Iatrogenesis: The Geriatric Giant

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Objectives

- Care providers will have a high index of suspicion for and be able to understand three drug-induced iatrogenesis

- Better outcomes with fewer iatrogenic complications will be realized by following the principles of appropriate prescribing for the elderly

Mr. S

- A 67 years old woman was brought to the ER by her husband after found confused, shivering & diaphoretic
- A week ago, she was started on Trazadone by her psychiatrist for insomnia & restlessness
- Three days ago, the pain clinic prescribed oxycodone for her back pain
- F/u with her NP next week

Mrs. S

- In the ER she appeared alert, extremely confused & shivering
- VS: 210/90, 100, 24, 40.3°C & 94% RA
- CT: Old CVA
- CXR: Normal
- Blood chemistry & CBC: WNL
- U/A & Blood cultures: Negative
- Physical exam: generalized rigidity, hyperactive bowel sounds & hyperreflexia to lower extremities.

Mrs. S

- PMHx: R-CVA with L hemiplegia, Depression, HTN, A-fib, GERD, Chronic back pain & Anxiety
- Meds: Effexor XR 150 mg OD, Celexa 20 mg OD, Metoprolol 25 mg BID, Digoxin 0.125 mg OD, Coumidin 2 mg OD, Losec 20 mg OD & Oxycodone 10 mg BID, Trazadone 50 mg @ hs
- Allergy: Penicillin

Differential Diagnosis

- Delirium
- Drug- induced delirium
- Serotonin Syndrome (SS)
- Neuroleptic Malignant Syndrome (NMS)
- Anticholinergic Toxicity (AchT)

Iatrogeny

- Creation of additional problems or complications form treatment
- “I will prescribe regimens for the good of my patients according to my ability & my judgment & never do harm to anyone” (Hippocrates, 400 BC)
- “All substances are poisons, there is none which is not a poison. The right dose differentiates a poison from a remedy” (Paracelsus, 1493-1541)

Serotonin Syndrome (SS)

- Not an idiopathic drug reaction
- Central & peripheral serotonergic hyperstimulation
- Over stimulation of serotonin receptors by two or more serotonergic drugs
  - SSRIs, TCAs, MAOIs and other serotonergic agents
- Clinical manifestations of SS range from barely perceptible to lethal
- Diagnosis is purely clinical

Mechanisms of Drugs in SS

- Increase synthesis of serotonin (L-tryptophan)
- Stimulates release of serotonin (Levodopa)
- Acts as a serotonin agonist (LSD)
- Increase postsynaptic responses to serotonin (Lithium)
- Prevents serotonin re-uptake (SSRIs)
- Prevents break down of serotonin (MAOIs)

