Pain control revision (particularly palliative)

Definition WHO: ‘an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage.’

40-80% of elderly in institutions are in pain; ¾ of cancer patients; 60% of pts with advanced disease get troublesome pain (similar for AIDS, cardiac, neuro)

Assessment of pain:

* What patient means when they complain of pain
* How symptom affecting pt’s life (sleep, normal activities, relationships)
* How pain makes pt feel
* Ideas & concerns about pain; pt’s expectations of you; pt’s goals for pain
* SOCRATES: characteristics, site, radiation, severity, onset, exacerbating/relieving, timing
* Associated features: bruising, redness, swelling, neuro deficit, depression
* Effects of interventions
* Antagonising factors that can be addressed (physical/emotional/social)
* Consider mechanism of pain to enable targeted drugs
* Can use pain assessment scales e.g. VAS
* Watch patient carefully, always examine (also has therapeutic value)
* Can use symptom monitoring by patients with diary/pain scales (also to monitor effect interventions); body chart may help
* Consider use of investigations e.g. XR

Specific pain features to determine cause:

* Exacerbated by slightest movement: skeletal instability-path #, nerve compression, soft tissue inflammation, local tumour infiltration
* Exacerbated by local pressure and/or active mvt e.g. myofascial muscle pain, skeletal muscle strain/spasm
* Exacerbated by straining bone on exam-bone mets, intermittent nerve compression due to skeletal instability
* Colic: bowel (infection, obstruction, chemo, drugs, RT), ureteric (obstruction/infection), bladder (infection, outflow obstruction, unstable)
* Other movement-releated: organ distension (tumour, infiltration, haemorrhage)
* Exclude trauma
* Regular episodes lasting mins at rest: colic-bowel, bladder, ureteric
* At rest with inspiration: rib mets, pleuritic (inflammation, tumour, infection, embolus), peritoneal inflammation, liver capsule stretch/inflammation, distended abdo
* Abnormal posture: altered tone, muscle spasm
* Skin changes: trauma, skin pressure damage, skin infiltration, infection, irritation, skin disease
* Neuropathic
  + Pain assoc peripheral nerve injury often superficial/burning ± spontaneous stabbing (neurodermatomal distribution)
  + Pain assoc compression peripheral nerve/plexus: deep ache, dermatomal
  + Often allodynia, hyperalgesia
  + May be sensory deficit
* During/after eating or feed refused? (dental, mucosal, distension stomach/bowel)
* Consider vascular disease or infection if cause uncertain

Neuropathic pain

* Cancer: mononeuropathy, plexopathy, polyneuropathy (paraneoplastic-glove & stocking), thalamic tumour
* MSCC
* Phantom limb pain
* Chronic surgical incision pain
* B12 peripheral neuropathy
* Polyneuropathy from drugs; chemo; thalidomide
* Radiation fibrosis→plexopathy
* Post-herpetic neuralgia
* Concurrent DM polyneuropathy
* HIV neuropathy

Assessment/clues in the frail/elderly/difficulty communicating

1. Verbal expression
   1. Crying when touched, shouting, , becoming very quiet, swearing, grunting, talking without making sense
2. Facial expression
   1. Grimacing, wincing, closing eyes, worried expression, withdrawn/no expression
3. Behavioural expression
   1. Hand pointing to body area, increasing confusion, grumpy mood
   2. Adaptive: rubbing/holding area, keeping area still, approaching staff, avoiding stimulation, reduced/absent function, reduced movement, lying/sitting, not eating, jumping on touch
   3. Distractive: rocking/rhythmic mvts, pacing, biting, gesturing, clenched fits
   4. Postural: increased muscle tension, altered posture, flinching, head in hands, limping
4. Physical expression
   1. Cold, pale, clammy, change colour, change vital sign if acute (BP, pulse)
   2. Sympathetic: ↑HR, ↑BP, dilated pupils, pallor, sweating
   3. Parasympthetic: ↓BP, ↓HR

Secondary effects of pain:

* Depression
* Exacerbates anxiety
* Interferes with social performance
* Negative impact on physical capability
* Prevent work, decrease income
* Encourage isolation
* Impaired quality of relationships & sexuality
* Family disharmony & stress
* Change existential beliefs
* Causes of failure to relieve pain:

|  |  |
| --- | --- |
| **Reasons** | **Consequences** |
| Belief that pain is inevitable | Unnecessary pain, fear, reluctance to ask for help |
| Inaccurate diagnosis of causes | Inappropriate treatment |
| Lack of understanding of analgesics | Use of inappropriate, insufficient or infrequent analgesics |
| Unrealistic objectives | Dissatisfaction with treatment (by pts & carers) |
| Infrequent review | Rejection of tx by pt |
| Insufficient attention to mood & morale | Lowered pain threshold |
| Pain erroneously interpreted as sign progression and approaching death | Reluctance to report/ask for help/accept, fear |
| Unable to communicate (coma, confusion, dysphasia, LD, dementia) | Pain not recognised or misinterpreted; don’t know type of pain; can’t take pain history |
| Staff/carers/family assessing pain | Their interpretation different to pt’s perception |

Abnormal sensations in neuropathic pain:

|  |  |
| --- | --- |
| **Dysaesthesia** | Spontaneous and evoked abnormal sensation |
| **Hyperaesthesia** | Increased non-painful sensitivity to non-painful stimulation e.g. touch |
| **Hyperalgesia** | Increased response (intensivty & duration) to a stimulus that is normally painful |
| **Allodynia** | Pain caused by stimulus that is not normally painful |
| **Hyperpathia** | Explosive and often prolonged painful response to non-painful stimulus |

## Acute severe pain

Acute: injured/diseased tissue; subsides as injury heals; can be worsened by fear; treat underlying cause

Causes of acute severe pain:

* Change in analgesia (e.g. conversion, not taking e.g. vomiting, change in uptake e.g. adhesion patch)
* Inflammation infection, irritation (PE, peritonitis-bowel perf), chemical damage (drug-induced GI mucosal damage, perianal skin burn from dantron)
* Ischaemia (PVD, MI)
* Fracture
* Tissue distension (e.g. bleed into liver mets→liver capsule pain)
* Muscle spasm (e.g. spinal mets, colic, skeletal muscle)
* Tissue rupture (bone #, fistula)
* Reduced ability to cope (fear, depression, past experiences)

Management acute severe:

Goals:

1. Achieve sufficient comfort for assessment
   1. Positioning
   2. Give usual PRN dose (injection for speed)
   3. Reassurance, company, distraction
   4. Lorazepam 0.5mg sublingual or midazolam 2.5mg SC/buccal in order to relax if overwhelming pain
2. Exclude causes requiring urgent management (<1hrs)
   1. MI, PE, #, MSCC, peritonitis
   2. Treat colic e.g. hyoscine bromide
3. Achieve comfort at rest within 4hrs
   1. Increase regular analgesia by 50%
   2. Check whether new type of pain
   3. Palliative care specialist esp if pain unchanged
   4. Consider use of ketamine
4. Plan for stable pain control within 24hrs
   1. Ensure good nights sleep
   2. Review support/treatment to cope with anxiety/low mood
   3. Consider spinal analgesia, nerve block if indicated (may need sedation until procedure)

* Give usual PRN analgesia
* History, exam for cause→treat cause
* Explain to pt & relatives
* Reassurance & distraction
* Consider simple treatments
* Increase regular analgesia
* Seek snr/specialist advice

## Chronic pain

Chronic: pain persisting >3-6m

Chronic pain may only complain of discomfort, seem depressed, may see pain as unending & meaningless, pain overflows to family & carer; s/e may be less acceptable if long-term; oral preferred; multiple approaches-tx may be complex

Goals: realistic targets (may not be able to eliminate), stop analgesia that doesn’t help, rehabilitation (reduce distress/disability)

Use pain chart to assess progress

Strategies for pain management:

* Prevention
  + Positioning, splinting, analgesia before procedures e.g. dressing changes
* Remove cause
  + Treat infection, diabetic nephropathy, refer for sx causes
* Drugs (start low and step up; step down if pain diminishes; stop if not helping)
  + Better to use regularly as PRN can result in vicious circle of pain, anxiety/fear with reduced tolerance to pain and so more pain
  + Steroids (compression nerve e.g. apical lung tumour; MSCC)
* Physical therapies (acupuncture, PT, TENS, relaxation, hypnosis)
* RT (pain from bone mets, nerve compression, soft tissue infiltration)
  + Bone mets
  + MSCC
  + Soft tissue infiltration: headache from brain mets; liver/splenic pain, para-aortic lymphadenopathy
  + Plexopathy (brachial plexus, lumbosacral plexus)
* Orthopedic surgery for painful bone mets
  + Cement augmentation (vertebra/kyphoplasty)
  + Surgical fixation if risk #
  + Treatment of pathological #
* Nerve blocks
  + Spinal analgesia with local anaesthetics (bupivacaine) ± opioids
  + Peripheral nerves-LA
  + Sympathetic nerve plexus with neurolytic agent (rarely done)
  + Coeliac plexus block with ethanol for epigastric visceral pain (infrequent)
  + Intrathecal phenol for nerve roots
* Modification of emotional response (antidepressants, anxiolytics)
* Modification behavioural response (e.g. back pain-rehab scheme)

## Types of analgesic

|  |  |  |  |
| --- | --- | --- | --- |
| **Primary** |  | **Secondary** |  |
| Non-opioids | Paracetamol, nefopam | Adrenergic pathway modifiers | Clonidine |
| Weak opioid agonists | Codeine, dihydrocodeine | Abx |  |
| Strong opioid agonists | Morphine, diamorphine, hydromorophine, oxycodone, fentanyl | Anticonvulsants | Carbamazepine, gabapentin |
| Opioid partial agonist/antagonists | Buprenorphine | Antidepresants | Amitriptyline, venlafaxine |
| NSAIDs | Ibuprofen (weak primary) | Antispasmodics | Hyoscine butylbromide |
| NO | 1:1 with oxygen: Entonox | Antispastics | Baclofen |
|  |  | Corticosteroids | Dexamethasone |
|  |  | Membrane-stabilising | Flecainide, mexiletine, lidocaine |
|  |  | NSAIDs | Ibuprofen (anti-inflammatory) |

## WHO steps:

1. Non-opioid
   1. paracetamol REGULARLY; 1g every 4-6hrs to max 4g
   2. if not try NSAID e.g. ibuprofen 200-400mg tds alone/combination (with food)
2. Weak opioid + non-opioid
   1. Paracetamol + codeine/dihydrocodeine
   2. Combinations have less dose-related s/e (but greater range s/e)
   3. 30mg codeine (no evidence for 8mg)
   4. Alternative is tramadol
3. Strong opioid + non-opioid
   1. Immediate release morphine or morphine solution
   2. 2 tablets co-codamol 30/500 equiv to 6mg morphine→5mg oral (less if elderly/RF)
   3. 2wks trial and only continue if benefit
   4. Increase dose by 30-50% every 24hrs until pain controlled if no undue s/e
   5. Care if elderly/renal insufficiency
   6. Oral route preferred (only other routes if N&V, exhaustion etc mean can’t tolerate or urgent pain control-not if just poor pain control as no more effective)
   7. Alternatives: diamorphine, diamorphine, fentanyl patch
4. Throughout:
   1. Co-analgesics: drugs, nerve blocks, TENS, relaxation, acupuncture
   2. Sx, PT
   3. Address psychosocial problems

