Prophylaxis of Bacterial Endocarditis 
Revisited

Paris 7 - Paris 5 Universities, France.
Prophylaxis of IE : 1950-2008

• IE persistent MORBIDITY → 50 % pts surgery required

• IE persistent MORTALITY : ≈ 20% pts

• Recommendations regularly updated

2007 AHA revision : Prophylaxis only for dental procedure, in pts with the highest risk from IE (incidence and outcome)
<table>
<thead>
<tr>
<th>MINIMAL</th>
<th>versus</th>
<th>MAXIMAL REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>DENTAL</td>
<td></td>
<td>GI - UROLOGIC</td>
</tr>
<tr>
<td>(upper respir.tract)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SINGLE PROC.</td>
<td></td>
<td>MULTIPLE PROC.</td>
</tr>
<tr>
<td>CARDIAC RISK</td>
<td></td>
<td>HIGH CARDIAC RISK</td>
</tr>
<tr>
<td>OUT PATIENT</td>
<td></td>
<td>IN PATIENT-GENERAL ANESTHESIA</td>
</tr>
</tbody>
</table>

Prophylaxis IE – CMI 1998
Swiss recommendations – 2000
P. Moreillon

1. Switzerland is not very original (at least for IE prophylaxis)
2. Clinical and animal studies indicate that IE is related to spontaneous bacteremia
3. Only selected high-risk patients are likely to benefit from prophylaxis
4. Single dose oral amoxicillin (2-3 g) is likely to be appropriate for prophylaxis against peni. R streptococci
5. Single dose oral amoxicillin is very effective against (amoxi-S) Van-S and Van-R E. faecalis
6. Single-dose oral amoxicillin should be proposed for high-risk patients undergoing UTI or lower GI tract procedures
Limited role of antibiotic prophylaxis against everyday versus procedure-related bacteriemia

Duval X & Leport C. Lancet Infectious Diseases 2008
France : Recommandations 2002

• To IMPROVE general *oral hygiene* and *education*

• To MAINTAIN the PRINCIPLE of antibiotic prophylaxis after *at risk procedures* in patients with *at risk cardiac conditions*

**BUT**

• REDUCE the INDICATIONS to situations where the *individual benefit* versus *individual and collective risk ratio* is the highest

Prophylaxie EI Reco -SPILF 2002
Changing Profile of Infective Endocarditis -1999
Results of a One-Year Survey in France

French Study Group on Infective Endocarditis

• **390** cases; 277 M / 113 F - age 59 yrs, [16-95]
30 cases / year / million inhabitants (age- and sex- standardized incidence)
### IE one-year French surveys: 1991 vs. 1999

<table>
<thead>
<tr>
<th>Incidence (CI 95%)</th>
<th>1991</th>
<th>1999</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall standardized</td>
<td>30.9 [27.9-34.1]</td>
<td>26.5 [23.9-29.6]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Standardized by UHD*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- prosthetic valve</td>
<td>6.9 [5.5-8.6]</td>
<td>4.7 [3.6-6.2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Standardized by pathogen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- oral streptococci</td>
<td>7.8 [6.4-9.5]</td>
<td>5.1 [4.0-6.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- group D streptococci</td>
<td>5.3 [4.1-6.9]</td>
<td>6.2 [5.0-7.9]</td>
<td>0.67</td>
</tr>
</tbody>
</table>

* UHD: underlying heart disease

Hoen et al. JAMA 2002
Estimated Risk of Endocarditis in Adults with Predisposing Cardiac Conditions Undergoing Dental Procedures With or Without Antibiotic Prophylaxis

Xavier Duval,1 F. Alla,2 B. Hoen,3 F. Danielou,2 S. Larrieu,4 F. Delahaye,5 C. Leport,1 and S. Briançon2

Figure 1. Age-specific prevalence of a predisposing cardiac condition among French adults (age, 25–84 years).

⇒3.3% French population
⇒ Predisposing cardiac condition

2805 pts Paquid and Canevas cohorts
Table 1. Estimated number of known predisposing cardiac conditions (PCCs) among French adults (age, 25–84 years) and of annual at-risk dental procedures among subjects with PCCs.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adults</th>
<th>Total</th>
<th>Protected procedures&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Unprotected procedures&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></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>
<td>1,042,189 (38)</td>
<td>1,704,195 (62)</td>
</tr>
<tr>
<td>95% CI</td>
<td>999,196–1,575,396</td>
<td>2,304,094–3,188,674</td>
<td>748,978–1,335,399</td>
<td>1,373,064–2,035,327</td>
</tr>
</tbody>
</table>

<sup>a</sup> Protected procedures were defined as invasive procedures in which antibiotic prophylaxis was administered.

