

Mighty Opium

In EMERGENCY: overdosed opium fiends, drug seekers and infectious complications

OD looks like this:

- Slowed respiratory rate, <13;
- Pinpoint pupils
- Coma
- Low blood pressure
- Pulmonary oedema

SALIENT FEATURES OF HISTORY:

WITHDRAWAL (heroin):

More nightmarish and prolonged with methadone

Signs and symptoms	Time to onset
First stage	8 hours
Yawning	
Perspiration	
Runny Nose and eyes	
Second stage	12 hours
Dilated Pupils	
Hair standing on end	
Muscle twitches	
Hot and cold flushes	
Bone, joint and muscle pain	
Anorexia	
Third stage	18-24 hours
↑ blood pressure	
↑ temperature	
↑ pulse rate	
Restlessness	
Nausea	
Insomnia	
Fourth stage	24-36hours
Feverish face	
Position-curling up	
Vomiting	
Diarrhoea	
Spontaneous ejaculation or orgasm (high dose withdrawal, quite scary)	

Related to injecting use:

Infections, endocarditis, vein state, transmissible diseases

Related to psychological consequences:

Symptoms of psychotic illness

→ **Symptoms of withdrawal** and evidence of tolerance

Symptoms resulting from malnutrition and anorexia

Symptoms resulting from poor self-care

Related to social consequences:

Withdrawal, failure in work, education or relationships

Related to forensic history:

Extent of legal repercussions, eg. assault, possession etc...

Withdrawal from **heroin**; onset 8-24 hours, duration 4 - 10 days.
 Withdrawal from **methadone**: onset 12 -48 hours, duration 10 -20 days

PHYSICAL EXAMINATION:

Look for track marks, abscesses, signs of poor self-care

Listen to the heart for murmur of endocarditis

Take temperature (is it high because of infection, or because of withdrawal?)

INVESTIGATIONS:

BSL especially if unsure what sort of coma this is

EUC especially if mental state changes are prolonged

LFT especially if using intravenously

Viral serology: Hep C is the major concern; HIV and Hep B also important

Urinalysis to look for heroin metabolites, chiefly morphine and 5-MAM

Echocardiogram to rule out endocarditis

Abdo Xray if constipated

MANAGEMENT

ACUTE: in the EMERGENCY setting:

Life and limb not threatened? **SEDATE AND OBSERVE. Diazepam 10mg PRN**
Severe intoxication? Unconscious overdose?

Immediate Effects:
Acute reversal of OD
Extreme unhappiness
Nausea, vomiting, diaphoresis
Hyperalgesia
Agitation / Anxiety
Hyperventilation

- **Secure airway (may need to intubate)**
- **Urinary catheter** (monitor output)
- **NALOXONE** in small increments, until you raise the dead
- **Regular chest auscultation:** looking for pulmonary oedema
- **Frusemide** if pulmonary oedema develops
- **IV fluids** if dehydrated

DETOXIFICATION:

Choice of setting very important; does this person need to be in hospital?
If they are motivated, they can detox at home.

Medications to treat symptoms of withdrawal

Involves the administration of various drugs to treat individual symptoms as they arise:

- | | | |
|-------------------------|--------------------------|-----------------------------------|
| - Nausea | metoclopramide (MAXOLON) | 10mg, 4-6 hours |
| - Muscle aches/pains | paracetamol | 5mg, 4-6 hours |
| - Muscle cramps | quinine | 300mg, twice a day |
| - Abdominal cramps | hyoscine | 20mg, every 6 hours |
| - Sleeplessness/anxiety | diazepam (VALIUM) | 10mg 6 hours. Stop after 3-4 days |
| - Diarrhoea | Lomotil as required | |

- **CLONIDINE:** weirdly central-acting blood pressure tablet; improves "the shakes"
- **Antidepressants** can help with the whole process

MAINTENANCE:

Methadone: long acting synthetic opioid, terrible withdrawal, daily dosing (with "take away" doses for patients who behave well and do as they are told). Plus it makes you desperately unhappy.

Buprenorphine

Studies have demonstrated buprenorphine to be:

1. More effective than systematic medications to relieve symptoms
2. More effective in retaining patients through the withdrawal episode
3. More effective in reducing heroin use in outpatient settings.

As with other treatment regimes, the aim of this treatment is the reduction of withdrawal symptoms and cravings.

Before commencing treatment, **patients must abstain from heroin for at least 6 hours**, take

no methadone for 24 hours and patients need to abstain from heroin use until stabilised on Buprenorphine.

WARNING!

Unsupervised use of other sedative drugs, such as benzodiazepines, alcohol, opiates, tricyclic anti depressants in combination with Buprenorphine **can be extremely dangerous, resulting in coma, respiratory depression and even death.**

NEUROPHARMACOLOGY OF OPIATE DRUGS

-G protein coupled opiate receptors: μ , δ , and κ

- 1) mu receptor activates G protein and thus adenylate cyclase
- 2) this leads to a fall in cAMP; which in turn leads to reduced activity of cAMP dependent protein kinase A (PKA)
- 3) Potassium channels activate, calcium channels de-activate; this results in a decrease in action potential and reduced neurotransmitter release. In total: a reduced electrical excitability of Mu-carrying neurons.
- 4) in the Ventral Tegmental Area, these neurons normally suppress the firing of dopaminergic neurons into the Nucleus Accumbens; thus disinhibition leads to over-excitation of the NATURAL REWARD SYSTEM, with buckets of dopamine getting dumped each time you inject.

Heroin uptake by opiate g-protein-coupled receptors

→ **Phosphorylation (inactivation) of Receptor**
→ **Underexpression of receptors (to combat heroin influx)**

THUS: loss of total excitability;

THUS NEED MORE DRUGS FOR SAME EFFECT

All opiate receptors are affected by heroine and morphine

Mu and Delta receptors:

- Analgesia (spinal / supraspinal)
- Behavioural
- Respiratory depression
- Reduced gastro-intestinal motility
- Pupillary constriction
- Physical dependence

Kappa Receptors: (methadone affects these selectively)

- analgesia (spinal)
- dysphoria / sedation

Actions of opiates

- **Analgesia**
 - acute & chronic pain
 - not very effective for neuropathic pain
- **Euphoria**
 - sense of contentment / well being
 - also sedation
 - with IV use, a sudden "rush"
- **Respiratory depression**
 - occurs with therapeutic doses
 - Due to Decreased sensitivity to raised P_aCO_2 in brain stem
- **Gastro-intestinal tract (intramural nerve plexuses)**
 - increased sphincter tone: decreased motility
 - constipation (side effect) : treat diarrhoea
- **Reduced Cough reflex**
 - not related to analgesia
 - codeine effective in sub-therapeutic doses
- **Pupillary constriction**
 - m & k receptors in oculomotor nucleus (III)
 - reversed by I.V. naloxone
- **Nausea & vomiting**
 - area postrema (medulla) - chemoreceptor trigger zone (CTZ)
 - in approximately 40% initially
 - usually transient with repeated administration