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PAIN MANAGEMENT IN THE PERIOPERATIVE PERIOD

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DISCLOSURE

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

None

A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (e.g. owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise) or organisational interests.

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LEARNING OBJECTIVES

- Explain the mechanisms of acute post-operative pain
- Describe different strategies used to manage post-operative pain
- Describe the classes of medications used to manage post-operative pain
- Describe the appropriate use of opioids in the post-operative period

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PHARMACIST COMPETENCY STANDARDS

Pharmacist competency standards* addressed include:

3.1.2, 3.3.2

*National competency standards framework for pharmacists in Australia, 2016

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EXPLAIN THE MECHANISMS OF ACUTE POST-OPERATIVE PAIN

- Transduction
- Transmission
- Modulation

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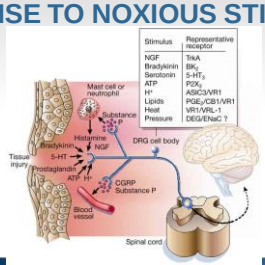
RESPONSE TO NOXIOUS STIMULUS



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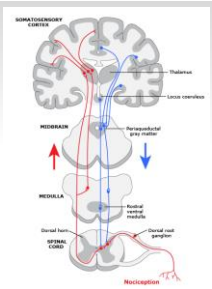

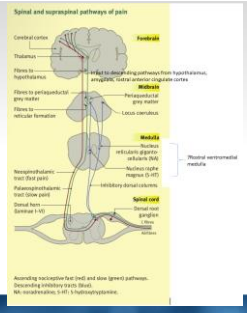

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MELZACK AND WALL GATE THEORY

- A-beta afferents inhibit A-delta and C at dorsal horn (principally at substantia gelatinosa) → ?mechanism for TENS

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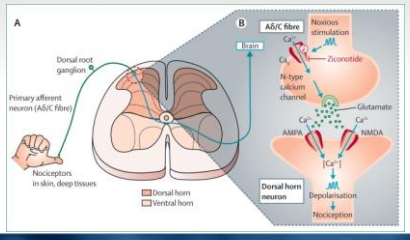
LONG-TERM CHANGES



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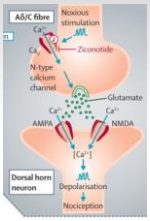
- Neurokinin receptors, AMPA receptors → setup long term potentiation
  NMDA receptors → maintain long term potentiation
- Repeated C fiber input → repeated EPSPs from AMPA activation at central post-synaptic membrane → progressive membrane depolarisation → removal of Mg plug in NMDA channel → Ca influx
  - → 2nd messenger systems (including phosphorylation of NMDA receptor)
  - → Increased substance P, glutamate
  - → Excitoctoxic death of inhibitory interneurons
  - → C-fos gene expression → memory and learning re pain
- End result
  - → Increased resting membrane potential closer to depolarisation threshold → increased response to normal nociceptive (hyperalgesia) and subthreshold inputs (allodynia)
  - → Widened receptor fields



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"Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"

IASP 1979

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DESCRIBE DIFFERENT STRATEGIES USED TO MANAGE POST-OPERATIVE PAIN

- Pharmacology
  - Systemic
  - Local
- Non-pharmacological
  - Education
  - Reassurance
  - Psychology

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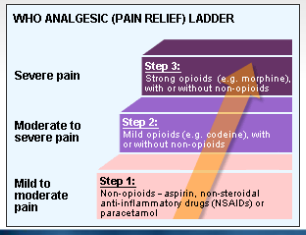
ANALGESIC LADDER



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SYSTEMIC

- "Simple" analgesics
  - Paracetamol NSAIDs
- Opioid analgesics
  - Classic – morphine, oxycodone, fentanyl
  - Atypical – buprenorphine, tapentadol, tramadol
- Antineuropathics
  - Antidepressants – TCA, SNRI (limited role in acute pain)
  - Gabapentinoid
- Other
  - Clonidine
- Advanced intravenous infusions
  - Ketamine
  - lignocaine

