Essential Pain Tips for Interns and Hospital Doctors

Pain definitions

- **Pain** is, '*an unpleasant sensory and emotional experience associated with actual or potential tissue damage.'* (IASP 1979)
- **Nociception** is, '*the process of encoding and transmitting tissue-damaging stimuli in the nervous system.' (*IASP 2008)
- **Allodynia** (*Gk* for 'other pain') is, *'pain due to a stimulus that is not normally painful.'*
- The word **'pain'** is derived from the Latin, *poenos,* meaning 'punishment' (e.g. *subpoena*).

Pain and nociception

- Pain and nociception and NOT the same thing.
- *Pain* is a conscious, unpleasant sensory & emotional **experience**.
- *Nociception* is simply **sensory-processing** of tissue damage.
- *Nociception can occur without producing pain* (e.g. under GA or local anaesthetic block).
- The uterus of a woman in labour generates lots of *nociception* but she won't *experience* pain with a good epidural block. Conversely…
- *Pain CAN occur without nociception***.** In other words…
- **It IS possible to experience pain *without* tissue damage**.
- In fact this is part of the official definition of pain—*potential* tissue damage is mentioned specifically. Some examples…

  -allodynia (touch-evoked pain)

  -squeezing your finger nail

  -phantom limb pain (there aren't any tissues left to be damaged)

  -back pain in a patient with a 'normal' spinal MRI

- The fact that **patients CAN experience pain without tissue damage is a key message** you should always remember in your medical career.

- The concept of **pain without damage** is poorly taught in health care, where medical fixes for *tissue damage pain* (x-rays, scans, nerve blocks, operations, pills, physiotherapy) are the norm. Insurance providers and lawyers also find the concept of *pain without damage* difficult to accept and may think its malingering. Patients too find this idea hard to understand and get the wrong idea—*"So my pain's not real then doc, it's all in my head?"*

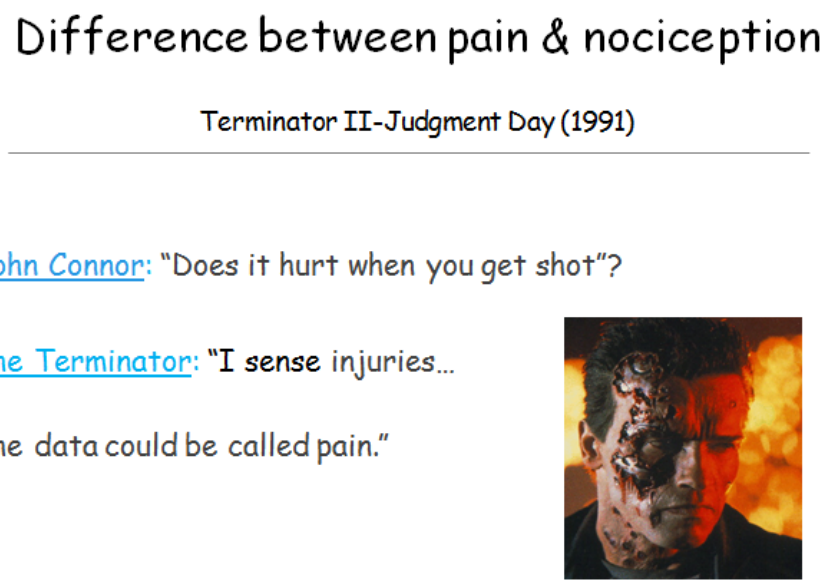


Figure 1

- Although nociception is the most common trigger or driver of pain, there at least five other factors that cause pain. The mnemonic is N.A.S.T.I (see table 2).

Table 2 **The 'N.A.S.T.I' causes of pain**

- **N**ociception
- **N**europathy (nerve damage)
- **N**ociplastic (central sensitization)
- **A**nxiety (see below)
- **S**tress (chronic stress or 'sickness response'; see below)
- **T**hreat (physical, psychological duress, especially in childhood)
- **I**nformation-scrambling (scrambling flow of sensory-motor information to/from cortex e.g. phantom pain).

Classification of pain

- **Acute pain** (<3M), **chronic pain** (≥3M), **cancer pain.**

- **Nociceptive pain:** *'pain due to activation of nociceptors.'*
  - This is 'alarm system' pain and protects tissues from damage.
  -Tissue damage pain.
  -The 'energy' released during tissue damage is converted to electric nerve signals.

