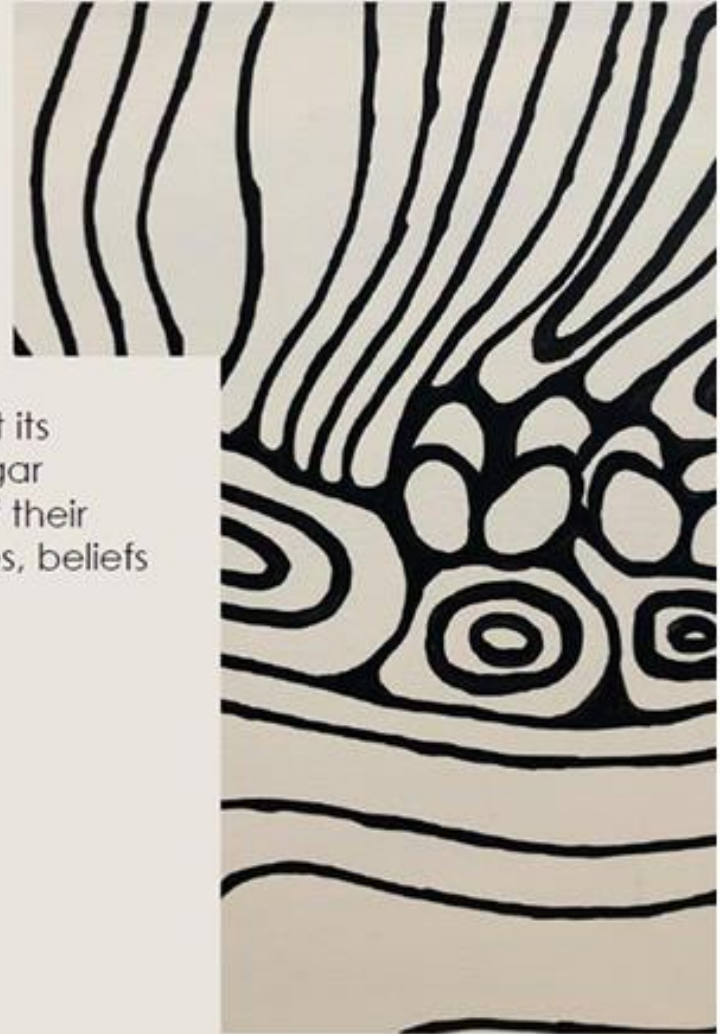


DENT 3005: Introduction to Pharmacology **Neurological drugs**

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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.



Learning Outcomes

Learning objectives

- 1) Understand the different types of neurological drugs and their mechanism of action
 - 1) Drugs for epilepsy
 - 2) Drugs for Parkinson's
 - 3) Drugs for migraines
 - 4) Drugs for Alzheimer's
 - 5) Drugs for MS
 - 6) Drugs for Myasthenia Gravis
 - 7) Other
- 2) Recognise oral and dental side effects of these drugs
- 3) Understand drugs interactions with dental medications
- 4) Applied knowledge to clinical scenarios



Neurological drugs

- Epilepsy
- Parkinson's disease
- Migraine
- Alzheimer's disease
- Multiple sclerosis

Epilepsy

- **Seizures:** transient uncontrolled electrical discharges
 - Causes: biochemical imbalance, structural
 - Partial Vs generalized
- **Epilepsy:** recurrent, unprovoked seizure, different types
- **Pharmacological targets**
 - Inhibitory GABA Vs excitatory glutamatergic pathways
 - Voltage gated membrane channels

Epilepsy

Seizure	Characteristics
Absence (generalized)	Sudden transient loss of consciousness
Myoclonic (generalized)	Convulsive movements of body
Tonic (generalized)	Muscle contractions forcing body into rigid & fixed positions
Tonic-clonic (generalized)	Collapse, followed by rigidity then violent convulsions, and deep sleep postictally, unresponsiveness, deep confusion
Aura (simple partial)	Usually experiencing sedation (e.g. olfactory, visual or aural) w/ no stimulus present
Jacksonian (simple partial)	Muscle spasms characterized by sequential involvement of body parts
Psychomotor (complex partial)	Transient aberrant behavior such as mood alteration, psychotic behavior or apparent drunkenness

