ANTIBIOTICS—

The Basics

K. David Stillwell, DDS, MAGD, FAAHD

April 2013
Antibiotic History I

• 1946: Civilian use of penicillin
• 1950’s: New antibiotics
  Tetracycline’s
  Cephalosporins
  Erythromycins
• 1960’s:
  Lincomycin

Antibiotic History II

• 1970’s:
  Clindamycin
  Vancomycin
• 1980-90’s:
  “Fine tuning” of present antibiotics (Zithromax) with no really new antibiotics
• 100+ antibiotics in use today in US
• Possible NEW antibiotic out.
Resistance!

- *Lancet 2/9/07:*
  - “The effect of a single course of antibiotics was felt as much as 180 days after treatment ended (in producing resistance in bacteria)”
  - “Physicians should take into account the striking ecological side-effects when prescribing antibiotics”

Resistance Growth

- **Each time** an antibiotic is taken a small number of microbes develop resistance genes
- These resistant microbes multiply in the absence of non-resistant microbes
- Can transfer these genes to other species of microbes through conjugation
- New strains then develop and the cycle continues
“Ideal” Antibiotic

• Targets one organism ("the" organism).
• No "friendlies" hit
• Side effects minimal (allergies, GI, etc.)
• One tablet a day (patient compliance)
• Take for a maximum of 3-5 days
• No resistant strains developed
• Low cost

Antibiotic Principles

1. **Presence of infection**: Patient should have an infection!
2. **Host’s defense**: Host should be able to mount a fight against defense—defense has “final say” and not antibiotic
3. **Eliminate source of infection**: This is especially true in dentistry
Antibiotic Choice

1. Know the organism (ID)
2. Know the sensitivity of organism
3. Desire a narrow spectrum of kill
4. Minimally toxic antibiotic
5. Cidal over static
6. Proven history for similar infections
7. Low cost

Why Bactericidal?

- Causes bacterial cell death NOT just slowing down cell growth
- Quicker than static in helping eliminate infection
- Produces longer lasting effects
- Better for short term dosing – AHA
- NEVER mix a cidal and static – get good medication history
Antibiotic Administration

- **Choices:**
  1. Dose
  2. Interval between doses
  3. Route of administration
  4. When to monitor (check-up on) the patient after antibiotic administration
- These are your choices

Antibiotic: Dose

- **MIC:** Minimum inhibitory concentration as determined by pharmaceutical industry
- Need 3 to 4 times MIC (typical dose)
- **Loading dose:** Usually double the standard dose then followed by recommended dosing—good idea for potentially “serious” infections or potentially compromised host
Antibiotic: Interval

- The interval is determined by the half life of the antibiotic.
- The interval is determined by the host’s clearance capacity. A measure of patient’s liver/renal function.
- The interval is also determined by the patient’s compliance level.

Antibiotic: Route

- Your choice of:
  1. Parenteral: IV and IM. Consider IM if worried about seriousness of infection or patient compliance – ER case?
  2. Sub Q: No real place in dentistry
  3. Oral: Comprises 99.9% of DMD/DDS antibiotics. However, least predictable due to variable absorption rates in gut.
Antibiotics: Patient Monitoring

• Wait a full 48 hours before changing dose, adding another antibiotic or switching antibiotics
• Most decisions after 72 hours depending upon patient response
• **MUST** see the patient before switching (Telephones have poor eyesight.)
• Make sure patient takes full Rx dose

Common Adverse Reactions:

• Allergy
• Nausea and vomiting
• Pseudomembranous colitis: *Clostridium difficile (becoming more resistant itself)*
• Inactivation of BC pill: controversial
• Renal/Liver toxicity: where is the antibiotic metabolized/eliminated?
Antibiotics

- Penicillin/Amoxicillin/Augmentin
- Cephalosporins
- Tetracyclines
- Erythromycins
- Clarithromycin
- Azithromycin
- Clindamycin
- Metronidazole

Penicillin/Amoxicillin

- 1929: Discovered by Fleming
- First mass produced during WW II
- Thought by science that it would “end the era of infections”. **The magic bullet**
- Resistant strains developed in early 50’s, shortly after civilian use began
- Amoxicillin: an extended spectrum penicillin
Penicillin VK

• Oral penicillin
• **CIDAL**: Inhibit enzymes responsible for the last stage of bacterial cell wall synthesis (Beta-lactams)
• Less than 50% absorption and eliminated by kidneys
• Narrow spectrum: Gram +
• **Resistance**: Continues to grow!!!! Beta-lactamase producers

Penicillin VK

• **Dosing**:  
  Rx: V-Cillin K 500 mg  
  Disp: 20 tabs  
  Sig: ii (2) tabs stat and i (1) tab q6h until gone  
• Use in dentistry is decreasing
Amoxicillin

• Oral derivative of ampicillin
• Extended-spectrum penicillin
• Cidal – similar to penicillin in action
• Broader spectrum: *H. influenzae* (middle ear infection in children/infants)
• Absorption: 60% (stays around longer)
• Dentistry: Common oral infections and AHA regimen

