2013 Webinar Series

State of the Science:

Dementia Evaluation and Management among Diverse Older Adults and their Families

STANFORD UNIVERSITY

Please visit our website for more information - http://sgec.stanford.edu/

Stanford Geriatric Education Center

2013 Webinar Series

State of the Science:

Dementia Evaluation and Management among Diverse Older Adults and their Families

Sponsored by Stanford Geriatric Education Center in conjunction with
American Geriatrics Society, California Area Health Education Centers,
& Community Health Partnership

STANFORD UNIVERSITY

Please visit our website for more information - http://sgec.stanford.edu/

Stanford Geriatric Education Center

Optimizing Geriatric Drug Therapy: Some Basic Issues

R.Ron Finley, B.S. Pharm., R.Ph.CGP
Clinical Professor, UCSF School of Pharmacy
Lecturer Dept. of Clinical Pharmacy (Emeritus)
Clinical Pharmacist, UCSF Memory and Aging Center

STANFORD UNIVERSITY

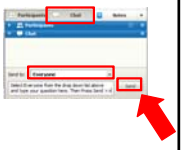
Feb 20, 2013

This project is/was supported by funds from the Bureau of Health Professions (BHPr), Health Resources and Services Administration (HRSA), Department of Health and Human Services (DHHS) under UB4HP19069, grant title: Geriatric Education Centers, total award amount: $184,125. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by the BHPr, HRSA, DHHS or the U.S. Government.

Stanford Geriatric Education Center

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.
***NOTE:** Continuing Education Participants must complete a final survey in order to receive CEU/CME credit*

Stanford Geriatric Education Center

State of the Science:
Dementia Evaluation and Management
among Diverse Older Adults and their Families
2013 WEBINAR SERIES

Optimizing Geriatric Drug Therapy: Some Basic Issues

Community Health Partnership CME Committee Members Disclosure Statements:

Continuing Medical Education committee members and those involved in the planning of this CME Event have no financial relationships to disclose.

Stanford Geriatric Education Center Webinar Series Planner Disclosure Statements:

The following members of the Stanford Geriatric Education Center Webinar Series Committee have indicated they have no conflicts of interest to disclose to the learners: Gwen Yeo, Ph.D. and Kala M. Mehta, DSc, MPH

Faculty Disclosure Statement:

Mr. Finley wishes to disclose a relationship with Novartis but his presentation will in no way promote any Novartis products and he will be generally referring to "pharmacological classes" of drugs not specific drugs. He will not be using any slides or materials supplied by Novartis.

Mr. Finley is also a consultant pharmacist for Eldercare and HGA Personal Care, both of which provide in home healthcare support and are not related to any pharmaceutical products.

Stanford Geriatric Education Center

About the Presenters

- **R.Ron Finley, B.S. Pharm., R.Ph.CGP**
- **Clinical Professor, UCSF School of Pharmacy**
- **Lecturer Dept. of Clinical Pharmacy (Emeritus)**
- **Clinical Pharmacist, UCSF Memory and Aging Center**
- **Consultant Pharmacist, Sutter Health, Brain Health Clinic**
- **Consultant Pharmacist,** Department of Aging and Adult Services, Medication Management Program
- **Consultant Pharmacist, Eldercare specialist and HGA Healthcare**
- **Speaker's Bureau: Novartis Pharmaceuticals**

Stanford Geriatric Education Center

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"

"biopsy the medicine cabinet"

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
- Phosphatidylserine

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

Absorption

"Last Year's Literature"

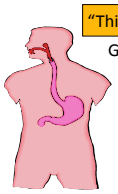
Gastric Acid Secretion

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

Sig: Take on an empty stomach

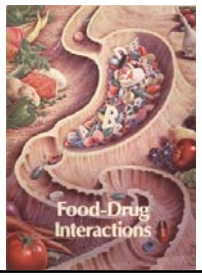
Sig: Take with food

PPI's

H2Blockers

Antacids

Metformin



B12

Magnesium

Calcium

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**

Distribution

Altered Physiology

Total Body Water

Lean Muscle Mass

Body Fat

Total Weight

Intra-cellular

H O H

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
    - congugation

- **Liver**

Pharmacogenomic Issues

CYP2D6 polymorphism (codeine, imipramine etc.)
6-14 % Caucasians
3-6% Hispanics
2-5% African Americans
5-10% Asian

CY2C19 (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, Hansten P, Horn,J 2013)

- **Liver**

Hepatic Metabolism: Drugs

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

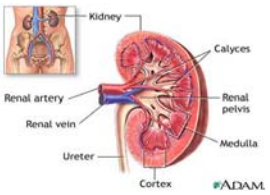
Distribution

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

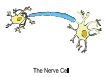
Many other drugs, Caution-especially in Severe Renal Impairment.

