LEARNING OBJECTIVES

• Outline the management of adverse drug effects in the oral cavity, especially xerostomia.
• Explain which drugs are most likely to cause drug-induced bruxism and orofacial movement disorders.
• Know where to find oral adverse drug effects in registered product information.
ORAL HEALTH TRACKER

ORAL HEALTH FACTS

- Only 51% of Australian adults (≥15 yrs) brush their teeth twice a day
- Only 69% of children (5-14 years) brush twice a day
- 26% adults have untreated tooth decay, 20% have gum disease
- Only 70% adults ≥65yrs visit dental practice once a year.
- Only 36% veterans ≥ 80yrs visited dentist in last 2 yrs. (Vets Mates)

ORAL HEALTH IN ELDERLY – PARTICULAR PROBLEM

• Ageing population living longer and keeping their teeth longer.
• Effects of ageing make maintaining good oral hygiene more difficult
  • Impaired mobility
  • Poor vision
  • Impaired manual dexterity

ORAL HEALTH ISSUES IN THE ELDERLY

• Dental caries
• Xerostomia
  • = Caries, probs chewing, swallowing, speaking
• Periodontal disease
  • Stomatitis
  • Gingivitis
  • Glossitis
• Bacterial infections
• Candidiasis
• Tooth loss

• Autoimmune disease
  • Bullous pemphigoid
  • Lichen planus
• Pre-malignant & malignant conditions
  • eg lichen planus
• Intra-oral pain
• Gingival enlargement
• Swallowing difficulty
EFFECTS OF SMOKING AND DRINKING

SMOKING

- Stains teeth and gums
- Nicotine vasoconstriction = impaired wound healing
- Dry mouth & periodontal disease = tooth loss
- **Oral cancer (RR =14x)**

ALCOHOL

- Trauma from accidents
- Dental staining
- Dehydration & dry mouth
- Sugar content & acid erosion = caries
- **Oral cancer (RR = 6x)**

[Source](https://www.dhsv.org.au/__data/assets/pdf_file/0008/3104/tobacco-alcohol-drugs-how-do-they-affect-your-mouth.pdf)
MANAGING DRUG-INDUCED ORAL PATHOLOGY

• Most adverse drug effects are DOSE and TIME related
• Can often be managed by reducing the dose or ceasing.
• Consider added risk from drug interactions

“Discovering that a symptom is caused by a drug presents an uncommon opportunity to effect a total “cure” by stopping the offending prescription or lowering the dose.” Prof Jerry Avorn BMJ. 2008 Apr 26; 336(7650): 956–957

DRY MOUTH – SUBJECTIVE OR OBJECTIVE

• Up to 40% people ≥65 years in community report dry mouth
• Up to 50% in aged-care facilities.


- Most objective dry mouth due to decreased saliva production.
- Drug induced: varies with drug type, dosage, duration, polypharmacy and drug interactions.
- TYPE: CV meds 7%, antidepressants 71%, bladder instability 80% of pts
- #1 drug = Oxybutynin, followed by other antimuscarinics.
- Risk also increases with the number of medicines used and with age.
MEDICATED INHALERS = >30!!!

ORAL ADVERSE EFFECTS FROM INHALERS

Dry mouth (antimuscarinics, beta agonists)
Dental caries
Oral candidiasis
Taste disturbance (dysgeusia)
Gingivitis
All exacerbated by poor technique!
DRUG-INDUCED TASTE DISTURBANCE

- Dysguesia: altered taste
  - Sweet
  - Sour
  - Salt
  - Umami
  - Bitter (metallic)
- Aguesia: loss of taste
  - terbinafine


TREATMENT OF DRY MOUTH

- Oral lubricants or saliva substitutes
- Cease or reduce dose of offending medication/s
- Deprescribe unnecessary medications
- Improve technique of antimuscarinic inhalers
- Minimise drug interactions adding to risk
SIALORRHOEA/ HYPERSALIVATION

• Cholinesterase inhibitors: donepezil, rivastigmine, galantamine
• Anti-D2 dopaminergics: Clozapine, risperidone, quetiapine
• Buprenorphine, lamotrigine, all sedatives
• Drooling from drug-induced parkinsonism: e.g. Prochlorperazine, metoclopramide

• TREATMENT:
  • Atropine 1% eyedrops
  • BOTOX
  • (Propantheline 15mg tablets: 1-3 tabs 3-4x day) = out-dated!

ORAL SIDE EFFECTS FROM ANTIMICROBIALS

• Oropharyngal candidiasis
• Nausea, reflux, loss of appetite
• Black hairy tongue
• Tooth discolouration
  • E.g. linezolid (yellow)
TOOTH DISCOLOURATION

• **Extrinsic** = occurs after the tooth has erupted into the mouth. The drug subsequently causes superficial discoloration.

• **Intrinsic** = drug interferes with odontogenesis and is permanent.

Figure 1. Extrinsic staining caused by a chlorhexidine mouthwash.  
Figure 2. A typical presentation of dental fluorosis.

