**Rob’s Top 5 Final Exam notes:**

**Definitions:**

**Substance use disorder:** A problematic pattern of substance use leading to clinically significant impairment or distress as manifested by at least 2 of 11 features occurring within a 12-month period

- CRPS: Control impaired, Risky use, Pharmacological criteria, Social impairment,

**Intoxication:** Reversible substance-specific syndrome due to recent ingestion of a substance

**Nociceptive vs Neuropathic pain**

- Neuropathic pain does not have transduction of pain signal

**Hyperpathia** – Increased reaction to a repetitive stimulus

**Hyperalgesia** – Increased sensitivity to a stimulus that usually causes pain

**Allodynia** – Pain due to a stimulus that does not usually cause pain

**Placebo (“Placere” = to please)**

1. The provision of a medication or procedure to a person for psychological benefit rather than physiological effect

**Nocebo** **(Latin – I will harm)**

1. Negative expectations of a patient about a procedure or medication create more negative effect than otherwise expected

**Tolerance:** Tolerance is a state of adaptation in which continuing exposure is associated with diminution of one or more effects of the drug over time. Drug tolerance is manifest as a need for increasing dose to achieve the same effect

**Dependence:** Physical dependence is a state of physiological adaptation that is manifest by a drug class-specific withdrawal syndrome induced by abrupt cessation, rapid dose reduction, and/or administration of an antagonist

**Symptom cluster –** A constellation of symptoms commonly seen together not necessarily linked

**Syndrome** – A collection of symptoms and signs that occur together and are connected to form a characteristic pattern

**Disease** – Deviation from normal structure or function of body part, organ, or system with a characteristic set of symptoms and signs

**Illness** – Fairly unclear term for a person’s perception of feeling unwell

**Complementary Medicine** - Therapies that are not considered an integral part of conventional medicine

**Alternative Medicine** - Used as an alternative to conventional medicine

**Intro sentences and details for specific conditions**

*Template:*

*Disease descriptions. Epidemiology. Subtypes / pain causing mechanisms.*

**PTSD:**

* Chronic pain co-occurs in 50%
* Shared vulnerability model and mutual maintenance hypothesis
  + Pain triggers memory, memory hyperarousal triggers pain

**EBM Treatments: (Charney et al, 2018)**

Prolonged exposure, EMDR, CBT = STRONG evidence of benefit

Sertraline, Paroxetine, Fluoxetine – Moderate evidence of benefit

Other drugs and therapies have limited or no evidence of benefit.

DSM 5 Diagnostic criteria: FIGHT - >1 month of symptoms

**Flight**. Avoidant symptoms, including efforts to avoid distressing memories, thoughts, or feelings about the traumatic event, as well as avoidance of external reminders.

**Intrusive symptoms,** such as distressing dreams, intrusive memories, and physiological distress when exposed to cues.

**Gloomy cognitions.** Negative cognitions and mood associated with the traumatic event.

**Hypervigilance.** Alterations in arousal, such as irritability, angry outbursts, reckless behavior, and exaggerated startle response.

**Trauma**. Exposure to actual or threatened death, serious injury, or sexual violence.

**Fibromyalgia**

Fibromyalgia (FM) is the most common cause of chronic widespread musculoskeletal pain, often accompanied by fatigue, cognitive disturbance, psychiatric symptoms, and multiple somatic symptoms. The etiology of the syndrome is unknown, and the pathophysiology is uncertain. Despite symptoms of soft tissue pain affecting the muscles, ligaments, and tendons, there is no evidence of inflammation in these tissues

**Fibromyalgia Risk factors:**

1. Mental health disorders e.g. depression, anxiety, OCD, PTSD
2. Obesity
3. Poor sleep
4. Physical inactivity
5. Catastrophising
6. Fear avoidance
7. Possible environmental triggers e.g. infections, trauma

**Fibromyalgia BETTER prognosis:** (these tend to do better with therapy)

1. Younger
2. More educated
3. Higher baseline depression scores
4. Lower tender point counts
5. Absent abuse history

**Fibromyalgia treatment principles: EULAR 2016** *(all Level 1A evidence. Strongest for physical therapy)*

* Nonpharmacological first line – Education, physical therapy, hydrotherapy, acupuncture).
* Psychological – mainly CBT and possibly psycho-pharmacological therapies
* Severe pain/pharmacological – Duloxetine, pregabalin, Tramadol, Amitriptyline

ACR 2016 Diagnostic Criteria

1. Widespread Pain index (WIT) and Symptom Severity Score (SSS)
   1. WPI > 7 and SSS > 5 OR WPI 4-6 and SSS > 9
2. Generalised pain: Pain in 4/5 regions (Upper, Lower, Right, Left, Axial)
3. Symptoms present for more than 3 months

**SCI:**

Chronic pain occurs in 70-80% of SCI patients with neuropathic pain in 50%. Average age is 33yo. Level of the injury in defined as the highest level there is retained sensory and motor function.

Neuropathic pain is listed as at level as classified by ASIA (dermatome level and within 3 below) and below level (below 3 levels below) pain is typically a central pain syndrome.

Pain is graded from A (worst) to E (best) – based upon completion of sensory and motor loss of function.

Pain is classified either as nociceptive, neuropathic, or other (e.g. Fibromyalgia).

Pathophysiology:

* Neuroplasticity
* Sprouting of new dendritic fibres
* Glial upregulation, activation and facilitation
* At-level – hyperexcitable neurones/irritated focus
* Below-level
  + Disinhibited polysynaptic pathways
  + Sensitised spinothalamic tract
  + Cortical remodelling with atrophy of motor and sensory cortex

Non-pharmacological therapeutic evidence: (2014 Cochrane suggested minimal evidence)

* Physical exercise - Meta-analysis shows mild-moderate benefit for MSK pain and nociceptive pain
* Hydrotherapy – Some evidence for nociceptive pain
* Transcranial direct-current stimulation – possible benefit for neuropathic
* Acupuncture – Benefit in some studies
* Lignocaine infusion can be trialled but minimal evidence available
* CBT and relaxation – No clear studies
* TENS – Unclear evidence

Pharmacological Therapeutic evidence:

* Pregabalin 150 mg daily up to 600 mg - NNT = 4 (30%) and gabapentin for neuropathic
* Duloxetine – one RCT showed benefit
* Amitriptyline mixed results and significant side effects
* Botox may help but limited evidence
* Baclofen may be helpful where there is evidence of spasticity in one trial
* Topical therapies and cannabinoids have insufficient evidence

**Table

Description automatically generated**

**Classification of SCI pain – 3 tier system – International SCI pain (ISCIP)**

* Nociceptive (MSK and Visceral)
* Neuropathic
  + At-level
  + Below-level
  + Above level/Other (E.g. carpal tunnel, CRPS)
* Other pain syndromes (e.g. Fibromyalgia)

**Assessment steps for SCI**

* Remember to think about:
  + Spinal stabilisation and operations
  + Assess for motor OVERactivity
  + Comfort and fit of orthotic devices – and are they contributing to pain
  + Psychological very important
  + Imaging if new pains
  + Visceral pain can be difficult but remember
  + Functional options and assistance
  + Educational inputs

**Peripheral traumatic neuropathy**

1. More common in younger males

* Many will recover function – up to a 33-50% ongoing symptoms
* Neuroma-in-continuity – Partially intact

**Pathophysiology of peripheral nerve trauma**

1. Peripheral
   * Lower threshold
   * Spontaneous firing (mechanical and chemical activity changes)
2. Central
   * Central changes with increased excitability
   * Reorganisation of somatotopic map

**Surgical options for neuroma**

1. Neurolysis
2. Nerve wrapping in fascia
3. Neuroma resection and reconstruction
4. Neuroma resection and relocation

**Phantom limb pain**

Noxious sensory phenomenon following the amputation of a body part. Incidence is between 25 and 85%. Most report pain on day one however 25% can develop over 1 week. Prevalence decreases with time.

**Pathophysiology of phantom limb pain**

* Peripheral
  + Nerve resprouting
  + Neuroma
  + Sodium channels
  + Lower threshold C fibres
* Spinal
  + Increased Glutamate and NMDA system
  + Loss in inhibitory interneuron activity
* Central
  + Cortical reorganisation
  + Extension of the neuronal receptive field

**Risk factors phantom limb pain**

* Demographics
  + Genetics
  + Female gender
  + Younger age
* Psychological
  + Anxiety
  + Depression
  + Catastrophisation
* Social
  + Poor social support
* Pain disease states
  + Fibromyalgia, migraine, IBS, irritable bladder, raynauds
* Presurgical pain
  + Increases the risk
* Intraoperative pain
  + Surgical technique
* Postoperative pain

**Prevention of post-amputation pain (BJA 2017)**

* Preoperatively
  + Gabapentin
* Surgery
  + Neuraxial block
  + Peri-neural catheter (Sciatic)
  + Low dose ketamine infusion/bolus
* Postoperatively
  + Ketamine
  + Tapentadol
  + Calcitonin
  + Memantine
  + Gabapentinoids

**Treatment of phantom limb pain**

* Physical
  + Desensitisation
  + Prosthesis use
  + Stump stocking
  + TENS
  + Mirror therapy
* Psychological
  + Stress-relaxation
  + Hypnosis
  + ECT
* Pharmacological
  + Antidepressants
  + Anticonvulsants
  + Opioids
  + NMDA receptor antagonists
* Other
  + Salmon calcitonin
  + Clondine
  + Botox
  + SCS maybe

**Post mastectomy pain syndrome**

1. Anterior chest wall pain, axilla, and medial upper arm >3 mths after surgery
2. Neuropathic pain features – burning, tingling, shooting, stinging
3. Intercostal nerves T3 to T6
4. Lateral cutaneous branch of the second intercostal nerve crosses the axilla to innervate the upper medial arm and anterolateral chest wall (Intercostobrachial nerve - ICBN)
5. ICBN most injured in axillary dissection

**Post mastectomy pain syndrome key management**

1. Gabapentin or carbamazepine in mainly neuropathic
2. Duloxetine if hot flashes
3. Neuroma identification and excision
4. Scar release with autologous fat grafting

**Post-stroke pain**

Leading cause of central neuropathic pain. Thoughts 10-50% will develop pain. Finnerup states 11% of all strokes. Move common in ischaemic and thalamic/brainstem strokes.

Five key pain complications following stroke include: Central post stroke pain, Nociceptive, Peripheral neuropathic, CRPS, and headache.

**Trigeminal Neuralgia**

Painful condition involving the trigeminal nerve. Classified into idiopathic, classic and secondary TN. Classic TN is associated with neurovascular compression within the trigeminal root entry zone. Secondary TN is caused by underlying disease such as tumour or multiple sclerosis.

ICHD-3 Diagnostic Criteria for TN

Recurrent paroxysms of unilateral facial pain in the distribution(s) of one or more divisions of the trigeminal nerve, with no radiation beyond1, and fulfilling criteria B and C

Pain has all of the following characteristics: (TN makes you LEaPS!)

* Lasting from a fraction of a second to 2 minutes
* Electric shock-like, shooting, stabbing or sharp in quality
* Precipitated by innocuous stimuli within the affected trigeminal distribution
* Severe intensity
* *Not better accounted for by another ICHD-3 diagnosis.*

**Parkinson Disease**

Progressive neurodegenerative disorder affecting dopamine producing neurones within the brain. Pain occurs in 30-85%. Four main types: Musculoskeletal, Dystonic (e.g. low dopamine), Neuropathic (due to disc disease and postural deformities), and central pain (usually abdominal and hard to describe).

**Multiple sclerosis**

Chronic inflammatory demyelinating disease of the CNS leading to motor, sensory and/or cognitive impairment. Its hallmark is demyelinated lesions in the CNS. Pain occurs in 25-90% of patients and causes comorbid disability and depression. Pain is typically: Primary (dysaesthetic, parosyxmal, TN, Migraine) or secondary (spasticity, contractures).

**MS pain features:**

1. Trigeminal neuralgia – commonly bilateral
2. Head pain (atypical facial pain, chronic TTH, migraine, pelvic pain)
3. Lhermitte’s sign (electric shocks down limbs or spine with neck flexion)
4. Paroxysmal motor symptoms
5. Seizures
6. Bladder difficulties
7. Muscle spasticity

**Syringomyelia**

Disorder of abnormal CSF circulation. Syrinx is a fluid filled cavity that lies within the spinal cord parenchyma or the central canal. Primary or Secondary. Pain is due to: Post-inflammatory, post-traumatic, chiari malformations, spinal cord tumours.

**Diabetic Neuropathy**

Most recognised cause of distal symmetric polyneuropathy but is not always painful. Prevalence in 25-50% of diabetics. Neuropathy from loss of myelination related to inflammatory processes generated by elevated BSL. Can cause direct nerve injury and changes to sodium channel expression.

**Pathophysiology of diabetic neuropathy:**

* Persistent hyperglycaemia (mitochondrial free radicals  Polyols  Wallerian degeneration)
* Autoimmune factors possible with antineural antibodies
* Microvascular mechanisms with endo and epineural changes
* Inflammatory activation with glia and cytokines
* Hyperglycaemia direct hyperalgesic effect

**Types of diabetic neuropathy:**

* Chronic sensorimotor distal symmetrical polyneuropathy (DSPN) – most common
* Small fibre neuropathy – (Burning in feet – usually leads to DSPN)
* Acute painful diabetic peripheral neuropathy – Severe sensory symptoms but little found on exam. Can resolve within a year)
* Focal and multifocal painflu neuropathies – Not well understood
* Cranial nerve palsy (sudden unilateral 3,4,5, 6 or 7. Often retroorbital pain. Recover in 3 months)
* Proximal diabetic neuropathy – Truncal and hip/thigh weakness. Stabilises and improves
* Truncal radiculopathy – Thoracic roots – acute pain over days to weeks with severe dysaesthesiaes in dermatomal pattern. Often full recovery

**Treatment of diabetic neuropathy**

1. Glucose control
2. Other risk factors (e.g. BP, smoking weight)
3. Neuropathic pain algorithm
   1. TCAs, SNRI, Gabapentinoids
   2. Lignocaine patch, tramadol
   3. Strong opioids
   4. Spinal cord stimulation can be considered
4. Psychological - CBT
5. Physical – exercise

**HIV**

Retrovirus which causes progressive failure of the immune system in humans. 50% of those infected will have neuropathy related pain. Pain is often due to antiretroviral therapy and its effects on inhibiting mitochondrial DNA polymerisation with errors in energy management. Pain presents as: Distal sensory neuropathy, Antiretroviral related, acute/chronic inflammatory demyelinating polyneuropathy, mononeuritis monoplex, infectious neuropathy e.g. HSV.

**Post herpetic neuralgia**

Most common long-term complication of VZV reactivation. Causes lancinating/burning pain in unilateral distribution lasting three or more months. Most commonly occurs In trigeminal nerve, geniculate ganglion, or ophthalmic affecting nerve 3,4, and 6.

**Guillian Barre Syndrome**

Inflammatory polyneuropathy with rapidly progressive, widespread, and severe weakness of limbs and cranial musculature with areflexia. Pain occurs in >75% of patients.

**Alcohol related neuropathy**

Alcoholic neuropathy is a primary axonal neuropathy with wallerian degeneration of the axons and seocondary demyelination of sensory and small motor fibres. Acetaldehyde has direct toxic effects on the nerve and pathophysiology is a combination of oxidative stress, microglia, and metabolic glutamate receptor errors. Thiamine affects larger fibres whereas alcohol specifically affects smaller fibres.

**Function GI Disorders**

Common disorders characterised by persistent and recurrent GI symptoms. These occur through abnormal functioning of the GI tract and gut-brain-microbiota relationship.

**CIPN**

Dose limiting side effect of chemotherapy causing primarily a sensory neuropathy and occasionally motor and neuropathic changes. 30-40% of patients treated with neurotoxic chemotherapy will develop CIPN.

**Cluster Headache**

Attacks of severe, unilateral pain which is orbital, supraorbital, temporal or any combination of these sites lasting 15-180 mins and occurring once every other day to eight times a day. Pain is associated with ipsiliateral conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis, or eyelid oedema with restlessnes and agitation. Men more common than females and age of onset 20-40 yo. Often clusters of attacks that can be separated by years.

**Chronic Post-Surgical Pain**

Chronic post-surgical pain (CPSP) is classified by the International Classification of Disease 11, as persisting pain for at least three months after surgery or tissue trauma, with the exclusion of other or pre-existing causes (such as infection and malignancy)

**Risk factors for chronic post-surgical pain:**

* **Preoperative**
  + Pain moderate to severe > 1 month
  + Genetic predispositions (e.g. COMT)
  + Female gender
  + Age (older less pain with hernia repair)
  + Compensation system
  + Reduced diffuse noxious inhibitory control
* **Operative**
  + Surgical approach
  + Surgical technique
  + Re-operation
  + Length of surgery > 3 hours
* **Postoperative**
  + Pain acute, moderate to severe postoperative pain
  + Acute neuropathic pain
  + Radiotherapy
  + Chemotherapy
  + Psychological factors such as anxiety, depression, catastrophising
  + Pain – moderate to severe on discharge

**Preventing CPSP**

* Pre-surgical pain coping skills training, exercise and education have little effect on long term outcomes (Cohen et al., 2021)
* Reducing BMI
* Managing preoperative pain
* Optimising comorbidities

**CRPS**

Complex regional pain syndrome (CRPS) primarily presents as a pain condition that usually affects a single limb with a composite of characteristic symptoms and signs. The central feature is severe often debilitating pain. This is accompanied by a collection of sensory, motor, autonomic, skin, and/or bone abnormalities. It presents as two types – Type 1 with no clearly defined pathological lesion and Type 2 – where a clear pathological lesion can be identified. It affects females more than males and the upper limb more than the lower limb.

Diagnostic Budapest Criteria

A clinical diagnosis can be made when four criteria are met. The first is continuing pain that is disproportionate to any inciting event.

