Dental Management of the Polypharmacy Patient

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The Oral systemic Connection

- Oral \[\rightarrow\] Systemic
- Systemic \[\rightarrow\] Oral
Objectives

- Common and emerging medications
- Oral manifestations of drug reaction and polypharmacy
- Dental treatment precautions and management of patients on multiple drug therapy.
Top 100 Drugs
Number of prescription (Mn) in USA 2012
imshealth

Total Market 4,078

1. hydrocodone/paracetamol (lortab, vicodin) 135.3
2. levothyroxine 107.5
3. lisinopril 90.8
4. simvastatin 86.1
5. metoprolol 78.1
6. amlodipine 66.0
7. omeprazole 65.7
8. metformin 61.6
9. salbutamol 61.5
10. atorvastatin 54.9
11 azithromycin 54.5
12 amoxicillin 52.0
13 alprazolam 49.2
14 hydrochlorothiazide 47.7
15 zolpidem 43.8
16 furosemide 41.9
17 fluticasone 41.4
18 sertraline 39.2
19 citalopram 38.9
20 gabapentin 38.0
21 tramadol 37.3
22 oxycodone/paracetamol 36.6
23 prednisone 34.0
24 warfarin 33.8
25 ibuprofen 33.4
Source: IMS Health, National Prescription Audit, Dec 2012
What is an iatrogenic illness?

- Physician-induced illnesses
  - Result from
    - Diagnostic procedures
    - Therapeutic intervention
  - Not a natural consequence of disease
  - Examples:
    - Complications of drug therapy
    - Nosocomial infections (MRSA)
    - Fluid and electrolyte disorders
    - Trauma
Polypharmacy

- Major concern in the elderly
  - Make up 13% of population
  - Account for 30% of all prescribed drug
Polypharmacy

- Concomitant use of multiple medications increases risk of:
  - Adverse drug reactions
  - Drug-drug interaction
  - Unwanted side effects
Polypharmacy

- Suboptimal prescribing
  - Inappropriate use
  - Underuse of medications

- Common in the elderly
- Leads to significantly increased morbidity
Polypharmacy

- Age-related changes in drug pharmacology
  - Kinetics (drug disposition)
  - Dynamics (target organ effects)
Polypharmacy

- Drugs absorption affected by:
  - Disease states (malabsorption)
  - Medications
    - Decrease absorption (e.g. antacids,
Drug distribution affected by:

- Age
  - Decreased water and lean body mass
  - Increased fat
    - Leads to increased serum concentration of water-soluble drugs
    - Leads to prolonged elimination of lipid-soluble drugs
  - Increased absorption across blood-brain barrier
Drug distribution affected by:

- Serum proteins
  - Drugs compete for serum proteins
  - Unbound drugs have more pharmacologic effect
  - May cause adverse drug reactions

- Eg: Coumadin patients given sulfa drugs or dilantin (excessive bleeding)
Polypharmacy

- Hepatic blood flow decreases with age
  - Decreases rate of drug metabolism
  - Increases risk of adverse drug reaction or overdose
  - First pass metabolism decreased
Polypharmacy

- Drug elimination
  - Primarily a function of the kidney
  - Decreased kidney function leads to slower elimination and increased drug levels. Requires lower maintenance doses of renally-excreted drugs
Target-organ responsiveness may be either increased or decreased

- Opiates – increased with age
- Beta-receptors – decreased with age
Drug interaction

- Activation of Cytochrom p450 and modulation of metabolism of another drug. Grapefruit juice interacts with 85 drugs including: benzodiazepines, amphetamines, statins, losartan, verapamil, levothyroxine, ambien, omeprazole, warfarin, oxycodone
Oral manifestations of drugs and oral adverse reaction

- Xerostomia
- Burning mouth
- Dysguesia
- Sialorhea, drooling
- Salivary gland swellings
- Gingival Hyperplasia
- Erythema Multiforme
- Ulcers
- Lichenoid reaction, pemphigus like lesions
- Hyperpigmentation
- Osteonecrosis of bone
Medications – which may enhance “dry mouth” or xerostomia

Over 400 prescription and OTC drugs have xerostomic effects.