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LOCAL

- Topical agents eg lignocaine patch
- Regional anaesthetic
  - LA injections

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DESCRIBE THE CLASSES OF MEDICATIONS USED TO MANAGE POST-OPERATIVE PAIN

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PARACETAMOL

- Mechanism – unclear
- Dose – 15mg/kg (upto 1g) q6h (max 4mg per day, 3mg in elderly or liver compromised)
- Side-effects
  - Liver impairment

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NSAIDS

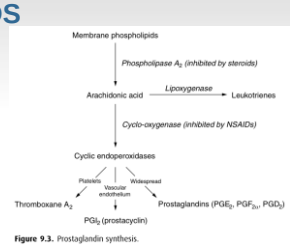

Figure 9.3. Prostaglandin synthesis.

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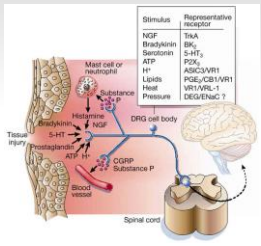

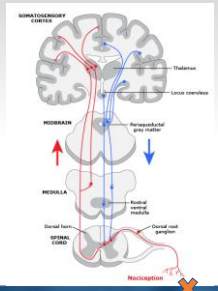

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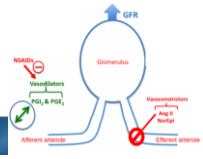
NSAID RISKS

	COX nonselective inhibitor	COX 2 inhibitor
GI	Peptic ulcers +++	Peptic ulcers +
Renal	Kidney injury	Kidney injury
Resp	Bronchospasm	?No effect
CVS	Increased risk MI/stroke Increase risk heart failure	Increased risk MI/stroke Increase risk heart failure
Haem	Platelet inhibition	No effect



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OPIOIDS

- Classic – morphine, oxycodone, fentanyl
- Atypical – buprenorphine, tapentadol, tramadol

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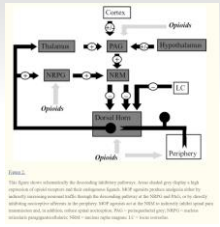

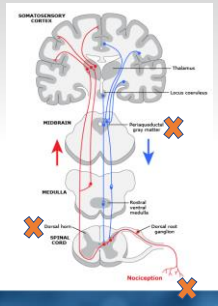

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OPIOID ADVERSE EFFECTS

Side Effects of Opioids

- – Respiratory depression
- – Nausea, vomiting
- – Urinary retention
- – Mental clouding
- – Tolerance & dependence
- – Ileus
- – Sedation**
- – Cough suppression**
- – Constipation**
- – Euphoria**
- – Pruritis
- – Biliary spasm

**These effects are occasionally desirable.

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EQUIANALGESIC DOSES

Not secure | http://www.opioidcalculator.com.au

Home

FPM FACULTY OF PAIN MEDICINE ANZCA — Opioid Calculator

Opioid	IV/IM (mg)	Oral (mg)
Morphine	10	30
Hydromorphone	2	7.5
Fentanyl	0.15-0.2	NA
Oxycodone	10	20
Methadone	10	15
Codeine	130	200
Buprenorphine	0.4	0.8 (SL)
Tramadol	100	100

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MORPHINE

- Reference opioid
- Hepatic metabolism, the primary metabolites of morphine after glucuronidation are:
  - Morphine-3-glucuronide (85%)
  - Morphine-6-glucuronide (10%)
- Morphine-6-glucuronide is mu-active (concern in renal failure)

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2012 DAVID
12 REASONS FOR CONSIDERING BUPRENORPHINE AS A FRONTLINE ANALGESIC IN THE MANAGEMENT OF PAIN