- **Neuropathic pain:** *'pain due to a lesion or injury of the somatosensory nervous system.'*
  - Nerve-damage pain.
  - Often a missed diagnosis.
  - 10% of surgical or trauma patients have it.
  - Being a problem of 'damaged wiring', neuropathic pain has 'electrical' qualities.
  - Electric shocks (paresthesiae, dysesthesiae), shooting, stabbing, burning, aching.
  - Altered sensation is common (e.g. numbness).
  - **Allodynia** is a hallmark of neuropathic pain (see below).

- **Nociplastic pain:** *pain in which there is no clear evidence of tissue or nerve damage.*
  - Fibromyalgia, IBS, headaches, non-specific chronic low back pain.

More about pain

- Pain is a complex and subjective **personal** experience.
- Pain is what the person-in-pain says it is.
- We should ALWAYS *believe* a person's pain.
- The only way we know a person's 'in pain' **is when they tell us** (verbal reports).
  (This is difficult for 'non-verbal' persons; infants, foreign-language speakers, dementia)
- *Pain behaviours* are subjective and often reflect *distress* rather than pain *per se*.
- You can't measure pain; *pain scores* are only a unidimensional measure of *intensity*.
- You can't *see* pain on an x-ray or scan.
- Pain is a *bio-medical-psychosocial-environmental* phenomenon.

Pain is personal (the pain phenotype)

- Ten-fold variation in the population's response to a given noxious stimulus (e.g. an electric shock), OR to a given dose of opioid analgesic.
- So, there's a wide *spectrum* of pain phenotypes in the population.
- This is reflects the different expressions of pain we seen in patients on a ward round.
- A person's pain phenotype is moulded over a lifetime by genetics, neurophysiology and importantly, by psycho-social and environmental factors.

Sensitization (amplification) of nociception (pain) in the CNS

- Over millions of years, the pain alarm has evolved 'amplifiers' (which makes the alarm 'ring' louder) so tissue damage is not ignored by the organism.
- It makes sense for an alarm to have an amplifier, just like a smoke detector which gets louder and is difficult to switch off.
- **Central sensitization** is the term which describes the process of nociceptive (pain) amplification in the central nervous system (CNS) (occurs mainly in the **dorsal horn** of spinal cord).
- **Central sensitization** is defined as *'increased nociceptive output for a given input to the CNS.'*
  -e.g. nociceptive impulses enter the spinal cord at 3 Hz and exit at 50 Hz.
  -also called ***wind-up.***
- *Central sensitization* is THE main reason we develop severe acute pain, and chronic pain.

How do we know that *central sensitization* has occurred in our pain patients?

- **Allodynia** is the *clinical sign* that central sensitization has occurred in the CNS (with the potential to develop severe acute pain or chronic pain).
- **Allodynia** is *touch pain* and feels like a having a warm shower after sunburn.
  - *Touch* feels painful (tissue paper or brush).
  - *Pressure* feels painful (toothpick or finger).
  - *Cold* feels painful (cold steel of a tuning fork, or ice).
  - Look for *allodynia* around a surgical wound for example and you are bound to find it.