- Anti-anxiety medications
- Antidepressants
- Antipsychotic
- Antihistamines
- Diuretics
- Anti-inflammatory NSAIDs
- Narcotic analgesics
- Anti-nausea drugs
Most xerogenicic drugs

- Amitriptyline
- Lithium
- Antihistamine
- HZT
- Tramadol
Xerostomia is the subjective feeling of oral dryness, which is often (but not always) associated with hypofunction of the salivary glands.

Hyposalivation is a clinical diagnosis (objective) that is made based on the history and examination, but reduced salivary flow rates have been given objective definitions.
Xerostomia - Hyposalivation

Subjective symptom

Objective sign

Not always correlated
Physiology of salivary glands: Saliva production

- **Unstimulated saliva**
  Secretions which enter the mouth in the absence of exogenous stimuli

- **Stimulated Saliva**
  Secretions in response to masticatory and gustatory stimulation or to other less common stimuli such as activation of the vomiting center

- **Total daily salivary flow** = 0.75-1.5 litres/day
  - 16 hours (daytime: US) x 0.3 ml/min = 300 ml
  - 7 hours (sleep: US) x 0.1 ml/min = less than 40 ml
  - 54 min. (meal: S) x 4 ml/min = 200 ml

- **Secretion**
  (US) 20% from parotid; 65% from SMX
  (S) 25% from SMX; 66% from parotid
The functions of salivary proteins

Antimicrobial activity: lysozyme, peroxidases, histatins
Hydration, lubrication, and protection against carcinogen and food toxins: mucins, proline-rich proteins
Remineralization: statherin, proline-rich proteins
Taste and digestion: gustin, amylase, lipase, proteases
Buffering: bicarbonate and phosphate ions, sialin
Mucosal integrity: water, mucins, growth factors

Growth factors
EGF (epidermal growth factor)
NGF (nerve growth factor)
  IGF I (Insulin like growth factor I)
  IGF II (Insulin like growth factor II)
TGF-alpha (transforming growth factor-alpha)
TGF-beta (transforming growth factor-beta)
bFGF (basic fibroblast growth factor)
Salivary gland impairment

Speech difficulties
Swallowing difficulties
Taste alteration
Social communication
Burning mouth
halitosis
candida
Diagnostic Tests for Oral Dryness

- Subjective questions
- No pooling in FOM
- Stringy, thick saliva
- Unstimulated sialometry
- < 1.5 ml/15 min = xerostomia
Age and xerostomia?

Despite the well supported association between age and dry mouth, controversial findings still exist. In a cohort of institutionalized elders >68 years old, the prevalence of xerostomia was shown not to be significantly related to age.
Gender and xerostomia

- Female sex as a risk factor for dry mouth has been well documented. Women have smaller glands and produce less saliva, and therefore have less functional capacity than men.
- Epidemiologic studies have demonstrated that women have a higher prevalence of xerostomia than men and that mean salivary flow rate in women is lower than in men.
In a cohort of institutionalized elders, Meds accounted for 42.3% of all cases of xerostomia. Nonmedicated subjects accounted for only 10% of xerostomia cases.

In 2 separate studies, >75% of hospitalized elders with medical conditions used medications with xerostomie side effects.

Xerostomia increases with the number of medications as well as the number of medical conditions.
CONCLUSION:

The use of medication increases the chance that an elderly person may present signs related to xerostomia and alterations in stimulated saliva flow and buffering capacity.
Management of Drug induced xerostomia
Be Proactive with patients!

- **Diagnosis**
  - R/O Sjögren’s
- **Treatment**
- **Patient awareness**
- **Aggressive prevention**
Treatment

- Artificial Saliva: Biotene
- Sugarless candy
- Sialagogues: Pilocarpine, Cevimeline
- Fluoride application
- Antifungal Medications
Management

Provide moisture & salivary flow

- Water, sip all day (6 glasses)
- Artificial saliva
- Sugar free hard candy or gum
- Ointments

Avoid dessicants

Alcohol, tobacco,
Goals of Oral Therapy

1. Restore/maintain oral health
2. Prevent future oral complications
   - Empower & Educate patient to take an active role in their oral health
3. Increase comfort & quality of life
Oral Management