Antiepileptics

First line	Second line
Focal (partial) seizures	
carbamazepine	lamotrigine ¹ , clobazam, gabapentin, lacosamide, levetiracetam ¹ , oxcarbazepine, phenobarbital, phenytoin, pregabalin, tiagabine, topiramate, valproate, zonisamide
Generalised tonic-clonic seizures	
valproate	carbamazepine ² , clobazam, lamotrigine ¹ , levetiracetam ¹ , oxcarbazepine ² , phenobarbital, phenytoin ² , topiramate
Absence seizures	
ethosuximide ³ , valproate	clobazam, clonazepam, lamotrigine
Myoclonic seizures	
valproate	clobazam, clonazepam, levetiracetam, phenobarbital
Infantile spasms	
prednisolone, tetracosactide	vigabatrin ⁴ , clonazepam, valproate
<p>¹ may be first line in females of child-bearing potential</p> <p>² do not use if juvenile myoclonic epilepsy is suspected (often presents with a tonic-clonic seizure) as it may be ineffective or worsen seizures</p> <p>³ does not prevent generalised tonic-clonic seizures which often coexist in juvenile absence epilepsy</p> <p>⁴ use only if no safer alternative</p>	

Barbiturates

- **MOA:** Prolong inhibitory postsynaptic potential
- **Drug interactions**
 - Phenobarbital + metronidazole
 - Other CNS depressants: monitor sedation
 - CYP3A4 substrates: clarithromycin, codeine, erythromycin, azoles, oxycodone, tramadol...
- **ADR**
 - Sedation, cognitive impairment, altered mood and behaviour
 - [Rare]: exfoliative dermatitis

Generic name	Brand Name
Phenobarbital	Phenobarb
Primidone	Mysoline

Benzodiazepines

- **[Neurology]** – *also in psychotropics*
- **MOA:** potentiate inhibitory effect of GABA
- **Drug interactions**
 - Other CNS depressants: monitor sedation
 - Alprazolam: itraconazole, ketoconazole → enhance sedation & respiratory depression
 - Diazepam + fluconazole → increase adverse effect
 - Midazolam + [CYP3A4 inh] → enhance sedation & respiratory depression
- **ADR:** fatigue, drowsiness, muscle weakness, ataxia, dry mouth, hypersalivation 😊 and many more

Generic name	Brand Name
Clobazam	Frisium
Clonazepam	Rivotril
Diazepam	Valium
Lorazepam	Lorazepam inj
Midazolam	Hypnovel inj

Ataxia refers to a loss of coordination and balance, resulting in clumsy or awkward movements, often affecting walking, speech, and fine motor skills.

Gabapentinoids

- **MOA:** bind to alpha-2 delta protein subunit of high threshold voltage-dependent calcium channels → reduce calcium influx & neurotransmitter release
- **Drug interactions:** other CNS depressants
- **ADR**
 - Drowsiness, sedation, dizziness, vertigo
 - Dysarthria
 - Ataxia
 - Tremor
 - Dry mouth
 - [Rare]: Steven Johnson's syndrome

