Q & A after the presentation

- We will reserve time at the end of the presentation for questions. If you have any questions, please use the “Chat” feature located on the right side of your screen. Please send your chat to everyone if possible.
- After the Q and A, We would like to ask each of the participants to answer the short evaluation questionnaire.

Please complete our short survey. We appreciate your feedback.

Optimizing Geriatric Drug Therapy: Some Basic Issues

About the Presenters

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Clinical “Pearl” #1: The Medication History

- Rx drugs
- OTC Drugs
- Social Drugs (caffeine, alcohol, nicotine)
- Vitamins and Minerals
- Herbal/Nutritional Supplements/Alternative treatments
- Illicit Drugs (MJ, Amphetamines, Narcotics)
- Medication Adherence
- Someone else’s drugs

Clinical Pearl #2 - Use The Drug “Iceberg Theory”
GH 73 year old African American male, retired chemical engineer with a recent diagnosis of mild Alzheimer’s Disease

- CC: GH reports “I have no get up and go”. Spouse reports, “He was very anxious, even before the AD diagnosis. We would like to start the Alzheimer’s medication”
- BP 120/80 HR 72 MMSE: 24 GDS: 2/30
- ADLS/IADLS: unable to select clothes, dresses with assistance, can no longer shop for groceries, needs assistance in preparing meals.
- Meds: Atenolol 25 mg daily, HCTZ 25 mg daily, alprazolam 0.25 mg orally four times daily.
- OTC: ASA 81 mg daily, Huperzine A 200 mcg twice daily, Mind Matrix, 3 tablets daily (started 7 days ago)
Mind Matrix Ingredients

- Gingko Biloba
- Acetyl L Carnitine
- St. John’s Wort
- L Glutamine
- DMAE (dimethylethanolamine)
- Bacopin
- Vinpocetin
- Phosphatidylyserine

RX galantamine ER 8 mg po daily

Two days later:
GH C/O:
“Severe nausea and one episode of vomiting since starting the galantamine”

- “Increased anxiety, “the alprazolam no longer seems to help”
- “Bruising over several areas of my arms”

How the Drug Travels Through the Body

- Absorption
- Distribution
- Metabolism
- Excretion

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Absorption

**“Last Year’s Literature”**
- Gastric Acid Secretion
- Gastric pH
- GI Blood Flow
- Gastric Emptying Time
- Esophageal Motility

**“This Year’s Literature”**
- Gastric Acid Secretion
- Gastric pH
- GI Blood Flow
- Gastric Emptying Time
- Esophageal Motility

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Absorption

- Oral
- Injectable (IM)
- Dermal
- Inhaled

- Reduced duration
- Extent not impaired
- Reduced muscle mass, circulation
- Physiological changes that impact absorption.
- Issues of dexterity, pulmonary function, cognition

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Sig: Take on an empty stomach
Sig: Take with food

PPI’s
- H2Blockers
- Antacids
- Metformin

B12
- Magnesium
- Calcium

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**Distribution**

**Altered Physiology**
- Total Body Water
- Lean Muscle Mass
- Body Fat
- Total Weight

**Clinical Significance**
- Impairs Homeostasis
  - Reduced volume for water soluble drugs
  - Less creatinine (Scr)
- Larger volume of distribution for lipophilic drugs
- May increase in "middle-aged" and decrease in very old.

**Metabolism**

- **Enzyme Induction**
- **Hepatic Blood Flow**
- **Mass**
- **Metabolism**
  - Phase I: Oxidation, Hydroxylation etc.
  - Phase II: Glucuronidation, conjugation

**Pharmacogenomic Issues**

- **CYP2D6** polymorphism (codeine, imipramine etc.)
  - 6-14% Caucasians
  - 2-5% Hispanics
  - 5-10% African-Americans
- **CYP2C19** (diazepam, omeprazole etc.)
  - 3-5% Caucasians
  - 12-23% Asians
  - 10-20% African Americans
- **CYP2C9** (warfarin, glyburide etc.)
  - 6-10% Caucasians
  - 10-14% African American
  - 8% Asian