- Complete dental exam-
  - Caries? Xerostomia? Periodontitis?
- Recall every 3-4 months
- Meticulous home oral hygiene
  - Brush, floss carefully
- Custom fluoride regimen
- Nutritional counseling
- Treat oral ulcers and fungal infections
Class V decay, Attachment loss
Hydration and Nutrition

- Drink plenty of fluids with meals – and throughout the day for hydration

- Liquid supplements if oral discomfort decreases regular food intake

- Room humidifiers help – *Keep clean*
New dental treatment considerations

- Dental Implants
  - Viable option in carefully chosen cases
Nutrition & Dryness

- Alcoholic and caffeinated drinks, increase oral dryness
- Alcohol containing mouthrinses, also dry oral tissues
Nutrition

- Nutrient absorption may be altered
  - Diet rich in proteins
  - Zinc
  - Iron
  - B vitamins
  - Vitamin C
  - Vitamin E
Lubricants/moisturizers

- Water or finely chopped ice chips
- Artificial saliva products
- Ointments
OTC - Salivary stimulants

- Sugarless gum
  - Xylitol

- Sugarless lozenge
  - Lemon or Cinnamon
Rx - Fluoride Products

- Toothpaste plus neutral sodium fluoride (Rx Prevident 5000 Plus)
- Neutral 1.1% sodium fluoride gel for use in custom trays
- Brush on gels
Burning Mouth Syndrome (BMS)
The Burning mouth syndrome

- Stomatodynia
- Stomatopyrosis
- Glossopyrosis
- Sore mouth
- Sore tongue
- Oral dysesthesia (abnormal and unpleasant sense of touch)
Burning mouth syndrome

Definition: “An intraoral burning sensation for which no medical or dental cause can be found”

International Headache Society
BMS Clinical presentation

* Pain involving the oral mucosa, tongue, hard palate or lips. described as “rawness”.

Onset is spontaneous but predisposing events such as dental treatment, trauma may occur.

* A mild discomfort on awakening, with increasing intensity throughout the day,
BMS usually does not interfere with sleep.

Burning and painful sensation can affect the urogenital and intestinal mucosa (vulvodynia). ACE inhibitors, xerostomia, dysesthesia and dysguesia may be associated.

A poor quality of life, anxiety are common
Burning mouth syndrome (BMS) - Differential diagnosis

- Local irritation (rough prosthesis or dental restoration)
- Contact hypersensitivity to dental materials
- Caustic oral rinses, tongue and cheek biting
- Oral candidiasis
- Lichen planus, BMP, pemphigus, migratory glossitis
- HSV, HZV
- Diabetes, hypothyroid, zinc def, vit B def, autoimmune markers may be elevated,
- xerostomia
- menopause
BMS (Etiology)

- Local factors
  - Trigeminal neuralgia
  - Atypical facial pain or neuralgia
  - TMJ dysfunction
  - Smoking
  - Submucous fibrosis
  - Fusospirochetal infection
  - Contact stomatitis (allergy)
  - Trauma to lingual nerve

- Systemic factors
  - Estrogen deficiency
  - Anxiety, stress depression
  - Parkinson’s disease
  - AIDS
<table>
<thead>
<tr>
<th>Local factors</th>
<th>Systemic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerostomia</td>
<td>Vitamin B deficiency (B1, B2, B6, B12)</td>
</tr>
<tr>
<td>Chronic mouth breathing</td>
<td>Folic acid deficiency</td>
</tr>
<tr>
<td>Chronic tongue thrust habit</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Chronic mechanical trauma</td>
<td>Chronic gastritis or regurgitation</td>
</tr>
<tr>
<td>Referred pain from teeth or tonsils</td>
<td>Chronic gastric hypoacidity</td>
</tr>
<tr>
<td>Angioedema</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>mercurialism</td>
</tr>
</tbody>
</table>
The literature yielded clinical cases in which oral burning sensation is described after the administration of drugs belonging to different therapeutic groups: antiretrovirals, antiseizure drugs, hormones and particularly antihypertensive medication. Curiously, among the different types of antihypertensive drugs, BMS was only associated with those compounds that act upon the angiotensin-renin system (ACE inhibitors and receptor blockers (ARB)).
Axonal degenerative changes in glossal terminal nerve fibers

Dysfunction of the small diameter afferent sensory fibers

Alterations of gonadal, adrenal and neuroactive steroid levels due to chronic stress
Burning mouth syndrome in Parkinson's disease: dopamine as cure or cause?

