ATB in dentistry

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Bacterial flora causing most odontogenic infections

- Microorganisms associated with odontogenic & periodontal infections **are well characterized:**

➢ **Bacterial:**

❖ aerobes

❖ anaerobes (75%)

➢ **Fungal:**

❖ candida

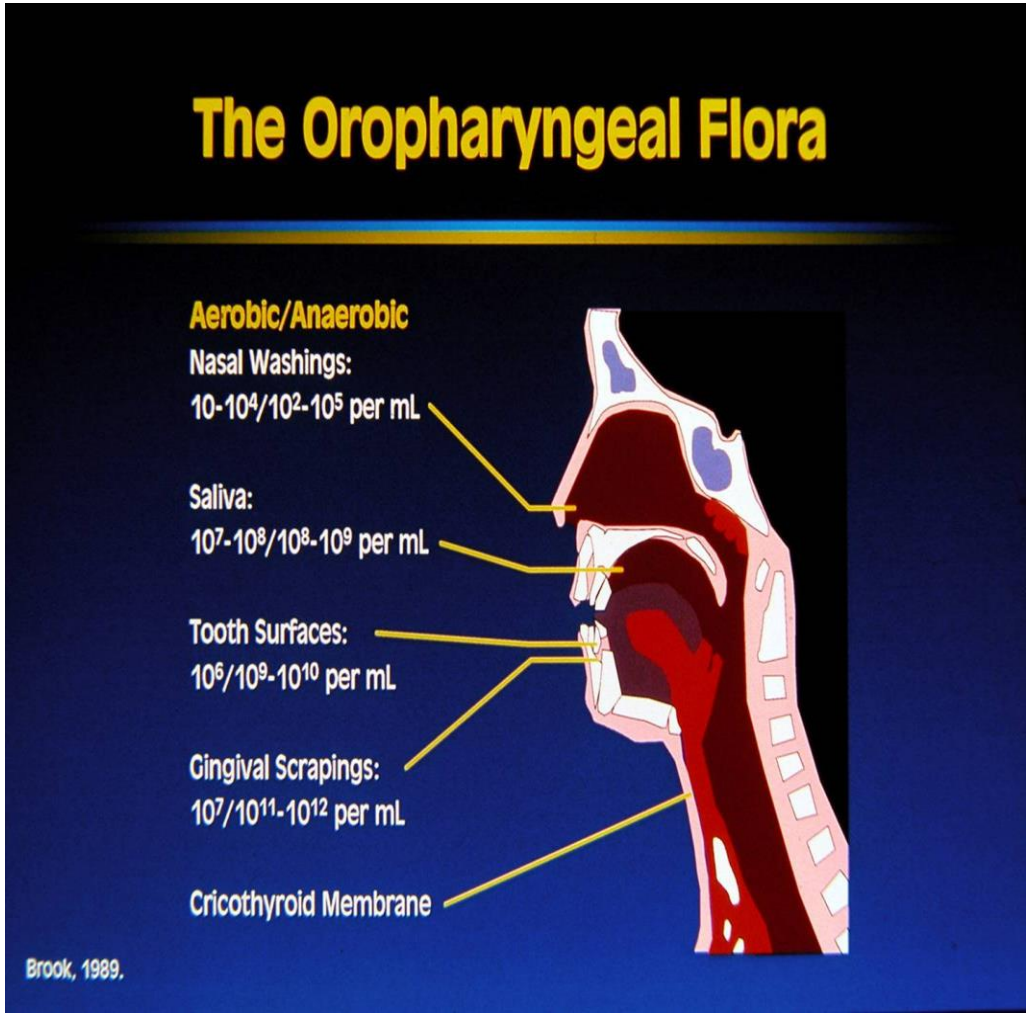


Table 2. The most common pathogens associated with dental infections.

Indication for antibiotics	Common pathogens (in order of prevalence)
Prophylaxis in patients with compromised immune systems caused by certain diseases or medications	*Streptococcus, Enterobacteriaceae, Moraxella, Lactobacillus, Corynebacterium, Fusobacterium, Bacteroides, Prevotella, Porphyromonas, Veillonella, Fusobacterium, Bacteroides, Prevotella, Porphyromonas*
Prophylaxis in patients at risk for developing bacterial endocarditis	*Streptococcus*
Treatment of an acute dental infection (gingivitis and periodontitis)	*Streptococcus, Actinomyces, Eubacterium, Leptotrichia, Fusobacterium, Bacteroides, Prevotella, Porphyromonas, Peptostreptococcus, Lactobacillus, Veillonella*

Brief Outline Of Oralmicroflora In Disease

INFECTIONS OF THE MOUTH	
Infection	Organism
Dental caries	Streptococcus mutans
Periodontal diseases	Bacteroides, Actinomyces
Surgical infection	
a) Dry socket	Actinomyces
b) Dental abscess	Oral streptococci
c) Osteomyelitis	Staphylococcus aureus
d) Ludwig's angina	β -haemolytic streptococci
e) Pericoronitis	Bacteroides

Mode of ATB use in odontogenic infections

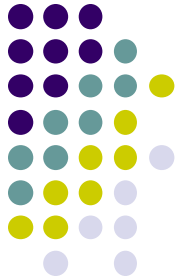
- **ATB are used in three general ways:**
  - as empirical therapy
  - as definitive therapy
  - as prophylactic & preventive therapy