At least one symptom in at least three of the following categories:

* Sensory: Hyperalgesia, allodynia
* Vasomotor: Temperature asymmetry, skin color changes, skin color asymmetry
* Sudomotor/edema: Edema, sweating changes, sweating asymmetry
* Motor/trophic: Decreased range of motion, motor dysfunction (eg, weakness, tremor, dystonia), trophic changes (eg, hair, nail, skin)

Must observe at least one sign in at least two of the following categories:

* Sensory: Evidence of hyperalgesia (to pinprick), allodynia (to light touch, temperature sensation, deep somatic pressure, joint movement)
* Vasomotor: Evidence of temperature asymmetry (> 1° C), skin color changes or asymmetry
* Sudomotor/edema: Evidence of edema, sweating changes, or sweating asymmetry
* Motor/trophic: Evidence of decreased range of motion, motor dysfunction (eg, weakness, tremor, dystonia), trophic changes (eg, hair, nail, skin)

There must be no other diagnosis that better explains the signs and symptoms

|  |  |
| --- | --- |
| CRPS  Cochrane review 2020 | ***USUAL NEUROPATHIC PAIN 101 evidence +***  *Cochrane 2020 – Review of evidence*  Low quality evidence that **bisphosphonates**, **calcitonin**, and IV **ketamine** may be better than placebo  Physiotherapy and OT - have greater evidence of efficacy <12 months  GMI and mirror therapy - may provide benefit but quality and quantity of evidence is low.  Sympathetic block - Low quality evidence of LACK of benefit  SCS – Moderate evidence of benefit over conventional therapy for pain and function. DRG may be further efficacious. |

**Brachial plexus injury**

**Post herpetic neuralgia**

**Pathophysiology of herpetic neuralgia**

* Degeneration of primary afferent neuronal cell bodies and axons
* Atrophy of the spinal cord dorsal horn
* Scarring of dorsal root ganglion
* Loss of epidermal innervation
* Sensitisation and deafferentation
* **Three subtypes**
  1. Irritable nociceptors (no sensory loss + allodynia and hyperalgesia)
  2. Deafferentation with allodynia (sensory loss and dynamic mechanical allodynia (brush) often present
  3. Deafferentation without allodynia (sensory loss but no allodynia due to complete loss of primary afferent neuron connection

**Prevention of AHN after HZ**

* Reduce pain and cease replication (antiviral)
* >50 yo, immunosuppressed, ophthalmic, severe rash
  1. Give them antivirals and TCA early
* Acute pain improves with steroid but no long term benefit
* Gabapentinoids, lignoication patches can be considered second line
* Neural blockades – but few studies

**Treatment of chronic PHN**

* Antineuropathics – TCA, Gabapentinoids, SNRI, 5% lignocaine patches
* Topical capsaicin (NNT 3.2)
* TENS may help
* SCS – maybe

**Somatic symptom disorder**

**Substance use disorder**

Substance use disorder (SUD) is the persistent use of drugs despite substantial harm and adverse consequences. Substance use disorders are characterized by an array of mental/emotional, physical, and behavioural problems.

Mnemonic is: ‘WITHDRAW THE substance’.

**W**ork, school or home obligation failures

**I**nterpersonal or social consequences

**T**ime spent too much for obtaining, using or recovering from effects of substance

**H**azardous use

**D**esire for the drug

**R**einstatement

**A**ctivities (important or recreational) given up

**W**ithdrawal

**T**olerance

**H**armful use

**E**xceed the intended amount or time

**Anxiety**

**Depression**

**Irritable bowel syndrome**

**Persistent pelvic pain**

Non-malignant pain within the pelvis of men or women for more than 6 months. Prevalence is high – 15-25%.

**Temporomandibular disorders**

Headache most prominent in the temporal regions, preauricular areas of the face and/or masseter muscle. Often unilateral but can be bilateral. It is the second most common cause of facial pain.

**Migraine**

**Cluster headache**

**Burning Mouth Syndrome**

Chronic condition of pain in the mouth, tongue, and palate. More common in older post-menopausal women. Uncertain cause however it has been associated with xerostomia.

**Burning mouth syndrome**

1. Daily burning of tongue lips or mouth
2. Women > Men 7:1
3. Age > 50 yo usually
4. Resolves in 2-3 years commonly

**TACs**

**Chronic widespread pain**

Wide spectrum of disease with pain affecting multiple sites. Affects 2-5 % of the population and is more common in women. Often associated with other conditions such as chronic fatigue and functional GI disorders. Can have significant disability.

**Whiplash**

**Risk factors for acute to chronic WAD**

1. Biomedical
   * Severe pain
   * Acute hospital admission
   * Headache
   * History of chronic pain
   * Female
   * Older
   * No seatbelt
   * High Neck Disability Index
2. Psychological
   * Depression
   * Anxiety
   * Mood disorder
   * High catastrophisation
3. Social
   * Low educational literacy
   * Litigation
   * Part time employment

**Mechanisms in biomedical dimension of pain**

**Reasons for Pain definition change 2019**

1. Cartesian (Mind-body interactions ignored)
2. Non-verbal (Ignores non-verbal and non-human)
3. Unpleasant (trivialises suffering)
4. More than symptoms (pain disease in its own right)
5. Accompanying notes (Repeated words in the statement)

**WHO Actions to address the Determinants of health**

1. Execute health sector’s role in governance for social determinants
   1. Advocating
   2. Monitoring
   3. Bringing together
   4. Developing capacity
2. Reorient health care services to reduce inequities
3. Institutionalise equity into health systems governance

**WHO Social determinants of health**

* Governance to address health inequities
* Promoting participation
* Role of the health sector and public health programs to reduce inequities
* Global action on social determinants with stakeholders
* Monitoring progress

**ICD-11**

1. ICD 10 pain was not represented systematically
2. Negatively impacted billing and therefore insurers and policymakers to identify the human and financial impact of chronic pain
3. Systematic classification of clinical conditions with chronic pain
4. Divides into subgroups defined by etiology or affected organ system
5. Allows subgroup where pain is not completely understood
6. Gathers pain codes into one place
7. Chronic primary pain should be acknowledged in its own right
8. May minimise further investigations/treatments in primary pain conditions

**ICD-11 Described by FPM**

1. Chronic pain is admitted as a taxonomic entity
2. Pain is a problem in its own right – in addition to underlying process or disease contributing

**Sensory fibres**

* Abeta – Touch and Vibration
* Adelta – Pinprick, sharp pain, Cold.
* C – Warmth

**Indication for nerve conduction studies**

* Only large, myelinated fibres can be tested
* Determine level of peripheral nervous system pathology is located
* Distinguish axon loss (loss of amplitude) from demyelinating conditions (slowed conduction)
* Electromyography may help with weakness (looking at myopathic vs neuropathic cause)
* Neurophysiology is NCS and EMG combined

**Mechanisms of placebo effect**

* Psychological
  + Expectations of response
  + Conditioning
  + Memory
  + Reward
  + Anxiety reduction
* Neurobiological
  + Role of prefrontal executive control and functional connectivity
  + Activation of endogenous opioids
  + Changes to regional brain activity with anxiety and relaxation
  + Autonomic responses

**Neurobiology**

* Primary afferent nerves innervate into
  + Rexedes lamina 1
    - Marginal zone – C-fibres and a few Adelta),
  + 2 (substantia gelatinosa – C-fibres and Adelta - & lots of interneurons)
  + 5 nucleus propius) (3,4,5, 6 has lost of Abeta fibres)
* Some travel in lasseurs tract called the intersegmental system
* Neurons in lamina 5 also receive non-noxious input. It is also where visceral inputs arrive. This the site for convergence theory for referred pain
* Anterior spinothalamic tract crude touch
* Lateral spinothalamic tract is pain and temperature
* These tracts go to the thalamus and synapse with third order neurons
* Projections go to primary and secondary somatosensory cortices
  + Primary somatosensory cortex – postcentral gyrus (parietal lobe)
  + Limbic system (emotion)
  + Anterior cingulate gyrus (ethics and decisions)
  + Insular cortex (Homeostatic emotions like hunger and pain)
* **Remember** – Dorsal columns travel up the SAME side until decussation in the medulla and these carry tactile sensation and limb proprioception – which can be sensitised

**Pathways:**

* Spinothalamic – Sensory-discriminative aspects of pain
* Spinoreticular and spinomesencephalic – meduall and midbrain for nociceptive information affecting arousal, homeostatic and autonomic responses – Affect/mood
  + Anterior cingulate cortex, insular, prefrontal cortex  PAG and Rostroventromedial medulla

**Modulation**

* **Segmental inhibition – *Gate theory (alpha beta fibres can close the gate)***
* **Endogenous opioids**
* **Descending inhibitory system**
  + Periacqueductal grey (around the acqueduct)
  + Locus Coeruleus (literally ‘blue spot’ – synthesis of noradrenaline!)
  + Nucleus raphe magnus (Releases serotonin. Main nucleus for descending inhibition. Gets message from PAG)

**Receptors at post-synaptic junction**

1. NMDA (allows glutamate in when activated leading to sensitisation)
2. AMPA
3. GABA
4. NK1
5. Opioid receptors
6. Alpha 2 adrenergic receptors

**Types of second order neurons**

1. Nociceptive specific
2. Wide dynamic range
3. Short projection neurons
4. Local interneurons

**Problems with Gate theory:**

1. Focus on cord and not on brain
2. Cannot explain phantom limb pain
3. No involvement of inflammation or immune system

**Features of sensitisation**

1. Increased response to less stimuli – Hyperalgesia
2. Response to stimuli not usually triggering pain – allodynia
3. Extension of receptive field (other areas of body triggering pain)
4. Spontaneous pain

**Peripheral sensitisation:**

1. Local inflammatory processes  upregulation of channels  increased excitability of the neuron and triggered firing by non-noxious stimuli
2. Collateral sprouting
3. Sympthetic-sensory coupling
4. Immune cells and chemical mediators worsen the process
5. Afferents may also begin to spontaneously fire
6. DRG cell bodies may increase receptor expression also triggering ectopic firing

**Central sensitisation**

1. Increased excitatory neurotransmitters e.g. substance P, glutamate, CGRP
2. Reduced inhibitory neurotransmitters and GABA sensing receptors e.g. GABA
3. Repetitive firing causes a sustained depoloarisation and susceptibility to repeated firing
4. Non-noxious stimuli can provide inputs arriving which can now trigger secondary hyperpathia
   1. By sensory afferents neurons collateralising and sending projections rostrally and caudally
   2. NMDA Mg plug is removed by repeated firing and glutamate can then activate the receptor. This causes influx of Ca, and lowers threshold allowing increased firing in these new/extended connections and areas
5. Decreased descending modulation (serotonin and noradrenaline)
6. Glial modulation
7. Neuroplasticity and pain matrix changes

**Referred pain:**

1. Visceral and somatic inputs converge on the same Wide dynamic range neurons called viscerosomatic convergence

**Immune cell involvement:**

1. Damaged neurons release ATP/heat-shock proteins that activate glia
2. Prostaglandins and NO can activate
3. They interconnect with each other when activated and reduce BBB
4. They can activate NMDA receptors through release of D-Serine
5. Opioids can activate,
6. Toll like receptor 4 on glia contributes to developing and maintaining chronic pain and is stimulated by local damaged neurons, M3G and methadone

**Paediatric pain neurobiology**

* **Nociceptors**
  1. Reduced ion channels on peripheral nociceptors
  2. May lead to reduced transduction
* **Neurons**
  1. Slower conduction
  2. Reduced frequency of firing due to incomplete myelination
* **Sensitisation**
  1. Faster resolution of increased sensitivity to noxious stimuli but not thermal
  2. NGF level high in immature possibly  more hyperalgesia
  3. Reflexes more pronounced in the very young
* **Central**
  1. Abeta fibres more overlapping with C-fibres in lamina 1 and 2
  2. Dorsal horn has a wider receptive field, lower threshold, fire longer
  3. Inhibitory interneurons more slowly than excitatory neurons
* **Central sensitisation**
  1. Glial immune response likely to lack activation and neuropathic pain less likely
  2. Descending inhibition and endogenous opioid system increases as age increases
  3. Likely effects on pain matrix though this has not been fully elucidated

**Gender differences in pain**

Females have

1. Lower pain thresholds
2. Greater ability to discriminate pain
3. Higher pain ratings
4. Less tolerance to noxious stimuli

**Female pharmacokinetic and pharmacodynamic differences**

1. Bioavailability – Gastric motility and drug absorption rates are different E.g. alcohol
2. Distribution – Altered volume of distribution with fat-soluble drugs, haemodilution, protein binding
3. Metabolism – CYP450 isoenzyme differences e.g. faster CYP3A midazolam metabolism
4. Excretion – Different rates of excretion
5. Receptor effects – Males are more sensitive to morphine

**Theories for female higher pain preponderance**

1. Vaginal canal route for internal trauma and invasion by pathogenic agents
2. Temporal patterns of pain
3. Sex hormone differences

**Geriatric pain pathway changes**

1. Loss of myelinated and unmyelinated nerve fibres
2. Loss of peripheral and central nervous pain processing and interneurons
3. Loss of descending inhibitory control particularly related to opioids
4. Pain threshold for action potential increases
5. FMRI shows spread of usual pain matrix across areas of the cortex
6. Loss of brain volume in hippocampus, prefrontal cortex and thalamus

**Indigenous pain factors**

* Experience of pain
  1. Beliefs of pain may differ from practitioner
  2. Physical pain may be overshadowed by emotional pain
  3. Contrasting results in research – different populations
* Expression of pain
  1. May be verbal or even non-verbal
  2. Reluctance to reveal for bravery in males
  3. Shame and stigma associated with origins of pain
* Assessment
  1. Difficulties describing and language barriers
  2. Hospital setting not comfortable
  3. Cultural safety – current scoring tools may not be suitable or validated
* Management
  1. They may not want to access healthcare and other barriers e.g. cost
  2. Previous experiences with healthcare may be negative

**Cultural competency defined**

* Set of integrated attitudes, knowledge, and skills to enable a healthcare professional to provide for patients of diverse cultures groups and/or communities
* Set of behaviours, attitudes and policies that come together in a system, agency or among professionals to enable effective cross-cultural work
* Cultural competency in one population may not translate to another
* Needs to be an ongoing process
* Cultural competency teaches behaviours and attitudes that respect and take into account a person’s cultural background

**Practical aboriginal consults**

* Common to avoid eye contact
* Body language more important than verbal content
* Never get involved in family politics
* Shyness is common. Long pauses are common.

**Pain in indigenous population**

* MSK pain high – 87% had some in the last week
* Back, shoulder and neck most common
* Less likely to seek health care
* Patients often present late
* PCA needs to be well explained
* CBT may not be suitable

**Predictors for developing chronic pain in adolescence**

* Female Gender
* Family dysfunction
* Childhood trauma
  1. Sexual and physical abuse
  2. Childhood neglect
* Genetics

**Predictors of disability due to pain**

1. Female gender
2. Multiple sites of pain
3. Anxiety and depression
4. School-related stress
5. Lifestyle factors
6. One/both parents with chronic pain

**Limitations of screening tools**

1. Only validated for patients with pain in a single location
2. Not helpful in widespread pain
3. Screening tools will miss 10-20%
4. Doesn’t help with cause
5. Cannot be used to assess response

**Neuropathic scoring systems:**

* **DN4** 
  + French Neuropathic pain group – in 2005
  + Clinician administered
  + Validated in a number of studies though strength is disputed in a systematic review in 2015
  + Language changes has made reliability difficult to extrapolate
  + Created before the redefinition of neuropathic pain in 2008
* **LANSS (Leeds Assessment of Neuropathic Symptoms and Signs)**
  + Self-reported

**IMMPACT six core domains - recommends for pain assessment:**

1. Pain numerical rating scale / Use of rescue analgesia
2. Physical functioning assessment (e.g. MDI or BPI)
3. Emotional functioning (e.g. Beck Depression Inventory)
4. Global improvement and satisfaction with treatment
5. Symptoms and adverse events
6. Disposition

**Grading neuropathic pain: - (Finnerup, 2016)**

* Possible neuropathic pain
  + Historical features of neuropathic pain and neuroanatomically possible
* Probable neuropathic pain
  + Sensory signs in the same neuroanatomically plausible distribution
* Definite neuropathic pin
  + Diagnostic test confirming a lesion or disease of the somatosensory nervous system

**Neuropathy terms / Classification (Wikipedia, 2021)**

* Distribution
  + Mononeuropathy – One nerve area
  + Symmetrical polyneuropathy – Same areas both side of body
  + Two or more areas in disparate areas – Mononeuritis multiplex
* Types of fibre involved
  + Motor
  + Sensory
  + Autonomic
* Distal axonopathy (long nerves are affected first e.g. diabetes)
* Demyelinating polyneuropathies – where myelin sheath is lost
* Cell bodies of neurons effected – motor neuron disease or sensory neuronopathy)
* Large fibre neuropathy = Loss of vibration and sensation of light touch with monofilament
* Small fibre neuropathy = autonomic nervous system function changes. Sweat test and tilt table test. Skin biopsy can also be used.

**Neuropathy investigations (Wikipedia, 2021)**

* B12
* CBC
* TSH
* HbA1c
* SEPP

**Nociplastic pain**

**Pain scoring in elderly**

1. Abbey pain scale (recommended by APS. 6 observations)
2. PainAD (for advance dementia. 5 observations)
3. PACSLAC (Difficulty communicating. Time consuming. 60 points)

**Limits to pain scores**

1. Most neuropathic scores were validated before definition changed in 2011 leading possibly to over or under diagnosis, therapeutic approach limitations, patient outcome measures affected
2. Often studied in single populations with single pain generators – external validity may be less clear
3. Validations studies have been supported by pharmaceutical companies at times
4. Nociplastic pain has not been considered
5. Absence of a gold-standard for neuropathic pain diagnosis
6. Can be overly simplistic
7. Sensory examination features are often limited

**Justification for MDT in chronic pain**

1. Cochrane review 2014 – Moderate evidence decreasing pain and disability in lower back pain
2. Gatchel 2014 – Review
3. National Pain Summit 2010 – recommendation

**QST testing**

* Standardised testing but trained investigators
* Evaluating function of unmyelinated C fibres, thinly myelinated A delta and thickly myelinated A beta fibres
* Sensory profile with 13 tests performed over 1 hour
* “Method of levels” – provides sub-threshold stimuli to assess for painfulness of stimuli
* Thermal testing – Temperature varies from 0-50 degrees Celsius
* Mechanical detection performed with monofilaments
* Vibration testing with tuning fork

**Electrophysiologic studies**

**EBM Majid**

**COVID-19 pain related**

|  |  |  |
| --- | --- | --- |
| **Scoring system** | **Pros** | **Cons** |
| LANSS | Interview and examination  Better sens/spec with exam 90/90%  Not evaluated in back pain specifically  Sensitivity for response to treatment  Now has a ‘self-reported’ version | Validated in pain settings but not primary care |
| DN4 | Designed in France and language altered to English |  |
| PAINAD | Observational scoring for advanced dementia  One of the best for both acute and chronic pain scoring  Distinguishes between painful and non-painful events  Correlates with other self-reported pain scales  One of the strongest tools for observation  Can be used to guide reduction in pain with treatment  Good interrater reliability and internal consistency | Training is generally required for its use  No testing on ethnic groups  Reliability evidence is lacking  Observational  Not validated in cultural groups  0-10 scale difficult to titrate against |
| ABBEY PAIN SCALE | Caregiver involved rating scale  Does not differentiate between distress and pain  Best to use while the patient is being moved/moving  Can repeat and compare results  Uses behavioural AND physiological measures |  |
| FLACC-R | Thought of as a behavioural scale not observational  Can be used for kids or those unable to communicate  Not recommended for Elderly | Not validated in special needs or ventilated |
| PAIN DETECT | Interview questions only  Originally designed for back pain  Sens/Spec ~ 80%  Uses graded answers not just yes/no |  |
| Wong-Baker Faces Scale | Rating scale using faces |  |
| ORT | Webster et al 2005  For use in adults  Predicting opioid risk  Administered and answered by the patient  Has 5 items  Validated screening tool for opioid use in chronic non-cancer pain  Modified ORT removed gender differences  Recent studies have not confirmed statsticically significant predictive values  **The brief risk questionnaire (similar) may be better at predicting aberrancy at 6 months**  ?Not recommended by BJA | Created using the DSM4 criteria |
| SOAPP-R | 14 Questions  Inter-item reliability is good  Good predictive validity  Predicting opioid risk in ongoing use  Self-reported by the patient  Better guide to see if future behaviour is at risk for opioid misuse |  |
| Current opioid misuse measure | Reviews current misuse  Performs well in the outpatient setting and may be best to use in telehealth  Sensitivity and specificity are in their 70s  Better to describe whether a person is currently misusing |  |
| ORBIT |  |  |
| PACSLAC -2 | Longer pain assessment in non-verbal adults  Discriminates between painful and non-painful events  Correlates with self-report scales  Recommended as one of the strongest tools  Content validity is good due to wide-ranging items  Good interrater reliability and internal consistency |  |
| Pain Medications Questionnaire | Risk tool for opioid misuse  Sensitivity and specificity was high |  |