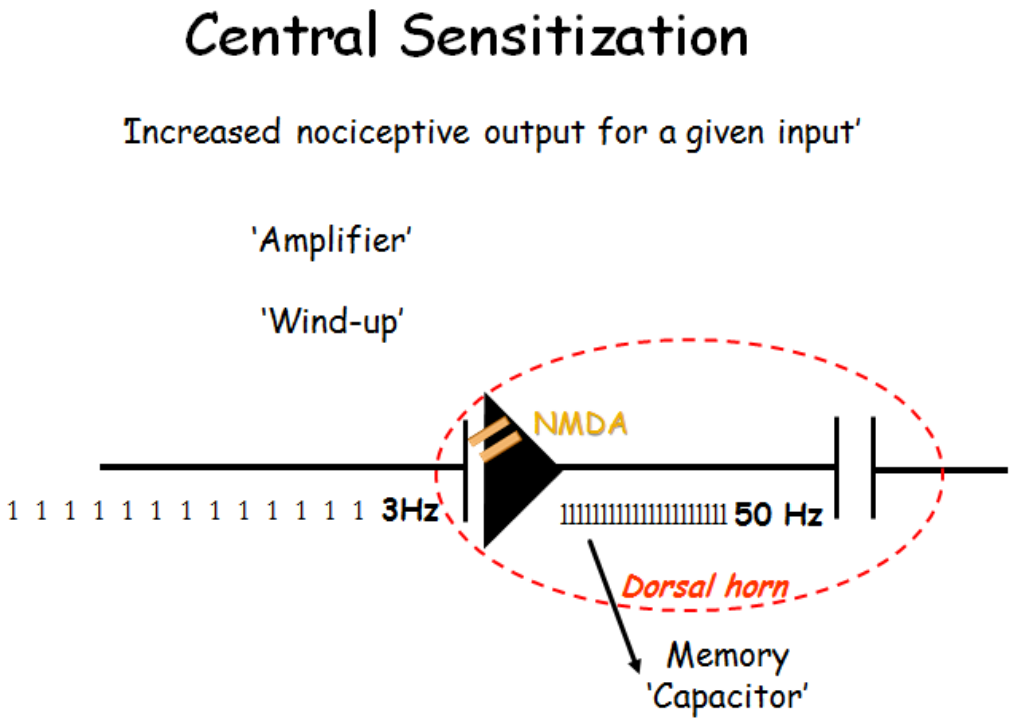


Figure 2

Figure 3

Inhibition (damping) of nociception in the CNS

- We also have an inbuilt pain *inhibitory* system called ***Conditioned Pain Modulation*** (CPM) centred in the midbrain, which inhibits nociception in the dorsal horn via descending spinal cord tracts. *Nor adrenaline and serotonin* are the inhibitory neurotransmitters released by the CPM system; that's how antidepressants, tramadol and tapentadol reduce pain.

- The CPM inhibitory system *is active all the time*, otherwise we would be overwhelmed by all sorts of bodily aches and pains, and not be able to sit on our seats due to the pressure on our ischiums (10kg/cm^2). Some unlucky people have poorly functioning inhibitory systems and develop severe pain problems.

- Severe acute pain and chronic pain usually reflects increased central sensitization (amplification) and/or a poorly-functioning CPM system (inhibition). Unlucky persons-in-pain may have both processes going on at the same time!

-

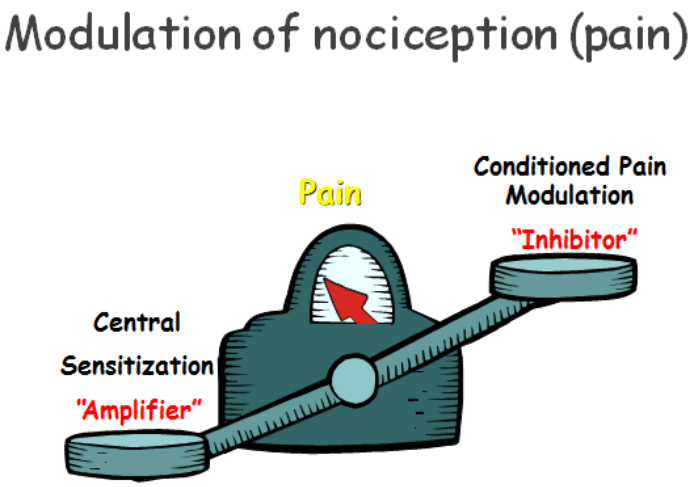


Figure 4

Pain and anxiety (fear) are the same thing

- **Pain and anxiety are essentially the same thing**—they are both 'alarm systems' that protect our tissues from damage.
- Pain is generated when SOME of our tissues are at risk of damage (a body region).
- *Anxiety* is generated when ALL of our tissues are at risk of damage ('dying').
- A **panic attack or phobia** are examples of how anxiety or fear might protect a person from total body damage (i.e. death).
- It make sense to be **scared** of a threat (such as a snake or sabre toothed tiger), run away and protect your tissues **before anything happens**, rather than first being bitten, sustaining tissue damage, experiencing pain and then responding.
- Anxiety probably evolved from primitive 'pain' systems in higher organisms (such as man).
- The same bits of the brain 'light up' with pain and anxiety (amygdala) and the same neurochemistry is involved.
- Epidemiology: There's a much greater chance of developing severe-acute pain or chronic pain after an injury or surgery with *major anxiety*, especially the 3 Ps, panic, phobia PTSD.