Generic name	Brand Name
Gapapentin	Neurontin
Pregabalin	Lyrica

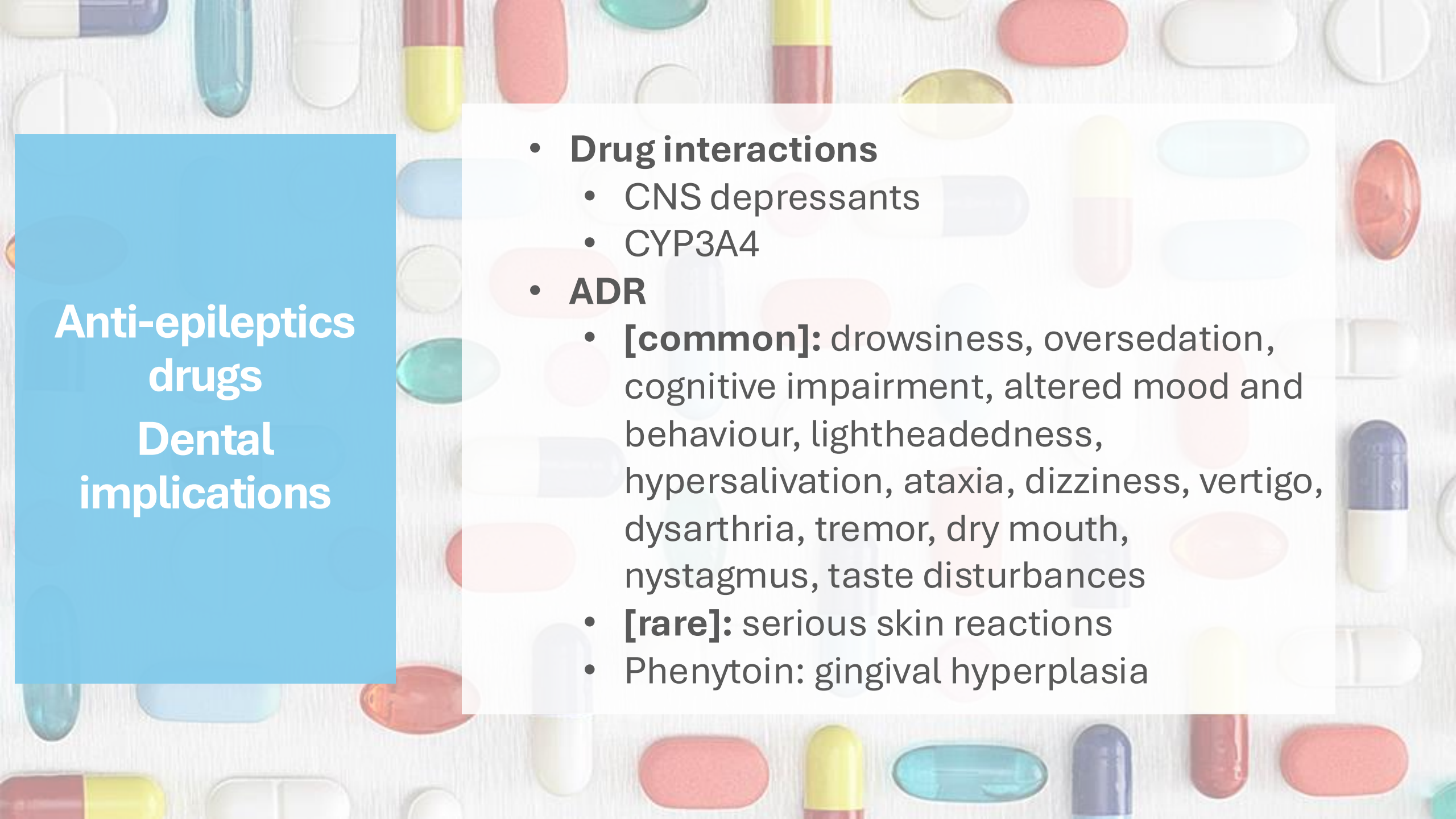
Selected drug (brand)	Selected ADR
Carbamazepine (Tegretol)	[common]: drowsiness, ataxia, dizziness, dry mouth [rare]: severe skin reactions, orofacial dyskinesia
Ethosuximide (Zarontin)	[common]: dizziness, drowsiness, ataxia [rare]: Steven Johnson's
Lamotrigine (Lamictal)	[common]: dizziness, ataxia, hyperkinesia [rare]: severe skin reactions
Levetiracetam (Keppra)	[common]: drowsiness, dizziness, vertigo, ataxia [rare]: severe skin reactions
Oxcarbazepine (Trileptal)	[common]: dizziness, tremor, ataxia, nystagmus [rare]: severe skin reactions
Phenytoin (Dilantin)	[common]: sedation, ataxia, nystagmus, vertigo, gingival hyperplasia [rare]: severe skin reactions
Topiramate (Topamax)	[common]: dizziness, nervousness, agitation, speech disorder [infrequent]: aphasia, nystagmus, taste disturbance
Valproate (Epilim)	[common]: ataxia, dizziness, tremor,

