NEW STRATEGIES FOR TARGETING ANTIBIOTIC USE IN CLINICAL DENTISTRY
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I. TARGETED INDICATIONS IN DENTAL PRACTICE

A. Therapeutic Indications

1. Acute cellulitis of dental origin
2. Acute pericoronitis with elevated temperature and trismus
3. Deep fascial space infections
4. Open fractures of the mandible and maxilla
5. Extensive, deep, or old (>6 hours) orofacial lacerations
6. Dental infection or oral surgery in the compromised host

B. Prophylactic Indications

1. Valvular heart disease
2. Prosthetic heart valve
3. Intravascular access device in place
4. Prosthetic joint replacement (first two years)

II. TARGETED PATIENTS AT INCREASED RISK OF OROFACIAL INFECTIONS

A. Patient-Specific Risk Factors

1. Immunocompromised by drug therapy or disease process
   a. drug therapy – methotrexate, cyclophosphamide, prednisone hydroxychloroquine, cyclosporine A, etc.
   b. disease process – SLE, rheumatoid arthritis, malnutrition, neoplastic disease, poor glycemic control in diabetics (A1c > 8%)

2. Impaired by trauma, surgery, reduced circulation, or implanted device
   a. hematomas and scar tissue – promote bacterial proliferation
   b. reduced circulation – may prevent antibiotic from reaching site
   c. implanted devices – intravascular devices are the leading cause of nosocomial infections and increase risk of endocarditis in some cases

3. Renal Insufficiency
   a. Tetracycline and minocycline are contraindicated in renal failure
   b. Dosage reduction necessary for amoxicillin, cefuroxime, cephalaxin, and fluoroquinolones
   c. No dosage reduction necessary for azithromycin, cefaclor, clindamycin, dicloxacillin, doxycycline, erythromycin, metronidazole
4. Diabetic Glycemic Control

**Correlation Between A1c and Mean Plasma Glucose**

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>Mean plasma glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>126mg/dl</td>
</tr>
<tr>
<td>7</td>
<td>154mg/dl</td>
</tr>
<tr>
<td>8</td>
<td>183mg/dl</td>
</tr>
<tr>
<td>9</td>
<td>212mg/dl</td>
</tr>
<tr>
<td>10</td>
<td>240mg/dl</td>
</tr>
<tr>
<td>11</td>
<td>269mg/dl</td>
</tr>
<tr>
<td>12</td>
<td>298mg/dl</td>
</tr>
</tbody>
</table>

Patient Risks Increased

**Importance of Glycemic Control in Dental Patients**

- Prevention of hyperglycemia
- Nonketotic hypertonicity/ketoacidosis
- Impaired wound healing
- Increased risk of oral infection
- Delayed gastric emptying could lead to aspiration during a procedure
- Prevention of hypoglycemia

5. Medico Legal Issues in Antibiotic Prescribing- *JADA April 2004 and January 2012*

**Reasons Why Antibiotics Fail**

- Inadequate drainage or debridement
- Antibiotic does not reach infection site
- Physical obstruction or open access
- Systemic disease alters host response
- Foreign body reaction
- Patient noncompliance
- Inadequate dose or duration
- Wrong antibiotic is chosen
- Development of bacterial resistance
- Concomitant therapy interferes

**Pitfalls in Antibiotic Prescribing**

- Antibiotic adverse effects not considered
- Cost of antibiotic not considered
- Rapid and inappropriate therapy changes
- Patient is not counseled or monitored
- Trying to treat viral infections
- Inappropriate drug or dosage selection
- Infecting agent not documented
- Failure to correct contributing factors
III. TARGETED ANTIBIOTIC SELECTION

A. Mechanism of action and spectrum of activity

**BACTERIOSTATIC**
- Tetracyclines
- Sulfonamides
- Macrolides
- Clindamycin (static/Cidal)

**BACTERICIDAL**
- Penicillins
- Cephalosporins
- Metronidazole
- Fluoroquinolones

**SPECTRUM OF ACTIVITY**
- Narrow
  - Penicillin VK
  - Erythromycin
  - Clindamycin
- Extended
  - Amoxicillin
  - Cephalosporins
  - Fluroquinolones
- Broad
  - Tetracyclines
  - Sulfonamides
  - Metronidazole
  - Fluroquinolones