Drugs Associated with SS

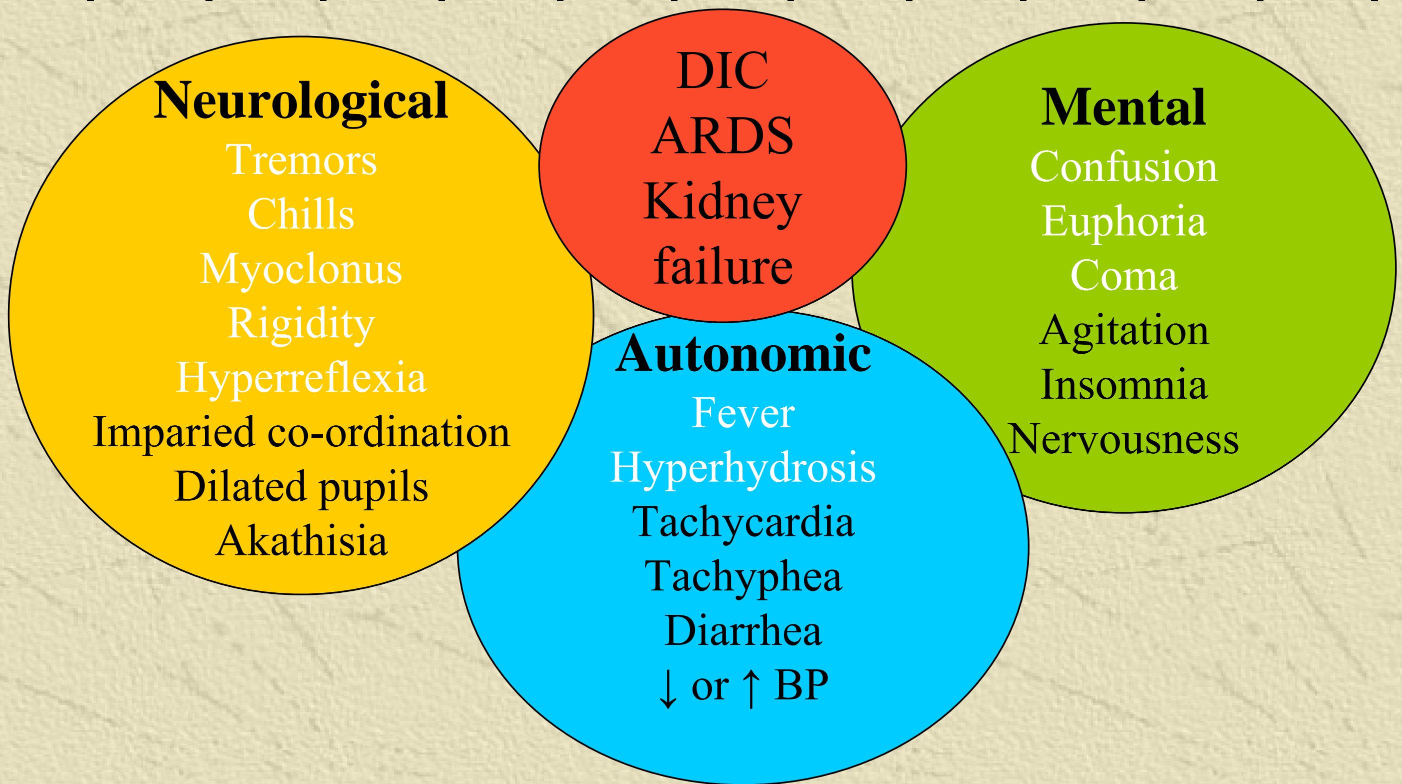
Tramadol, venlafaxine, and mirtazapine

Netherlands The Journal of Medicine 2004: 62 (9) 309-313

Opiates Associated with SS

- Fentanyl
- Sufentanil
- Loperamide
- Meperidine
- Methadone
- Oxycodone
- Pentazocine
- Propoxyphene

Clinical Features of SS



4 major symptoms or 3 major symptoms plus 2 minor ones

A SS Situation

N Eng J Med 2005: 352 1112-20

Neuroleptic Malignant Syndrome (NMS)

- Rare, potentially life threatening
- Introduction of agents that block dopamine signaling
- Reduced dopamine signaling resulting from sudden withdrawal of dopamine agent
- Agitation, dehydration, simultaneous use of two or more antipsychotics, parental administration, use of restraints, male gender & previous brain injury

Clinical Features of NMS

Cardinal Features of NMS

* Hyperthermia
* Rigidity
* Autonomic Instability
* Altered Consciousness

Associated Features of NMS

* Akinesia
* Tremor
* Dystonias
* Dysphagia
* Dyspnea
* Sialorrhea
* Fluctuating BP
* Tachycardia
* Diaphoresis
* Incontinence
* Pallor
* Flushing

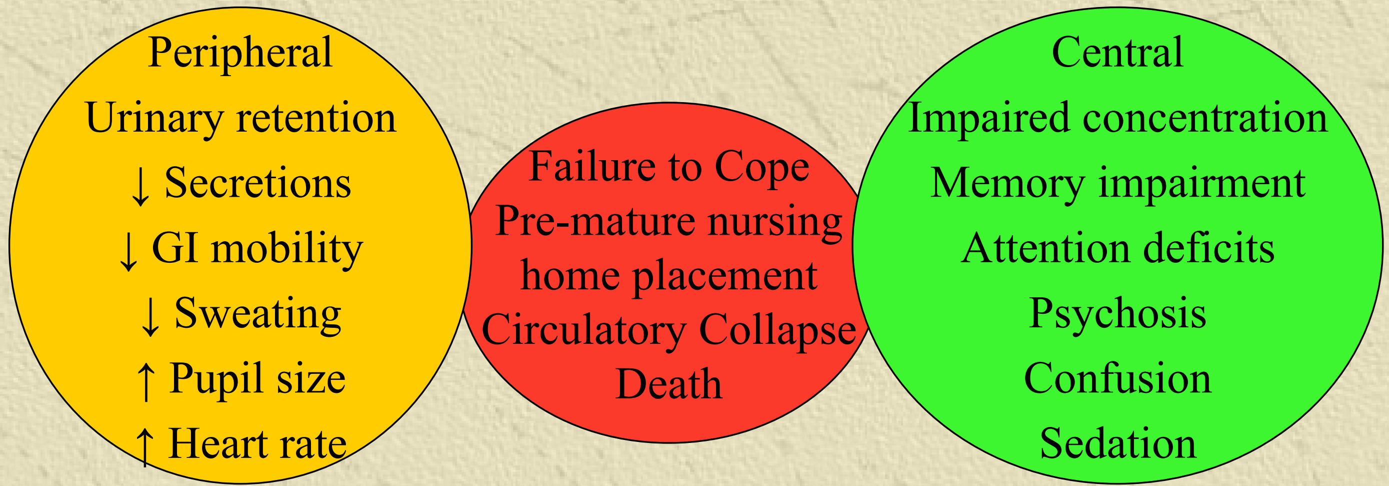
Psychiatric Quarterly,2001: 72 (4), 325-36