<table>
<thead>
<tr>
<th>Amoxicillin</th>
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<tbody>
<tr>
<td><strong>Dosing option 1:</strong></td>
</tr>
<tr>
<td>Rx: Amoxicillin 500 mg</td>
</tr>
<tr>
<td>Disp: 20 tabs</td>
</tr>
<tr>
<td>Sig: 2 tabs STAT and 1 tab q8h until gone</td>
</tr>
<tr>
<td>• Allergy: Like penicillin: 1-10% with .02% being fatal (300 deaths/year)</td>
</tr>
</tbody>
</table>
Amoxicillin

• Dosing option 2:
  Rx: Amoxicillin 875 mg
  Disp: 10 tabs
  Sig: 2 tabs STAT and 1 tab bid until gone

• Allergy: Like penicillin: 1-10% with .02% being fatal (300 deaths/year)

Augmentin

• Amoxicillin
• Clavulanic acid: Blocks the Beta-lactamase inhibitors for resistant bacteria
• Used for S. aureus, H. influenzae
• Used for combination skin and soft tissue infections. Use is declining
• Rx: Augmentin 500 mg (500 mg amoxicillin and 125 mg clavulanic acid)
Adverse Affects: Penicillin/Amoxicillin

- Allergy: Penicillin 10% and amoxicillin reportedly higher?
- N&V: Both pretty low
- P. Colitis: Both reported - but low
- BC Inactivation: Both yes
- Toxicity: Very low. If Rx for dialysis patients the dosage must be adjusted

Cephalosporins

- 1948: Discovered in a Sardinian sewer
- 20+ cephalosporins used in US today
- Act by interfering with enzymes that form bacterial cell wall Cidal
- Classified according to generation (1 – 4) The higher the generation, the less used in dentistry and more effect on anaerobic bacteria
Cephalosporins II

- Resistance: Once active against *Staph aureus*. The resistance is growing quickly.
- Absorbed well (oral forms) and excreted by kidneys. Higher generations metabolized more in liver.
- Dental: Used 5th in line for penicillin allergy (20%); ANUG; TJR replacement prophylaxis and sinus exposures.

Adverse Effects: Cephalosporins

- Allergy: 1 – 7% reported
- N&V: Low
- P. Colitis: Reported – low
- BC inactivation: Probably
- Toxicity: Low - like penicillin
- Other: Blood dyscrasias (IV)
Cephalosporins

- **Dosing:**
  Rx: Cephalexin (Keflex) 500 mg
  Disp: 20 tabs
  Sig: 2 tabs stat and 1 tab q6h until gone

- **Allergy:** 20% cross over with penicillin (rash)

Tetracyclines

- Clinically introduced in 1953
- Probably most misused antibiotic in US, resulting in multiple resistant strains
- **Static:** Inhibit protein synthesis by interfering with 30-S subunit of bacterial ribosome
- Classified according to length of action
- General use: Severe acne and rickettsial diseases (Lyme/RMSF)
**Tetracyclines II**

- Resistance: Growing rapidly because of low dosing
- Absorbed well in empty stomach. No heavy metals (dairy products)
- Metabolized by liver
- Dental: Used for penicillin allergic patients (4th in line) and for periodontal disease. High levels in bone and crevicular fluid.

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**Adverse Effects: Tetracyclines**

- Allergy: Lowest of antibiotics
- N&V: Low/moderate
- P. Colitis: Very low
- BC Inactivation: Very high
- Toxicity: Low in dental doses
- Death: Ø
- Other: Phototoxic reactions and tooth discoloration
**Tetracycline**

- **Dosing:**
  
  - **Rx:** Doxycycline (Vibramycin) 100 mg
  - **Disp:** 10 tabs
  - **Sig:** 1 tab q12h day one; then 1 tab qd until gone

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**Erythromycin**

- Discovered in 1952 from soil in Philippines Islands
- Macrolide antibiotic
- Static: Inhibit protein synthesis by binding to the 50-S subunit
- Various forms based upon stability in GI tract
- General use: URIs
Erythromycin II

- Resistance: Bacteria rapidly become resistant (particularly staph)
- Absorbed poorly with resultant GI irritation
- Metabolized in liver (P-450 cytochrome system)
- Dental: Can be used in penicillin allergic patient. However, I see no benefit unless it's the only antibiotic around.

Adverse Effects: Erythromycin

- Allergy: Low
- N&V: Very high
- P. Colitis: Reported but low
- BC Inactivation: Yes
- Toxicity: Yes
- Other: Interacts with other meds for metabolism in the liver and cause them to rise to toxic levels
Erythromycin Side Reactions

- Hismanal
- Digitalis
- Theophylline
- Tegretol
- Coumadin
- Cyclosporine A
- Many others!
- BAD ANTIBIOTIC!!!!!