Stress and pain

- **Stress** is *any factor that disturbs the normal physiological homeostasis of an organism*.
- Stress is a **threat** to the organism's organs and tissues.
- *Stress* may be physical trauma, illness or (importantly) psychosocial load factors ('yellow flags') such as *duress* during the development years of childhood.
- Pain and anxiety are part of our whole-body response to *stress.*
- The body reacts to *stress* by generating an *acute stress response* (fight or flight) or a *chronic stress or sickness response* (like the flu-curl up in bed and wait for tissues to heal).
- The *acute stress response* is usually associated with *acute pain.*
- The *sickness response* is seen in 30% of *chronic pain* patients (e.g. fibromyalgia, chronic fatigue syndrome).
- There is a major neuro-immune and endocrine component to the stress response.

Figure 5

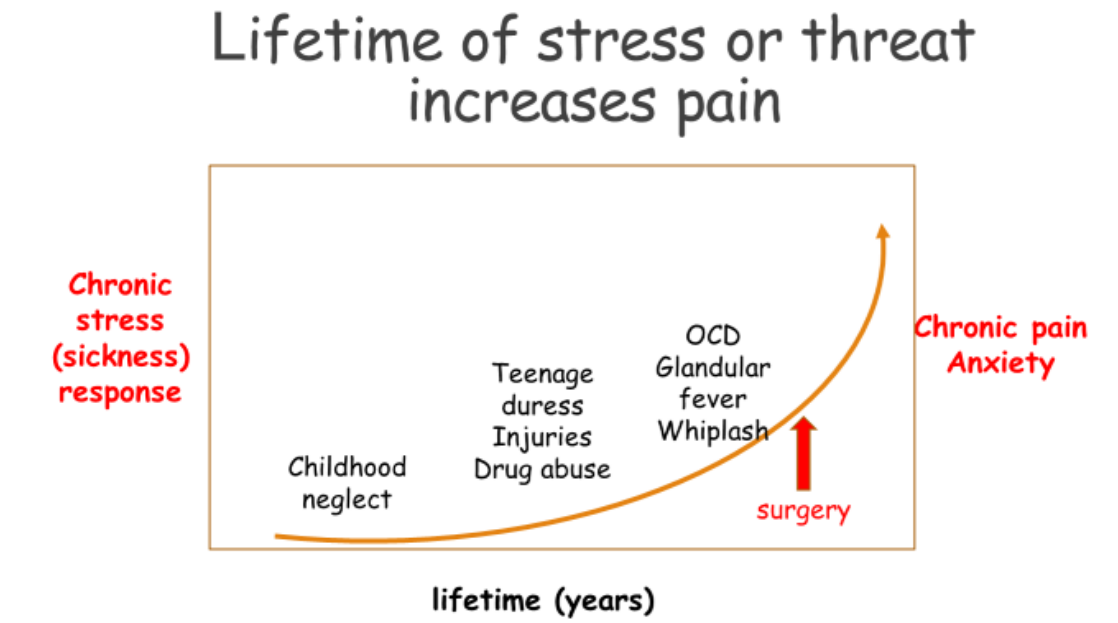


Figure 6

Acute Pain

Acute Pain Services

Acute pain

- Defined as '*pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease.'* (Ready 1992)
- Alarm-system pain (that protects tissues from damage).
- Usually a clear cause (e.g. fracture, appendicitis, sunburn).
- Usually nociceptive, inflammatory or wound pain.
- Neuropathic pain in 10% of cases (e.g. shingles, 'sciatica').
- Pain is proportional to the amount of tissue damage (except for a paper cut!).
- Pain decreases as tissues heal.
- Adaptive, protective emergency response.
- Pain behaviours attract help from others (crying, splinting a limb, calling an ambulance, labour pain).
- Evolutionary advantage: acute pain is highly preserved in nature (down to level of crustaceans).

Acute Pain Services (APS)

- APS's developed in the 1990s to improve peri-operative pain management.
- Many have now expanded into comprehensive care systems (pain, nausea, sleep, anxiety).

APS Team

- Nurses, doctors, pharmacists (psychologists, physiotherapists).
- Nurse driven, medically-supervised and protocol-structured.