Coon EA¹, Laughlin RS.
BMS - Management

- Eliminate potential local and systemic factors
- Reassure the patient that this is not a fatal disease
- Antidepressants - Elavil
- Cognitive behavioral therapy CBT
- Alpha lipoic acid
- Gabapentin, clonazepam, capsaicin, topical steroids
Long term prognosis for idiopathic BMS is variable

One third - one half of patients experience a spontaneous or gradual remission month or years after onset of symptoms.

Other, may continue to experience symptoms through the rest of their life.

Patient should be reassured that this is benign and not a symptom of oral cancer.
Practical approach to management of BMS

- R/O xerostomia and candida
- R/O anemia, iron vit B12
- Alpha lipoic acid 600mg/d
- Clonazepam 1.5mg/d
- Elavil 10mg/d
- Distraction techniques
- Psychotherapy
Dysgeusia

Dysgeusia is a distortion of the sense of taste. Dysgeusia is also often associated with ageusia, which is the complete lack of taste, and hypogeusia, which is the decrease in taste sensitivity.
Dysgeusia (persistent abnormal taste)

- Found in appx 2 million adult Americans
- Dysguesia may be associated with underlying systemic conditions or by radiation therapy
- Trauma, tumors or inflammation of the peripheral nerves cause transient hypogeusia rather than dysgeusia
- Cold, URI produce mild dysgeusia
- CNS neoplasms produce dysgeusia and not ageusia
- Dry mouth and meds, depression, periodontal disease and candidiasis
# Dysgeusia and hypogeusia (etiology)

## Local factors
- Oral candidiasis
- Oral trichomoniasis
- Desquamative gingivitis
- Oral glvanism
- Periodontitis/gingivitis
- Chlorhexidine rinses
- Oral lichen planus
- xerostomia

## Systemic factors
- Vitamin A,B deficiency
- Zinc, Iron deficiency
- Overdose of vit A,B
- Food sensitivity or allergy
- Sjogren’s syn
- Chorda tympani nerve damage
- Anorexia, bulimia, cachexia
- Severe vomiting
Drugs associated with dysgeusia

- Anticoagulant
- Antihistamine
- Antihypertensive or diuretic
- Antimicrobial
- Antineoplastic
- Antiparkinsonian
- Antipsychotic
- Antirheumatic
- Antiseptic
- Antithyroid
- Hypoglycemic
- Opiates
- Sympathomimetic
- Vasodialtor
Systemic factors associated with dysgeusia

- Temporal arteritis
- Brain stem ischemia
- Migrane
- CNS tumor
- Gustatory nerve trauma
- Herpes zoster
- URI
- Chronic gastritis or regurgitation
- Bell’s palsy
- Head and neck radiation
- Liver dysfunction
- Crohn’s disease
- Familial dysotonomia
- Addison dis
- Alcoholism
- Medication (200 type)
- Anxiety, depression
- Pesticide ingestion
- Lead, copper or mercury poisoning
Management

- Discern dysgeusia from smell problem
- Taste and smell center (tests for 4 primary taste—sweet, sour, salty, bitter) in non odorous solution.
- If taste is described as metallic or rancid it may be associated with smell problem.

The altered taste may require a stimulus such as certain foods or liquids. If no stimulus is required the dysgeusia is classified as a “phantom taste”. Two thirds of patients experience spontaneous resolution within 10 month.
DRUG RELATED GINGIVAL HYPERPLASIA

- Associated with phenytoin for more than 50 years, valporic acid, vigabatrin
- Other drugs: numerous Ca channel blockers such as nifedipine and immunosuppressant - cyclosporine
- Prevalence related to phenytoin is approx 50%
- Cyclosporine and Ca channel blockers approx 25%
- Degree of gingival enlargement related to:
  - patient's susceptibility
  - level of oral hygiene
Clinical Features

- Starts after 1 to 3 months of drug use
- Originates in interdental papillae and spreads
- Anterior and facial most frequently involved
- Can cover portion or all of the crown
- Edentulous areas generally not affected
Treatment & Prognosis