ATB

- Relatively **small number of ATB** are required to effectively manage dental infections

- **MOA** (unique to microbial cells):
  - synthesis interruption of **structural components**
  - specific alteration of **metabolic functions**

Group of basic *PNCs*



- ***Penicillin G*** (*procaine* or *benzathine PNC*):
  - very active against **G+ cocci** (frequently cause oral, pharyngeal, pulmonary infections)
  - ***Neisseria gonorrhoeae*** & ***Treponema pallidum*** (still a first-line agent for treating syphilis & gonorrhea)
- ***Phenoxymethyl PNC*** (*penicillin V*):
  - spectrum similar to PNC G (⇓ active against Neisseria species & several anaerobes)
  - susceptible to a variety of β-lactamases (most strains of *Staphylococcus aureus* & many species of *Bacteroides* - seldom causative agents in oral infections, but resistant strains of Bacteroides = cause for *PNC* failure)
  - agent of choice for mild to moderate intraoral infections

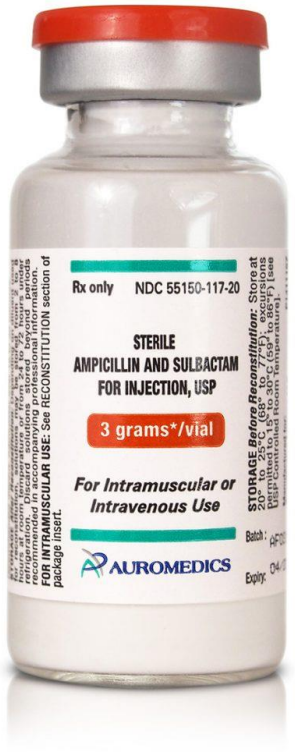
Penicillinase-stable *PNC*

- ***Oxacillin*** (*dicloxacillin*):
  - primarily indicated in the management of infections attributed to *Staphylococcus aureus* (over 90% are resistant to PNC G & V)
  - these microbes **are rarely if ever present in odontogenic infections**
  - both *oxacillin* & *dicloxacillin* are less active than *PNC V* against odontogenic pathogens

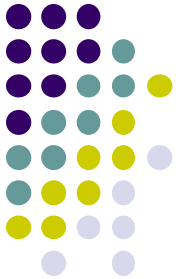
Group of *aminopenicillins*

Ampicillin

- ***Ampicillin***
  - first derivative to have an extended spectrum including several G-organisms (*Haemophilus influenzae* & *Escherichia coli*, but these are **rarely, if ever, associated with intraoral infections**)
  - a possible exception may be infections that also involve the maxillary or nasal sinuses (*Haemophilus influenzae*)
  - reserved for parenteral use (because of lower bioavailability)



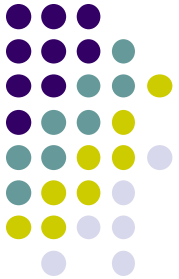
Group of *aminopenicillins*
Amoxicillin



- ***Amoxicillin***

- identical spectrum as *ampicillin*
- equally active against *Streptococci* as *PNC V*
- greater oral bioavailability (reason of *ampicillin* reservation for parenteral use)
- bioavailability is also superior to that of *PNC V* (replacing *PNC V* in guidelines for the prophylaxis of infective endocarditis)
- the only **advantages of amoxicillin for dental infections** are greater bioavailability & a longer half-life (favors its use if the leading cause of therapeutic failure is lack of patient compliance)
- ***clavulanic acid*** is combined with *amoxicillin* to act as a "suicide molecule" (protecting it from β-lactamases)

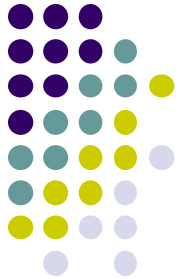
Clavulanic acid



- Structure similar to that of *PNC*:
  - weak antimicrobial action
  - strong affinity for β-lactamase
- Resistance among *streptococci* & most other dental pathogens **is not attributed to β-lactamase**

- *Amoxicillin + clavulanic acid* is indicated in refractory odontogenic & periodontal infections that (on some occasions) become colonized by PNC-resistant *Bacteroides* & *Prevotella* species that produce this enzyme:
  - however, these species are anaerobic & highly susceptible to ***metronidazole*** (which is less expensive)

Cephalosporins
First-generation



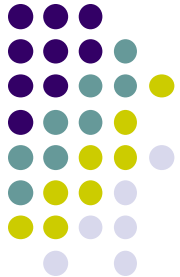
- Offer few advantages over *PNCs* in the management of dental infections:

- spectrum of activity includes that of *PNC V* for odontogenic microbes
- also active against most strains of *Staphylococcus aureus* (not susceptible to β-lactamases produced by this species)
- an alternative for the *PNC*-allergic patient
- certain agents have PK advantages that allow less frequent dosing (long elimination half-life of ***cefadroxil*** allows twice daily p.o.)
- ***cefazolin*** is the standard first-generation agent for parenteral use

Cephalosporins
Second & third-generations

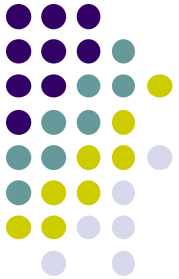
- Exhibit an even broader spectrum & greater resistance to β-lactamase:
  - several of the third-generation agents also demonstrate antipseudomonal activity
  - they are **rarely if ever indicated for managing oral infections** (too often prescribed inappropriately for infections that could be managed using less expensive agents)

