

DRUG INTERACTIONS EVERY  
ED PROVIDER SHOULD  
KNOW

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DISCLOSURES



- I have no financial disclosures, receive no funding from drug companies and have no financial interests in any of the medications we will discuss.

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OBJECTIVES

- Review scenarios that should make us worry about drug interactions
- Review specific drug interactions to be on the look out for
- Review drug interactions that we can avoid by careful medication selection

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WHEN TO ASK YOURSELF IF THIS COULD BE A DRUG INTERACTION

- Delirium
- Falls
- Syncope
- GI Bleeds
- Acute Renal Failure
- Congestive Heart Failure

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HIGH RISK PATIENTS

- Elderly
- Renal – CKD patients won't clear drugs as quickly, at risk for hyperkalemia, beware of DOAC + colchine or digoxin, TUMS can inhibit the absorbtion of Quinolones, tetracycline and macrolides, do not use NSAIDS with even mild AKI
- Substance Abuse
- Mental Illness
- Polypharmacy (anyone on 5 or more drugs)

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PAY PARTICULAR ATTENTION

- Antibiotics
- Analgesics
- Cardiovascular Drugs

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## CASE ONE

• A 32 year old woman presents with near syncope. She is on Fluoxetine for Depression and has been taking Imodium recreationally. Her EKG shows a widened QRS and a QTc of 685. While in your emergency department she goes into Torsades. What is the treatment of choice?

- IV Magnesium
- Sodium Bicarbonate

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## AGENTS THAT PROLONG QT

Table 2

## Drugs Associated with QT Prolongation and TdP

Antiarrhythmics	Antimicrobials	Antidepressants	Antipsychotics	Others
Amiodarone	Levofloxacin	Amitriptyline	Haloperidol	Cisapride
Sotalol	Ciprofloxacin	Desipramine	Droperidol	Sumatriptan
Quinidine	Gatifloxacin	Imipramine	Quetiapine	Zolmitriptan
Procainamide	Moxifloxacin	Doxepin	Thioridazine	Arsenic
Dofetilide	Clarithromycin	Fluoxetine	Ziprasidone	Dolasetron
Ibutilide	Erythromycin	Sertraline		Methadone
	Ketoconazole	Venlafaxine		
	Itraconazole			

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## TOP QT PROLONGING NON-PSYCHOTROPIC MEDS

- Antibiotics – clarithromycin, levofloxacin, erythromycin
- Antihistamines – diphenhydramine, hydroxyzine
- Antiemetics – ondansetron, droperidol, promethazine
- Antiarrhythmics – quinidine, amiodarone
- Antivirals – Anti- HIV meds
- Antifungals - fluconazole

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CASE TWO

- A 24 year old woman presents diaphoretic, tachycardic and febrile. She is taking an SSRI. Admits to also using cocaine and methamphetamines. On physical exam you notice spasticity and clonus.
- What do you need to consider?
- Serotonin Syndrome

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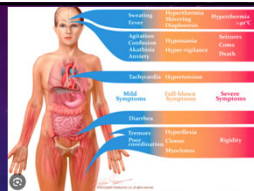
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SEROTONIN SYNDROME



- Life threatening drug interaction leading to increased serotonin – Libby Zion
- Clonus, spasticity, tachycardia, restlessness, diaphoresis
- 2 SSRIs and antipsychotic (Common causes)
- Fentanyl, cocaine, Flexeril, methadone, propofol (more rare)

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SERATONIN SYNDROME - CAUSES

- \* **ANTIDEPRESSANT MEDICATION**
  - ~ SSRIs & SNRIs
  - ~ TCAs
  - ~ MAOIs
- \* **OPIOIDS**
  - ~ TRAMADOL
- \* **OTHER MEDICATIONS**
  - ~ ONDANSETRON
  - ~ CIPROFLOXACIN
  - ~ SUMATRIPTAN
- \* **ILLICIT DRUGS & DIETARY SUPPLEMENTS**

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### SERATONIN SYNDROME - DIAGNOSIS

- \* PRESENTATION
- \* EXCLUDING OTHER POSSIBLE CAUSES
- \* HUNTER SEROTONIN TOXICITY CRITERIA (HSTC):
  - ~ 1. MUST TAKE SEROTONERGIC MEDICATION
  - ~ 2. SPONTANEOUS CLONUS
- \* RULE OUT NEUROLEPTIC MALIGNANT SYNDROME (NMS)

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### SERATONIN SYNDROME – SIGNS AND SYMPTOMS

