AWSOME

Anaesthesia Written ShOrt answer & Multiple choice Examination Course

# Pain

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# Learning Outcomes

- Definitions
- Pain Pathway
- Notes on Paracetamol
- NSAIDS what you need to know
- Opiates how they work
- Answering a chronic pain question
- Acute vs Chronic pain
- Assessing Pain
- Antineuropathics
- CRPS
- Phantom Limb Pain
- CPSP

# Definitions

- **Nociception**
  - *Neural process encoding noxious stimulus*
- **Pain**
  - *Unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*
- **Neuropathic Pain**
  - *Pain caused by a primary lesion or disease of the somatosensory nervous system*
- ***Chronic Pain***
  - *Pain persisting beyond the time of healing and frequently with no clearly identifiable cause*
- **Wind Up**
  - *progressive, frequency-dependent increase in the excitability of wide dynamic range nociceptive neurons to repetitive stimulation from primary afferent nociceptive C-fibers*
- **Central Sensitization**
  - *Increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold afferent input.*

# Definitions

- Hyperalgesia
  - *Increased pain from a stimulus that normally provokes pain*
- Allodynia
  - *Pain due to a stimulus that does not normally provoke pain*
- Hyperasthesia
  - *Increased sensitivity to stimulation, excluding the special senses*
- Dysasthesia
  - *An unpleasant abnormal sensation, whether spontaneous or evoked*
- Parasthesia
  - *An abnormal sensation, whether spontaneous or evoked*

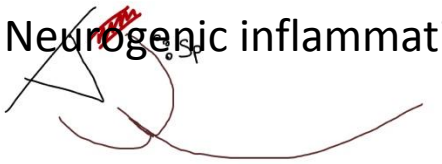
# Pathway

Lymphocytes, Mast cells and Platelets:
'Inflammatory soup'
With specific receptor subtypes