Clarithromycin

- Macrolide antibiotic (Biaxin)
- Developed in the 80’s (tweaked)
- Very well absorbed if full or empty stomach
- Greater range of spectrum than Emycin
- Half life of 8 -12 hours
- Use: URIs and ulcers (*Helicobacter pylori*)
- Does not have as much P-450 as Emycin
Clarithromycin II

• Dosing:
  Rx: Clarithromycin 500 mg
  Disp: 12 tabs
  Sig: 1 tab q12h until gone

**Dental:** Used last in line for penicillin allergy. Be sure to question patients who have a history of ulcers (cidal vs. static)

Azithromycin

• Macrolide antibiotic (Zithromax)
• Developed in the 90’s.
• Travels with the macrophages to site of infection and has long half life (68 hours)
• Sensitive to stomach contents.
• “Thought” to have less P-450 activity
• Used primarily for URI’s
• Expensive
• Resistance is increasing!!!!
**Azithromycin II**

- **Dosing:**
  - Rx: Azithromycin 250 mg
  - Disp: 5 tabs (Z-pack)
  - Sig: 2 tabs stat then 1 tab qd until gone
- **Dental:** 3rd in line for penicillin allergy (AHA). Maybe used more in future for routine oral infections?

**Clindamycin**

- Discovered 1970 (Lincomycin)
- Static and cidal depending upon dose. Works similarly to Emycin and the 50-S subunit inhibiting protein synthesis
- Excellent spectrum for dental infections (some anaerobes and *S. aureus*)
- Resistance is on par with other antibiotics – jury is still out
Clindamycin II

• 90% absorbed even with full stomach contents. Metabolized in the liver – watch for the liver impaired
• Excellent penetration into bone. Used in general medicine for the treatment of refractory bone infections
• Side Affect: Diarrhea—implicated in pseudomembranous colitis (bad rap as use increases)
• Low allergy potential

Clindamycin III

• Dosing:
  Rx     Clindamycin 300 mg
  Disp:  20 tabs
  Sig:   2 tabs stat and 1 tab q6-8h until gone
• Dental: Becoming more of a first round antibiotic of choice for infections. The antibiotic for penicillin allergy!
• Can be expensive
**Metronidazole**

- *Flagyl*
- Clinical use 1960
- Only against obligate anaerobic bacteria
- *Cidal*. Inhibits DNA replication
- Metabolized in liver
- Dental: Used for periodontal infections involving *B. fragilis* and as “bump” with amoxicillin

**Metronidazole II**

- **Dosing:**
  - Rx: Metronidazole 500 mg
  - Disp: 20 tabs
  - Sig: 1 tab q6h until gone
- Other: Side effects include: metallic taste, GI disturbances, candidal super infections and patients NOT to drink EtOH (disulfiram reactions)
Newest Antibiotic

- Telithromycin (Ketek)
- Classified as “Ketolide antibiotic”
- Used to be approved for: acute bacterial sinusitis (H-flu and S-aureus) and acute exacerbations of bronchitis
- However, reports of fatal life-threatening respiratory failure and liver toxicity have been reported
- Now only for community pneumonia

Most Recent ADA Guidelines
JADA, April 2004

1. Make an accurate diagnosis
2. Use appropriate dosing schedule
3. Consider using narrow spectrum antibiotics
4. Avoid unnecessary use (viral infections)—if treating empirically, revise treatment if results available
5. Know side effects and drug interactions
6. Educate patient on medication
The Penicillin Allergic Patient

- Reported in 1 – 10% of patients in US
- Severity is “generally” determined by the route of administration (Penicillin G via IM is highest reaction)
- Determine type:
  1. Acute: Severe anaphylaxis
  2. Accelerated: within 30 minutes
  3. Delayed: after 30 minutes
- If positive: other allergies?

The Penicillin Allergic Patient

- Flow Chart:
  1. Clindamycin
  2. Azithromycin
  3. Doxycycline
- Previous recommendation of cephalosporins OK in the delayed type of reaction but NOT in acute/immediate
- If patient has many allergies, follow up 24 hours and use clindamycin
The PCN “Resistant” Patient

- When things do not go smoothly
- When do I increase dose?
- When do I change antibiotics?
- When do I call OMFS?
- Why is it always my mother-in-law?
- Why does this happen to me?
- Can I get my resort hotel deposit refunded?

PCN Resistant Infection

- Do NOT rush decision to change antibiotics. Wait at least 48-72 hours.
- Slightly Better?: Wait another 24 hours.
- Staying Same?: If not on clindamycin then change and wait 48 hours. If on clindamycin, is the source eliminated?
- Getting Worse?: Refer to OMFS. Weird bugs and/or host resistance is compromised.
If You MUST Rx Antibiotics

• If you routinely Rx antibiotics for surgical procedures (surgical extractions, periodontal surgery, implants, etc), a new study showed that a single preoperative dose is as effective at preventing infections as a 24-48 hour dose
• The hospital study compared 1g of Ancef vs. 24-48 hours in orthopedic procedures

Philosophy

• Be consistent!
• Do NOT jump from one antibiotic to another without due cause
• Good Dental Antibiotics: 99.9% cases
  1. Amoxicillin
  2. Clindamycin
  3. Azithromycin
  4. Doxycycline
Practical Pharmacology for the Dental Team

“Antibiotics, Antibiotic Premedication, and Anticoagulants”

ASDA Annual Scientific Session
Saturday, April 6, 2013

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“...TO SCRIPT, OR NOT, TO SCRIPT...”

That Is The Question!!