Macrolides



- *Erythromycin* - prototypic macrolide (historically as an alternative for patients allergic to *PNC* because it had reasonable activity against most *PNC*-sensitive microbes - no longer the case & *Streptococci* & *staphylococci* resistant to *erythromycin* are also resistant to *clarithromycin* & *azithromycin*)
- *Clarithromycin* & *azithromycin* – could be used in prophylaxis for endocarditis (effective on G- anaerobes & spirochetes)
- *Macrolides* have little activity against periodontal pathogens (in recent years their activity against streptococcal species has declined)
- *Macrolides* produce a high incidence of nausea & the majority of these agents ⇓ cytochrome P450 enzymes (in addition to growing resistance among odontogenic pathogens):
  - furthermore, *azithromycin* continues to be a concern for promoting cardiac arrhythmias in susceptible patients

Tetracyclines

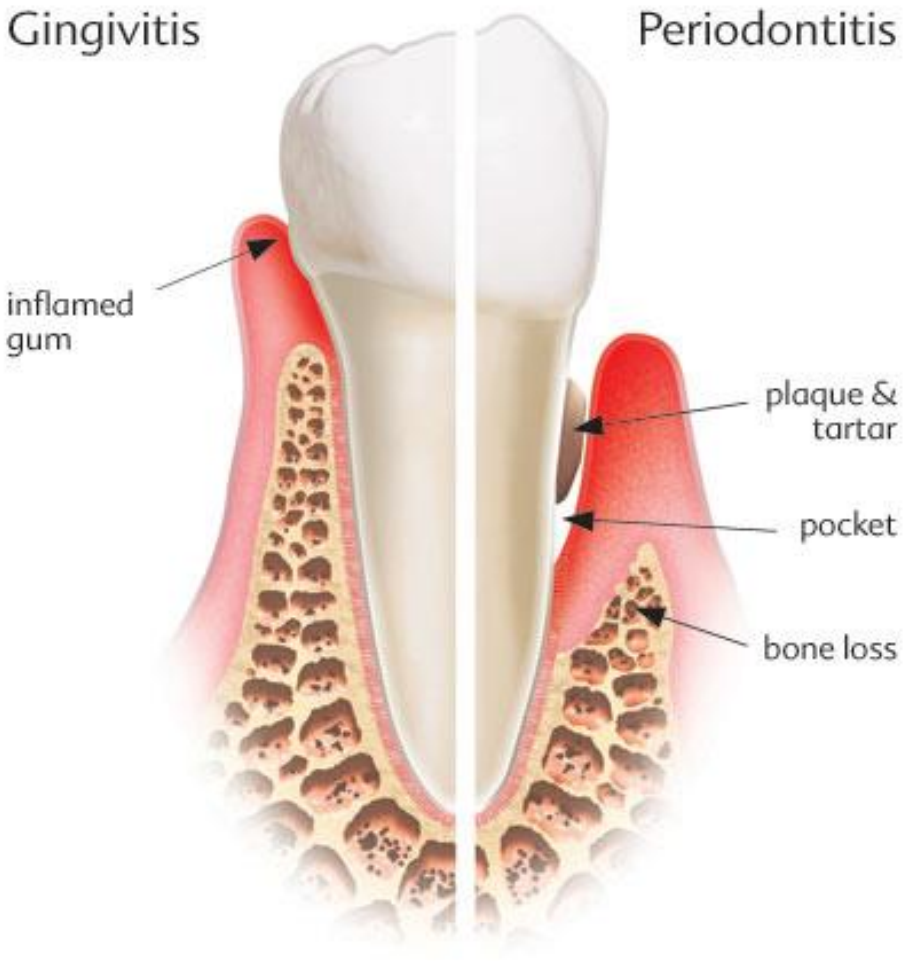


- Have a wide spectrum of activity (but microbial resistance has ⇑ to the extent that they are seldom first-line agents for medically treated infections - sinus & respiratory infections caused by *Haemophilus influenzae* & pneumonococci are exceptions: most of the strains remain sensitive)
- Less antimicrobial resistance to *doxycycline* & *minocycline* & these are generally preferred for periodontal infection
- *Doxycycline (Vibramycin)* ⇑ skin sensitivity to sunlight (leading to intense sunburn & generalized erythema) but offers several advantages:
  - it is well absorbed in the presence of food & has an extended elimination half-life that allows for **once-daily dosing**
  - it is eliminated primarily in feces & this makes it particularly attractive for patients having hepatic or renal compromise

Doxycycline
Dental practice

It is:

- useful adjuncts for managing **periodontal infections** in dental practice (highly active against many of the microorganisms implicated in gingival & periodontal disease)
- exhibits high bioavailability in the gingival sulcus
- unreliable for managing odontogenic infections due to streptococcal resistance



Doxycycline
Indications

- Effective against:

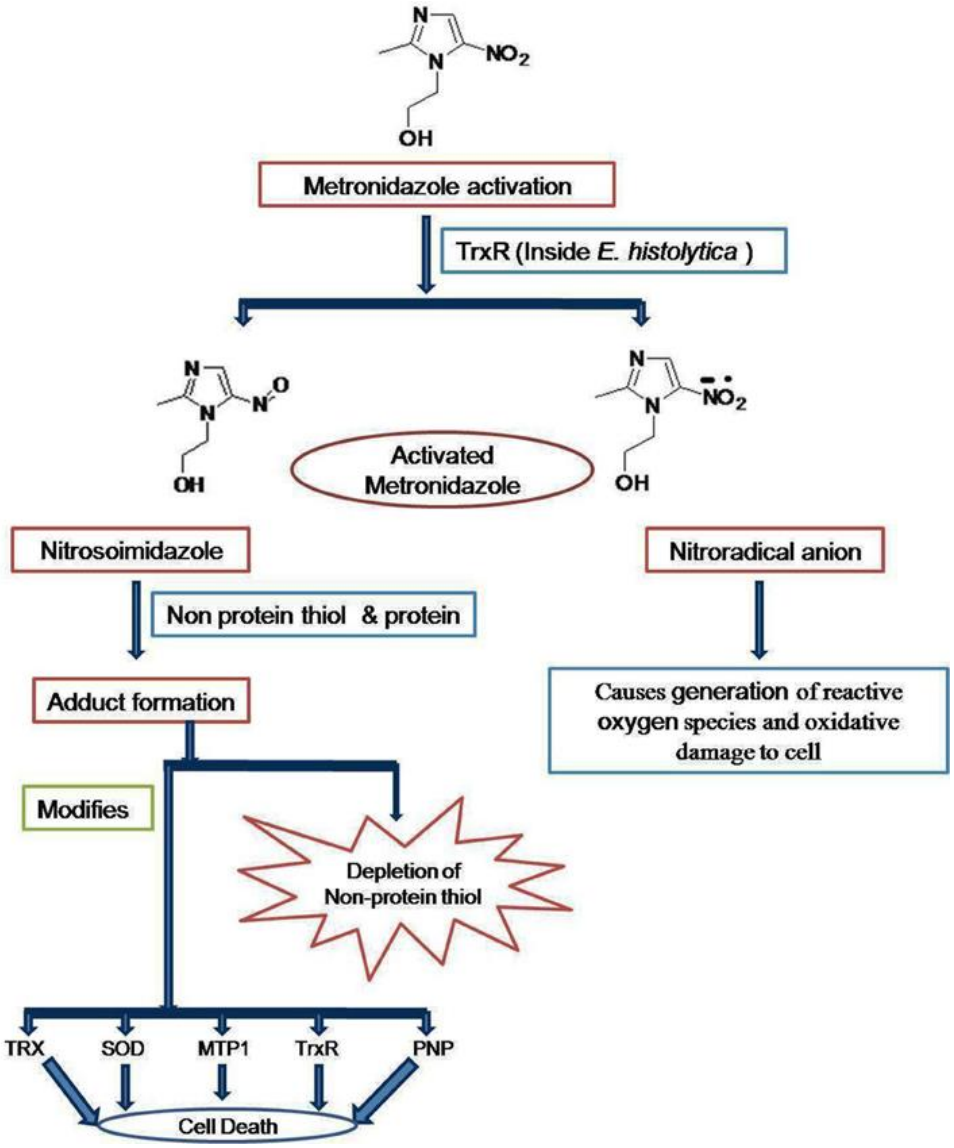
Actinomycetemcomitans:

- a G-, facultative anaerob, non-motile, rod-shaped oral commensal
- often found in association with **localized aggressive periodontitis**
- even at subantimicrobial doses, *doxycycline* ⇓ the activity of collagenases that contribute to the pathogenesis of periodontal destruction

Indicated in:

- localized aggressive periodontitis
- other aggressive periodontitis
- refractory periodontitis

Metronidazole
MOA



- **Converted into an active form** by reduction of it´s nitro-group in anaerobic microorganisms:
  - this binds to DNA & prevents formation of nucleic acid
  - bactericidal against most anaerobic organisms