- (1) buprenorphine is effective in cancer pain
- (2) buprenorphine is effective in treating neuropathic pain
- (3) buprenorphine treats a broader array of pain phenotypes than do certain potent mu agonists, is associated **with less analgesic tolerance**, and can be combined with other mu agonists
- (4) buprenorphine produces **less constipation** than do certain other potent mu agonists, and does not adversely affect the sphincter of Oddi
- (5) buprenorphine **has a ceiling effect on respiratory depression but not analgesia**
- (6) buprenorphine causes **less cognitive impairment** than do certain other opioids
- (7) buprenorphine is **not immunosuppressive** like morphine and fentanyl
- (8) buprenorphine does not adversely affect the hypothalamic-pituitary-adrenal axis or cause hypogonadism
- (9) buprenorphine does not significantly prolong the QTc interval, and is associated with less sudden death than is methadone
- (10) buprenorphine is a safe and effective analgesic for the elderly
- (11) buprenorphine is one of the **safest opioids to use in patients in renal failure and those on dialysis**
- (12) **withdrawal symptoms are milder and drug dependence is less** with buprenorphine

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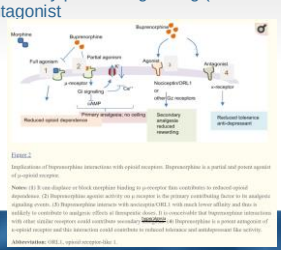
BUPRENORPHINE

- Mechanism – high affinity partial long-acting (slow offset) mu agonist, kappa antagonist



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- Dosing
  - SL – 200-400mcg SL q6-8h prn
- Kinetics
  - SL onset time = 30-60mins
  - SL peak clinical effects = 1-4 hours
  - SL duration of action increases with dose – < 2mg = 6-12 hours, 16-32mg = 24-72 hours
  - Metabolised mostly by liver, excreted mostly by liver, no dose-adjustment in ESRF
  - Do not use Suboxone in liver failure as will get excessive systemic naloxone

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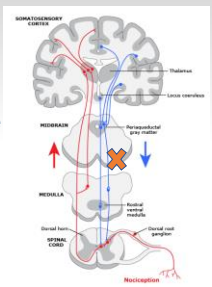
TAPENTADOL

- Partial opioid agonist
- Inhibits neuronal uptake of noradrenaline



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- Opioid side-effects
  - Ilius
- Avoid in patients at risk of seizures
  - PHx of seizures
  - Seizure threshold lowering meds (Eg. many psychiatric drugs)
- Accumulation in renal impairment

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- Is tapentadol safer than classic opioids? Jury is out

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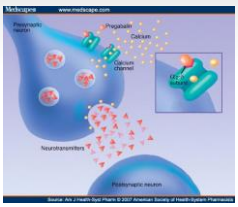
GABAPENTINOIDS

- "For nerve pain"



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- CNS – sedation, lethargy, poor concentration, dizziness, unsteadiness, blurred vision, tremor
- Resp – resp depression
- Other – weight gain, peripheral oedema
- Abuse of euphoric effect, addiction
- Suicide risk (esp young, depressed, risk factors for substance abuse)

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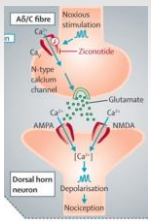
KETAMINE

- NMDA antagonism
- Other effects?
  - Proaminergic? → increased descending inhibitory modulation
  - Opioid agonist?
  - Anti-inflammatory?
- Analgesic
- Anti-hyperalgesic
- Anti- central sensitisation ?role in prevention of chronic pain?



