CONTROVERSIAL ISSUES IN ANTIBIOTIC PROPHYLAXIS

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I. ANTIMICROBIAL PROPHYLAXIS: PRINCIPLES & PRACTICE

A. RISK FACTORS FOR POST-OPERATIVE INFECTIONS:
   1. Proportional to the degree of bacterial contamination during surgery – dirty vs. clean surgeries
   2. Virulence of the infective organism –
   3. Host factors – immunocompromised?

B. TIMING OF SURGICAL PROPHYLAXIS

IV REGIMENS: Recommend a single dose given just prior to surgery
Give follow-up dose when: drug has short t1/2, for prolonged surgeries, ↑ blood loss
PO REGIMENS: Peak plasma concentration of antibiotic should occur when surgery begins

C. SOURCES OF BACTERIAL CONTAMINATION

EXOGENOUS: Due to poor aseptic technique, high O.R. traffic, colonized surgeons

ENDOGENOUS: Flora from patient’s skin, GI, GU, or respiratory tract, dirty wounds (pus)
**most common cause of post-op infections**

D. ANTIMICROBIAL AGENTS

MECHANISM OF ACTION ??: ↓ Level of bacteremia and bacterial growth after adherence
Prevents adherence of bacteria to defect or prosthetic device

- Direct prophylaxis against the most likely infective organisms:
  - Usually normal skin flora
  - Target specific organisms

- For dental procedures: Coverage of Viridans streptococci
  - Amoxicillin preferred by A.H.A. (American Heart Association) over penicillin VK citing better absorption & more prolonged serum levels

F. HEALTH QUESTIONNAIRE IDENTIFIERS

Possible Risk from Oral Bacteremia:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>?</th>
<th>a. Artificial heart valve replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>b. History of bacterial endocarditis</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>c. Congenital heart disease (type ____________________________)</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>d. Acquired valvular heart disease or heart murmur</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>e. History of post-streptococcal glomerulonephritis</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>f. Organ transplantation</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>g. Prosthetic joint replacement (when__________________________)</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>h. Artificial implant or graft of any kind other than above (list ____________)</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>i. Systemic lupus erythematosus (SLE)</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>j. Immunosuppression? Asplenic?</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>?</td>
<td>k. Physician requests antibiotic coverage for reasons other than above (reason________)</td>
</tr>
</tbody>
</table>
II. ANTIBIOTIC PROPHYLAXIS FOR PATIENTS WITH TOTAL JOINT REPLACEMENTS

<table>
<thead>
<tr>
<th>Joint</th>
<th>Candidates</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Replacement</td>
<td>Usually over 55 years old</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td></td>
<td>Reasonable weight</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td></td>
<td>Significant joint stiffness, instability or deformity</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td></td>
<td>Daily pain limits work, recreation &amp; daily activity</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td></td>
<td>80-90% successful for 10 years</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td></td>
<td>Loosening is biggest problem</td>
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</tr>
<tr>
<td></td>
<td>By 10 years up to 20% will require revision</td>
<td>By 10 years up to 20% will require revision</td>
</tr>
<tr>
<td></td>
<td>80-90% successful for 10 years</td>
<td>80-90% successful for 10 years</td>
</tr>
<tr>
<td>Hip Replacement</td>
<td>Usually over 55 years of age</td>
<td>Pain relief in 90-95% of patients.</td>
</tr>
<tr>
<td></td>
<td>Pain limits work, recreation and daily activities</td>
<td>90% are successful for up to 10 years</td>
</tr>
<tr>
<td></td>
<td>Pain not relieved by meds, use of cane or physical restrictions</td>
<td>90% are successful for up to 10 years</td>
</tr>
<tr>
<td></td>
<td>Significant stiffness of joint</td>
<td>90% are successful for up to 10 years</td>
</tr>
<tr>
<td></td>
<td>Loosening is biggest problem</td>
<td>90% are successful for up to 10 years</td>
</tr>
<tr>
<td></td>
<td>By 10 years up to 20% will require revision</td>
<td>By 10 years up to 20% will require revision</td>
</tr>
<tr>
<td></td>
<td>Removal results in leg shortened 1-3 inches</td>
<td>Removal results in leg shortened 1-3 inches</td>
</tr>
</tbody>
</table>

