Toxidromes

Anticholinergic Syndrome

Agitated delirium (fluctuating LOC, slurred speech, picking at objects, confusion) associated with peripheral muscarinic blockade (mydriasis, ↑HR, dry mouth/skin, flushing, ↑T, ↓bowel sounds, urinary retention). Potentially life-threatening.
Examples: Benztropine, antihistamines, TCA, antipsychotics, atropine, *Datura* species
Mx:

- Resus: ABC, O_2, BDZ for fits, correct ↓BSL or ↑T.
- Supportive: Quiet well lit environment. IV fluids, IDC for retention, BDZ for agitation.
- Inv: ECG, paracetamol screening tests. Drug level, UEC, CK may be appropriate.
- Antidote: Physostigmine centrally acting acetylcholinesterase inhibitor may help & aid Dx.

Cholinergic Syndrome

Potentially lethal ↑central & peripheral ACh activity at muscarinic & nicotinic receptors. Affects CNS (agitation, confusion, fits, coma), NMJ (fasciculation, weakness), parasympathetic (miosis, ↑secretions, D&V, ↑urination, ↓HR) & sympathetic (mydriasis, sweating, ↑HR, ↑BP)
Mnemonics: **DUMBELS** (diarrhoea, urination, miosis, bronchospasm, emesis, lacrimation, salivation) or **SLUDGE** (salivation, lacrimation, urination, diaphoresis, GI upset, emesis)
NB: ↑HR > ↓HR (as may be hypoxic, vasodilated). Usually miosis in warfare nerve agent poisoning.
Examples: OP, carbamates, nerve agents (e.g. Sarin), anti-Alzheimer agents (e.g. donepezil), myaesthenia gravis Rx (neostigmine, physostigmine).
Mx:

- PPE & decontaminate patient for OP
- Resus: ABC, suctioning airway secretions, O_2, atropine++, intubation, BDZ for fits.
- Supportive: Well ventilated environment & PPE. IV fluids, IDC for monitoring.
- Inv: ECG, paracetamol screening tests. Cholinesterase level, CXR, ABG, UEC.
- Antidotes: Atropine & pralidoxime (for OP or nerve agents).

Sympathomimetic syndrome

Features include anxiety, delusions, paranoia, diaphoresis, piloerection, ↑HR, ↑BP, hyperreflexia, tremor, mydriasis, arrhythmias and seizures.
Examples: salbutamol, amphetamines, cocaine, MDMA, ephedrine, pseudoephedrine
Mx:

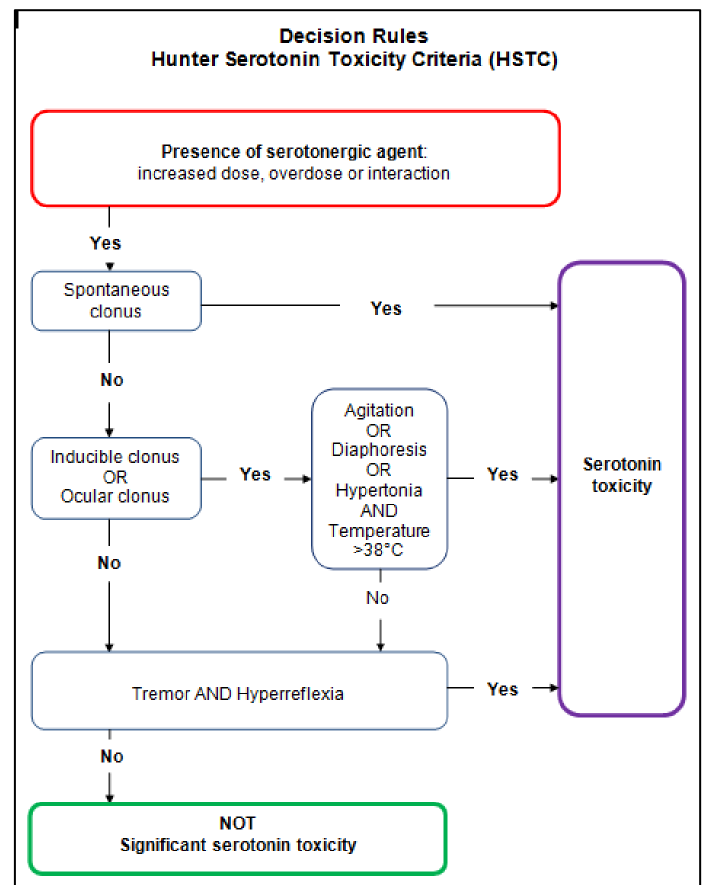
- Resus: ABC, O_2, BDZ for fits, correct ↑T.
- Supportive: Quiet well lit environment. IV fluids, BDZ for agitation.
- Inv: ECG, paracetamol screening tests. Drug level, UEC, CK may be appropriate.
- **B-blockers are contraindicated** as unopposed alpha action may → ↑HT, coronary spasm.

