Commonly used Drugs in Dentistry

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Objectives

- Review common drugs used in dentistry and used by our patients
- Review mechanism of action
- Review side effects of these drugs

Drugs that we use/prescribe

- Local anesthetics
- Pain control
- Antibiotics

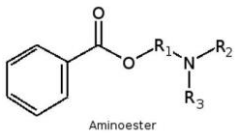
Drugs our patients take

- Anti-hypertensives
- Diabetic
- Anti-coagulants
- Anti-resorptive
- Herbal supplements

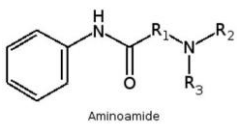
Local Anesthetics

Molecular structure

- Molecular structure
  - Lipophilic group (aromatic ring)
  - intermediate chain (ester or amide)
  - ionizable group (usually a tertiary amine)
- Metabolism
  - Ester: Pseudocholinesterase
  - Amide: Liver metabolism by cytochrome P450



Aminoester



Aminoamide

Local Anesthetics

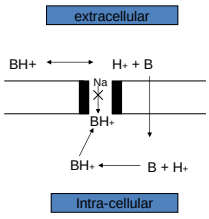
Types

- Ester
  - Cocaine (1860)
  - Procaine (Novocain-1905)
  - Tetracaine (Topical Ophthomology)
  - Benzocaine (Topical)
- Amide
  - Lidocaine (Xylocaine)
  - Mepivicaine (Carbocaine)
  - Bupivicaine (Marcaine)
  - Articaine (Septocaine)

Local Anesthetics
Mechanism of Action

Blockage of voltage gated Na channels

- The drug must penetrate the neuron to act on intracellular end of the Na channel
- Affect small fiber nerves first
  1. C fibers (pain)
  2. A delta (Pain, temp)
  3. A beta (Touch, Pressure)
  4. A alpha (motor, Proprioception) fibers



Local Anesthetics
Properties

Type	Lipid solubility **Potency**	Protein binding (%) **Duration**	pKa **Onset**	Notes
2% Lidocaine (Xylocaine)	2.9	65% (medium)	7.8 (fast)	standard
2% Mepivacaine (Carbocaine)	1	75% (medium)	7.7 (fast)	fastest on/off
0.5% Bupivacaine (Marcaine)	30	95% (long)	8.1 (moderate)	Slowest on, longest off
4% Articaine (Septocaine)	49.5	95% (long)	7.8 (fast)	Strongest, do not use for blocks

JADA, Vol 131, May 2000

Local Anesthetics
Maximum dose

Anesthetic	Maximum Dosage		Maximum total dosage	Carpules	mg/carpule
	mg/kg	mg/lb			
2% Lidocaine 1:000,000 epi (Xylocaine)	7	3.2	500 mg	8	34 - 36mg
3% Mepivacaine plain (Carbocaine)	4.4	2.0	300 mg	5	51 - 54mg
4% Articaine 1:100,000 epi (Septocaine)	7.0	3.2	500 mg	6	68 - 72mg
0.5% Bupivacaine 1:200,000 epi (Marcaine)	1.3	0.6	90 mg	10	8.5 - 9mg

Adapted from Stanley Malamed, Handbook of Local Anesthesia, Fifth Edition

Local Anesthetics
Toxicity

- CNS
  - Initial: restlessness, confusion, peri-oral numbness, vertigo, tinnitis, slurred speech, auditory/visual hallucination and tonic-clonic seizures
  - Late: CNS depression respiratory collapse and death
- Cardiac
  - Initial: Hypertension, tachycardia
  - Late: Decreased contractility and cardiac output, hypotension
  - Later: Sinus Bradycardia, ventricular dysrhythmias, circulatory arrest

Local Anesthetics
Epinephrine

- Increases duration of action
- Hemostasis (max effect takes 7 minutes)
- Hydro-dissection of surgical plane

- Avoid IAN blocks in patients with unstable/significant coronary artery disease to avoid intravascular entry
  - No more than 0.04mg = 40 ug epinepherine (2 carpules)

Local Anesthetics
Pregnancy

Epinephrine

- Decreases uterine blood flow and activity
  - Needs to be a intravascular injection
    - Aspirate and inject slowly!!

No significant contraindication for the careful use of lidocaine with epinephrine in pregnant patients

Compendium of Continuing Education in Dentistry, September 2012

Local Anesthetics
Pregnancy

- Category B
  - Lidocaine
- Category C
  - Articaine
  - Bupivacaine
  - Mepivacaine

United States FDA Pharmaceutical Pregnancy Categories

A	Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
B	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.
C	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
E	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Local Anesthetics
Allergy

- Mostly adverse reaction to epinephrine
  - Rapid heart rate
- Rare allergy to agent itself
  - Ester are metabolites resemble para-aminobenzoic acid which can elicit allergic reaction
- Allergy to components of anesthetic
  - Methylparaben: multi use vials
  - Bisulfites: preservative for vasoconstrictor
  - Sulfa: articaine has small amount
- Consider referral to allergist

Local Anesthetics
Methemoglobinemia

Hemoglobin deficiency occuring when hemoglobin is oxidized to methemoglobin and cannot bind or carry oxygen

- Excessive doses of Articaine (> 500 mg/6 carpules) or Prilocaine (> 600 mg)
- Accumulation of oxidized metabolite, ortho-toluidine
- Decreased pulse oximetry reading, cyanosis, dark blood
- Reversal with 1-2 mg/kg methylene blue IV over 5 minutes