<sup>b</sup> Unprotected procedures were defined as invasive procedure in which antibiotic prophylaxis was not administered.
Risk of IE in at-risk cardiac pts after at-risk dental procedures

≈ 30 - 40 IE /year in France (2.4%)

POPULATION-based STUDIES (France 2003)

900 000 at-risk dental procedures performed per year, on at-risk pts, without prophylaxis

Risk of IE after at-risk procedures

1 /50 000 in pts with native valvulopathy

1 /10 000 in pts with prosthetic valve
Estimated Risk of Endocarditis in Adults with Predisposing Cardiac Conditions Undergoing Dental Procedures With or Without Antibiotic Prophylaxis

Xavier Duval, F. Alla, B. Hoen, F. Danielou, S. Larrieu, F. Delahaye, C. Leport, and S. Briançon

Clinical Infectious Diseases 2006;42:e102–7

Results. After standardization, extrapolation of results to the age-equivalent general population (39 millions subjects) indicated the following: first, 3.3% (95% confidence interval [CI], 2.6%–4%) of the subjects had PCC, 2.7 million (95% CI, 2.3–3.2 million) of whom had undergone at least 1 at-risk dental procedures within the survey year, and the procedures were unprotected in 62% of cases; second, 37 (95% CI, 18–68; 2.7%) of the 1370 annual IE cases in France were possibly related to unprotected procedures. Thus, the risks of developing IE were estimated to be 1 in 46,000 for unprotected procedures (1 in 10,700 and 1 in 54,300 for subjects with prosthetic and native valve PCC, respectively) and 1 in 150,000 for protected procedures.

At most 1 /10 700 at-risk procedures (in PV pts) could be responsible for ONE IE

Evolution of French recommendations 2002

**When**: one hour before an **at risk** procedure

**For Whom**: pts with **at risk cardiac conditions**… and other **non cardiac risk factors**

<table>
<thead>
<tr>
<th>Procedures</th>
<th>1992</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-All dental</td>
<td>-<strong>Invasive</strong> oral or dental</td>
</tr>
<tr>
<td></td>
<td>-Almost all extradental</td>
<td>- Extradental procedures: list</td>
</tr>
<tr>
<td>Patients</td>
<td>-Prosthetic cardiac valves</td>
<td>1/ <strong>CARDIAC CONDITIONS</strong></td>
</tr>
<tr>
<td></td>
<td>-Cyanotic congenital cardiopathies</td>
<td>(*) high risk group</td>
</tr>
<tr>
<td></td>
<td>(except IAC)</td>
<td>(**) lower risk group</td>
</tr>
<tr>
<td></td>
<td>-History of IE</td>
<td>2/ <strong>HOST FACTORS</strong></td>
</tr>
<tr>
<td></td>
<td>-Valvulopathies (AI, MI, AS)</td>
<td>-Visceral deficiencies</td>
</tr>
<tr>
<td></td>
<td>-Mitral prolapsus with regurgitation</td>
<td>-Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>-Bicuspid aortic valve</td>
<td>-Age &gt; 65 years</td>
</tr>
<tr>
<td></td>
<td>-Obstructive cardiomyopathy</td>
<td>-Immunodepression</td>
</tr>
</tbody>
</table>

(*help for choosing if prophylaxis optional)
ANTIBIO-PROPHYLAXIE EI

France 2002

Groupe A : Cardiopathie à HAUT RISQUE
Gestes bucco-dentaires à risque RECOMMANDÉE

Groupe B : Cardiop. à RISQUE MOINS élevé

Gestes bucco-dentaires non à risque : NON recommandée

Gestes bucco-dentaires non à risque : NON recommandée

Prophylaxie EI Reco -SPILF 2002
Arguments for the OPTIONAL prescription

- **Age > 65 years**
- **Associated conditions**
  - Cardiac, renal, respiratory, hepatic insufficiency
  - Diabetes mellitus
  - Acquired, constitutional or therapeutic ID
- **Oral or dental condition**
  - Especially inadequate oral or dental hygiene
- **Procedure**
  - Heavy bleeding (intensity duration)
  - Technically difficult procedure (prolonged …)
  - AB may be initiated within the hour following the procedure
- **Patient’s informed opinion**