## Co-analgesics & adjuvants:

* Antidepressants (low dose for nerve pain & sleep disturbance assoc with pain; larger doses for 2° depression)
* Anticonvulsants (neuropathic pain e.g. gabapentin)
* Steroids (pain due to oedema)
* Muscle relaxants (muscle cramp pain)
* Antispasmodics (bowel colic)
* Antibiotics (infection pain)
* Night sedative (if lack sleep lowers pain threshold)
* Anxiolytic (anxiety making pain worse; also relaxation exercises)

## Specific types of pain

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| --- | --- | --- |
| Type pain | Features | Management |
| Soft tissue | Localised ache, throbbing, gnawing | Good response to non-opioid ± non-opioid |
| Visceral | Poorly localised deep ache  May be referred to specific sites | Good response to non-opioid ± non-opioid |
| Bone pain | Well localised, aching, local tenderness, worse on mvt/straining | Try NSAIDs and/or strong opioids (variable response)  Pregabalin (nerve endings in bones)  Consider palliative RT, strontium (prostate ca) or IV bisphosphonates  Refer to orthopaedics if lytic mets at risk # (consider pinning) |
| Abdo pain | Constipation: periodic, pain at rest  Bowel colic: constipation, obstruction, drugs, RT, chemo, bile, infection)  Ureteric colic: infection/obstruction  Bladder:infection, outflow obstruction, unstable bladder | Constipation most common-treat  Colic: loperamide 2-4mg qds or hyoscine hydrobromide 300μg tds or **hyoscine butylbromide** (Buscopan) via syringe driver 20-60mg/24hrs  Liver capsule pain: dexamethasone 4-8mg/d or NSAID + PPI  Gastric distension: antiacid ± antifoaming agent (Asilone) or prokinetic e.g. metoclopramide/domperidone 10mg tds before meals  Upper GI tumour: often neuropathic; consider coeliac plexus block, refer to palliative care team  Consider NSAIDs as cause  Manage acute/subacute obstruction (see emergencies) |
| Neuropathic | Difficult to describe; burning/shooting; dysaesthesia; assoc motor/sensory loss; dermatomal distribution of pain (or radicular/nerve territory) | May respond to simple analgesia  Max dose tolerated opioid (often poor response); refer to specialist  Can add **amitriptyline 10-25mg nocte** (see below) (titrate up)  May prefer **pregabalin** (less sedating than amitriptyline)  Add carbamazepine 100mg 8hrly or if not tolerated gabapentin 100mg 8hrly (titrate up); also consider pregabalin, phenytoin, valproate  Clonazepam (give in evening for night)  If nerve compression from tumour try dexamethasone 4-8mg od (higher dose may help in SCC)  Consider TENS, acupuncture, nerve block  If fails to respond can consider specialist for ketamine, spinal analgesia  Duloxetine-esp for DM (non-malignant)? |
| Rectal |  | Topical rectal steroids  TCA e.g. amitryptiline 10-100mg nocte  Anal spasm: glyceryl trinitrate ointment 0.1-0.2% bd  Referral for local RT |
| Muscle pain | Pain on active movement; may have tender spot | Paracetamol and/or NSAIDs  Muscle relaxant e.g. diazepam 5-10mg od, baclofen 5-10mg tds, dantrolene 25mg od to max 75mg tds  Physio, aromatherapy, relaxation, heat pads |
| Bladder pain/spasm |  | Treat reversible cause, ↑ fluid, regular toileting  Oxybutynin 5mg tds, tolterodine, propiverine, trospium  Amitriptyline 10-75mg nocte  If catheterised try 20mL intravesical bupivacaine 0.25% for 15 mins tds or oxybutynin  NSAIDs  Dexamethasone for tumour related bladder inflammation  Terminal: hyoscine butylbromide 60-120mg/24hrs or glycopyrronium SC |
| Pain of short duration (incident) | Occurs episodically on mvt, weight bearing, dressing changes | Short-acting opioid e.g. fentanyl citrate 200μg lozenge sucked 15mins prior or breaththrough dose oral morphine 20mins prior  Consider spinal routes for analgesia, orthopaedic intervention for spinal stabilisation & strengthening weight-bearing bones, gaseous NO |
| Skin pressure pain |  | Pressure relieving aids, position changes  Topical ibuprofen get, oral paracetamol, oral diclofenac  If severe: ketamine, spinal analgesia |

# Opioids

Reduce transmission of nociceptive stimuli to conscious brain through inhibition at opioid receptors in brain stem, spinal cord and possibly peripheral nerves

Morphine absorbed from SI→metabolised in liver to active metabolic morphine-6-glucuronide M6G→kidney excretion

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|  | Morphine |
| Indications | Mod-severe pain esp visceral |
| C/I | Acute resp depression, risk paralytic ileus, ↑ICP, head injury (interferes with pupil responses), coma? |
| Caution | Impaired resp function (COPD), asthma (avoid in acute attack), hypotension, urethral stenosis, shock, MG, BPH obstructive bowel disease, biliary tract disease, convulsive disorders  Pregnancy: resp depression & withdrawal in neonate if during delivery; gastric stasis & aspiration pneumonia in mother  Reduced dose: elderly/debilitated, hypothyroid, adrenocortical insufficiency  May ppt coma in hepatic impairment (avoid/reduce)  RF (↑risk toxicity & myoclonus) |
| S/e | N&V (esp initially) (30% nausea, 10% vomiting)-nausea improves after 5-10d; poor gastric emptying in 20-25%-no tolerance  Dry mouth (50%)  Constipation (90%)-doesn’t improve (no tolerance)  Drowsiness (10%), confusion (10%)-tolerance to sedation 3-5d but little tolerance to confusion, misperceptions (↓ as tolerance)  Hallucinations (often need to change dose/opioid)  Reduced RR (<1%)-tolerance 1-3d  Addiction (<1%)  Myoclonic jerks (uncommon)-usually sign toxicity  Common: brady/tachycardia, palpitation, oedema, OH, hallucination, vertigo, euphoria/dysphoria, dizziness, confusion, drowsiness, sleep disturbance, headache, sexual dysfunction, difficulty micturition, urinay retention, ureteric spasm, miosis, visual disturbance, sweating, flushing, rash, urticarial, pruritis, biliary spasm  Larger doses: muscle ridigity, hypotension, resp depression  Long term: hypogonadism, adrenal insufficiency (amenorrhoea, reduced libido, infertility, depression), hyperalgesia (reduce dose/switch)  Avoid driving at start of therapy and after dose change |
| Interactions | Special hazard with pethidine; possibly other opioids & MAOIs  Not recommended to inject with cyclizine as may aggrevate severe HF |
| Notes | Repeated dose can cause dependence & tolerance; avoid abrupt withdrawal  Reduce dose if poor renal function  Start early and use regularly to prevent pain even if pain free |