Intracellular:
K, H, ATP

Metabotropic and ion channel receptors

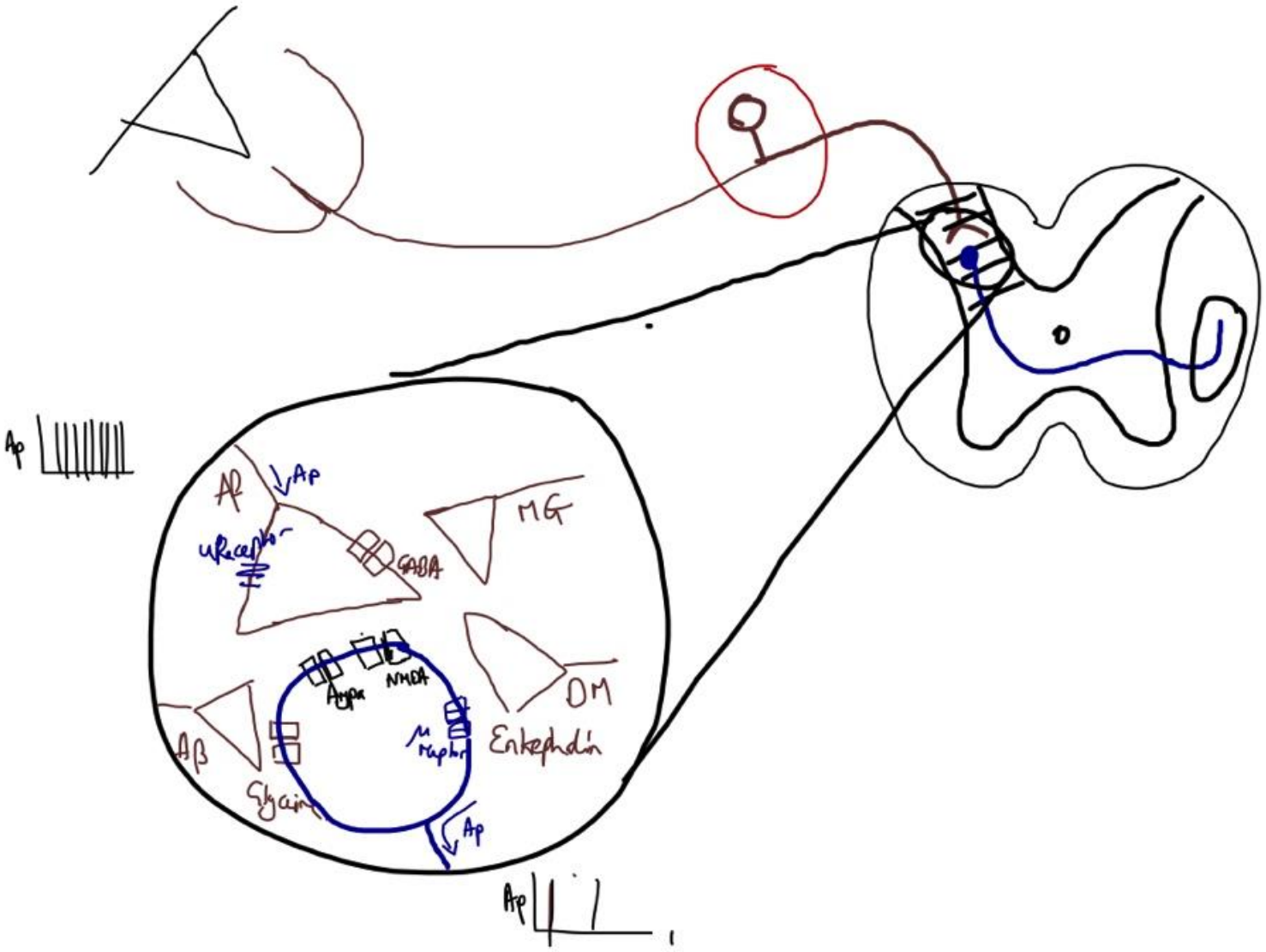
Neurogenic inflammation



Basement membrane depolarisation

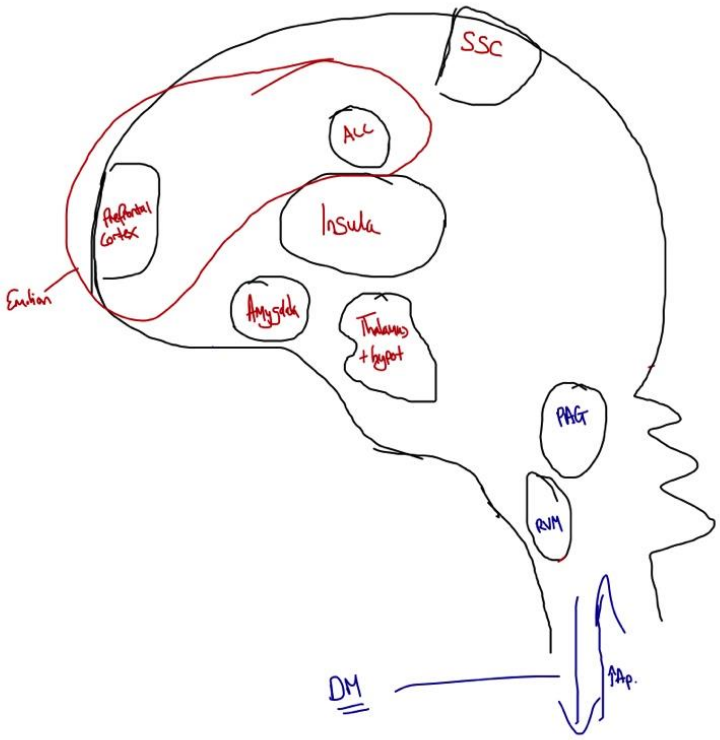
Metabotropic
Prostanoid- PGE2
Histamine
Serotonin
Bradykinin
Opiod
Tachykinin

Ionotropic
TRP- heat, H, capsaicin
ASIC-H
Purine-ATP
Serotin-5HT3
NMDA-Glutamate
AMPA-Glutamate

