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Practical Aspects

Exam Focus

- opioid tolerant
- persistent post surgical pain
- opioid dependant patients
- phantom/chronic pain
- post herpetic neuralgia
- CRPS
- Cancer pain
- Burn pain
- Spinal Cord Injury Pain
- New analgesics

PCA Requirements

- patient delivered bolus of IV opioid analgesia
- helps deal with the marked variation of post operative pain experienced by patients
- patients end up titrating analgesia to between the minimum analgesic requirement and their minimum toxic concentration
- inherent safety by disallowing patient to overdose once they become sedated

Requirements:

- understanding of how the PCA works
- ability to press the button (cognitive ability and physical ability)
- normal psychological status; may be inappropriate in the very anxious

Limitations:

- unable to used in patients who
 - ▶ cognitive deficits and who forget to push button
 - ▶ very old and very young
 - ▶ inability to push button (severe arthritis or muscle weakness of hands)
- delivery of opioid analgesia – side-effects of opioids including: nausea and vomiting, respiratory depression, pruritis, constipation, sedation
- drug may be dangerously administered by people other than patient
- susceptible to equipment failure and power surges (rare)
- must be programmed adequately
- some concern of PCA's masking signs of compartment syndrome (PCA ok as long as limb observation continue throughout duration of PCA treatment)
- some patients 'don't trust the PCA' and others fear the PCA may overdose them
- need to be used with caution OSA as are more susceptible to respiratory depression (use small dose, no infusion, and monitor closely)
- ↑ed monitoring by nursing staff:
 - ▶ 1-4hrly obs depending on length of time established
 - ▶ can effect night time sleep
 - ▶ being asleep means can get behind in analgesia

Opioid Sparing Anaesthetic

- Consideration needs to given to this prospectively rather than being ignored and having to be instituted later.
- The same principles apply with altered doses for paediatrics.

Preoperatively:

Paracetamol 1 gram

Gabapentin 600 mg. reduced if frail and elderly to 300 mg.

etoricoxib 120mg

Discuss epidural/regional or PCA

Intra operative:

Ketamine at least a bolus with induction 0.2 - 0.5 mg/kg

Paracetamol IV if not used previously or over 4 hours.

COX 2

Clonidine 1-6 micrograms / kg as tolerated

Tramadol 3-4mg/kg loading.

Lignocaine Loading 1.5 mg / kg + infusion 1.5 mg/kg/hour

Rectus or wound catheter if no epidural

Mac requirements are substantially reduced with the sedative effects of Gabapentin and Clonidine as can be seen with CNS monitoring.

Post operative:

If PCA consider adding

- Ketamine
- Clonidine

Regular

- Paracetamol
- Tramadol
- Cox 2
- Gabapentin 300mg BD or reduced to 100mg BD in the elderly

Opioid Dose Equivalents

- **Morphine 10mg IV =**

- ▶ Morphine 30-60mg PO =
- ▶ Fentanyl 100-200mcg IV =
- ▶ Pethidine 100mg IV = Pethidine 250mg PO =
- ▶ Codeine 175mg PO =
- ▶ Tramadol 100mg IV = Tramadol 100mg PO =
- ▶ Oxycodone 20mg PO =
- ▶ Methadone 10mg PO (acute use) (in chronic patients may ↓oral methadone dose to 1-4mg)
↳ ie Iv morphine : oral methadone = 1:1

PO morphine (mg/24hrs)

PO morphine : methadone

<90	3:1
90-300	8:1
>300	12:1

- breakthrough opioid dosing = 24hr dose/6 ⇒ give 4-6hrly

Methadone Switch

- opioid naive:

- ▶ start 5mg bd and change at D3-5
- ▶ max 30mg/d (=100mg oral morphine)

- on opioids:
 - ▶ convert opioids to methadone equivalent (be conservative)
 - ▶ give 50% to 2/3rds as regular, and a breakthrough prescription
 - ▶ after 1-2days assess and can ↑ regular dose
- methadone dosed once or twice daily depending on metabolism
- methadone OBA 40-90%
- can give methadone subcut
- use specialised service

Opioid Tolerant Patients

- set up expectations
- deserve high quality anaesthetic
- continue normal opioids - liaise with local pharmacy
- patient may require x2-3 more opioid dosing peri-op
- Plan:
 - ▶ Multimodal analgesia eg ketamine, clonidine
 - ▶ regional technique
 - ▶ Review x2/day
 - ▶ avoid withdrawal
 - ▶ attenuate tolerance - there is a role for opioid rotation
 - ▶ address psychosocial issues - home support
 - ▶ start d/c planning early

Acute Pain

Definitions

- pain
 - ▶ = individual, multifactorial experience influenced by culture, previous pain events, beliefs, mood & ability to cope
 - ▶ = an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
- nociception = sensory nervous system's response to certain harmful or potentially harmful stimuli
- Duration of pain defines acute (<30d) ⇒ subacute (1-3months) ⇒ chronic (>3 months)
 - ↳ arbitrary lengths
- hyperalgesia = noxious stimuli producing more pain than normal expected:
 - ▶ primary hyperalgesia = due to periph sensitisation where stimulus at site produces more pain
 - ▶ secondary hyperalgesia = ↑ed responsiveness in a zone surrounding injured tissue
 - ↳ due to central sensitisation
- allodynia = previously non painful stimuli is now very painful
- Placebo = inert substance which intended to cause beneficial effect
- Nocebo = inert substance which causes adverse effect
- Neuropathic pain: demonstrable lesion/disease which satisfies established neurological diagnostic criteria
- Tolerance = progressive ↓response to repeated drug dosage
- Dependence = experience abstinence syndrome after stopping drug or giving antagonist
- Addiction = Characterised by craving, compulsion, continuing use despite harm
- Pseudo-addiction = under treated pain giving rise to addiction like behaviour

Classification

- Pain =
 - ▶ Physiological ⇒ nociceptive (= warning system)
 - ▶ Pathological ⇒ (=no physiological benefit)
 - Neuropathic
 - Dysfunctional eg fibromyalgia, CRPS

Neuropathic Pain

- diagnosis can be difficult - can classify into:
 - ▶ Certain
 - ▶ Probably
 - ▶ Possible
- supporting factors to diagnosis:
 - ▶ pain in defined anatomical territory
 - ▶ Hx relevant disease
 - ▶ partial or complete sensory loss
 - ▶ confirmation of nerve lesion by recognised test
 - ▶ pain worse at night
- Diff locations of pain by cause:
 - ▶ peripheral ⇒
 - trauma
 - Peripheral neuropathy
 - ▶ Central ⇒
 - SCI
 - Stroke
 - MS

Physiological Aspects of Acute Pain

Pain Pathways

- ascending = mainly stimulating
- descending = mainly inhibiting

Ascending pathways

- start in periph tissues & terminate in contralateral somatosensory cerebral cortex (precentral gyrus)
- generally 3 orders of neurons - ie 3 synapses in pathway

1st order Neurons

- A δ - and C-fibers
- cell bodies lie in dorsal root ganglion
- terminate on second order neurons in dorsal horn
- C fibres terminate in lamina 1 & 2 aka substantia gelatinosa
- A δ terminate lamina 1 + 5
- myelinated:unmyelinated = 1:4 for cutaneous nerves
- pain receptors (nociceptors) respond to various stimuli eg mechanical, chemical, thermal:
 - A δ = mechano-thermal
 - C fibre = polymodal

Interneurons

- stay at that spinal level
- integrate signal in spinal cord between laminae

2nd Order Neurons

- lie in dorsal horn (lamina 1-5)
- diff types of neurons:
 - nociceptive specific:
 - high threshold
 - located in superficial layers of dorsal horn
 - respond selectively to painful stimuli
 - wide dynamic range:
 - found in deeper laminae
 - respond to painful & non painful stimuli
 - \uparrow firing in proportion to intensity of stimulus in graded fashion
 - Do not signal pain in normal non-painful stimuli eg from A β
 - ↳ but if sensitized (allodynia) then non-painful stimuli may be perceived as painful
- form tracts up spinal cord:
 - may cross over at same level or after 1-2 segments
 - ascend up anterolateral funiculus as 1 of 3 tracts:
 - spinothalamic
 - (spinoreticular)
 - (spinomesencephalic)
 - synapse with 3rd order neurons at various levels