K. David Stillwell, DDS, MAGD, FAAHD
UAMS Center for Dental Education
“...it is time for some investigators to scientifically debunk a supposedly well established linkage. This is the theory that there is a causal relationship between dental care and bacterial endocarditis...”
J. R. Hupp (contd.)

“...without any strong scientific evidence, and now requires dentists to give certain patients potentially harmful antibiotics to manage bacteremias. The harm includes altering flora, triggering allergic reactions, and exposing dentists to unwarranted litigation should the patient inadvertently not receive the antibiotic regimen. Here's a hypothetic linkage begging to be undone.”

AHA Regimen History

2. 1977—IM penicillin (big dog dose) 1 hour before followed by 500 mg orally every 2 hours for 2 doses
3. 1984—Oral penicillin 2 grams 1 hour before and 1.0 gram 6 hours later
4. 1990—Amoxicillin 3 gram 1 hour before and 1.5 gram 6 hours later
5. 1997—Amoxicillin 2 grams 1 hour before

Circulation 2007; 116:1736-54
Peter B. Lockhart, DDS, et al

- "The evidence base for the efficacy of antibiotic prophylaxis in dental practice"
  - 2007 major review of 8 medical conditions and devices (290 references)
  - Analyzed the prevalence in dental practice and the frequency of mention in dental literature for antibiotic premedication (AP) prior to dental treatment

Lockhart, JADA 2007

- *Eight Medical Conditions—*
  1. Cardiac: native heart valve disease, prosthetic valves and pacemakers
  2. Hip, knee and shoulder prosthetic joints
  3. Renal dialysis shunts
  4. Cerebrospinal fluid shunts
  5. Vascular grafts
  6. Immunosuppression secondary to cancer and cancer chemotherapy
  7. Systemic lupus erythematosus (SLE)
  8. Insulin dependent (Type 1) diabetes mellitus
Lockhart Conclusions

- Controversy and confusion
- Lack of sound scientific evidence
- Problems of identifying what dental office procedures that increase risk
- Focus should be on rigorous oral hygiene to decrease oral bacteremia

“The weight of evidence suggests that the practice should be stopped in most, if not all, of these eight groups.”

Circulation, JAHA 2007

“Prevention of Infective Endocarditis – Guidelines from the American Heart Association”

- Agencies involved—AHA Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on CV Disease in the Young, Council on Clinical Cardiology, Council on CV Surgery and Anesthesia, ADA
- 23 individuals (2 DDS/DMD) and 153 citations
- Major revision provided more conservative guidelines (Tables 1-6)
IE versus SBE

- IE is infective endocarditis
- This term replaced subacute bacterial endocarditis (SBE) which is fast fading off into the sunset
- IE can be bacterial, viral or fungal
- IE is an uncommon—but life threatening—disease

Reasons for Revisions

1. Infective Endocarditis (IE) is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental procedure

2. Prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo dental procedures

TABLE TWO—Circulation 2007; 116: 1736-54
Reasons for Revisions

3. The risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.

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.

Estimated Risk Rates

- **IE from a dental procedure on patients with underlying cardiac conditions**—
  - Mitral valve prolapse: 1 per 1.1 million
  - Congenital heart disease: 1 per 475,000
  - Rheumatic heart disease: 1 per 142,000
  - Prosthetic valve in place: 1 per 114,000
  - Previous IE: 1 per 95,000
High Risk Cardiac Conditions

- Prosthetic cardiac valve
- Previous infective endocarditis (IE)
- Congenital heart disease (CHD)
  - Unrepaired cyanotic CHD
  - Repaired CHD during first 6 months of healing
  - Repaired CHD with residual defects
- Cardiac transplantation patients who develop cardiac valvulopathy

"Except for conditions listed above, antibiotic prophylaxis is no longer recommended"

Cardiac Conditions Eliminated

- Mitral Valve Prolapse—with or without regurgitation
  - MVP was previously the most common condition that dental profession was required to prescribe antibiotics
- Murmurs—only those specifically attributed to IE or prosthetic valves
Etiology of IE

- An infection of the heart valves or endocardium (bacterial most common)
- Most often associated with cardiac defects—usually on the valves
- Bacteria, virus and fungi can colonize
- Today, can have 10-80% mortality rate depending upon organism

Pathophysiology of IE

- Bacteria enter blood stream and attach to damaged endocardium (eddies and tide pools) with vegetation formation
- Vegetations can—
  - Damage cardiac valve structure
  - Become detached (embolic) and spread to vital organs
  - Cause a general systemic infection
Prosthetic Heart Valves

- Two types—
  1. Mechanical: first introduced in 1952
  2. Biologic (tissue): introduced early 60’s
- Mechanical include reciprocating ball, tilting disk and semicircular hinged
- The tissue valves are usually porcine or bovine valves treated with glutaraldehyde

Prosthetic Valve Complications

- 60% of patients will develop serious problems within 10 years
- PV endocarditis can develop both early and late (2 months of placement)
  - Oral strep are implicated in late infections
- The 6 month survival rate for PVE can be as high as 65% (late) or only 35% (early)
- Patients who had “native” IE are more prone to PVE— so beware!
Transient Bacteremia Studies

- Tooth extraction: 10-100%
- Periodontal surgery: 36-88%
- Scaling and root planing: 8-80%
- Routine cleaning: up to 40%
- Endodontic procedures: up to 20%
  - Brushing and flossing: 20-68%
  - Toothpicks: 20-40%
  - Food chewing: 7-51%

Duration of Bacteremias

- After extractions—
  - Positive for up to 10 minutes
  - Drops sharply after 10-30 minutes
  - Small percentage positive after 30-60 minutes

“There may not be a risk in the frequency, nature, magnitude, and duration associated with a dental procedure compared with that resulting from routine daily activities.”
Continuing AP Indications

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

* Do not need for anesthetic injections, dental radiographs, placement of RPDs, adjustment and/or placement of orthodontic brackets, shedding of deciduous teeth and bleeding from trauma.