Serotonin Syndrome

Spectrum (mild-lethal) of serotonin toxicity mostly via $5HT_2$ receptors from drug interactions (e.g. MAOI+SSRI), drug OD, recreational drug use or rarely therapeutic drug use. Rapid onset of CNS changes (anxiety, agitation, confusion), autonomic stimulation (↑HR, mydriasis, diaphoresis, hyperthermia, flushing), & neuromuscular excitation (clonus, hyperreflexia, myoclonus, tremor, rigidity). *E.g.:* Antidepressants (SSRI,SNRI,TCA,MAOI,St.John's Wort,Li), Analgesics (tramadol, pethidine,fentanyl,dextromethorphan), Recreational drugs (cocaine,MDMA,amphetamine), linezolid

Hunter Serotonin Toxicity Criteria: (see diagram)
In the presence of a serotonergic agent:

- Clonus (inducible, spontaneous [lower>upper limb] or ocular)
- Agitation
- Diaphoresis
- Tremor
- Hyperreflexia [lower>upper limb]
- Fever & hypertonia common in life-threatening cases



Sternbach's Criteria (less sens/spec than HSTC)

1. Recent addition or increase in a known serotonergic agent
2. Absence of DDx (infection, drug abuse, withdrawal, etc.)
3. No recent addition or increase of a neuroleptic agent
4. At least three of the following symptoms: Mental status changes, Agitation, Myoclonus, Fever, Hyperreflexia, Diaphoresis, Shivering, Tremor, Diarrhoea, Incoordination

Mx:

- Resus: ABC, O_2, intubate if coma, recurrent seizures or hyperpyrexia
- Treat hyperpyrexia (paralyse, ventilate, cool, ??consider **dantrolene**) and ↓BSL
- Supportive: Quiet/bright env. Stop 5HT drugs. IV fluids, BDZ for agitation/HT.
- Inv: ECG, paracetamol screening tests. Drug level, UEC, CK, Trop may be appropriate.
- Antidotes: **cyproheptadine** 12mg stat PO then 4-8mg q4-6h (mod tox), **chlorpromazine** 25-50mg IV then rpt PO/IV q6h (intub or not absorbing, e.g. post charcoal). **Olanzepine** 10mg SL may be useful too.

Neuroleptic Malignant Syndrome (Dopamine blockade)

Rare but potentially lethal Cx of neuroleptics characterised by slow onset neuromuscular rigidity (lead pipe or cog-wheel rigidity, bradykinesia, mutism, staring, dystonia, dysarthria, invol movements), altered mental status & autonomic instability (↑T, ↑HR, ↑BP, arrhythmias).
Dx: Severe muscular rigidity, pyrexia with 2 of (diaphoresis, ↑BP, ↑HR, incontinence, dysphagia, mutism, tremor, altered LOC, leucocytosis, ↑CK or evidence of muscle injury) in a patient on a antipsychotic where not explainable by another drug, condition or psychiatric disorder.
RF: >1 neuroleptics, haloperidol, depot fluphenazine, young, M, genetics, dehydration, PMH.
DDx: acute lethal (malignant) catatonia, malignant hyperthermia, serotonin syndrome, anticholinergic syndrome, sympathomimetic syndrome, encephalitis, metabolic encephalopathies
Mx:

- Resus: ABC, O_2, if coma or hyperpyrexia (>39.5°C) then intubate
- Treat hyperpyrexia (paralyse, ventilate, cool, consider **dantrolene**) and ↓BSL
- Usual supportive care. Avoid dopamine antagonists. Cease neuroleptics.
- BDZs are controversial but are used in mild cases.
- **GTN** or **nitroprusside** may be used initially for HT
- **Bromocriptine** may be also used for autonomic instability or severe cases.
- Inv: ECG, CXR, ABG, CK, FBC, UEC, CMP, LFT, Cultures, CT/MRI brain, ±LP.
- Antidotes: **Bromocriptine**, **dantrolene**, ECT

Withdrawal Syndromes

Alcohol withdrawal

Usually develops between 6-24hrs after last drink.

Features: Autonomic excitation (tremor, agitation, sweating, ↑HR, ↑BP, N&V, ↑T), neuro-excitation (hyperreflexia, nightmares, hallucinations, generalised seizures), delirium tremens (severe form, mort ~8%, ↓LOC, autonomic & neuro-excitation, respiratory/CVS collapse, death).

Mx:

- Consider other CX of EtOH abuse (Wernicke's, dehydration, malnutrition, infections, pancreatitis, gastritis, liver disease, SDH, ketoacidosis, loss of social support).
- Inpatient (severe, ↓LOC, fits, hallucinations) vs outpatient (motivated)
- If florid DT or fitting – resus, IVC, BDZ, treat hypoglycaemia
- Monitor with Alcohol Withdrawal Scale (AWS)
- If significant symptoms by AWS, give **diazepam** 5-20mg PO q1-8h
- Give **thiamine** 100mg PO/IV OD
- Ensure adequate fluids, electrolytes, nutrition
- Consider blood tests (FBC, UEC, LFT, coags, lipase)

Sedative-hypnotic withdrawal

Onset usually 2-10d after abruptly stopping drug – though short acting drugs e.g. GHB may produce symptoms earlier.

Features: Similar to EtOH withdrawal. Agitation, insomnia, inattention, palpitations, hyperacusis/photophobia, hallucinations, spasticity, occasionally severe with seizures/delerium.

Mx:

- Restart sedative or change to longer acting one and taper dose over weeks

Opioid withdrawal

Unlike other withdrawal syndromes, although unpleasant not usually life-threatening. Onset after cessation depends on drug, dose/frequency and degree of dependence. E.g. <6hrs for heroin or >2 days for methadone.

Features: Anxiety, restlessness, insomnia, craving, yawning, lacrimation, rhinorrhoea, salivation, anorexia, N&V, Abdo cramps, diarrhoea, mydriasis, diaploresis/piloerection, flushing, joint/muscle aches, ↑HR & ↑BP if severe.

Mx:

- Usually outpatient management unless severe.
- Opioid replacement – methadone or buprenorphine with slow tapering
- Rapid detoxification using naltrexone, buprenorphine, or clonidine
- Supportive care – may include
    - **Metoclopramide** (N&V)
    - **Buscopan** (abdo cramps)
    - **Paracetamol** (myalgia)
    - **Diazepam** (agitation)
    - **Clonidine** - test with 75mcg PO if no postural hypotension then 50-300mcg PO tds & tapered over 5d.
- Counselling