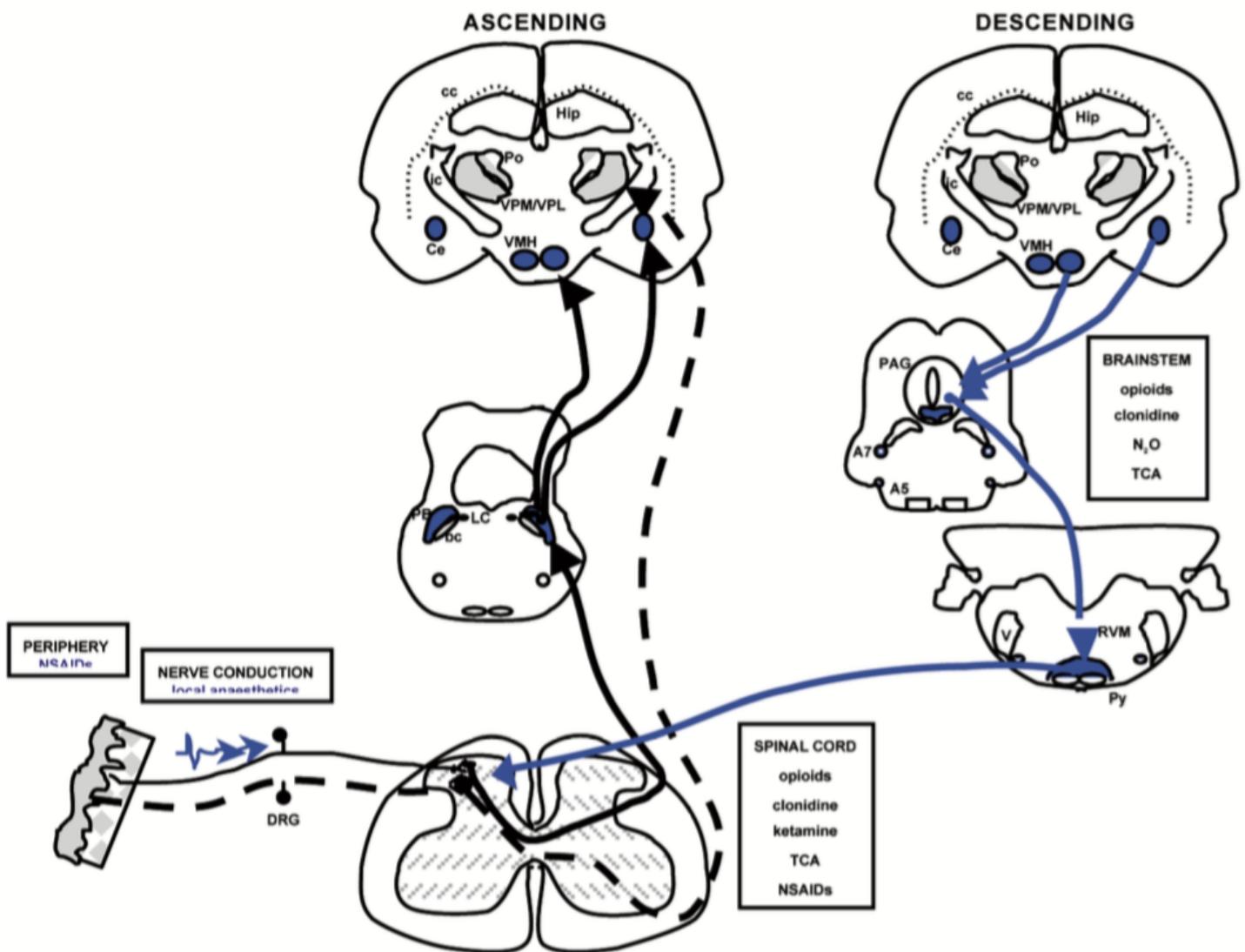
3rd Order Neurons

- lie in thalamus, brainstem or cortex
- spinothalamic - 2nd order terminate on 3rd order in thalamus:
 - anterolateral - discriminatory pain
 - medial - emotive-motivational pain
- spinoreticular -
 - terminate in several brainstem nuclei:
 - Nucleus reticularis paragigantocellularis lateralis,
 - nucleus subceruleus,
 - nucleus reticularis pontis caudalis
 - medullary raphe nuclei
 - responsible for:
 - activation of descending inhibitory pathways
 - arousal
 - activation motor & autonomic reflexes
- spinomesencephalic tracts:
 - terminate in:

- superior colliculus
- nuclei cuneiformis
- periaqueductal grey (PAG)
- impt in
 - activating descending inhibitory pathway & autonomic reflexes
 - coordinated affective motor responses to pain
- 3rd order neurons ⇒
 - somatosensory cerebral cortex (precentral gyrus)
 - ↳ role of this not fully understood
 - cingulate gyrus - role in emotion

Descending Pathways

- arise from diff areas:
 - hypothalamus - β endorphin neurones link ⇒ Nucleus Raphe Magnus (NRM)
 - periaqueductal grey (PAG) - α_2 receptors eg in clonidine analgesia
 - locus ceruleus (LC)
 - (Nucleus paragigantocellularis lateralis)
- descend down dorsolateral funiculus, synapse in dorsal horn lamina 1,2,5
- in dorsal horn may release:
 - serotonin
 - NA
 - enkephalins
 - others eg substance P, GABA, CCK, thyrotrophin releasing hormone (TRH), somatostatin
- endogenous opiate system:
 - PAG & NRM ⇒ descending pathway to spinal level inhibitory interneurons
 - Mu opioid receptors found:
 - 1st order afferent presynaptic membrane
 - 2nd order afferent post synaptic membrane in thalamus
 - proenkephalin = endogenous ligand
- importance of descending pathways:
 - activation via external factors eg stress battle field
 - acupuncture
 - spinal cord stimulation
 - drugs eg tramadol - serotonergic & noradrenergic effects work here

Figure 1.1 The main ascending and descending spinal nociceptive pathways

Classification of Pain Fibres & Receptors

- A δ fibres:
 - from high threshold mechanoreceptors
 - enter lamina 1,5,10 of dorsal horn
 - release glutamate
 - = small myelinated fibres 2-5 μ m
 - fast conduction 6-30m/s
 - well localised & well differentiated pain ie fast pain
 - poor response to opioids
- C-fibres:
 - from polymodal nociceptors
 - enter lamina 1 & 2 of dorsal horn
 - release substance P
 - smaller unmyelinated <2 μ m
 - slow conduction 0.5-2m/s
 - poorly localised/burning pain follow acute injury
 - good response to opioid
- A β fibres
 - conduct non-noxious stimuli eg low threshold touch/pressure/mechano/thermal stimuli
 - unmyelinated fibres

- conduction velocity 30-70ms
- sensitisation ⇒ normal Aβ fibres input being interpreted as pain (allodynia)
- Sleeping/silent nociceptors:
 - unmyelinated
 - chemically sensitive - only activated in inflam & tissue damage
 - only activated after high intensity prolonged stimuli (eg >10mins) BUT then remain active for hours
- sympathetic fibres:
 - may proliferate in DRG
 - ↑ed in chronic pain

Effects of acute pain on Systems

CVS – tachycardia, hypertension, increased SVR -> increased myocardial O₂ consumption, altered regional blood flow as per autonomic nervous system, reduced mobility, venous stasis -> increased risk of DVT->PE

RESP – abdomino-thoracic wall pain -> diaphragmatic splinting and weak cough, decreased lung volumes, atelectasis, sputum retention -> chest infection and hypoxaemia

GI – delayed gastric emptying and reduced intestinal motility

GU – urinary retention

ENDOCRINE – release of vasopressin, ALD, rennin, AG, cortisol, glucagons, GH and catecholamines, decrease in insulin and testosterone -> catabolic state, impaired wound healing and immune function, Na⁺ and H₂O retention, increased fibrinogen and platelet activation and increased metabolic rate

Psychological Aspects of Acute pain

- fear avoidance beliefs ⇒ poor outcome (in back pain)
- association between anxiety, pain, catastrophising, depression & stress causing:
 - chronic pain
 - disability
 - higher post op pain
 - ↑PCA demands