Other antiepileptics

- [Acetazolamide](#)
- [Brivaracetam](#)
- [Cannabidiol](#)
- [Carbamazepine](#)
- [Ethosuximide](#)
- [Lacosamide](#)
- [Lamotrigine](#)
- [Levetiracetam](#)
- [Oxcarbazepine](#)
- [Perampanel](#)
- [Phenytoin](#)
- [Rufinamide](#)
- [Stiripentol](#)
- [Sulthiame](#)
- [Tiagabine](#)
- [Topiramate](#)
- [Valproate](#)
- [Vigabatrin](#)
- [Zonisamide](#)

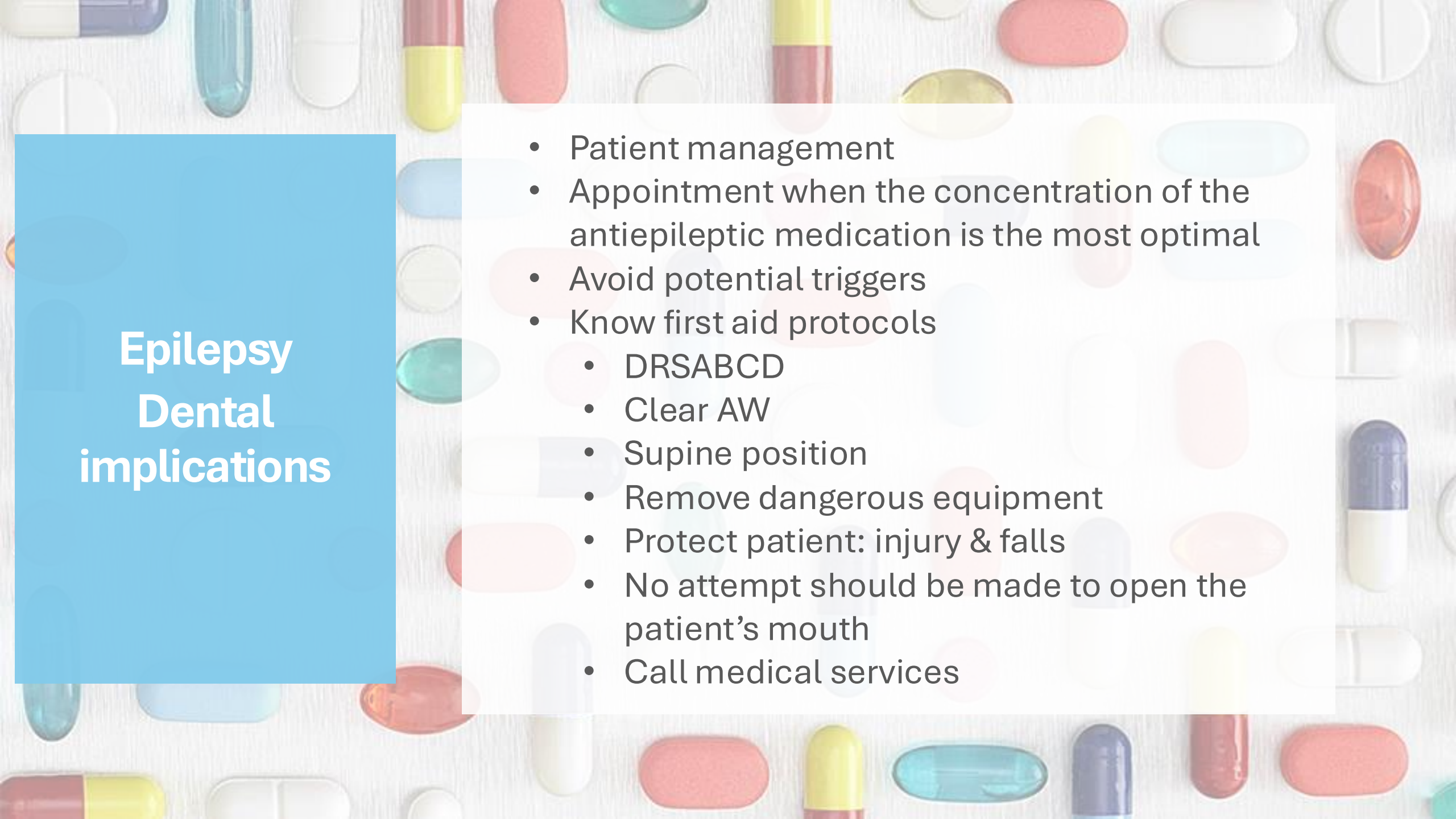


Serious skin reactions



Anti-epileptics drugs Dental implications

- **Drug interactions**
 - CNS depressants
 - CYP3A4
- **ADR**
 - **[common]:** drowsiness, oversedation, cognitive impairment, altered mood and behaviour, lightheadedness, hypersalivation, ataxia, dizziness, vertigo, dysarthria, tremor, dry mouth, nystagmus, taste disturbances
 - **[rare]:** serious skin reactions
 - Phenytoin: gingival hyperplasia



Epilepsy Dental implications

- Patient management
- Appointment when the concentration of the antiepileptic medication is the most optimal
- Avoid potential triggers
- Know first aid protocols
 - DRSABCD
 - Clear AW
 - Supine position
 - Remove dangerous equipment
 - Protect patient: injury & falls
 - No attempt should be made to open the patient's mouth
 - Call medical services

Parkinson's Disease

- Usually **older** population
- **Characteristics:** tremor, difficulty coordinating fine movements, hypokinesia, shuffling gait, skeletal muscle rigidity
- **Normal muscle movement:** balance muscarinic cholinergic and dopaminergic activities
