THE UNIVERSITY OF WESTERN AUSTRALIA

DENT 3005:Introduction to Pharmacology

Endocrine drugs: Drugs for obesity

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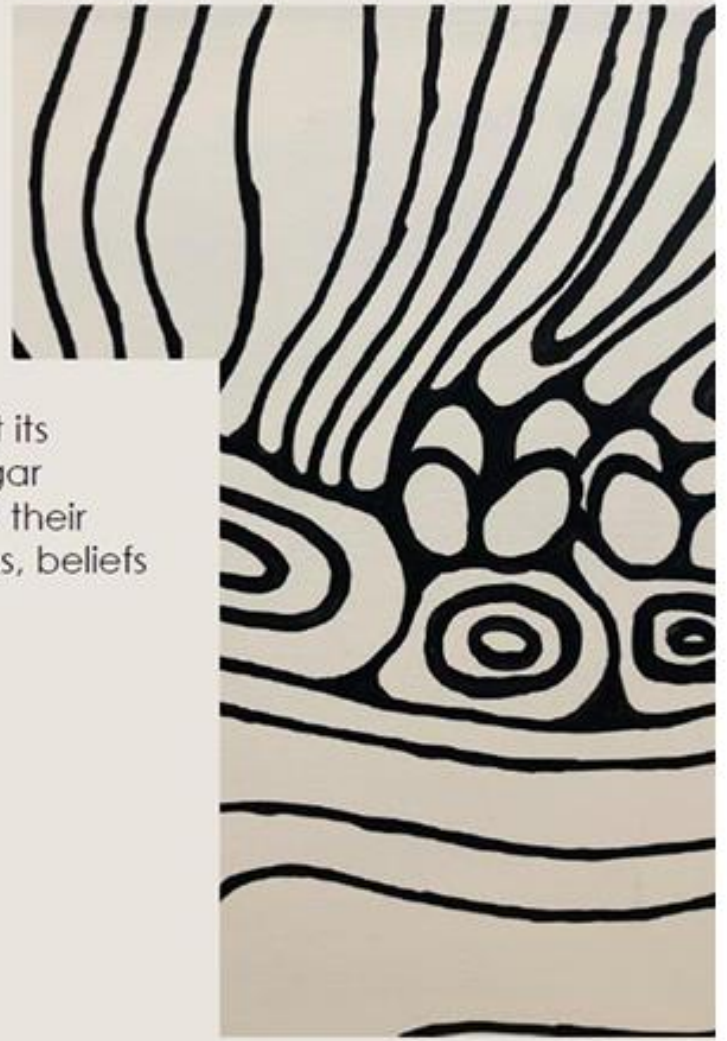
Acknowledgement of country

The University of Western Australia acknowledges that its campus is situated on Noongar land, and that Noongar people remain the spiritual and cultural custodians of their land, and continue to practise their values, languages, beliefs and knowledge.



Artist: Dr Richard Barry Walley OAM

Learning Outcomes

Learning objectives

1) Understand the different types of drugs for obesity
2) Recognise oral and dental side effects of these drugs
3) Understand drugs interactions with dental medications
4) Identify and understand the oral health implications of obesity
5) Applied knowledge to clinical scenarios

Obesity

- Linked to lots of health issues: heart disease, musculoskeletal problems, HTN, T2DM, cancers…
- Obesity (BMI >30) or in overweight people (BMI >27)
- However BMI alone is not always an accurate indicator
  - Overestimate: body builders, performance athletes, pregnant people
  - Underestimate: elderly, people w/ physical disability
- A person's waist circumference is a better predictor of health risk than BMI
  - Recommended to use in combination w/ BMI values

Waist circumference
For men:
- **94 cm or more** – increased risk
- **102 cm or more** – substantially increased risk

Waist circumference
For women:
- **80 cm or more** – increased risk
- **88 cm or more** – substantially increased risk

Drugs for obesity (in GI lectures)

- **Orlistat**
  - MOA: inH GI lipases
  - Fecal urgency/incontinence
- **Phentermine**
  - MOA: sympathomimetic w/ CNS stimulatory effect
  - CNS overstimulation
    - Restlessness, nervousness, tachycardia, agitation, HTN, dry mouth!
- Dietary and lifestyle factors

Generic name	Brand Name
Orlistat	Xenical
Phentermine	Duromine

Drugs for obesity

- These are al indicated as an adjunct to lifestyle modification in obesity
- **Liraglutide (T2DM) & Semaglutide (T2DM)**
  - Analogues of glucagon-like peptide-1 (an incretin)
  - ADR: gastrointestinal sx, hypoglycaemia (+SU/insulin)
- **Tirzepatide (T2DM)**
  - Agonist at glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptors
  - ADR: gastrointestinal sx, hypoglycaemia (+SU/insulin)
- **Naltrexone w/ bupropion**
  - MOA: Not fully understood; may be due to effects on the appetite regulatory centre