**Table 1. Drugs Causing Extrinsic Tooth Discoloration**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Discoloration Caused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhexidine</td>
<td>Yellow/brown</td>
</tr>
<tr>
<td>Oral iron salts</td>
<td>Black</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>Yellow or grey-brown</td>
</tr>
<tr>
<td>Essential oils</td>
<td>Yellow/brown</td>
</tr>
</tbody>
</table>

**Table 2. Drug-related Intrinsic Tooth Discoloration**

<table>
<thead>
<tr>
<th>Drug-related Permanent Tooth</th>
<th>Discoloration Caused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoride</td>
<td>White/brown discoloration</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Yellow + brown/grey</td>
</tr>
<tr>
<td>Minocycline</td>
<td>Green-gray/blue-grey</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Greenish</td>
</tr>
</tbody>
</table>

TETRACYCLINES CAUSE MULTIPLE PROBLEMS

• Minocycline-induced intrinsic tooth discolouration
• Can also cause blue-grey discolouration of
  • Erupted teeth
  • Oral mucosa, gums
  • External skin

GINGIVAL HYPERPLASIA

• ALL calcium channel blockers
  • Dihydropyridine most likely, espec. amlodipine
• Other drugs:
  • Phenytoin (~50% pts) only 17 reports on TGA DAEN
  • Valproate (rare)
  • Cyclosporin (up to 30% pts) only 14x reports TGA DAEN
• Oral hygiene also contributes to GH.

Look for in combination products e.g. Exforge, Amlodipine/Valsartan Novartis (amlodipine/valsartan).
LICHENOID REACTIONS

- Oral lichen planus (OLP) quite common: 1-2% population.
- White, lacy painful lesions on oral mucosa. Often misdiagnosed as fungal.
- **Drug-induced “lichenoid lesions”** mimic OLP clinically and histologically
- Drugs implicated *:
  - beta-blockers, ACE inhibitors, thiazides, CCBs, sulphonylureas, anti-malarials, gold, penicillamine, allopurinol
- Often seen in close proximity to amalgam and other metallic restorations.


ORAL SIDE EFFECTS **ANTIDEPRESSANTS AND ANTIPSYCHOTICS**

- Xerostomia, stomatitis, glossitis
- Nausea and reflux
- Taste disturbances
- Memory problems –impaired ADLs
- Oro-buccal-lingual dyskinesia
- Bruxism and tooth grinding
DRUG–INDUCED MOVEMENT DISORDERS

• **Orobuccolingual dyskinesia (OBLD)**
  - well-coordinated continual movements of the mouth, tongue, jaw, and cheeks
  - may include lip smacking, cheek puffing, and tongue thrusting. May resemble chewing motions.

• **Drugs involved**
  - Metoclopramide & Prochlorperazine
  - 1st generation antipsychotics (haloperidol, chlorpromazine, fluphenazine)

DRUG–INDUCED BRUXISM

• “A repetitive jaw-muscle activity characterised by clenching or grinding of the teeth and/or bracing or thrusting of the mandible, which may occur during the day or night.”

• Occurs in up to 20% children and adults, especially at night.

• **SSRI antidepressants** = most common drug cause.

• **SNRIs, amphetamines and atomoxetine** **chlorpromazine**, also reported.

• **Onset** – can occur from first dose. Usually within first week or days of dose increase.

• Treatment for bruxism and temporomandibular joint dysfunction will not succeed until drug cause eliminated or reduced.
INTRAORAL HAEMORRHAGE

- **Risk factors include**
  - thrombocytopenia, defective vascular integrity,
  - altered coagulation, periodontal disease

- **Drugs** which contribute
  - Antiplatelet agents
  - Anticoagulants, heparinoids,
  - Herbal remedies assoc’d with bleeding eg. Turmeric, garlic, fish oil, krill oil, ginkgo, meadowsweet, devils claw etc.
  - Drug-induced thrombocytopenia e.g. quinine, methotrexate
  - Corticosteroids – weaken the integrity of oral mucosa

OSTEONECROSIS OF THE AW (ONJ)

- ONJ is exposure of mandibular or maxillary bone through lesions in the gingiva that do not heal.
- Lesions are more common in the mandible than maxilla.
- Most frequent after invasive dental procedures, such as extractions, but can also occur spontaneously.
- May be asymptomatic for weeks or months until exposed bone lesions appear.
- Originally assoc’d with bisphosphonates (BRONJ), now wide range of drugs.
MOST COMMON DRUGS ASSOC’D WITH ONJ

• **DENOSUMAB** (Xgeva, Prolia)
  - Oncology use > osteoporosis
  - Short-acting, so schedule extractions to end of dosage interval

• **Bisphosphonates** - prev. 10 yrs
  - Intravenous > oral
  - Oncology setting > community
  - Drug holiday still helps

• **Corticosteroids**: systemic use increases ONJ risk significantly

Anti-angiogenic drugs

• **Anti-VEGF drugs**: Bevacizumab, Aflibercept

• **Tyrosine kinase inhibitors**: Sunitinib, Sorafenib,
  - M-Tor inhibitors
  - Sirolimus, everolimus
  - Methotrexate

PHARMACIST’S ROLE IN ONJ PREVENTION

1. Don’t frighten anyone!
2. Help calculate ONJ risk from ALL risk factors.
3. Manage all modifiable risks and monitor.
WHERE TO FIND ORAL ADRS IN PRODUCT INFO

There is no “dental” or “oral” section for ADRs in the PI.

- GASTROINTESTINAL = dry mouth, taste disturbance, mouth ulcers, ONJ
- PSYCHIATRIC: bruxism, tardive dyskinesia,
- NERVOUS SYSTEM or SPECIAL SENSES: dysgeusia, tardive dyskinesia
- DERMATOLOGICAL: oral mucosal disorders, tongue effects, stomatitis.
- MUSCULOSKELETAL: osteonecrosis of the jaws.

PHARMACIST’S ROLE

- Educate on maintenance of good oral health
- Identify, manage and prevent oral ADRs
- Advise on limitations of product information for oral ADRs.