- **Parkinson's disease:** dopaminergic fibres and/or dopamine receptor degenerate
- **Rationale tx:** provide sx relief
- **Pharmacological:** dopamine agonists, anticholinergics, MAO-B, others

Dopamine agonists

- **MOA:** stimulate dopamine receptor
- **Drug interactions**
 - Apomorphine: clarithromycin, erythromycin, fluconazole → prolong QT
 - Bromocriptine + erythromycin: increase ADR
 - Cabergoline + clarithromycin, itraconazole: increase ADR
- **ADR**
 - Dizziness, drowsiness
 - Orthostatic hypotension
 - Dyskinesia
 - Impulse control disorders

Generic name	Brand Name
Apomorphine	Movapo inj
Pramipexole	Sifrol
Rotigotine	Neupro
Ergot derivative	
Bromocriptine	Parlodel
Cabergoline	Dostinex

Anticholinergics

- **MOA:** block muscarinic actions of acetylcholine
- **Drug interactions**
 - Benztropine, trihexyphenidyl: nil dental interactions
- **ADR**
 - Dizziness, drowsiness
 - Orthostatic hypotension
 - Dyskinesia
 - Dry mouth

Generic name	Brand Name
Benztropine	Benztrop
Trihexyphenidyl	Artane

Tertiary amines

[Atropine, Atropine \(antidote\)](#)

[Benztropine](#)

[Darifenacin](#)

[Hyoscine hydrobromide](#)

[Orphenadrine](#)

[Oxybutynin](#)

[Solifenacin](#)

[Tolterodine](#)

[Trihexyphenidyl](#)

Quaternary amines

[Glycopyrronium \(anaesthesia\)](#)

[Hyoscine butylbromide](#)

[Propantheline](#)

Monoamine oxidase inH type B

- **Aka MAOB inH**
- **MOA:** inH MAOB, reduce breakdown of dopamine, may block dopamine re-uptake
- **Drug interactions:** nil dental interactions
- **ADR**
 - Orthostatic hypotension
 - Dyskinesia