Prophylaxie El Reco -SPILF 2002
Rational for IE prophylaxis: 1950-2002

- Invasive procedure at risk of bacteriemia
- Cardiopathy at risk of IE
- BACTEREMIA
- IE
Rational for IE prophylaxis 2002

Cardiopathy at risk of IE

Invasive procedure at risk of bacteriemia

BACTEREMIA

(Severe) IE

Other non cardiac host factor at risk of IE
AHA : IE prophylaxis Workshop
May 2004

• Poor compliance with recommendations
• Poor understanding of reco.
• Portal of entry usually unknown
• Known underlying conditions associated with IE
• Some dental procedures cause bacteremia
• Low number of preventable cases
• High morbidity and mortality of IE

F. K. Gould¹*, T. S. J. Elliott², J. Foweraker³, M. Fulford⁴, J. D. Perry¹, G. J. Roberts⁵, J. A. T. Sandoe⁶ and R. W. Watkin⁷

¹Department of Microbiology, Freeman Hospital, Newcastle upon Tyne, UK; ²Department of Microbiology, Queen Elizabeth Hospital, Birmingham, UK; ³Department of Microbiology, Papworth Hospital, Cambridge, UK; ⁴Postgraduate Dental Department, University of Bristol, Bristol, UK; ⁵King’s College Dental Institute, London, UK; ⁶Department of Medical Microbiology, Leeds Teaching Hospitals NHS Trust, Leeds, UK; ⁷Department of Cardiology, Queen Elizabeth Hospital, Birmingham, UK

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**High-risk cardiac factors requiring antibiotic prophylaxis**

- Previous infective endocarditis
- Cardiac valve replacement surgery, i.e. mechanical or biological prosthetic valves
- Surgically constructed systemic or pulmonary shunt or conduit

**Dental procedures requiring antibiotic prophylaxis**

- All dental procedures involving dento-gingival manipulation
<table>
<thead>
<tr>
<th>Procedures</th>
<th>Anecdotally associated with endocarditis?</th>
<th>% Bacteraemia</th>
<th>Requires IE prophylaxis?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophageal varices–sclerotherapy</td>
<td>yes$^{21,22}$</td>
<td>10–50$^{23,24}$</td>
<td>yes</td>
</tr>
<tr>
<td>Oesophageal stricture dilatation</td>
<td>yes$^{25}$</td>
<td>21–54$^{23,26–29}$</td>
<td>yes</td>
</tr>
<tr>
<td>Oesophageal varices–Bandining</td>
<td>no</td>
<td>6$^{23}$</td>
<td>no*</td>
</tr>
<tr>
<td>Oesophageal laser therapy</td>
<td>no</td>
<td>35$^{23}$</td>
<td>yes</td>
</tr>
<tr>
<td>Endoscopy–upper</td>
<td>yes$^{30–33}$</td>
<td>4$^{23}$</td>
<td>no*</td>
</tr>
<tr>
<td>Sigmoidoscopy/colonoscopy</td>
<td>yes$^{34–37}$</td>
<td>0–9$^{23,26,38}$</td>
<td>no*</td>
</tr>
<tr>
<td>ERCP</td>
<td>no$^{39}$</td>
<td>6–11$^{23}$</td>
<td>yes</td>
</tr>
<tr>
<td>Percutaneous endoscopic gastrostomy</td>
<td>no</td>
<td>0$^{40}$</td>
<td>no*</td>
</tr>
<tr>
<td>Echocardiography–transoesophageal</td>
<td>yes$^{41}$</td>
<td>1–13$^{42,43}$</td>
<td>no*</td>
</tr>
</tbody>
</table>
Recent Evolution of guidelines

Time to Scale Back (Durack, 1992)

Duval X & Leport C. Lancet Infectious Diseases 2008
Comparison of recent guidelines that have reduced indications for prophylaxis of IE