*The Top 100 Drug Interactions: Human Pharm 2013*
Hepatic Metabolism: Drugs

- propranolol, metoprolol, pindolol
- amitriptyline, nortriptyline, desipramine,
- donepezil, rivastigmine, galantamine
- lorazepam, diazepam, oxazepam,
- cimetidine, ranitidine, famotidine
- enalapril, benazepril, moexepril
- acetaminophen, codeine, morphine

Distribution

Protein Binding
- Albumin
  - alpha 1 acid-glycoprotein

Clinic Significance
- Albumin - 12 to 15%
  - Alph 1 acid glycoprotein + in old age and disease

Kidney

- GFR
- Renal plasma flow
- Active Secretion
- Renal Concentrating
  - ability
  - impaired homeostasis

(Note renal function does not decline in approximately 30% of adults > 65 years of age.)
Kidney Clearance: Drugs

- digoxin
- allopurinol converted (liver) to oxypurinol
- cimetidine, ranitidine, famotidine
- amantadine, pramipexole
- tobramycin, vancomycin, penicillin,
- captopril, enalapril, benazepril, lisinopril
- atenolol, nadolol
- disopyramide
- memantine
- trimethoprim

Many other drugs, Caution especially in Severe Renal Impairment.

What approach should be used in estimating creatinine clearance in elderly patients, particularly when the serum creatinine concentration is low?

\[
\text{Cl}_{\text{cr,pred}} = \frac{[140 - \text{Age}] \times \text{Wt}}{[\text{Scr}] \times 72} \times 0.85 \text{ for women}
\]

(Cockcroft D W & Gault M H. Prediction of creatinine clearance from serum creatinine. Nephron 16:31-41, 1976. [Departments of Medicine, Queen Mary Veterans Hospital, Montreal, Quebec, and Memorial University, St. John, Newfoundland, Canada])

Neurological Changes with Aging

Neurotransmitters: dopamine, serotonin, norepinephrine, GABA, acetylcholine

- Loss of Nerve Cells
- Regeneration of Nerve Cells
Pharmacodynamics
(What the drug does to the body)

- More Sensitive to:
  - Anticholinergic
  - Benzodiazepines
  - Central nervous system depressants
  - Anticoagulants [warfarin]
  - General anesthetics

- Less sensitive to adrenergic β-blockers
- Less sensitive to some noradrenergic drugs (isoproterenol)

Drugs with Significant Anticholinergic Activity
- Atropine and Belladonna alkaloids (scopolamine patch)
- Benzotropine, Trihexyphenidil
- Tricyclic antidepressants
- Antihistamines (diphenhydramine, chlortrimeton etc.)
- Phenothiazines (prochlorperazine, promethazine etc.)
- Clonazepam
- Dizynapine
- Paroxetine
- Oxybutynin, Tolerodine
- Cylophenazonine, Tizanidine
- Meclizine
- Diphenoxylate/atropine
- Disopyramide

Drug Interactions Not to Miss
- warfarin/metronidazole
- warfarin/TMP-Sulfa
- warfarin/cimetidine
- Warfarin/fluvasatin
- ciprofloxacin/Mylanta
- fluoxetine/codeine
- paroxetine/desipramine
- grapefruit juice/3A4
- Phenytoin/theophylline
- Increased INR
- Increased INR
- Increased INR
- Impaired absorption
- Impaired conversion to MS
- Increased desipramine
- Decreased metabolism
- Decreased theophylline

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Drug Disease Interactions

- Alzheimer’s disease
- Esophageal reflux
- Heart failure
- Depression
- Constipation
- Anticholinergics, CNS depressants
- CCB’s, Anticholinergics
- All NSAID’s
- Clonidine, Progestins, Tamoxifen, Interferon, Beta Blockers?
- Opiates, Anticholinergics, Iron, etc.