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- Hallucinations, delirium, flare of psychiatric symptoms
- Sedation
- Liver impairment
- Bladder cystitis

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LOCAL

- Topical agents eg lignocaine patch
- Regional anaesthetic
  - LA injections

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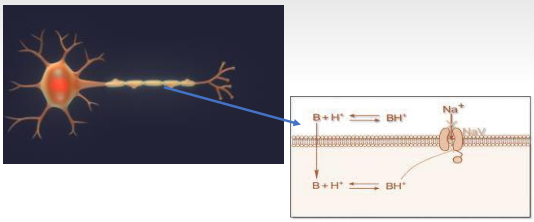
LOCAL ANAESTHETICS



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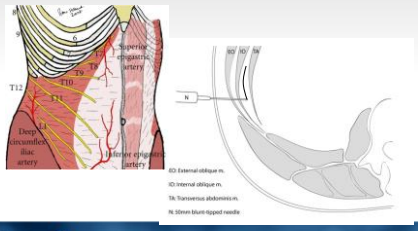
REGIONAL ANALGESIA



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DESCRIBE THE APPROPRIATE USE OF OPIOIDS IN THE POST-OPERATIVE PERIOD

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JAMA Surgery | Original Investigation

New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults

Chad M. Brummett, MD; Jennifer F. Waljee, MD, MPH, MS; Jenna Goesling, PhD; Stephanie Moser, PhD; Paul Lin, MS; Michael J. Englesbe, MD; Amy S. B. Bohnert, PhD, MHS; Sachin Kheterpal, MD, MBA; Brahmajee K. Nallamothu, MD, MPH

- Retrospective
- Used US insurance claim information between 2012 and 2015
- 36 177 patients opioid-naïve patients who had operations which required some postop opioid use
  - 29 068 minor surgery
  - 7109 major surgery

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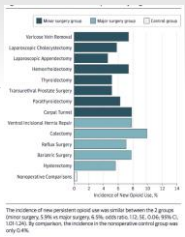
- Rate of persistent opioid use > 3 months
  - 5.9% minor surgery
  - 6.5% major surgery
  - Not significantly different between minor and major surgery



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- Risk factors
  - Preoperative tobacco use OR 1.35 (1.21-1.49)
  - Preoperative alcohol or other substance abuse OR 1.34 (1.05-1.72)
  - Mood disorders OR 1.15(1.01-1.30)
  - Anxiety OR 1.25 (1.10-1.42)
  - Preoperative pain
    - Back pain OR 1.57 (1.42-1.75)
    - Neck pain OR 1.22 (1.07-1.39)
    - Arthritis OR 1.56 (1.40-1.73)
    - Centralised pain OR 1.39 (1.26-1.54)

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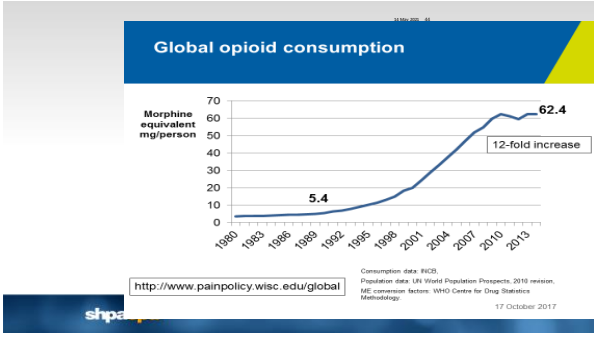

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- Recent evidence suggests that the first month after starting opioid medication is critical.

Days of opioid use	Risk of persistent opioid use at one yea
12 days	24%
21 days	35%
31 days	43%

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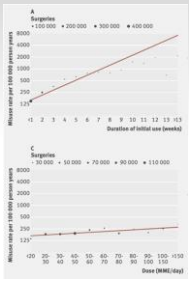
- Retrospective, looked at surgical administrative database of pts 2008-2016
- 1 015 116 opioid-naïve patients undergoing surgery



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GOVERNMENT INITIATIVES

- Prescriber
  - Opioid education to prescribers & public
  - Prescription drug monitoring
    - Victoria - Safescript
  - GP prescribing dose caps
- Dispensing
  - Codeine rescheduling
  - Limited dispensing pack sizes
- Other
  - Drug buy-back programs
  - Support services – harm-minimisation programs (ORT, take-home naloxone)