B. Activity Against Common Oral Pathogens

<table>
<thead>
<tr>
<th>Aerobic Bacteria</th>
<th>Frequency</th>
<th>Anaerobic Bacteria</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci</td>
<td></td>
<td>Gram-negative bacilli</td>
<td></td>
</tr>
<tr>
<td>Streptococcus Viridans</td>
<td>very common</td>
<td>Peptostreptococcus</td>
<td></td>
</tr>
<tr>
<td>B-Hemolytic</td>
<td>unusual</td>
<td>Porphyromonas (Bacteroides)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>rare</td>
<td>Prevotella (Bacteroides)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fusobacterium</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacteroides fragilis</td>
<td></td>
</tr>
</tbody>
</table>

1. The typical odontogenic infection is composed of a mix of aerobic and anaerobic species
2. The timeline of infection may show: AEROBES-------MIXED-------ANAEROBES.
3. Obtain cultures & sensitivities for: antibiotic failures, recalcitrant infections, suspected osteomyelitis, impaired host defenses, post-op wound infections, etc.

IV. ANTIBIOTIC THERAPY GUIDELINES

A. Antimicrobial prescribing in the USA is 80% empirical therapy.

1. Target causative organism -empirical or lab
2. Patient drug and medical history - ALLERGIES vs ADVERSE REACTIONS??
3. Patient counseling - adverse effects, compliance, therapeutic endpoints, cost
4. Positive response expected in 48 hours, continue therapy 72 hours after symptom resolution
5. Combination therapy: 3 possible effects - indifferent (additive) - synergism – antagonism
   - Cidal + Cidal or Static + Static
6. Best combination: penVK qid + metronidazole qid, or amoxicillin tid + metronidazole tid

V. ANTIBIOTIC CLASSES

A. ORAL PENICILLINS – FDA Pregnancy Category B

<table>
<thead>
<tr>
<th>Classification</th>
<th>t(^1/2) (h)</th>
<th>OK with food?</th>
<th>Pediatric Dose</th>
<th>Activity against oral pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gm'</td>
<td>Aerobes</td>
</tr>
<tr>
<td>Natural</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>1</td>
<td>no</td>
<td>150-250 U/kg/d</td>
<td>+</td>
</tr>
<tr>
<td>Penicillin VK</td>
<td>1</td>
<td>yes</td>
<td>25-50mg/kg/day</td>
<td>+</td>
</tr>
<tr>
<td>Penicillinase-Resistant</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>.75</td>
<td>no</td>
<td>12-25mg/kg/day</td>
<td>staph only</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>.75</td>
<td>no</td>
<td>37mg/kg q 6h</td>
<td>staph+strep</td>
</tr>
<tr>
<td>Aminopenicillins</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1.5</td>
<td>yes</td>
<td>40-50mg/kg/day</td>
<td>+</td>
</tr>
<tr>
<td>Amox/potassium clavulanate (Augmentin,G)</td>
<td>1.5</td>
<td>yes</td>
<td>40-45mg/kg/day</td>
<td>+</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1.5</td>
<td>no</td>
<td>50-100mg/kg/day</td>
<td>+</td>
</tr>
</tbody>
</table>

**ORAL PENICILLINS USEFUL IN DENTISTRY**
1. INDIVIDUAL AGENTS

Amoxicillin advantages over penicillin
- more complete absorption
- longer duration of activity
- TID administration

Amoxicillin disadvantages over Pen VK
- broader spectrum
- poor anaerobe activity
- more side effects/less efficacy

2. ADVERSE EFFECTS

Hypersensitivity

- 3 - 10 % of population is allergic to penicillins (more frequently with IV/IM than PO route)
- IgE Mediated acute reaction - PCN binds to protein and acts as a hapten to which Ab develop
- True anaphylactic reactions to penicillin are 1/7,000 to 1/25,000 instances of PCN use
  * mortality occurs once in every 50,000 - 60,000 treatment courses
  * sx. begin 10-20 min. after ingestion, antihistamines are of little effect
- Cross-reactivity to cephalosporins occurs in 3-5% of patients
  * Cephalosporins are contraindicated with pt history of severe or immediate penicillin reaction (urticaria, angioedema, anaphylaxis)

