>
<th>H/C @ CMU</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 yr, old Girl</td>
<td>TOF/PA PO. total correct. &amp; RV to PA conduit 2 yrs</td>
<td>3 weeks</td>
<td>Yes</td>
<td>No growth</td>
</tr>
<tr>
<td>17 yr. Female</td>
<td>TOF/PA PO. Total correct. RV to PA conduit 10 yr. &amp; mild conduit stenosis</td>
<td>3 weeks</td>
<td>Yes</td>
<td>No growth</td>
</tr>
<tr>
<td>22 yr. Male</td>
<td>TOF PO. total correction 15 yr. and Post re-op for PVR 2 yr.</td>
<td>2 months</td>
<td>Yes</td>
<td>+Enteroc occi</td>
</tr>
</tbody>
</table>
4 yr. girl, Post-op total correction TOF/PA with RV to PA conduit 2 years

- Fever 4 weeks after oral and IV antibiotics treatment @ local hospital
- CRP : 96.0 mg/L, ESR 10 mm./hr
Computed Tomography (CT) Scan
Delayed diagnosis increased mortality in IE-CHD

- Advanced technologies CT/PET in diagnosis
- **Education**: ↑ pts. awareness of this condition
- Promptly report: symptoms suggestive of IE
- Maintaining good dental & skin hygiene
- Education all medical practitioners:
  
  *High index of suspicious to early diagnosis & refer CHD centers take hemo-culture before giving antibiotic*

Montanaro C, In J Cardiol, 2017
Education*high risk patients*

These are some common symptoms, which may come and go, or may not all be present:

- Fever
- Swells or chills especially at night
- Fluid build-up on chest or legs
- Muscle or joint aches
- Swollen lymph nodes
- Persistent cough
- Headache
- Nausea or poor appetite
- Weight loss
- Rash
- Fatigue
- Breathlessness

**Consider infective endocarditis**

**Diagnosis**

It most commonly presents as a flu-like illness.

It is difficult to diagnose because the symptoms are similar to those of other conditions.

**SEEK URGENT MEDICAL ATTENTION**

Tell the doctor you are worried about infective endocarditis.

Inform him or her about any recent:

- Invasive dental, medical or surgical procedures
- Skin wounds
- Tattooing or piercing
- Intravenous lines
- Intravenous drug use

Patient information leaflet: BMJ, 2017
Summary:

• Characteristics of children & adult CHD population constantly change with novel surgical & interventional technique

• IE was most common in pts.with complex CHD ,VSD, left sided lesions(AV), post invasive (cath/surgery)<6mo. and prosthetic material was involved

• Early detection, early refer and endocarditis team are crucial to decrease morbidity & mortality

• Primary prevention of IE is vital included good dental heath & skin hygiene and antibiotic prophylaxis in high risk pts.