Clinical Issues

- Constipation
- Adverse Reactions to Cholinesterase Inhibitors
- Use of Antipsychotics
- Use of Benzodiazepines
- Selecting a SSRI
- Dosing venlafaxine
- Treating AD Related Behavior Issues with Mood Stabilizers
- Therapeutic Issues in Pain Management
- Two Basic Drug Categories to Assess for Every Patient

Treating Constipation
Docusate (Colace®) vs Placebo = The Winner Is---?
Placebo!


PS: How much sodium is contained in one docusate 100 mg capsule?

Donepezil, Galantamine, Rivastigmine and Nausea, Diarrhea

- Before giving up on cholinesterase inhibitor consider:

Dosing Tips

- Reduce dose
- Titrate slowly
- Divide dose (twice daily)
- Consider starting memantine first
  - Titrate memantine up to max dose and then start cholinesterase inhibitor
Venlafaxine (Effexor)

- RX: venlafaxine SR 75 mg orally daily for depression.
- Goal: Manage depression with a “dual acting” antidepressant.

“At doses less than 225 mg per day the drug functions more as a SSRI than a dual inhibitor of 5-HT and NE.”


Two basic drug categories to always assess when evaluating a patient’s medications?

Anticholinergics and CNS Depressants

Anticholinergics: many antihistamines, antispasmodics, TCA’s etc.

CNS Depressants: many antihistamines, benzodiazepines, many antidepressants, antipsychotic agents etc.

Paroxetine and Fluoxetine
- Acetaminophen with codeine
- Aripiprazole
- Metoprolol
- NSAIDS
- Tamoxifen
- Warfarin (?)

References:
http://www.fda.gov/CDER/drug/drugReactions/testQuestions.htm
The Top 100 Drug Interactions, 2008 Edition; Hansten and Horn. H&H publications, Freeland WA
http://www.hanstenandhorn.com/books
Drug Interactions. LexiComp.com

Equivalent Doses of BDZ’s
- Lorazepam 1 mg = 5 to 10 mg of Diazepam = Alprazolam 1 mg = Clonazepam 0.25 to 0.5 mg= Oxazepam 10 mg = Chlordiazepoxide 25 mg

(http://www.benzo.org.uk/manual/bzcha01.htm)
(http://www.vhpharmsci.com/vhformulary/tools/benzodiazepines-comparison.htm)

Valproate (VA) in Dementia
- Cochrane Review: December 2010
- The new meta-analysis of pooled results showed no improvement of agitation among valproate treated patients, compared with controls, and showed an increase in adverse events (falls, infection, gastrointestinal disorders) among valproate treated patients.
- Authors’ conclusions:
  - The updated review corroborates the earlier findings that valproate preparations are ineffective in treating agitation among demented patients, and that valproate therapy is associated with an unacceptable rate of adverse effects. More research on the use of valproate preparations for agitation of people with dementia is needed. On the basis of current evidence, valproate therapy cannot be recommended for management of agitation in dementia.
  - Plain language summary: No evidence of efficacy of valproate preparations for treatment of agitation in people with dementia
Perspective
ACNP White Paper: Update on Use of Antipsychotic Drugs in Elderly Persons with Dementia

- "Not only are psychosis and agitation common in persons with dementia but they also frequently cause considerable caregiver distress and hasten institutionalization of patients.
- At the same time, there is a paucity of evidence-based treatment alternatives to antipsychotics for this population. Thus, there is insufficient evidence to suggest that psychotropics other than antipsychotics represent an overall effective and safe, let alone better, treatment choice for psychosis or agitation in dementia; currently no such treatment has been approved by the FDA for these symptoms.
- Similarly, the data on the efficacy of specific psychosocial treatments in patients with dementia are limited and inconclusive. The goal of this White Paper is to review relevant issues and make clinical and research recommendations regarding the treatment of elderly dementia patients with psychosis and/or agitation.

Neuropsychopharmacology (2008) 33, 957–970; doi:10.1038/sj.npp.1301492; published online 18 July 2007

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Summary
Q & A

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