Generic name	Brand Name
Rasagiline	Azilect
Safinamide	Xadago
Selegiline	Eldepryl

Other drugs for Parkinson

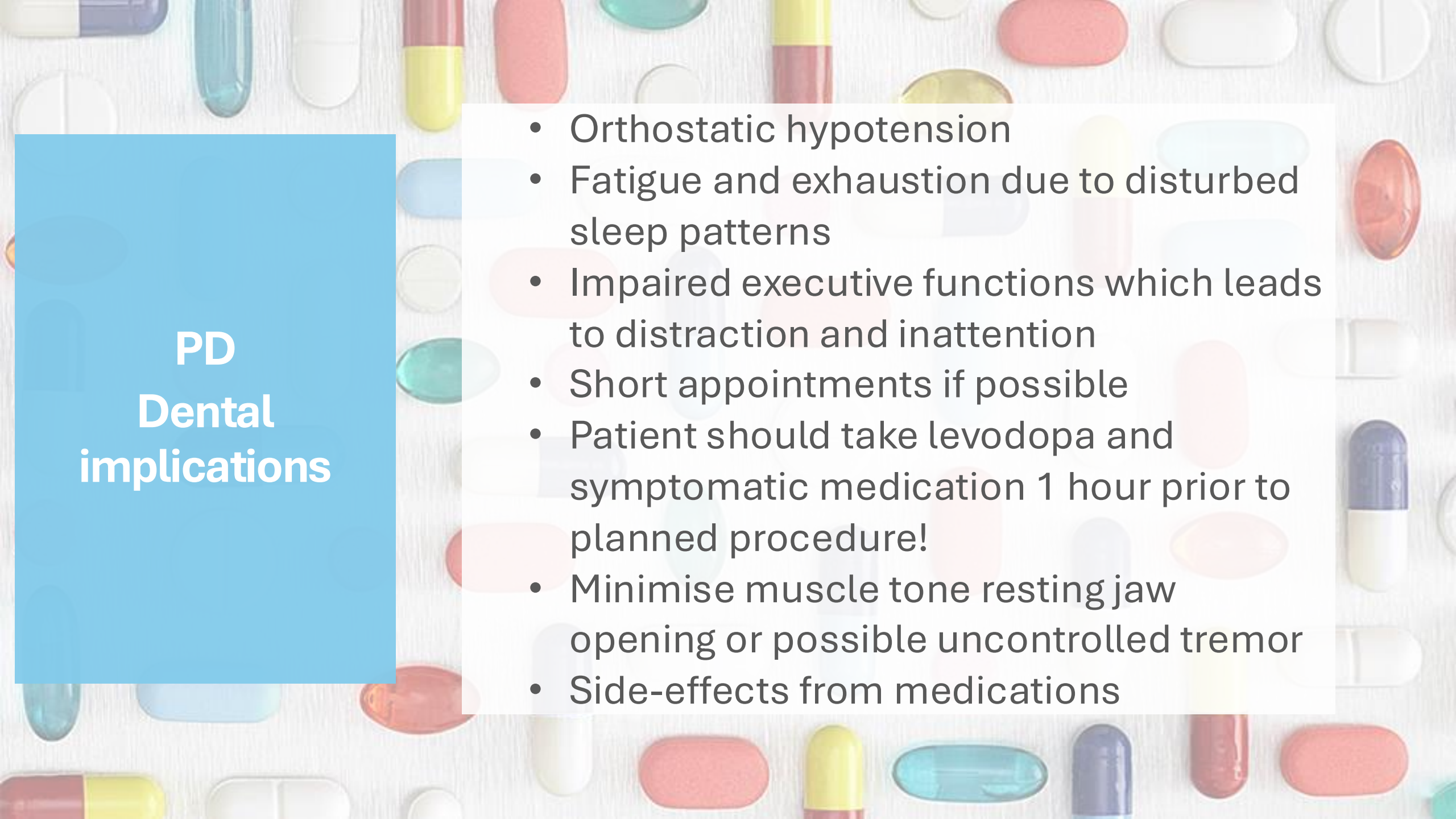
- **Drug interactions:** Entacapone + adrenaline: dental relevance?
- **Amantadine [ADR]:** Orthostatic hypotension, dizziness, dry mouth
- **Entacapone [ADR]:** Orthostatic hypotension, dry mouth, dyskinesia
- **Opicapone [ADR]:** Dry mouth, dizziness, dyskinesia
- **Combination [ADR]:** orthostatic hypotension, dyskinesia, drowsiness, impulse control disorder

Generic name	Brand Name
Amantadine	Symmetrel
Entacapone	Comtan
Levodopa + benserazide + carbidopa	Madopar Kinson, Sinemet
Levodopa + carbidopa & entacapone	Carlevent, Lecteva
Opicapone	Ongentys



Drugs for PD Dental implications

- Drug interactions
 - QT prolongation drugs
 - CYP3A4
- ADR
 - [common]: Dizziness, drowsiness, orthostatic hypotension, dyskinesia, impulse control disorders, dry mouth