**Ethics/Legal**

**AHPRA and notifiable conditions**

1. Practicing while intoxicated by drugs or alcohol
2. Sexual misconduct in the practice of the profession
3. Placing the public at risk of substantial harm because of impairment (health issue)
4. Placing the public at risk because of a significant departure from accepted professional standards

**Risk factors for vulnerable health professionals**

1. Depression
2. Drugs (including alcohol)
3. Dimming (burnout)
4. Disruptive behaviour (personality problems like narcissism)

**Four pillars of ethical principles**

* Beneficence
  + Must weigh appropriate pain relief against need to protect individuals and society from addiction, diversion and trafficking
* Non-maleficence
  + Tension with leaving pain untreated causes harm versus giving long term opioids that cause harm
* Autonomy
  + Requires informed consent. Clinicians must be able to provide that information
* Justice
  + Equitable access becomes difficult where demand for a treatment may clash with clinical judgement and costs to society

**Mandatory Notifications**

1. Practicing while intoxicated by alcohol or drugs
2. Sexual misconduct in practice of the profession
3. Placing the public at risk of substantial harm because of impairment (health issue)
4. Placing the public at risk because of a significant departure from accepted professional standards

**Australian Charter of Healthcare Rights**

1. Access
2. Safety
3. Respect
4. Partnership
5. Information
6. Privacy
7. Give feedback

**Montreal declaration 2010 – Rights to...**

1. Article 1 – Pain management without discrimination
2. Article 2 – Acknowledgement of their pain and informed on how it can be assessed and managed
3. Article 3 – Access to appropriately trained professionals

**Types of complementary medicine for pain management**

* Whole medical systems (e.g. homeopathy, Chinese medicine)
* Mind-body medicine (relaxation, mediation, yoga)
* Biologically based practices (dietary supplements, shartk cartilage)
* Manipulative therapies (Chiropractic and osteopathic)
* Energy therapies (Qigong, reiki, EM therapy)

**EBM**

**Definitions**

* NNT
  1. The number of patients needed to treat with a specific drug to obtain 1 patient with a defined degree of pain relief (usually 30 or 50%)
  2. Calculated as the reciprocal of the absolute risk difference
* NNH
  1. The number of patients needed to be treated for 1 patient to withdraw from the trial due to adverse effects.
* Mean – Sum of all divided by number of values
* Median – Middle value when in order
* Mode – Most frequent number
* Standard deviation – quantify the amount of variation in a set of data
* Variance – Measures the amount of spread in values
* Range – Difference between smallest and largest
* Standard error – Standard deviation of sampling distribution
* P value – Probability that when the null hypothesis is true, statistical summary would be the same as or greater magnitude than the actual results

**Grading of EBM**

* Systematic reviews and RCTs (Level 1 and 2)
* Comparative clinical studies RCTs and observational (Level 3)
* Expert clinical judgement (level 4)

**Distinguishing high-quality papers**

* Critical Appraisal Skills Programme
  1. Valid
  2. Worth continuing
  3. Results
  4. Context

**Limitations of EBM in Spinal pain**

* Classification is fluid – a reductionist structural diagnosis is difficult to confirm
* Psychosocial factors vary widely and are difficult to control for
* RCTs are not well supported or financially confirmed

**Conditions**

**Risk factors for acute to chronic WAD**

1. Biomedical
   * Severe pain
   * Acute hospital admission
   * Headache
   * History of chronic pain
   * Female
   * Older
   * No seatbelt
   * High Neck Disability Index
2. Psychological
   * Depression
   * Anxiety
   * Mood disorder
   * High catastrophisation
3. Social
   * Low educational literacy
   * Litigation
   * Part time employment

**Risk factors for chronic pelvic pain:**

* Age (increased in reproductive group)
* Patients with post-surgical pain
* Psychological morbidity e.g. depression
* Psychological maladaptive coping e.g. catastrophising
* Recurrent STIs

**Suspected IBS pathophysiology:**

1. GI motility disorder with altered serotonin signalling
2. Visceral hypersensitivity disorder triggering sensitised nociceptors in gut wall
3. Intestinal barrier disorder with loss of tight-junctions. Inflammatory responses ++
4. Bile acids may affect intestinal permeability in response to different foods
5. Increased intestinal permeability following acute gastroenteritis from infection
6. Bacterial overgrowth
7. Intestinal microbiota imbalance with gut-brain communication complications
8. Low grade mucosal inflammation
9. Genetics contribution

**Cardinal signs of parkinson’s disease (BRIT)**

1. Bradykinesia
2. Rigidity
3. Instability (postural)
4. Tremor

**Parkinson’s – Kings Parkinson Pain Scale – 2015 (CONFORM)**

1. **7 Domains – Severity and Frequency**
   1. **C**hronic pain
   2. **O**rofacial pain
   3. **N**octurnal pain
   4. **F**luctuation-related Pain
   5. **O**edema/swelling and discolouration
   6. **R**adicular pain
   7. **M**usculoskeletal pain

**PD-Pain Classification System (PD-PCS) – NEW Parkinsons system suggested**

* Ideally to differentiate between PD specific pain and other causes

**Specific treatments in Parkinson’s disease:**

* Levodopa/Carbidopa (Dopamine precursor)
* Duloxetine – Improves pain
* Deep brain stimulation – Improves ‘off’ pain can last up to 2 years
* Opioids – constipation clearly an issue
* MOAB maybe – may be neuroprotective
* Anticholinergics - Mainly if tremor pain – Benztropine

**Pudendal neuralgia**

* Burning or sharp pain in the ‘saddle’ area
* Avoid activities compressing the nerve e.g. cycling
* U-shaped cushion
* Pelvic physiotherapy for down-training
* Cease straining with bowels and bladder
* Antineuropathic agents

**Sickle cell disease**

* Single point mutation in B-globin
* Low oxygen leads to sickling
* Sickling leads to chronic inflammation, vascular damage and anaemia
* **Acute pain – Vaso-occlusive episodes**
  1. Severe sudden and unpredictable
  2. Often 1 week
  3. Triggered by cold weather, over-exertion, dehydration, tobacco smoke, psych distress
  4. Can occur and cause pain in: bones, muscles, mesentery, organs
* **Chronic pain** – Not well understood – likely highly sensitised
  1. Ulcers, avascular necrosis, neuropathic pain, arthritic pain
* **Multi-organ injury**
  1. Sequestration crisis (blood pooling in an organ)
  2. Aplastic crisis

**Management of Sickle Cell Acute pain crisis**

1. Opioid analgesia
2. Paracetamol as anti-pyretic
3. NSAIDs – but caution
4. Fluid replacement as required
5. Thromboprophylaxis – Heparin commonly 5000U TDS
6. Incentive spirometry

**Acute Pain**

**Poorly managed acute pain complications**

1. VTE
2. PONV
3. Bowel and urinary complications
4. Prolonged length of stay in hospital
5. Hospital readmissions
6. Progression to chronic pain
7. Substance use disorder

**Benefits of APS**

1. Reduced pain
2. Less side effects
3. Reduced postoperative mortality and morbidity
4. Reduced incidence of persistent post-operative pain
5. Cost-effective

**AIMS in Acute pain in opioid-tolerant patients**

1. Adequate and appropriate full work up/review
2. Provision of effective analgesia
3. Prevention of withdrawal from opioids
4. Involvement of multidisciplinary and other specialist teams
5. Manage comorbidities – depression, anxiety, mental health
6. Organise appropriate management on discharge

**PRACTICAL acute pain in opioid-tolerant patients**

1. Multimodal analgesia
2. Ketamine and gabapentinoids to attenuate hyperalgesia and tolerance
3. Regional analgesia maximised
4. Opioids still commonly needed – best via a PCA
5. Pain scores are often higher – titrate to functional outcomes

**Reducing long term opioid use**

* Manage patient pain expectations perioperatively
* Hospital specific recommendations and guidelines
* Setting default quantities of prescribed opioids
* Policy interventions limiting first time opioid scripts to 7 days
* Having known about monitoring programs
* Medical student education

**OIVI**

* Monitor with continuous pulse oximetry, and continuous capnography in those receiving supplemental oxygen
* Cause:
  + Central respiratory depression - Depression of respiratory drive with reduction in respiratory rate and/or depth of breathing
  + Sedation - Depression of consciousness (and therefore arousal)
  + Obstruction - Depression of supraglottic airway muscle tone
* **Cannot just rely on respiratory rate without sedation monitoring**
* **Many patients do NOT have clear risk factors**
* **Avoid with opioid-sparing medications**
* **Risk factors:**
  + Obesity
  + Sleep disordered breathing
  + COPD
  + Renal disease
  + Cardiac disease
  + Neurlogical disorder
  + ASA 3 or 4
  + Age > 65 years
* **Contributing factors**
  + Administration of sedatives
  + Administration of opioids by multiple routes
  + Continuous infusion of opioids
  + Multiple prescribes

**Sedation score:** (aim for less than 2)

* 0 Wide awake
* 1 Easy to rouse
* 2 Easy to rouse but doesn’t stay awake
* 3 Difficult to rouse

**Bromage score**

* 0 = Patient has full movement
* 1 = Partial movement (can just move hips/knees/feet)
* 2 = Almost complete (only move feet)
* 3 = Complete (unable to move feet or knees)

**Functional Assessment Score**

* A = No limitation
* B = Mild limitation
* C = Unable to complete activity due to pain

**Recognition of OIVI**

1. Sedation more reliable than decreased RR
2. Continuous CO monitoring best way

SPO2 less reliable – patients often on oxygen

**ORT in acute pain**

1. Both should be continued

**PCA practical safety**

1. Antireflux and antisyphon

**Factors for prescribing on a PCA**

1. Bolus dose of opioid
2. Loading dose (usually at zero – loading done BEFORE it commences)
3. Concentration
4. Dose duration (rate)
5. Lockout interval

**General orders for PCA**

* Oxygen at 2-4 L/min while orders are in effect
* No systemic opioids or sedatives to be given outside of APS instruction
* Naloxone to be immediately available
* One-way anti-reflux siphon valve always used between patient and PCA machine
* Cease PCA if patient becomes confused
* If inadequate analgesia, contact APS (Scores > 7 or FAS = C)
* If resp rate < 7 and sedation score < 2 notify APS

**Excessive sedation management**

* If sedation score = 2 then halve bolus dose and cease background infusion. Increase to hourly sedation scores until <2 for > 2 hrs
* If sedation score = 3 (irrespective of RR) or sedation score = 2 AND respiratory rate < 7 then perform MET call an give 100 mcg naloxone IV stat. Repeat 2 minutely up to 400 mcg. Cease PCA

**Risks of PCA continuous infusion**

1. PCA will not be able to be pressed if patient is too sedated
2. Continuous infusion removes this safety

**Evidence for IV PCA**

1. Provides better analgesia
2. Higher opioid use
3. Higher incidence of pruritis but not much else
4. Similar analgesic outcome regardless of opioid used

**Regular monitoring required on PCA (hourly for 6 hours and then 2nd hrly when stable)**

1. Pain scores
2. Functional ability
3. Sedation scores
4. Respiratory rate
5. Other side effects

**Inadequate analgesia with a PCA**

1. Reassess the patient
2. Another cause for the change in pain?
3. Neuropathic pain?
4. Opioid side effects being treated (so patient not avoiding pressing)
5. Chest patient on multimodal options also
6. Give extra opioid to ‘reload’ if needed
7. Consider re-education
8. Consider prescription change
9. Check equipment

**Overly sedated on a PCA (Sedation score 2 or more)**

* Check no other reason for sedation
  1. Another sedative agent
  2. Another opioid given
  3. PCA correctly programmed
  4. Prescription appropriate
  5. Antireflux and antisyphon valves in place
  6. PCA pump functioning properly
* Reduce amount of opioid patient can receive from PCA (e.g. halve the bolus)
* Naloxone may be considered if RR <7

**Benefits of epidural analgesia**

1. Better pain relief particularly with movement
2. Possibly reduced respiratory, cardiac, and GI complications and less postoperative mortality

**Complications of Epidural**

1. Neurological (spinal cord or nerve injury)
2. Epidural haematoma
3. Epidural space infection (abscess or meningitis)
4. Postdural puncture headache
5. Migration of epidural catheter

**Monitoring after epidural placement**

* Nondrug treatment orders should include advice about antiplatelet/anticoags
* Monitoring – Vitals and motor/sensory function
* Motor and sensory function monitored for 24 hs after removal

**Absolute and relative contraindications for epidural and intrathecal analgesia**

* Untrained staff
* Patient refusal
* Contraindications to needle or catheter placement e.g. infection
* Present of a dural puncture

**Intrathecal for Chronic pain**

* Evidence for use in cancer pain and spasticity (level 1 for baclofen)
* Chronic non cancer pain evidence is far less clear

**Opioids decrease ventilation mechanisms**

* Depression of respiratory drive
* Depression of CNS in general and reduced consciousness
* Depression of supraglottic airway tone (snoring)

**Assessment of acute pain**

* Unidimensional measures
* Assessment of function (FAS)
* Requires pain at rest and with movements assessment

**How to monitor for OIVI**

* Measure arterial or end-tidal CO2 levels
* Sedation scores
* Respiratory rate (though least reliabile)
* Oxygen saturation levels (though patients often on O2 making this difficult)

**APS Standard orders**

* Drugs to use
* Education of nursing, medical staff and patients
* Monitoring requirements including analgesic and OIVI
* Response to inappropriate analgesia
* Response and treatment of side effects
* Nursing procedures and protocols
* Equipment used

**Benefits of patient centred approach**

* Humanitarian right to pain relief
* Addresses patients’ medical needs
* Leads to improved safety, quality, and cost effectiveness
* Greater staff satisfaction
* Greater patient satisfaction

**Tramadol vs Tapentadol**

* Tramadol SSRI and SNRI, Tapentadol just SNRI
* Tramadol not a controlled drug
* Tramadol has active metabolite M1
* Tramadol relies upon CYP2D6 metabolism

**APS role:**

* Education health professionals and organisations
* Advanced analgesic techniques
* Impreve analgesic regimes
* Standardise use of equipment and ‘standard’ orders
* 24-hour available pain personnel
* Quality improvement
* Research role

**Key steps in an ERAS program**

* Presurgery
  1. Education
  2. Counselling
  3. Carbohydrate drinks
  4. Epidurals for pain
* During surgery
  1. Fluid management
  2. Judicious opioids
  3. Reduce surgical trauma/incision
  4. Minimise transfusion
* Post-surgery
  1. Early mobilisation
  2. Early removal of drains and tubes
  3. Early transition to oral pain meds
  4. Early allowance of food

**Benefits of ERAS**

1. Increased patient satisfaction
2. Less postoperative complications
3. Decreased length of hospital stay
4. Improved use of hospital resources

**Principles of pain management in ERAS**

1. Use multimodal analgesia
2. Use regional analgesia
3. Avoid opioids as possible
4. Transition to orals early

**Benefits of epidural analgesia**

1. Better general analgesic effect
2. Lower side effects and sedation
3. Decreased morbidity
4. BUT higher rates of pruritis, urinary retention, motor blockade

**Additives with morphine intrathecal/epidural**

* Clonidine – extends motor blockade
* Adrenaline – improved analgesia with slower drug clearance
  1. Vasoconstriction concerns do not occur

**Contraindications to ketamine (0.1-0.3 mg/kg/hr)**

1. Active psychosis
2. Pregnancy
3. Severe liver disease
4. Poorly controlled cardiovascular disease
5. Elevated intracranial pressure and intraocular pressure

**Harms of extended-release opioids in Acute pain**

1. Increased risk of opioid-related adverse events
2. Extended length of hospital stay
3. Increased 28-day readmission rates
4. Difficulties in titrating dosage
5. Opioid requirement differs significantly for different patients.
6. Increased risk of OIVI
7. Down titration and pain severity reduces is more difficult
8. Side effects are maintained for a longer period if they occur
9. Increased risk of persistent opioid use at 30 days
10. Less effective analgesia, requires higher dose

**Opioid free vs Opioid sparing**

1. Unclear what role nonopioid components play due to lack of evidence
2. Additional equipment, monitoring and resources
3. Does not decrease the risk of persistent opioid use
4. Arguably unrealistic in clinical practice

**International Multidisciplinary consensus – prevent harms in surgical patients 2021 Anaesthesia**

1. All patients should have OIVI risk mitigated
2. Optimise preoperative pain and psychological risk-factors. Manage expectations.
3. Opioids provided for functional outcome rather than unidimensional scores
4. Multimodal analgesia is the aim
5. Long-acting opioids should not be used routinely
6. Patient-centred approach to limiting number of tablets and duration at discharge
7. Automated post-discharge amounts should be avoided
8. Hospitals should mitigate OIVI risk with sedation assessment
9. Modifiable OIVI risk should be addressed
10. Patients advised on safe storage and disposal of unwanted opioids

**Harms of preoperative opioid use**

1. Increased surgical infection risks
2. Revision surgery
3. Higher readmission rates
4. Longer lengths of hospital stay
5. Higher medical costs after surgery

**Risks of neuraxial opioids**

1. Respiratory depression
2. Sedation
3. Nausea and vomiting
4. Pruritis
5. Urinary retention
6. Reduced GI motility

**Pharmacokinetics of intrathecal opioids**

* Hydrophilic medicines have a SLOWER onset of action and longer half-life in CSF with greater dorsal horn bioavailability and greater cephalad migration compared to lipophilic

**Rationale for Intraspinal analgesia**

* Improved quality of analgesia (lower pain scores and better function)
* Lessen impact of pain (cognitive, psycho)
* Lessen toxicity of pharmacology (e.g. constipation)
* Improve QOL
* Cost – May be cost effective in some settings
* Improved life expectancy – possibly due to lower opioid doses
* May assist anti-cancer therapy tolerability
* Reduction of central sensitisation