Benefits of an APS

- Improved pain management.
- Improved patient safety and monitoring (e.g. epidurals, opioids).
- Surveillance; 'picking-up other problems' (compartment syndrome, hypoxia, acute abdomen, withdrawal, anxiety, systems errors e.g. drugs).
- Quality improvement.

- Education & research.
- Requirement of hospital accreditation.

Why should we treat acute pain 'optimally'?

- Humanitarian (pain relief is a basic human right).
- Reduces the acute stress response (acute coronary syndrome, DVT, ileus, catabolism).
- Facilitates post-surgical and injury rehabilitation (We're designed to wander the African savannah, so we need to get patients back to this evolutionary state-'wandering the wards').
- Reduces risk of acute-to-chronic pain transition (which occurs in 20% of cases).

  -remember, all chronic pain starts as acute pain.

  -preventive analgesia reduces development of central sensitization.
- Reduces psychological distress (PTSD).

Facilitating early rehabilitation after surgery or injury

- Until the 1980s it was accepted that post-surgical or injured patients had to *rest-in-bed* to allow their bodies to heal.

- In the 1990s, the new concept of **post-surgical/injury rehabilitation** turned the tradition of *bed rest* on its head.

- Instead, patients were *mobilised and fed as soon as possible*.

- **Remember, we evolved to wander the African savannah**, not lay in bed for 10 days after a laparotomy or motor bike accident—we never would have survived such traumas in Neolithic Africa!

- Most complications following surgery or injury are ***'stasis effects'*** (the result of lying in bed) e.g. chest infection, ileus, urinary retention, DVT, pressure sores etc.
- Analgesia should *facilitate mobilization* (but, there's a 'Catch 22'-see opioids below).

- **The job of the APS is to facilitate rehabilitation (particularly walking and coughing)** and provide the best possible analgesia with least side effects (especially due to opioids) so patients can do ''laps around the ward within hours of a laparotomy'.

Multimodal analgesia is the mainstay of acute pain management

- **Multimodal analgesia** is *the rational use of two or more analgesics to improve pain and reduce adverse effects.*

- Usually consists of an OPIOID +/- paracetamol +/- NSAID/COX 2-inhibitors +/- adjuvants (pregabalin, clonidine, IV lignocaine, ketamine) +/- regional analgesia with local anaesthesia.

Rationale for multimodal analgesia

- Opioid sparing (dose reduction).
- Improved analgesia.
- Reduced (opioid) adverse effects.
- Preventive analgesia (reduces acute-to-chronic pain transition).

- **Opioid are nervous system inhibitors *but they also slow everything else down***;

  -brain (groggy, falls risk)

  -breathing and coughing (chest infection)

  -gut (nausea, vomiting, ileus)

  -bladder (urinary retention)

  -mobility (DVT and pressure sores)

  -immune and endocrine systems (infection risk)

- **The opioid 'catch 22':** We're using opioids (which slow everything down) to provide analgesia to help get the patient up-and-moving. That is why opioid dose sparing is important.

- **A little bit of opioid sparing makes a lot of difference**: For every 3 mg of IV morphine per day you save, the patient will have one less side effect.

- **Adjuvant analgesia:** Paracetamol, NSAIDs/COX 2-inhibitors, pregabalin, clonidine, IV ketamine and IV lignocaine, each reduce the opioid dose and relate adverse effects (e.g. nausea and vomiting) by about 30% (this is not cumulative).

- The best adjuvant analgesics are **local anaesthetics,** such as in nerve blocks.

Preferred opioids for acute pain

- *Fentanyl* (PCA): no renal accumulation.
- *Hydromorphone:* PCA or oral.
- *Oxycodone* (orally): effective analgesic, minimal renal accumulation.
- *Tramadol:* less impairment of respiratory and gut function, good for neuropathic pain, **accumulates in renal impairment**, interacts with antidepressants, seizure risk; maximum 400 mg/d.
- *Tapentadol:* opioid and noradrenergic agonist, good for mixed nociceptive and neuropathic pain.
- *Buprenorphine* (sublingual) (Temgesic™): less respiratory depression, no oral route needed and no renal accumulation.

Adjuvant analgesics

- **PARACETAMOL:** Prescribed *regularly*: If liver disease or resection, alcoholism, <45 kg, reduce dose or cease altogether.