Pain Medications

- Opioids
- NSAIDS
- Acetaminophen

Opioids

- Naturals
  - Codeine
  - Morphine
- Semi-synthetics
  - Hydrocodone
  - Oxycodone
- Synthetics
  - Meperedine
  - Fentanyl
  - Tramadol

Opioids
Mechanism of action

- Binds opioid receptors (3 groups) found in CNS, PNS and GI tract

Mu 1 supraspinal analgesia bradycardia sedation	**Mu 2** respiratory depression Euphoria physical dependence
Delta spinal analgesia respiratory depression	**Kappa** spinal analgesia respiratory depression sedation

Opioids
Side Effects

- Desirable
  - Analgesia
  - Adjunctive with sedation and anesthesia
  - Anti-tussive
- Undersirable
  - N/V
  - Constipation
  - Pruritis
  - Sedation
  - Mental clouding

Opioids
Metabolism

- Hepatic metabolism into active metabolites
  - Drug interactions
  - Individual specific response: good and bad metabolizers

Opioids
Natural

- Codeine
  - Both naturally occurring (opium poppy) or synthesized from morphine
  - Combination with acetaminophen, ASA or NSAIDs
  - Active metabolite: morphine → M3G, M6G
  - Analgesic effect depends on individual's liver metabolism
  - Paroxetine, Fluoxetine, diphenhydramine, bupropion block metabolism
- Morphine
  - Not commonly used in dentistry
  - Mimics endogenous endorphins
  - Works much better IV than PO (extensive first pass metabolism, 40-50% reach CNS
  - Active metabolites: M3G, M6G

Opioids
Semi-Synthetics

- Hydrocodone
  - Derived from codeine
  - w/Acetaminophen (Vicodin, Norco), w/Ibuprofen (Vicoprofen)
  - Active metabolite → hydromorphone
    - Good/poor metabolizers have similar response
- Oxycodone
  - Derived from thebaine (poppy derivative)
  - w/Acetaminophen (Percocet), w/Aspirin (Percodan)
  - Immediate or extended release (Oxycontin)
  - Many metabolites
    - Good/poor metabolizers

Opioids
Synthetics

- Meperidine
  - Longer onset
  - Metabolite normeperidine cause undesirable effects
    - Dysphoria, tremors, seizures
    - MAOI → Life threatening serotonin syndrome
    - Hypertensive crisis, hyperpyrexia, cardiovascular collapse
- Fentanyl
  - Rapid onset, short duration of action
  - 100 times more potent than morphine (high lipophilicity)
  - Transdermal patch, lollipops, IV

Opioids
Synthetic hybrid

- Tramadol
  - Weak opioid agonist + inhibitor of seratonin and norepinepherine reuptake system
  - Metabolite O-desmethyltramadol is potent opioid receptor agonist
  - Side effects: HA, N/V, seizure, somnolence
  - Low respiratory effects and abuse potential

Opioids
Comparison of potency

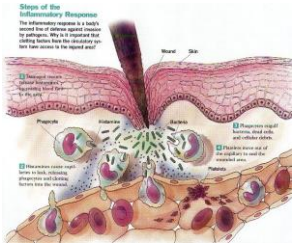
Opioid	Strength	Equivalent Dose
Codeine	1/10	30 mg
Tramadol	1/10	30 mg
Demerol	.36	8.3 mg
Hydrocodone	.6	5 mg
Morphine PO	1	3 mg
Oxycodone	1.5-2	1.5-2 mg
Morphine IV/IM	4	.75 mg
Hydromorphone	5	.6 mg
Fentanyl	50-100	0.03-0.06 mg

Pain Medication

- Opioids
- NSAIDS
- Acetaminophen

Inflammation

- Local tissue damage → Release of inflammatory mediators
  - Cytokines
  - Substance P
  - Prostaglandins
  - Leukotrienes
  - Kinins
  - Histamine
  - Seratonin



Inflammation

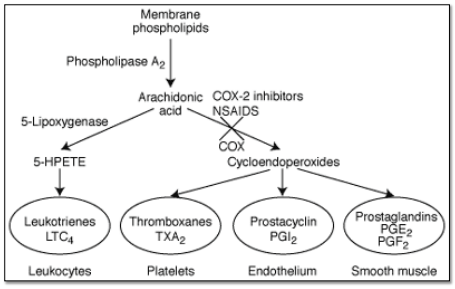
- Prostaglandins

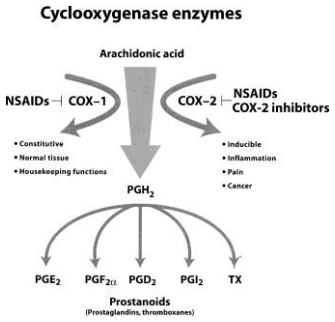
E1, E2, F1α, F2 α	Increase vascular permeability Inflammation
D2	Increase hyperalgesia in sensory afferent nerves Inhibit platelet adhesion
Thromboxane	Increase vascular permeability Inhibit platelet adhesion
Prostacycline	Decrease vascular tone Reduce platelet adhesion

Prostaglandins

- Maintains homeostasis of different organ systems.
  - GI
    - Creates mucosal lining that is protective
  - Kidney
    - Control blood flow, renin release and salt/water resorption
  - Heart
  - Brain
  - Vasculature
    - Platelet function