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Adult Regimens

- **Oral**: Amoxicillin 2 gm 30-60 minutes before dental procedure
- **Allergic to penicillin**: Cephalexin (2 gm)*, clindamycin (600 mg), azithromycin (500 mg) or clarithromycin (500 mg) 30-60 minutes before dental procedure
- **Unable to take oral**: Ampicillin (2 gm IV/IM) or cefazolin (1 gm IM/IV) 30-60 minutes before dental procedure

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* TABLE FOUR—Circulation 2007; 116: 1736-54

* TABLE FIVE—Circulation 2007; 116: 1736-54
Child Regimens

- **Oral**: Amoxicillin (50 mg/kg)
- **Allergic to penicillin**: Cephalexin (50 mg/kg), Clindamycin (20 mg/kg) or Azithromycin/clarithromycin (15 mg/kg)
- **Non-oral**: Ampicillin (50 mg/kg) IV/IM or Cefazolin (50 mg/kg) IV/IM

If Regimen NOT Taken

- If dosage of antibiotic is *inadvertently* not administered then.................
  - The dosage may be administered up to **TWO** hours after the procedure.
  - This should be considered **ONLY** when the patient forgot to take dosage.
  - Don’t use as routine in your office!
Already on AHA Antibiotic

- If patient is being treated for another infection, and the antibiotic is a class similar to amoxicillin or penicillin—
  - Change antibiotic to a different class that still works on S. viridans
  - Consider clindamycin, azithromycin or clarithromycin
- If not sure, delay dental treatment 10 days after antibiotic completion

Summary of Major Changes

1. Concluded that bacteremia resulting from daily activities is much more likely to cause IE than bacteremia associated with a dental procedure.
2. Concluded that only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis even if prophylaxis is 100% effective.
Summary of Major Changes

3. Antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of IE.

4. Limit recommendations for IE prophylaxis to those conditions listed in Table 3.

5. Antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease (except those listed in 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 the highest risk of outcome (Table 3).

7. Antibiotic prophylaxis solely to prevent IE is not recommended for GI or GU tract procedures.
Total Joint Replacement

- “Antibiotic Prophylaxis for Dental Patients with Total Joint Replacements”
  - ADA and AAOS Joint Consensus Advisory Statements (July 1997 then July 2003 update)
  - Antibiotics **not indicated** for pins, plates, screws, nor for dental patients with TJR after two years
  - Consider premedication for **small number** of patients at risk for hematogenous TJ infection
TJR Patients “At Risk?”

1. **Immunocompromised**
   - Rheumatoid arthritis
   - Systemic lupus (SLE)
   - Insulin-dependent (Type 1) diabetes
2. **First two years post-TJR surgery**
3. **Hemophilia**
4. **HIV infection**
5. **Previous prosthetic joint infection**

**TABLE ONE: JADA 2003;134;R55-99**

2003 TJR Antibiotic Regimens

- No penicillin allergy—
  - Cephalexin, cephradine or amoxicillin
  - 2.0 grams PO one hour before

- Penicillin allergy—
  - Clindamycin 600 mg (PO or IV) one hour before

**Consider Azithromycin 500 mg PO one hour before**
**AAOS Unilateral Statement**

- “Antibiotic Prophylaxis for Bacteremia in Patients with Joint Replacements”
  - Released February 2009, updated November 2010
  - Recommended AP for all TJR patients prior to any invasive procedure that causes bacteremia
  - Failed to provide ongoing guidance for “penicillin-allergic” individuals

[www.aaos.org/about/papers/advistmt/1033.asp](http://www.aaos.org/about/papers/advistmt/1033.asp)

**AAOM Rebuttal Statement**

- “The Dental Treatment of Patients with Joint Replacements—A position paper from the American Academy of Oral Medicine”
  - Released just after the new AAOS guideline
  - Concluded: The new AAOS position should not replace the 2003 joint consensus statement
  - Implications: Until resolved, dentists have 3 options—
    - Inform patients about AP risk and let them decide
    - Individually follow the 2003 guidelines
    - Suggest to the orthopedist that both parties follow the 2003 guidelines

[JADA 2010; 141:667-671](http://jada.ada.org/content/141/7/667)
New 2012 Practice Guidelines

- “Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures”
  - Joint AAOS/ADA statement released 12-18-2012
  - 17 review organizations, 140 citations, 3 new clinical guideline recommendations
  - Replaces 2009 AAOS “Informational Statement”
  - Conclusions—
    - Evidence insufficient to recommend routine antibiotics for joint replacement patients undergoing dental procedures
    - No direct evidence that routine dental procedures cause prosthetic joint infections