Generic name	Brand Name
Liraglutide	Saxenda inj
Semaglutide	Ozempic
Tirzepatide	Mounjaro inj
Naltrexone w/ bupropion	Contrave

Drugs for Obesity Dental implications

- **Orlistat**: Be mindful of long procedures → faecal urgency/incontinence may require bathroom breaks
- **Phentermine**: dry mouth → higher risk of caries and oral discomfort
  - Avoid with **tramadol** (serotonin toxicity)
- **Naltrexone + Bupropion (Contrave)**
  - ADR: dry mouth
  - Blocks opioid receptors → opioid analgesics ineffective
  - Bupropion inhibits CYP2D6 → avoid tramadol, oxycodone
  - Pain relief limited to **paracetamol and NSAIDs**
  - Increases seizure risk with **benzodiazepines**
- **Liraglutide & Tirzepatide**: similar considerations as in diabetes lecture → GI side effects, hypoglycaemia
- **Obesity considerations**
  - Linked with comorbidities: **HTN, diabetes, OSA**
  - **OSA** → snoring, mouth breathing → impacts saliva and increases decay risk
  - Check **dental chair weight limits** for patient safety

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DENT 3005:Introduction to Pharmacology

Endocrine drugs: Drugs affecting bone

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Learning Outcomes

Learning objectives

1) Understand the different types of drugs affecting bones
2) Recognise oral and dental side effects of these drugs
3) Understand drugs interactions with dental medications
4) Understand pathophysiology and risk factors for medication-related osteonecrosis of the jaw (MRONJ)
5) Understand management for these patients in the dental setting
6) Applied knowledge to clinical scenarios

Osteoporosis

- Characteristics: low bone mineral density (BMD) and microarchitectural deterioration of bone tissue → bone fragility, increased fracture risk.
- Risk factor for minimal-trauma fracture: falls, old age, osteoporosis
- Rationale for drug therapy: To prevent fractures and associated morbidity in people with low BMD or history of fracture
- Assess underlying conditions: hyperthyroidism, hyperparathyroidism, deficiencies (vit D), medications , cancer and many more

	Drugs affecting bones
Drug therapy	Calcium: routine management Vitamin D: correct vitD deficiency Bisphosphonates: 1st line osteoporosis Denosumab: alternative to bisphos. Raloxifene Romosozumab HRT: controversial

Bone metabolism

- Aka bone remodelling
- A lifelong dynamic process – involving continuous remodelling of bone
  - Osteoclasts are bone-resorbing cells that break down old bone
  - Osteoblasts are bone-forming cells that create new bone
- Chemical mediators
  - Glucocorticoids, PTH, vit D, RANKL
- Parathyroid: 4 small glands in the neck, regulate calcium and phosphorus
  - Release of calcium by bones into blood stream
  - Absorption of calcium from food by intestines
  - Conservation of calcium by kidneys

Bisphosphonates

- MOA: Decrease bone resorption by inhibiting osteoclasts
- Oral formulation: alendronate, ibandronic acid, risedronate
- Injectables: Pamidronate, zoledronic acid
- MRONJ risks
- Consider full dental assessment and complete any dental procedures: the MGP should liaise w/ the dentist

Generic name	Brand Name
Alendronate	Fonat, Fosamax Plus
Ibradronic acid	Bondronat
Pamidronate	Pamisol inj
Risedronate	Actonel
Zoledronic acid	Aclasta inj Osteovan inj Deztron inj Zometa inj

Postmenopausal osteoporosis

- **Denosumab:** human monoclonal antibody
  - Binds RANKL & prevent activation of RANK receptor
  - Reduce formation & activity of osteoclast → reduce bone resorption
- **Raloxifene:** Estrogen agonistic effects on bone mass and lipid
- **Romosozumab:** bones sclerostin & inhibit its activity
  - Increases bone formation & decrease bone resorption
- **Teriparatide:** active fragment of human parathyroid hormone
  - Promotes bone formation and increases BMD.