PD Dental implications

- Orthostatic hypotension
- Fatigue and exhaustion due to disturbed sleep patterns
- Impaired executive functions which leads to distraction and inattention
- Short appointments if possible
- Patient should take levodopa and symptomatic medication 1 hour prior to planned procedure!
- Minimise muscle tone resting jaw opening or possible uncontrolled tremor
- Side-effects from medications

Migraines

- **Headache:** mod-severe throbbing/pulsing pain
 - Other accompanying sx: nausea, vomiting, photosensitivity, phono sensitivity, aura...
- **Tx rationale**
 - Relief headache and assoc sx
 - Prevent recurrent migraine
 - Improve QOL
- **Treatment**
 - Non-pharmacological
 - Pharmacological: sx relief, acute & preventative

Triptans

- **MOA:** action at 5HT_{1B/1D} receptors appears to reduce calcitonin gene-related peptide levels and modulate nociception
- **Drug interactions**
 - Eletriptan [CYP3A4 inh]: erythromycin, fluconazole
- **ADR**
 - Sensations (tingling, heat, pain, heaviness, tightness)
 - Dizziness, drowsiness
 - Dry mouth

Generic name	Brand Name
Eletriptan	Relpax
Naratriptan	Naramig
Rizatriptan	Rixalt, Maxalt
Sumatriptan	Imigran
Zolmitriptan	Zoltrip, Zomig

Calcitonin gene related peptide antagonist

- **AKA CGRP antagonists**
- **MOA:** inH CGRP vasodilation
 - Erenumab blocks CGRP receptors
- **Drug interactions**
 - Limited information available
- **ADR:** not dentally related

Generic name	Brand Name
Eptinezumab	Vyepti inj
Erenumab	Aivomig
Fremanezumab	Ajovy inj
Galcanezumab	Emgality

Other drugs to prevent migraine

- **MOA:** 5HT₂ antagonist
- **Drug interactions**
 - Other CNS depressants
- **ADR**
 - [common]: sedation
 - [infrequent]: dry mouth, dizziness

Generic name	Brand Name
Botulinum toxins	Botox, Xeomin, Dysport
Pizotifen	Sandomigran



Drugs for migraine Dental implications

- Drug interactions
 - CNS depressants
 - CYP3A4
- ADR
 - [common]: Sensations (tingling, heat, pain, heaviness, tightness), dizziness, drowsiness, dry mouth
- Migraine triggers: avoid
 - Ensure patient have acute relief medications

Alzheimer's Disease

- A form of dementia
- Characteristics: neuronal cell loss, brain shrinkage, enlarged ventricles, significant histological changes in brain tissue
- Progressive deterioration
- Pathophysiology: neuronal cell death, B-amyloid plaques, neurofibrillary tangles
- Reduction in Ach and raised glutamate?
- Pharmacological: inH acetylcholinesterase, glutamate receptor antagonists

Anticholinesterases

- **MOA:** decrease breakdown of acetylcholine
- **Drug interactions [Galantamine]**
 - QT prolongation: clarithromycin, erythromycin, fluconazole
 - [CYP3A4 inh]
- **ADR**
 - Drowsiness, dizziness, tremor, increased sweating, hypertension, fainting

Generic name	Brand Name
Donepezil	Arazil, Aricept
Galantamine	Galantyl, Reminyl
Rivastigmine	Exelon

Other drugs for Alzheimer's

- **MOA:** N-methyl-D-aspartate (NMDA) antagonist
- **Drug interactions:** limited information
- **ADR**
 - [common]: confusion, dizziness, drowsiness, headache, agitation, hallucinations, dyspnoea
 - [infrequent]: anxiety

Generic name	Brand Name
Memantine	Ebixa, Memanxa



Drugs for AD Dental implications

- **Drug interactions**
 - QT prolongation drugs
 - CYP3A4
- **ADR**
 - [common]: Drowsiness, dizziness, tremor, increased sweating, hypertension, fainting, confusion, headache, agitation, hallucinations, dyspnoea
 - [infrequent]: anxiety