Prostaglandin Pathway





NSAIDs

- analgesia, antipyretic, anti-inflammatory

Non-selective (COX 1, COX 2) Ibuprofen (Motrin, Advil) Naproxen (Aleve)	**Partial-selective (COX 2 > COX 1)** Etodolac (Lodine) Meloxicam (Mobic) Nabumetone (Relafen)
Salicylates (irreversible COX1) Aspirin	**COX-2 inhibitors** Celecoxib (Celebrex) FDA alert Rofecoxib (Vioxx) withdrawn from market

NSAIDs
Equipotency

	Low Dose	Medium Dose	High or Max Dose
Ibuprofen (Motrin)	400mg tid	600mg tid-qid	800mg qid
Naproxen (Aleve)	250mg tid	500mg bid	1250mg/day (divided)
Etodolac (Lodine)	200mg tid	400mg bid	1200mg max
Meloxicam (Mobic)	7.5mg qd	7.5mg qd	15mg qd
Nabumetone (Relafen)	1000mg qd	1000mg bid	2000mg/day (qd or divided bid)
Celecoxib (Celebrex)	200mg qd	200mg bid	200mg bid
Rofecoxib (Vioxx)	12.5mg qd	25mg qd	50mg qd for max of 5 days (acute pain)

NSAIDs
Side Effects

- GI
  - Gastritis
  - Ulceration
  - Bleeding (prolonged usage)
- GU
  - Chronic renal failure
    - Decrease blood flow and glomerular filtration*
- Other
  - Severe allergic reaction
  - Tachycardia
  - Edema
  - Dizziness
  - Headache
  - Increased liver enzymes

Pain Medication

- Opioids
- NSAIDS
- Acetaminophen

Acetaminophen

- Analgesic, antipyretic, mild anti-inflammatory
- Mechanism of action unknown
  - Reduces prostaglandins by inhibition of COX??
- Hepatotoxic
  - Metabolite NAPQI (N-acetylimidoquinone) is toxic to liver
  - < 4,000 mg per day for adults
  - Use narcotic formulations with less tylenol (325 vs 500 mg)

Pain Management Strategies

- 2 medications with different mechanisms of action are better than a lot of 1 medication
  - NSAIDs around the clock for pain and inflammation
  - Narcotics to supplement, alternate or as needed
- Begin pain medication before or right after treatment to counteract initial hyperalgesia
- Take medication ahead of pain, not after experiencing it

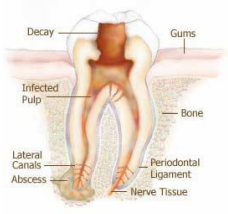
Antibiotics

- Penicillins
- Cephalosporins
- Clindamycin
- Metronidazole
- Fluoroquinolones

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Antibiotics
Indications

- Cellulitis or abscess
- Pericoronitis
- Osteomyelitis
- Prophylactic
- Preventative?



Cellulitis/Abscess

- Progression
  - Tooth
  - Bone
  - Fascial planes/Soft tissue
  - Deeper fascial planes
  - Potentially fatal

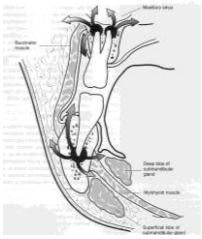
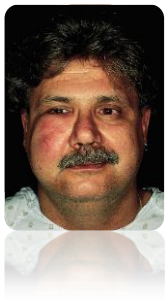


Table 15-1 Borders of the Deep Spaces of the Head and Neck

	Borders					
Space	*Anterior*	*Posterior*	*Superior*	*Inferior*	*Superficial or Medial**	*Deep or Lateral**
Buccal	Corner of mouth	Masseter m., pterygomandibular space	Maxilla, infraorbital space	Mandible tissue and skin	Subcutaneous	Buccinator m.
Infraorbital	Nasal cartilages	Buccal space	Quadratus labii superioris m.	Oral mucosa	Quadratus labii superioris m.	Levator anguli oris m., maxilla
Submandibular	Ant. belly digastric m.	Post. belly digastric, stylohyoid, stylopharyngeus mm.	Inf. and med. surfaces of mandible	Digastric tendon	Platysma m., investing fascia	Mylohyoid, hyoglossus sup. constrictor mm.
Submental	Inf. border of mandible	Hyoid bone	Mylohyoid m.	Investing fascia	Investing fascia	Ant. bellies digastric m.†
Sublingual	Lingual surface of mandible	Submandibular space	Oral mucosa	Mylohyoid m.	Muscles of tongue*	Lingual surface of mandible†
Pterygomandibular	Buccal space	Parotid gland	Lateral pterygoid m.	Inf. border of mandible	Med. pterygoid muscle*	Ascending ramus of mandible†
Submasseteric	Buccal space	Parotid gland	Zygomatic arch	Inf. border of mandible	Ascending ramus of mandible*	Masseter m.†
Lateral pharyngeal	Sup. and mid. pharyngeal constrictor mm.	Carotid sheath and scalene fascia	Skull base	Hyoid bone	Pharyngeal constrictors and retropharyngeal space*	Medial pterygoid m.†
Retropharyngeal	Sup. and mid. pharyngeal constrictor mm.	Alar fascia	Skull base	Fusion of alar and prevertebral fasciae at C6-T4	—	Carotid sheath and lateral pharyngeal space†
Pretracheal	Sternothyroid-thyrohyoid fascia	Retropharyngeal space	Thyroid cartilage	Superior mediastinum	Sternothyroid-thyrohyoid fascia	Visceral fascia over trachea and thyroid gland