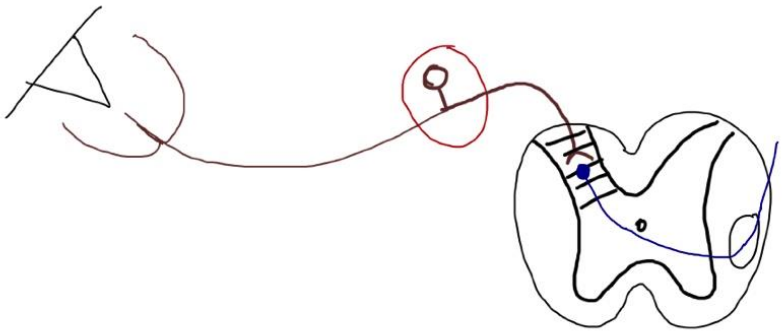

Ap
Ap
Aδ
Ap
MG
GABA
NMDA
OM
Aβ
Enkephalin
Ap
Ap

# Pain Pathway

- ***Insult***, sensitise and or stimulate nociceptor
- A delta, C fibre depolarisation,
- Action Potential
- DRG
- DH, Lamina, Substantia Gelatinosa
- Synapse and summate, Interneurons, descending modulating neurons, microglial
- Wind up, Sensitization,
- Decussate
- Anterior lateral Spinothalamic tract




Via NA, 5HT3



# Pain Pathway

- **Brainstem**, PAG, RVM

- **Mid Brain**
- Thalamus and hypothalamus , Insula,
- Amygdala (emotions, stress)
- Anterior cingulate cortex (affect, attention)

- **Cortex**, post central gyrus S1 S2

# Acute pain assessment

- History (SOCRATES) and examination,
- Uni-dimensional sensory intensity assessments
  - These are reliable, validated, sensitive and easy,
  - Verbal categorical rating scale
    - 4 point none, mild, moderate, severe
    - Cons: less reliable than vas, comprehension, language
  - Numerical rating scale
    - 0-10/100 0 being no pain 10/100 worst possible pain
    - Instant,
  - Visual Analogue Scale
    - Gold standard
    - 10cm line horizontal, no pain to worst pain imaginable without anchors
    - Cons, requires equipment and accurate measurement in mm, cognition

# Acute pain assessment

- At risk individuals
  - Neonates
    - COMFORT (distress in ventilated neonates)
    - CRIES
  - Children from 3 years
    - Faces pain scale
    - 5 Faces depicting increasing distress
  - Elderly
    - Abbey score – 6 domains from physiological changes to vocalisation and expressions

# Paracetamol

- Mechanism remains uncertain.
  - Centrally acting
  - Effects descending modulation via 5HT, cannabinoid, opioid, nitric oxide
  - Antipyretic action ?COX3
- Pharmacokinetics
  - Bioavailability of 60-90%
  - Highest absorption small bowel
  - IV therapeutic plasma concentration after 20 mins
  - Rectal absorption unpredictable.
  - Hepatic metabolism via CP450
  - NAPQI accumulates in OD