**Standard order requirements when using epidural**

* Specific drug orders
  + Drug name
  + Dosage of bolus
  + Infusion rate
* Nondrug orders
  + Cannot have
    - CNS depressants
    - Other opioids
    - Antiplatelets
    - Anticoagulants
  + Supplemental oxygen orders
  + Need to maintain IV access while epidural in place
  + Contact instructions
* Monitoring requirements
  + Assessment of pain scores / function scores
  + Functional activity scale scores
  + Sedation scores
  + Vital signs
  + Motor and sensory function checks
  + Record of amount of drug given
  + Medication for any side effects
  + Time to check infusion pump program
* Guidelines for inadequate analgesia
* Guidelines for side effect management
* Name and signature of prescribing doctor

**Standard PCEA order**

* Bolus doses of 2-4 mL with back-ground infusion of 6-12 mL/h with lockout 10-20 mins

**Complications of epidural analgesia**

* Insertion related
  + Postdural puncture headache
  + Nerve or spinal cord injury
  + Epidural haematoma
  + Epidural abscess/meningitis
  + Catheter migration
* Equipment related
  + Catheter/filter
  + Leakage/disconnection
  + Infusion pump malfunction
  + Incorrect program
  + Gravity flow
* Drug related

**Management for dural puncture headache**

* History to rule out other cause
* Bed rest as required (patient comfort)
* Analgesia (non-opioids +/- caffeine)
* Hydrate
* Blood patch if required

**Acute pain management in opioid dependent patients**

* Supportive non-judgemental environment
* Establish if other drugs misused
* Analgesic plan
  + Maximise non-opioid
  + Use increased doses compared to naïve patients – but watch for side effects
  + Change from parenteral to oral formulations of opioids as soon as possible
* Withdrawal management plan
  + Continue ORT or replace with appropriate opioid
  + Consider withdrawal symptoms of other drugs
* Minimise stress
* Allow for MDT planning

**Naloxone use in respiratory sedation**

* 400 mcg vial of naloxone in 9ml of Saline – labelled and checked
* 40-100mcg of naloxone every 2 minutes – wake patient up enough to protect airway
* Can give 2-4 mg of naloxone prior to intubation *(?Extubation)*

**Opioid induced hyperalgesia**

1. Dorsal horn has increased glutamate and NMDA
2. Neuroplastic changes in the rostral ventromedulla
3. M-3-G may have pronociception effects in the CNS
4. Reduction of descending inhibition through CCK, serotonin and substance P
5. Increased TRPV1 receptors peripherally
6. Calcium channel upregulation

**Opioid immunosuppression mechanism**

1. Immunomodulator effects through the sympathetic nervous system
2. Affects on HPA axis
3. Affect cell-mediate and humoural immunity
4. Decreased cell line maturation

**Opioid side effect mechanisms**

* *Analgesia* – CLOSED Ca2++ channels presynaptically, OPEN K+ postsynaptically. Descending inhibitory changes
* *Euphoria –* Likely dopaminergic and reward centres
* Sedation – Mechanism unclear. Theory is agonism at CNS neurons and inhibition of firing
* *Respiratory depression –* Pre-Botzinger complex in the pons affecting breathing rate. Depression of hypoxic ventilatory response.
* *Cough suppression –* Inhibiting tachykinergic transmission of excitatory non-adrenergic non-cholinergic (eNANC) nerves in the airway
* *Miosis –* Activation of pupillary sphincter muscle
* *N&V –* Brainstem chemoreceptor trigger zone activation. Possibly vestibular effect also
* *Hypotension –* Peripheral arterial and venous vasocilation
* *GI effects –* Reduced motility and increased resting tone. Delayed passage leads to reabsorption of fluid and constipation.
* *Biliary pain –* Spasm of the sphincter of oddi
* *Renal function reduced –* Due to reduce renal plasma flow. Bladder tone increased
* *Pruritis –* likely from histamine release

**10 Universal precautions for prescribing opioids**

* Diagnosis with appropriate differential diagnosis
* Psychological assessment and risk for addiction
* Informed consent
* Develop treatment agreement
* Pre and post intervention assessment planning
* Consider a trial as part of multimodal approach
* Reassess pain score and level of function
* Regularly assess the five A’s
* Periodically review pain and comorbidity diagnoses
* Document

**Extra effects of methadone**

1. Serotonin reuptake inhibitor
2. NMDA antagonist
3. Noradrenaline effects
4. Toll-like receptor 4 acivation and pro-glial
5. Binds cardiac hERG potassium channels to prolong QT

**Extra things about buprenorphine**

1. Can displace other opioids
2. Slower binding than fentanyl
3. Dissociates slowly too
4. Low occupancy 5-10% can give analgesic effect
5. Sublingual bioavailaibilty of 30% vs only 6% orally

**Opioid metabolism**

Table

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Table

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**Neuraxial pharmacokinetics**

**Spread of drug in CSF is affected by:**

* Characteristics of injectate (e.g. Baricity, volume, dose, concentration, temp etc)
* Clinical technique (needle type, level of injection, patient position)
* Patient characteristics (age, height, weight, sex, pregnancy)

**Drug features:**

* pKa (pH at which ionised and unionised at equal amounts)
* Molecular weight
* Lipid solubility

**Spinal Pain**

**Acute to chronic lower back pain**

1. Australian data 75% return to baseline pain and disability level at 12 months
2. Negative prognostic factors:
   * Older age
   * Compensable injury
   * Higher pain intensity
   * Reduced activity before consultation
   * Longer duration before consultation
   * Feeling of depression
   * Perceived risk of persistence

**DON’T USE TERM SCIATICA**

**Mechanical causes of lumbar spinal stenosis**

* Narrow spinal canal or foramina by:
  + Degenerative change e.g. facet OA
  + Ligamentum flavum hypertrophy
  + Bulging discs
* Symptoms from venous congestion or ischaemia of the nerve roots in the cauda equina due to compression

**Modic changes**

* Vertebral endplate abnormalities seen on MRI
* Thought to be pro-inflammatory response but structural damage allowing microbial infiltration, autoimmune reactions, or both.
* This worsens nociceptor stimulation by chemical or mechanical stimuli
  + Type 1: Bone marrow oedema in vertebral body and hypervascularised
  + Type 2 – Fatty replacements of red bone marrow in vertebral body
  + Type 3 – Subchondral bone sclerosis

**Key facts to quote about back pain**

1. Number one cause of disability in the world
2. Increased 50% since 1990
3. Worse in low- and middle-income countries
4. US 135 billion spent in 2016

**Risk factors to develop lower back pain**

1. Back specific
   * Previous episodes of back pain
   * Chronic conditions (asthma, headache, diabetes)
2. Mental health
   * Poor mental health (distress and depression)
3. Demographics / General health
   * Genetic influences
   * Obesity
   * Smoking
   * Low level of physical activity
4. Specific tasks
   * Awkward postures
   * Heavy manual tasks

**Negatives of back pain imaging (compared with no imaging)**

1. Higher medical costs
2. Increased health care utilisation
3. More work absence

**SPACE trial**

1. Showed opioids use was not more effective than non-opioid management of chronic back pain, hip and knee pain with OA

**Cannabis in back pain**

1. 4-year observational trial
   * Cannabis users had greater pain
   * Cannabis users had lower self-efficacy
   * No evidence cannabis reduced pain severity or interference
   * No evidence cannabis had an opioid sparing effect

**High level neuroscience education no better than sham education for back pain**

**Two views of back pain**

1. Mechanistic
2. Neuromatrix

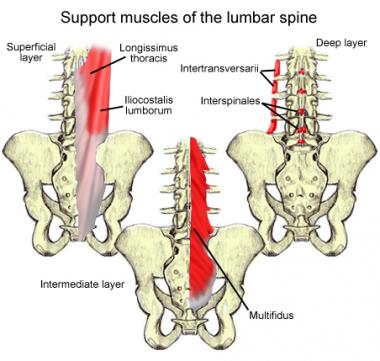
**Flag colours for back pain (Flag colours for complicating factors of acute back pain)**

1. Red – Serious pathology
2. Orange – Psychiatric symptoms (depression, personality disorders)
3. Yellow – Beliefs, judgements, emotional responses, pain behaviours
4. Blue – Perceptions about work and health – too onerous and will cause injury
5. Black – System or contextual issues e.g. legislation, conflict insurance, solicitous fam

**Red flags back pain**

* Poor evidence
* History of cancer is best 75% sens/spec
* Steroid and trauma for vertebral body fractures





Diagram

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**Acute lower back pain treatment**

* NSAIDs – Small effect
* Muscle relaxants – minimal short-term benefit
* Acupuncture vs sham – Small
* Massage – Helpful at 1 week not 5
* Heat – Some help
* Spinal manipulation – small effect

**Controversies in back pain taxonomy**

* Taxonomical vs clinical classifications
* Pain described as locational (e.g. low back pain) or anatomical (e.g. spondylosis)
* Locational – Hard to argue this is a ‘diagnosis’
* Anatomical – Hard to truly correlate clinical findings with anatomical pathology
* Neither of these consider the sociopsychological involvement

**Terminology problems**

* ‘Non-specific’ may de-legitimise the sufferer
* ‘Degenerative changes’ is not a helpful radiological term
* Chronic secondary musculoskeletal pain also describes pathophysiological findings – trying to pacify those who remain focused on a mechanistic/anatomical description
* ‘Mechanical’ spinal pain is often used where there is no clear altered structural finding but pain is induced

**Reasons to refer to spinal surgeon in back pain**

* History of progressive leg weakness or cauda equina
* Clinical signs of upper motor neurone lesion
* Acute radiculopathy not responding to conservative management
* History of acute trauma with possibly unstable fractures
* History of malignancy with spinal involvement
* Evidence of infective process
* Spinal canal stenosis with claudicant leg pain
* Spondylolisthesis, particularly in young adult, with progression of defect
* Syringomyelia on investigations
* Single level intervertebral disease with failed conservative management

**Visceral Pain**

**Summary of neuropathic/nociceptive/nociplastic?**

1. Out of proportion to nociceptive stimulus
2. Amount of pain sensed and underlying pathology mismatch
3. Change in way pain is transduced, translated, transformed, and received at cortex
4. This suggests a neuropathic component though there is a nociplastic component possibly

**Visceral pain questionnaires**

* LANSS
* PainDETECT
* DN4

**Gut-Brain Axis**

1. Bidirectional - Vagus nerve feedback from brain to gut (ANS, ENS, HPA axis)
2. Bidirectional - Gut feedback to the brain -
   1. Immune – cytokines and chemokines
   2. Endocrine – HPA
   3. Neural pathways of feedback – Autonomic with para/symp arms
   4. Microbial metabolites e.g. fatty acids
3. Epigenetics – phenotypic expression of genes
   * Often environmental changes
   * Methylation can be induced by maternal neglect, emotional deprivation etc
   * Widespread changes in the glial cells and other CNS cells
   * Can impact upon the way we behave and perceive the world

**Direct Microbiota effects**

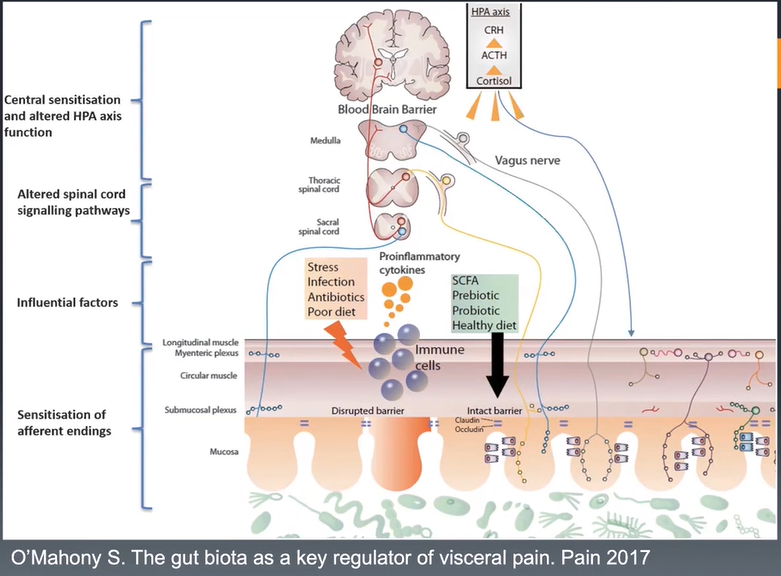
1. Neurogenesis
2. Myelination
3. Activation of microglia
4. Neuroinflammatory processes

**Microbiota local effectors (direct or indirect)**

1. TRPV1 receptor activation
2. Serotonin receptors
3. Cannabinoid receptors
4. Ion channels
5. Neurohormonal (opioids, endocannabinoids, monoamines such as serotonin creation)
6. Altered intestinal permeability

**Ganglia memory bits**

* Stellate ganglia – Sympathetic of head, neck, and arms
* Thoracic splanchnic nerves – form from the coeliac ganglion – Upper gut
* Inferior hypogastric plexus -



**Visceral innervation – Key points**

1. Organs innervated by two nerves
2. Viscera are midline structures so bilateral innervation
3. Cell body of vagus nerve is in the NODOSE and rostral jugular ganglia
4. Vagus nerve projects to CNS via the nucleus of the solitary tract
5. Spinal afferents TRAVERSE pre and post paravertebral ganglia to spinal cord
6. Terminates in superficial laminae 1 and 2
7. Transduction from unencapsulated free nerve endings
8. These free nerve endings are polymodal

**Visceral sensitisation**

1. ABeta fibres can become sensitised and undergo phenotypic switching
2. They may also have terminals into other laminae
3. Viscero-somatic convergence can cause referred pain
4. Convergence-facilitation is where these inputs may sensitise dorsal horn neurons also causing somatic cross-talk

**Visceral pathways to brain**

1. Uses medial/slow pathways
2. Spino-parabrachial-limbic and dorsal columns
3. Terminates in the limbic brain (primitive mid-brain)
4. Vegetative motor response (e.g. rest and digest/rest and recover) rather than fight/flight

**Chronic pain in visceral organs mechanisms**

1. Massive injury signal --> nothing.
2. Neurochemical release with biochemical and morphological changes
3. Sprouting and microneuromata formation with ectopic firing
4. Basket like sympathetic fibre growths around DRG sensitising them
5. Dendritic growths causing rewiring and convergence

**Evidence for visceral procedures (Very minimal generally)**

* SCS for angina
* Neurolytic coeliac plexus block for pancreatic cancer
* *Other things tried – but minimal evidence*

**Issues in clinical trials for procedures**

* Often excludes demographics at higher risk/more complicated
* Device company sponsored – sponsorship bias
* Definition of successful outcome varies
* Duration of follow up is often short
* Blinding is difficult
* Recruitment is complex
* Funding and costs are high

Table

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**Pain Related to Cancer**

**Bony Metastases Diseases:**

* PBKTL (Lead Kettle) – Prostate, Breast, Kidney, Thyroid, Lung

**Solid organ pain mechanisms**

* Expansion with pressure
* Tumour infiltration to sensitive tissues or nerves
* Inflammatory responses sensitise transmission
* Tumour factors release e.g. prostaglandins, TNFalpha
* Acidosis from local tissue damage and tumour tissue
* Proteolytic enzymes
* Local pressure effects causing ischaemia
* Stretched serosal and associated tissues

**Hollow viscus pain** **mechanisms**

* Stretch receptor activation
* Distension, impaction
* Ischaemia of tissue wall
* Pronociceptive factors released by tissues
* Secretion problems secondarily

**Bone pain mechanisms**

* Direct infiltration of sensory neurons within bone marrow
* RANK system changes causing osteoclast activation
* Mechanical bone strength loss and associated further degradation/damage
* Periosteal covering pressures
* Direct C-fibre activation by pronociceptive ligands released from tumour tissue

**Indirect cancer pain mechanisms**

* Cachexia
* Osteoporosis
* Muscle spasms
* Treatment related issues

**Mucositis definition**

* Painful inflammation, ulceration and dysfunction of mucous membranes in response to chemo/radiotherapy/bone marrow transplant

**Mucositis pathophysiology**

* Toxicity of ‘high turnover’ epithelial cells in mucous membranes due to toxins
* Decreased saliva and mucous  secondary inflammation, necrosis, ulcers, blisters
* Can develop further inflammation and infection

**Mucositis management**

* Monitor mucous membranes
* Avoid mucosal irritants: smoking, alcohol etc.
* Hydration and nutrition
* Gut care e.g. PPI, probiotics, dirrhoea and nausea management
* Topical agents – Honey, sucralfate, ice chips, lignocaine gel, topical clonazepam
* PCA opioid as required
* IV paracetamol
* IV ketamine
* IV clonidine or benzo for anxiety
* Pregabalin by NG
* (AVOID TCAs and NSAIDs)

**Serotonin syndrome**

* Increases serotonin levels at the post-synaptic 5HT receptor (e.g. reduced uptake, reduce metabolism, increased synthesis, altered receptor activity)
* Classic Triad of MAN
  1. Mental status – agitation, anxiety, confusion, hypomania
  2. Autonomic function – Hyperthermia, tachycardia, sweating, flushing, mydriasis
  3. Neuromuscular activity – Clonus/myoclonus, shivering, tremor, hypertonia
* Symptoms commonly occur within 24 hrs of starting/changing the drug
* Cyproheptadine is a serotonin antagonist that can be used in treatment
* ***Neuroleptic malignant syndrome – similar to serotonin syndrome but more autonomic symptoms and stiffness of the muscles. Treatment is withdrawal of the agent and symptomatic support***
  1. ***Mental status changes***
  2. ***Muscular rigidity***
  3. ***Hyperthermia***
  4. ***Autonomic instability***

**Patient Centred care (Aus commission on Safety and Quality in Health care)**

* Healthcare organisations, healthcare providers, and policy-makers actively working wih consumers to ensure that health information, systems and services meet their needs

**Management of Sickle Cell Chronic pain**

* Depression, anxiety and sleep dysfunction
* Hydroxyurea preventative in paeds and adults
* Transfusions

**Cancer epidemiology**

* 1 in 3 men by 75yo
* 1 in 4 women by 75yo
* Most common: Prostate, colorectal, breast, melanoma, and lung cancer
* 40% have pain at time of diagnosis
* >75% will develop pain at some point

**‘Total pain’**

* Concept of pain involving also emotional, social, and spiritual components

**Compare and contrast cancer and non-cancer pain**

* Cancer pain
  1. Often progressive
  2. Goals curative to palliative as disease progresses
  3. Interventions which would otherwise be unsuitable can be considered
  4. ‘New pain’ may be a harbinger of concern
  5. Cancer treatments often may cause pain
  6. Multidisciplinary teams may involve others e.g. religious/spiritual leaders
  7. New risk of acute pain presentations e.g. raised ICP

**WHO original cancer pain relief guide**

* By mouth
* By the clock
* By the ladder
* For the individual
* Attention to details

**Mechanisms of cancer pain**

* Nociception directly from cancer e.g. invasion, compression, ischaemia
* Nociception indirectly from cancer e.g. pressures sores, MSK complications, falls
* Pain from treatment e.g. hormonal, surgery, chemotherapy , radiotherapy
* Pain from co-morbid disease e.g. mechanical spinal
* Pain contributed by sociopsychospiritual components