2012 AAOS/ADA Recommendations

- Consider discontinuing routine prophylactic antibiotics for dental patients with hip/knee TJR
- The routine use of oral antimicrobials in TJR patients prior to dental procedures shows no clear benefit-to-risk advantage
- Without evidence linking poor oral health to prosthetic joint infection, TJR patients should maintain appropriate oral hygiene
CV Implantable Devices

- “Summary of the Update on Cardiovascular Implantable Electronic Device Infections and their Management”
  - AP is not recommended for dental or other invasive procedures to prevent CIED infections

JADA 2011;142(2):159-165
Wrap up Recommendations

- Must record AP in patient record—
  - Any premed indications
  - Any physician consult if one done
  - That patient took antibiotic
  - When patient took antibiotic
  - What antibiotic taken and at what dosage

"Don’t assume anything!"

Questions???

- Will TJR guidelines change again?
- Are we to use the same list of dental procedures requiring coverage for TJR as published in 2003?
- What if a MD wants us to keep on using the 1997 AHA IE/SBE guidelines?
- What if a patient who has been using the 2003 guidelines wants us to cover them with the 2010 AAOS recommendation?
Answers

- TJR guidelines: Appears that we are still “obligated” to use the old 2003 guidelines despite new guidelines.
- If an MD insists on using old guidelines (after you sent him/her the new)— have the MD write the script and document in the patient record.
- For patients wanting to use old guidelines—advise your patients, give them a copy of the new guidelines and stick by your guns on this one.
- It is going to take a couple of years to train your patients (and especially) the MDs. You take the initiative.

Summary

- Finally getting common sense involved
- New regimens are more realistic for the dental profession
- The numbers of consults will decrease
- With the growing trend of antibiotic resistance, look for further diminution or even elimination of prophylaxis
- Stay tuned for future changes and updates
AHA GUIDELINES FOR PREVENTION OF INFECTIVE ENDOCARDITIS (2007)

TABLE 1: Cardiac conditions associated with high risk of adverse outcomes from endocarditis for which prophylaxis with dental procedures is recommended:

1) Prosthetic cardiac valve
2) Previous infective endocarditis
3) Congenital heart disease (CHD)
   a. Unrepaired cyanotic CHD, including shunts and conduits
   b. Completely repaired CHD with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure.
   c. Repaired CHD with residual defects at the site or adjacent to the site of prosthetic patch or prosthetic device.
4) Cardiac transplantation patients who develop cardiac valvulopathy.

TABLE 2: Dental procedures for which endocarditis prophylaxis is recommended for patients in Table 1 (above):

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

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

TABLE 3: Regimens for antibiotic prophylaxis

<table>
<thead>
<tr>
<th>Situation</th>
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<th>Regimen Single Dose 30-60 minutes before procedure</th>
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<td>Amoxicillin</td>
<td>2 g</td>
<td>50 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Unable to take oral Medication</td>
<td>Ampicillin OR</td>
<td>2 g IM or IV*</td>
<td>50 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefazolin OR</td>
<td>1 g IM or IV</td>
<td>50 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriazone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin Oral</td>
<td>Cephalaxin**† 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</td>
<td>500 mg</td>
<td>15 mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin and unable to take oral medication</td>
<td>Cefazolin OR</td>
<td>1 g IM or IV</td>
<td>50 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ceftriaxone† OR</td>
<td>600 mg IM or IV</td>
<td>20 mg/kg IM or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td></td>
<td></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 ampicillins.
## 2011 RX on the Market

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug</th>
<th>Drug</th>
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<tbody>
<tr>
<td>Aspirin</td>
<td>Plavix</td>
<td>Pletal</td>
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<tr>
<td>Reopro</td>
<td>Ticlid</td>
<td>Integrlin</td>
</tr>
<tr>
<td>Angiomax</td>
<td>Activase</td>
<td>Coumadin</td>
</tr>
<tr>
<td>Effient*</td>
<td>Fragmin</td>
<td>Lovenox</td>
</tr>
<tr>
<td>Pradaxa*</td>
<td>Orgaran</td>
<td>Heparin</td>
</tr>
<tr>
<td>Streptase</td>
<td>TPA</td>
<td>TNKase</td>
</tr>
</tbody>
</table>

*Recent

## Implications in Dentistry

1. Our patients can bleed excessively!
2. Anticoagulants can react (predictably or unpredictably) with meds we Rx or those our patients already take: OTC/herbals/Rx
3. Why: What is the underlying disease for these anticoagulants?
Why our Patients Use

- CVA/Stroke-**long term**
- CAHD/Anti-arrhythmias-**long term**
- Thrombophlebitis-**short term**
- DVT-**short term**
- Post Surgery (Heart valve and TJR)-**short and long term**
- Hemodialysis-**long term**

Anticoagulant Categories

1. Direct Acting: Heparin
2. Direct Acting: Low molecular weight heparins
3. Indirect Acting: Coumarins
4. Platelet Inhibitors: ASA, etc.
5. Thrombin inhibitor (Newest)
**Time Summary**