Dental procedures

<table>
<thead>
<tr>
<th>Guideline</th>
<th>High cardiac risk*</th>
<th>Moderate cardiac risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>French 2002</td>
<td>Recommended</td>
<td>Optional</td>
</tr>
<tr>
<td>BSAC 2006</td>
<td>Recommended</td>
<td>Abandoned</td>
</tr>
<tr>
<td>AHA 2007</td>
<td>Recommended</td>
<td>Abandoned</td>
</tr>
</tbody>
</table>

List of dental procedures

Recommended

Optional

Abandoned
Comparison of recent guidelines that have reduced indications for prophylaxis of IE

Extra dental procedures

<table>
<thead>
<tr>
<th>Indications for prophylaxis</th>
<th>High cardiac risk*</th>
<th>Moderate cardiac risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>French 2002</strong></td>
<td>Recommended</td>
<td>Optional</td>
</tr>
<tr>
<td>List of procedures</td>
<td>or optional **</td>
<td>or not recommended **</td>
</tr>
<tr>
<td><strong>BSAC 2006</strong></td>
<td>Recommended</td>
<td>Recommended</td>
</tr>
<tr>
<td>List of procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AHA 2007</strong></td>
<td>Abandoned*</td>
<td>Abandoned</td>
</tr>
</tbody>
</table>

* Except respiratory and skin procedures
A 44-year old woman

- Asymptomatic Barlow’s disease (mitral regurgitation)
- Diabetes mellitus
  - Retinopathy, nephropathy; Biguanids, insulin
- Inadequate dental hygiene, previous dental extractions with antibioprophylaxis

→ Needs tooth’s extraction

⇒ Antibioprophylaxis ?

US ? UK ? France ?
IE antiobioprophylaxis
COST- EFFECTIVENESS approach
ADVERSE EVENTS (AHA 2007)

• **Non severe** (rash, diarrhea, gastro-intestinal upset): common but usually not severe and self limited (single dose) / documented *Clostridium difficile* colitis after a single dose of prophylactic clindamycin: 1 case report

• **Fatal anaphylactic reactions**:  
  - Single dose of penicillin: 15 to 25 / 10^6 pts, 1-3 deaths/ 10^6  
  - Single dose of cephalosporin: 1 / 10^6 pts  
  - Single dose of macrolid or clindamycin: « extremely rare ». Clarithromycin: cost-effective?
Resistance of viridans streptococci
IE french surveys

- **Oral streptococci**
  - R erythromycin
    - 2%, 1991 → 21%, 1999
  - R penicillin
    - 5%, 1991 → 11%, 1999

- **Gastro-intestinal streptococci**
  - 80% R erythromycin; 35% R pristinamycin

Bouvet et al. MMI 2002
STRATEGY for IE prophylaxis – Summary 2007

General consensus on principle for prophylaxis:

FOCUS on HIGHEST RISK situations

Consensus:
high cardiac risk – invasive dental procedures

Debate in other situations:
moderate cardiac risk; extra-dental procedures;
other predisposing host factors

Monitoring IE profile
Cost-effectiveness modelizations
Practitioners and patients feed back
Better identification of at risk cardiac pts:

IE prophylaxis card,
echocardiography report specifying the at-risk cardiac group

General hygiene measures

including oral, dental, skin… (education)

reduce the risk of bacteremia (spontaneous or procedure-related)

Discourage some procedures: limit invasive care

Propose systematic twice yearly dental appointment
PRÉVENTION DE L’ENDOCARDITE INFECTIEUSE
Recommandations 2002

Nom, Prénom : ________________________________

CARDIOPATHIE À RIQUE MODÈLE D’ENDOCARDITE INFECTIEUSE (EI) (GROUPE B) :
☐ LA, LI, RA, bicuspidie A
☐ PVM avec IM / étalonnage
☐ Cardioïdopathie congenitale non cyanogène
☐ CMH obstructive

Remis par le Dr. : ________________________________
à : ____________________________________________
 tel : __________________________________________


Cette carte doit être systématiquement montrée à votre médecin / votre dentiste
En cas de soin dentaire à risque, traitement antibiotique préventif facultatif, à discuter avec eux.