## Opioids in palliative care (NICE)

Initial titration:

* Regular oral sustained-released morphine (e.g. 10-15mg twice daily)
* OR immediate release morphine (20-30mg/d)
  + Start 5-10mg every 4hrs (2.5-5mg if elderly/cachexic; 2.5mg if very elderly or RF)
  + (if opioid naïve then start 2.5mg)
  + If on 30mg codeine 4hrly=180mg codeine→approx 18mg morphine→5mg 4hrly
* Rescue doses of oral immediate-release for breakthrough pain (5mg)
* Adjust dose until good pain control (balance with s/e)
  + Increments 25-50% every 3d until pain controlled or s/e

First-line maintenance treatment:

* Oral sustained release morphine first line for advanced/progressive disease requiring strong opioids
  + Oral preferred as gives more control and less disruptive
  + Effective PCA unless can’t be ingested/absorbed
  + Pain is chronic so need regular analgesia
  + If pain at night/first thing in morning is problem then try increasing evening dose by 50% (don’t wake at night to give)
  + Once on MR if need dose increase use increments 1/3-1/2 of dose
* Consider specialist advice if inadequate control
* Consider transdermal patches only if oral not suitable and analgesic requirements are stable
  + Transdermal fentanyl 12microgram patch = 45mg oral morphine daily
  + Transdermal buprenorphine 20microgram patch = 30mg oral morphine daily
* Consider subcut opioids if oral not suitable and analgesic requirements unstable

Breakthrough pain:

* Transitory exacerbations of pain common, sometimes predictable
* Usually short duration 20-30mins and rapid onset
* Patients should always have access to extra analgesia for these episodes
* First-line: oral immediate-release morphine (e.g. oromorph: action 30mins; lasts 3hrs)
  + Same dose as pt is taking as 4hrly dose as an additional dose
  + If occurs regularly before next dose analgesia due increase background dose
  + Previous guidance: 1/6 of daily dose (but this may be too high for many)
  + Can try alternative routes e.g. sublingual, buccal, SC if doesn’t act fast enough
* Incident pain
  + Specific activity e.g. getting dressed, dressing change (avoid if possible)
  + Consider analgesia 20mins prior
  + Ibuprofen, immediate release opioid at 50-100% of 4hrly background dose, oral transmucosal fentanyl citrate 20mg lozenge or lorazepam 0.5mg sublingual (anxiety)

Seek specialist advice if mod/severe renal/hepatic impairment; reduce dose if kidney impairment as kidney excretion (no need to reduce if poor liver function)

Early use is best; regular even if pain free

Always discuss patient concerns around addiction, tolerance, s/e, fear that treatment implies final stages of life

Provide written info: when/why opioids used, how effective likely to be, how long should last, how/when/how often to take, side effects, signs toxicity, safe storage, follow up, further prescribing, contacts 24/7; implications for driving/alcohol interactions

### Management of side effects

* Constipation
  + Prescribe laxatives regularly at effective dose
  + Inform that may take time to work and adherence important
  + E.g. sodium docusate, bisacodyl 1-2 nocte
* Nausea
  + Advise that nausea may occur when starting/increasing but usually transient
  + If persists, prescribe and optimise anti-emetics before considering switching opioids
  + (prescribe regular antiemetic for 2wks e.g. haloperidol 1.5mg nocte)
  + Can often be stopped after 2wks
* Drowsiness
  + Advise that mild drowsiness/impaired concentration may occur when starting/increasing but usually transient
  + Advise that may affect ability to drive and other manual tasks (avoid ≥1wk after starting)
  + If persistent or mod/severe CNS s/e then consider dose reduction if pain controlled or switching opioids if not
* Hallucinations: usually need change of dose or opioid
  + Can prescribe haloperidol
* Myoclonic jerks
  + Reduce dose + midazolam/diazepam stat + PRN
* Gastric stasis: metoclopramide
* Hyperalgesia
  + Reduce dose of causal opioid and optimise adjuvants; consider alternative opioid/ketamine
  + Uncommon, more with high dose IV/spinal
* Pruritis
  + Chlorphenamine (antihistamine)

## Guide to equivalent doses:

Nb. Morphine 8-10 times more potent than codeine so if on 8 co-codamol 30/500→equivalent 24-30mg morphine

Strongest opioids (fentanyl, buprenorphine, hydromorphone)

|  |  |  |  |
| --- | --- | --- | --- |
| **Drug** | **Route** | **Dose** | **Conversion from oral morphine 10mg 4hly (60mg/24hrs)** |
| Codeine | PO | 100mg | 600mg/24h (100mg 4hrly) |
| Pethidine | PO | 100mg | “ |
| Diamorphine | IM, IV, SC | 3mg | /3 = 20mg/24hrs in syringe driver |
| Dihydrocodeine | PO | 100mg?? | X5 morphine? |
| Hydromorphone | PO | 2mg | /7.5 = 8mg in divided doses over 24hrs |
| Hydromorphone | SC | 1mg | /10=6mg/24h |
| Morphine | PO | 10mg |  |
| Morphine | IM, IV, SC | 5mg | /2 = 30mg/24hrs syringe driver |
| Oxycodone | PO | 6.6mg | /2 = 30mg oral oxycodone in divided doses over 24hrs |
| Tramadol | PO | 100mg |  |
| Fentanyl |  |  | Daily morphine dose in mg/3 = fentanyl in μg/hr |