**Critical history features in cancer pain**

* Organ involved
* Type of cancer
* Stage of cancer
* Past and current treatments
* Treatments planned
* OTHER symptoms

**Epidural drawbacks in cancer pain**

* Less reliable than intrathecal space due to fibrosis, bleeding, tumour involvement
* Placement can have issues
* Epidural drug requirements are 5-10x higher
* Epidural infection difficult to detect

**Breakthrough pain**

* Occurs when pain ‘breaks through’ base level of analgesia
* Incident pain – Pain on movement or activity

**Palliative care symptom control**

* N&V = Haloperidol 0.5 – 1.5 mg at night
* Respiratory distress = Sit up, fan on face, morphine 2.5 mg q4h, Benzo
* Non-productive Cough = Pholcodeine 30 mg loading dose – 5-10 mg QID, Morph 2.5 mg QID
* Productive cough = Expectorant, neb saline, Hyoscine hydrobromide for secretions
* Pruritis = Cooling menthol on skin, loratadine 10 mg daily, Cholestyramine if bile related

**Headache and Orofacial pain**

**Chronic daily headache**

* Presence of headache on at least 15 days per month for at least 3 months
  1. Can be primary or secondary

**Medication overuse headache (rebound)**

* Headache on 15 days/mth
* Overuse for more than 3 months of drugs used for acute headache
* Intake of simple analgesics > 15 days per month
* Intake of complex headache analgesics > 10 days per month
* Not explained by another cause

**Red flags for primary headache**

* Subacute and/or progressively worsening headaches over time
* New or uncharacteristic headache
* Any headache maximal at onset
* New headache after the age of 50
* Persistent headache from a Valsalva
* Systemic signs e.g. fever, weight loss, scalp tenderness etc.
* Presence of neurological signs
* Seizures

**Red flags for secondary headache (SNOOP)**

* Systemic symptoms
* Secondary risk factors (e.g. pregnancy, HIV)
* Neurological examination (deficits)
* Onset (sudden/thunderclap)
* Older (New, sudden, progressive, >50 yrs)
* Pattern change (new symptoms)
* Precipitants (Valsalva, sexual activity)

**Vascular features suggesting migraine**

* Pounding quality
* Duration 4-72 hrs
* Lateralised
* N&V
* Sono or photo-phobia
* Disabling intensity

**Migraine pathophysiology**

* Prodrome phase – Hypothalamus activation
* Aura – Cortical spreading depression – activates trigeminovascular system
  1. Trigeminovascular system arise from trigeminal ganglion and innervates vessels, pia mater, dura mater, and venous sinuses.
  2. Trigeminal nerve and upper cervical roots converge at the trigeminal nucleus caudalis – these signals then are transduced to the thalamus for further signal progression
* Headache (ictal)
  1. Activation of nociceptors in trigeminal system through the trigeminal ganglion sensitising between ganglion and CNS
  2. Repeated triggering of this system may lead to sensitisation and lead to migraine consistent symptoms and non-headache symptoms
  3. Calcitonin-G related peptide and PACAP play a role in migraine with levels increased during migraine attacks and resolve with triptan treatment
* Postdrome
* Interictal

**Acute treatment**

* Migraine specific (triptans)
* NSAIDs
* Dopamine antagonists (metoclopramide)

**Management tips for ALL headaches**

* Migraine diary
* Normalisation of normal life as able
* Don’t overuse acute analgesics
* Try and lead healthy lifestyle

**Classifications for secondary headache**

* Medication-related
* Post-traumatic
* Intracranial pressure disorders
* Structural (Cervical / head and neck disorders)
* Metabolic
* Vascular
* Neoplastic
* Cervicomedullary lesions (chiari)
* Infections
* Other

**Pathophysiology of TMJD**

* Trauma to joint
* Disc displacement
* Teeth issues e.g. grinding
* Malocclusion of the jaw
* Cartilage damage
* Localised inflammation

**Management of TMJ**

* Non-pharmacological
  1. Behavioural techniques (e.g. addressing teeth grinding, stress mmnt)
  2. Physical therapy for muscle issues if identified
  3. Dental input (e.g. malocclusion)
* Pharmacological
  1. NSAIDs
  2. Amitriptyline
  3. Gabapentin
* Interventional
  1. Periarticular/interarticular injections
  2. Botox injections (if muscle spasm)
  3. Surgery including arthrocentesis

**Prognosis of TMJD**

* Remember 40% resolve on their own – 60% had a complete resolution with treatment at 2 yrs
* 50-90% gain a pain relief response

**TACS to remember**

* Cluster headache (episodic (cycles of 7 days to 1 yr – 1 mth between) or chronic)
  1. Unilateral pain
  2. Periorbital or temporal
  3. 15-180 mins
  4. Ipsilateral autonomic features
  5. Restless and agitated
  6. One every day to 8/day in cycles
* Paroxysmal Hemicrania (episodic or chronic (cycles or periods for >1 yr with remission < 1 mth)
  1. Shorter duration of attacks
  2. >5 attacks per day during active periods
  3. ABSOLUTE response to indomethacin
     + (150-225mg daily in divided doses for 2 weeks)
* Hemicrania continua (Unremitting – does not stop for 1 yr without >1 day break) (Remitting – continuous but more than 1 day between)
  1. Strictly unilateral
  2. Present for >3 months
  3. Absolute response to indomethacin
     + (May have some migrainous features)
* Short-lasting unilateral neuralgiform headache attacks (SUNHA) – Two types **BOTH NEED AN MRI TO EXCLUDE POSTERIOR FOSSA LESIONS**
  + - Moderate to severe unilateral pain in orbital, supraorbital, temporal or trigeminal regions.
    - Attacks are short 1-600s.
    - Single stabs or in salvos
    - At least one attack per day but often hundreds
  1. SUNCT (Short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing)
     + Has above plus significant ipsilateral conjunctival injection and tearing
  2. SUNA (Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms)
     + Has above and only one or neither of tearing or injection but other autonomic features

**Contraindications to migraine treatments**

* Triptans and ergots
  1. CAD
  2. Uncontrolled hypertension
  3. History of stroke or CVD
  4. Brainstem aura or hemiplegic migraine
  5. Use of different triptans or ergots within 24 hrs
  6. Pragnancy

**Indications for prophylaxis**

* > 3-4 attacks per month
* QOL affected
* Patient’s choice
* Medication overuse headache
* Adverse effects from antimigraine meds
* Uncommon headache disorders

**Cluster headache treatment**

* High flow 100% oxygen (12-15 L/min)
* Sumatriptans

**Cluster headache prevention**

* Verapamil 240-480 mg daily (orally in 3 doses)
* Valproate

**Treatment of SUNA/SUNCT**

* First line: Lamotrigine 400 mg daily
* Second Line: Oxcarbazepine (better than…) and Carbamazepine
* Topiramate
* Gabapentin/pregabalin
* Duloxetine
* Mexiletine
* IV lidocaine (90% improved!)
* GON block (37% improved)

**PATHOPHYS OF EACH HEADACHE**

**Whiplash details and risk factors**

***Pharmacology:***

**Neuropathic pain meds: - Finnerup**

**First Line. NNT Dose Timing**

Gabapentin IR/SR 7.2 1200-3600mg/day bd/tds

Pregabalin 7.7 300-600mg/day bd

SNRI Duloxetine 6.4 60-120mg/24h od

Venlefaxine 6.4 150-225mg/24h od

TCA’s (amy/nor) 3.6 25-150mg/24h od/bd

**Second-Line**

Capsaicin 10.6 1-4 patches to area 30-60min q3months

Lignocaine patch 1-3 patches 12h on/off

Tramadol 4.7 200-400mg/day SR bd

**Third-Line**

Botulinum toxin A 1.9 50-200 units/3 months

Strong opioids 4.3

**Morphine Mechanisms of action**

* Works on Mu, Kappa and Delta receptors

**Opioid receptor actions:**

1. Mu – Analgesia, depression, Euphoria, Physical dependence, Respiratory sedation
2. Delta – Analgesia, inhibit dopamine
3. Kappa – Analgesia, diuresis, dysphoria

**Opioid risk of fatal overdose**

1. Slow release and long-duration opioids
2. Co-prescription of opioids and benzodiazepines
3. Sleep-disordered breathing
4. Reduced renal and hepatic function
5. Older age
6. Pregnancy
7. Mental health disorders including SUDs

**Opioid induced tolerance, dependence, reward**

1. Receptor decoupling and downregulation
2. Modulation of NMDA receptors
3. Reduced glutamate transporters
4. Glia up-regulation

**Opioid types at receptors:**

1. Mu = ALL
2. Kappa – Oxycodone and Buprenorphine
3. NOP/ORL-1 Buprenorphine

**Metabolism of opioids**

1. CYP2D6 = Codeine, Tramadol, Oxycodone

**Long acting versus short acting (CDC review)**

* NOT proven that longer acting medications have lower risk of abuse
* Do not provide superior relief for constant pain than short-acting opioids
* THEY ONLY recommend them in opioid tolerant patients

**Use of opioids in Chronic Non-cancer pain – FPM 2015**

1. Lack of evidence supporting long term effectiveness
2. Substantial evidence of long term harms
3. Tolerance limits long term use
4. Increased risk of opioid induced hyperalgesia
5. Functional outcomes are often worse long term
6. Mental health is often worse long term

**Opioids long term harms**

1. Immunosuppression
2. Sleep apnoea
3. Osteoporosis
4. Hormonal changes – reduced fertility and sexual dysfunction
5. Increased MI risk

**Prescription of opioids for CNCP requires (FPM 2020)**

1. Demonstration of benefit
2. Active surveillance of harms
3. Periodic attempts at dose minimisation

**Prescribers of opioids for CNCP require:**

1. Understanding of the clinical pharmacology of opioids prescribed
2. Efficacy and harms of those opioids
3. Interactions of opioids with other drugs
4. The regulatory requirements imposed by the jurisdiction in which they practise

**Describe the 5+3A’s of opioid documentation**

* Analgesia
* Activity
* Adverse effects
* Affect
* Aberrant behaviour

(Adequate Assessment, Adequate documentation, Agreement of goals and conditions)

**Opioids in elderly**

1. Most studies are in younger populations
2. Renal and liver decline with time
3. Decreased cardiac output
4. Altered body composition – more fat and less water
5. Altered protein binding
6. Increased comorbidities
7. Increased polypharmacy

**Concepts for opioid rotation**

1. Potency
2. Equianalgesia
3. Equi-mu agonism (eg. Tapentadol 30% agonist)
4. Cross-tolerance
   1. NB: Studies often on single doses

**Opioid’s effect driving by**

* Sedation
* Reduced reaction times, reflexes, and coordination
* Reduced peripheral vision and night driving
* Decreased concentration

**Driving rules with opioids**

* No opioid better than any other
* Once dose is stabilised the person can drive as neuroadaptation occurs rapidly
* Stable dose of opioid does not confer increased risk of crash
* Dose should be stabilised over several weeks
* Conditional licence if in a treatment program and in remission for 3 months with no other contraindication to driving

**Strategies to improve appropriateness of opioid use**

* Standardised definitions and laws across states and territories
* Effective national surveillance and scripting program
* Up-scheduling of codeine
* Improved analysis of PB prescriptions
* State and territory systems to support continual and coordinated care for complex patients
* Improved use of opioids in acute settings
* Support for the 'medical home' concept
* Adequate education and supporting for general practice
* Improved collaboration with pharmacists
* Education of health professionals of non-pharmaceutical EBM treatments

**Gabapentinoids**

* Increased risk of OIVI
* Dramatic increase in poisonings and deaths in AUstralia since 2013
* One in seven Australians dispensed is at high risk of misuse
* Pure overdoses are relatively safe but high risk when combined with other substances

**Route of administration**

1. Fentanyl and Buprenorphine work because they are so lipophilic!
2. Can get through the stratum corneum of the epidermis

**Mechanisms of opioid induced bowel dysfunction**

1. KOR, MOR, DOR in enteric nervous system from mid oesophagus to rectum
2. Effect’s motility, and ion and water transport
3. Opioids cause reduced neurotransmitter release and neuronal excitability
4. Contractions are non-propulsive
5. Increased absorption and decreased fluid secretion
6. Increased anal sphincter tone
   1. NB: Avoid lactulose and sorbitol – increased gas

**Mechanism of opioid induced nausea and vomiting**

1. Opioids trigger MOR in the chemoreceptor trigger zone
2. Can trigger vestibular apparatus
3. Inner ear has DOR and KOR – unclear effect

**Mechanisms of tolerance**

* Innate: Genetic makeup
* Acquired
  1. Cells internalise their mu and delta opioid receptors
  2. Endogenous opioids are not strong enough once exogenous ones are removed (withdrawal)
  3. Intercellular second-messenger systems are down regulated (G proteins and adenylyl cyclase/cAMP) with high levels of potent exogenous opioids.

**Mechanism of opioid induced hyperalgesia**

1. Opioids activating toll-like receptor 4 on Glial cells
2. Increased glutamate release and cytokines
3. Long term potentiation of dorsal horn

**Mechanism of opioid tolerance**

* Innate = pharmacogenetics e.g. CYP2D6 polymorphisms
* Acquired
  1. MOR receptor desensitisation
  2. NMDA receptor changes
  3. Upregulation of drug metabolism and excretion
  4. MOR receptor endocytosis and recycling

**Reason for buprenorphine in substance use disorder**

1. Partial agonist
2. No intensity of mood alteration and no intense high with use
3. However, still prevents cravings and withdrawal symptoms
4. Binds tightly to mu receptor preventing other opioids from binding

**Analgesics in pregnancy**

* Paracetamol is ok
* NSAIDs (Avoid generally – definitely in first and third trimesters)
* Opioids no evidence of congenital defects. Risk of neonatal abstinence syndrome if taken in later parts of pregnancy
* Codeine – Not for breast feeding
* Duloxetine appears to be safe (limited numbers in studies)
* TCAs - Safe

**Ketamine for the management of chronic pain FPM Statement (2021)**

1. Paucity of quality evidence in CNCP
2. Unclear studies with reduction of pain versus reduction of opioid dosage
3. There is suggestive that benefit of ketamine may outlast the expected duration of the drug indicating possible effect on desensitising neuronal circuits

**Proposed mechanisms of ketamine**

* Inhibition of NMDA
* Intrinsic analgesic effect (opioid receptors, monoamine systems, cholinergics)
* Central antinociceptive effects
* Attenuation of opioid tolerance and hyperalgesia
* Cytokine effects (reduction)
* Brain Derived Neurotrophic Factor (BDNF) effects (effects on depression)

**Pharmacokinetics**

* Tmax = Time to maximum dosage
* Bioavailability = Proportion of drug in circulation and able to have an active effect
* Volume of distribution = Amount of drug in the body (dose) to the concentration of a drug (C)
* Biotransformation = Process of chemicals being converted in the body by enzymatic reactions to products that are more hydrophilic

**Pharmacodynamics of Drugs**

* Dose response: Measured response to a particular dose – helps calculate therapeutic window (ED50)
* Potency: The concentration (EC50) or dose (ED50) of a drug required to produce 50% of that drugs maximal effect
* Tolerance: Larger doses required to gain the same effect
* Efficacy: Maximum effect expected from this drug

**Analgesics in breast feeding**

* Not for codeine specifically
* Not for Aspirin (Reye’s syndrome risk)

**Psychological factors and Problematic substance use**

**Risk factors for suicidality in chronic pain (Racine 2018)**

1. Social
   1. Unemployed
   2. Disability
   3. Childhood/adulthood adversity
2. Psychological
   1. Depressive symptoms
   2. Anger problems
   3. Harmful habits
   4. Hopelessness/helplessness/burdensomeness
   5. Insomnia
3. Biomedical
   1. Family history of depression/suicide
   2. Pain severity
   3. Male gender
   4. Prescription pain medication access

**CBT factors**

1. Chronic pain psychoeducation
2. Relaxation techniques
3. Behavioural activation coupled with time-based pacing
4. Sleep hygiene
5. Cognitive restructuring
6. Communication skills
7. Maintenance and relapse prevention

**Risk factors for substance use disorder**

1. Biomedical
   * Family history of substance abuse
   * Personal history of substance abuse
   * Opioid exposure at a younger age
   * Higher pain levels
   * Multiple pain complaints
2. Social
   * History of criminal/legal problems
   * Regular contact with high-risk people
   * Past problems with employers, family members, friends
   * Risk taking behaviours
   * Heavy tobacco use
3. Psychological
   * History of depression/anxiety
   * Previous treatment programs including AA

**Opioid Risk Tool**

* Written by Webster 2005
* Adult patients in primary care settings before prescribing opioids
* Answered by the patient
* 5 items
  + (Personal history of SU, Family history of SU, Age 16-45, Childhood sexual abuse, psychological illness)
* Validated for future aberrant opioid use in chronic non-malignant pain
* Modified ORT removes the gender differences

**Red flags of aberrant drug-taking behaviours**

* Seeking
  + Doctor shopping
  + Borrowing / stealing / hoarding
  + Sex for drugs
  + Opioids more than one source
* Benefitting
  + Selling their script
  + Forgery
  + Reporting lost/stolen meds
* Abnormal pain behaviours
  + Disproportionate pain
  + Negative interactions with providers
  + Anxiety or desperation over symptoms
* Maladaptive coping
  + Drinking alcohol
  + Using other substances
  + Raising opioid dose on their own

**Benefits of a pain team**

* Evidence of greater functional improvements compared to regular PT
* Multidisciplinary Biopsychosocial rehab = for reduced pain and disability in chronic low back pain.
  + More effective than usual care (moderate quality evidence)
  + More effective than physical treatments (low quality evidence)

**Substance dependence changes for DSM5**

* Difference between terms ‘dependence’ and ‘abuse’ was not clinically useful
* Created diagnostic orphans – those that fit two criteria of one but none of the other
* Hierarchical structured did not follow clinical relationship between abuse and dependence
* Abuse diagnosis had significant reliability problems

**ICD-11 vs DSM 5 substance use disorder**

* Sub-types are categorised differently
* Polysubstance removed from both
* Gambling and gaming added to both
* DSM 5 SUD very broad – over 2000 combinations to get diagnosis
* Craving added to DSM 5 to bring in line with ICD-11

**Procedural evidence**

**Spinal cord stimulation**

1. Failed back surgery syndrome
2. CRPS
3. Peripheral vascular disease
4. Refractory angina
5. Painful diabetic neuropathy
6. Brachial plexitis

**Paediatric pain medicine**

**Complications when transitioning child to young adult pain clinic**

* Biomedical
  + Pharmacokinetic and pharmacodynamics change with age
  + Restricted opioid use
  + Contact difficulties for follow up
  + Health education level possibly low
  + Consent issues
* Psychological
  + Mood diagnoses, cutting, suicidality
  + Modelling of behaviour from adults
  + Acute psychological stressors
  + Previous trauma
  + Attachment style
  + Independence developing
* Social
  + Cultural
    - Language, rurality, ATSI, LGBTQI+
  + Home
    - Home setting, family support, family unit, finances
  + Education
    - Schooling, school avoidance, learning difficulties, future planning,
  + Activities
    - Hobbie and sport restrictions, risk taking behaviours, cigs/alc/drugs
  + Spiritual
    - Church factors, Existential