Progression from acute -> chronic pain

- early analgesic interventions reduce the incidence of chronic pain after surgery
- **risk factors for development of chronic pain** =
 - severity of pre and postoperative pain,
 - intraoperative nerve injury
 - psychological vulnerability ie anxiety, pain catastrophising, depression , stress
- strategies to ↓chronic pain:
 - periop ketamine
 - (thoracotomies) - use of epidural
 - (gynae LSCS & hysterectomy) - spinals
- gabapentin - conflicting evidence on effect

Mechanisms of Acute & Chronic Pain

PERIPHERAL NERVES

PRIMARY AFFERENT NOCICEPTORS

- skin and visceral
- are sensitised by a multitude of mediators and neurotrophins
- damaged nerves can form neuromas and sprout -> ectopic impulses sent centrally
- acute treatment: NSAIDS, opioid agonists, LA
- chronic treatment: Na⁺ channel blockers (LA, mexiletine, anticonvulsants)

SYMPATHETIC AFFERENT INTERACTIONS

- ie. CRPS II (causalgia)
- increased pain in response to stimuli % sympathetic nerves
- **treatment: sympathetic blockade (plexus or regional), alpha adrenergic blockade (guanethidine, resperine)**

DORSAL HORN

CENTRAL SENSITIZATION

- increased responsiveness of nociceptive neurons in the CNS to their normal afferent input

WINDUP

- increased responsiveness of dorsal horn neurones
- mediated by NMDA receptor

LONGTERM POTENTIATION

- increased responsiveness of dorsal horn neurones
- has NMDA and non-NMDA components

SPROUTING

- nerves in dorsal horns grow and connect with neurons going to brain

LOSS OF INHIBITION

- from surrounding cells + descending pathways
- **treatments: AMPA receptor antagonists (none available), NMDA receptor antagonists (ketamine, dextromethorphan)**

ASCENDING SPINAL TRACTS

- spinothalamic
- spinomesencephalic
- spinoreticular
- spinocervicothalamic
- post-synaptic dorsal column pathway
- **treatments: peripheral neurectomy, ganglionectomy, DREZ, cordotomy, brain lesions**

BRAIN

- anterior cingulate cortex
- insular cortex
- primary somatosensory cortex
- secondary somatosensory cortex
- prefrontal cortex
- thalamus

- neurotransmitters involved: noradrenaline, beta-endorphin, GABA, serotonin...

- treatments:

1. Opioids receptors (opioids)
2. GABA receptor (anticonvulsants, BZD, stimulation techniques – TENS, acupuncture)
3. Alpha adrenoceptors (TCA's, clonidine, dexmedetomidine)
4. 5HT receptors (TCA's)
5. psychological help (cognitive, behavioural, pharmacological)

Pre-emptive and preventative analgesia

- Preventative analgesia =
 - ▶ Analgesic intervention which have an effect on postop pain/analgesic consumption that exceeds the expected duration of action of the medicine
- Pre-emptive analgesia =
 - ▶ analgesic intervention given pre-incisional causing significant effect on post-operative pain relief
- Pre-emptive interventions pre-incision have very poor evidence **except (some evidence):**

- ▶ ketamine
 - ▶ epidurals,
 - ▶ LA infiltration
 - ▶ NSAIDS
- Preventative analgesia shown evidence with:
- ▶ lignocaine (regional or IV)
 - ▶ Ketamine

Genetics

- CYP2D6 polymorphisms affect plasma conc of active metabolites of codeine, oxycodone & tramadol:
 - ▶ ultrarapid metabolisers ⇒ ↑ risk of codeine & tramadol toxicity
- Mu opioid OPRM1 polymorphism on relevant in Asian populations

Assessment and Measurement of Acute Pain

- Site
 - Onset
 - Character
 - Radiation
 - Associations
 - time Course
 - Exacerbating/Relieving factors
 - Severity
-
- regular assessment of pain ⇒ better pain management
 - good correlation between
 - ▶ verbal rating scales (mild, moderate, severe)
 - ▶ numerical scales (1-10)
 - self reporting encouraged
 - visual analogue scales (two extremes on a scale that patient marks, normally 100mm long)
 - assess pain with regard to static and dynamic scores
 - uncontrolled/unexpected pain should prompt review of diagnosis

Provision of safe and effective Acute Pain management

- an acute pain management service may improve pain relief and reduce the incidence of side effects
- no good evidence in favour of preop pain education effecting outcomes significantly (except in specific situations & for carers)
- written info is better than verbal info

Analgesic drugs

Opioids

Systemic

- dextropropoxyphene has low analgesic efficacy
- tramadol:
 - ▶ effective in treating neuropathic pain
 - ▶ less respiratory depression and GI dysfunction @ equipanalgesic dose of other opioids
 - ▶ not with MAOI
 - ▶ care if high dose SSRI (fluoxetine >20mg), TCA (amitryp >50mg)
- ↓PONV post op - use drugs in combination of classes:

- ▶ droperidol, ondanestron cyclizine, metoclopramide and dexamethasone
- ▶ PC6 acupuncture/acupressure effective in ↓PONV
- ▶ IV Paracetamol - also ↓s pain (but doesn't ↓opioid requirement)
- ▶ haloperidol, transdermal scopolamine
- remi hyperalgesia or acute tolerance - reversed by NMDA antagonists (ketamine & Mg)
- naloxone, naltrexone and nalbuphine -> effective for
 - ▶ opioid-induced pruritis
 - ▶ opioid induced urinary retention
- opioid adverse effects are dose-related
 - ▶ PCA morphine = higher analgesic efficacy in females
- opioid sparing drugs = gabapentin, non-selective NSAIDs, IV lignocaine, ketamine
- pethidine is not superior to morphine in treatment of renal or biliary colic (discourage use)
- post op O2 -> increases SpO₂, reduces tachycardia and myocardial ischaemia
- renal impairment and PO morphine -> increased levels of M3G and MG6
- sedation score better than RR - for early onset opioid ventilatory impairment
- age, rather than weight: is a better predictor of opioid requirement

Intrathecal

- morphine & fentanyl prolong LA block
- fentanyl has fewer adverse effects
- morphine gives better post op analgesia post Caesar
- intrathecal morphine ≥300mcg ⇒ ↑risk of resp depression

Epidural

- analgesia efficacy: morphine = fentanyl but fentanyl has ↓ed side effects
- morphine can provide pain relief for up to 48hrs but more resp depression than PCA
- epidural pethidine better analgesia & sedation than IV pethidine post Caesar

Peripheral

- no effect of morphine injected into joints or peripherally
- topical opioids inconclusive

Oxycodone

Indications

- cancer pain
- chronic pain
- ? neuropathic pain (diabetes neuropathy, post-herpetic neuralgia)
- ? acute pain

Dosage -

- 1mg IV morphine = 2mg oxycodone = 3mg PO morphine
- reduce or extend dosing interval in renal impairment
- **0.1mg/kg**

Onset - 30min (oxynorm)

Pharmaceutics

- PO
- oxynorm (capsule and elixir) – given 4-6 hrly
- oxycontin (tablet)
- not licensed for breast feeding or children
- liposolubility similar to morphine

Pharmacokinetics

Absorption

- bioavailability 50-90% (increased compared to morphine)

Distribution

- protein binding 40%

- Vd 2-3L/kg

Metabolism

- hepatic via PYP3A4 via N-demethylation (effected less than pathway used by morphine in hepatic dysfunction)
- minor metabolite (oxymorphone) is active

Elimination

- urine (some eliminated unchanged)
- t_{1/2} oxynorm = 4 hours (increased by renal failure, hepatic impairment and in women)
- t_{1/2} oxycontin = 8 hours

Pharmacodynamics

Mechanism of action;

- mu & kappa agonist
- binds less avidly than morphine

RESP

- respiratory depression

CNS

- somnolence
- dizziness
- hallucinations (less than morphine)
- withdrawal if stopped quickly

GI

- N+V (less than morphine)
- constipation (more than morphine)

SKIN

- pruritis (less than morphine)
- sweating

IMMUNE

- less immunosuppressive effects than morphine

Interactions

- cyclosporine – decreases bioavailability -> increase dose of cyclosporin
- fluoxetine – increased plasma levels of oxycodone + increase risk of serotonin syndrome
- quinidine – increased plasma level of oxycodone
- rifampicin – increased oxycodone clearance

