Amphetamines

In EMERGENCY:

People on speed will not come in to ED unless in serious trouble, eg:

**ACUTELY UNPLEASANT INTOXICATION:** one night it got out of hand…

- Disorientation and possibly delirium or psychosis
- Headache due to massively increased blood pressure
- Dyskinesia, twitchiness due to dopaminergic effects
- Agitation due to dopaminergic and cholinergic effects
- Formication? not sur what this is caused by
- Symptoms of stroke …it might actually BE a hemorrhagic stroke!
- Chest pain you can actually have an MI because of vasoconstriction
- Palpitations due to tachycardia and/or arrhythmia
- Dry mouth a sympathetic overdrive effect
- Nausea and vomiting sympathetic, or related to intoxication
- Diarrhea due to sympathetically increased gut motility
- Difficult micturition due to sympathetic overdrive
- Diaphoresis as above
- Erythematous painful rashes, needle marks if they inject
- Infected deep ulcerations (echyma) from scratching

**HYPERTHERMIA!!**

**SALIENT FEATURES OF HISTORY:**

**WITHDRAWAL:**

- opposite to intoxication
- Deprssion
- Dysphoria
- Reduced Concentration
- Prolonged disturbed sleep
- extreme hunger
- anxiety
- psychosis
- exhaustion and confusion

- 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
- Related to social consequences:
  - Withdrawal, failure in work, education or relationships
- Related to forensic history:
  - Extent of legal repercussions, eg. assault, possession etc…

**PHYSICAL EXAMINATION:**

- Weight loss? clinical emaciation?
- Hyperactivity, confusion, and agitation (may combine to produce severe hyperthermia, which can be worse in physically restrained individuals)
- Diaphoresis
- Dilated pupils
- Elevated blood pressure
- Tachycardia
- Increased alertness, hypervigilance, paranoia
- Euphoria
- Confusion or agitation
- Grinding teeth (“bruxism”)
- Skin flushing
- Infected deep ulcerations (echyma) in patients with formication
- Skin track marks, cellulitis, abscesses, phlebitis, or vasculitis with IV use
INVESTIGATIONS:

- **BSL** especially if mental state changes are prolonged
- **EUC** especially if mental state changes are prolonged
- **LFT** especially if using intravenously, or in severely hyperthermic patients
- **ECG** if there is a cardiac complaint
- **Creatine Kinase** to look for rhabdomyolysis
- **Urinalysis** to look for heme, a sign of rhabdomyolysis
- **Head CT, if stroky** because it would suck to miss a subarachnoid bleed

MANAGEMENT

**ACUTE: in the EMERGENCY setting:**

- **Life and limb not threatened? SEDATE AND OBSERVE.** Diazepam 10mg.
- **Acute oral ingestion?** Activated Charcoal p.o. …

**Severe intoxication?**
- Secure airway
- Urinary catheter (monitor output)
- Midazolam to control behaviour, agitation, and seizures
- ECG monitoring: so you can cardiovert in time
- **Regular chest auscultation:** looking for pulmonary oedema
- Frusemide if pulmonary oedema develops
- **Aggressive Cooling of hyperthermic patients**
- IV fluids if dehydrated

**ACUTE PSYCHOSIS?**
- **Regular chest auscultation:** looking for pulmonary oedema
- Frusemide if pulmonary oedema develops
- **Aggressive Cooling of hyperthermic patients**
- Lorazepam to control agitation (Midazolam may be needed instead)
- Beta Blockers to reduce heart rate and anxiety
- HALOPERIDOL or CHLORPROMAZINE for psychotic features

**AMMONIUM CHLORIDE:**
Can increase the rate of excretion of amphetamine

**DETOXIFICATION:**

- **Still psychotic?**
  - Olanzapine 2.5 to 5 mg bd for 2-3 weeks
  - OR Risperidone 0.5 to 1 mg bd for 2-3 weeks

- **Ugly withdrawal?**
  - Mirtazapine30 to 60mg nocte for insomnia (a sedating antidepressant)
  - Alternatively an SSRI .. for a looong time

**MAINTENANCE:**

- **SSRIs may have to continue as long as necessary**
- Ditto antipsychotic agents.
- Relapse is normal.
NEUROPHARMACOLOGY OF AMPHETAMINE

**Absorption:**
After oral ingestion of amphetamine, peak effect at 2 hrs.
Absorption is complete in 4-6 hours. Levo-amphetamine metabolised 40% slower than dextro.
Amphetamine is largely unaffected during metabolism. The entire dose is probably eliminated in the urine over a period of several days.
Metabolism produces Phenylacetone, benzoic acid, and hippuric acid less than 25%; 4-hydroxyamphetamine, 4-hydroxyxynorephedrine, and norephedrine less than 10%.

**Pharmacology:**
Dextro-AMPH has a greater affinity for CNS receptors, while levo-AMPH seems to mediate the cardiovascular effects of speed.
CVS effects are mediated by noradrenaline release, producing vasoconstriction even at low doses. Tachycardia follows. Sympathetic effects develop in proportion to dose.

**Administration** plays an important role. Oral AMPH effects are divorced from the act of ingestion by about 30 to 60 minutes, and the dopamine spike in the Nucleus Accumbens is lower and blunter.
With injection, the dopamine rises immediately and massively, and so the reward system is activated. The pleasure of the effect is married to the act of injecting or snorting. Hence IV use of amphetamine appears to have a greater addictive potential.

**Excretion:**
Depends on urine pH. Acidic urine will result in greater excretion. Difference of 60% excreted per 24 hrs with acidic, down to 3% with alkaline.

**IN SUMMARY:** amphetamine increases release and reduces reuptake of catecholamines and of noradrenaline in particular. This is responsible for 90% of its effects. The oral dose of these stimulants, which produce amphetamine-type subjective effects in humans, correlated with their potency in releasing NE, not DA, and did not decrease plasma prolactin, an effect mediated by DA release.
However, it is likely that adaptive dopamine channel remodeling is responsible for the negative symptoms of amphetamine withdrawal from chronic use.