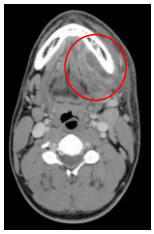
Cellulitis

- Early infectious process spreading to surrounding fascial planes and soft tissue
- Rubor (erythema), Dolor (pain), Tumor (swelling), Calor (heat), loss of function
- No drainable abscess
- Treatment
  - Antibiotics
  - Remove offending agent
  - Consider surgical exploration to change flora



Abscess

- Advanced infection
- Organized fluid collection
- Treatment
  - Antibiotics
  - Requires I+D, possible OR
  - Hospital admission/IV abx



Micro-organisms in dental infections

Organism	Percentage
ANAEROBIC	75
Gram-positive cocci	30
■ *Streptococcus spp.*	*33*
■ *Peptostreptoccus spp.*	*65*
Gram-negative cocci (Viellonella spp.)	4
Gram-positive rods	14
■ *Eubacterium spp.*	
■ *Lactobacillus spp.*	
■ *Actinomyces spp.*	
■ *Clostridia spp.*	
Gram-negative rods	50
■ *Bacteroides spp.*	*75*
■ *Fusobacterium spp.*	*25*
Miscellaneous	6

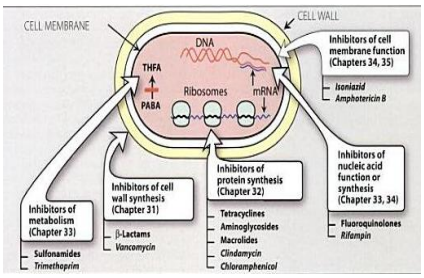
Excerpted from Contemporary Oral and Maxillofacial Surgery, Third Edition, 1998

Micro-organisms in dental infections

Organism	Percentage
AEROBIC	25%
Gram-positive cocci	85
■ *Streptococcus spp.*	*90*
■ *Streptococcus (Group D) spp*	*2*
■ *Streptococcus Group spp. Staphylococcus spp.*	*6*
■ *Eikenella spp.*	*2*
Gram-negative cocci (*Neisseria spp.)*	*2*
Gram-positive rods (*Corynebacterium spp.)*	*3*
Gram-negative rods (*Haemophilus spp.)*	*6*
Miscellaneous and undifferentiated	4

Excerpted from Contemporary Oral and Maxillofacial Surgery, Third Edition, 1998

Antibiotics
Mechanism of action



Antibiotics
Mechanism of action

- Bactericidal
  - Kills bacteria
  - Pencillins, fluoroquinolones, metronidazole
- Bacteriostatic
  - Limit growth of bacteria by interefering with bacterial cellular metabolism
  - Works together with body's immune system to remove micro-organisms
  - In higher doses, can be bacteriocidal
  - Clindamycin, macrolides

Antibiotics
Penicillin family

- Inhibits cell wall synthesis by interfering with transpeptidaton or cross-linkage, thus exposing the osmotically less stable membrane → cell lysis
- Bactericidal
- Allergy is common (10%)
- Dosing: QID
- Cost
  - 500mg tabs (#30) = $26
  - 500mg q6h x 7 days
- Can combine with Flagyl broaden spectrum of coverage. Cost effective combination.

Antibiotics
Amoxicillin

- More gram-negative coverage
- Can be dosed TID or BID
- Recommended as first line for prophlyaxis

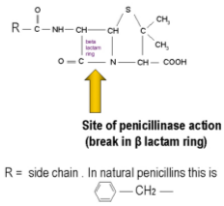
Antibiotics
Penicillin resistance

Beta-Lactam Ring

- Cleaved by beta-lactamases produced by resistant bacteria

Beta-lactamase inhibitors

- Clavunic acid
- Sublactam
- Tazobactam



Antibiotics
Augmentin

- Amoxicillin + clavunic acid
  - B-lactamase inhibitor
- Dosing BID
- Good for more severe odontogenic infections
- First line for sinusitis
- IV forms:
  - Ampicillin + sublactam (Unsasyn)
  - Pipercillin + tazobactam (Zosyn)

Antibiotics
Cephalorosporins

- β-lactam antibiotic
- 4 generations (gram positive → gram negative)
- 1st generation good for oral organisms
  - Cephalexin (Keflex)
- Bactericidal, less susceptible to β-lactamases
- 10% cross-reactivity in PCN allergic pts

Antibiotics
Clindamycin (Cleocin)

- Inhibits protein synthesis by binding to the 50s ribosomal subunit of bacteria.
- Bacteriostatic; bactericidal in higher doses
- Good against oral organisms (Strep, Staph, Bacteroides) and majority of anaerobes
  - MRSA
- Achieves high levels in bone, excellent penetration in abscesses
- First line option in penicillin allergic patients

Antibiotics
Clindamycin (Cleocin)

- Dosage
  - 150-450 mg PO q6-8h
  - Higher doses for active infection
  - Elixir is rancid (switch to Azithromycin)
- Cost
  - 150 mg (30 ea) : $24.99
  - 300 mg (30 ea) : $79.99

Antibiotics
Metronidazole (Flagyl)