Tapentadol

- 50-200mg/day
- compared to tramadol:
 - ▶ not metabolised to active morphine component
 - ▶ ↓ resp depression
 - ▶ ↓tolerance/addiction
- similar to tramadol
- ↑ed NA reuptake inhibition & ↓ed 5HT effects

Hydromorphone

- x5 potency of morphine

Dihydrocodeine

- Doesn't require metabolism to become active
- Otherwise same PD of codeine

Buprenorphine

- = partial agonist

- no active metabolism
- clinically equipotent to other opioids
- ceiling effect on SE's ie ↓constipation, ↓RR
- can reverse with naloxone but may need higher doses and long infusions
- good for neuropathic pain
- ↓opioid induced hyperalgesia
- patches, sublingual options available
- elim half life 24-72hr & cant co-dose with other opioids ∴ if patch not taken off 3d prior to op then need to other analgesic options eg ketamine, regional

Paracetamol

- effective analgesic
- same side effects as placebo
- hepatotoxicity extremely rare

NSAIDS & COX 2 Inhibitors

Systemic

- NNT = 1.6-4.2
- effective analgesics of similar efficacy for acute pain
- NSAIDS + paracetamol = more analgesia
- with careful selection of patients NSAID induced renal impairment is low
- aspirin + some NSAIDS increase perioperative bleeding after tonsillectomy except in paed
- NSAIDS reduce opioid consumption
- NSAIDS increase perioperative blood loss
- COX 2 inhibitors and NSAIDS have similar effects on renal function
 - ↳ slight ↓in risk with COX2 inhibitors
- COX 2 inhibitors vs NSAIDS:
 - ▶ ↓bronchospasm in aspirin induced respiratory disease
 - ▶ no effect on platelet function
 - ▶ same peptic ulcer rate as placebo (decreased compared to NSAIDS)
- COX 2 inhibitors -> don't give in patients with lots of vascular risk factors
- parocoxib & valdecoxib DO NOT increase risk of cardiovascular disease after non-cardiac surgery
 - ↳ post CABG they do cause ↑CVS/stroke risk ∴ contraindicated
- COX 2 inhibitors and NSAIDS are associated with the same rates of adverse CVS effects (MI)
- surgical complications:
 - ▶ short-term use of COX 2 inhibitors do not affect bone healing after spinal fusion
 - ▶ effect on colo-rectal anastomosis leak is unclear
- VIGOR study looked @ rofecoxib vs naproxen and found significant increase in MI in rofecoxib group (patients on low-dose aspirin were excluded)
- benefit of low dose aspirin in CVS disease is reversed by co-administration of other NSAIDS - esp ibuprofen

Non-Systemic

- topical NSAIDS (except indomethacin) are effective in periph MSK injuries (with systemic side effects no more than placebo)
- NSAID peri/intra-articular injections is unclear **except** for arthroscopy where is better than IV
- topical NSAIDS good for corneal abrasions

Contraindications

Absolute

- history of GI bleeding or ulceration
- known hypersensitivity to NSAIDS
- severe liver dysfunction
- cardiac failure
- dehydration
- hypotension
- hypovolaemia
- hyperkalaemia

- pre-existing renal impairment
- uncontrolled HT
- aspirin-induced asthma

Relative

- impaired hepatic function
- DM
- bleeding or coagulation disorders
- vascular disease
- operations where there is a high risk of bleeding (cardiac, major vascular, hepatobiliary)
- operations where absence of bleeding important (eye and neurosurgery)
- non-aspirin induced asthma
- concurrent use of ACE I, diuretics, anti-coagulants, methotrexate, cyclosporine and other nephrotoxic agents
- pregnant & lactating women
- age >65 (renal impairment more common)

Nitrous oxide & Inhalational Agents

- obs: some analgesic efficacy in labour no effect on neonate
 - ▶ but nausea & dizziness in mother
- effective analgesic in many pain situations
- methoxyflurane - effective analgesic with rapid onset esp in prehospital setting
- neuropathy and bone marrow suppression = rare but serious complication
- supplement with vitamin B12, methionine & folate

NMDA antagonists

- help in avoiding remi hyperalgesia
- ketamine:
 - ▶ thoracic pts: opioid sparing, ↑ed time to first analgesic request, ↓chronic pain, ↓opioid induced PONV, useful in allodynia, hyperalgesia and opioid tolerance
 - ▶ ↓pain in opioid tolerant pts
 - ▶ concerns:
 - abuse esp South East Asia & china
 - toxicity - cog impairment & liver toxicity
- ↳ only sig issue if using infusion > 2-3 days
- Mg2+
 - ▶ as adjunct to morphine = opioid sparing & ↓pain scores
 - ▶ post spinal:
 - prolongs duration of sensory block
 - ↓s post op pain scores
- Methadone:
 - ▶ NMDA ant agony as well as opioid
 - ▶ Lacks active metabolites ∴ excellent in renal failure
 - ▶ half life up to 5 days (4-190hours)
- Regional:
 - ▶ epidural ketamine (no preservative) (with opioid) ⇒ ↑pain relief & no ↑adverse effects
 - ▶ caudal ketamine - benefit with no ↑adverse effects in adults

Antidepressants

- 3-4 weeks onset
- TCA's & SNRIs effective in; chronic neuropathic pain, chronic headaches & chronic back pain
- in neuropathic pain -> TCA's better than SSRI's
- antidepressants reduce the incidence of chronic neuropathic pain after acute zoster & breast surgery

Anticonvulsants

- gabapentin, pregabalin -> effective in chronic neuropathic pain
- gabapentin and pregabalin -> reduce post operative pain, opioid requirements but increase the risk of sedation

Gabapentin

- anticonvulsant and used to modulate acute and chronic pain
- oral agent
- structurally related to GABA but acts on non-GABA receptors (voltage sensitive calcium channels in CNS -> inhibit Ca²⁺ uptake and thus release of neurotransmitters)
- dose 300mg od titrated up to 800mg tds (if required)
- if using as single prop dose then need >600mg
- peak plasma level in 3 hours
- t_{1/2} 6 hours
- no hepatic metabolism
- renally eliminated
- side effects; sedation, dizziness, diplopia, nausea, ataxia, nystagmus, tremor, bilat LL oedema

Acute surgical pain

- multiple trials have revealed the following:
 - can be used peri-operatively and has been shown to decrease postoperative analgesic requirements and pain (level 1 evidence) – mastectomy, lap chole, hysterectomy, spinal surgery)
 - has anti-hyperalgesia and anti-allodynia effects
 - requires titrating up to an adequate dose over a number of days (shown to not influence analgesia requirement in day case surgery)
 - effective for post-amputation phantom limb pain
 - improves quality of opioid analgesia
 - reduces opioid requirements (only few trials have shown this)
 - reduces/prevent opioid tolerance
 - relieves anxiety (preop medication)
 - does not depress respiratory function (important in the respiratory cripple)
 - no effect on gastric and duodenal mucosa (unlike NSAIDS)
 - no effect on platelets (haemostasis maintained)
 - no effect on renal function
- reduced movement-evoked pain -> improved functional recovery
- limitations of its use include; sedation, dizziness & only available orally

Chronic surgical pain

- used when chronic surgical pain has a neurogenic component - low NNT (4) for treatment of chronic neuropathic pain states that may be induced post surgery
- benefit demonstrated in diabetic neuropathy, spinal surgery and phantom limb pain modulation
- this is currently a lack of evidence in the area
- has equal efficacy to TCA's but is more readily tolerated by patients.