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INDUSTRY INITIAITIVES

- Responsible advertising
- Creation of abuse-deterrent opioid formulations

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HOSPITAL INITIATIVES

- Opioid education programs
- Limited dispensing pack sizes
- See pic above

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ALFRED OPIOID STEWARDSHIP PROGRAM

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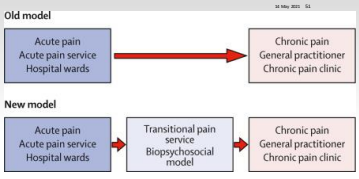

New models of best practice concerning early management of post-surgical and post-traumatic pain and disability identify the peri-operative period and early weeks after hospitalization as vital to reduce chronic pain and disability

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PRINCIPLES OF APPROPRIATE USE OF OPIOIDS IN THE POST-OPERATIVE PERIOD

- Multimodal analgesia
- Lowest dose of opioid required for shortest time required
  - Continuous re-assessment of 4 As – analgesia, activity, adverse effects, aberrant behaviour
  - Decrease opioids first
  - Discharge planning with community GP
- ?Alternative opioids preferred?
- Check Safescript

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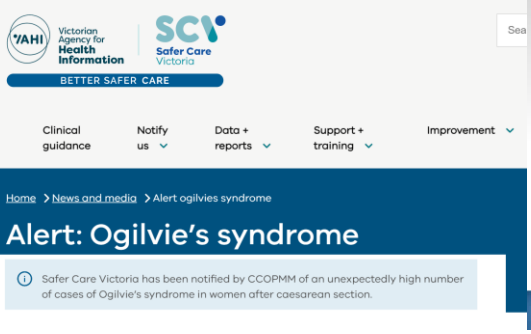

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- Aberrant behaviours
  - Abuse – wrong dose, wrong route
  - Addiction
  - Diversion
  - Other – unsanctioned dose-escalation, obtaining prescriptions from multiple doctors, forging prescriptions, losing prescriptions or seeking early refills, sharing medication with family members, co-using other substance abuse

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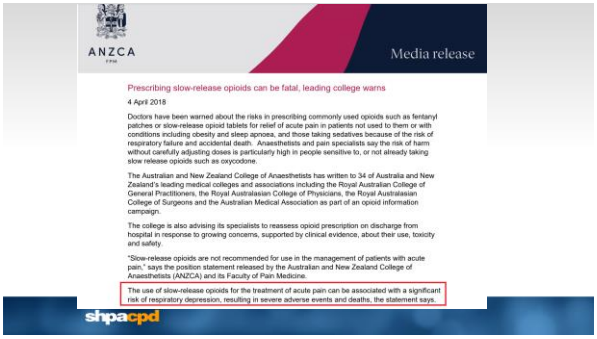

ANZCA

Media release

Prescribing slow-release opioids can be fatal, leading college warns

4 April 2018

Doctors have been warned about the risks in prescribing commonly used opioids such as fentanyl patches or slow-release opioid tablets for relief of acute pain in patients not used to them or with conditions including obesity and sleep apnoea, and those taking sedatives because of the risk of respiratory failure and accidental death. Anaesthetists and pain specialists say the risk of harm without carefully adjusting doses is particularly high in people sensitive to, or not already taking slow release opioids such as oxycodone.

The Australian and New Zealand College of Anaesthetists has written to 34 of Australia and New Zealand's leading medical colleges and associations including the Royal Australian College of General Practitioners, the Royal Australasian College of Physicians, the Royal Australasian College of Surgeons and the Australian Medical Association as part of an opioid information campaign.

The college is also advising its specialists to reassess opioid prescription on discharge from hospital in response to growing concerns, supported by clinical evidence, about their use, toxicity and safety.

"Slow-release opioids are not recommended for use in the management of patients with acute pain," says the position statement released by the Australian and New Zealand College of Anaesthetists (ANZCA) and its Faculty of Pain Medicine.

The use of slow-release opioids for the treatment of acute pain can be associated with a significant risk of respiratory depression, resulting in severe adverse events and deaths, the statement says.

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QUESTIONS?

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