- **Non-selective NSAIDs:** The most effective analgesics for acute pain (and best at opioid-sparing), but they have adverse *effects so need to be cautious*.

- **NSAID adverse effects:** Renal impairment (prostaglandins keep renal vasculature open at times of haemodynamic stress, after trauma or surgery), acute peptic ulceration (within 48 hours), bleeding, possibly acute cardiovascular events.

- **COX 2-selective inhibitors** (parecoxib, celecoxib): *Less bleeding and acute gastric ulceration compared with non-selective NSAIDs,* otherwise all the same risks, including renal.

- **PREGABALIN (gabapentin):** Good for acute pain, neuropathic pain, opioid sparing and may reduce chronic pain. Good premedication and anxiolytic. Reduces urinary retention, nausea, vomiting and itch. Only available via oral route (can open capsule into 5 ml water for NGT).

- **CLONIDINE:** Oral or intravenous; for pain, anxiety, sedation, agitation, withdrawal. Check heart rate and blood pressure before starting. Care in elderly or haemodynamic instability.

- **KETAMINE:** Improves analgesia in opioid-resistant pain (tolerance, hyperalgesia, neuropathic pain).

- **BENZODIAZEPINES:** For severe anxiety, post-operative nausea and vomiting, BNZ or drug withdrawal. **Beware mixing BNZ and opioids**—higher risk of respiratory depression. Sublingual or oral lorazepam or oral clonazepam are preferred.

Routes of administration: oral versus parental (intravenous)

- **If your mouth (gut) works, use it!**

- Often start with *parenteral analgesia e.g. PCA* (nil-by-mouth) and change to oral route as soon as intake is established for 24 hours **(wait for NGT to be removed and oral fluids to be established)**.

- Beware prescribing oral opioids and sedatives ***unless gastric function is clearly established***. Cases of patients suddenly absorbing many days' worth of drugs when gastric function recovered, leading to 'dose-dumping', sedation and death.

- **Subcutaneous administration of opioids** via S/C butterfly or cannula is an effective alternative for patients who are nil-by-mouth.

- **Many hospitals use an *hourly-prn* oral opioid protocol,** using *oxycodone or hydromorphone immediate release, or tramadol immediate release.*

- Remember, it takes *5 half-lives to reach plasma steady-state concentration.* If most opioids have a half-life of 3 hours, that's 5 x 3 or 15 hours before steady-state analgesia is achieved if the prescription is written as *3/24 prn*.

- **Controlled Release (CR) opioids** (e.g. Oxycontin CR, Targin MR, MS Contin, Hydromorphone MR, transdermal 'patches', methadone, suboxone, Tapentadol MR).

- As a general rule, if patients are on CR opioids for chronic pain or addiction, *these should be continued* in the perioperative period. If nil-by-mouth, convert to an intravenous or transdermal (patch) equivalent.

- **Do NOT routinely prescribe CR opioids** or transdermal patches for acute pain management—risk of narcotisation.

- However can prescribe CR opioids for **'step down'**, when patients are using high doses of PCA or oral *prn* opioids, to allow for weaning.

- Do not use oral CR opioids (e.g. Oxycontin CR) in patients with *an ileostomy or short gut*—drug will be dumped in stoma bag before being absorbed.

What we need to know for every patient on the APS round

The 3Rs

- **R**espiratory function (sleep apnoea, COPD, CO_2 retention risk)
- **R**enal function (drugs that accumulate)
- **R**egular medications or recreational drugs

Also

- Pain scores (rest, movement), sedation score, respiratory rate
- Function (cough, deep breath, mobilise, drink [oral route], eat)
- Analgesia doses used over 24 hours (e.g. PCA fentanyl)
- Side effects (sedation, cognition, nausea, vomiting, ileus, urinary retention, itch)
- Are they moving legs or limbs (for epidurals or nerve blocks)?

- Chronic pain
- Pre admission analgesia use
- Anxiety, depression, chemical coping
- Drug and alcohol use (nicotine, caffeine, benzodiazepines, antidepressants)

Analgesia Q & A

Q. Which analgesics accumulate in renal impairment?

- Pethidine (nor-pethidine toxicity and fits)
- Morphine
- Tramadol
- Pregabalin and gabapentin
- Dextropropoxyphene
- Codeine
- Hydromorphone (a bit less)

Q. Which are the safest opioids in pregnancy or breast feeding?

- Buprenorphine.