A. STATISTICS
- Overall risk is 5 in 10,000 (0.05%) for development of late infection in joint prosthesis due to hematogenous spread of bacteria
- Early joint prosthetic infections (< 1 year) are most often caused by Staphylococcal organisms which were probably buried at the time of surgery
- Historically, over 90% of orthopedic surgeons want all patients with large prosthetic joints to receive antimicrobial prior to invasive dental procedures

B. GUIDELINES FOR ANTIMICROBIAL PROPHYLAXIS
- Recommends lifelong antimicrobial prophylaxis only for patients at increased risk of hematogenous total joint infection

C. PATIENTS AT INCREASED RISK OF LATE INFECTION
   IMMUNOCOMPROMISED – IMMUNOSUPRESSED
   - Disease: insulin-dependent diabetes (Type 1), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), other collagen vascular disorders
   - Drugs: glucocorticoids (>5mg prednisone/day or its equivalent), immunomodulators or antineoplastics
   - Treatment: radiation therapy

   OTHER PATIENTS AT INCREASED RISK
   - Patients with chronic infections: e.g. urinary or respiratory tract infections, chronic periodontitis
   - Malnourished
   - Hemophiliacs

ORTHOPEDIC RISK
- Patients with history of post placement complications – previous infection in joint, recent dislocation, recent capillary hemorrhage near prosthesis, re-operated joints, etc.
- Joint in place less than 2 years

D. SCREENING QUESTIONS FOR PATIENTS
   YES NO ? DO YOU HAVE ANY ARTIFICIAL JOINTS? (if yes, answer questions below)

1. How long have you had the prosthetic joint? (date of surgery ________________)
   (note: if 2 yrs. or less = premedicate, if greater than 2 years = no need for premedication unless "yes" to questions 2 and/or 3)

2. YES…NO…? Have you had any problems with the joint since it was replaced?

3. YES…NO…? Is your immune system suppressed by disease, medications or treatments?
E. PRESCRIPTIONS

Rx: Amoxicillin 500 mg capsules or Cephalexin 500 mg capsules
Disp: # 4
Sig: Take 4 capsules p.o. 1 hr. prior to dental appointment

- Amox is for patients NOT allergic to penicillin
- Cephalexin is a 1st generation cephalosporin with good strep. coverage and active against staphylococcal organisms

Rx: Clindamycin 150 mg capsules
Disp: # 4
Sig: Take 4 capsules p.o. 1 hr. prior to dental appointment

- For patients with penicillin allergy
- 150 mg capsules available generically

Rx: Cefazolin 1 gram or Ampicillin 1 gram
Administer: I.M. or I.V.
Sig: 1 hr. prior to procedure

- For patients unable to take oral medications AND NOT allergic to penicillin

Rx: Clindamycin 600 mg
Administer: I.V.
Sig: 1 hr. prior to procedure

- For patients unable to take oral medications AND penicillin allergic

F. DENTAL MANAGEMENT OF PATIENTS WITH TOTAL JOINT REPLACEMENTS

♦ Updated health history with each visit
♦ Reinforce home-care procedures and use chemotherapeutic measures to reduce bleeding
♦ Immediate and aggressive treatment of acute and newly recognized chronic infections
♦ Avoidance of regular daily bacteremia

III. PROPHYLAXIS FOR OTHER IMPLANTS AND DEVICES

A. NO PROPHYLAXIS NECESSARY:
   • Breast implants  
   • Intraocular lenses  
   • Dental implants  
   • Cochlear implants  
   • Cardiac Pacemakers  
   • A.I.C.D. (Artificially Implanted Cardiac Defibrillators)  
   • Orthopedic Plates, Pins, Screws, and Wires  
   • Hernia Repair Mesh, Vascular Screens