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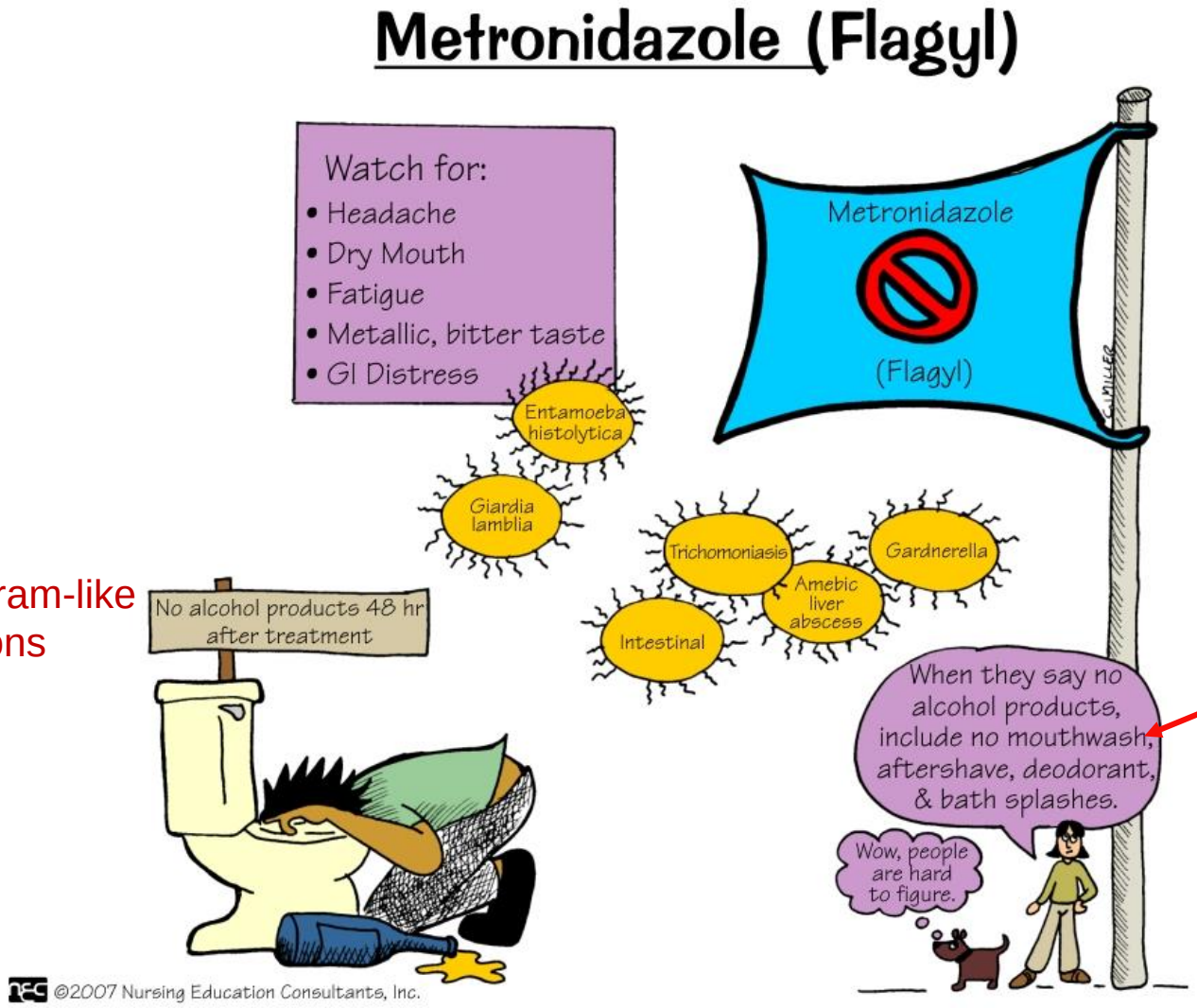
Metronidazole
Clinical use

- **Indications in dentistry:**
  - very useful for treating severe odontogenic & periodontal infections (where anaerobes are able to thrive)
  - only for obligate anaerobes
  - effective in *Bacteroides spp.* (periodontal infections)
  - acute ulcerative gingivitis
  - chronic, aggressive or refractory periodontitis
  - it may be combined with *β-lactams* when managing severe refractory infections (inactive against aerobic & facultative streptococci)
- **Other indications:**
  - trichomoniasis *(Trichomonas vaginalis)*
  - giardiasis *(Giardia lamblia)*
  - amoebiasis *(Entamoeba histolytica)*

Metronidazole

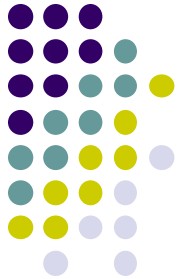
SE



Disulfiram-like reactions

Dental

Clindamycin
Use in dentistry



- ⇓ protein synthesis (but, unlike the *macrolides,* it is bacteriocidal)
- G+ bacteria & G- anaerobes, most species of *Bacteroides*, including *Bacteroides fragilis* (often implicated in severe orofacial infections)
- Infections where significant **anaerobic** infection is suspected
- Premedication (*PNC* allergy)
- Its cost & predilection for *Clostridium difficile* infection limit its routine use for dental infections in favor of *β-lactams* (should not be deterrents to **using *clindamycin* when indicated** - *Clostridium difficile* infection may be a complication associated with *amoxicillin & cephalosporins* as well)

Antifungal drugs

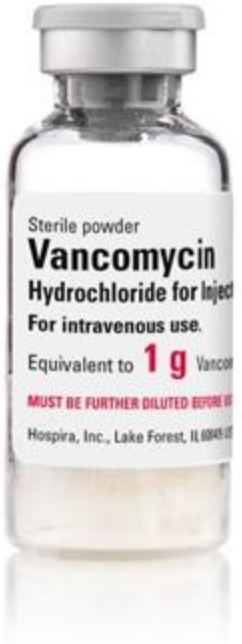
Treatment of oropharyngeal candidiasis:

- Azole derivatives are preferred
- *Clotrimazole* is generally preferred (based on cost & little risk for side effects & drug interactions)
- *Fluconazole* (Diflucan) & *miconazole* (Loramyc) are also available for oral administration:

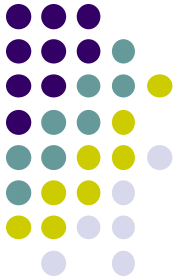
- these 2 azoles also ⇓ several families of cytochrome P450 enzymes & should be avoided in patients taking *warfarin, statins, antiretrovirals* & any drug known to prolong QT intervals

Miscelaneous ATB

- The following agents have little or no indications for managing odontogenic or periodontal infections:
  - *gentamicin*
  - *tobramycin*
  - *vancomycin*
- The newer generations of *β-lactame* ATB *(carbapenems, monobactams)* are also active against *Pseudomonas species* (but they are far more expensive)