- Disrupts bacterial nucleic acid synthesis
- Bactericidal against anaerobic species
- Do not drink alcohol!
  - Disulfiram-like reaction: flushing, tachycardia, palpitations, N/V
- Treatment of chose for C. difficile associated diarrhea
- Resistance non-existent
- Prescribe in combination with aerobic covering abx

Antibiotics
Metronidazole (Flagyl)

- Dosage Forms
  - Tablets, IV
- Dosing
  - 500-750 mg q 6-12 h
- Cost
  - 250mg (#90) $16
  - 500mg (#30) $13

Antibiotics
Macrolides

- Azithromycin (Zithromax), Erythromycin
- Drug of choice for URI, pneumonias
- Binds to 50S subunit of bacterial ribosomes, inhibiting bacterial protein synthesis
- Bacteriostatic

Antibiotics
Fluoroquinolones

- ciprofloxacin (Cipro), levofloxacin (Levaquin), moxifloxacin (Avelox)
- Inhibit DNA gyrase and topoisomerase involved in DNA replication.
- Bacteridicdal
- Good for gram-negative bacteria
  - Greater gram positive coverage with levofloxacin and moxifloxacin
  - Greater anaerobic coverage with moxifloxacin
- Not recommended for children (joint toxicity in animals)

Antibiotics
Moxiflocaxin (Avelox)

- Second-line, broad spectrum abx for odontogenic infections
  - Concern for emerging antibiotic resistance
- Excellent for intra-oral organisms
- Dosage forms
  - 400 mg, PO/IV
- Dosage
  - 400mg po or IV once daily x 5-10 days
- Cost
  - Expensive (no generic)
  - 400mg tab (#30) $490

Antibiotics
Resistance

- Serious, growing problem
- Causes
  - Overuse and misuse of antibiotics
  - Poor patient compliance with antibiotic regiment
  - Evolutionary potential of bacteria
- Superbugs resistant to multiple antibiotics
  - MRSA: staph aureus resistant to penicillin, methicillin, tetracycline, erythromycin
  - VRE: enterococcus resistant to vancomycin, linezolid

Antibiotics
Resistance

- Mechanisms
  - Drug inactivation or modification (penicillins)
  - Alteration of target site (penicillins)
  - Alteration of metabolic pathoway
  - Reduced drug accumulation (fluoroquinolones)

Antibiotics
Adverse reactions

Diarrhea

- Mild cases are common (1 in 3 people)
- Loose stools, more frequent BMs
- Caused by alteration/imbalance of colonic micro-organsims
- Changes in carbohydrate metabolism and decreased fatty acid absorption cause an osmotic diarrhea
- Can occur with ANY antibiotic
  - More commonly: penicillins, clindamycin, fluoroquinolones, cephalosporins
- Probiotics may be protective

Antibiotics
Adverse reactions

C. Difficile colitis

- Serious problem, significant cause of mobidity/mortality among elderly hospitalized patients
- Clostridium difficile is natural colonizer in 20% of patients
- Symptoms: watery diarrhea 10-15 times daily, abdominal pain/cramping, fever, leukocytosis, foul odor
- Treatment
  - Stop offending agent
  - Flagyl 500 mg PO TID
  - Vancomycin PO

Antibiotics
Prophylaxis for cardiac patients

American Heart Association

- Revised in 2007 to cover only the highest risk patients
  - No convincing evidence that antimicrobial prophyaxis provides significant benefit in preventing infective endocarditis
- Procedures involving manipulation of gingival tissue, periapical region of teeth, or perforation of oral mucosa
  - Does not include routine cleaning
- Highest risk cardiac conditions only
  - Prosthetic heart valves
  - Prior history of infective endocarditis
  - Unrepaired cyanotic congenital heart disease
  - Completely repaired congenital heart defects with prothetic material
  - Repaired congenital defects with residual defects
  - Cardiac valvulopathy in a transplanted patient

Antibiotics
Prophylaxis for orthopedic patients

American Academy of Orthopedic Surgeons, 2013

- Antibiotic prophylaxis administered prior to dental procedures for 2 years after prosthetic joint implantation, unless patient is immunocompromised

Antibiotics
Summary

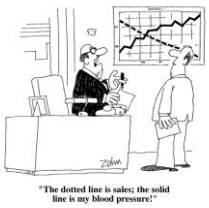
- Amoxicillin is good first line drug for odontogenic infections
- Augmentin is good for secondary space or sinus involvement
- Penicillin/Flagyl is a cost effective option
- Clindamycin is first line for PCN allergic patients
  - Use higher dose for active infections
- Azithromycin is suitable third alternative or when elixir is needed in PCN allergic patients
- Moxifloxacin is an expensive, last resort option
- Be conservative in prescribing antibiotics to avoid development of resistance and adverse reactions
- Start with smaller guns so you have a backup option

Drugs our patients take

- Anti-hypertensives
- Diabetic medications
- Anti-coagulants
- Anti-resorptive
- Herbal supplements

Anti-hypertensives

- 29-31% of American adults (58-65 million) have hypertension
- Options for therapy
  - Diuretics
  - Angiotensin-converting enzyme (ACE) inhibitors
  - Angiotensin II receptor blockers (ARBs)
  - Calcium channel blockers
  - Beta blockers
  - Combination therapy



Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

Which drug to choose?

