Guidelines ESC 2015 Endocarditis: Evolution or Revolution?

Prophylaxis

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www.eurovalvecongress.com
I disclose the following financial relationships:

Consultant for Boehringer ingelheim
Paid speaker for Edwards Lifesciences
• IE is a rare but severe disease

Incidence of infective endocarditis in the study population, by age and by microorganism

- Incidence 34 / million / yr.
- In-hospital mortality 23%

- Antibiotic prophylaxis was proposed before invasive procedures to prevent IE in patients at risk.

- Changes in recommendations for antibiotic prophylaxis over the last decade.

- Conflicting findings from recent observational data.
Antibiotic Prophylaxis in IE

- **Expert guidelines & consensus conferences**
  - Switzerland: 1984, 2000
  - ESC: 2004
  - France: 1992, 2002

- **All types of procedure in any patient at risk**
- **All types of procedure optional in intermediate-risk patients**

(Duval and Leport
*Lancet Infect Dis* 2008;8:225-32)
Rationale for restricting antibiotic prophylaxis in IE

• Concerns on bacteraemia as a surrogate endpoint of IE.

• Respective roles of:
  • high-grade bacteraemia during invasive dental care
  • low-grade bacteraemia during daily life

• Low risk of IE after dental care in practice.

• No convincing proof of the clinical efficacy of prophylaxis.

• The potential benefit of antibiotic prophylaxis should be weighed against the risks for the individual and the community.
Continuous low-grade vs. transient high-grade bacteraemia

Adapted from P. Moreillon

(Duval and Leport
Lancet Infect Dis 2008;8:225-32)
Continuous low-grade vs. transient high-grade bacteremia

- Rats inoculated with the same Strep intermedius inoculum: either by **bolus** 1ml in 1 min or by **continuous** infusion over 10 h

  ![Graph showing bacteremia levels](image)

- Continuous low-grade bacteremia induces experimental IE
- Bacteremia levels required to infect vegetation after bolus are much higher than those required after continuous infusion

**Estimated Risk of IE with or without Antibiotic Prophylaxis**

- **Estimation of the number of cases of IE occurring after at-risk dental care, with or without antibiotic prophylaxis** from 559 definite IE in the French survey on IE 1999
- **Estimation of the number of at-risk dental care procedures in patients with known predisposing heart disease** from 2,805 patients of the Paquid and Canevas cohorts


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adults</th>
<th>At-risk dental procedures per year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%) of patients or yearly procedures</td>
<td>1,287,296</td>
<td>2,746,384</td>
</tr>
<tr>
<td>95% CI</td>
<td>999,196–1,575,396</td>
<td>2,304,094–3,188,674</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Estimated Risk of IE with or without Antibiotic Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 IE 1/150,000</td>
</tr>
<tr>
<td>37 IE 1/46,000 Native 1/54,000 Prosth. 1/10,700</td>
</tr>
</tbody>
</table>

Risk-benefit analysis
Intermediate risk of IE

- Risk of IE
  - Occurrence of IE after unprotected dental procedure 1/50,000
  - In-hospital death due to IE (20% mortality) 1/250,000

- Risk of antibiotic prophylaxis
  - Death/anaphylaxis due to amoxicillin 1/75,000

No AB prophylaxis
AB prophylaxis

1 death / 250,000

1 death / 75,000
Risk-benefit analysis
High risk of IE

- Risk of IE
  - Occurrence of IE after unprotected dental procedure: 1/10,000
  - In-hospital death due to IE (20% mortality): 1/50,000

- Risk of antibiotic prophylaxis
  - Death/anaphylaxis due to amoxicillin: 1/75,000

No AB prophylaxis
1 death / 50,000

AB prophylaxis
1 death / 75,000
Antibiotic Prophylaxis in IE: NICE Guidelines

- **Expert guidelines & consensus conferences**
  - Switzerland: 1984, 2000
  - ESC: 2004
  - France: 1992, **2002**

![Diagram showing the timing of expert guidelines and consensus conferences]
Rationale for NICE Guidelines

- Downgrading of the risk of IE after dental care.
- No indication if there is no proof of efficacy.
- Antibiotic prophylaxis is cost-ineffective.

Limitations

Reliability of estimations of the risk of IE after dental care.
Antibiotic Prophylaxis in IE: 2009 ESC Guidelines

Expert guidelines & consensus conferences

- Switzerland: 1984, 2000
- ESC: 2004, 2009
- France: 1992, 2002

All types of procedure in any patient at risk

All types of procedure, optional in intermediate-risk patients

All types of dental care in any patient at high risk

Only certain dental care procedures in any patient at high risk

No AB prophylaxis
Main principle of prevention of infective endocarditis

1. The principle of antibiotic prophylaxis when performing procedures at risk of IE in patients with predisposing cardiac conditions is maintained.

