AN UPDATE ON 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 – HA-MRSA or CA-MRSA?
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:

YES NO ? a. Artificial heart valve replacement
YES NO ? b. History of bacterial endocarditis
YES NO ? c. Congenital heart disease (type ______________________)
YES NO ? d. Acquired valvular heart disease or heart murmur (no longer necessary to ask)
YES NO ? e. History of post-streptococcal glomerulonephritis
YES NO ? f. Organ transplantation
YES NO ? g. Prosthetic joint replacement (when____________________)
YES NO ? h. Artificial implant or graft of any kind other than above (list ______________________)
YES NO ? i. Systemic lupus erythematosus (SLE)
YES NO ? j. Immunosuppression? Asplenic?
YES NO ? k. Physician requests antibiotic coverage for reasons other than above (reason_________)
II. ANTIBIOTIC PROPHYLAXIS FOR PATIENTS WITH TOTAL JOINT REPLACEMENTS

A. GUIDELINES FOR ANTIMICROBIAL PROPHYLAXIS – TIMELINE FROM 2003 THROUGH 2016


- February 2009 AAOS Information Statement recommends lifelong antimicrobial prophylaxis for all patients with total replacements of large weight-bearing joints even though no new evidence for the change exists.

- Given this new “Information Statement”, Orthopedic Surgeons now bear prescriptive responsibility if the dentist does not deem premedication to be appropriate. See Clinical Infectious Diseases, 1/1/10 and JADA;141;667-671. (Position Paper from the AAOM on Dental Treatment of Joint Patients); Also see JADA December 2011.

- Evidence-based recommendation issued December 18, 2012 with guideline writing committee appointed.

This clinical practice guideline, with three recommendations, is based on a systematic review of the correlation between dental procedures and prosthetic joint infection (PJI).

- Recommendation one, which is based on limited evidence, supports that practitioners consider changing their longstanding practice of prescribing prophylactic antibiotics for patients who undergo dental procedures. Limited evidence shows that dental procedures are unrelated to PJI.

- Recommendation two addresses the use of oral topical antimicrobials (topical antibiotic administered by a dentist) in the prevention of PJI in patients undergoing dental procedures. There is no direct evidence that the use of oral topical antimicrobials before dental procedures will prevent PJI.

- Recommendation three is the only consensus recommendation in the guideline, and it supports the maintenance of good oral hygiene.

B. ADA Constitutes 2014 Committee and Publishes Clinical Recommendations in January 2015

Management of patients with prosthetic joints undergoing dental procedures

Clinical Recommendation:
In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection.

For patients with a history of complications associated with their joint replacement surgery who are undergoing dental procedures that include gingival manipulation or mucosal incision, prophylactic antibiotics should only be considered after consultation with the patient and orthopedic surgeon.* To assess a patient’s medical status, a complete health history is always recommended when making final decisions regarding the need for antibiotic prophylaxis.

Clinical Reasoning for the Recommendation:
- There is evidence that dental procedures are not associated with prosthetic joint implant infections.
- There is evidence that antibiotics provided before oral care do not prevent prosthetic joint implant infections.
- There are potential harms of antibiotics including risk for anaphylaxis, antibiotic resistance, and opportunistic infections like Clostridium difficile.
- The benefits of antibiotic prophylaxis may not exceed the harms for most patients.
- The individual patient’s circumstances and preferences should be considered when deciding whether to prescribe prophylactic antibiotics prior to dental procedures.

* If drugs where antibiotics are deemed necessary, it is most appropriate that the orthopedic surgeon recommend the appropriate antibiotic regimen and when reasonable write the prescription.
C. AAOS Appropriate Use Criteria (AUC) for Total Hip and Knee Replacement Patients Undergoing Dental Procedures (Approved September 23, 2016 and published September 28, 2016)

We recognize that in the office setting, some specific laboratory values and other patient data are not always readily available. This also may include timely access to published scientific studies that can support clinical decision-making. Appropriate Use Criteria (AUC) specify when it is appropriate to perform a clinical procedure or service. An “appropriate” procedure is one for which the expected health benefits greatly exceed the expected health risks. Ideally, AUC are evidence-based, but in the absence of sufficient evidence, may be derived from a “consensus of expert opinion” and “accepted practice”.

With this AUC, we have attempted to define clinical situations in which antibiotic prophylaxis in certain at-risk dental patients could reduce a theoretical risk of post-surgical prosthetic joint infection. This AUC was developed as a decision support tool to facilitate the treatment of defined “high risk” and “immune compromised” patients who are on the more severe end of the clinical spectrum of disease. In the absence of readily available laboratory data or suggestive clinical suspicion, it would be reasonable to assume that most patients will fall outside of these criteria and therefore lay outside the confines of our strict definitions. As always, sound judgment should guide clinical decisions about when it may be necessary or prudent to delay a dental procedure until more information is available.

Assumptions:

Planned Dental Procedures
- The chance of oral bacteremia being related to joint infections is extremely low, with no evidence for an association.
- Oral bacteremia frequently occurs secondary to activities of daily living such as tooth brushing and eating.
- Virtually all dental office procedures have the potential to create bacteremia.