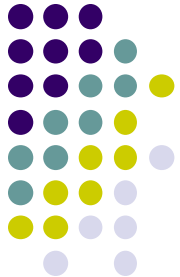


Aminoglycosides



- The most significant risk for infective endocarditis is in patients:
  - having a prior history of this infection
  - those with prosthetic valves
- In these cases, some cardiologists may prefer that an *aminoglycoside* such as *gentamicin* be added to the prophylactic regimen
- This is based on the synergistic influence *aminoglycosides* have with cell wall inhibitors *(β-lactames)* in killing **enterococci** & **resistant strains of *Streptococcus viridans***

Gentamicin & tobramycin

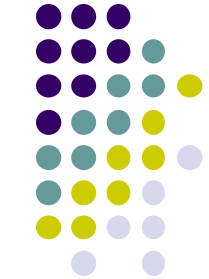


- *Gentamicin* & *tobramycin* are used most commonly & are the primary agents used to treat infections caused by G- rods (most notably *Pseudomonas species)*
- Although most ATB that ⇓ protein synthesis are bacteriostatic, the ***aminoglycosides*** **are frequently bactericidal**
- Toxicity includes:

➢ **Nephrotoxicity** - fairly common, generally reversible following discontinuation

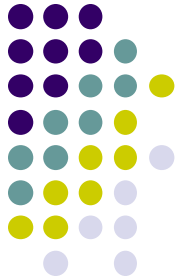
➢ **Ototoxicity** (either the auditory or vestibular) - may be permanent (**tinnitus** is the earliest sign of auditory toxicity, whereas **headache** & **nausea** generally indicate the onset of vestibular toxicity)

Vancomycin



- For high-risk patients allergic to *β-lactams, vancomycin* may be requested (does not require the addition of *gentamicin*);
  - must be administered by i.v. infusion (over 30 - 60 min. preoperatively)
  - ⇓ cell wall synthesis (active against most G+ cocci, including most species of streptococci, staphylococci & enterococci - resistant strains are a growing problem)
- Reserved for serious infections caused by organisms that are resistant to first-line agents or in cases of serious allergy *(β-lactams* - in the prophylaxis in the heart valve patient)
- Can produce pseudoallergic reactions, rapid i.v. infusion may trigger **histamine release** (erythematous or urticarial reactions, flushing - redman syndrome), tachycardia, hypotension):
  - the most significant untoward reactions are **ototoxicity** & **nephrotoxicity** (more likely when administered concurrently with an aminoglycoside)