Q. What is the *major* determinant of opioid dose in adults?

- Age
- ***100 - Age*** *= mg of* IV *morphine required in 24 hours* after major surgery or trauma.

  (Remember, this is a rough estimate)

Q. What is the most important sign of opioid toxicity (narcotisation)?

- Sedation, sedation, SEDATION!
- Sedation develops long before there's a decrease in the respiratory rate.
- *The brain is the most sensitive total body monitor* we have.
- If the patient's getting drowsy, something's going on—don't ignore it!
- Write **withhold if sedated** next to orders for opioids and sedatives; sometimes inexperienced staff will treat the pain score and ignore the sedation!
- **Safety:** Oxygen, oxygen, OXYGEN for everyone!

Q. What are the 5th and 6th vital signs?

- Pain score and sedation score, respectively.

Epidural and regional nerve catheters with local anaesthesia infusion

- Infuse **ropivacaine** (less risk of LA toxicity compared with bupivacaine).
- Be familiar with the signs and symptoms of LA toxicity and how to manage it.

  http://www.aagbi.org/sites/default/files/la_toxicity_2010_0.pdf
- Intravenous **Intralipid** is the 'antidote' for LA anaesthetic toxicity.

Epidural analgesia

- Epidurals improve pain, cardio-respiratory and gut function and reduce DVT risk.
- Reduces risk of chronic pain in some cases (thoracotomy).
- BEST indications: Poor respiratory function (COPD, OSA), major thoraco-abdominal surgery; labour pain.

- Epidurals don't always work perfectly.
- 20% failure rate within two days (an ineffective epidural is worse than no analgesia at all).
- Hypotension, motor block.
- Need a urinary catheter.
- Not compatible with regional or systemic infection or impaired coagulation.
- Rare but serious complications:

  -paralysis (haematoma) 1/50 000
  -epidural abscess 1/2000
  -direct neural trauma 1/2000

When to call the APS for help in a patient with an epidural catheter

- *Acute neurological emergency?*

  -can't move legs

  -incontinent (usually has a urinary catheter)

  -back pain

  -fever ≥38.5C

- *Motor block:* don't assume it's just the local anaesthetic, call the APS.

  -need to exclude rare catastrophes such as **epidural haematoma and paralysis.**

- *Hypotension:* Fluid, Pump, Pipes

  -Fluids: volume, blood loss; Pump: cardiac rhythm (AF), heart failure; Pipes: vasodilators (e.g. ACE inhibitors), sepsis.

  -consider withholding antihypertensive drugs, especially ACE or angiotensin II inhibitors.

  -check level of block to ice: higher than **T4 (nipple line)** means block is too high.

- *Altered consciousness or seizure*.

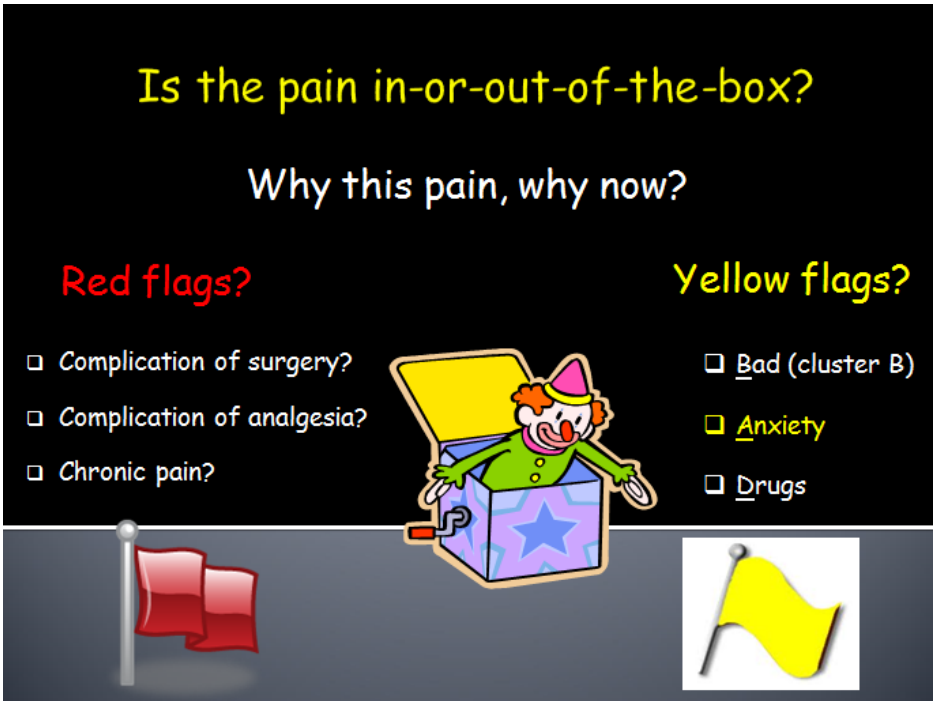
  -local anaesthetic toxicity, hypotension, stroke.