B. PENILE PROSTHESES

BACKGROUND: 30% of men over 40 yrs. have erectile problems due to:
- arteriosclerotic disease, endocrine problems
- medications (25%) e.g. antihypertensives, diuretics alcohol, tobacco
MANAGEMENT: Defer elective dental treatment until 3 months post-op
ANTIBIOTIC PROPHYLAXIS?? Not unless immunosuppressant co-morbidities are present

C. VASCULAR GRAFTS

BACKGROUND: 1 – 5 % incidence of infections
- varies with the site of graft placements
- organisms often originate from bowel or skin
MANAGEMENT: Antibiotic prophylaxis is indicated for grafts < 6 months old
- pseudointima (connective tissue & fibrin) forms on the inner surface of the graft
- physician consult to determine size, type and location of graft
D. INTRAVASCULAR ACCESS DEVICES

BACKGROUND:

- Central (tunnel) I.V. lines
  - Broviac or Hickman lines - for chemotherapy
  - Uldall catheters - for hemodialysis, plasmaphoresis
- Infections primarily due to skin contamination
- Increased risk with newer grafts

MANAGEMENT: No invasive procedures within 6 weeks of graft placement or revision

- Hemodialysis patients (JADA. Dental Considerations for the Patient with Renal Disease. 127:211-19, 1996)
  - at ↑ risk of S.B.E., Viridans group Strep is responsible for 17% of I.E. cases in renal failure patients
  - ? mechanism – long term cardiac valve problems with hemodialysis patients
  - consult hemodialysis clinic for definitive guidelines-most use AHA recommendations
  - home maintenance of oral hygiene is crucial to avoid shunt infection

E. CEREBROSPINAL FLUID SHUNTS

- Ventriculoatrial shunts (ventriculooatriostomy)– at risk, premedicate
  - old procedure where tube from brain ventricle empties into heart atrium
- Lumboperitoneal shunts – negligible risk, no prophylaxis needed
- Ventriculoperitoneal shunts – negligible risk, no prophylaxis needed
  - Most common procedure performed today
  - Used to treat hydrocephalus, post-stroke injury
  - Used to treat normal pressure hydrocephalus (NPH) which is a reversible cause of dementia

IV. PROPHYLAXIS FOR THE PREVENTION OF SUBACUTE BACTERIAL ENDOCARDITIS (SBE) – NEW GUIDELINES IN CIRCULATION, APRIL 19, 2007

2007 AHA Guidelines for the Prevention of Infective Endocarditis

A. Regimens for a Dental Procedure

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen – Single dose 30-60 minutes before procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin</td>
<td>2 g</td>
</tr>
<tr>
<td>Oral</td>
<td></td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>Oral</td>
<td>Allergic to penicillins or ampicillin</td>
<td>2 g IM or IV*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg IM or IV</td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>Ampicillin</td>
<td>2 g IM or IV</td>
</tr>
<tr>
<td></td>
<td>OR Cefazolin or ceftriaxone</td>
<td>1 g IM or IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg IM or IV</td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin and unable to take oral medication</td>
<td>Cefazolin or ceftriaxone†</td>
<td>1 g IM or IV</td>
</tr>
<tr>
<td></td>
<td>OR Clindamycin</td>
<td>600 mg IM or IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 mg/kg IM or IV</td>
</tr>
</tbody>
</table>

*IM – intramuscular; IV – intravenous.
**or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.
†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria.
with penicillins or ampicillin

B. Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from Endocarditis For Which Prophylaxis with Dental Procedures Is Recommended (Table 3.)