Fluoroquinolones

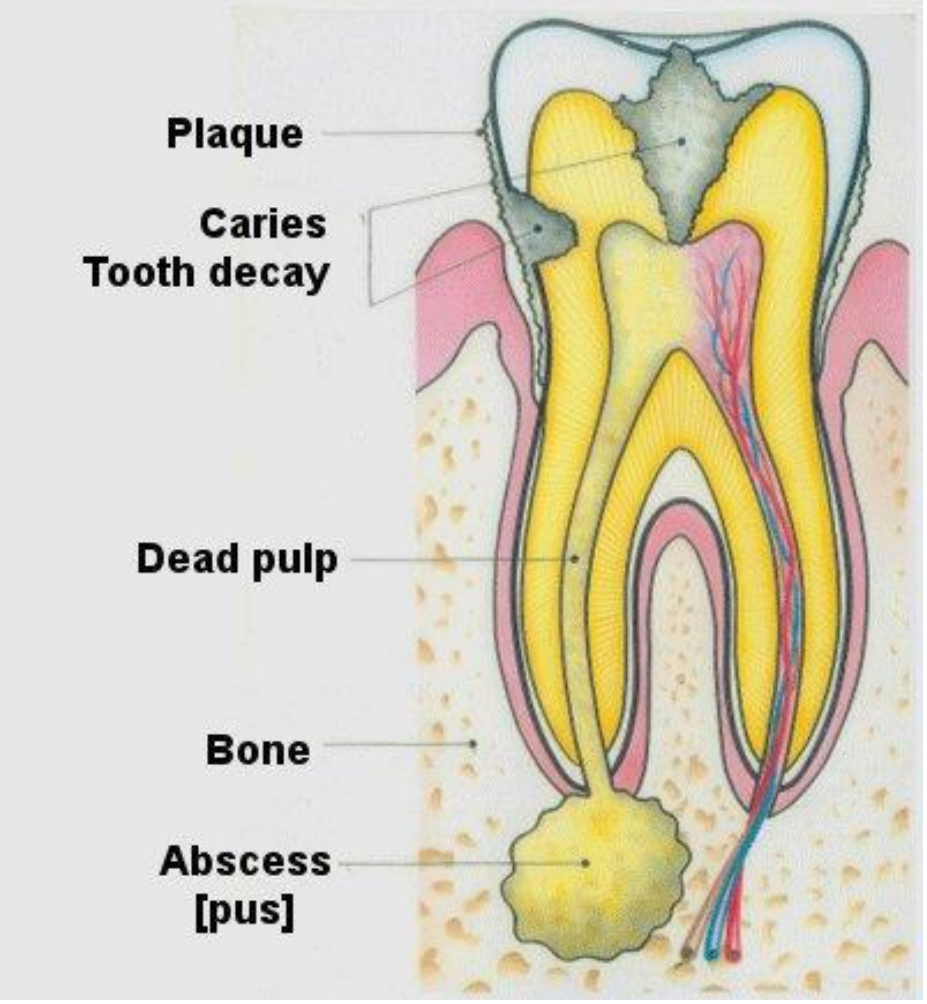


- Broad-spectrum antibacterial agents that ⇓ DNA gyrase
- *Ciprofloxacin* - active against most staphylococci & a variety of G- microorganisms:
  - poor activity against most streptococci & all anaerobes (this negates its use for odontogenic & periodontal infections - generally consist of mixed aerobic & anaerobic flora)
- Newer generations have broader activity:
  - *Levofloxacin* - good antistreptococci but poor anaerobic activity
  - *Gemifloxacin* offers added anaerobic coverage (their cost generally renders them inappropriate for dental-related infections)

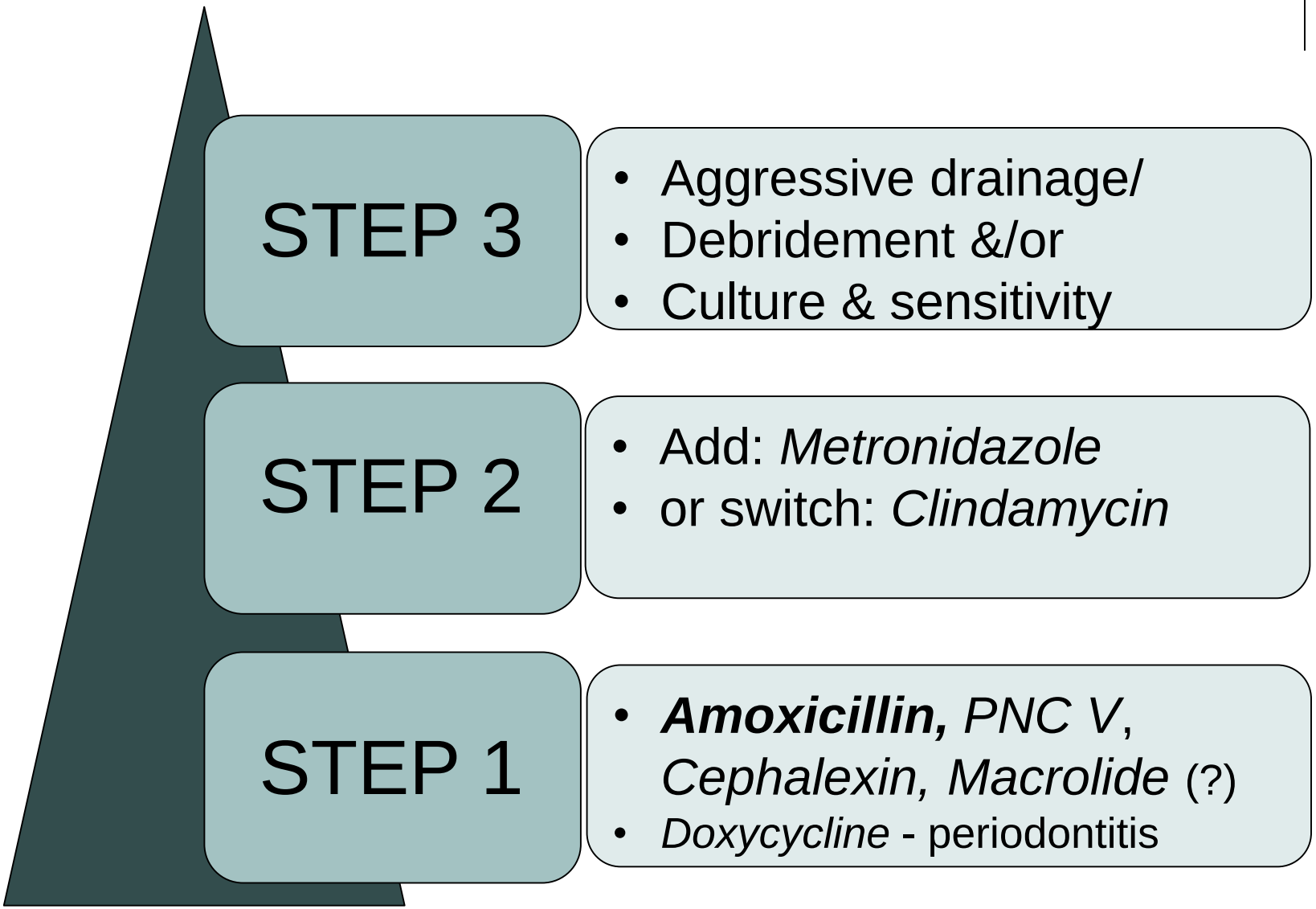
Dental procedures that require endocarditis prophylaxis

- **In risky patients:**

  - tooth extraction
  - periodontal surgery
  - subgingival dental prophylaxis
  - endodontic surgery
  - incision & drainage of infection



Step approach to empiric ATB therapy

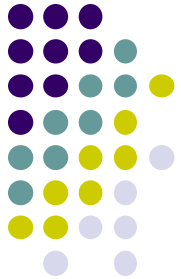


ATB & Dosages

For Dental Infections

Preparation	Conventional dosing schedule
Penicillin V	500 mg QID
Amoxicillin	500 mg TID
Cephalexin	500 mg QID
Cefadroxil	500 mg BID
Clindamycin	300 mg TID or QID
Metronidazole	500 mg TID or QID
Doxycycline	100 mg QID or BID

