Serotonin Syndrome, Neuroleptic Malignant Syndrome, MH

Serotonin Syndrome
10% mortality rate

Causes
5HT agonist, Usually due to >1 drug
Sertraline, SSRIs, Li, MAOI, St John’s wort, TCA, SNRI
Illicit drugs: LSD, cocaine, amphetamines, E
Analgesia: Pethidine, fentanyl, tramadol, sumatriptan
AntiParkinsons: L dopa, bromocriptine

Clinical Features
Onset <12hrs (faster than NMS; 60% within 6hrs)
Fever (milder than in NMS)
Muscle rigidity (esp legs; occurs late)
NM hyperactivity: akathesia, hyperreflexia, clonus; myoclonic jerks; seizures
Autonomic hyperactivity: incr HR/RR/BP, sweating, mydriasis, hyperactive bowel sounds, diarrhoea
Altered LOC: agitation, confusion, change in behaviour/cognition
Metabolic acidosis, rhabdo (rare), ARF, seizures, DIC

Management
25% ETT rate (if coma, recurrent seizures, incr T >39.5, severe rigidity)
Benzos
Barbs and paralysis if severe
GTN or nitroprusside for HTN
Observe at least 8hrs
Cyproheptadine: 8mg PO - 4mg PO Q4h; 5-HT receptor antagonist
Chlorpromazine 50-100mg IV - 50-100mg Q6h or olanzapine 5mg PO

Neuroleptic Malignant Syndrome
5-30% mortality
Dopamine blockade in basal ganglia and hypothalamus - hyperthermia due to sustained muscle contraction (EPSE) or elevated T set point

Causes
Dopamine agonists
Occurs after starting/incr dose/adding 2nd drug, within 2/52 (in 2/3)
Typical/atyptical antipsychotics (haloperidol, chlorprom, olanzapine, quetiapine, risperidone)
Antiemetics (chlorpromazine, maxalor, stemetil)
Antihistamines

Patient factors: young, male, agitated, organic brain disease, dehydration, malnutrition, Hx NMS
Drug factors: high potency (Haloperidol), high dose, rapid incr in dose, depot meds

Clinical Features
Develops over 24-72 hrs
Hyperthermia
Rigidity
NM: tremor, incontinence; decr reflexes
Autonomic instability: incr HR/RR/BP, sweating but pallor, mydriasis or normal pupils; normal BS’s
Altered LOC (dysphagia, aphony, dysarthria, staring, bradykinesia)
Rhabdomyolysis
Renal failure
RS/CV failure, ARF, MOF, DVT, NCPO, PE, pneumonia, seizures, rhabdo, dehydration

**Investigations**
WCC up to 30; CK > 1000; incr LFTs; incr K/phos/Ur/Cr/plt; myoglobinuria; ARF; metabolic acidosis

**Serotonin syndrome vs neuroleptic malignant syndrome**
NMS idiosyncratic reaction after prolonged exposure to neuroleptics or after withdrawal dop agonist
NMS develops over days or weeks
NMS - hyperthermia, severe muscle rigidity, rhabdo (not mydriasis, diarrhoea, hyperreflexia)
NMS frequently associated with multi-organ failure

**Management**

**Goals**
1. early recognition
2. withdrawal of precipitants
3. aggressive supportive care
   - cooling
   - IVF
   - treat rhabdo
   - monitor electrolytes
   - cardiovascular support
   - bicarbonate if severe acidosis that is unresponsive to specific treatment
   - Bromocriptine: 2.5mg PO TDS - incr to max 5mg Q4h; dopamine agonist; in mod/severe cases
   - Dantrolene: 1mg/kg IV load - 1mg/kg QID IV; controversial; in severe cases

**Malignant Hyperthermia**
Mainly autosomal dominant
Disorder of skeletal muscle
Due to increased free Ca2+ ions in muscle cells - ie a peripheral problem, not CNS (like SS & NMS)
70% mortality untreated, 7% mortality with trt

**Causes**
Suxamethonium
Inhaled General Anaesthetics (not NO)
Amide Local Anaesthetics (lignocaine, bupivacaine)
**Assoc with:** Muscular dystrophy, osteogenesis, congenital (skeletal, abdominal hernias), SIDS, phaeo

**Clinical Features**
Onset over mins-hrs. Fever: >38.8
Muscle rigidity: generalised rigidity, trismus
NM changes: decr reflexes
Autonomic changes: Incr HR/BP/RR, normal pupils; ileus; sweaty and mottled
Altered LOC: agitation
Resp acidosis (incr ETCO2) and metabolic acidosis; rhabdo

**Complications**
ARF: hypovolaemia, rhabdo
APO: cardiogenic, ARDS
Other: coagulopathy, cerebral oedema, compartment syndromes
Investigation

Bloods: CK >20,000, incr Ca/K/phos/Mg/BSL/Ur/Cr/coags
2-3x incr ETCO2 (early sign)
Late decr BSL/phos
Early met acidosis - late resp acidosis
Urine: myoglobin (+ive peroxidase test)
Muscle biopsy

Management

Cease Anaesthetic, 100% O2
If unable to cease switch to N20/opiates/benzos/propofol
Use non-depolarising NMJ blocker
Cooling
Correct electrolytes; IVF; inotropes as needed; procainamide / verapamil for arrhythmias; avoid lignocaine

Dantrolene
1mg/kg bolus
Then 3mg/kg (up to 10mg/kg)
Then 1-2mg/kg 6 hourly for 24-48hrs
Incr Ca uptake by SER - decr intracellular Ca - decr muscle tone
Investigate patients and family (muscle biopsy)