<table>
<thead>
<tr>
<th>Prophylaxis with Dental Procedures Is Recommended for Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic cardiac valve</td>
</tr>
<tr>
<td>Previous infective endocarditis</td>
</tr>
</tbody>
</table>

**Congenital heart disease (CHD)**
- Unrepaired cyanotic CHD, including palliative shunts and conduits
- Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure**
- Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

Cardiac transplantation recipients who develop cardiac valvulopathy

* Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease (CHD).

**Prophylaxis is recommended because endothelialization of prosthetic material occurs within 6 months after the procedure.

C. Dental Procedures for which Endocarditis Prophylaxis is Recommended for Patients

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa *

*The following procedures and events do not need prophylaxis: routine anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthetic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth and bleeding from trauma to the lips or oral mucosa.

D. Primary Reasons for Revision of the IE Prophylaxis Guidelines

1) IE is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental, GI tract or GU tract procedure.
2) Prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo a dental, GI tract, or GU tract procedure.
3) The risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotics.
4) Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.

E. Summary of Major Changes In The 2007 Updated Document

1) We concluded that bacteremia resulting from daily activities is much more likely to cause IE than bacteremia associated with a dental procedure.
2) We concluded that only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis even if prophylaxis is 100% effective.
3) Antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of IE.
4) Limit recommendations for IE prophylaxis only to those conditions listed in Table 3.
5) Antibiotic prophylaxis is no longer recommended for any other form of CHD, except for Table 3.
6) Antibiotic prophylaxis is recommended for all dental procedures that involve manipulation of gingival tissues or periapical region of teeth or perforation of oral mucosa only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).
Antibiotic prophylaxis is recommended for procedures on respiratory tract or infected skin, structures or musculoskeletal tissue only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).

F. SAMPLE ADULT ANTIBIOTIC PREMEDICATION PRESCRIPTIONS

**RX:** Amoxicillin 500 mg capsules  
**Disp. #4**  
**Sig:** Take 4 capsules p.o. 1 hour before dental appointment  
- For patients NOT penicillin allergic:  
  - Pediatric dose: 50 mg/kg not to exceed adult dose!  
  - Amoxicillin is available in 500 and 250 mg capsules, and 250 mg chewable tablets and 250 mg/5 ml susp.  
  - Amoxicillin ≠ ampicillin ≠ penicillin VK

**RX:** Clindamycin 150 mg capsules  
**Disp. #4**  
**Sig:** Take 4 capsules (600 mg) p.o. 1 hour before dental appointment. Take with food or milk.  
- For patients with penicillin allergy  
  - Pediatric dose: 20 mg/kg  
  - Clindamycin is a lincomycin, therefore not cross-reactive with the erythromycin family

**RX:** Cephalexin 500 mg capsules  
**OR**  
**Cephradine 500 mg capsules**  
**Disp. #4**  
**Sig:** Take 4 capsules p.o. 1 hour before dental appointment  
- Pediatric dose: 50 mg/kg  
- Cephalexin (generic Keflex®) is less expensive than cephradine (generic Velosef® or Anspor®)  
- Also comes in a 250 mg/5ml suspension  
- Avoid cephalosporins if patients allergic reaction was either - urticarial, angioedema, anaphylaxis or unknown

**RX:** Clarithromycin (Biaxin®) 500 mg tablets  
**Disp. #1**  
**Sig:** Take one tablet p.o. 1 hour before dental appointment.  
- Pediatric dose: 15 mg/kg  
- An erythromycin with low GI irritation

**RX:** Azithromycin (Zithromax®) 250 mg tablets  
**Disp. #2**  
**Sig:** Take 2 tablets p.o. 1 hour before dental appointment.  
- Pediatric dose: 15 mg/kg  
- Less drug interactions than macrolides, low incidence of GI irritation  
- Very expensive, no therapeutic advantage over Biaxin® or EES