- *Anticoagulants*: major risk is epidural haematoma on *insertion* or *withdrawal* of epidural catheter.
- **DO NOT systemically anticoagulate patients** with an epidural catheter.

  WARFARIN, HIGH-DOSE HEPARIN (low molecular weight or infusion), RIVAROXABAN, FIBRINOLYTICS, CLOPIDOGREL, TIROFIBAN etc.

Pain trouble shooting: Is the pain presentation 'out-of-the-box'?

- When a patient's pain is out-of-the-box; that is…it's worse than expected…
- Always ask yourself WHY NOW?
- We are always obliged to firstly exclude **red flags** (serious biomedical conditions that should not be missed).
- Psychosocial factors **(yellow flags)** such as anxiety, drugs, alcohol and personality may also drive increasing pain.



Red flags (biomedical complications)

- Complications of surgery or trauma (e.g. compartment syndrome, acute abdomen).
- Complication of analgesia technique (e.g. epidural or IV PCA disconnected, not absorbing oral analgesia, not replacing pre-op baseline opioid analgesia).
- Chronic pain, or developing a new pain condition (e.g. neuropathic pain).

Yellow flags (psychosocial drivers of pain & distress) (B.A.D)

- **B** reminds us that some people have 'difficult' (or even pathological) personalities such as cluster B.
- **A**nxiety is *the major yellow flag* to look out for and manage.
- **D**rugs: *anything to do with drugs e.g. withdrawal, addiction, chemical coping, intoxication etc.*
- *Sometimes there are multiple yellow flags* e.g. the angry, 'risk-taking' drunk driver on the trauma ward, (cluster B personality + anxiety + substance abuse + withdrawal + 'impulse control' problems).
- So, never forget the psychosocial dimension of pain!

Substance use problems on the ward

- Common problem (alcohol and tobacco are still the most commonly used drugs).
- **Always get a comprehensive drug and alcohol history** from EVERY patient (often missed).
- Patients may undergo *withdrawal* during hospital admission.
- Patient may also be *intoxicated (or overdose)* in hospital e.g. visitors bringing drugs or alcohol, patients inject drugs.

Simple Tips

- Alcohol withdrawal chart.
- Nicotine patch. Nicotine is a much 'stronger' drug than opioids. An opioid dependent patient will frequently forsake their morphine PCA so they can go off the ward for a cigarette!
- Benzodiazepine withdrawal and supplementation (IV, oral, sublingual).
- 'Discontinuation syndromes'-suddenly ceasing antidepressants.
- **Clonidine** is very helpful for withdrawal.

Withdrawal: you rebound to the drug's opposite arousal state!

Uppers go down

- Those taking 'uppers' (e.g. amphetamines) become *sleepy* in withdrawal.

  -think about this in patients who are unusually sleepy and you can't find a cause.

Downers go up

- Those taking 'downers' (e.g. opioids, benzodiazepines, alcohol, cannabis) become *stimulated.*

Worried about opioid abuse in your patient?

- Monitor doses, consider using transdermal patches for dose control, use elixirs ONLY whilst in hospital (so they can't spit out tablets and inject them after the nurse leaves).
- Involve drug and alcohol services early.
- Beware patients who frequently go off the ward or with visitors who may supply drugs.
- If a patient is prescribed high doses of opioids prior to admission (e.g. Oxycontin CR) and you convert them to equivalent opioid doses post operatively, **watch them closely**; they may become **narcotised**, *when they've not actually been taking their opioids but and instead are diverting them*!

Resources:

Acute Pain Management: Scientific evidence 4rd Ed 2015 via www.anzca.edu.au