**Principles for transition from child to adult services**

* Systematic and formal process
* Early preparation
* Identify transition coordinator
* Good communication
* Individual transition plan
* Empower young person
* Follow up and evaluation

**CRPS**

**Causes**

* **Peripheral MSK**
  + Fractures, sprains, surgery, dislocation, immobilisation, tendonitis etc.
* **Peripheral Nerves/DRG injury**
  + Trauma and injury to brachial plexus and specific nerve sites
* **CNS**
  + Post-stroke, tumours, traumatic brain injury
* **Visceral**
  + Can occur after MI
* **Idiopathic**
  + Spontaneous in <10%

**Mechanisms**

* Genetic predisposition
* Inflammation / peripheral sensitisation
* Reduced nociceptor neurone density
* Increased expression of adrenergic receptors
* Sympathetic-sensory afferent coupling
* Spinal central sensitisation
* Changes in cortical representation
* Emotional arousal

**Evidence base for CRPS treatment**

* Evidence for: Ketamine, Gabapentin, DMSA, Corticosteroids, Bisphosphonates, CCB, SURGICAL sympathectomy, SCS, Physio, OT
* *No evidence for: Paracetamol, TCA, pregabalin, phenytoin, carbamazepine*
* *No evidence for: rehab or psych treatments*
* *Insufficient evidence for: NSAIDs, Opioids, LA, Capsaicin, Muscle relaxants, Botox, amputation, TENS, or IT baclofen*
* *Not helpful: IV sympathetic block, IV treatments, Percutaneous symp blocks*

**Approach to acute CRPS**

* Early referral to specialised service
* MDT and multimodal approach
* Physio-motor imagery
* CBT – address fear avoidance
* Avoid opioid / wean / cease
* Cease smoking
* Address PTSD (if injury related)
* Pharmacological approach
  + Pain processing
    - Gabapentin/PEA/Ketamine
    - Compound creams
    - PRF to DRG
  + Autonomic
    - PRF to sympathetic chain?
  + Immune aspect
    - Prednisone
    - Bisophosphonates
    - Aspirin
    - Vit C

**Approach to chronic CRPS**

* Early referral
* MDT and multimodal
* CBT – address fear avoidance
* Remove opioids
* Cease smoking
* Treat PTSD
* Pharmacology
  + Intensive PMP
  + Ketamine infusion
  + Lignocaine infusion
  + SCS

**Prevention of CRPS**

Primary prevention

* Vitamin C 500 mg daily for 50 days from injury

Secondary prevention

* Operations postponed until CRPS 1 signs are minimal
* Regional anaesthetic techniques
* Stellate ganglion block
* Multimodal analgesia
* Daily subcut calcitonin (to help prevent relapse)

Physical therapy

* Desensitisation
* Reactivation
* Pacing
* RE-engage with regular activities
* Self-management focus

Functional therapy

* Reduce contractures
* Improve function at home
* Address vocational issues
* Aim for return to work
* Reduce sick days

**CRPS four pillars of care**

1. Education
2. Pain relief
3. Physical rehabilitation
4. Psychological intervention

**CRPS physical therapy**

1. Gentle limb movement
2. Frequent attention to affected limb
3. Normalising sensation – desensitisation
4. Increase to active use as able
5. Graded motor imagery
6. Tactile discrimination
7. Stress loading

**Pharmacological therapy for CRPS**

1. Usual neuropathic agents (though not extensively studied)
2. NSAIDs may be used however AEs must be considered
3. Bisphosponate - Pamidronate can be used as a one off IV dose 60mg
4. Corticosteroids – 40 mg daily for 2 weeks and then wean – some evidence of benefit in small RCTs
5. Sympathetic blocks (evidence is unclear)
6. SCS – Some RCTs to suggest benefit
7. Vitamin C for prevention has mixed outcomes of low-quality evidence
8. Clonidine topically or lidocaine topically
9. Calcitonin – possibly some low-level evidence

**Risks of CRPS with limb amputation**

1. Development of phantom limb pain
2. Development of stump pain preventing prosthesis
3. CRPS in the remaining part of limb
4. CRPS occurring in other limbs
5. Delayed wound healing

**CRPS pathophysiology pathways**

1. Aberrant inflammatory mechanisms
2. Elevated cytokine signalling / Immune
3. Vasomotor dysfunction – sympathetic/afferent coupling
4. Maladaptive neuroplasticity
5. Possibly loss of disinhibition

**CRPS clinical course**

* Minor or moderate tissue injury --> limb is painful, red, and warm --> Cold and swollen --> allodynia, hyperalgesia, sweating, hair, nails and muscle changes --> motor control can be reduced and then hyperpathia --> hypoesthesia, hypolalgesia, and hypotheraesthesia can occur
* Dystonia, tremor and myoclonus may develop

**CRPS epidemiology**

* Incidence increases to age 70
* Women 3-4 times more common than men
* Arm 60% and leg in 40%
* Triggered most commonly by fracture, sprain or elective surgery

**CRPS risk factors**

* Psychological factors
  + Unlikely anxiety and depression – conflicting studies
* Immobilisation
  + Experimental suggestion that immobility is a risk
* Epidemiology
  + ACE inhibitor use
  + Migraine hisory
* Demographics
  + Women more severe than men but NOT increased risk
* Genetics
  + Possibly genetic polymorphisms in TNFalpha

**Chronic widespread pain**

**Problems with the term ‘medically unexplained symptoms’**

* Relies upon someone to have a medically unexplained symptom – the reliability of this notion is limited
* Diagnosis is based on the absence of evidence
* Reinforces mind-body dualism
* Providing a psychiatric diagnosis for medical science’s shortcomings is illogical
* Unacceptable to patients to be labelled with a psychiatric disorder or that their suffering is not genuine
* They do not form a coherent category – just an absence of something

**Basis of Somatic symptoms and related disorders**

* Prominent somatic symptoms with significant distress and impairment and disruption in daily life

**Subcategories of Somatic Symptoms in DSM5**

* Somatic symptom disorder
* Illness anxiety disorder (hypochondriasis)
* Conversion disorder (Functional neurological symptom disorder)
* Psychological factors affecting other medical conditions
* Factitious disorder
* Other specified
* Unspecified

**Myofascial pain syndrome**

* Regional pain from hyperirritable spots in skeletal muscle
* Causes are unknown – trauma/repetitive strain/postural
* No diagnostic criteria (three main bits)
  + Taut muscle
  + Exquisite tenderness over that muscle
  + Reproduces the person’s pain
* Minimal evidence for any treatments. Maybe botox. Maybe dry needling

**Fibromyalgia**

* Most common in women 20-55yo
* Prevalence increases with age
* Presentation – *at least 3 months not explained by another*
  + Pain – Multisite (usually >6 sites)
  + Fatigue
  + Sleep disturbance
* Psychiatric symptoms co-occurring
  + 30-50% at diagnosis also have depression/anxiety
* Headache’s co-occurring
  + 50%

**Fibromyalgia diagnostic criteria (2010 American College of Rheumatology)**

* WPI > 7 and SSS > 5 (75)
* WPI 4-6 and SSS > 9 (469)
* Symptoms for > 3 months
* Not explained by another
* *ACTTION-APS Pain Taxonomy group tried to define further in 2019. Multisite pain defined as 6 or more sites from possible 9*

**Pathophysiology of Fibromyalgia**

* Temporal summation of pain
* Decreased endogenous pain inhibition
* Upregulation of pronociceptive peptides e.g. substance P
* Brain pain dysregulation
  + Morphology changes
  + Neurotransmitter changes
  + Resting state connectivity changes

**Evidence of therapeutics**

* Education – 2019 Systematic review showed reduced pain intensity and anxiety
* Exercise – 2017 Systematic review improves QOL and aerobic exercise may reduce pain and improve physical function
* Pharmacology
  + Gabapentinoids – 2018 Systematic review improved pain and sleep - pregabalin (NNT = 14)
  + TCA some benefit - 2015 Systematic review (NNT = 4)
  + Benefit from duloxetine - 2013 SR (NNT = 8)
* Address comorbidities (no specific evidence base) (sleep, mood, IBS)

**Describe difficulties in labelling CWP**

* ICD-10 required pain to be described in terms of its underlying pathophysiological process
* If this process could not be defined, the pain condition was classed as psychiatric in nature and classified under somatoform disorders
* Increasing pain understanding demonstrates these are likely conditions in their own right
* Terms like ‘functional’ never made sense – improving function?

**Definition of Chronic primary pain**

* Persists for longer than 3 months
* Associated with significant emotional distress and/or functional disability
* Symptoms not better accounted for by another diagnosis
* *It is then described in terms of location*

**Chronic widespread pain diagnosis**

* Diffuse musculoskeletal pain in 4 of 5 body regions and 3 or more body quadrants and axial skeleton
* With significant distress and/or functional disability

**CWP Pathophysiology theory**

* Persistent activation of evolutionarily conserved physiological system designed to defend and repair organism from challenges to homeostasis
* SP/NK1R pathway activation (Substance P and Neurokinin 1 pathway)

**Somatic Symptom Disorder evolution**

* Introduced in DSM 5 and replaces 3 DSM 4 entities (somatisation disorder, pain disorder, and undifferentiated somatoform disorder)
* Introduced because:
  + Questionable label of ‘medically unexplained pain’
  + Previous diagnoses were conditions of exclusion
* Criticised by:
  + Diagnostic inflation (though ultimately this has not been proven)
  + Fear of misdiagnosing a medical illness as SSD
  + Inadequate field testing
* Risks of SSD category
  + Stigma
  + Overlooked diagnoses with failure to investigate new or worsening symptoms
  + Increased risk of inappropriate psychotropic meds
  + Gender concerns (women more commonly diagnosed than men)

**Somatic Symptom Disorder - Diagnostics**

* A - One or more somatic symptoms that are distressing or result in significant disruption of daily life
* B – Excessive thoughts, feelings, or behaviours related to the somatic symptoms or associated health concerns as manifested by one of the following
  + Disproportionate and persistent thoughts about the seriousness of ones symptoms
  + Persistently high level of anxiety about health or symptoms
  + Excessive time and energy devoted to these symptoms or health concerns
* C – Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically > 6 months)
* SPECIFICATIONS
  + With predominant pain
  + Persistent > 6 months
  + Mild/Moderate/Severe

**Evidence of therapeutics for SSD**

* Cochrane 2015 – Minimal evidence for pharmacological therapies
* Cochrane 2014 – CBT, mindfulness, psychodynamic and integrative therapies – superior to usual care – but limited studies.

**Risk factors for SSD**

* Epidemiological
  + Female
  + Lower socioeconomic
  + Lower education
* Comorbidities
  + History of sexual abuse
  + History of childhood chronic illness
  + Concurrent medical disorders
  + Health anxiety
  + Psychiatric disorder
  + Family history of chronic illness

**Functional Neurological Symptom Disorder**

* One or more symptoms of altered voluntary motor or sensory function
* Clinical features are incompatible between symptoms and recognised medical/neuro conditions
* Symptoms not better explained by medical or mental health disorder
* Clinically significant distress in social, occupational, or other areas of functioning

**Assessment of FND patient**

* Ask about all effects upon life
  + Sleep
  + Pain
  + Fatigue
  + Memory
  + Concentration
* Ask about depression/anxiety as common in this group
* Ask about functional comorbid conditions
* PHQ15 can be used as a questionnaire

Topical issues:

**Covid-19**

**Benefits of telehealth: (IASP, 2021)**

1. Savings
2. Avoidance of travel
3. Reduction in delays
4. Improved patient satisfaction, compliance and QOL
5. Avoids physical interaction with challenging patients/families
6. Improved time management
7. E-mail communications easily documented
8. Less dedicated patient wait areas and supports
9. Can be performed even if the doctor is not in the clinic
10. Allows remote communication between clinicians also

**Cons of telehealth: (IASP, 2021)**

1. Communication less effective
2. Lack of paper interaction
3. Lack of universal access
4. Upgrade tools for remote care
5. Time consuming patients education on use
6. Requires high level equipment/software
7. Requires internet access
8. Lack of body language
9. Arguably weaker clinical alliance with patients
10. Manual skills cannot be perfectioned

**Barriers to telehealth: (IASP, 2021)**

1. Lack of evidence-based research on long-term outcomes
2. Unforeseen harms are unknown
3. Potential inequity in access
4. Use in elderly and disabled is unknown

**Steps in successful telehealth consult: (IASP, 2021)**

1. Verbal consent
2. Patients aware of possible limitations
3. There is suggestion to only do phone after initial F2F appts if possible
4. Confidentiality should be maintained

**Health system impacts of COVID-19 (IASP, 2021)**

1. Pharmacological drug access and shortages
2. Closure of multidisciplinary services
3. Confinement measures leading to loss to follow up
4. Fear of going to health appointments
5. Increased non-medical use of illicit or prescribed substances

**Possible secondary causes of pain from COVID-19 (IASP, 2021)**

1. Herpes zoster
2. HIV
3. Enteroviruses
4. Zika
5. Guillain-Barre
6. Myelitis
7. Stroke
8. Encephalitis
9. Worsening of co-morbidities

**Cannabinoids (Nature, 2017)**

1. Exerts its actions through THC and CBD
2. THC activates CB1 and CB2 receptors
3. CBD does not activate these receptors
4. CBD may reduce psychotropic effects of THC
5. CB1 is mostly in CNS and PNS
6. CB2 is mostly in immune cells and peripheral

**Cannabinoids and chronic pain: (FPM statement)**

1. FPM states doctors are urged not to prescribe cannabinoids for non-cancer pain unless part of a clinical trial
2. IASP states there is a lack of evidence for cannabinoids to be used to treat pain. Systematic reviews that have been completed have been critiqued heavily and are difficult to pool/compare
3. TGA in 2017 recommended that only use of cannabis in clinical trials is recommended due to the paucity of appropriate evidence for their use
4. There is a critical lack of evidence that cannabis provides a consistent benefit for any type of non-cancer pain
5. Evidence is either unsupportive or of low quality so no scientific conclusion can be drawn

**End of life cares (FPM 2017 submission to NZ parliament)**

1. Patient advocacy – Protect patient’s rights and ability to exercise those rights
2. Health advocacy – Ensure research into palliative care is not an unintended casualty
3. Practitioner advocacy – Practitioners are protected through legislation
4. Skill safety – Appropriate education and support should be provided
5. Priority – Alleviation of patient suffering
6. Access – Those in rural and remote areas and disadvantaged should have equal access
7. Coercion – Avoided at all costs and in all facets
8. Medical practitioners right to conscientious objection
9. Predictions at end of life are difficult
10. Psychiatric assessment is not required in all settings unless there are concerns about capacity