- **1 to 2 seconds**: Platelet adhesion, Exposed subendothelium
  - ADR thromboxane

- **10 to 20 seconds**: Platelet aggregation, Platelet release
  - Thrombin

- **1 to 3 minutes**: Platelet plug, Fibrin formation

- **3 to 5 minutes**: Consolidation, Retraction
  - Fibrin stabilization

**Coagulation Pathways**

- **Contact activation** starts the intrinsic pathway
- **Tissue thromboplastin** starts the extrinsic pathway

- **Common pathway**
  - Activated X
  - IX
  - VIII

- **Intrinsic Pathway**
  - Factor IX
  - FIX
  - FVII
  - FVIII
  - FIX

- **Extrinsic Pathway**
  - FVIII
  - FVII
  - FIX
  - FVIII

- **Fibrin clot**
Heparin Anticoagulation

- Strongest organic acid in body.
- Produced from mast cells. Harvested from beef/porcine lungs and GI tissue.
- Must be formulated into heparin sulfate.
- Does NOT break down existing clots.

Heparin Anticoagulant

- **Anticoagulant mechanism:**
  Binds with antithrombin III: which accelerates the rate at which antithrombin III inactivates factors XIIa, Xla, Xa, IXa, VIII and V.
  Inactivates thrombin itself.
Heparin Statistics

- Must be given intravenously or SubQ.
- Cannot be given intramuscularly.
- Short half life of 1 to 3 hours.
- Monitored by aPTT (PTT)
- Reversal agent: protamine sulfate

Hemodialysis AV Fistula
Heparin and Dental Tx

• **NO** routine dental treatment!!
• **Medical consult a MUST**
• Better managed by OMFS.
• Better managed in hospital setting.

LMW Heparin

• Low molecular weight heparins:
  - **Lovenox** (enoxaparin)
  - **Normiflo** (ardeparin)
  - **Arixtra** (fondaparinux)

  More “long-term” than conventional heparin. Can be given every 12 hours by self injection subQ
**LMW Heparin**

- **Indications**: Prevention of DVT usually after TJR of knees and hips
- Severe CV disease patients
- Use is increasing: especially in a protocol when stopping coumadin therapy for oral surgery.
- **Length of treatment**: Usually can be given for 14 days post operative
- Medical consult is a MUST

**Coumarin Anticoagulants**

- **Coumadin (Warfarin)**
- **Actions**: Competitively inhibits Vitamin K which is essential for the synthesis of factors II, VII, IX, and X in the liver
Coumadin Statistics

• Given PO
• Long half-life (1 to 2 days)
• Monitored by INR and PT
• Antidote: Vitamin K
• #36 Rx med in 2010

Coumadin Uses

• “Less” critical anticoagulation
• Longer term therapy than heparin
• Atrial fibrillation
• Pulmonary disease
• Post cardiac surgery (valves)
• Post TJR surgery
• Congestive heart failure
Coumadin and Dental Tx

• Consult a MUST if invasive dental treatment planned: ask why?
• Medical risk versus dental treatment issues (????)
• Lab values: know current INR status or most recent “trends”

Laboratory Tests

• Prothrombin Time (PT)
• International Normalized Ratio (INR)

These two lab tests are the MOST common way to evaluate current status of anticoagulation.
Laboratory Tests

• **PT:** Normal control is 12-15 seconds
  1.5 to 2 times normal for adequate hemostasis for dental procedures.

• **INR:** Normal is 1.0
  3.0-3.5 is adequate hemostasis for most dental procedures.

Laboratory Tests

• **GOAL**— Establish a level of anticoagulation that will provide minimum thrombosis risk and achieve workable hemostasis for required dental procedures.

• A compromise !!!!!
Coumadin Therapeutic Levels

- Treatment of venous thrombosis
  Range of 2.0-3.0
- Prevention of pulmonary embolism
  Range of 2.0-3.0
- Prevention of systemic embolism
  Range of 2.0-3.0
- Prosthetic heart valves: 2.3-3.5

Prosthetic Valve Patients

- **Location**: Aortic usually requires more anticoagulation than mitral.
- **Type**: Caged ball usually requires more anticoagulation than bi-leaflet.
- Keep INR at 3.0-3.5
AFib Patients

- Kept at INR 1.5-2.0
- 17 times greater risk of stroking when INR at 1.0.
- If below 3.5 do not alter for “routine” dentistry.

Current INR????