3. DRUG INTERACTIONS

Bacteriostatic antibiotics
Oral contraceptives
Methotrexate

B. ORAL CEPHALOSPORINS – FDA Pregnancy Category B

<table>
<thead>
<tr>
<th>Classification</th>
<th>t1/2 (min)</th>
<th>OK with food?</th>
<th>Pediatric Dose</th>
<th>activity against oral pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gm+</td>
</tr>
<tr>
<td>First Generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalexin (Keflex, g)</td>
<td>50-80</td>
<td>yes</td>
<td>25-50mg/kg/d (4)</td>
<td>+</td>
</tr>
<tr>
<td>Cefadroxil (Duricef, Ultracef, g)</td>
<td>78-96</td>
<td>yes’</td>
<td>30mg/kg/day (1)</td>
<td>+</td>
</tr>
<tr>
<td>Cephadrine (Anspor, Velosef, g)</td>
<td>48-80</td>
<td>yes</td>
<td>25-50mg/kg/day (4)</td>
<td>+</td>
</tr>
<tr>
<td>Second Generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefaclor (Ceclor, G)</td>
<td>35-54</td>
<td>yes</td>
<td>20-40mg/kg/day (3)</td>
<td>+</td>
</tr>
<tr>
<td>Cefuroxime (Ceftin, G)</td>
<td>80</td>
<td>yes’</td>
<td>10-15mg/kg bid (2)</td>
<td>+</td>
</tr>
<tr>
<td>Cefprozil (Cefzil, G)</td>
<td>78</td>
<td>yes’</td>
<td>15-30mg/kg/day (2)</td>
<td>+</td>
</tr>
<tr>
<td>Loracarbef (not available now)</td>
<td>60</td>
<td>no</td>
<td>15-30mg/kg/day (2)</td>
<td>+</td>
</tr>
<tr>
<td>Third Generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefdinir (Omnicef)</td>
<td>100</td>
<td>yes</td>
<td>14mg/kg/day (1-2)</td>
<td>+</td>
</tr>
<tr>
<td>Cefixime (Suprax)</td>
<td>180-240</td>
<td>yes</td>
<td>8mg/kg/day (1-2)</td>
<td>+</td>
</tr>
<tr>
<td>Cefpodoxime (Vantin)</td>
<td>120-180</td>
<td>yes’</td>
<td>10mg/kg/day (2)</td>
<td>+</td>
</tr>
<tr>
<td>Cefditoren (Spectracef)</td>
<td>144</td>
<td>no</td>
<td>4.5mg/kg bid</td>
<td>+, -</td>
</tr>
</tbody>
</table>

1. INDIVIDUAL AGENTS

1st generation: best gram + coverage of all cephalosporins
2nd generation: best anaerobe coverage of all cephalosporins
3rd generation: oral agents provide NO oral anaerobe activity

2. ADVERSE EFFECTS

Hypersensitivity
Oral candidiasis

3. DRUG INTERACTIONS

Bacteriostatic antibiotics
Anticoagulants
Antacids, H2 blockers, PPIs (cefdinir, cefuroxime)
C. ORAL MACROLIDES – FDA Pregnancy Category B (except Biaxin)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Tpeak(h)</th>
<th>OK with food?</th>
<th>Pediatric Dose</th>
<th>activity against oral pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin Base</td>
<td>3</td>
<td>no</td>
<td>30-40mg/kg/day</td>
<td>+</td>
</tr>
<tr>
<td>Boots E-Mycin (EC)</td>
<td>6</td>
<td>yes</td>
<td>(3-4)</td>
<td>-</td>
</tr>
<tr>
<td>Abbott Ery-Tab (EC)</td>
<td>3f, 2nf</td>
<td>yes</td>
<td>(3-4)</td>
<td>-</td>
</tr>
<tr>
<td>Abbott PCE (PC)</td>
<td>3</td>
<td>no?</td>
<td>(3-4)</td>
<td>-</td>
</tr>
<tr>
<td>P-D ERYC (EC)</td>
<td>3</td>
<td>no</td>
<td>(3-4)</td>
<td>-</td>
</tr>
<tr>
<td>Erythromycin Ethylsuccinate</td>
<td>2</td>
<td>yes</td>
<td>Base dose x 1.6</td>
<td>+</td>
</tr>
<tr>
<td>Erythromycin Stearate</td>
<td>3</td>
<td>no</td>
<td>30-40mg/kg/day</td>
<td>+</td>
</tr>
<tr>
<td>Azithromycin (Zithromax,g)</td>
<td>2-3</td>
<td>Caps-no</td>
<td>Day 1: 10mg/kg</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tabs-yes</td>
<td>Days 2-5: 5mg/kg</td>
<td>+,-</td>
</tr>
<tr>
<td>Clarithromycin (Biaxin,g) Preg C</td>
<td>1.7</td>
<td>yes</td>
<td>15mg/kg/day (1-2)</td>
<td>+</td>
</tr>
<tr>
<td>Dirithromycin (Dynabac,g)</td>
<td>6</td>
<td>yes</td>
<td>Not given</td>
<td>+</td>
</tr>
</tbody>
</table>