PreGabalin

- more potent x4 (50-100mg bd)
- more predictable metabolism
- bd dosing rather than tds
- faster onset of action, ↓side effects

Local Anaesthetics - Membrane Stabilisers

Systemic

- effective in chronic neuropathic pain (particularly peripheral nerve trauma)
- perioperative IV lignocaine for abdo surgery reduces:
 - ▶ opioid requirement
 - ▶ PONV
 - ▶ duration of ileus
 - ▶ length of hosp stay
- ↳ analgesic effect lasts >8hrs post cessation of infusion

Regional

- lignocaine more likely to cause transient neurological symptoms than bupivacaine/ropivacaine
- epidural quality better with opioids
- periph nerve block infusions should avoid lignocaine as less effective & ↑ motor block
- CVS & CNS toxicity less severe with ropivacaine or levo-bupivacaine compared to bupivacaine
- use US
- in accidental overdose: resuscitation less likely to be successful with bupivacaine

Alpha-2-agonists (clonidine, dexmedetomidine)

Systemic

- both lead to:
 - ▶ adv: ↓ post op pain, ↓ opioid consumption, ↓ PONV, same PACU time
 - ▶ adverse effects limit use: ↓ HR, hypotension

Regional

- intrathecal clonidine/dexmedetomidine ⇒ ↑ duration of analgesia
 - ↳ but also seen with addition of adrenaline
- eye blocks - clonidine good effect but side effects as above
- dexmedetomidine in brachial plexus blocks can prolong effects of LA

Salmon Calcitonin & bisphosphonates

- Bisphosphonates ↓ bone pain in metastatic breast Ca & multiple myeloma
- Calcitonin
 - ▶ reduces pain and improves mobilisation after an osteoporotic vertebral #
 - ▶ post amputation: ↓ acute pain but not chronic pain or phantom pain

Cannabinoids

- no role in acute pain
- appear to be mildly effective in treatment of chronic neuropathic pain (including MS & HIV pain)
- adverse effects may limit use: dizziness, cognitive changes, psychosis

Steroids

Systemic

- dex ⇒
 - ▶ ↓ post op pain, ↓ opioid needs to limited extent
 - ▶ ↓ PONV, ↓ fatigue, ↑ recovery
 - ▶ pre-op admin more effective than intraop
 - ▶ risk of hyperglycaemia

Regionals

- lumbar epidural steroid injection effective for short term relief
- addition of dex to regional LA ⇒ prolonged duration of sensory & motor block
- concerns:
 - ▶ septic arthritis
 - ▶ safety of epidural injection

Routes For Drugs

Oral

- NSAIDs & COX 2 inhibitors – same side effects if given IV, PO or PR
- paracetamol combined with tramadol or codeine are more effective
- paracetamol given periop ⇒ variable plasma concentrations which may be subtherapeutic in some

Parenteral

- morphine SC is just as effective as IM
- don't use transdermal fentanyl for acute pain (safety and can't titrate)
- intranasal/buccal/sublingual fentanyl good for breakthrough pts in cancer (opioid tolerant)
- in severe pain use IV bolus titration

PCA

- provide better analgesia
- better patient satisfaction
- opioid consumption slightly higher
- no difference in PONV
- increased pruritis
- no difference in length of hospital stay
- adding ketamine to morphine in pump only useful in thoracic surgery
- adding naloxone may decrease N+V and pruritis
- addition of a background infusion:
 - ▶ ↑ risk of resp depression
 - ▶ doesn't improve pain relief or sleep or decrease number of demands
- little evidence that one PCA opioid is better than the other - base it on individuals
- intra-nasal and SC PCA can be as effective as IV
- routine addition of anti-emetics not needed (select cases carefully)
- practical:
 - ▶ pt must have adequate analgesia prior to commencement of PCA
 - ▶ dose based on Hx prior opioid use, age, renal function etc
 - ▶ must have antisiphon valves & antireflux valves
 - ▶ avoid use of norpethidine
- morphine may not be perfect PCA opioid:
 - ▶ long equilibration half time
 - ▶ active metabolites

PCEA

- adv:
 - ▶ lower total doses of LA
 - ▶ decreased N+V
 - ▶ less motor block
 - ▶ fewer anaesthetic interventions
- disadv:
 - ▶ less effective analgesia
 - ▶ more pruritis

Epidural analgesia

- epidural gives better analgesia for all surgery than IV opioids:
 - ▶ post sternotomy
 - ▶ AA surgery
 - ▶ abdo surgery
- reduced oxygenation and reduced pulmonary infections compared with IV opioids
- thoracic epidural -> improves bowel recovery, decreases ventilator hours, MI, respiratory failure, gastric complications and renal impairment + decreases pneumonia in patients with rib #'s, preserves total body protein after upper abdominal surgery (with nutritional support)
- lumbar epidural -> reduces graft occlusion in peripheral vascular surgery
- permanent nerve damage = very low (key is to diagnose haematomas and abscesses early)
- chlorhexidine 0.5% or povidone-iodine impregnated dressings -> reduce incidence of catheter colonisation
- generally benefits incl:
 - ▶ ↓ pain
 - ▶ ↓ arrhythmias
 - ▶ ↓ duration of intubation & ventilation
 - ▶ ↓ MI
 - ▶ ↓ resp failure
 - ▶ ↓ GI complications
 - ▶ ↓ renal injury
 - ▶ ↓ chronic pain
 - ▶ ↓ ileus
- disadv:
 - ▶ ↑ hypotension

- ▶ ↑length of stay
- ▶ ↑urinary tract infection
- ▶ risks of placing: infection, haematoma (decompression within 8hrs ↑s chance of recovery)
- Triggers for MRI epidural problems:
 - ▶ fever
 - ▶ evidence of catheter site infection
 - ▶ back pain or any neuro change

Intrathecal analgesia

- morphine (100-200mcg) offers effective analgesia with low risk of adverse effects for 24hrs
 - ↳ use lowest poss dose
- morphine, fentanyl and sufentanil -> no neurotoxicity or POCD
- side effects:
 - ▶ ↑urinary retention
 - ▶ N&V
 - ▶ pruritus ⇒ naloxone or serotonin antagonists
 - ▶ ↓ventilatory drive - monitor for 24hours
- intrathecal Mg to opioids prolongs effect

Other regional and LA techniques

- specific surgeries:
 - ▶ intra-articular LA is only minimally effective
 - ▶ breast surgery: PVB > compared to iV analgesia
 - ▶ thoracic surgery: continuous PVB infusion > epidural = same analgesia but fewer side effects
 - ▶ abdo surgery: wound catheters good (no benefit found in ortho surgery)
 - ▶ lap chole: intraperitoneal LA -> improves early post pain
 - ▶ TKJR:
 - adductor canal block as good as fem nerve block with less quads weakness
 - continuous femoral nerve blockade -> compared to epidural analgesia (fewer side effects)
 - continuous lumbar plexus blockade and continuous femoral blockade much the same efficacy
 - local infiltration injection of LA improves analgesia for 32hrs compared to IV analgesics
 - ▶ shld ops: continuous interscalene catheter
 - ▶ LSCS & laprascopic surgery: TAP blocks improve analgesia in short term
- bupiv should not be used intra-articular - risk of cartilage destruction
- wound infiltration for small cuts good (no point in big cuts)
- continuous LA wound infusion -> better analgesia, less PONV, less time in hospital and no difference in wound infections

Non-pharmacological techniques

- psychological therapies, music, distraction, TENS, acupuncture and physio -> all can be effective

Specific clinical settings

Postoperative Pain

- acute neuropathic pain occurs after trauma and surgery
- multimodal analgesia \Rightarrow \downarrow pain & \downarrow opioid need
- adhere to ERAS protocols
 - acute neuropathic pain should be treated as chronic pain: ketamine, opioids, gabapentin

Post Amputation Pain Syndromes

- Three phenomena after amputation
 1. phantom sensation
 2. stump pain
 3. phantom pain

Phantom Sensation

- any sensation experienced in the where the amputation limb use to be
- paraesthesia in missing limb
- sensation that it is present
- usually immediately straight after amputation sometime can be delayed

Stump pain

- associated with surgery and usually resolves once wound heals
- can persist and may be secondary to a neuropathic process
- can be difficult to treat
- refer them on to limb centres to optimize prothesis
- may required surgical revision if pathology found (bone spurs, infection, osteomyeliitis)

Phantom limb pain

- experienced by around 70%

Symptoms;

- pain in first week, may induced by spinal or epidural for an unrelated procedure, shooting, burning, cramping, aching in distal area of phantom limb, pain can be constant with varying intensity, variable spontaneous resolution rates, can affect the breast post mastectomy

Risk factors

- pre-amputation pain, presence of persistent stump pain, bilateral limb amputations, lower limb amputation

Mechanism

- ? central re-organisation in brain in spinal cord from peripheral afferent input

1. peripheral mechanisms – ectopic discharge from nerves or dorsal root ganglia, increased sensitivity of neuromas, sympathetically mediated afferent input
2. spinal cord mechanisms – reorganisation from degeneration of unmyelinated C fibers, central sensitisation of dorsal horns \rightarrow hyperalgesia
3. supraspinal mechanisms – errors occurring in the cortical remapping process \rightarrow overamplification