- *Ideally* test on day of surgery if altering schedule
- Look at past compliance
- YOU NEVER take patient off coumadin unilaterally (yourself)
**INR and Dental Treatment**

- “Routine” dentistry: *NO* need to modify 3.5 and under
- Periodontal surgery: *NO* need to modify 3.5 and under
- Scaling and curettage: *NO* need to modify 3.5 and under

**Coumadin Interactions**

- Herbal medicines - *increase*
- Alcohol – *increase/decrease*
- Analgesics - *increase*
- Antidepressants - *increase*
- Antimicrobials - *increase*
- Diuretics - *increase*
Specific Interactions

• Alternative Herbal Meds:
  CQ10       Ginseng
  Garlic     Ginger
  Ginko biloba “Others”

• Analgesics:
  ASA/ NSAIDS     Propoxyphene
  Acetaminophen   Coxibs – very little

Specific Interactions

• Antimicrobials:
  E-mycin         Miconazole
  Clindamycin     Tetracyclines
  Metronidazole

• Antidepressants: Tricyclics/SSRI’s

• Diuretics: Thiazides
Platelet Inhibitors

- Usually related to acetylation of COX resulting in decreased platelet ADP release and secondary aggregation
- Vary in strength and length of action
- Vary in permanency of inhibition

Platelet Phase

- Platelets “swarm” to injured vessel—primary platelet aggregation
- “Sticky” plug formed by platelets sticking to each other—secondary platelet aggregation
- Begins seconds after injury
Platelet Inhibitors

**INDICATIONS:**
- History of CAHD
- Post angioplasty or cardiac stents
- Post TIA/CVA
- Post TJR

IIb/IIIa Inhibitors
- **Plavix** (clopidogrel) - tabs
- **Effient** (prasugrel) – tabs/new**
- **Reopro** (abciximab) – injection
- **Brilinta** (ticagrelor) – newest/more potent
- **Cangrelor** – injection/ very short half-life

Combined with aspirin
- **Aggrenox** (dipyridamole) - tabs
**Clopidogrel (Plavix)**

- Blocks ADP receptors—*inhibits* platelet aggregation
- Has a slow onset (takes 3-5 days unless a loading dose of 300-600 mg is given)
- Platelet function is *normal 5-7 days after discontinuation*
- Patients on both ASA and Plavix—can discontinue Plavix *but not ASA*
- 2009: #3 Rx in terms of $$ ($5.5 billion) and #7 in total prescriptions (26.5 million)

**Plavix “Black Box” Warning**

- **FDA (3/2010)—new warning that Plavix can be less effective in “poor metabolizers”**
- Poor Metabolizer: 2% to 14% of patients
- Variant of *CYP2C19* gene associated with poor metabolism of the drug (7 different variants)
- Platelet function testing produces *8X decrease* in stent thrombosis

Eur J Cardio; MADONNA study; 2012
Platelet Inhibitors and Dentistry

- **NO** specific lab test (bleeding time versus POC platelet function testing)
- Remember the **duration** of action
- Generally **NOT** as potent as coumadin
- Tend to “ooze more”

Thrombin Inhibitors

[Diagram of thrombin inhibitor pathways]

Ann Thorac Surg 2012;94;1761-1781
Thrombin Inhibitors

- **Pradaxa** *(dabigatran etexilate)*
- *Newest kid on the block*
- Developed because of the many side effects, dosing problems and drug interactions of coumadin
- Primary use: reducing risk of stroke and systemic embolism in patients with non-valvular **atrial fibrillation**

Pradaxa

- **Mechanism of action**: Categorized as a direct thrombin inhibitor. Thrombin (Xa) is necessary for the *conversion of fibrinogen to fibrin* in the coagulation cascade. This in turn inhibits the development of a thrombus.
- **Normal dosage**: 75mg twice a day
- **Drug interactions**: Not many (some antifungals)
Pradaxa

• **Surgery and interventions**: If possible discontinue 2 days before invasive or surgical procedures and begin day after.
• However, like coumadin, you must weigh risks of thrombus formation versus need for hemostasis *(Be careful)*.
• Unlike coumadin, no specific lab test to monitor and drug has not been around long enough to gage. Recommend ????

Rivaroxaban (Xarelto®)

• Rivaroxaban is an *oral Factor Xa inhibitor*
  – Blocks the active site of factor Xa and does not require a cofactor like antithrombin III
• Indication
  – Prophylaxis of DVT in patients undergoing knee or hip surgery replacement
  – 11/4/11: FDA approved rivaroxaban for prevention of stroke and systemic embolism in non-valvular atrial fibrillation
Xa Inhibitors and Dentistry

• **Laboratory Testing:** Thrombin clotting time (TT) or aPTT for those patients exhibiting bad bleeding—sensitivity questionable

• **Adverse Reactions:** Nausea/dyspepsia is primary followed by excess bleeding

• **Interactions:** Antifungals, herbals (bilberry, alfalfa), ASA, verapamil, grapefruit increase bleeding

• Phenytoin and St. John Wort – decrease bleeding

Anticoagulant Summary 1

• Good medical and Rx history

• Medical consult??

• *MUST* consider the seriousness of underlying medical condition

• Categorize *BOTH* medications and proposed dental treatment

• You *do NOT* take them off meds
Anticoagulant Summary 2

• “Stopping antiplatelet medications prior to a surgical procedure places a patient at greater risk of permanent disability or death than continuing the therapy, specifically increasing the risk thromboembolism, MI and cerebral vascular accident.”*
• *Aubertin MA, Gen Dent, May/June 2008

Anticoagulant Summary 3

• Keep these patients in the dental chair 10 to 15 minutes longer than normal—good initial hemostasis is your best friend
• Gelfoam and/or topical thrombin
• Infiltrate local with epinephrine 1:50000
• Thorough post-operative instructions
• Call patient that evening—keeps you sleeping better
• Be prepared— you will see more each year.