**Radiology**

**Evidence and therapeutics table**

|  |  |
| --- | --- |
| **Condition** | Therapeutic evidencial statements (Sept 2021)  *Be aware – if NOTHING written about something – then its stance is one of the (101) statements.*  *Strongest grouped together at the top otherwise ‘weak or absent evidence of benefit’* |
| Trials to quote by name | **ROCKET** – Australian Trial looking at Ketamine benefit at 3 and 12 months  **SPORT**  **SPACE trial**   * Showed opioids use was not more effective than non-opioid management of chronic back pain, hip and knee pain with OA   **HUNT Trial** 2020 –   * Longtitudinal study – Significant association between depressive symptoms and pain. Association was stronger in patients with catastrophisation.   **MINT trial 2013** – Managing Injuries of the Neck Trial   * Stepped care approach following whiplash injury over 12 month period * Outcome was Neck Disability Index * Suggested psychoeducational interventions in ED are no more effective than usual care advice for reducing burden of acute whiplash injuries * Physiotherapy was more effective in multiple sessions rather than one. Benefit was return to work earlier   **PROMISE trial 2014** - MINT continued essentially   * Showed no benefit in intensive physio program over simple education for chronic whiplash-associated disorders (after they had already had symptoms for 3 mths)   **POINT Study –** Pain and Opioids IN Treatment (2015)   * Higher OME associated with higher physical and mental health issues, aberrant opioid use, probelms with opioids, and opioid dependence. * Cannabis use is common in CNCP (25%) but not evidence that cannabis use improved patient outcomes   **LAIDBack Study –** Showed 1 in 5 asymptomatic people over 75 have evidence of spinal canal stenosis |
| Neuropathic Pain(101) | **First Line. NNT**  **NNH**  TCA’s (amy/nor) 3.6 14  SNRI Duloxetine 6.4 8  Venlafaxine 6.4  Gabapentin IR/SR 7.2 12  Pregabalin 7.7 8    **Second-Line**  Capsaicin 10.6  Lignocaine patch 4.4  Tramadol 4.7    **Third-Line**  Botulinum toxin A 1.9  Strong opioids 4.3- DNP 2.6  PHN- 1st Line TCA 2.6, Pregabalin 3.9, Lig 4.4  DPN 1st Line TCA 3.6, SNRI 4.5, Pregabalin 5    CINP- Duloxetine Moderate Benefit  Trigeminal Neuralgia- Carbamazepine 1.7 |
| Acute pain | Paracetamol - NNT 3.6 for 1g PO and 4.0 for IV  Opioid - NNT with morphine 10 mg IV = 2.9 for 50% reduction  Gabapentin - NNT 11 for reduction of postoperative pain and reduced rescue analgesia NNT 6 for reduction in PONV at 24hrs  **Position statement**  Long-acting opioids should be avoided in Acute pain management – ANZCA/FPM 2018  Statement recently shown to result in clinical reduction in SR and CR analgesic use in acute settings (2021) |
| Chronic pain – General  Reference:  **COHEN, VASE and HOOTEN 2021 – Chronic pain: Lancet 2021** | CBT – Cochrane 2020 - systematic review showed CBT, but **NOT** behavioural therapy, provides small benefit in the short term but not when compared to an active control  Physical therapy - Cochrane reviews suggest  Exercise is more beneficial for function (strong evidence of small effect) than pain relief (conflicting evidence for small effect)  Better for MSK than neuropathic  No one exercise better than another  Yoga, Tai Chi - Little evidence of effect beyond regular exercise (RCTs)  Chiropractor - Maybe slightly better than active comparators – but quite unclear standardising of therapy (Meta analysis)  TENS – Cochrane review - Low quality evidence due to flawed study. Small benefit in NeuP, conflicting evidence in non NeuP. May be useful for short lasting breakthrough pain  Music – Better for depression than pain (RCTs)  High dose opioids - Cochrane 2017 - No high-quality evidence to show how well high-dose opioids work for CNCP.  Position statement |
| CRPS | ***USUAL NEUROPATHIC PAIN 101 evidence +***  *Cochrane 2020 – Review of evidence*  Low quality evidence that bisphosphonates, calcitonin, and IV ketamine may be better than placebo  Ketamine infusion may provide benefit up to 12 weeks after provision  Physiotherapy and OT - have greater evidence of efficacy <12 months  GMI and mirror therapy - may provide benefit but quality and quantity of evidence is low.  Sympathetic block - Low quality evidence of LACK of benefit  SCS – Moderate evidence of benefit over conventional therapy for pain and function. DRG may be further efficacious. |
| Spinal Cord Injury  Bryce, T.N. Opioids should not be prescribed for chronic pain after spinal cord injury.*Spinal Cord Ser Cases* **4,**66 (2018). <https://doi.org/10.1038/s41394-018-0095-2>  Siddall, P. Management of neuropathic pain following spinal cord injury: now and in the future. *Spinal Cord* **47,**352–359 (2009). https://doi.org/10.1038/sc.2008.136 | ***USUAL NEUROPATHIC PAIN 101 evidence + however LESS efficacious than other conditions***  ***Pharmacological agents are minimally efficacious in the management of chronic post spinal cord injury pain***  Pregabalin has small evidence of benefit in pain scores and sleep. Though further recent trial suggested no benefit for gabapentin.  *MSK requires addressing the acute MSK cause. Treatment will depend upon that condition (e.g. carpal tunnel). Use the WHO ladder.*  Botox - RCT of 40 patients injected in maximal pain area showed some benefit  Ketamine – Shown to be more effective than placebo for below-level pain though evidence is weak  Valproate *–* Recent study suggests no better than placebo  Venlafaxine and duloxetine - case reports of benefit only  TCA – No significant benefit over placebo  Procedures have limited benefit  Intrathecal baclofen – Some evidence of benefit for chronic spasticity. Mixed evidence of benefit for neuropathic pain.  Intrathcal morphine and clonidine – showed some benefit but limited duration/administration options.  Opioids – There are no high quality RCTs supporting use of opioids either acutely or chronically for SCI specifically  SCS – Better with ‘at level’ and incomplete lesions  Deep brain stimulation – Not shown to be helpful  CBT – Evidence of benefit for mood but not pain scores  Cognitive motor imagery - not know. Mixed results currently. |
| Phantom Limb Pain  (UpToDate 2021) | Low to moderate quality trials with usual agents (Gaba, Ketamine, TCA, lidocaine)  Mirror therapy, virtual reality, peripheral nerve stimulation – small trials – difficult to draw meaningful conclusions  Suggest treating as neuropathic pain 101. |
| Chronic post-surgical pain | **Clear Benefit**  Ketamine – ASME Level 1 cochrane - >24 hrs reduces incidence  *Procedural regional analgesia*  Thoracotomy – Meta-analysis benefit for epidural  Breast cancer – Meta-analysis benefit for regional  Caesarian – Meta-analysis spinal over GA  Phantom limb pain – Level 3 – reduced with epidural  CBT may have some evidence of reduced CPSP severity  Lignocaine – Preventative effect for ACUTE post op pain and CPSP - Level 1.  **Unclear**  Surgery – minimally invasive better acute pain but no evidence for CPSP.  Surgery – sparing intercostobrachial nerve in mastectomy does not affect hyperalgesic effects  **No benefit**  Neuroeducation – no clear evidence of benefit on CPSP  Gabapentin – No evidence of benefit – Lvl 1 cochrane |
| Low back pain | **CBT and ACT –** Evidence of reduced disability and catastrophising (systematic reviews)  **Exercise** – No single modality has been shown to be more beneficial than another – Walking, aerobic, stretching, yoga, core exercises (2016 Systematic review). May help prevent relapse.  **Spinal manipulation** – 2011 & 2018 Meta analysis – Short-term effects on pain reduction compared to routine  **Acupuncture** – Mixed results in studies. Well blinded trials show little to no benefit from acupuncture versus sham.  **Massage** – Short term efficacy in 25 trials.  **Lumbar Supports** – RCT showed some benefit at 30 and 90 days but not recommended as reinforces psychological sequelae of back problem  **Bed mattress –** Soft better than hard in small RCTs  **TENS** – Meta analysis of 9 trials – no benefit.  **NSAIDs** – Slightly more effective than placebo in RCTs  **Paracetamol** – Conflicting results  **Duloxetine**  - 2021 meta-analysis – more effective than placebo for pain and disability at 3 months. Benefit was small.  **TCAs** – 2021 Meta Analyssi benefits at 3 mths similar to SNRI  **Opioids** – Systematic reviews and meta-analyses have few high quality and no long-term trials. Small improvements versus placebo in the evidence available however clearly risk of harms.  **Tramadol** – Minimal evidence  **Benzodiazepines** – Some reduction in pain in systematic trials but risk of dependence is very high  **Gabapentinoids** – No benefit if no radiculopathy. Some small or unclear benefits if they have radiculopathy.  **Glucosamine** – Not helpful |
| Back pain – procedural  (UpToDate 2021) | **ESI for Radicular lumbar pain from disc** –  Small benefits for shorter term pain and function vs placebo. Some benefit for reduction in leg pain and disability at 2 weeks and decreased surgery at 3 months (Systematic review 2015)  **ESI For spinal stenosis** – Low quality evidence of minimal benefit  **Spinal fusion** – Systematic reviews have not shown benefit between surgical and non-surgical management for chronic back pain. Comparators remain difficult, elderly are often excluded from trials, and few randomised trials.  **Lumbar disc replacement** – Systematic review 2012 – Bias and sponsorship of trials. No significant difference between groups in pain scores.  **Discectomy** – open or micro – RCTs show similar outcomes at 2 years. Studies were not blinded. SPORT outcomes showed no better pain outcomes after three months, 4 and 8 years. Secondary outcomes were better (e.g. sciatic bothersomeness and patient satisfaction)  **Micro vs Open discectomy** – Small trials have shown no significant difference  **Physiotherapy after surgery** – unclear benefit  **Spinal stenosis and spondylolisthesis**   * Laminectomy – some evidence of benefit over non-surgical at 4 years but gone by 8 years. Observational cohorts have favoured surgery but varies and benefits decline with time. * Spacer implants – Good improvements at 6 months, 2 and 4 years. Higher rates of subsequent surgery and complications. Less helpful in spondylolisthesis. * Decompression surgery in spondylolisthesis – Unclear results   **Spinal cord stimulation after surgery** – Significant benefits over conventional medical management. No RCTs have looked at SCS outside of post-surgical. |
| Chronic widespread pain (particularly fibromyalgia)  Kia, S., & Choy, E. (2017). Update on Treatment Guideline in Fibromyalgia Syndrome with Focus on Pharmacology. *Biomedicines*, *5*(2), 20. https://doi.org/10.3390/biomedicines5020020 | **Amitriptyline** – Meta analysis – benefit for pain, sleep and fatigue NNT = 4  **Pregabalin/Gabapentin** – Cochrane review benefit on sleep, fatigue and QOL at 8 weeks. NNT = 14  **Duloxetine (RCTs)** – Dose 60 mg / day – particularly with comorbid mental health concerns – NNT = 8  **SSRI** – No benefit over placebo (Cochrane)  **Opioids** – no evidence of benefit and suggestion of harms  (Tramadol may be considered in some countries guidelines)  **Cannabinoids** – No clear evidence of benefit in available current studies  **NSAIDs** – No evidence of benefit in small studies  **Ketamine** – Strong negative evidence of benefit |
| Pelvic Pain | **Progesterone** is more effective than placebo (Medroxyprogesterone acetate) Cochrane  **Gabapentin** may be more efficacious than amitriptyline (Cochrane). Use of pregabalin and gabapentin is extrapolated from use in fibromyalgia and neuropathic pain in general.  **SNRI** – Evidence extrapolated from other areas of use  **TCA** – Evidence extrapolated from other areas of use  **NSAIDs** – very low level of evidence. Societal guidelines generally support their use. Useful specifically in dysmenorrhea (NNT = 3). Naproxen better than cox-2  **Intravaginal diazepam** – Very limited evidence of use. No evidence of benefit at this time.  **Topical amitriptyline** – no evidence of benefit – too minimal studies to draw conclusions |
| Visceral pain |  |
| Somatic Symptom Disorder | Cochrane 2015 – Minimal evidence for pharmacological therapies  Cochrane 2014 – CBT, mindfulness, psychodynamic and integrative therapies – superior to usual care – but limited studies. |
| CRPS | Evidence for: Ketamine, Gabapentin, DMSO, Corticosteroids, Bisphosphonates, CCB, SURGICAL sympathectomy, SCS, Physio, OT  *No evidence for: Paracetamol, TCA, pregabalin, phenytoin, carbamazepine*  *No evidence for: rehab or psych treatments*  *Insufficient evidence for: NSAIDs, Opioids, LA, Capsaicin, Muscle relaxants, Botox, amputation, TENS, or IT baclofen*  *Not helpful: IV sympathetic block, IV treatments, Percutaneous symp blocks*   1. Bisphosponate - Pamidronate can be used as a one off IV dose 60mg 2. Corticosteroids – 40 mg daily for 2 weeks and then wean – some evidence of benefit in small RCTs 3. Sympathetic blocks (evidence is unclear) 4. SCS – Some RCTs to suggest benefit 5. Vitamin C for prevention has mixed outcomes of low-quality evidence 6. Clonidine topically or lidocaine topically 7. Calcitonin – possibly some low-level evidence |
| Osteoarthritis | **Intra-articular injections** - Recommended by some guidelines – Evidence of reducing cartilage volume however |
| Irritable bowel syndrome  Camilleri M. (2018). Management Options for Irritable Bowel Syndrome. *Mayo Clinic proceedings*, *93*(12), 1858–1872. [https://doi.org/10.1016/j.mayocp.2018.04.032)](https://doi.org/10.1016/j.mayocp.2018.04.032) | *Evidence:*  *FODMAPS NNT = 2.2*  *General dietary change NNT = 9*  *Psyllium addition for 12 weeks NNT = 4-7*  *Probiotics NNT = 7*  *Antispasmodics NNT = 5*  *Peppermint oil NNT = 2.5*  *TCAs NNT = 4*  *SNRI NNT = 4*  *Rifaximin NNT = 10*  *(*Camilleri M. (2018). Management Options for Irritable Bowel Syndrome. *Mayo Clinic proceedings*, *93*(12), 1858–1872. [https://doi.org/10.1016/j.mayocp.2018.04.032)](https://doi.org/10.1016/j.mayocp.2018.04.032) |
| General Headache Therapies | **CBT**  Systematic review gave mixed results (2015)  Shown to help with mood and not the disability of pain intensity scales  **Relaxation**  Not shown in a systematic review to have major positive effects on intensity or disability  **Mindfulness**  Evidence of benefit for pain reduction 2018 meta-analysis  **Sleep hygiene**  Too few studies. Maybe some benefit. Unclear.  **Exercise**  Aerobic exercise has been shown to reduce migraine attacks (RCT)  Physical therapies evidence remains unclear  **Diet**  Ketogenic diet, low calorie, low fat and low glycemic diets have been shown in case series to reduce daily headaches  **Massage**  Small RCTs show some benefits  Possibly greater benefit in tension-type headaches  **Acupuncture**  Acupuncture has been shown in Cochrane review to be at least equivalent to prophylactic medication for migraine |
| Evidence in acute migraine | **Simple analgesics**  Paracetamol reduces headache from moderate/severe to none in 2 hours in 1 in 5. 1 in 10 for placebo  **Non-steroidal anti-inflammatory drugs**  Level A evidence of benefit for migraine attacks  Single-dose of 1000mg of aspirin is very helpful  From Mod/severe to non by two hours in 1 in 4 people vs 1 in 10 with placebo.  **Antiemetics**  Addition often helps reduce nausea and vomiting and NNT is 4 for a significant reduction in pain in migraine  **Triptans**  RCTs and systematic reviews have shown triptans to be beneficial.  May be better given earlier in the treatment  Use with NSAIDs may be more efficacious than either alone - systematic review 2016  **Ergotomines**  Binds to 5Ht 1b/d receptors (same as triptans)  RCTs are a bit more unclear regarding efficacy/benefit than triptans  **CGRP**  Meta-analyses in 2021 suggest better than placebo acute migraine treatment with rimegepant [UPDATE: Hepatotoxicity – drug withdrawn] . More trials are needed  **Opioids**  Should not be used as first line therapy. High risk of return to ED with a repeat headache within 7 days of first visit  They are not as effective as migraine-specific medications  Risk of developing MOH and chronic migraine  **Nerve blocks**  Case series showed benefit for occipital nerve blocks  Possible benefit also for sphenopalatine blocks |
| Evidence in migraine prophylaxis | **Beta-blockers**  RCTs show benefit for migraine prevention (50% of patients will have 50% reduction)  And for Ag2 blockers (candesartan)  **CCBs**  Evidence is weaker and conflicting that CCBs and ACE are effective but still possible  **Sodium valproate**  Better than placebo in systematic reviews  **TCA**  Effective in 4 trials - However not recommended by NICE guidelines  **Topiramate**  Better than placebo  Several systematic reviews and meta analyses  **Pizotifen**  Little clinical trials of efficacy. NICE found minimal benefit.  **CGRP**  Monoclonal antibodies directed against the CGRP receptor or ligand - erenumab  Modestly effective for migraine prevention in placebo-controlled trials. |
| Trigeminal Neuralgia | **Carbamazepine**  Best studied for Classic TN - shown to be effective in systematic reviews NNT < 2  100-200 mg twice daily to maintainence 600-800 mg  Oxcarbazepine - Better tolerability than carbamazepine. Suggested both are equally effective.  **Gabapentin**  Shown to be possibly effective and fewer side effects than carbamazepine in 2016 meta-analysis - but studies were poor  **Clonazepam**  ***Not listed in UpToDate***  **Baclofen**  Limited evidence suggests a possible benefit  **Microvascular decompression**  Up to 90% reduction in pain however this reduced with time to 75% at 5 years  Mortality 0.2%  Hearing loss in up to 10% of patients however  **Radiofrequency ablation**  Similar efficacy to microvascular decompression however possibly mire complications with dysaesthesia in 12 %  **Balloon compression**  *As above - same studies*  **Radiosurgery / Gamma Knife**  Lag time of 1 month for onset of relief  Possibly less efficacious than RF or microvascular decompression  Worsening facial sensory impairment in 9-37% |

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| Red flags for back pain | Only previous cancer has strong evidence. | Cochrane 2013 |
| EVIDENCE FOR INTERVENTIONS | https://onlinelibrary.wiley.com/doi/full/10.1111/papr.12786 |  |
| **COHEN, VASE and HOOTEN 2021 – Chronic pain: Lancet 2021** | | |

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**Chronic back pain Intervention and evidence**

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| **Intervention** | **Magnitude of Effect** | **Strength of Evidence** |
| NSAID  Pain  Function | Small to mod  Small to no | Mod  Low |
| Strong Opioids  Pain  Function | Small  Small | Mod  Mod |
| Tramadol  Pain  Function | Mod  Small | Mod  Mod |
| Buprenorphine  Pain | Small | Low |
| Duloxetine  Pain  Function | Small  Small | Mod  Mod |
| Exercise  Pain  Function | Small  Small | Mod  Mod |