See BNF for batch equivalents

Reasons to change:

* Attempt to reduce significant s/e when original drug achieved good pain control
* Improve pain control when s/e prevented upward titration
* Safer drug in RF (morphine not well tolerated) e.g. methadone, fentanyl
* Shortage of supply
* High doses opioids with apparent tolerance to analgesic effects
* Hallucinations
* Different route administration e.g. transdermal patch, diamorphine SC
  + Can sprinkle contents of capsules on food immediately before swallowing
  + Liquid morphine
  + Sublingual buprenorphine
  + Piroxicam orodispersible (NSAID)
  + Breakthrough: oral transmucosal fentanyl citrate (Actiq) or buccal/SL/nasal
  + Buprenorphine/fentanyl transdermal patches
  + Morphine suppositories
  + Syringe drivers SC
  + Spinal analgesia

Reasons for lack response to opioids:

* Pseudo-opioid-resistant pain
  + Underdosing
  + Poor alimentary absorption of opioid (rare unless ileostomy)
  + Poor alimentary intake due to vomiting
* Semi-opioid-resistant pain
  + Bone pain
  + Skeletal instability
  + ↑ICP
  + Neuropathic
  + Activity-related
  + Pressure sores, skin damage
  + Inflammation e.g. infection
* Opioid-resistant pain
  + Muscle spasm
  + Abdo cramps (colic) (bowel, ureter, bladder)
  + Spiritual pain (chronic unremitting pain; refer for psychosocial/spiritual support and/or complementary therapy)

General points if meds not working:

* Is diagnosis correct? (e.g. path #)
* Is method of evaluating pain sound? (e.g. become more mobile so more activities provoke pain)
* Something happened to alter perception of pain? (e.g. emotional distress)
* Concordance
  + Patient beliefs (e.g. ‘natural’)
  + Lifestyle choices (s/e, inconvenience of multiple dosing)
  + Lack understanding of condition and/or way to take meds
  + Practical: forgetful, can’t open containers
  + Use simple language, discuss reasons for treatment and consequences if not treated
  + Seek pt’s views and agree on action before prescribing
  + Explain what drug is, function, mechanism of action
  + Keep regimens simple (OD/BD)
  + Seek pt’s views on how they will manage regimen within schedule/routine
  + Discuss s/e
  + Clear verbal & written instructions; rpt info and ask pt to rpt back to you
  + If necessary arrange review within short time of starting
  + Address pt questions
  + Monitor rpt prescriptions
* More likely causes of apparent ‘intolerance’
  + Dose too high
  + Titration too rapid (should be 25-50% every 3d)
  + Conversion ratio incorrect
  + Other causes confusion e.g. infection, drugs, biochemical
  + Constipation-manageable

## Opioid toxicity:

* Drowsiness/coma
* Hypotension
* Pinpoint pupils
* Confusion (incl hallucinations)
* Vomiting
* Respiratory depression
  + If ≥8 and easily rousable & not cyanosed→’wait and see’; consider reducing/omitting next dose; stop syringe drivers temporarily to allow plasma levels to decrease then restart at lower dose
  + If <8 and barely rousable/unconscious/cyanosed→naloxone 400μg in 10mL normal saline and give 0.5-1mL IV every 2 minutes until resp status satisfactory up to max 10mg; if doesn’t improve consider diagnosis; may need further doses as short acting
* Muscle rigidity/myoclonus
  + Consider RF (myoclonus)
  + Rehydrate, stop other exacerbating meds, switch opioid
  + Or clonazepam 2-4mg/24h
* Subacute: slowly progressive somnolence & resp depression; common in RF; withhold for 1-2 doses then reintroduce at 25% lower dose
* Increased toxicity if: RF, dehydration, other analgesics e.g. NSAIDs, reduced hepatic function, weight loss, amitryptiline

Causes of deterioration on stable dose of opioids: disease advancing; concurrent cause drowsiness e.g. hypercalcaemia, taken higher dose/error, not eliminating morphine as well (renal impairment)

## Prescribing controlled drugs

All strong opioids come under Misuse of Drugs Regulations 1985

Buprenorphine, codeine injection, dihydrocodeine injection, diamorphine, dipipanone, morphine >10mg/5ml, morphine solid & injectable forms, fentanyl, hydromorphone, pentazocine, methadone, pethidine, phenazocine

Most opioids schedule 2: storage CD cupboard; register; prescription writing

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| --- | --- | --- | --- |
| Schedule | Examples | Controls |  |
| 1 | Cannabis, MDMA | Have to apply for license from Home Office e.g. research |  |
| 2 | Morphine, diamorphine, cocaine, methadone, other strong opioids | Storage, register, prescription writing |  |
| 3 | Temazepam, midazolam, flunitrazepam, pentazocine, methylphenobarbitone, buprenorphine | Variable (often treated as S2) |  |
| 4 | Other BZDs, anabolic & androgenic steroids, ketamine?, zolpidem | Prescription <30d recommended; must be denatured before disposal |  |
| 5 | Codeine, medicinal opium or morphine <0.2% | OTT |  |

Community: FP10

* Must use own handwriting in ink (not typed)
* State name and address of patient
* Name of drug
* Form of drug (tablets, ampoules etc)
* Strength of preparation
* State dose precisely
* State total quantity or numbers of doses in figures AND words
  + E.g. Morphine sulphate solution 20MG in 1ML; 20MLS 4 hourly; 50MLS (fifty MLS)
* If PRN must state min interval and max 24h dose
* Signed and dated by prescriber (for FP10 must be prescriber’s address)