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

$$Cl_{cr\ (ml/min)} = \frac{(140 - Age)(Wt)}{(72)(S_{cr})} \times 0.85 \text{ women}$$

(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



The Nerve Cell

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 B-blockers
- Less sensitive to some noradrenergic drugs (isoproterenol)

(Chan P. Pharmacokinetic and pharmacodynamic considerations in geriatrics. California J of Health System Pharmacy. 2010;22 (5): 5-12)

Drugs with Significant Anticholinergic Activity

Atropine and Belladonna alkaloids (scopolamine patch)
Benztropine, Trihexyphenidil
Tricyclic antidepressants
Antihistamines (diphenhydramine, chlortrimeton etc.)
Phenothiazines (prochlorperazine,promethazine etc.)
Clozapine
Olanzapine
Paroxetine
Oxybutynin, Tolterodine
Cylclobenzaprine, Tizanidine
Meclizine
Diphenoxylate/atropine
Disopyramide

Drug Interactions Not to Miss

warfarin/metronidazole	Increased INR
warfarin/TMP-Sulfa	Increased INR
warfarin/cimetidine	Increased INR
Warfarin/fluvastatin	Increased INR
ciprofloxacin/Mylanta	Impaired absorption
fluoxetine/codeine	Impaired conversion to MS
paroxetine/desipramine	Increased desipramine
grapefruit juice/3A4	Decreased metabolism
Phenytoin/theophylline	Decreased theophylline

Drug Disease Interactions

- **Alzheimer's disease** — **Anticholinergics, CNS depressants**
- **Esophageal reflux** — **CCB's, Anticholinergics**
- **Heart failure** — **All NSAID's**
- **Depression** — **Clonidine, Progestins, Tamoxifen, Interferon. Beta Blockers?**
- **Constipation** — **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!

Hurdon V, Viola R, Schroder C.How useful is docusate in patients at risk for constipation? A systematic review of the evidence in the chronically ill. J Pain Symptom Manage. 2000 Feb;19(2):130-6

Chapman RW, Sillery J, Fontana DD, Matthys C, Saunders DR. "Effect of oral dioctyl sodium sulfosuccinate on intake-output studies of human small and large intestine. Gastroenterology. 1985 Sep;89(3):489-93

Hawley PH, Byeon JJ. J Palliat Med. A comparison of sennosides-based bowel protocols with and without docusate in hospitalized patients with cancer. 2008 May;11(4):575-81

- 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”
Psychotropic Drug Handbook 8th edition, 2007, Lippincott

Stanford Geriatric Education Center

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

Stanford Geriatric Education Center

Anticholinergics and CNS Depressants

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

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

J Mintzer and A Burns Anticholinergic side-effects of drugs in elderly people. J R Soc Med. 2000 September; 93(9): 457–462. PDF: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1298101

Stanford Geriatric Education Center

Paroxetine and Fluoxetine

- Acetaminophen with codeine
- Aripiprazole
- Risperidone
- Nortriptyline
- 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 =
  Chlordiazapoxide 25 mg

(Psychotropic Drug Handbook, Perry P et al 8th edition,Lippincott, Williams and Wilkins)
(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.
- The role of shared decision making and caution in using pharmacotherapy for these patients is stressed.
- Neuropsychopharmacology (2008) 33, 957–970; doi:10.1038/sj.npp.1301492; published online 18 July 2007

Stanford Geriatric Education Center

Authors

- Dilip V Jeste*,1,2, Dan Blazer3, Daniel Casey4, Thomas Meeks1, Carl Salzman5, Lon Schneider6, Pierre Tariot7 and Kristine Yaffe8
- **1Department of Psychiatry and Neurosciences, University of California, San Diego, CA, USA; 2VA San Diego Healthcare System, University of California, San Diego, CA, USA;**
- **3Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA;**
- **4Department of Psychiatry and Neurology, Oregon Health and Science University, Portland, OR, USA;**
- **5Department of Psychiatry, Massachusetts Mental Health Center, Jamaica Plain, MA, USA;**
- **6Department of Psychiatry, Neurology, and Gerontology, University of Southern California, LosAngeles, CA, USA;**
- **7Department of Psychiatry, Medicine, Neurology, and Aging/Developmental Biology, University of Rochester, Rochester, NY,USA;**
- **8Department of Psychiatry, Neurology, and Epidemiology/Biostatistics, University of California, San Francisco, CA, USA**

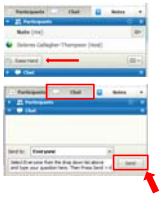
Stanford Geriatric Education Center

Summary

Stanford Geriatric Education Center

Q & A

- We now have some time to answer your 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.
***NOTE:** Continuing Education Participants must complete a final survey in order to receive CEU/CME credit*

Stanford Geriatric Education Center

Thank You for Participating!

Reminder: Please complete our short survey.
We appreciate your feedback.
***NOTE:** Continuing Education Participants must complete a final survey in order to receive CEU/CME credit*

Stanford Geriatric Education Center