Diagnostic Criteria for NMS

Anticholinergic toxicity (AchT)

- Acetylcholine (Ach) decreases with aging
- Ach reduced in people with cognitive impairment
- Cholinergic disturbances is the central lesion in delirium
- "unavoidable" or as a normal part of aging or disease process
- Anticholinergic load: an accumulation of anticholinergic burden from a number of medications

Anticholinergic Drug Effects



Neurogenic bladder
UTI, BPH
Pneumonia
Constipation
Hyperthermia& Heat stroke

Depression & Dementia
Schizophrenia exacerbation
Dental/speech problems
Weight loss
Poor vision & Falls

Common Anticholinergic Medications

Amitriptylin
Atropine
Benztropine
Captopril
Cimetedine
Clozapine
Codeine
Diazepam
Digoxin
Furosemide
Haloperidol
Hydroxyzine
Hydralazine
Imipramine

Ipratropium bromide
Isosorbide dinitrate
Meclizine
Nifrdipine
Oxybutyin
Oxycodone
Prednisone
Promethazine
Quinidine
Ranitidine
Scopolamine
Theophyllin
Trifluoperazine
Warfarin

Anticholinergic Risk Scale (ARS)

Arch Intern Med 2008: 168 (5) 508-513

ARS ..

Arch Intern Med 2008: 168 (5) 508-513

Cholinergic Rebound

- Withdrawal of drugs with high anticholinergic activity
- N & V, loss of appetite, malaise, diarrhea, sweating, anxiety, insomnia, rhinnorrhoea
- Movement disorders: dyskenesia, akathesia & parkinsonism
- Mistaken as the side-effects of new medication

Differentiation of SS, NMS & AchT

SS	NMS	AchT
proserotonergic drug	Dopamine antagonist	Anticholinergic agent
Mydriasis	Normal pupils	Mydriasis
Sialorrhea	Sialorrhea	Dry mucosa
Hyperactive bowel - sounds	Normal or decreased- bowel sounds	Decreased or absent - bowel sounds
Diaphoresis	Pallor, diaphoresis	Erythema (hot & dry)
Hyperreflexia	Bradyreflexia	Normal reflexes
Clonus	Lead-pipe rigidity	Normal muscle tone
Hyperthermia > 41.1	Hyperthermia > 41.1	Hyperthermia < 38.6
Agitation, coma	Stupor, alert, mutism, coma	Agitation, delirium

Ways to ‘Healthy’ Prescribing

- Pharmacologic ‘debridement’
- ‘Brown bag’
- Polypharmacy
- Application of Beers’ criteria
  - http://www.dcri.duke.edu/ccge/curtis/beers.html
- Consideration of current indications
- Evaluation of side-effects
- Risk/benefit analysis
- Renal dosing

Ways to ‘Healthy’ Prescribing

- Quality of life/goals of care
- Drug holidays
- Prescribing cascade
- Drug-drug interactions
- Drug-disease interactions
- Drug-herb interactions
- Inappropriate prescriptions
- Compliance

Drug-Disease Interactions

Disease	Drug	Potential adverse outcome
Benign prostatic hypertrophy	α-agonists, anticholinergics	Urinary retention
Dementia	Anticholinergics, benzodiazepine	Increased confusion

Primary Care Clinic Office Pract 2005: 32 755-775

Drug-Drug Interactions

Primary Care Clinic Office Pract 2005: 32 755-775

Drug-Herb Interactions

Arch Intern Med 1998;158(20):2200–11.

The SEA -Squared Model

Safety: is the medication safe based on clinical trials and clinical experience?

Soundness: is the medication in keeping with the patient's goals for care?

Effective: has the medication been shown to have a positive outcome in clinical trials?

Efficacious: will the medication prove beneficial in the "real world"?

Appropriate: is the medication approved for this indication? Would its use be consistent with the current standard of care?

Affordability: can the patient afford the medication?

Primary Care Clinic Office Pract 2005: 32 755-775

“Pearls to Remember”

- Any symptom in an elderly patient should be considered a drug side effect until proved otherwise”
- Start low & go slow”
- “A pill for every ill has become an ill from every pill”

Thank You