- Discontinuation of the medication
- Substitution of one Ca channel blocker for another
- Plaque control, scaling, and gingivectomy
- Peridex rinse
- Cyclosporine hyperplasia least responsive to plaque control, replace with tacrolimus
ERYTHEMA MULTIFORME

- Blistering, ulcerative mucocutaneous condition
- Uncertain etiology - immunologically mediated?
- Triggering factors in 50%
  - preceding infection
    - Herpes
    - Mycoplasma
  - drugs and medications
    - antibiotics
    - analgesics
Clinical Features

- Young adults 20s or 30s
- Men > women
- Self-limiting, usually 2 to 6 weeks
- 20% recurrent episodes, usually in the spring and autumn
Clinical Features

- Skin - 50%, variety of appearances
  - Flat, round, and dusky-red on extremities
  - Concentric circular erythematous rings
    - a target or bull's-eye
- Oral lesions large, shallow ulcers with irregular borders
- Hemorrhagic crusting of the vermillion zone of lips
Stevens-Johnson Syndrome

- EM Major
- Severe form of disease
- Usually triggered by a drug rather than infection
Treatment and Prognosis

- Oral lesions – topical steroids
- More severe disease - systemic steroids
DRUG REACTIONS

- Stomatitis medicamentosa - several different patterns:
  - anaphylactic stomatitis
  - intraoral fixed drug eruptions
  - lichenoid drug reactions
  - lupus-like eruptions
  - pemphigus-like drug reactions
  - nonspecific vesiculoulcerative lesions

- Fixed drug eruptions - recur at same site
DRUG REACTIONS

- Relatively common disease
- Immunologically mediated - caused by a variety of drugs
- Reticular or erosive with fine white striations or multiple eroded, ulcers
DRUG REACTIONS

- Common on buccal mucosa, tongue, gingiva, palate
- Desquamation of surface epithelium - erosive form
- Many agents implicated - new drugs identified frequently
- Some of the categories are:
  - Antihypertensives
  - Analgesics
  - Antidepressants
  - Antipsychotics
  - Antibiotics
  - NSAIDs
Treatment and Prognosis

- Localized reactions - topical steroids
- If discontinuation of the medication is contraindicated, palliative care can be provided
- Steroids often ineffective if offending medication is continued
CONTACT ALLERGIES

- Foods, chewing gums, dentifrices, mouthwashes, topical anaesthetics, restorative materials, acrylic denture materials and denture adhesives, metal alloys

Cinnamon and amalgam - unique patterns

- Oral mucosa is much less sensitive than skin
  - period of contact is often brief
  - saliva dilutes and removes many antigens
Clinical Features

- Acute or chronic
- Distinct female predominance
- Burning is the most frequent symptom
- Acute – mild, barely visible erythema to a brilliantly red lesion with or without edema
- Chronic - erythematous or white and hyperkeratotic
PLASMA CELL GINGIVITIS

- First reported 1960s -70s with allergic reaction to cinnamon chewing gum
- Also to herbal toothpaste, mouthwash, mint candy, peppers used for cooking
- Gingiva - diffuse enlargement with bright redness and loss of stippling
- Edentulous areas are less affected
- With chewing gum, lips and tongue involvement also seen
Histology and Treatment

- Thickened, edematous and inflamed epithelium with multiple microabscesses
- Intense inflammatory consisting primarily of plasma cells
- Complete and thorough history
- Elimination of possible allergens
- Idiopathic cases may have to be treated with topical or systemic steroids
- Many do not respond to any treatment
(Rituximab) is a unique therapy that selectively targets CD20-positive B-cells, shown to play an important role in non-Hodgkin B cell lymphoma and rheumatoid arthritis.
chemosteonecrosis of bone (bisphosphonate and biological drugs)
Background

- Bisphosphonates are used to treat osteoporosis, Paget dis, myeloma, metastatic solid tumors
- Main mechanism of action: inhibition of osteoclastic activity (they also affect apoptosis, adhesion and invasion), slight inhibition of osteoblastic activity as well
- Oral and intravenous preparations
- First reports of ONJ about 10 years ago.
- Systematic review of the literature (450 cases up to early 2010): Mandible>maxilla (2:1); 60% had prior dental procedure (Ann Int Med, May 2006)
Reclast
Reclast
Denosumab
A retrospective review of patients’ medical and dental charts at the University of Florida (UF) and the associated Veterans Administration Medical Center (VAMC) between 01/04-02/07
Summary of Results