- Goal is < 140/90 mm Hg
- All agents are roughly equally effective in lowering BP
  - Good response in 30-50% of patients with mild hypertension
- Wide interpatient variability
  - Patients respond differently to different medications
  - Side effect profile
- Race/Age considerations
  - Younger people respond better to ACE inhibitors or ARBs
  - African Americans respond better to diurectics and poorly to ACE inhibitors or beta blockers

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

Which drug to choose?

- First line drugs
  - Thiazide diuretics (African Americans)
  - calcium channel blockers
  - ACE inhibitors (diabetics, younger age)
  - ARBs (diabetics, younger age)
- Start with one drug, assess patient response, side effects
  - Start 2 drugs initially if BP is 20/10 mm Hg above goal
- Increase dose (side effect profile increases) one step
- If ineffective, try drug 2 (50% chance of responding)
- If ineffective, try drug 3 (60-80% chance of responding)

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

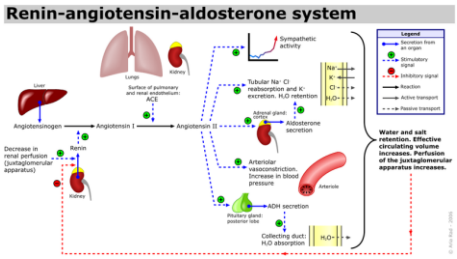
Thiazide diuretic

Chlorthalidone

- Inhibits sodium reabsorption in renal ascending loop of Henle
- Reduce extracellular fluid volume, cardiac output → decrease BP
- Preferred first-line drug (esp in African-Americans)
- Adverse effects
  - Electrolye abnormalities (hypokalemia, alkalosis)
  - photosensitivity

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

ACE inhibitors
ARBs



Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

ACE inhibitors

Lisinopril (Prinivil), enalapril (vasotec), ramipril (Altace), quinapril (Accupril)

- First line therapy for patients with
  - Diabetics (kidney protective)
  - heart failure
  - asymptomatic LV dysfunction
  - STEMI
  - Chronic kidney disease
- Adverse effects
  - Cough
  - Hypotension
  - Metabolic abnormalities (hyperkalemia)

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

angiotensin II receptor blockers (ARB)

Valsartan (Diovan), lorsartan (cozaar)

- Acts on renin-angiotensin-aldosterone system
- Good for those intolerant to ACE inhibitors
- Indications and efficacy similar to ACE inhibitors
  - Particularly pts with severe hypertension with LVH on ECG
- Adverse effects
  - Angioedema
  - Hypotension

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

calcium channel blockers

Amlodipine (Norvasc)

- Inhibit release of calcium
  - Vascular smooth muscle: reduce contraction, vasodilation
    - Dihydropyridine class
  - Cardiac muscle: reduce force of contraction and conduction of heart beat
- Adverse effects
  - Peripheral edema

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Anti-hypertensives

beta blockers

Metoprolol (Lopressor), atenolol (ternormin), carvedilol (coreg)

- Block beta receptors in sympathetic nervous system
  - Decrease heart rate
  - Decrease renin secretion
- Not recommended as first line therapy, especially ages > 60
  - Inferior protection against stroke risk
  - Small increase in mortality
- Good after MI and stable pts with HF or asymptomatic LVD
- Adverse effects
  - Heart failure
  - Beta blocker withdrawal
  - Bronchoconstriction
  - Depression, fatigue, sexual dysfunction

Choice of therapy in primary hypertension: Recommendations, 2013 UpToDate

Diabetic Drugs

- Metformin
- Glipizide
- Insulin

Diabetes Overview

- Hyperglycemia associated with microvascular and macrovascular complications
- Increased risk for infections, poor healers
- Causes
  - Lack of endogenous insulin (absolute in type 1; relative in type 2)
  - Resistance to insulin a target sites (muscle, fat and liver)
- Risk factors
  - Obesity (90% type 2 diabetics are obese)
  - Race (Native Americans, Hispanics, African Americans, Asians)
  - Family history
- Presentation
  - Asymptomatic
  - Polyuria, polyphagia, polydipsia
  - Blurred vision, extremity paresthesia, yeast infections

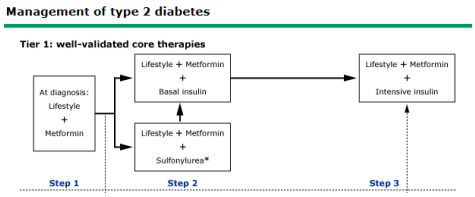
Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetes Overview

- Diagnosis
  - HbA1c > 6.5%
  - Fasting plasma glucose level of ≥ 126 mg/dl
  - 2 hr plasma glucose level of ≥ 200 mg/dl
  - Random plasma glucose of ≥ 200 mg/dl in a patient with symptoms
- Treatment
  - Lifestyle modifications
    - Diet (caloric restriction, low carbohydrate)
    - Weight loss (5-10% loss associated with improvements in risk factors)
  - Medications

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Treatment Algorithm



Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Metformin

- Biguanide
- First line choice for treatment of type 2 diabetes
- Decreases hepatic glucose production, increases peripheral insulin sensitivity
- Generally reduces HgA1c by 1.5% points
- Often leads to modest weight reduction or stabilization
- Cardiovascular benefits
- Adverse effects
  - GI related (diarrhea, N/V, flatulence)
  - Lactic acidosis (rare but serious)