2. Antibiotic prophylaxis must be limited to patients with the highest risk of IE undergoing the highest risk dental procedures.

3. Good oral hygiene and regular dental review are more important than antibiotic prophylaxis to reduce the risk of IE.

4. Aseptic measures are mandatory during venous catheter manipulation and during any invasive procedures in order to reduce the rate of health care-associated IE.
Cardiac conditions at highest risk of endocarditis

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis should only be considered for patients at highest risk of IE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Patients with a prosthetic valve, including transcatheter valve, or a prosthetic material used for cardiac valve repair.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Patients with previous IE.</td>
<td></td>
<td></td>
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<tr>
<td>3. Patients with congenital heart disease.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. any cyanotic congenital heart disease</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>b. congenital heart disease repaired with prosthetic material whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if there remains residual shunt or valvular regurgitation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic prophylaxis is not recommended in other forms of valvular or congenital heart disease.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>
Heart diseases at risk for IE

- Risk of IE (incidence)

Heart valve prosthesis

Cyanotic CHD

Previous IE

AR, MR, AS

Mitral valve prolapse with MR / thickening

Bicuspid aortic valve

- Risk from IE (mortality/morbidity)
Prophylaxis in highest-risk patients according to the type of procedure at risk

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Dental procedures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Antibiotic prophylaxis should only be considered for dental procedures</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>requiring manipulation of the gingival or periapical region of the teeth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>or perforation of the oral mucosa.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Antibiotic prophylaxis is not recommended for local anaesthetic injections</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>in non-infected tissues, treatment of superficial caries, removal of sutures,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dental X-rays, placement or adjustment of removable prosthodontic or</td>
<td></td>
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<tr>
<td>orthodontic appliances or braces, or following the shedding of deciduous teeth</td>
<td></td>
<td></td>
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<tr>
<td>or trauma to the lips and oral mucosa.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B. Respiratory tract procedures</strong></td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>• Antibiotic prophylaxis is not recommended for respiratory tract procedures,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>including bronchoscopy or laryngoscopy, transnasal or endotracheal intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C. Gastrointestinal or urogenital procedures or TOE</strong></td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>• Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cystoscopy, vaginal or caesarean delivery or TOE.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D. Skin and soft tissues procedures</strong></td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>• Antibiotic prophylaxis is not recommended for any procedure.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TOE = transoesophageal echocardiography.

www.escardio.org
# Prophylaxis for dental procedures at risk

<table>
<thead>
<tr>
<th>Situation</th>
<th>Antibiotic</th>
<th>Single-dose 30-60 minutes before procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergy to penicillin or ampicillin</td>
<td>Amoxicillin or Ampicillin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 g orally or i.v.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg orally or i.v.</td>
</tr>
<tr>
<td>Allergy to penicillin or ampicillin</td>
<td>Clindamycin</td>
<td>600 mg orally or i.v.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 mg/kg orally or i.v.</td>
</tr>
</tbody>
</table>

<sup>a</sup>Alternatively, cephalexin 2 g i.v. for adults or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.

“Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin or ampicillin due to cross-sensitivity”.
Non-specific prevention measures

<table>
<thead>
<tr>
<th>These measures should ideally be applied to the general population and particularly reinforced in high-risk patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in others.</td>
</tr>
<tr>
<td>• Disinfection of wounds.</td>
</tr>
<tr>
<td>• Eradication or decrease of chronic bacterial carriage: skin, urine.</td>
</tr>
<tr>
<td>• Curative antibiotics for any focus of bacterial infection.</td>
</tr>
<tr>
<td>• No self-medication with antibiotics.</td>
</tr>
<tr>
<td>• Strict asepsis control measures for any at-risk procedure.</td>
</tr>
<tr>
<td>• Discourage piercing and tattooing.</td>
</tr>
<tr>
<td>• Limit the use of infusion catheters and invasive procedures when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3–4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.</td>
</tr>
</tbody>
</table>
Antibiotic prophylaxis for the prevention of local and systemic infections before cardiac or vascular interventions