Generic name	Brand Name
Denosumab	Prolia inj Xgeva inj
Raloxifene	Evista Ralovista
Romosozumab	Evenity inj
Teriparatide	Teriparatide Lupin inj Terrosa inj

Vitamin D

- MOA: regulate calcium homeostasis & bone metabolism
  - Increase intestinal & renal absorption of calcium & phosphate
  - Promote bone mineralisation
- **Calcitriol:** active form of vit D
  - Rapid onset, short duration
- **Cholecalciferol:** a precursor to calcitriol
  - Slow onset, prolonged duration
- ADR due to hypercalcemia
  - Nausea, vomiting, constipation, anorexia, apathy, muscle weakness, headache, thirst and polyuria

Generic name	Brand Name
Calcitriol	Calitrol Rocaltrol Sical
Cholecalciferol	Ostevit Caltrate Ostelin

Other drugs affecting bone

- **Calcitonin Salmon aka salcatonin**
  - Natural hormone involved in calcium regulation & bone metabolism
  - Inhibit bone resorption, increase urinary excretion of calcium & phosphate
  - Indication: Paget's disease, hypercalcaemia
- **Calcium**: supplement, adjunct to osteoporosis
- **Cinacalcet**
  - Increase sensitivity of calcium sensing receptors on parathyroid glands
  - Indication: hypercalcaemia

Generic name	Brand Name
Calcitonin Salmon	Miacalcic inj
Calcium	Caltrate and many more
Cinacalcet	Cinacalcet

MRONJ

- **Rare complication of osteoporosis therapy**
- **Definition:** *an area of exposed bone in the maxillofacial region that has persisted for more than eight weeks in a patient receiving bisphosphonates, denosumab, or anti-angiogenic therapy for cancer, with no history of radiation therapy to the jaws or obvious metastatic disease*
- **Aetiology:** multifactorial
  - Dose, duration pre-existing oral disease type of procedure**, genetic polymorphism
  - **extraction, implant insertion, periodontal scaling

Stage of osteonecrosis of the jaw	Features
Stage 0 [NB1]	symptomatic (eg pain) radiographic changes no exposed bone
Stage 1 [NB1]	asymptomatic exposed bone no inflammation or infection
Stage 2	symptomatic (eg pain) exposed bone adjacent soft tissue inflammation or secondary infection
Stage 3	symptomatic (eg pain) full thickness bone involvement pathological fracture extensive soft tissue infection and fistulae

NB1: Stage 0 and stage 1 require follow up and monitoring, but no treatment.

Patient management

- **Maintain optimal oral health**
  - Comprehensive exam (pulp tests and radiographs)
  - Eliminate caries: extractions, restorations
  - Establish healthy periodontium: debridement, extractions
  - Oral hygiene and dietary patient education
  - Invasive tx completed before or within 6mo of starting medication
  - Ensure optimal fit for denture
- **AB prophylaxis:** not recommended to reduce risk of MRONJ
- There is no evidence that drug holidays reduce the risk of MRONJ

Figure 13.34 Management advice for patients at risk of medication-related osteonecrosis of the jaw undergoing a bone-invasive dental procedure

- Inform the patient of the risk of medication-related osteonecrosis of the jaw and obtain consent for the procedure.
- See advice on Drug holidays and scheduling of procedures.
- Do not use antibiotic prophylaxis to reduce the risk of medication-related osteonecrosis of the jaw—there is insufficient evidence to support this practice. However, an active infection should be treated.
- Ensure optimal oral hygiene before and after the procedure.
- Reduce the plaque load with mechanical debridement and pre- and post-procedural chlorhexidine mouthwash.
- Minimise trauma and periosteum stripping, and close any mucosal flaps that are raised with sutures.
- Monitor the oral wound until it heals—healing may be slow.
- Do not debride nonhealing wounds.
- Refer to a specialist if bone is still visible at 8 weeks.

Drugs affecting bones

Dental implications

- **Key medications:** Bisphosphonates, denosumab, romosozumab
- **Major dental concern:** MRONJ (rare but serious), risks increase with invasive dental procedures
- **Other oral implications**
  - **Bisphosphonates:** (rare) glossitis (inflammation of the tongue, smooth appearance)
    - Interaction with NSAIDs: increased risk of gastric ulceration
  - **Denosumab:** (rare) lichen planus
  - **Romosozumab:** (rare) MRONJ
- **Dental management strategies**
  - Prioritize **preventive dental care** before starting therapy
  - Monitor oral health closely during treatment
  - Avoid or carefully monitor **NSAID use** with bisphosphonates
- **Key takeaway: b**enefits of therapy generally **outweigh risks**, but proactive **dental assessment and management** are essential

Figure 13.32 History taking to assess the risk of medication-related osteonecrosis of the jaw

Has the patient ever received treatment for any bone or calcium disorders or malignancy?

Antiresorptive drugs are used to treat:

- osteoporosis
- Paget disease of the bone
- cancer with spread to the bone (eg breast, prostate, liver, lung, kidney)
- multiple myeloma.

Romosozumab is used to treat osteoporosis.

Is the patient currently receiving or have they previously received treatment with an antiresorptive drug or romosozumab?