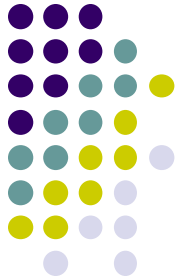
SE
GIT



- With the exception of **allergy**, adverse effects attributed to ATB are **surprisingly infrequent**, but:

- most agents are implicated in producing nausea, dyspepsia & diarrhea
- the incidence of diarrhea attributed to those ATB commonly used in dentistry ranges from 2 - 10% (may be as high as 25% with amoxicillin/clavulanic acid)
- mild diarrhea may be managed using antiperistaltics & changing the ATB to a narrower spectrum if possible (however, it becomes a more significant event if it is the result of *Clostridium difficile)*

SE
Allergy

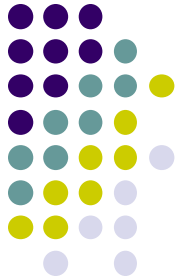


- *PNCs* & *cephalosporins* raises concern regarding cross-allergenicity (related more to similarities in the R side chains as to *β-lactame* ring):

- it is generally accepted that patients having a history of IgE-mediated reaction to a *PNC* should be managed using a non -*β-lactam* ATB
- urticaria (hives) is immunoglobulin E mediated (but accounts for only 10% of all exanthematous drug reactions)
- majority of cutaneous reactions to *PNCs* are pruritus or rash; (these are not immunoglobulin E-mediated & any potential for crossreaction is unlikely)

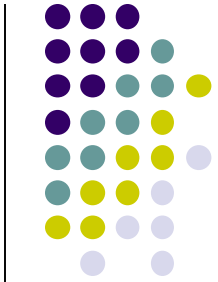
Managing *PNC*-allergic patients

Clarify nature of reaction



Hives or anaphylactiod	• IgE-mediated, cross reaction possible • Avoid all *β-lactams*
Pruritus or rash	• Non IgE-mediated, cross reaction unlikely • Use alternate *PNC* or *cephalosporin*
Dyspepsia, nausea or diarrhea	• No issue • Avoid offending formulation

Surgical prophylaxis

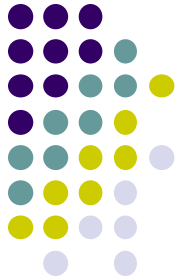


- The surgical site is currently not infected, but may become contaminated during surgery:

- this condition is not present when removing **abscessed** or **periodontally compromised teeth** (infection is currently present & it is frequently unnecessary after the offending reasons are surgically removed)
- an adequate serum concentration should be established no earlier than **2 hours** before a surgical incision
- in this case a dose may be repeated at intervals corresponding to 1 - 2 elimination half-lives for the drug used

Surgical prophylaxis

Suggested routine regimens



Preparation	Dosing schedule
Penicillin V	2 g PO/1 h preop; ± 1 g q 6 h x 1
Amoxicillin	**2 g PO/1 h preop; ± 1 g q 6 h x 1**
Cephalexin	2 g PO/1 h preop; ± 1 g q 6 h x 1
Clindamycin	600 mg PO/1 h preop; ± 300 mg q 6 h x 1
Intravenous regimens	
Cefazolin	1 g IV 30 min preop; ± postop PO as above
Clindamycin	600 mg IV 30 min preop; ± postop PO as above

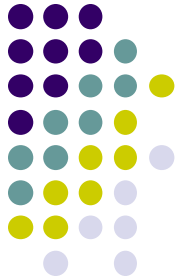
Medical prophylaxis

Examples of conditions that may be associated with **poor immune status** include the following (dentists often provide a course of ATB when performing dental surgery for these patients):

- Poorly controlled diabetes
- Systemic lupus erythematosus
- End-stage renal disease undergoing dialysis
- Evidence of significant malnutrition or alcoholism
- Symptomatic HIV – positive patients
- Patients receiving immunosuppressant drugs or radiation to head & neck
- Patients receiving anti-osteoprosis therapy *(bisphosphonates, denosumab)*

Prevention of infective endocarditis

IE



- It is reasonable before dental procedures (that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa) in patients with the following:

- Prosthetic cardiac valves (including transcatheter-implanted prostheses & homografts)
- Prosthetic material used for cardiac valve repair (such as annuloplasty rings & chords)
- Previous IE
- Unrepaired cyanotic congenital heart disease or repaired congenital heart disease (with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device)
- Cardiac transplant with valve regurgitation (due to a structurally abnormal valve)

Regimens for prevention of IE

2017 American Heart Association

Preparation	Dosing schedule
Standard regimen	
Amoxicillin	**PO: 2 g; 1 h preop**
Ampicillin	IM/IV: 2 g; 1/2 h preop
Penicillin allergy	
Clindamycin	PO: 600 mg; 1 h preop IV: 600 mg; 1/2 h preop
Clarithromycin or *azithromycin*	PO: 500 mg; 1 h preop
Cephalexin (first-generation)	PO: 2 g; 1 h preop
Cefazolin (first-generation)	IM/IV: 1 g; 1/2 h preop


COSMETIC DENTAL SURGERY
SO WHADDA YOU THINK?