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| Drug Class | Mechanism of Action | Rationale for use in Pain | Evidence in Acute Pain | Evidence in Chronic Pain | Adverse effects |
| Paracetamol | Antipyretic-  1/ Inhibition of PG synthesis in the HT  2/ Weak inhibition of peripheral cyclooxygenase  3/ Interactions with endocannabinoid system, TRPV1 receptor and central 5HT pathways (descending inhibition)  4/ Potential inhibition of NO syntheses with effects on NMDA  Ultimately MOA unknown | -First line analgesic for mild to mod pain | * effects comparable to low dose naproxen, inferior to NSAIDs, but act synergistically * Synergistic with opioids   Efficacy for acute pain - Paracetamol 500 mg NNT 3.5 | Cancer Pain- do not work | -Hepatotoxicity with OD due to production of NAPQ1 and exhausting supply of liver’s glutathione   * can lead to haemolysis in G6PD deficiency * Can enhance effect of warfarin * Little or no GI or renal effects |
| NSAIDs | Inhibits breakdown of Arachidonic Acid by inhibiting enzyme cyclooxygenase to eicosanoids including PGE2, prostacyclin and TXA2  nsNSAIDs- antipyretic, antiinlammatory, antiplatelet, analgesic  Met in the liver  Ex in the kidney  Most half lives 2-3 hours (ex piroxicam (50-60 hours), higher half life, higher AE | 1/ PGE2 and prostacyclin- anti-inflammatory effects  2/ Reduction in prostaglandin in periphery- analgesic effect  reduces formation of prostaglandins in the SC and the brain and reduces central sensitisation  3/ Antipyretic- effect of a decrease in prostaglandin concentration in HT  1st line use in Dysmenorrhoea and migraines | * Sole Rx for mild to mod pain * Synergistic effect with opioids (opioid sparing) * Reduction in incidence of adverse effects of opioids * Synergistic effect with paracetamol   Diclofenac 100 mg - Efficacy NNT - 2.3  Ibuprofen 200 mg - Efficacy NNT - 2.1  Celecoxib 400 mg - Efficacy NNT - 2.6 | Cancer Pain- no high quality evidence and sign adverse events | -GI erosions- prostaglandin mediated protective fx of mucus production, blood flow and inhibition of gastric acid secretion is inhibited   * Renal toxicity- prostaglandin mediated vasoldilatory action mainatin renal blood flow and GFR inhibited * Plt fx- TXA2 presence inhibtion- Aspirin only NSAID to irreversibly inhibit COX1 * Resp- bronchospasm due to lipoxygenase pathway producing more leukotrienes |
| Opioids | Opioid 7 transmembrane receptor couple to GPCRs on neuron  1/ Close VGCa channels on presynaptic nerve terminals and therapy reduce transmitter release (Glutamate, ACh, NA, 5HT and substance P)  and  2/ open K channels and hyperpolarise thus inhibit post synaptic neurons  3/ Inhibit Adenylate cyclase> dec breakdown of ATP to cAMP therefore dec NT release    Sites on afferent pain pathway  A. Some effects may be mediated by opioid receptors on peripheral sensory nerve endings.  B. Dorsal horn at the post synaptic membrane and presynaptic membrane  C. Possible site of action in the in brain (amygdala, ACG, VPL nucleus , and spinal cord regions involved in transmission and modulation of pain.  Sites on descending inhibitory   1. Midbrain PAG 2. Medulla/Pons- RVM 3. Locus coeruleus indirectly controls pain transmission by enhancing descending inhibition to the dorsal horn.   -Act on descending inhibitory pathway indirectly by inhibiting the inhibitory (GABAergic) interneuron to enhance inhibition of nociceptive processing |  |  |  | Resp  - OIVI   * Cough supression * Sleep disordered breathing   CNS   * Sedation, euphoria, dysphoria, N&V, miosis, cognitive impairment, delirium, muscle rigidity, myoclonus, seizures, impairment of driving   GI, GU   * delayed gastric emptying, constipation, spasm sphincter of odd, urinary retention, cholestasis   CVS   * vasodilation (helpful in MI), bradycardia, prolonged QT (methadone)   Pruritis  Allergy  Tolerance, OIH, physical dependence- may be seen 7-10 days of commencing opioid  Other   * Serotonin Syndrome * Immunosupression * Endocrinopathies * Inc risk of early and late post op complications * Inc risk of falls, fractures and other trauma * PPOU, diversion, misuse |
| Tramadol | Centrally acting synthetic analgesic, structurally related to opioids  Naloxone only inhibits 30% of effect. Enhances serotonin release and inhibits reuptake of noradrenaline and serotonin | 150 mg - NNT = 2.9 |  |  |  |
| Tapentadol | -modest mu opioid receptor affinity and signifanct NA reuptake inhibiting action.   * only modestly reduced by naloxone, but strongly reduced by alpha2 adrenoceptor antagonist * Binding to NA transporter was stronger than tramadol, but less for 5HT transporter than tramadol * Reduced GI profile eg nausea * Risk of seizures and serotonin syndrome | Lower rates of doctor shopping  Reduced GI adverse effects  Unlikely to get serotonin syndrome  Mu load approximately 40% (compared to 100% for typical opioid)  Very very rare in drug overdose |  |  |  |
| SSRI | Inhibition of serotonin transporter SERT thereby decreasing reuptake and allowing more serotonin available in the synaptic cleft |  | Minimal role acutely |  |  |
| SNRI | Inhibition of SERT and NA transporter NET on the presynaptic nerve terminal and allowing more serotonin and noradr available in the synaptic cleft |  | 1/ Perioperative use may have beneficial effects on postop pain and opioid use (limited data)- mastectomy | CIPN- Better than Placebo  1st line therapy for NeuP  2/ 1A evidence for FM if mood disturbance |  |
| TCA | Inhibition of SERT and NA transporter NET on the presynaptic nerve terminal and allowing more serotonin and noradr available in the synaptic cleft   * potent antagonist at H1 receptor (antihistamine and sedative) * Blockade of alpha adrenoceptors (orthostatic hypotension) |  | 1/ Acute HZ to prevent PHN    Minimal role otherwise acutely | 1/ First line for NeuP  2/ IA evidence for FM if sleep disturbance | * postural hypotension * Dysphoria * Agitation * Confusion * Urinary retention * Sedation * Combination with SSRIs, SNRIs and tramadol may increase risk of serotonin toxicity * Prolonged QT * CI in CVD and cardiac arrthymias |
| Gabapentin | Binding of alpha-2-delta submit of the neuronal VG calcium channels, but may include others including the NMDA receptor   * Modulate but do not block these channel and thus reduce the influx of calcium ions in hyper excitable neuronal states. As intracellular ca conc control the release of EAAs such as glutatmate, these medicines reduce synaptic glutamate conc and subsequent NSMDA receptor activation- explains their efficacy in reducing central sensitisation * Relies on an active transport mechanism for uptake through the gut wall and shows saturation kinetics, non linear dose response relationship * Low potency + above make titration over a wide dose range necessary. |  | 1/ Initially thought to dec postoperative pain, opioid requirements and opioid related AE, however, AE and size of benefits have been overestimated most likely due to inclusion of trials with higher risk of bias  2/ Inc concern with OIVI in combo with opioids  3/ Reasonable choice for acute NeuP | 1/Useful in PHN, DPN, mixed NeuP, SCI | * Peripheral oedema * Weight gain * Overdose esp with other sedatives * Sedation |
| Pregabalin | Same MOA, but differ in potency and PK  Linear dose response relationship  Longer half life  Higher oral BA and potency  Excreted unchanged by kidney- needs dose adjustment in KI, cleared extensively by dialysis and patient commonly require a post dialysis booster dose |  | Perioperative gabapentinoids reduce postoperative pain and opioid requirements (lvl Q)  Reduce postoperative nausea and vomiting and pruritis (S)  Increased risk of sedation and visual disturbance | As above  1/ No preventive effect on CPSP, but is a preventive effect on CPSNeuP  2/ 1A evidence for FM if severe pain disturbance  3/ SCI | -Peripheral oedema   * Weight gain * Overdose esp with other sedatives * Sedation * Acute suicidality * Dizziness * Ataxia * Potential for misuse |
| Carbamazepine | Sodium channel blocker at presynaptic terminal of glutamate neuron |  | 1/ TN | 2/ TN | * blurred vision * Drowsiness * Ataxia * Vertigo * Nausea * Leukocytosis * Thrombocytopaenia * Blood dycrasias, hepatic dysfunction, SJS |
| Lamotrigine | Sodium channel blocker at presynaptic terminal of glutamate neuron |  |  | 1/ SCI for incomplete at level or below level SCI  2/ HIV, antiretroviral neuropathy- small study showed improvement=n=227 |  |
| Topiramate | Likely acts through several cellular targets  1/VGNa channels  2/ GABAa receptor subtypes  3/AMPA or kainate receptors  Weak inhibitor of carbonic anhydrase |  |  | 1/ Migraine prevention | - impaired expressive language fx, verbal memory and cognitive slowing |
| Ketamine | 1/ Inhibition of NMDA Receptor   * Non competitive antagonist @ sub anaesthetic conc * If so would only expect analgesic in central sensitisation bc NMDA is not in the normal pain pathway * Antihyperalgesic, antiallodynic, tolerance protective (Visser, Shug 2006)   2/ Intrinsic analgesic effect   * Higher conc- interact with spinal and central opioid receptor * Monoamine system- agonist and alpha and beta adrenergic receptors> inc dopamine activity * Cholinergic antagonist @ CNS muscarinic and nicotinic receptor * Possible other effects on purinergic and adenosine receptor system * LA effect   3/ Central Antinociceptive effects   * Enhanced descending inhibition, anti-inflammatory effects (Neisler 2013) * Reduction of temporal summation in nociceptor reflex model   4/ Opioid sparing due to attenuation of tolerance (Kissing et al 2000)  5/ Prevention of OIH  6/ Cytokine effection  - inhibition of TNF alpha and IL6 gene expression in LPS activated macrophages |  | -Preemptive analgesia- Perioperative Ketamine dec risk of CPSP- NNT 12 @ 3 months    -Level I (Lakowski 20211)   * up to 40 % dec opioid consumption * Inc time to first analgesic request * Dec pain scores if severe        * Phantom Limb Pain * Reduces opioids, pain intensity and postoperative N&V - Level 1 * Reduces risk of chronic post surgical pain - Level 1 * Reduced OIH and tolerance associated with remifentanil - Level 1 * Useful in neuropathic pain following spinal cord injury - Level 1 * Reduces post operative pain and opioid requirement in opioid-tolerant patients - Level 2 | CRPS  -Moderate evidence supporting Ketamine infusion to provide improvements in pain for up to 12 weeks- Level II evidence   * Weak to no evidence to support infusion in SCI, Mixed NP, PLP, PHN, FM, Cancer pain, Ischaemic pain, migraine or LBP   Cancer Pain   * Not much difference to placebo NNT25 NNH 6   Palliative Care   * No evidence |  |
| Benzodiazepine | Acts at the GABAa receptor to influence GABA binding to increase Cl ions to hyperpolarize cell to inhibit transmission of action potential. Inhibits networks of neurons associated with anxiety and arousal |  |  |  |  |
| Local Anaesthetics | -block voltage gated sodium channels in cell membranes- prevent the influx of sodium ions into cells and thereby the generation of AP and the conduction of nerve impulses   * also modify a number of other neuronal membrane channels or even receptors * Some effects on GPCR explain anti-inflammatory effect * Block all nerve conduction in all sensory and motor fibres including sympathetic nerve fibres- may lead to vasodilation   Lignocaine Editorial Anaes 2021   * Below clinically relevant levels- acts on M1, M2, NMDA receptors * Above levels- P2X7, NaV1.8, TLR4, nAChR, HCN | Topical- PHN, TN, Radiculopathies, Peripheral Neuropathies (post thoracotomy, meralgia paraesthetica, intercostal neuralgia)  Neuroaxial- intraoperative, postoperative, cancer/palliative  Systemic lignocaine- intraoperative, Diabetic Peripheral Neuropathy | 1. Perioperative lidocaine- dec pain and opioid requirements, dec incidence and duration of ileum, and length of hospital stay (Level I CR) 2. In breast surgery and other surgeries less CPSP at 3,6,12 months 3. Effect extends > 8 hours after cessation 5.5 half lives 4. Perioperative IV lignocaine reduces pain and opioid requirements to a limited extent (Level 1) 5. It reduces nausea, but NOT vomiting, incidence, and duration of ileus, and hospital stay duration (level 1) 6. Perioperative lignocaine has effects beyond its half-life (level 1) 7. Perioperative lignocaine reduces chronic post surgical pain at 3 mths vs placebo (level 1) | 1. Chronic neuropathic pain (Level II CR) 2. Strong evidence for use in peripheral nerve traumas (Level I) 3. SCI | Increasing blood conc   * Lightheadedness * Circumoral/tongue numbness * Tinnitus, visual disturbances * Muscular twitching * Drowsiness * Unconsciousness * Convulsions * Coma * Resp arrest * CV depression and arrhythmias * VF and cardiac arrest |
| Calcitonin | Peptide hormone which regulates calcium homeostasis  -Analgesic effects mediated by modulation of serotonergic mechanisms  -may also act as its own NT in the CNS |  | 1. Efficacy in acute PLP < 7days 2. Acute pain due to vertebral body fractures 3. Acute pain due to SCI | 1/ CRPS based on limited evidence | Nausea and vomiting  Interacts with 5HT3 antagonistic antiemetics  Flushing, drowsiness and allergic runs  Hypocalcaemia |
| Bisphosphonates |  | Bone pain from metastatic disease | 1/ Acute pain from OP crush fractures  Reduce pain in CRPS type 1 in early phase of disease (level 1)  Pamidronate has been snown to reduce pain with osteoporotic vertebral compression fractures (level 2) | Cancer Pain  - Reduces Pain scores   * Reduces skeletal related events   CRPS (Level I)  - should be considered <6 months to decrease pain | Osteonecrosis of jaw |
| Corticosteroids | Synthetic Steroid hormone- powerful antiinflammatory effect and immunosuppressive  Transcortin binds and transports glucocorticoids around blood stream   * Bind to glucocorticoid receptor intracellularly to either up regulate or down regulate certain genes * Inflammation- activates NFKappa B- activates genes of cell to produce MRNA tranlates inflammatory cytokines- leading to inflammation * Glucocorticoid inhbitis NFKappa B> suppresses inflammation * Inhibits production of eicosanoids by inhibiting phospholipase A2 and COX enzyme * Immunosupression due to decrease in production of number of white blood cells due to decreased cytokine production | Cancer related bone pain, Visceral pain  CRPS | 2/ Perioperative dec N&V, postop fatigue, length of hospital stay and slightly lower pain scores and opioid consumption | Cancer Pain   * Weak evidence * Some studies showed significant pain relief for a short period of time * Not able to determine benefit in specific cancers * Side effect profile particularly in long term not studied * 1/ Brachial plexitiis * 2/ CRPS- early phase * Safe 10mg TDS for up to 2/12 | * GI- ulceration * Long term- immunosupression, cushings- due to mineralocorticoid receptor action * Osteoporosis- due to inhibition of osteoblastic activity and stimulation of osteoclastic activity |
| Clonidine + Dexmedotomidine | -alpha-2adrenoceptors are located on peripheral sensory nerve terminal and in the spinal cord and brain stem.   * peripherally and centrally, a2a agonism has an inhibitory effect on pain transmission. * Endogenous activation is by NA, receptors in SC are though to be primarily responsible for the analgesic effects * Usually used in combination with other analgesic medicines | * useful in mx of withdrawal from opioids, benzodiazepines and alcohol * May be effective in treatment of NeuP | -conflicting results for opioid sparing and dec N&V- effect outweighed by adverse events of bradycardia and hypotension  Evidence for their use in opioid-withdrawal symptoms  Perioperative use does NOT reduce pain intensity but reduces opioid consumption and postoperative N&V (Level 1)  Clonidine can exten effects of opioid when used neuraxially (level 1) | CRPS  -may show some benefit with SMP (low quality evidence) | -bradycardia, hypotension  -sedation  -bradycardia  -dizziness   * dry mouth * Dec bowel motility |

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|  | Pain |  |  |  |  |  |  |  |  | Management |  |  |
| Headache | Location | Nature | Intensity | Freq | Duration | Demo | Diagnostic Feature | Asso Features |  | Abortive | Prophylaxis | Procedure |
| Migraine | Hemicranial or Global | Throbbing, Pulsating | Mod-severe intensity | **Common**  5x att  **Chronic** 15d/mth>3mth | 4~72h, typically 24h | ♀(3) 15% > ♂(1) 8%  18% of pop  Before 40yo  Can be familial | -Reversible neurology  -Worse with movement | -Aura 20%  -Autonomic  -Cortical Spreading Depression  -Movement  -phono/ photophobia/ nausea | 15/month  3 months  >5 attacks  Migranous | Triptan: cerebral vasoconstriction by blocking serotonergic receptors  Ergotamine  Aspirin 1000mg  NSAIDs | βBlocker  CaBlocker  Topiramate  Valproate  Gabapentin  TCA  Mg  CGRP | GON – PRF  Sphenopalatine ganglion block  Trigger pt inj  Cervi MBB/RFN  Botox  Trig nn block |
| Cluster Headache  TAC | Unilateral Orbital, Supraorbital, Temporal |  | Severe, very severe | -**Episodic** 1/52~1yr with painfree>1 mth  -**Chronic** >1yr or painfree<1mth | 15~180 min | 0.1% of pop  20~50yo  Can be familial  ♂(4)>♀(1) | 5 attacks in 10 days, (max 8/day) | Conj inj, lacrimation, nasal cong, sweating, ipsi miosis, ipsi eyelid oedema, ptosis, agitation |  | Verapamil 240mg/d upto 960mg/d – takes weeks for effect  Oxygen therapy  Triptan  CGRP – maybe |  | Occipital nn or Frontal nn stim  Sphenopalatine block |
| Hemicrania  TAC | Unilateral, Orbital, Supraorbital, Temporal |  | Mod-Severe | **Paroxysmal**: 5~30min, multiple/day  **Continua**:Daily, continuous | Depends on Paroxysmal Vs Continua | 1 in 50,000  No male dominance  ♀(2)>♂(1)  3rd decade of life | Responsive to Indomethacin | Conj inj, Nasal cong, Rhinnorrhoea, Ptosis, Miosis |  | Indomethacin 150mg OD upto 225mg OD  Cox-2 if not tolerating  Lamotrigin 50~200mg/d  Topiramate |  | Stimulation |
| SUNCT  TAC | Unilateral  Around eyes | Burning, stabbing, electrical | Mod-severe | Average 60 attacks/d (upto 200) | 5s~5min | ♂>♀  50s | NOT responsive to Indomethacin/O2 | Conj inj, Nasal cong, Rhinnorrhoea, Ptosis, Miosis |  | Lamotrigine  Topiramate  Gabapentin  IV lignocaine  Mythylpred |  |  |
| TTH | Bilateral | Pressing, tightening | Mild-mod | Infreq <12d/yr  Freq 12~180d/yr  Chronic >180d/yr | Short or Continuous | Most common form of HA  Life prev 78%  2~3% chronic  ♂=♀  Onset 25~30yo  Peak 30~39yo  🡫with age |  | Greater med overuse  More disability  Higher person/society cost  Only 1 of Photo- or Phonophobia allowed  Pericranial mm tender  Myofascial sensitisation | Similarity with Mig  Sonophobia  Photophobia  Neck pain  Trigger: dehydration, menstruation, stress, strong ordour, sleep  **NO N+V** | NSAIDs  Panadol | Amitriptyline 75mg 🡫 by 30% in a wk  Also venlafaxine, mirtazepine |  |
| MOH |  |  |  | 15d/mth |  |  | Pre-existing 1o Headache  Nearly daily (>3/mth) use of medications  >15d/mth of simple med use  >10d/mth of ergot,triptan,opioid,combo analgesia  Headache/analgesia diary | -🡩headache freq  -New Moring headache  -Non-descriptive pain – not like primary pain  -Escalating dose  -Headache predictable post analgesia |  | Education  CBT  Discontinuation  Tapering off  If complicated pt, inpatient management  If not, outpatient management |  |  |
| Medication withdrwal headache |  |  |  |  |  |  | Consider the headache pattenrs attributable to a substance or its withdrawal |  |  |  |  |  |
| Trigeminal neuralgia | Trigeminal distribution  Unilat V Bilat | Burning neuropathic pain | Severe |  | Min - hours | 0.0125% of pop /yr  ♀>♂  After 50yo |  |  |  | Carbamazepine (90%) – sig s/e  Gabapentin, Pregabalin  Lamotrigine  Baclofen  Amitriptyline |  | Gamma knife  Surgery – high risk |
| Post Herpetic neuralgia | Dermatomal distribution  Unilateral | Neuropathic | Severe |  | PHN: >4mth post H.z rash onset  Subacute HN: 4/52 ~ 4/12  Acute HN: <4/52 | 9~35% of herpes zoster patient  🡩 with age | **Mechanism**: neuro damage due to reactivation of Varicella-zoster virus | Can have senstisation  **Risk factors**:  -older age  -🡩acute pain  -🡩rash severity  -Opthalmicus  -severe prodromal pain | After healing of herpes zoster rash  May test for Ab to H.zoster | TCA, Gabapentinoid, duloxetine (Strong recom)  **Gabapentin**: upto 1800mg/d 3 doses  **Pregabalin** upto 600mg/d  Amitriptyline: upto 100mg nocte  Nortriptyline: 30~75mg/d  Topical lidocaine (strong recom)  Topical capsaicin (weak recom)  Strong opioid: 2nd line (strong recom) | | Intrathecal methylprednisolone  Botox |
| Burning mouth syndrome | Anywhere in mouth but typically in tip or side of tongue | Burning discomfort | Intensity fluctuates | Daily  >2h/day  > 3 mth |  | Peri-/post menopausal woman  ♀(6):♂(1)  0.01~4% of pop | Lingual nn block with lig  -relieved:peripheral  -not relieved:central  2ndary e.g. candidasis |  |  | Psychotherapy + topical clozepam  Amitriptyline  Gabapentin  Duloxitine |  |  |
| Cervicogenic headache |  |  |  |  |  |  |  |  |  |  |  |  |
| Post Craniotomy  Headache  PCH |  |  |  | Immediate: 80%  Often resolves in 7/7  ♀>♂  25% 🡪 persistent pain  Post fossa, Sub occipital craniotomy |  |  |  |  |  | Early NSAIDs  Multimodal: NSAIDs, anticonvulsants, analgesics  Surg tech  Fat graft with dura closure  LA for wound  Periop gabapentinoid  Ѱ |  | GON- strong evidence |
| Secondary headaches related to disorders of intracranial pressure 🡩 |  |  |  |  |  |  |  | Morning pain  Visual obscuration  Vomit with little nausea  Pappilloedema  Neck stiffness |  |  |  |  |
| Secondary headaches related to disorders of intracranial pressure 🡫 |  |  |  |  |  |  |  | Pain 🡩 on standing  🡫 on lying |  |  |  |  |