## Practical considerations

* Ensure pt has access to meds including over weekend (prescribe extra)
* Dosette box may help
* Tell pt about s/e and how to manage (ensure opioid prescribed anti-emetic & laxative)
* Inform district nurse, out of hours etc of plan
* Set review date and tell pt/carer how/who to contact
* Prescribe short-acting dose morphine for breakthrough pain if on MR

## Specific opioids:

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| Name | Morphine | |
| Indications | Most valuable opioid for severe pain  Cough in terminal care | |
| Regimens/doses | Acute | Regular 10mg every 4hrs then adjust  (elderly 5mg) |
| Chronic | Start 5-10mg every 4hrs then adjust  (2.5-5mg if elderly/cachexic)  20-30mg/d if opioid naïve (40-60mg if on regular weak opioid)  Increase by 25-50% every 3d until controlled or s/e (increments ≤1/3-1/2 total dose every 24hrs)  30mg 4hrly usually adequate but some require 200mg |
| Breakthrough | Titrate separately (approx. 1/10-1/6 of regular 24hr dose); equivalent 4hrly dose as extra dose  E.g. 30mins before painful activity (e.g. dressing) at 50-100% of 4hrly background dose |
| Preparations | Oral | Oral solution morphine hydrochloride: 5mg in 5ml chloroform water (dose volume 5-10ml)  Oromoph: morphine sulphate 10, 30 or 100mg/5ml (action 30mins, lasts 3hrs) (use if dose >13mg/5ml)  Sevredol tablets (morphine sulphate 10mg, 20mg, 50mg) (immediate release) |
| Modified release | Once pain controlled switch to MR with last dose or within 4hrs of immediate release; increase by 1/3-1/2 every 12 or 24hrs if necessary  12hrs: Morphgesic, Zomorph, MST (5, 10, 30, 60, 100, 200mg tablets, oral suspension)  24hrs: MXL (30, 60, 90, 120, 150, 200mg); can sprinkle contents caplets on food |
| SC/IM | Half dose of oral (10, 15, 20, 30mg/ml morphine sulphate) |
| Rectal | 15-30mg every 4hrs (10, 15, 20, 30mg suppositories) |
| Slow IV infusion | 5mg every 4hrs then adjust; 1mg/ml |
|  | MR epidural | Depodure |
|  | Topical | Pressure ulcers, oral mucositis, vaginal fistula, rectal ulceration; 0.1% gel (Intrasite) kept in place with Opsite dressing |
| Max dose | None |  |
| Side effects | Constipation in nearly all, N&V, euphoria, mental detachment, hallucinations/confusion/nightmares are very uncommon s/e | |
| Contraindications/cautions | Active metabolites (M6G, M3G) accumulate in renal impairment; little effect in liver impairment unless severe | |
| Notes | Tolerance not seen usually; withdrawal if stopped abruptly but not if reduced slowly over 5d; once on stable dose usually able to drive etc; addiction unlikely | |
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| Name | Buprenorphine | |
| Properties | Opioid agonist & antagonist; longer duration of action | |
| Indications |  | |
| Regimens/doses | Acute |  |
| Chronic |  |
| Breakthrough |  |
| Preparations | Sublingual | 200-400μg every 6-8hrs |
| IM or slow IV injection | 300-600μg every 6-8hrs |
| Transdermal (BuTrans) | 5, 10 or 20μg/hr for 7d (start at 5)  Adjust at intervals ≥3d (assess effect only after 72hrs)  Wait 24hrs after removal before other opioids |
| Rectal |  |
| Slow IV infusion |  |
|  | MR epidural |  |
| Max dose | None | Max 2 patches at any one time |
| Side effects | May precipitate withdrawal including pain if opioid dependent  Diarrhoea, abdo pain, vasodilation, dyspepsia, anorexia | |
| Contraindications/cautions | Only partially reversed by naloxone  Abuse potential; can cause dependence | |
| Notes | Increased absorbtion from patch with increased temp e.g. fever  Apply patch to dry, non-hairy, non-irritated site on upper torso; site on different area | |

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| Name | Diamorphine (heroin) | |
| Properties | Powerful opioid; greater solubility so smaller injection volume | |
| Indications | May be less N&V; good for emaciated; preferred for syringe driver as high solubility | |
| Regimens/doses | Acute | SC/IM 5mg every 4hrs (up to 10mg in well-muscled) |
| Chronic | Start 2.5-5mg every 4hrs then adjust |
| Breakthrough |  |
| Preparations | SC/IM | 1/3 dose of oral morphine dose |
| IV infusion | Start 5-10mg over 24hrs then adjust |
| Slow IV injection | ¼-1/2 of IM dose |
| Max dose | None |  |
| Side effects | Anorexia, taste disturbance, asthenia, ↑ICP | |
| Contraindications/cautions |  | |
| Notes |  | |