- 3 A's:**
- \* ALTERED MENTAL STATE
    - ~ AGITATION, RESTLESSNESS, or ANXIETY
  - \* NEUROMUSCULAR ABNORMALITIES
    - ~ OCULAR CLONUS, HYPERREFLEXIA, TREMORS, RIGIDITY of MUSCLES
  - \* AUTONOMIC HYPERACTIVITY
    - ~ TACHYCARDIA, HYPERTENSION, DIAPHORESIS, MYDRIASIS, FLUSHED SKIN, ARRHYTHMIAS, VOMITING, or DIARRHEA
- MILD:**
- \* TREMORS, SWEATING, TACHYCARDIA, HYPERTENSION, & NAUSEA
- SEVERE:**
- \* FEVER, HYPERACTIVE BOWEL SOUNDS, CLONUS, AGITATION, HYPERTHERMIA, & DELIRIUM
  - \* AS CONDITION WORSENS, RHABDOMYOLYSIS, MYOGLOBINURIA, RESPIRATORY & KIDNEY FAILURE

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### SERATONIN SYNDROME - TREATMENT

- Discontinue serotonergic drugs
- Supportive care
- Rarely need serotonin antagonist such as cyproheptadine, or clozapine
- Usually resolves in 24 hours
- If not look again for other causes

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### NEUROLEPTIC MALIGNANT SYNDROME

- Antipsychotics + Fever, tachycardia, AMS, sweating, **hyporeflexia and rigidity**

Serotonin Syndrome vs Neuroleptic Malignant Syndrome		
Serotonin Syndrome		Neuroleptic Malignant syndrome
More acute (hours)	Onset	More gradual (days/weeks)
SSRIs, SNRIs, MAOIs, tricyclic antidepressants, synthetic opioids, illicit drugs	Aetiology	Anti-psychotics, sudden cessation of dopaminergic agents e.g. Levodopa
Tachycardia, raised BP, hyperthermia, diaphoresis, rigidity, altered mental state	Presentation	Tachycardia, raised BP, hyperthermia, diaphoresis, rigidity, altered mental state, delirium
Hyporeflexia, clonus, tremor	Neurological signs	Hyporeflexia, "lead pipe" rigidity
Dilated	Pupils	Normal
Diarrhoea, increased bowel sounds	Gastrointestinal features	Normal
Can be raised but generally more associated with neuroleptic malignant syndrome	Creatinine kinase (CK)	Raised. Can cause acute kidney injury
Stop serotonergic drugs IV fluids and cooling Benzodiazepines Cyproheptadine	Management	Stop antipsychotics IV fluids Dantrolene Bromocriptine

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### DRUGS WITH NARROW THERAPEUTIC WINDOW

- Warfarin
- Anticoagulants
- Insulin
- Oral hypoglycemics
- Anticonvulsants
- Immunosuppressants

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### BE ESPECIALLY VIGILANT ABOUT ACCURATE MEDICATION LIST WHEN PRESCRIBING

- Antibiotics
- NSAIDS
- Opiates (Methadone QT)

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“ANTIS”

- Antibiotics (esp Macrolides and Fluoroquinolones)
- Antidepressants (QT prolongation, Citalopram, Lithium, Serotonin Syndrome)
- Anticoagulants (bleeding)
- Antiemetics (QT prolongation – Zofran, droperidol, Gravol, Phenergan)
- Antipsychotics (QT prolongation, Haldol)

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OVER SEDATION

Alcohol + benzo + opiate + antipsychotic

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SPECIFIC SCENARIOS



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ACE/ARB + TMP/SMX

Can cause life threatening **hyperkalemia!** TMP is a potassium sparing diuretic

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SULFONUREAS + TMP/SMX

Hypoglycemia!

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WARFARIN + TMP/SMX

Elevated INR and bleeding!

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WARFARIN + ACETAMINOPHEN

Increased INR and Bleeding!

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WARFARIN + CIPROFLOXACIN

Elevated INR and bleeding!

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QUINOLONES + LIPITOR

Can cause **rhabdomyolysis**

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AMLODIPINE + BIAXIN

Can cause significant hypotension

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AMIODARONE

Watch out for statins, beta blockers, DOAC, CCB

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NSAIDS

- Gastroenterology and nephrology hate these
- Even aspirin + ibuprofen carries 2x greater risk of GIB than either alone
- COX-2 are easier on the stomach but still effect kidneys

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### TAKE HOME POINTS

- Vast topic with over 1000 interactions
- Need accurate med list
- Same pharmacy every time
- Watch out for common players
  - Fragile at risk patients
  - TMP/SMX
  - Quinolones
  - Macrolides
  - DOACs/Warfarin
  - NSAIDS
- Good return precautions and review potential side effects prior to discharge

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### REFERENCES

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- EM Cases Podcast: Episode 184 Must Know Drug Interactions
- <https://www.osmosis.org/answers/serotonin-syndrome>

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