**RX:** Erythromycin Ethylsuccinate. 400 mg tablets (EES®)  
**Disp. #4**  
**Sig:** Take 4 tablets (1600 mg) p.o. 2 hours before dental appointment.  
- Pediatric dose: 32 mg/kg (of EES®)  
- 400 mg EES = 250 mg erythromycin base activity  
- EES is better tolerated than erythromycin base or stearate  
- Still acceptable for AHA guideline prophylaxis  
- Pediatric dose for erythromycin base/stearate is 20 mg/kg

NOTE: Consider writing "DAW" (Dispense As Written) orders for erythromycin products when used for prophylaxis

**Oral liquids for adults who have forgotten to take premedication at home:**

**RX:** Amoxicillin 250 mg/5 ml suspension  
**Disp. #40 ml**  
**Sig:** Take 40 ml one-half to one hour before dental appointment  
- Suspension is a powder that must be reconstituted prior to use- tastes good  
- Reconstituted suspension expires in 14 days with or without refrigeration

**RX:** Erythromycin ethylsuccinate 400 mg/5 ml susp.  
**Disp. #20 ml**  
**Sig:** Take 20 ml one-half hour before dental appointment  
- Suspension is commercially available premixed  
- Must be refrigerated, has a shelf life of about 2 years.  
- Suspension is better tolerated (GI) than tablets

**RX:** Cleocin® 75 mg/5 ml solution  
**Disp. #40 ml**  
- Solution must be reconstituted & expires in 14 days  
- Do NOT refrigerate
V. OTHER CONDITIONS THAT MAY REQUIRE ANTIMICROBIAL PROPHYLAXIS

A. SYSTEMIC LUPUS ERYSHEMATOSUS (SLE)

BACKGROUND:
- SLE is an inflammatory autoimmune disease whereby pathogenic antigen-antibody complexes harm a variety of organs & systems including the skin, kidneys, blood vessels, joints and the heart
- 50% of SLE patients demonstrate cardiac valve abnormalities at autopsy
- SLE patients have an increased prevalence of cardiovascular abnormalities
- Incidence of Infective Endocarditis: 
  - SLE = 1 - 7%
  - RHD = 0.8 - 1.2%
  - Prosthetic heart valve = 1.1%

MANAGEMENT: Progressive SLE patients should be regularly evaluated for the detection of new heart murmurs and should be questioned about cardiac valve disease at dental visits.

B. ASPLENIC PATIENTS

BACKGROUND (JADA: Dental Considerations in Asplenic Patients. 127:1359-1363, 1996)
- Patients who are functionally or anatomically asplenic fail to clear organisms from the bloodstream and are at an increased risk of overwhelming bacteremia
- Reasons for splenectomy
  - Encapsulated organisms pose the highest risk - primary pathogens of concern are S. pneumoniae, H. influenzae, N. meningitidis, β-hemolytic streptococci
- Splenectomy confers life-long risk from sepsis in both adults and children (2 - 4%)
- Recommend dental prophylaxis with current AHA regimen when needed

C. SOLID ORGAN TRANSPLANTATION

- Infectious Disease Rates of Patients
  - 80% have “normal” rate of infections
  - 10% chronic or progressive viral infections
  - Hepatitis B or C, cytomegalovirus, EPV etc.
- Theoretically at ↑ risk from transient bacteremias
- 5-10% recurrent or chronic rejection
  - Increased immunosuppressive dosages
  - Most likely to develop opportunistic infections
- Immunosuppressive regimens
  - Cyclosporine or tacrolimus
  - Infection is most common life-threatening complication

MANAGEMENT:
- Defer elective dental treatment until at least 6 months after transplantation

D. CORONARY ARTERY STENTS

BACKGROUND: (JADA. Coronary Artery Stents. Vol 131: 797-801, 2000)
- Studies in pig hearts reveal endothelial damage for up to 3 months after insertion
- Neo-vascularization begins in 72 hours and neointima is complete in 30 days

MANAGEMENT:
- Reasonable to premedicate patient for 1-3 months post stent insertion
- American College of Cardiology New Guidelines for Antibiotic Use