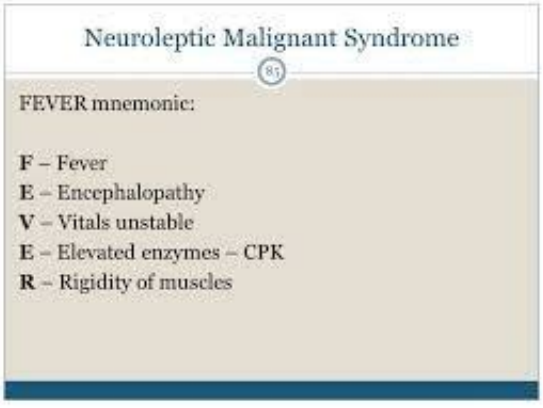
Neuroleptic Malignant Syndrome

What is it?
It is a life –threatening reaction to neuroleptic agents. NMS is a "syndrome" that is often missed.

Symptoms evolve over hours/days and each of the key features is present in 97-100 % patients. Two of four cardinal features suggest the syndrome.

1) ***MS change****: agitated delirium most common – including catatonia – not typically psychotic symptoms. Stupor and coma are not uncommon.*
2) ***Muscular rigidity:*** *increased tone and resistance in all ROM (lead pipe rigidity)* ***–*** *drooling and speech impairment common.*
3) ***Hyperthermia:*** *> 38°C common, and even > 40°C – many believe this is central feature.*
4) ***Autonomic Instability:*** *tachycardia, labile/high BP, tachypnea – profuse sweating*



Differential diagnosis?
Meningitis, heat stroke, serotonin syndrome (unique to SS: shivering, hyperreflexia, myoclonus and ataxia), malignant catatonia (behavioral prodrome distinguishes this, and motor sx are usually more "waxy," with less severe lab abnormalities), malignant hyperthermia (genetic disorder - can't use certain anesthesia).

Lab changes?
Elevated CK (greater than 1000 IU/L more specific for NMS) is common and r/t muscle rigidity. Elevated WBC (10,000 – 40,000). Myoglobinuric acute renal failure can occur secondary to rhabdomyolysis.

How common is NMS?
1-3 % of patients taking neuroleptics. All ages, but more common in young men, and most likely to occur during the first two weeks of treatment. It is NOT dose dependent and CAN occur at any time. **Up to 20% mortality.**

Which medications?
First generation (e.g. Haldol, Prolixin) more likely to be associated with NMS, but all neuroleptics can cause it, including anti-emetics. Rapid w/d of Parkinson's meds can also cause it.

What causes it?
Unknown, but central dopamine blockade is leading hypothesis. Hypothalamic dysregulation putatively causes hyperthermia and VS instability.
Other theories include sympathetic nervous system disruption.

Treatment?
Stop causative agent, supportive care. No RCT data but case reports include benzodiapdepines, Dantrolene (a direct skeletal muscle relaxant used in malignant hyperthermia –reduces fever), Bromocriptine (a DA agonist to restore balance), Amantadine (alternative DA agonist). ECT inpatients unresponsive to meds.

Prognosis?
5-20 % mortality. Usually resolves in two weeks, but chronic sx can persist. Worse with depot meds and baseline neurological probs. SUD also worsens prognosis.

Restarting Neuroleptics:
Wait minimum 2-4 weeks, use lower potency meds, start slow, and avoid lithium and dehydration.

Serotonin syndrome and neuroleptic malignant syndrome: Distinguishing features

	Serotonin syndrome (SS)	Neuroleptic malignant syndrome (NMS)
Onset	Within 24 hours	Days to weeks
Neuromuscular findings	Hyperreactivity (tremor, clonus, reflexes)	Bradyreflexia, severe muscular rigidity
Causative agents	Serotonin agonist	Dopamine antagonist
Treatment agents	Benzodiazepine, cyproheptadine	Bromocriptine
Resolution	Within 24 hours	Days to weeks

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