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| Name | Fentanyl | |
| Indications | Chronic intractable pain  Best parenteral option if renal failure  Less constipation than morphine, less sedation | |
| Regimens/doses | Acute |  |
| Chronic |  |
| Breakthrough | Oral 100μg rpt if necessary after 15-30mins  Oral transmucosal fentanyl citrate lozenge 200mg for incident pain 20mins prior  if >4 episodes adjust background analgesia  PecFent: 100μg in one nostril; max 2 sprays and 4hrs between episodes |
| Preparations | Transdermal patch | Start 12μg or 24μg for 72hrs if opioid naïve  Evaluate after 24hrs and adjust at 48-72hr intervals in steps 12-25μg/hr  Don’t give MR opioids when stating; give IR opioid PRN for ≥12hrs after starting |
| Oral | Abstral, Effentora |
|  | Nasal spray | PecFent: |
| Max dose | Consider alternative if >300μg/hr of patch  Max 800μg per episode for breakthrough; no more than 2 units for each episode | |
| Side effects | Abdo pain, dyspepsia, diarrhoea, GORD, stomatitis, anorexia, HTN, vasodilation, SOB, asthenia, myoclonus, anxiety, tremor, appetite changes, rhinitis, pharyngitis, paraesthesia  Risk fatal resp depression esp if opioid naïve | |
| Contraindications/cautions | Little effect of renal impairment; accumulates in liver impairment | |
| Notes | Takes ≥17hrs for plasma conc to decrease by 50%  Monitor for 24hrs after removal due to long action  Can take 14hrs to reach steady state  IR morphine PRN for >12hrs when changing to fentanyl until it reaches steady state and to prevent morphine withdrawal syndrome esp diarrhoea  Reduce/stop laxatives 24hrs before starting and then retitrate | |

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| Name | Oxycodone | |
| Indications | If can’t tolerate morphine (too much sedation/nausea) | |
| Regimens/doses | Acute |  |
| Chronic | 5mg every 4-6hrs; can increase BD but usually every other day  Renal impairment: 2.5mg every 6hrs |
| Breakthrough |  |
| Preparations | Oral | Oxynorm |
| Modified release | Longtec, Oxycontin  10mg every 12hrs then increase |
| SC/IM | Start 5mg every 4hrs (infusion 7.5mg/24hrs) |
| IV infusion | Start 2mg/hr then adjust |
| Slow IV injection | 1-10mg every 4hrs |
| With naloxone | Targinact: 10mg/5mg every 12hrs |
| Rectal MR | Dolocodon |
| Max dose | None | 400mg/d  Targinact: 40mg/20mg every 12hrs |
| Side effects | Diarrhoea, abdo pain, anorexia, dyspepsia, dyspnoea, impaired cough reflex, asthenia, anxiety, chills, bronchospasm | |
| Contraindications/cautions | Accumulates in liver impairment & renal impairment | |
| Notes |  | |

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| Name | Pethidine | |
| Indications | Prompt but short-lasting  Less constipation  Not for severe continuing pain | |
| Regimens/doses | Acute | Oral 50-150mg every 4hrs |
| Chronic |  |
| Breakthrough |  |
| Preparations | Oral |  |
| Modified release |  |
| SC/IM | 25-100mg every 4hrs |
| IV infusion |  |
| Slow IV injection | 25-500mg every 4hrs |
| With naloxone |  |
| Rectal MR |  |
| Max dose |  |  |
| Side effects | Restlessness, tremor, hypothermia, convulsions in overdose | |
| Contraindications/cautions |  | |
| Notes | Weaker than morphine and dihydrocodeine but stronger than cocaine | |

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| Name | Tramadol | |
| Properties | Opioid and enhances serotonergic & adrenergic pathways; synthetic analogue codeine | |
| Indications | Rapid absorption orally (analgesia <1hr)  Safe in elderly & RF as metabolised in liver  May help neuropathic | |
| Regimens/doses | Acute |  |
| Chronic | 50-100mg every 4hrs |
| Breakthrough |  |
| Preparations | Oral | Also available dispersible |
| Modified release | 12 or 24hrs |
| SC/IM/IV | 50-100mg every 4-6hrs |
| Rectal MR |  |
| Max dose | 400mg/d oral |  |
| Side effects | Fewer s/e, less resp depression & constipation, less addiction potential  Diarrhoea, retching, fatigue, paraesthesia, N&V at higher doses | |
| Contraindications/cautions | Can cause serotonin toxicity if with other drugs affecting serotonin esp in elderly) | |
| Notes | Less addiction potential; not a controlled drug; lowers seizure threshold | |

## Weak opioids

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| Name | Codeine | |
| Indications | Mild-mod pain (weak opioid)  Cough suppression | |
| Regimens/doses | Acute |  |
| Chronic |  |
| Breakthrough |  |
| Preparations | Oral | 30-60mg every 4hrs |
| Modified release |  |
| IM | 30-60mg every 4hrs |
| IV infusion |  |
| Slow IV injection |  |
| With paracetamol | 8mg/500mg x2 every 4-6hrs  Also available 15/500; 30/500 usually for palliative |
| Rectal MR |  |
| Max dose |  | 240mg/d oral; max 8 tablets co-codamol |
| Side effects | Constipation (more than tramadol), abdo pain, N&V, anorexia, seixures, hypothermia, andidiuretic, muscle fasciculation | |
| Contraindications/cautions | Metabolism varies considerably; marked increased toxicity if ultra-rapid metaboliser and reduced effect in poor metabolier  5-10% of pop have CYP2D6 (lack hepatic enzyme to convert to morphine) | |
| Notes | Always give laxative e.g. bisacodyl 1-2 nocte  Max dose due to increased adverse effects relative to pain control and tablet burden  Not controlled drugs so prescribing easier | |

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| Name | Dihydrocodeine | |
| Indications | Similar to codeine | |
| Regimens/doses | Acute |  |
| Chronic |  |
| Breakthrough |  |
| Preparations | Oral | 30-60mg every 4-6hrs  Severe: 40-80mg |
| Modified release | 60-120mg every 12hrs |
| IM/SC | Up to 50mg every 4-6hrs |
| IV infusion |  |
| Slow IV injection |  |
| With paracetamol | Co-dydramol 10/500mg |
| Rectal MR |  |
| Max dose |  | 240mg/d |
| Side effects | Higher doses co-codamol may cause more N&V  Paralytic ileus, abdo pain, diarrhoea, seizures, paraesthesia | |
| Contraindications/cautions |  | |
| Notes |  | |