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative screening of nasal carriage of <em>Staphylococcus aureus</em> is recommended before elective cardiac surgery in order to treat carriers.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Peri-operative prophylaxis is recommended before pacemaker or implantable cardioverter defibrillator implantation.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Elimination of potential sources of dental sepsis is recommended &gt;2 weeks before implantation of a prosthetic valve or other intracardiac or intravascular foreign material, except in urgent procedures.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Peri-operative antibiotic prophylaxis should be considered in patients undergoing surgical or transcatheater implantation of a prosthetic valve, intravascular prosthetic, or other foreign material.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Systematic local treatment without screening for <em>Staphylococcus aureus</em> is not recommended.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>
Guidelines changes and incidence of IE

3 prospective nationwide surveys on IE with individual case validation

• 323 IE cases in 1991
• 331 IE cases in 1999
• 339 IE cases in 2008

(Duval et al. J Am Coll Cardiol 2012;59:1968-76 )
Guidelines changes and incidence of IE

No increase in the incidence of IE due to oral streptococci between 1999 and 2008

(Duval et al. J Am Coll Cardiol 2012;59:1968-76)
No increase in IE due to viridans streptococci in Olmsted County

- between 1999 and 2010 (DeSimone et al. Circulation 2012;126:60-4)
Guidelines changes and incidence of IE US

No change in hospital discharges with and ICD code of IE due to viridans streptococci in the Nationwide Inpatient Sample database

1999-2010

1999-2011

Guidelines changes and incidence of IE

Incidence of IE in England

Analysis of ICD discharge codes with a primary diagnosis of IE in 19,804 patients (UK, 2000-2013): increased incidence after 2008

(Dayer et al. Lancet 2015;385:1219-28)
Guidelines changes and incidence of IE

Incidence of IE in England

High and intermediate-risk patients

(Dayer et al. Lancet 2015;385:1219-28)
Incidence of IE in England
Limitations of the analysis

• Concerns about the true incidence of IE:
  • Coding quality (diagnosis, high vs. lower risk)
  • No data on causative microorganisms

• Confounding factors:
  • Number of hospital admissions
  • Number of patients with intracardiac devices
  • Number of invasive procedures
  • Population ageing

• Temporal relationship.

(\textit{Dayer et al.} \textit{Lancet} 2015;385:1219-28)
(\textit{Duval and Hoen} \textit{Lancet} 2015;385:1164-5)
Incidence of IE in England
Temporal Relationship

Statistical testing for slope change was significant (p<0.0001) at all time points between April 2003 and May 2010

(Iung, Tubiana, Alla, Lavielle Lancet 2015;386:529 (correspondence))
Guidelines changes and incidence of IE
Temporal trends in the US

Nationwide Inpatient Sample (NIS) database
- 457,052 hospitalisations for IE between 2000 and 2011
- Analysis of trends in incidence according to microorganisms

(Pant et al. J Am Coll Cardiol 2015;65:2070-6)
Guidelines changes and incidence of IE
Temporal trends in the US: contrasting findings

NIS database 2000-2011
Trends in incidence (per 100,000)

![Chart showing trends in incidence of IE](chart.png)

Medicare 1999-2010
262,658 hospitalisations for IE ≥ 65 yrs

![Chart showing Medicare data](chart2.png)

(Pant et al.
*J Am Coll Cardiol* 2015;65:2070-6)

(NIS database 2000-2011)

(DeSimone et al.
• There is no revolution in ESC Guidelines, which continue to recommend antibiotic prophylaxis in high-risk patients undergoing the highest risk dental procedures.

• Oral and cutaneous hygiene measures are likely to be the most effective approach for preventing IE and should be applied in intermediate- and high-risk patients.

• Non-specific infection control measures are mandatory in routine practice to reduce healthcare-associated IE.

• Specific prospective surveys are needed to better ascertain the impact of prevention measures.
Antibiotic Prophylaxis in IE

- **Expert guidelines & consensus conferences**
  - Switzerland: 1984, 2000
  - ESC: 2004
  - France: 1992, **2002**

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**FR**

All types of procedure in any patient at risk

**UK**

All types of procedure, optional in intermediate-risk patients

**US**

Only certain dental care procedures in any patient at high risk
Bacteraemia of Oral Origin

290 patients needing tooth extraction randomized:

<table>
<thead>
<tr>
<th></th>
<th>Toothbrushing</th>
<th>Extraction + placebo</th>
<th>Extraction + amoxicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº pts</td>
<td>98</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Bacteraemia (%)</td>
<td>32%</td>
<td>80%</td>
<td>56%</td>
</tr>
<tr>
<td>Stepto. Viridans (%)</td>
<td>48%</td>
<td>70%</td>
<td>49%</td>
</tr>
</tbody>
</table>