Immunocompromised Status
1. Severely immunocompromised patients include:
   a. Patient with Stage 3 AIDS as defined by the Centers for Disease Control and Prevention (CDC) Guidelines when the immune system becomes severely compromised due to reduced CD4 T lymphocyte counts (<200) or opportunistic infection as defined by CDC<sup>8</sup> see list of diseases below.
   b. Cancer patient undergoing immunosuppressive chemotherapy with febrile (Celsius 39) neutropenia (ANC <2000) OR severe neutropenia irrespective of fever (ANC <500)
   c. Rheumatoid arthritis with use of biologic disease modifying agents including tumor necrosis factor alpha or prednisone >10 mg per day. Methotrexate, Plaquenil not considered immunocompromising agents.
   d. Solid organ transplant on immunosuppressants
   e. Inherited diseases of immunodeficiency (e.g., congenital agammaglobulinemia, congenital IgA deficiency)
   f. Bone marrow transplant recipient in one of the following phases of treatment:
      i. Pretransplantation period
      ii. Preengraftment period (approximately 0-30 d posttransplantation)
      iii. Postengraftment period (approximately 30-100 d posttransplantation)
      iv. Late posttransplantation period (≥100 d posttransplantation) while still on immunosuppressive medications to prevent GVHD (typically 36 months post transplantation) (see Table reference below)

*Opportunistic illness in AIDS: (as per CDC<sup>5</sup>)*

Glycemic Control
1. A1C scores should be recent within 3-6 months.
2. Acucheck spot check in dental office blood glucose level is equivalent to a patient self-report.
3. Blood glucose tests are assumed to be random (not necessarily fasting).
D. 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: Azithromycin 250mg tablets  
Disp: # 2  
Sig: Take 2 tablets p.o. 1 hr. prior to dental appointment

- For patients with penicillin allergy  
- Doesn’t inhibit P450 3A4  
- Does prolong QT interval

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
E. DENTAL MANAGEMENT OF PATIENTS WITH TOTAL JOINT REPLACEMENTS

- Updated health history with each visit and explain why you ask at every 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 their recommendation-some still use AHA recommendations
  - home maintenance of oral hygiene is crucial to avoid shunt infection

E. CEREBROSPINAL FLUID SHUNTS

- Ventriculoatrial shunts (ventriculoatriostomy)-- 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
  o Most common procedure performed today
  o Used to treat hydrocephalus, post-stroke injury
  o Used to treat normal pressure hydrocephalus (NPH) which is a reversible cause of dementia

IV. PROPHYLAXIS FOR THE PREVENTION OF SUBACUTE BACTERIAL ENDOCARDITIS (SBE) – 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>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin</td>
<td>2 g</td>
<td>50 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Oral An allergic to penicillins or ampicillin</td>
<td>Cephalexin**† OR</td>
<td>2 g</td>
<td>50 mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clindamycin OR</td>
<td>600 mg</td>
<td>20 mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Azithromycin or clarithromycin</td>
<td>500 mg</td>
<td>15 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>Ampicillin OR Cefazolin or ceftriaxone</td>
<td>2 g IM or IV*</td>
<td>50 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin and unable to take oral medication</td>
<td>Cefazolin or ceftriaxone† OR Clindamycin</td>
<td>1 g IM or IV</td>
<td>50 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>600 mg IM or IV</td>
<td>20 mg/kg IM or IV</td>
<td></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.)

Prosthetic cardiac valve

Previous infective endocarditis

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. 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

**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  
**Sig:** Take 40 ml one-half hour before dental appointment  
- Solution must be reconstituted & expires in 14 days  
- Do NOT refrigerate  
- Taste and smell are less than desirable
V. OTHER CONDITIONS THAT MAY REQUIRE ANTIMICROBIAL PROPHYLAXIS

A. SYSTEMIC LUPUS ERYTHEMATOSUS (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

**BACKGROUND:** (Clin Transplant. A Survey of Dental Care Protocols. 19: 15-18, 2005)
- 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 (tacrolimus, mycophenolate, prednisone)
  - Most likely to develop opportunistic infections

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

D. CORONARY ARTERY STENTS

The report published in JADA can be summarized for the dental professional as follows:

1. Dental professionals and other healthcare providers who perform invasive or surgical procedures and are concerned about periprocedural and postoperative bleeding must be made aware of the potential catastrophic risks of premature discontinuation of antiplatelet (thienopyridine) therapy. The dental professional should contact the patient’s physician if issues regarding the patient’s antiplatelet therapy are unclear, in order to discuss optimal patient management strategy.

2. Elective procedures for which there is significant risk of perioperative or postoperative bleeding should be deferred until patients have completed an appropriate course of thienopyridine therapy. The course of this therapy is suggested as 12 months after drug-eluting stent implantation if they are not at high-risk of bleeding.

WHAT ABOUT ANTIBIOTIC PREMEDICATION??

* According to the 2007 AHA SBE Prophylaxis guidelines, antibiotic prophylaxis is not indicated as stated in the last section called “other considerations”.