## Other opioids

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| Name | Notes |
| Diapanone | Less sedating  Contains anti-emetic (not used regularly) |
| Hydromorphone hydrochloride | Very similar to morphine  May be used in renal impairment or if inadequate pain relief/intolerable s/e with other opioids  Palladone capsules: can sprinkle content capsules on soft food  1.3mg is equivalent to 10mg morphine (factor 7.5) every 4hrs then titrate up  MR available  PO, SC, IM, IV, spinal; widely used in USA where diamorphine not available |
| Methadone | Less sedating  Longer action, accumulates over several days  Occasionally if excitation or pain worse with morphine  If prolonged use not >twice daily (avoid accumulation & toxicity) |
| Tapentadol | Opioid agonist and inhibits NA reuptake  Less N&V & constipation |
| Meptazinol | Weak opioid  Onset 15 mins, lasts 2-7hrs  Low resp depression |

# Non-opioids

NSAIDs/paracetamol: reduce inflammation and/or PG synthesis and thereby reduce stimulation of nociceptors on peripheral nerves

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| Name | Indications | Dose/preparation | | Side effects | Notes |
| Nefopam | Persistent unresponsive pain | 60mg TDS then adjust (usually 30-90mg) | | Little/no resp depression  Antimuscarinic s/e  Sympathomimetic s/e |  |
| NSAIDs | Chronic disease with pain & inflammation  MSK pain  Dysmenorrhoea  2° bone tumours  Bone pain | Ibuprofen | 1.2-1.6g/d in 3-4 divided doses (200-400mg TDS)  Incident pain 20mins prior | Bleeding risk  Bronchospasm in asthma, fluid retention, renal impairment, oedema, pain, nausea, GI ulcer, hypersensitivity, vascular events | Protect with PPI if GI ulcer or dyspepsia/GORD  NOT in myeloma (risk renal impairment) and beware in elderly  Relatively c/I in HF/HTN  Avoid if mod/severe RF  Lowest effective dose |
| Naproxen | 250-300mg BD (PO/PR) | More s/e |
| Diclofenac | 50mg TDS (PO/SC/PR) | More s/e esp hepatic |
| COX-2 inhibitors | Preferred to NSAIDs if risk GI s/e (history PU, aspirin, warfarine, SSRIs) | Celecoxib | 200mg od/bd | Lower risk s/e  Only if low risk CVS disease |  |
| Paracetamol | Mild-mod pain  Pyrexia  Few s/e | PO | 0.5-1g every 4-6hrs  Max 4g/d | Rare  Liver damage on OD  Main problem is tablet burden | Caution alcohol dependence, liver insufficiency, chronic malnutrition or dehydration  Check when last given  Max dose restricted by hepatotoxicity |
|  | IV infusion | 1g every 4-6hrs over 15 mins (if >50kg) |
| Gabapentin | Neuropathic pain | 300mg OD on d1, BD on d2 then TDS on d3 (or start TDS)  Max 3.6g/d (600mg tds) | | N&V, gingivitis, diarrhoea, abdo pain, dyspepsia, constipation, dry mouth, flatulence, altered appetite, HTN, vasodilation, oedema, SOB, cough, pharyngitis, confusion, emotional lability, depression, vertigo, anxiety, drowsiness, insomnia, headache, mvt disorders, tremor, fever (more) | |
| Pregabalin | Neuropathic pain | Lecture: 25mg BD  BNF: 150mg in 2-3 divided doses; increase after 3-7d to 300mg/d  Max 600mg/d in divided doses  (titrate dose to creatinine clearance)  Nb. Can’t put in syringe driver | | **Dry mouth, constipation**, vomiting, flatulence, oedema, **dizziness, drowsiness, fatigue**, irritable, ↓attention, disturbed muscle control & mvt, speech disorder, **impaired memory**, paraesthesia, euphoria, **confusion**, malaise, appetite change, insomnia, wt gain**, sexual dysfunction**, **visual disturbance, tremor**  Uncommon: agitation, hallucinations, myoclonus, panic, sweating | |
| Amitryptiline | Unlicensed neuropathic pain  (enhance central inhibition by increase synaptic serotonin) | 10mg nocte then increase every 2wks up to max 75-150mg if necessary | | TCA |  |
| Nortryptiline | Better tolerated than amitryptiline | 10mg nocte up to 75mg | | TCA |  |
| Carbamazepine | Neuropathic | 200mg BD increase slowly to max 1.5g/24h | |  |  |
| Dosulepin | Neuropathic pain | 25-75mg nocte | |  |  |
| Lofepramine | Neuropathic pain  Esp for elderly/frail | 70mg nocte  Up to 70mg BD after 5-7d | |  |  |
| Capsaicin | Neuropathic  Counter-irritation | Topical  Small amount 3-4x/d | | Intense burning during initial treatment | Wash hands after application and not after hot shower/bath |
| Lidocaine | Neuropathic  Post-herpetic neuralgia | Topical (impregnated plasters)  5% plasters for post-herpetic neualgia  OD up to 12h then 12h plaster-free | |  |  |
| Ketamine | NMDA recetor-channel blocker  Severe pain  Persistent movement-related pain  Some neuropathic pains | Oral, buccal SC infusion | | Well tolerated low doses  If >400mg/24h: drowsiness, euphoria/dysphoria, hallucinations, HTN | Anaesthetic |
| BZD | Muscle spasm  Difficulty sleeping  Incident pain with anxiety | Clonazepam 250-500μg nocte  Lorazepam 0.5mg sublingual | |  | Only specialists |
| Dantrolene | Skeletal muscle relaxant  Chronic severe spasticity  Muscle pain | 25mg daily increased weekly to max 100mg QDS (usually 75mg tds) | | Potentially life-threatening hepatotoxicity reported at high doses  Diarrhoea, N&V, resp depresion |  |
| Dexamethasone | Nerve root/trunk compression  MSCC  Anti-cancer in breast, lymphoma, myeloma, prostate Ca | 4-8mg OD  16mg OD | |  |  |