- **treatment;** should be MDT and multimodally based

1. opioids (good for acute pain)
2. gabapentin (good in neuropathetic pain but not proven in phantom limb pain)
3. carbamazepine (good in neuropathetic pain but not proven in phantom limb pain)

4. NMDA antagonists
 5. calcitonin
 6. betablockers (not good efficacy)
 7. pre-emptive analgesia with epidural
 8. continuous regional blockade via nerve sheath catheters post amputation provides good analgesia but doesn't prevent phantom limb pain
 9. physical treatments – acupuncture, heat, cold, U/S, TENS, massage, adjustment of prostheses, manipulation of stump (all have reported some success)
 10. cortical reorganisation therapy useful ie mirror therapy, sensory discrimination, motor imagery
 11. explanation, reassurance, psychotherapy, hypnosis, CBT – all have reported some success
- ↓ing incidence of severe phantom limb pain:
- ▶ prophylactic ketamine
 - ▶ perioperative epidural analgesia
 - ▶ calcitonin, morphine, ketamine, gabapentin and sensory discrimination training

Acute neuropathic pain post surgery

- doesn't usually occur in isolation (associated with nociceptive pain from inflammation and tissue damage)
 - burning, shooting pain
 - pain may extend beyond the territory of a single peripheral nerve
 - poorly responsive to opioids
-
- allodynia = pain following a normal innocuous stimulation
 - hyperalgesia = pain out of proportion to a normal painful stimuli
 - dysaesthesias = spontaneous unpleasant abnormal sensations

Management:

Principles = reducing hyperexcitability and reducing activity of NMDA receptor

IV options:

1. NMDA antagonist (IV ketamine 5mg/hr)
2. Membrane stabiliser (IV lignocaine 5mg/kg over 30min -> 0.5-1.5mg/kg/hr)

Oral options:

1. TCA's/SNRI
2. Gabapentin/Pregabalin/Capsacin
3. Opioids - try to avoid due to long term issues

Rescue options:

1. Epidural/Regional

NeuroSurg

- cranial:
 - ▶ scalp blocks are good for early analgesia
 - ▶ morphine best opioid
 - ▶ risk of chronic headache
 - ▶ pain can be under-estimated
- spinal surgery:
 - ▶ gabapentin - opioid sparing, & better functional outcome at 3/12
 - ▶ NSAIDs - opioid sparing
 - ▶ local infiltration opioid sparing esp if deeper than just subcut
 - ▶ lignocaine infusion - opioid sparing
 - ▶ NSAID use for <14 days does not ↓risk of bony union (except if high dose ketorlac)

Acute pain post cord injury

- IV opioids, ketamine and lignocaine -> decrease acute spinal cord injury pain
- gabapentoids are effective in treatment of spinal cord injury

Acute Burns

- pain can be nociceptive +/- neuropathic
- background pain, intermittent or procedure related
- biosynthetic dressings advs: ↓time to heal, ↓pain during dressing changes
- effective dressing change options:
 - ▶ distraction therapy
 - ▶ lorazepam
 - ▶ PCA with ketamine & midaz
- PCA opioids effective
- gaba ↓pain post burn

Acute back pain

- Acute LBP non specific in 95% of cases
- further Ix only if red flags
- stay active, heat pack, verbal info and behavioural therapy -> are beneficial for neck and back pain
- soft collars bad
- early treatment and education can stem the tide towards chronic back pain

Acute MSK pain

- shld pain:
 - ▶ topical & oral NSAIDs
 - ▶ exercises
 - ▶ ultrasound
 - ▶ subacromial steroid injection useful in early stages
- hollistic approach impt
- use pain ladder
- extended analgesics (anticonvulsants, antidepressants, mm relaxants) should not be used routinely

Day Stay Surgery

- paed:
 - ▶ ketamine in caudal ⇒ prolongs analgesia but not motor block (some concern re neurotoxicity)
- best practise:
 - ▶ laparoscopic work: use wound infiltration & intraperitoneal instillation (up to 6hrs)
 - ▶ Simple analgesia good: NSAIDs, cox 2 inhibitors, Dex
 - ▶ single shot PNBs - earlier d/c, less opioids, quicker rehab, less sleep disturbance
 - ▶ PVBs good in breast & hernias
 - ▶ dexmed in PNBs can prolong duration of action
 - ▶ continuous PNB infusions safe at home if adequate resources & educations

Acute Medical Pain

Abdominal pain

- analgesia does not interfere with diagnosis
- renal/biliary colic:
 - ▶ give NSAIDS (help ↓opioid need) + opioids
 - ▶ IV NSAID pain relief faster than oral
 - ▶ α blockers for stones ⇒ ↓pain episodes & analgesic requirements
 - ▶ IV paracetamol = IV morphine in efficacy
 - ▶ buscopan not useful
 - ▶ no role for pethidine > morphine
- IBS:
 - ▶ antispasmodis & TCAs good
 - ▶ bulking agents - no effect
- dysmenorrhoea:
 - ▶ NSAIDS superior to paracetamol
 - ▶ TENS, magnesium, vit B, acupuncture are effective

Acute herpes zoster infection

- caused by Herpes Zoster Virus
- severe pain -> vesicular rash in the distribution of a nerve root
- history of chicken pox, immunocompromised \Rightarrow malaise, fever \Rightarrow cutaneous lesions in dermatomal distribution
 - \hookrightarrow if ophthalmic symptoms \Rightarrow eye emergency
- Rx based on clinical diagnosis - dont wait for bloods (PCR), serology
- Rx:
 - ▶ Analgesia – simple + opioid PCA may be needed (all effective at reducing pain)
 - ▶ start antivirals within 72 hours of rash
 - good for \downarrow ing length of acute pain
 - no effect on incidence, severity, duration of postherpetic neuralgia
 - ▶ Anti-depressants – TCA's -> possible decreased in acute pain, but does significantly decrease risk of developing post herpetic neuralgia
 - ▶ (Corticosteroids) -> only modest:
 - \downarrow quality of life,
 - \downarrow time to healing of lesions
 - \downarrow incidence of post-herpetic neuralgia \hookrightarrow **but** with an \uparrow in secondary bacterial infection
 - ▶ topical lignocaine
 - ▶ Capsaicin - need high doses. poorly tolerated
 - ▶ Eye treatments; topical steroids, topical antibiotics, topical antivirals, glaucoma medications (effective @ decreasing damage and reducing infection risk)

Acute Cardiac Pain

- effective analgesics: morphine, GTN

Sickle cell crises

- analgesia:
 - ▶ opioid PCA
 - ▶ zinc
 - ▶ IV corticosteroids - \downarrow pain and hospital stay
 - ▶ +/- hyperbaric O₂
- hydroxyurea - \downarrow s
 - ▶ frequency of acute crises
 - ▶ life threatening complications
 - ▶ transfusion requirements
- no evidence to \downarrow pain:
 - ▶ IVF
 - ▶ Regular O₂
- avoid pethidine - risk of seizure with nortryptiline

Acute Headache

- migraines - significant placebo effect
 - ▶ triptans
 - (fastest onset with highest efficacy = s/c)
 - 30-40% may not respond
 - ▶ aspirin & NSAIDs
 - ▶ metoclopramide (esp with paracetamol), droperidol
 - ▶ prochlorperazine, chlorpromazine - esp in ED
 - ▶ droperidol, NSAIDS
 - ▶ not effective:
 - opioids esp pethidine - may be effective but carry large side effect risk
 - IV Mg
- tension -> acupuncture, metoclopramide, chlorpromazine, caffeine, aspirin, paracetamol, NSAIDS
- cluster headache -> sumatriptan, high flow O₂,
- PDPH ->
 - ▶ use small needles,

- ▶ prophylactic bed rest not effective
- ▶ patch is best treatment
- ▶ analgesia:
 - effective: morphine, aminophylline, hydrocort, gabapentin
 - not effective: dex
 - inconclusive: fentanyl, caffeine, indomethacin

Acute Pain & Neuro disorders

- MS - effective agents:
 - ▶ neuropathic pain: anticonvulsants, (maybe cannabinoids)
 - ▶ spasticity: cannabinoids
- MS cannabinoids ⇒ 1% risk of severe psychopathological effects