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Glipizide

- Short-acting sulfonylurea
- Stimulates release of insulin from pancreatic beta cells
- Reduces HbA1c 1-2%
- Effectiveness decreases over time
- Adverse effects
  - Hypoglycemia
  - Weight gain

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Insulin

- Type 1 diabetic (absolute insulin deficiency)
- Type 2 diabetics
  - Traditionally reserved for those who have failed PO agents
  - Data support using insulin earlier and more aggressively
  - Inducing normoglycemia improves endogenous insulin secretion and insulin sensitivity resulting in better glycemic control

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Insulin

- Rapid acting (lispro, aspart, glulisine)
  - Given before meals
  - Continuous infusion via insulin pump to provide basal levels (Type 1)
- Intermediate to long acting (NPH, lantus,)
  - Given once or twice daily to provide basal insulin levels

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Insulin

Insulin type	Onset of action	Peak effect	Duration of action
Lispro, aspart, glulisine	5 to 15 minutes	45 to 75 minutes	Two to four hours
Regular	About 30 minutes	Two to four hours	Five to eight hours
NPH (Humulin)	About two hours	4 to 12 hours	18 to 28 hours
Insulin glargine (Lantus)	About two hours	No peak	20 to >24 hours
Insulin detemir (Levemir)	About two hours	Three to nine hours	6 to 24 hours*
NPL	About two hours	Six hours	15 hours
Insulin degludec	About two hours	No peak	>40 hours

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Diabetic drugs

Insulin

- Adverse effects
  - Hypoglycemia
  - Weight gain

Initial management of blood glucose in adults with type 2 diabetes, 2013 UpToDate

Anticoagulants

- Aspirin
- Clopidogrel (Plavix)
- Warfarin (Coumadin)
- Dabigatran etexilate (Pradaxa)

"Oh waiter! Will you pass me the anticoagulant please?"

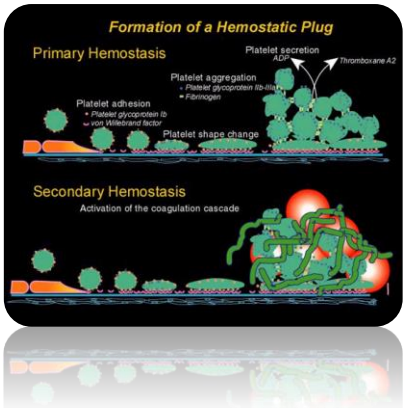
Hemostasis

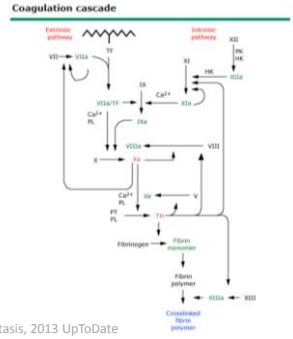
- Blood clot formation at site of vessel injury
- 4 stages
  1. Platelet plug formation
  2. Coagulation cascade
  3. Antithrombotic control mechanisms, termination of clotting
  4. Fibrinolysis (removal of clot)

Overview of hemostasis, 2013 UpToDate

ASA
Plavix

Coumadin
Pradaxa





Overview of hemostasis, 2013 UpToDate

Anticoagulants
Antithrombotics

- Aspirin, Plavix
- Primary and secondary prevention of
  - Heart attack
  - Stroke
  - Peripheral vascular disease
  - Coronary artery stent thrombosis

Anticoagulants
Aspirin

- Irreversible COX 1 inhibition, preventing thromboxane A2 formation (binds platelet molecules together)
- Strong evidence for benefits of ASA in decreasing risk of CVD events in a wide range of patients
  - Primary prevention of first CV event in moderate to high risk patients
  - Secondary prevention of CVD after vascular event
- No difference in efficacy between low vs high dose
- Adverse effects
  - Bleeding (GI)

Benefits and risks of aspirin in secondary and primary prevention of cardiovascular disease, 2013 UpToDate

Anticoagulants
clopidogrel (Plavix)

- Irreversible inhibition of ADP receptor on platelets (activation of platelets)
- Undergoes liver metabolism to its active form
  - Poor metabolizers have decreased response
- Uses
  - Patients intolerant to ASA (GI ulcer)
  - In combination with ASA after coronary stent placement to prevent thrombosis
- Adverse effects
  - Bleeding
  - Less GI side effects vs ASA

Antithrombotic therapy for percutaneous coronary intervention, 2013 UpToDate

Anticoagulants
Management of patients on ASA/plavix

- Do not hold ASA/plavix for patients undergoing routine extractions
  - Use local hemostatic measures (gelfoam, collaplug, surgicel,…)
  - Hold firm manual pressure and do not discharge until hemostasis is confirmed
  - Life threatening thromboembolic event vs minor bleeding
- For larger surgeries
  - Talk to physician, assess risk level
  - May be able to hold 1 antiplatelet agent if on ASA + plavix
  - May be able to hold both for 4 days
    - Compromise: some platelet action with less risk of thromboembolic event
  - Platelets lifespan is 7 days

Antithrombotic therapy for percutaneous coronary intervention and secondary prevention of stroke, 2013 UpToDate

Anticoagulants
warfarin (coumadin)

