put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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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…

More likely scenario:
The speeding patient presenting in ED will more likely be in the grip of an **amphetamine psychosis.**
This is usually paranoid, with delusions of persecution, speech pressure, auditory hallucinations and extreme agitation.

Disorientation and possibly delirium or psychosis
Headache due to massively increased blood pressure
Dyskinesia, twitchyness due to dopaminergic efects
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 (ecthyma) from scratching
HYPERTHERMIA!!

SALIENT FEATURES OF HISTORY:

WITHDRAWAL:
-opposite to intoxication
= Depression
= 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 (ecthyma) 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. …

AMMONIUM CHLORIDE:
Can increase the rate of excretion of amphetamine

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**

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-hydroxynorephedrine, 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, procuding vasoconstriction even at low doses. Tachycardia follows. Sympathetic effects develop in proportion to dose.

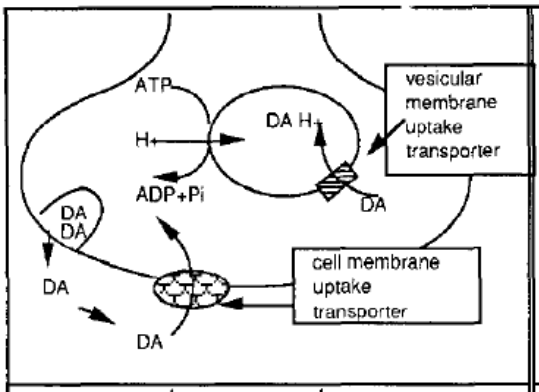
ADMINISTRATION

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.

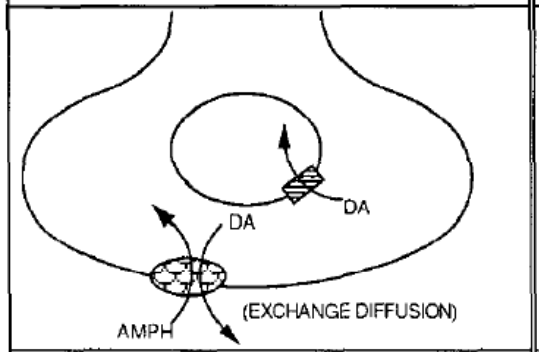
EXCRETION:

!! **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.

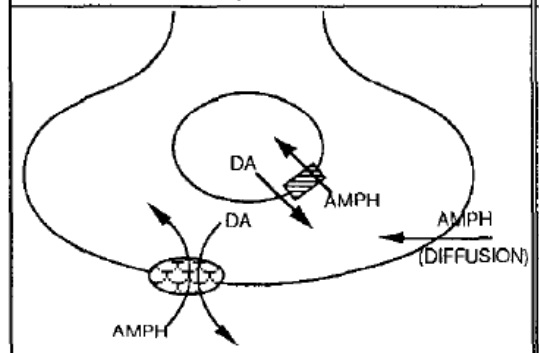
AT THE RECEPTOR LEVEL:



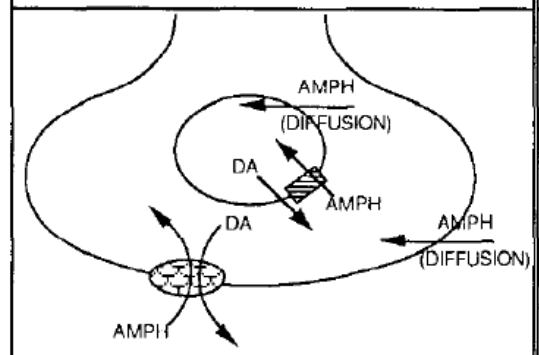
A. Impulse-dependent exocytotic release of dopamine and pH-dependent vesicular storage of dopamine.
Cell firing causes exocytotic release of dopamine into the extracellular space. The dopamine is taken back into the nerve terminal through the uptake transporter. Dopamine is taken up into the vesicle through a second transporter. It is held inside the vesicle by a proton gradient maintained by an ATP-dependent proton pump.



B. Low doses of AMPH (1-5mg/kg?) cause release of dopamine through:
1. exchange diffusion across the cell membrane.



C. Moderate doses of AMPH (5 mg/kg - ?) cause release of dopamine through:
1. exchange diffusion across the cell membrane,
2. passive diffusion of AMPH into the cell,
3. an interaction between AMPH and the vesicular membrane transporter.



D. High doses of AMPH cause dopamine release through:
1. exchange diffusion across the cell membrane,
2. passive diffusion of AMPH into the cell,
3. an interaction between AMPH and the vesicular membrane transporter,
4. passive diffusion of AMPH into the storage vesicle: alkalinization of the vesicle.

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 the 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.