Orofacial pain

- acute dental pain = NSAIDs
- dental extraction:
 - ▶ simple pain ladder
 - ▶ Cox 2s are just as good as NSAIDs
 - ▶ steroids ⇒ ↓swelling not ↓pain
- tonsillectomy:
 - ▶ simple pain ladder
 - ▶ avoid NSAIDs - use Cox2s to ↓risk of bleeding (analgesia just as good)
 - ▶ dex - ↓pain, ↓PONV, ↓time to resumption of oral intake & no adverse effects
 - ▶ LA to tonsillar bed or peritonsillar infiltration may be effective
 - ▶ Abx dont effect pain
 - ▶ preop gaba ↓post op pain

Trigeminal Neuralgia

- = a chronic pain state characterised by brief, severe radiating pain in the distribution of the trigeminal nerve
- most commonly seen in mandibular & maxillary distribution
- described as 'a red hot needle' or 'forked lightning pain in the face'
- pain usually unilateral
- triggered by non-noxious stimulation of the ipsilateral nasal and perioral region
- minimal or no sensory loss
- aetiology unknown (?structural abnormality in the trigeminal root adjacent to the pons ?compression of a root by an aberrant vein or artery)
- incidence 5/100,000

Treatment options

Acute treatments = opioids +++

1. carbamazepine (beneficial in 70% of cases, first line treatment)
2. phenytoin
3. TCA's
4. clonazepam (initial success but quickly ineffective)
5. gabapentin (used as second line agent with some benefit)
6. simple analgesics (some use)
7. trigeminal nerve blocks (temporizing measure only)
8. acupuncture
9. lamotrigine (added to carbamazepine when needing additional treatment)
10. topiramate
11. baclofen (moderate effect)

Operative interventions

12. microvascular surgical decompression of the trigeminal nerve (2/3 pain free @ 10 years however death rate 0.2-1% and persistant facial numbness 1%)

13. destructive lesions

- alcohol injection or radiofrequency coagulation (high initial success, 1/3 free of symptoms @ 3 years)
- surgical destruction (some success but numbness 15%)
- stereotactic gamma knife radiosurgery (up to 80% free of pain in short term but has a significant side effect profile)

Pain + HIV infection

- neuropathic pain common:
 - ▶ treat normally
 - ▶ other effective agents: cannabis, lamotrigine
- beware of interaction with anti-retrovirals

Acute cancer pain

- PO transmucosal fentanyl effective for breakthrough pain
- pt education key for optimising pain management
- neuropathic pain in ~40%
- breakthrough analgesia should be one-sixth of total regular daily opioid dose (except with methadone)
- is sudden severe pain ≈ possibility of medical emergency & should be investigated
- transdermal only useful for background pain

Acute pain in ICU

- remi no better than other opioids
- sedation holidays
- GBS –
 - ▶ plasma exchange improves outcome incl analgesia
 - ▶ gabapentin and carbamazepine effective
- opioids 1st line analgesia in ventilated patients
- routine monitoring of pain using scores imp

Acute pain in ED

- use morphine (avoid pethidine)
- give analgesia (doesn't change diagnostic yield)
- NSAIDs + opioids for colic
- FNB for # NOF
- buffering lignocaine with bicarb ⇒ ↓pain on infiltration

Prehospital Analgesia

- IV morphine, fentanyl & tramadol equally effective
- N2O & methoxyflurane effective
- ketamine safe & effective
- early effective analgesia of trauma pain ⇒ ↓PTSD
- oral transmucosal fentanyl effective alternative to IV morphine

Discharge Meds Post Acute Pain

- short term opioids can lead to long term use
- ↑risks with recent opioid use:
 - ▶ ↑falls risk
 - ▶ impaired driving
- risk of people keeping unused opioid tablets and sharing them with others

Specific patient groups

Paediatrics

- pain measurement can be carried out @ all ages
- neonates :
 - ▶ experience pain
 - ▶ pain & injury in early life may have adverse long-term effects
 - ▶ more info needed on ideal dosing to gain max benefit & avoid side effects
 - ▶ breastfeeding/breast milk or sucrose reduces the behavioural response to heel stick in neonates
- distraction, hypnosis and combined cognitive-behavioural interventions reduces pain and distress associated with needle-related procedures
- specific drugs:
 - ▶ paracetamol linkage to asthma is inherently confounded
 - ▶ serious adverse events after NSAIDs are rare in children over 6 months of age (avoid aspirin)
 - ▶ intraoperative dexamethasone administration reduces acute pain and nausea and vomiting after tonsillectomy
 - ▶ avoid codeine - esp post T&A
 - ▶ tramadol: similar efficacy to opioids with
 - similar or ↓ed N&V, sedation & fatigue
 - **but** less constipation & pruritus
 - less vent impairment **but** active metabolite M1 remains a concern for ultrametabolisers esp if high risk of opioid induced vent impairment
 - ▶ ketamine:
 - low dose IV bolus shows no ↑risk of N&V, sedation, agitation, hallucinations in paed
 - peritonsillar infiltration ↓s pain score
 - no benefit over placebo for minor operations
 - high dose, long term ketamine neurotoxic in animals. unclear in humans
 - preventing remi induced hyperalgesia unclear in paed
 - ▶ clonidine:
 - premed vs midaz: ↓post pain score, ↓N&V
 - periop benefits: anxiolysis, ↓emergence agitation, facilitate opioid withdrawal
 - ▶ dex post tonsillectomy:
 - does not ↑overall bleeding risk but ↑s re-operation rate for bleeding
- regional:
 - ▶ caudal and dorsal penile nerve block provides perioperative analgesia for circumcision
 - ↳ topical not enough in neonates
 - ▶ caudals:
 - clonidine in caudal -> increased duration of analgesia and increased quality of block
 - ketamine prolongs analgesia (but not motor block) - concern around neurotoxicity remain
 - ▶ complications of epidural infusions are rare
 - ▶ placement of neuraxial blocks under GA not associated with ↑ed complications
- PCAs:
 - ▶ good down to 5yrs old
 - ▶ NCA/parent controlled effective with education (but ↑ed use of rescue meds ie naloxone)
 - ▶ is the best option for kids with mucositis from chemo
 - ▶ may be useful to have background infusion with bolus to cover movement pain
- procedural analgesia:
 - ▶ sweet solutions ↓pain in neonates
 - ▶ EMLA effective but amethocaine is superior for reducing needle insertion pain
 - ▶ topical LA & entonox are effective
 - ▶ adjuncts are effective: music therapy, distraction, cold & vibration
- trauma:
 - ▶ intranasal fentanyl = IM morphine
 - ▶ prehosp intranasal fentanyl or methoxyflurane = IV morphine

The Pregnant Patient

- avoid NSAIDS:
 - ▶ early pregnancy ⇒ miscarriage
 - ▶ particularly after 32 weeks ⇒ ductal closure
- opioids in pregnancy doesn't cause malformations but may cause neonatal abstinence syndrome if used long term
- morphine & fentanyl fine for acute pain
- paracetamol:
 - ▶ inconclusive assoc with use in pregnancy and childhood wheezing/asthma

PREG & Classes A,B,C,X

Labour Analgesia

- CSE vs epidural analgesia ->
 - ▶ not significant analgesic difference -> but increase urinary retention in CSE group
 - ▶ CSE improves speed of analgesia onset, but doesn't change satisfaction & ↑s pruritus
- epidurals:
 - ▶ = best form of pain relief
 - ▶ ↑duration of second stage & rate of instrumental delivery
 - ▶ no ↑Caesar rate or back pain
 - ▶ low conc mixes better: ↓2nd stage, ↓assisted delivery, better ambulation, ↓urinary retention
 - ▶ bupiv = ropiv
- inhaled analgesia:
 - ▶ inhaled volatiles vs N2O give better pain relief but more drowsiness
 - ▶ N2O:
 - analgesia = pethidine but less than epidural
 - Nausea, vomiting, dizziness
 - no adverse effect on newborn
- IV analgesia:
 - ▶ non opioid analgesia alone dont work
 - ▶ opioids - short term effects on newborn
 - ▶ remi PCA better than pethidine, N2O but inferior to epidural
- complimentary:
 - ▶ 1:1 midwife ⇒ ↓analgesia needs
 - ▶ water births good
 - ▶ acupuncture good
 - ▶ massage good for 1st stage
 - ▶ relaxation & yoga good; music doesn't work
 - ▶ doesn't work in labour: TENS, hypnosis, biofeedback, aromatherapy