# Paracetamol

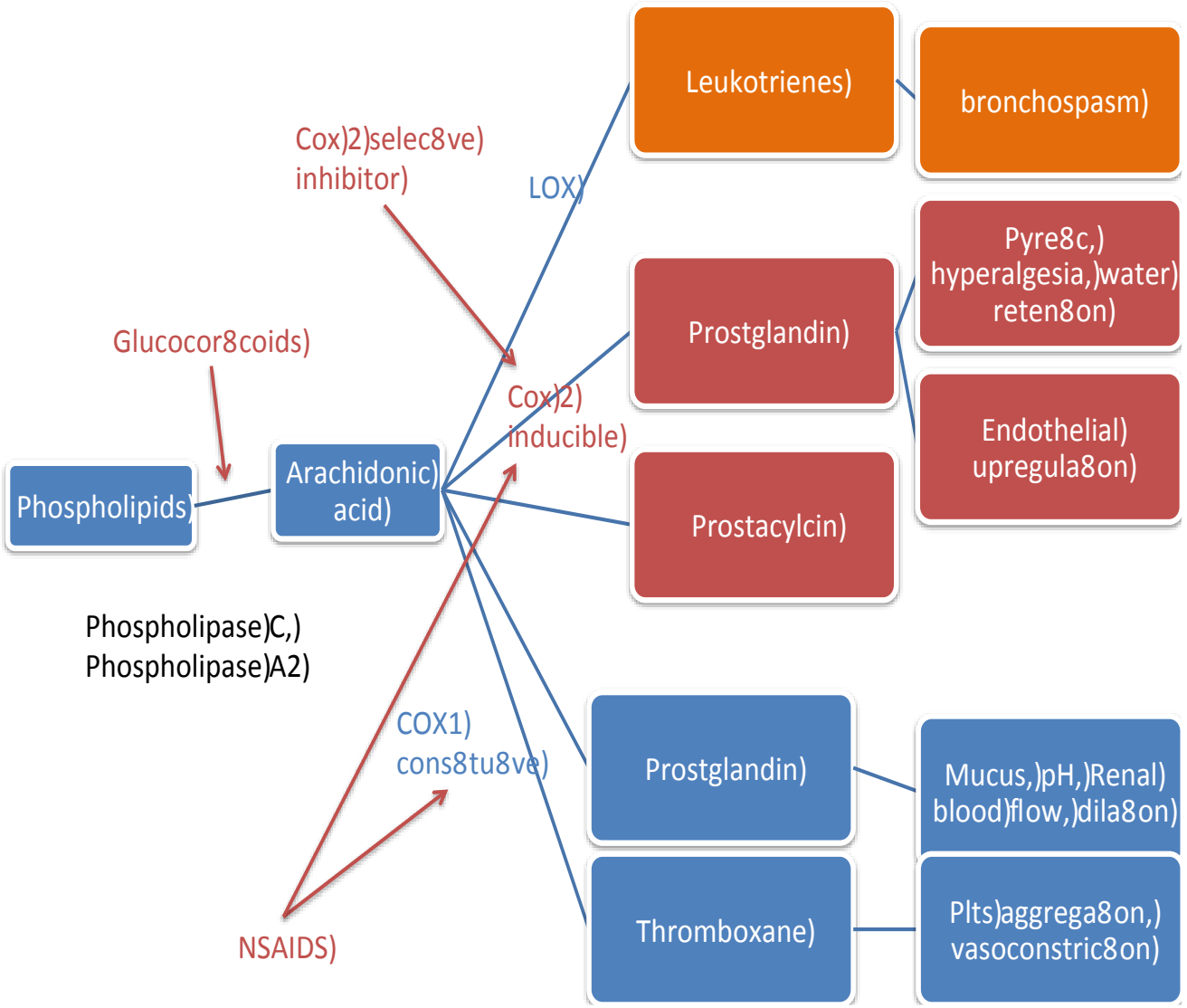
- Severe liver disease and renal disease 1g tds recommended
- NNT 3.7-1.87
- Reduces post operative morphine consumption but not as much as NSAIDS.
- Loading dose of 2g IV or oral is safe
- Some 5 HT3 inhibitors  are contraindicated

Table 1 MHRA guidelines for i.v. paracetamol dosing in children

| | Dose per administration | Max. daily dose |
|---|---|---|
| Term newborn infants, up to children , 10 kg | 7.5 mg $kg^{-1}$ | 30 mg $kg^{-1}$ |
| Weight 10–33 kg | 15 mg $kg^{-1}$ | 60 mg $kg^{-1}$ up to max. 2 g |
| Weight 33–50 kg | 15 mg $kg^{-1}$ | 60 mg $kg^{-1}$ (max. 3 g) |
| Weight . 50 kg | 1 g | 4 g |

# NSAIDS

- NS COXi peripheral and central nociceptive pathway
  - Reduce peripheral and central sensitisation
- Evidence based statements
  - nsNSAIDS and COX2 reduce post op opiate requirements
  - Increase post op bleeding 2.4% vs 0.4%(without)
  - Decreased PONV (with pca vs pca plus placebo)



# NSAIDS

- 1998
  - 100’000 hospitalisations in the USA due to GI NSAID complications with a mortality of 5000
- 2 – 12x increased risk of GI complications
- Dyspepsia in 60% of patients on NSAIDS
- Endoscopic ulceration in 30% of patients on NSAID for a week
- 4x more likely to develop a GI ulcer on a NSAID
- Coxibs decrease GI risk by ½ to a third

- Also diclofenac hepatotoxic

- S.E. profile is independent of route,
  - Rectal NSAIDS increase diarrhoea and increased rectal irritation, gastric erosions the same

# NSAIDS GI risk factors

- Patient
  - Concurrent Aspirin use
  - High dose NSAID
  - Elderly
  - Steroids
  - Anticoagulants
  - Previous ulcer or H.pylori