Si décision de traitement antibiotique préventif
Prendre une seule prise, par la bouche, dans l’heure précédente
Si pas d’allergie connue aux β-lactamines : Amoxicilline : 3 g
(spois < 60 kg ; 2 g - enfant : 35 mg/kg)
Si allergie connue aux β-lactamines : Pristinamycine : 1 g (enfant 25 mg/kg),
oc Gidamycine : 600 mg (enfant : 25 mg/kg)

Dans tous les cas, en cas de fièvre (en particulier dans les semaines suivant un soin dentaire) :
- prévenir votre médecin
- lui présenter cette carte
- ne pas prendre d’antibiotiques sans son avis

Prévention de l’endocardite infectieuse
Recommandations 2002

Nom, Prénom : ________________________________

CARDIOPATHIE À RIQUE ÉLEVÉ D’ENDOCARDITE INFECTIEUSE (EI) (GROUPE A) :
☐ Prothèse valvulaire
☐ Antécédent d’EI
☐ Cardioïdopathie congenitale cyanogène

Remis par le Dr. : ________________________________
à : ____________________________________________
 tel : __________________________________________


Cette carte doit être systématiquement montrée à votre médecin / votre dentiste
En cas de soin dentaire à risque, traitement antibiotique préventif impératif

Prendre une seule prise, par la bouche, dans l’heure précédente
Si pas d’allergie connue aux β-lactamines : Amoxicilline : 3 g
(spois < 60 kg ; 2 g - enfant : 75 mg/kg)
Si allergie connue aux β-lactamines : Pristinamycine : 1 g (enfant : 25 mg/kg),
oc Gidamycine : 600 mg (enfant : 25 mg/kg)

Dans tous les cas, en cas de fièvre (en particulier dans les semaines suivant un soin dentaire) :
- prévenir votre médecin
- lui présenter cette carte
- ne pas prendre d’antibiotiques sans son avis
PREVENTION OF BACTERIAL ENDOCARDITIS
Wallet Card

This wallet card is to be given to patients (or parents) by their physician. Healthcare professionals: Please see back of card for reference to the complete statement.

Name: __________________________
needs protection from BACTERIAL ENDOCARDITIS because of an existing heart condition.

Diagnosis: ________________________
Prescribed by: ____________________
Date: ____________________________

Healthcare Professionals – Please refer to these recommendations for more complete information as to which patients and which procedures need prophylaxis.

The Council on Scientific Affairs of the American Dental Association has approved this statement as it relates to dentistry.

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American Heart Association | American Stroke Association

Learn and Live
National Center
7272 Greenville Avenue
Dallas, Texas 75231-4596
americanheart.org
In any case,
Visit your GP in case of FEVER after a procedure,
with or without AB prophylaxis
BLOOD CULTURES before starting any ANTIBIOTIC
Evolution in the strategies for IE prophylaxis: where do we go? (ECCMID, April 2008)

Valvular diseases
At risk procedures

Antibiotics for
Streptococcus sp. IE

2002 – 2007

• Other risk factors? (diabetes…)
• Other bacteria? (staphylococci)

Other prophylactic means?
Prophylaxis against infective endocarditis

Implementing NICE guidance

2008

NICE clinical guideline 64
IE Prophylaxis - 2008

Expert guidelines & consensus

- Suisse: 1984, 2000
- ESC: 2004
- France: 1992, 2002

All types procedures all at risk pts

All types proc. Optionnal: moderate risk pts

All types proc. high risk pts

Only dental proc. high risk pts

NO PROPHYLAXIS

NICE : How this guidance changes practice?

Antibiotic prophylaxis has not been proven to be effective and there is no clear association between episodes of IE and interventional procedures.

We recommend that antibiotic prophylaxis is no longer offered routinely for the interventional procedures listed in this guideline.
Decisions for your patient
A case-based approach: 76-year-old man

• Calcified aortic stenosis
• Diabetes mellitus; Sulfamides
• Facial cellulitis 6 months ago; successful outcome with oral pristinamycin
• Basal cell carcinoma of the nasal wing

→ Needs a surgical resection

⇒ Antibioprophylaxis?

US? UK? France?
Prophylaxis of IE - 2008
the JUST MESSAGE?

SIMPLE
CONSENSUAL
for
EFFICIENCY

CLEAR
PROGRESSIVE
for
ACCEPTABILITY

IMPACT of CHANGES to be EVALUATED
EI 2008

Régions concernées :

Signalements : 1er décembre 2007 - 30 mars 2009

Protocole et renseignements pratiques sur www.endocardite.fr