Post Caesar

- TAP blocks good only when intrathecal morphine not used
- PCA, epidural, neuraxial morphine good but ⇒ ↑nausea & pruritus
- LA, paracetamol, some NSAIDS & morphine, fentanyl & oxycodone are considered safe in lactating patients
- avoid repeated codeine/oxycodone if possible or observe infant for CNS depression

The Elderly Patient

- pain threshold increased ⇒ tendency to under treat pain
- pain tolerance decreased
- frequency and intensity of pain decreased
- ↑ed chance of POCD, delirium, CNS effects of opioids ⇒ difficulty with self reporting
- age related decrease in opioid requirements (variability exists)
- drugs:
 - ▶ start all low and titrate up
 - ▶ topical NSAIDS effective with lower systemic levels & ↓complications

- ▶ avoid oral NSAIDs and COX 2 Inhibitors

Others

Aboriginal Peoples

- use verbal descriptor scale (rather than numerical rating scales)
- renal impairment more common
- pain may be under reported due to cultural background

Maori Peoples

- ischaemic pain tolerated for longer
- dental pain, gout, joint pain more intense
- major healthcare inequalities

OSA Patients/Resp Comprised Patients

- eg Pneumothorax, thyroid masses
- high risk pts
- avoid opioids - high complications & very sensitive to them
- strategies:
 - ▶ regional
 - ▶ CPAP
 - ▶ high monitoring environment
 - ▶ multimodal analgesia without opioids
- CPAP doesn't increase risk of anastomotic leak after upper GI surgery

Opioid Induce Ventilatory Impairment

- Features:
 - ▶ ↓central drive
 - ▶ ↓airway reflex
 - ▶ ↓cough
- Rx:
 - ▶ open airway
 - ▶ Ventilate with O2 if unresponsive
 - ▶ CPR if needed
 - ▶ naloxone

The Opioid-tolerant patient

- report higher pain scores
- lower incidence of opioid-induced N+V
- need up to 2-3x opioid requirement
- clonidine ↓s opioid withdrawal symptoms
- remifentanyl ⇒ opioid induced hyperanalgesia - attenuate with:
 - ▶ propofol
 - ▶ ketamine
 - ▶ gaba
- ketamine may reduce opioid requirements
- PCA's need to have a basal to replace usual opioid dose and use a higher bolus dose
- use reverse analgesic ladder to withdraw from pain relief

Patients with a substance abuse disorder

- naltrexone should be stopped at least 24 hours prior to elective surgery
- patients who have completed naltrexone therapy -> are not only opioid naïve but may be opioid sensitive
- no cross tolerance between alcohol, benzos, CNS stimulants **and** opioids
- continue methadone if at all possible

Renal Failure

- avoid NSAIDs
- Opioids choice:
 - ▶ fentanyl (10-20% urine - liver metab'ed)
 - ▶ Alfentanil (liver metab)
 - ▶ Buprenorphine (liver metab)
 - ▶ methadone (liver metab)
- paracetamol & ketamine good choice
- caution with gaba, morphine, tramadol
- Oxycodone - some accumulation of something over time even though no "active metabolite"
 - ↳ better may options may be buprenorphine, methadone, fentanyl PCA/patch

Liver Failure

- titrate all drugs slowly
- Paracetamol is fine but if ALT x4 normal \Rightarrow ↓dose or withhold
- reduced dose to 2-3g/day if:
 - ▶ <50kg
 - ▶ ↓albumin
 - ▶ Malnourished
- ketamine fine if norm LFTs

Cancer Patients

- COX 2 awesome
- use regional where able but opioids needed to minimise pain
- need to avoid SNS activation

Chronic Pain

Introduction

- complex problem
- multimodal approach
- simple analgesics (paracetamol, NSAIDs, codeine) -> have failed
- we're often involved in the titration of stronger medications (opioids)
- also 'non-analgesic' drugs – anti-depressants, anti-epileptics and anti-arrhythmics

Specific Drug Agents

Anti-depressants

- 50% of patients have depression
- however, pain specialists prescribe for analgesic effects -> in this context -> onset quicker and dose required lower
- ? mechanism -> increased serotonin or monoamine levels or enhanced inhibition in spinal cord
- first generation TCA's (amitryptiline, doxepine, clomipramine)
- indications = chronic neuropathic pain (post-herpetic neuralgia, diabetic peripheral neuropathy, central pain)

Anti-epileptic drugs

- effective
- trigeminal neuralgia -> phenytoin and carbamazepine
- good evidence in post-herpetic neuralgia and diabetic neuropathy
- also used in post-stroke pain syndrome, phantom limb pain and pain post spinal cord injury
- mechanisms dependent on agent:
 - phenytoin, lamotrigine and carbamazepine -> Na⁺ channel blockade ⇒ membrane stabilisation
 - Na⁺ valproate -> increases GABA release
 - Gabapentin & Pregabalin -> blockade of Ca²⁺ channels

LA and Anti-arrhythmics

- damaged tissue = damaged nerves -> send spontaneous and continual discharge to the spinal cord via afferents
- LA and anti-arrhythmics suppress the hyperexcitability via a non-specific Na⁺ blockade
- IV lignocaine main drug used -> useful in acute pain, post-herpetic neuralgia, post thoracotomy pain and CRYPs

Perioperative Management of the Chronic Pain Patient

Preoperative assessment

- risk factors:
 - moderate -> severe pain lasting more than 1 month pre-op
 - repeat surgery
 - psychological vulnerability (neuroticism, emotional distress, poor social setting)
 - sickness benefit (secondary gain)
 - pre-existing neuropathic pain
 - already on analgesics (including opioids), anti-depressants and anti-epileptics
- prolonged inactivity
- neurological deficits from pain syndrome
- must be aware of tolerance, drug adverse effects and interactions
- decreased organ function reserves
- increased risk of adverse effects from pain responses
- under report their actual medication use (particularly with opioids -> at risk of withdrawal)

- anaesthetic considerations of the drugs patients are on – COX inhibitors, anti-convulsants, ketamine, benzodiazepines, TCA's, LA
- be aware of threshold = 30mg of IV morphine for >2-4 weeks ≈ at risk of a withdrawal
- calculate daily opioid requirements and provide a background infusion rate for NBM time
- keep chronic medications going if possible
- stop NSAIDS 24 hour prior to OT if high bleeding risk
- consider Major Depressive Disorder or Anxiety Disorder & treat accordingly
- monitor for the development of significant pain

Intraoperative management

- if chronically using opioids -> may have 2 to 4x the opioid requirements of the opioid naïve.
- establish and continue background opioid requirements throughout OT
- consider regional techniques esp in high risk surgery:
 - amputation, thoracotomy, extensive breast surgery, cholecystectomy, inguinal hernia)

Postoperative management

- have higher pain scores and need more analgesics despite technique used
- likely to be hysterical and hypochondriacs
- compliance with PCA less and often have them for longer
- review 3x/day to assess and manage pain and side-effects
- advise the acute and chronic pain teams of patients status
- after 2nd post operative day, decrease the patients opioid intake step-wisely back to baseline
- switch from IV to oral opioid as soon as possible

Chronic Regional Pain Syndrome

Type I

- formally called **reflex sympathetic dystrophy**
- continuous pain (allodynia or hyperalgesia) in part of an extremity after trauma but doesn't correspond to the distribution of a single peripheral nerve
- worse on movement
- associated with sympathetic overactivity: cool, clammy -> pale, cold with tissue atrophy and stiffness
- usually occurs within weeks of trauma
- osteoporosis may be present
- treatment: mobility, physio, rehabilitation, sympathetic nerve blocks

Type II

- formally called **causalgia**
- burning pain in the distribution of a partially damaged nerve
- median, ulnar and sciatic most common
- usually occurs within a month of injury
- may radiate beyond the nerves normal distribution
- symptoms made worse by cutaneous stimulation and emotional upset
- thought to be secondary to abnormal connections between efferent sympathetic nerves and somatic fibres at the site of injury
- skin classically cold, moist and swollen -> atrophic -> disuse and osteoporosis
- treatment: sympathetic nerve blocks