# Vigor Trial

- Rofecoxib vs Naproxen
  - 5x MI rate
    - Chance
    - Naproxen has aspirin like protective effect
    - Rofecoxib is slightly cardiotoxic
- Ratio of COX1: COX2 important, too highly cox2 increase CVS complications
  - including BP and CCF
  - Also aspirin and NSAID CNS complications

# Renal effects of NSAIDS

- PGE2 and PGI2 maintain renal perfusion by preferentially dilating renal arterioles in hypovolemia……
  - ACEi, furosemide, hypervolemia
- Direct interstitial fibrosis and pupillary necrosis

# Bone Growth

- 25% non-union if smoke and take NSAIDS
- And long term
  - Vertebral fracture 2.9X

# Opioids

- Mechanism of action
  - Opioid receptors GPCRi
    - Present throughout periphery/ peripheral and CNS
    - Most active in DH and PAG
      - Pre and postsynaptic nerve fibres
      - When stimulated cause hyperpolarisation via
      1. Open K channels
      2. Close calcium channels
      3. Inhibit cAMP → increased Protein Phosphorylation → activates protein kinases and leads to gene transcriptional changes

# PCA

- Evidence suggests
  - Efficacy
  - Safety
  - Patient satisfaction
  - Possible lower cost
- However it is not a one size fits all solution
- Equally efficacious to provide prn analgesia if system in place but within busy wards etc this is often not the case

# PCA

- PROBLEMS
  - Patients fear addiction
  - Even in pain they wont press the button more than 4x an hour
  - Compared to epidural more post operative pulmonary complications
  - Elderly and OSA and hypervolemia
- Prescription
  - 2mg resp depression high, 0.5mg pain relief poor
  - Background infusion increased side effects but no improvement in pain

# Opioid induced hyperalgesia

- opioid induced hyperalgesia where by rapidly escalated opiate doses precipitate a pro-nociceptive state as opposed to an analgesic effect
- Diffuse hyperalgesia and allodynia
- Probably via effects on NMDA and Sp
- Role for ketamine, clonidine
- Ondansetron?

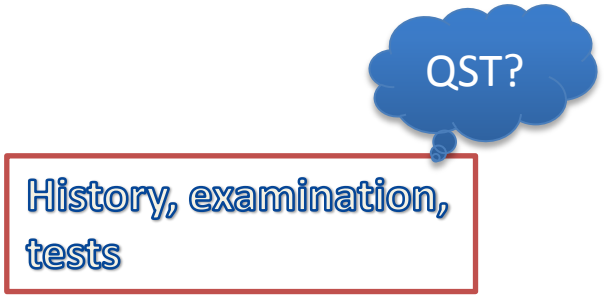
# Opioid Tolerant Patient

- Increased analgesic requirements
  - Tolerant
  - Up regulated nociceptive system
  - Down regulated endorphin system

- Continue chronic opiates as long as possible
- Use good multimodal analgesia and regional where possible
- PCA is a good option on top of normal opiates
- If unable to then equivalence calculation through oral morphine
- Incomplete cross tolerance
- Current evidence suggests ***no*** equivalence
- ***Treat new opiate initially as though they are new….***

# Chronic Pain Questions

- Assessment
  - Bio-psychosocial
  - Pain assessment
    - SOCRATES
    - Nociceptive vs Neuropathic vs Mixed
    - Multidimensional scales
      - Brief Pain inventory
      - McGill pain questionnaire
  - Psychosocial assessment
    - Social History (impact on life SF36)
    - Functional ability assessment (Roland Morris, Oswestry back pain)
    - Psychiatric history (risk assessment) (bidirectional effect)
    - GAD7, PHQ9,HAD



# IMPACT requirements

**Table 1** Content of a four-page minimal-requirement pain assessment tool for pain clinics[22]

| Domain | Instruments for measurement |
|---|---|
| Patient's characteristics | Categories from the Statistical Registry |
| Pain | Body chart and three NRS pain intensity at worst, least, and average last 24 h (from BPI) |
| Coping/catastrophizing | Two Qs from Coping Strategies Questionnaire |
| Health-related quality of life | Eight Qs from SF-8<br>Two Qs from EORTC QLQ-C30 |
| Physical functions | 10 Qs from SF-36 |
| Emotional functions | Five Qs from SF-36 (MHI-5) |
| Three more pain-related Qs | Duration of pain condition<br>Economic impact of pain condition<br>Ongoing compensation process? |
| Patient rating of improvement and satisfaction with treatment | Three Qs in follow-up questionnaire |