Antiresorptive drugs can be taken orally (either daily, once weekly or once monthly), or can be administered intravenously or subcutaneously and given less frequently (eg once or twice yearly). Antiresorptive drugs available in Australia are:

- alendronate
- denosumab
- ibandronic acid
- pamidronate
- risedronate
- zoledronic acid.

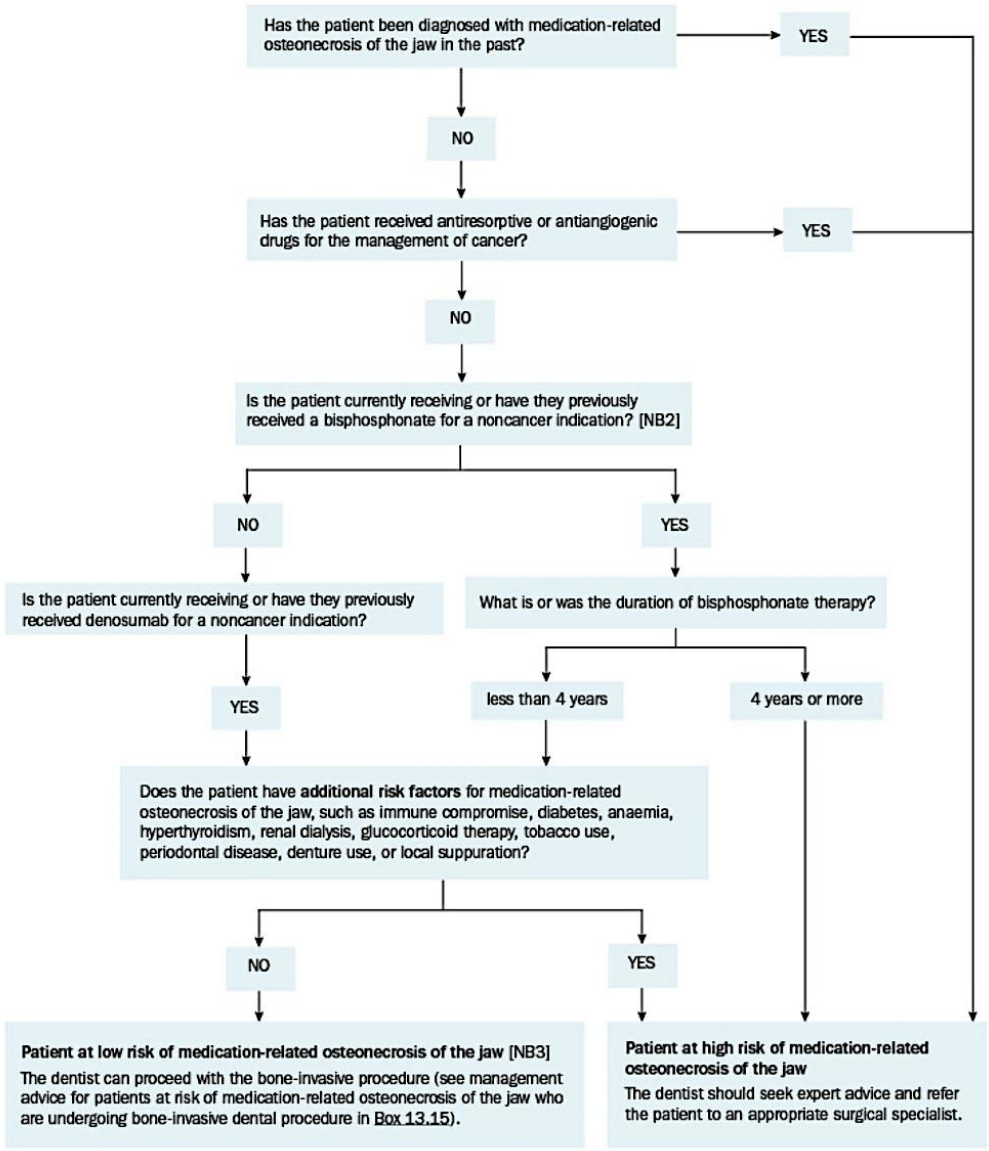
Romosozumab is given subcutaneously once monthly.

Has the patient received an antiangiogenic drug for the management of cancer?

Antiangiogenic drugs are used as targeted therapies for specific cancers. Some antiangiogenic drugs (cabozantinib, lenvatinib, sunitinib [tyrosine kinase inhibitors] and bevacizumab [a monoclonal antibody-targeting VEGF]) have been associated with an increased risk of medication-related osteonecrosis of the jaw; the risk may also be increased with other drugs that have a similar mechanism of action.

If the patient has received any of the treatments above, see Figure 13.33 for further risk assessment.

VEGF = vascular endothelial growth factor



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