1. INDIVIDUAL AGENTS

Clarithromycin (Biaxin) advantages over erythromycin base:
- 3% GI irritation as opposed to 30% for older agents, BID dosing
- better activity against S. pyogenes than erythromycin, cefaclor or doxycycline
- better anaerobe coverage than erythromycin
- pregnancy C classification by FDA

Azithromycin (Zithromax): 2-4 fold less active than erythromycin against most strains of strep., no risk of QT interval prolongation. Azalide has limited drug interactions compared to macrolides

Dirithromycin (Dynabac): same as erythromycin base but once daily

2 ADVERSE EFFECTS

Cholestatic jaundice (estolate salt = Ilosone)  Taste disturbances (Clarithromycin)
Gastrointestinal disturbances  Oral candidiasis

3. DRUG INTERACTIONS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Carbamazepine</th>
<th>Ergotamine</th>
<th>CCBs (diltiazem, verapamil)</th>
<th>“Statins”</th>
<th>Cyclosporine</th>
<th>Theophylline</th>
<th>Bromocriptine</th>
<th>Disopyramide</th>
<th>Tolterodine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfentanil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiocoagulants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azole antifungals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bromocriptine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

D. ORAL FLUOROQUINOLONES – FDA Pregnancy Category C

<table>
<thead>
<tr>
<th>Drug*</th>
<th>t1/2 (h)</th>
<th>OK with food?</th>
<th>Usual Adult Dose</th>
<th>activity against oral pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gm’ Aerobes</td>
</tr>
<tr>
<td>Ciprofloxacin (Cipro, G)</td>
<td>5</td>
<td>yes</td>
<td>500mg bid</td>
<td>-</td>
</tr>
<tr>
<td>Gemifloxacin (Factive,G)</td>
<td>7</td>
<td>yes</td>
<td>320mg qd</td>
<td>+</td>
</tr>
<tr>
<td>Levofloxacin (Levaquin,G)</td>
<td>8</td>
<td>yes</td>
<td>500mg q24 h</td>
<td>++</td>
</tr>
<tr>
<td>Moxifloxacin (Avelox,G)</td>
<td>10</td>
<td>yes</td>
<td>400mg qd</td>
<td>+</td>
</tr>
<tr>
<td>Norfloxacin (Noroxin)</td>
<td>6</td>
<td>no</td>
<td>400mg q 12h</td>
<td>-</td>
</tr>
<tr>
<td>Ofloxacin (Floxin)</td>
<td>8</td>
<td>yes</td>
<td>400mg q12h</td>
<td>+,-</td>
</tr>
</tbody>
</table>

*not indicated for children or adolescents except for cystic fibrosis
1. ALL FLUOROQUINOLONES HAVE A BLACK BOX WARNING FOR ACHILLES TENDON RUPTURE!!

2. ADVERSE EFFECTS
   Arthropathies: contraindicated for children, adolescents, pregnant or lactating women
   CNS stimulation/toxicity
   Gastrointestinal disturbances
   Photosensitivity-worst with sparfloxacin
   QT interval prolongation risk

3. DRUG INTERACTIONS
   Antacids (Fe, sucralfate, zinc)
   Antiarrhythmics (Spar)
   Anticoagulants
   Antineoplastics
   Cimetidine
   Cyclosporine
   NSAIDS (increased CNS stimulation)
   Probenecid
   Theophylline
   Caffeine (Cipro)

E. MISCELLANEOUS AGENTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>t1/2 (h)</th>
<th>OK with food?</th>
<th>Pediatric Dose</th>
<th>activity against oral pathogens</th>
<th>activity against oral pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aerobes</td>
<td>Anaerobes</td>
</tr>
<tr>
<td>Clindamycin (Cleocin,g) FDA B</td>
<td>2</td>
<td>yes</td>
<td>15-30mg/kg/day (3-4)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Metronidazole (Flagyl,g) FDA B</td>
<td>8</td>
<td>yes</td>
<td>30mg/kg/day (3-4)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>6-12</td>
<td>no</td>
<td>25-50mg/kg/d (4)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Tetracycline HCL(Sumycin,g)</td>
<td>15-25</td>
<td>yes</td>
<td>2-4mg/kg/day (2)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Minocycline (Minocin,g)</td>
<td>11-18</td>
<td>yes</td>
<td>4mg/kg x 1 day, 2mg/kg/day</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