# Chronic Pain Questions

- Management
  - Multidisciplinary
    - Education
    - Pharmacology
      - Topical
      - Systemic
      - Interventional
    - Physiotherapy, Psychology
      - Group: Pain Management Program
      - One to one
      - CBT, ACT,CT

# Neuropathic Pain

- Gabapentinoids
  - Pregabalin (NICE first line)
  - Antiepileptics
  - GABA synthetic analogue with no GABA action
  - Site of action is cerebral and spinal pre and postsynaptic Voltage gated N type Calcium Channels on alpha 2 delta subunit
  - Some evidence to support perioperative use
    - Reduce pca requirements, ?reduced CPSP

# Neuropathic pain

- Gabapentanoids
  - PO only
  - Pregabalin more potent, faster onset of action, better oral bioavailabilty, bd rather than tds
  - better s.e. profile
    - Sedation Dizziness, blurred vision, ataxia, increased suicide risk
  - Renal excretion decrease dose if GFR <60
  - Safe in O.D.

# Antineuropathics

- TCA
  - Amitriptyline
  - Active metabolite Nortriptyline
  - Action is descending modulation via NA, 5HT and Ach
  - Side-effects related to Ach activity
  - Dry mouth, blurred vision, urinary retention, prolonged QT
  - Increased morbidity in elderly
  - Dangerous in O.D

# Antineuropathics

- Duloxetine (“dual”)
  - Antidepressant and generalised anxiety disorder
  - Serotinin NA reuptake inhibitor
  - First line for diabetic peripheral neuropathy

# Complex Regional Pain Syndrome

- syndrome associated with severe pain in a distal limb with associated peripheral sensory, vaso- motor, sudomotor/oedema and motor/trophic changes

- Budapest Criteria
  - Pain beyond expectation
  - No other diagnosis
  - Three symptoms from 4 categories including asymmetry of temperature, sweating, trophic changes, tremor
  - Two signs from hyperalgesia, allodynia, motor dysfunction, decreased ROM, colour, oedema

# CRPS

- Consequence of neurogenic inflammation mediated by cytokines leading to functional and structural changes in central and peripheral nervous system.
- Incidence varies but ?2% post fractured wrist
- Course majority pain free at 2 yrs
- Risk factors
  - women, post fractures, upper limbs

# CRPS management

- Prevention
  - 500mg vitamin C daily for 50 days
- Management
  - Diagnosis, education,
  - Physiotherapy, OT, Rehab
  - Pharmacology- antineuropathics, pamidronate,
  - Intervention Spinal cord stimulator
- Avoid surgery in that limb for 1 yrs post resolution of symptoms avoid amputation

# Phantom Limb Pain

- Chronic post amputation pain
  - Phantom limb pain (noxious sensory phenomena in missing limb)
  - Stump pain (neuropathic or inflammatory)
  - Mechanical pain
- Very high incidence up to 85%
- Immediate or delayed
- Phantom limb RF- pain pre amputation, post op stump pain, chemotherapy, passive coping strategies, catastrophising

# Prevention of PLP

- Pre intra and post op epidural NNT 5.8
- Ketamine probably
- ? LA nerve infusions
- Management (biopsychosocial as above) plus
  - Calcitonin infusion
  - Ketamine by infusion>24hrs
  - Opiates NNT 5.8
  - Contralateral trigger points
  - Lignocaine infusion
  - SCS

# Chronic Post Surgical Pain

- pain outlasting healing usually longer than 2 (-3) months following surgery different to pre-surgery
- Incidence is surgery specific
  - Severe pain usually 5-10%
  - Pain 30-80%
- High risk surgery- thoracic, Inguinal hernia, breast, amputation, lap choly, post op infection, wound break down
- High risk patients- female?, young, pain at site of surgery, severe post op pain, Catastrophising Anxiety, depression,
- Rx, Chx,

# Review

- Definitions
- Pain Pathway
- Acute pain assessment
- Notes on Paracetamol
- NSAIDS what you need to know
- Opiates how they work and more
- Answering a chronic pain question
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# Suggested reading



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# References


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