- Shands side: 15 patients (14 MM, 1 Pr CA); VA side: 12 patients (2 Br, 2 H&N, 1 RCCA, 2 PrCA, 5 MM)
- Total of 27 patients
- 12 patients received sequential A/Z, 11 had Z, 3 had A
- 10 had prior dental procedure
- Median length of treatment 29 mo (range, 7-88)
- 21 Mandible, 4 Maxilla, 2 both
Summary of Results II

- Three centers involved with different incidence:
  1. Shands- BMTU: 13%* in MM, while only 4% in those receiving Aredia
  2. Shands Cancer center: 1.7%
  3. VAMC: 4.2%

*In 2 & 3, mostly solid tumors*
Interferon Alpha

Antiviral agent that modulates functions of the immune system in hepatitis C affected subjects
Oxcarbazepine

- Oxcarbazepine is an aromatic antiepileptic drug indicated for the treatment of partial seizures as both monotherapy and adjunctive therapy in adults and children with epilepsy (analogue of carbamazepine) and is considered to be much safer due to its different metabolic
Certolizumab injection is used to relieve the symptoms of Crohn's disease in people who can no longer be helped by other medications. Certolizumab injection is in a class of medications called tumor necrosis factor (TNF) inhibitors. It works by blocking the activity of TNF, a substance in the body that causes inflammation.
Cimzia (side effects)

- Swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs
- Hoarseness, shortness of breath, difficulty swallowing or breathing
- Chest pain, sudden weight gain
- Hives, rash, especially on the cheeks or arms that worsens in the sun
- Pale skin, blistering skin, dizziness
- Extreme tiredness, numbness or tingling
- Problems with vision, weakness in the arms or legs
- Joint pain, loss of appetite
- Red scaly patches and/or pus-filled bumps on the skin
- Receiving certolizumab injection may increase the risk of developing leukemia (cancer that begins in the white blood cells) and other types of cancer in adults and children.
Cimzia (side effects)

- blood and lymphatic system malignancies (including lymphoma and leukaemia), solid organ tumours, non-melanoma skin cancers, pre-cancerous lesions (including oral leukoplakia, melanocytic nevus), benign tumours and cysts (including skin papilloma)
Drugs affecting oral bleeding

- Platelets function and aggregation
- Coagulation cycle
**Bleeding Disorders**

Table 6 Common drugs affecting platelets

<table>
<thead>
<tr>
<th>Functional impairment</th>
<th>Thrombocytopenia</th>
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</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Heparin or analogues</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Chemotherapeutic agents</td>
</tr>
<tr>
<td>Ticlopidine, clopidogrel</td>
<td>Quinidine</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Quinine</td>
</tr>
<tr>
<td>Clofibrate</td>
<td>Trimethoprim-sulfamethoxazole</td>
</tr>
<tr>
<td>Sulphinpyrazone</td>
<td>Methyldopa</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Furosemide</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Histamine H$_1$ antagonists</td>
<td>Cephalosporins</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Carbamazapine</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Valproic acid</td>
</tr>
</tbody>
</table>

NSAIDs = nonsteroidal anti-inflammatory drugs

Bleeding Disorders

Oral findings

- Petechiae/purpura
- Ecchymosis
- Gingival bleeding

Photo courtesy of Dr. Brad Neville

Photo courtesy of UFCD Oral Biopsy Archive
Bleeding Disorders

Anticoagulation
Bleeding Disorders

Anticoagulation agents

- Warfarin
- Antiplatelet drugs
- Aspirin/NSAIDs
- New oral drugs
Bleeding Disorders

Anticoagulation - Warfarin

- Warfarin (Coumadin) *oral* anticoagulant
  - Synthetic derivative of coumarin
  - Inhibit biosynthesis of vitamin K-dependent coagulation proteins: Factors VII, IX, X and prothrombin
  - Monitor by INR (values range 2.0-3.5)
  - Long half life – needs to be stopped 2-3 days prior to surgery
  - Reversal agents: vitamin K (slow), fresh frozen plasma (rapid), rFVIIa, Prothrombin Complex Concentrates (2,7,9,10; Profilnine*), FEIBA
Many medications affect the activity of warfarin:
- Antibiotics: metronidazole, erythromycin, ciprofloxacin
- Anticonvulsants: phenytoin
- Antacids: cimetidine
- Anti-cholesterol: simvastatin
- Antineoplastic agents
- Vitamin K
- Foods: bananas, lettuce
Bleeding Disorders