Multiple sclerosis

- **Disease of nervous system**
 - Demyelination → [slowed, distorted, blocked] neural transmission
 - Plaques: scar tissue
- **Unpredictable course**
 - Progressive Vs Relapsing-Remitting forms
- **Four common syndromes**
 - Spinal syndrome: most common
 - Other syndrome [brainstem, cerebral, cerebella]
- **Pharmacological**
 - Immunosuppressants
 - Sx relief

Symptom	Drug
Depression/pain	TCA's
Incomplete bladder emptying	A-blockers
Infections	AB's
Neuralgia	Carbamazepine
Spasm/spasticity	Diazepam/ baclofen

Sphingosine 1-phosphate receptor modulator

- **MOA:** preventing lymphocytes leaving lymph nodes
- **Drug interactions**
 - Fingolimod & Siponimod: CYP3A4 inH
- **ADR**
 - Hypertension, infection
 - Basal cell carcinoma: check patients for skin cancer

Generic name	Brand Name
Fingolimod	Gilenya
Ozanimod	Zeposia
Siponimod	Mayzent

Fumarates

- **MOA:** exact mode of action unknown
- **Drug interactions**
 - Limited information
- **ADR**
 - [common]: flushing
 - [rare]: serious opportunistic infections

Generic name	Brand Name
Dimethyl fumarate	Tecfidera
Diroximel fumarate	Vumerity

Other drugs for MS

- Additional reading on MOA
- Most don't have detailed drug interactions
- ADR: related to immunosuppressant effects
 - Infections

[Alemtuzumab \(neurology\).](#)

[Cladribine \(neurology\).](#)

[Fampridine](#)

[Glatiramer](#)

[Interferon beta](#)

[Nabiximols](#)

[Natalizumab](#)

[Ocrelizumab](#)

[Ofatumumab](#)

[Teriflunomide](#)



Drugs for MS Dental implications

- Drug interactions
 - CYP3A4
- ADR
 - [common]: Hypertension, infection, basal cell carcinoma, flushing, infection

Myasthenia gravis

- **Autoimmune neuromuscular disorder** causing weakness and fatigue of voluntary muscles
- **Cause:** antibodies destroy acetylcholine receptors (AChRs) at neuromuscular junction
- **Effect:** impaired nerve-to-muscle communication → muscle weakness (e.g. limbs, speech, chewing)
- **Treatment:** cholinesterase inhibitors increase acetylcholine availability
 - Overdosage → cholinergic crisis
- **Goal:** enhance neuromuscular transmission, improve muscle strength

Anticholinesterases in MG

- **MOA:** inH cholinesterase
- **Drug interactions:** no dental implication
- **ADR**
 - [common]: increase salivation
- **Monitor Cholinergic crisis**
 - Excessive sweating, involuntary defecation and urination, miosis, nystagmus, bradycardia, hypotension, increased muscle weakness

Generic name	Brand Name
Edrophonium	Not marketed AUS
Neostigmine	Neostigmine inj
Pyridostigmine	Mestinon



Drugs for MG Dental implications

- Drug interactions
 - No dental implication
- ADR
 - [common]: increase salivation
- Monitor cholinergic crisis

Other neurological drugs

Generic name (brand)	MOA	Selected ADR	Selected drug interaction
Baclofen (Clofen) <i>Chronic spasticity associated with MS</i>	GABA _B agonist	Hypotension, drowsiness, dizziness, seizures, ataxia, tremor, nystagmus	Drugs causing CNS and respiratory depression
Dantrolene (Dantrium) <i>Chronic spasticity associated with spinal cord injury</i>	A direct acting skeletal muscle relaxant	Drowsiness, dizziness, nervousness, seizures	Drugs causing CNS depression
Riluzole (Rilutek) <i>Amyotrophic lateral sclerosis (ALS)</i>	May act by inhibiting glutamate neurotransmission	Drowsiness, dizziness,	Drugs causing CNS depression
Tetrabenazine (Tetrabenazine) <i>Some dystonic syndromes</i>	Depletes levels of dopamine in the CNS	Drowsiness, parkinsonism, akathisia, agitation, anxiety, confusion, orthostatic hypotension, dysphagia, choking	Drugs causing CNS depression Drug causing QT prolongation

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