1. CLINDAMYCIN is Pregnancy Category B
   a). Cross-reaction with erythromycins because they are all “mycins”??
   b). Adverse effects:
      Gastrointestinal disturbances
      Morbilliform skin eruptions
   c)BLACK BOX WARNING: Clostridia Difficile Induced Colitis (CDIC)
      caused by overgrowth of Clostridia difficile which produces a toxin
      Four requirements for CDIC:
      1. Presence of Clostridia difficile in GI tract
      2. Altered gastrointestinal flora
      3. Presence of Toxin A and B
         - must have toxin receptors in gut
      4. Predisposing factors
         * potential adverse effect of all antimicrobial agents - especially ones that affect obligate anaerobes (ampicillin, Augmentin, cephalosporins)
         * S/Sx: profuse, watery diarrhea 1-20 times/day, bloody diarrhea in 5-10 % of cases, foul smelling, abdominal cramping, nausea, fever and leukocytosis
         * risk factors: recent hospitalization, recent broad-spectrum antibiotic use, history of colitis, advanced age, recent instrumentation of lower bowel
   d). Drug interactions
      Succinylcholine Erythromycin Kaolin-Pectin

2. METRONIDAZOLE
   a.) BLACK BOX WARNING: Metronidazole has been shown to be carcinogenic when given chronically to rats and mice. Avoid use in children except for approved indication (amebiasis).
b.) Adverse effects – taste disturbances, peripheral neuropathy, GI irritation
   - mutagenic effect demonstrated with in vitro assays as well

c.) Interaction with ethanol and disulfiram (Antabuse) may lead to gastrointestinal distress and N/V.
   Avoid alcohol during and for 1 day after discontinuing metronidazole. Preg Category B

d). Drug interactions
   | Anticoagulants | Disulfiram | Ethanol (IV diazepam, IV SMZ/TMP) |
   | Lithium       | Phenytoin  |                             |

3. TETRACYCLINES
a). Adverse effects
   - Esophageal ulceration
   - Toxicity - outdated tetracycline
   - Pregnancy – hepatotoxicity. Pregnancy Category D due to pediatric tooth discoloration

b). Drug interactions
   | ALL TETRACYCLINES | DOXYCYCLINE | TETRACYCLINE |
   | Antacids, bismuth | Phenobarbital | Food (milk, dairy) |
   | Iron salts        | Phenytoin    | Cholestiplol   |
   | Oral contraceptives |            | Zinc sulfate   |

c). Periodontal infections
   Advantages in periodontal infections:
   - high concentration in GCF
   - good activity against A.A
   - binds to root surfaces
   - anticollagenase activity

d). Periodontal abscesses – tetracyclines are NOT the drugs of choice

e). Compliance considerations: cost, GI irritation, doses per day

4. OXALODINONES – Linezolid (Zyvox) 400mg and 600mg tablets
a) reserved for resistant gram positive pneumonias and CA-MRSA
b) NOT effective for oropharyngeal anaerobes

F. PATIENT-SPECIFIC ANTIBIOTIC SELECTION CRITERIA

1. History of allergy to penicillin
   a. Avoid all penicillins
   b. Avoid cephalosporins if hives, angioedema, anaphylaxis, or unknown history is reported

2. History of antibiotic-associated diarrhea
   a. Use narrow spectrum agent if possible- consider flora support with Florajen3 probiotic supplement
      Best choice is pen VK with/without metronidazole
   b. Avoid 2nd and 3rd generation cephalosporins
   c. Avoid clindamycin and amoxicillin/clavulanic acid (Augmentin,G)

3. Inadequate response to penicillin VK
   a. Add metronidazole 1000-2000mg/day in four divided doses to pen VK
   b. Stop pen VK and initiate clindamycin 300mg qid or q 6h.
   c. Stop pen VK and initiate Augmentin 500/125 tid or q 8h.

4. Allergy or intolerance to penicillins, cephalosporins, macrolides, clindamycin
   a. Reserve agents include levofloxacin or moxifloxacin
   b. May combine fluoroquinolone with metronidazole for resistant anaerobic infections

5. Patient may be pregnant
   a. Use penicillins, cephalosporins, clindamycin
   b. Avoid clarithromycin, all fluoroquinolones and tetracyclines
   c. Macrolides may be too hard on gut