Antiplatelet drugs

- Platelets are an important contributor to arterial thrombi
- Antiplatelet therapy important in prevention and treatment

Medications:
- Aspirin
- NSAIDS
- Clopidogrel (Plavix), Ticlopidine (Ticlid) inhibit platelet aggregation
- Prasugrel (Effient)
- Eptifibatide (Integrilin), Abiximab (Reopro)
- Dipyridamole (Persantine)
Bleeding Disorders

Aspirin/NSAIDS

- Inhibits platelet cyclooxygenase preventing synthesis of thromboxane
  \[ \text{A}_2 \rightarrow \downarrow \text{platelet aggregation} \]

- Aspirin – irreversible

- NSAIDS – reversible

- Rarely a problem in minor oral surgery
FDI Information for Healthcare Professionals: Concomitant Use of Ibuprofen and Aspirin
New Information [9/2006]

Ibuprofen can interfere with the anti-
platelet effect of low dose aspirin (81 mg per day), potentially rendering aspirin less effective when used for cardioprotection and stroke prevention. Healthcare professionals should advise consumers and patients regarding the appropriate concomitant use of ibuprofen and aspirin.
Aspirin and Ibuprofen

- Patients who use immediate release aspirin (not enteric coated) and take a single dose of ibuprofen 400 mg should dose the ibuprofen at least 30 minutes or longer after aspirin ingestion, or more than 8 hours before aspirin ingestion to avoid attenuation of aspirin’s effect.
New oral anticoagulants

- dabigatran (Pradaxa)
  Direct thrombin inhibitor, prevents it from catalyzing fibrinogen into fibrin

- rivaroxaban (Xarelto)
  Factor Xa inhibitor, prevents conversion of prothrombin (FII) to thrombin
  No reversal agents but short half lives (5-9 hrs)
  May need to discontinue 24 hrs before surgery if concerned about complications from excessive bleeding/impaired hemostasis
Management of patients on anticoagulation medication
Bleeding Disorders

- Consult with physician
- Obtain baseline studies: INR, PT, aPTT, platelet count, platelet function test (rarely ordered)
- Schedule patient to coincide with hematology correction eg. platelet transfusion, factor replacement
- Good surgical technique
- Augment clotting with use of local measures such as sutures, gelfoam, surgicel, antifibrinolytics
- Post operative instructions, close follow up
- Do not give aspirin/NSAIDS
Bleeding Disorders

Management of the patient on warfarin

- Consult with patient’s physician re safety of stopping warfarin

INR 2.0-3.0 dose does not need to be altered

INR 2.5-3.5 dose may need to be altered

INR >3.5 dose adjustment
Bleeding Disorders

Management – warfarin therapy

• Stop warfarin 2-5 days prior to surgery
• Obtain INR on day of procedure or day before
• Good surgical technique
• Local measures, post operative instructions
• Do not give aspirin/NSAIDS
• Restart warfarin night of procedure, follow up with physician
• Careful post operative follow up
Management of the patient on antiplatelet therapy

- Consult with physician re safety of stopping medication
- Stop medication for 7-10 days ???
- Local measures
- Post operative instructions
- Restart medication next day if no bleeding
Bleeding Disorders

Local measures for hemorrhage control

- Pressure
- Sutures
- Gelfoam with thrombin
- Oxycel, surgicel, microfibrillar
Antifibrinolytic agents

- **Tranexamic acid** — synthetic antifibrinolytic. 25mg/kg PO TID starting prior to procedure, continue 7-10 days. Also available as a mouthwash.

- **Aminocaproic acid** — synthetic antifibrinolytic, used as an adjunct with factor replacement. Administer PO or IV.
Bleeding Disorders

Regulation

Clot formation

Excessive thrombosis

Clot dissolution

Excessive bleeding
Thank You!!