- Rat poison
- Inhibits vitamin-K dependent clotting factors (II, VII, IX, X), protein C/S.
- Peak effect in 36-72 hrs
- Indications
  - Atrial Fibrillation
  - Prosthetic heart valve
  - Deep vein thrombosis/pulmonary embolism
  - Anti-phospholipid syndrome
- Shortcomings
  - Interacts with food, other medications
  - Difficult to manage, requires multiple blood draws

Therapeutic use of warfarin, 2013 UpToDate

Anticoagulants
warfarin (coumadin)

Management

- Can do routine extractions with INR < 3.0-3.5
  - Most patients will be in this range
  - Use local hemostatic measures
- Larger surgical procedures in higher risk patients may require bridging
  - Enoxaparin (Lovenox)
  - Heparin IV

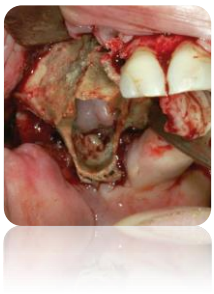
Anticoagulants

dabigatran etexilate (Pradaxa)

- Direct thrombin inhibitor
- Undergoes liver metabolism to convert to active form
- Maximum effect within 2-3 hrs after ingestion, half life 12-14 hrs
- Indications
  - Deep vein thrombosis/pulmonary embolism
  - Atrial fibrillation
- Lower rates of both embolic events and major bleeding vs warfarin
- Does not require laboratory monitoring, less susceptible to dietary/drug interactions
- Drawbacks: BID dosing, higher cost, no reversal agent

Anti-resorptives

- Bisphosphonate
  - Alendronate (Dosamax)
  - Ibandronate (Boniva)
  - Pamidronate (Aredia)
  - Risedronate (Actonel)
  - Zoledronic acid (Reclast, Zometa)
- Denosumab (Prolia)



Anti-resorptive related osteonecrosis of the jaws (ARONJ)

- Formerly BRONJ
- Use: osteoporosis, metastatic bone disease, bony malignancy
- Osteoblastic bone formation ↔ osteoclastic bone breakdown
- Osteoclastics are inhibited, thus breaking the normal cycle of bone turnover
- Necrosis of the jaw can occur spontaneously but more commonly associated with tooth extractions
- Frequency difficult to assess (no good clinical trials)
  - <1% with PO meds (osteoporotic patients)
  - 13% with IV meds (cancer patients)

Managing the care of patients receiving antiresortive therapy for prevention and treatment of osteoporosis, ADA 2011

Anti-resorptive related osteonecrosis of the jaws (ARONJ)

- Risk factors
  - > 65 years
  - Prolonged use of AR agents (> 2 yrs)
  - Smoking
  - Denture wearing
  - Periodontitis
  - Diabetes

Managing the care of patients receiving antiresortive therapy for prevention and treatment of osteoporosis, ADA 2011

Anti-resorptives

Bisphosphonates

Appendix 1 Bisphosphonate Preparations Currently Available in the US *

	Primary Indication	Nitrogen Containing	Dose	Route	Relative Potency**
Etidronate (Didronel)	Paget's Disease	No	300 -750 mg daily for 6 months	Oral	1
Tiludronate (Skelid)	Paget's Disease	No	400 mg daily for 3 months	Oral	50
Alendronate (Fosamax)	Osteoporosis	Yes	10 mg/day 70 mg/week	Oral	1,000
Risedronate (Actonel)	Osteoporosis	Yes	5 mg/day 35 mg/week	Oral	1,000
Ibandronate (Boniva)	Osteoporosis	Yes	2.5 mg/day 150 mg/month	Oral	1,000
Pamidronate (Aredia)	Bone Metastases	Yes	90 mg/3 weeks	IV	1,000 – 5,000
Zoledronate (Zometa)	Bone Metastases	Yes	4 mg/3 weeks	IV	10,000 +

Anti-resorptives

denosumab (Prolia)

- Monoclonal antibody targeting RANKL, key component in pathway for osteoclast formation and activation
- Not considered first line for postmenopausal women with uncomplicated osteoporosis
- Can be initial therapy for pts at high risk for fracture, intolerant, unresponsive to other therapies, impaired renal function

Anti-resorptives

Management recommendations

Based on expert clinical opinion; no good evidence exists

- Prior to anti-resorptive therapy, patients should seek dental consultation to optimize oral health
- During anti-resorptive therapy, prior to extraction/implant
  - <3 yrs on PO medications (unless on corticosteroids): proceed
  - > 3 yrs on PO medications: 3 month holiday before/after treatment
  - IV medications: drug holiday efficacy unknown; can consider burying roots + endo
- Good informed consent

AAOMS Position Paper on BRONJ, 2009 Update

Herbal Supplements

- 60 million Americans used herbal supplements on a regular basis
- Less than 10% of herbal supplement users inform their physicians before surgery
  - View that herbals are "natural" and do not have side effects
- Herbal supplements have significiant medicinal activity and potential for adverse effects and drug interactions

Overview of herbal medicine and dietary supplements, UpToDate 2013

Herbal Supplements

Bleeding

- Ginkgo biloba
  - Antioxidant properties, vascular problems, memory loss, dementia, macular degeneration
  - Antiplatelet effects: interacts with NSAIDs
- Garlic
  - Lowers BP, lowers cholesterol, cardio-protective
- Ginger
  - Nausea, motion sickness, aids digestion
- Ginseng
  - Increases physical/mental energy, enhances performace

Overview of herbal medicine and dietary supplements, UpToDate 2013