

## Pharmacotherapy of BPSD

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## Pharmacological interventions

- ◆ Reducing medication errors.
- ◆ Reducing potentially inappropriate medication prescription.
- ◆ Reducing adverse drug events.
- ◆ Pharmacological interventions for pain.
- ◆ Pharmacological interventions for medical conditions.
- ◆ Pharmacological interventions for cognitive deficits and BPSD.

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## Anti-dementia drugs

- ◆ Approved by FDA
- ◆ Cholinesterase inhibitors approved for mild to moderate AD: donepezil (aricept), galantamine (razadyne), rivastigmine (exelon) and tacrine (cognex).
- ◆ NMDA receptor antagonists approved for moderately severe to severe AD: memantine (namenda).

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## Dosage

- ◆ Donepezil: 5mg in morning, may increase to 10 mg after 4 weeks.
- ◆ Galantamine extended release preparation: 8 mg with food in morning, increase to 16 mg after 4 weeks, may increase to 24 mg after another 4 weeks.
- ◆ Rivastigmine: 1.5 mg with food twice a day, increase to 3 mg twice a day after 4 weeks. May increase to 4.5 mg twice a day after 4 more weeks and 6 mg twice a day after 4 more weeks.

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## What to expect?

- ◆ No change for a year, then gradual decline.
- ◆ 2-3 months per year of less decline in cognition and possibly function.
- ◆ Mild decrease in future behavioral problems.
- ◆ One out of four benefit.
- ◆ Small number of people show a dramatic benefit.

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## Adverse effects

- ◆ Nausea, vomiting, diarrhea, weight loss.
- ◆ Rare: dizziness.
- ◆ Do not initiate these meds in patients with active peptic ulcer disease, exacerbation of COPD and symptomatic bradycardia (slow heart rate) until the problem has been well controlled. If a person is already on these meds, avoid discontinuing it.

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## Memantine

- ◆ Numbers needed to treat: 3-7. Thus, one out of every 3-7 people given the medicine will benefit.
- ◆ Beneficial effect very modest. Less decline compared to not giving the medicine.
- ◆ A small subgroup may 'improve' noticeably.

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## Dosage

- ◆ Memantine: 5 mg once a day for 1 week, then 5 mg twice a day for 1 week, then 5 mg in morning and 10mg at bed time for 1 week and then 10 mg twice a day.
- ◆ In patients with severe renal (kidney) problems: do not increase beyond 5 mg once or twice a day.

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## Adverse effects

- ◆ Confusion, headache, dizziness, constipation.
- ◆ Rare: hallucinations.

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## Drug interactions

- ◆ Donepezil or Galantamine: with fluoxetine, fluvoxamine, nefazodone, paroxetine, carbamazepine, ketoconazole, tramadol.
- ◆ Galantamine: codeine.
- ◆ Donepezil: may displace valproate, digitalis, warfarin, tolbutamide from protein binding sites.
- ◆ Anticholinergic drugs block the effects of donepezil, galantamine, rivastigmine.

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## Drug interactions

- ◆ Memantine: avoid detromethorphan, ketamine, amantadine.

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## Nootropics

- ◆ Hydergine 3-6 mg/d: preliminary evidence suggests modest beneficial effect. Improves metabolism of brain cells, modulates serotonin and dopamine.
- ◆ Piracetam: preliminary data show modest benefit.
- ◆ Nicergolene: preliminary data show modest benefit.

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### Anti-oxidants

- ◆ Selegiline: 10mg/day
- ◆ Delayed nursing home placement.
- ◆ Risk of falls and syncope.

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### Anti-oxidants

- ◆ Initial study suggested Vit E 2000 IU beneficial. Risk of falls and bleeding.
- ◆ Later studies found more than 400 IU vitamin E associated with increased all cause mortality.
- ◆ Generally not recommended. May take less than 400 IU.

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### Psychiatric medications

- ◆ Antidepressants: most useful for severe depression in people with dementia.
- ◆ Antipsychotics: most useful for behavioral emergencies.
- ◆ Anti-anxiety drugs: benzodiazepines for emergency situations.

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## Anti-depressants

- ◆ Those with least likelihood of drug-drug interactions: citalopram (celexa), escitalopram (lexapro), sertraline (zoloft): first line agents.
- ◆ Venlafaxine (effexor), duloxetine (cymbalta) and mirtazapine (remeron) as second line agents.
- ◆ Bupropion (wellbutrin), paroxetine (paxil) as third line agents.

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## Antipsychotics

- ◆ Increased mortality: rate of death 4.5% compared to 2.6%.
- ◆ Increased stroke risk: 1.6-1.7 times more.
- ◆ ?Risk of accelerated decline.

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## Anti-anxiety medications

- ◆ Antidepressants
- ◆ Buspirone (buspar)
- ◆ Benzodiazepines (lorazepam [ativan], alprazolam [niravam, xanax, xanax-XR], clonazepam [klonopin]).

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### Over-the-counter drugs

- ◆Gingko. small beneficial effect. 120-240 mg/d in two divided doses. Standardized preparation. Care reports of bleeding in brain.
- ◆Acetyl L Carnitine (preliminary evidence of modest benefit in people with mild AD and depression)
- ◆Huperzine (preliminary data of modest benefit: effect similar to aricept)

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### Over-the-counter drugs

- ◆DHEA-S: preliminary data showing modest benefit. Effect similar to memantine.
- ◆Vinpocetine: preliminary data showing modest benefit. Increases cerebral blood flow.
- ◆Alpha-lipoic acid: animal data showing potential benefits.

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### OTC psychiatric drugs

- ◆SAMe (depression)
- ◆St. John's wort (depression)
- ◆Fish oil (EPA 1 gm/d) (depression)
- ◆Chamomille tea (sleep)
- ◆Valerian (sleep)
- ◆Melatonin (sleep)

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## Ethical issues

- ◆ Increased longevity
- ◆ Increased insight may cause recurrence of anxiety, depression, irritability.
- ◆ Caregivers may need to renegotiate stages of illness and behavior already dealt with (such as wandering, exit seeking).

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## Other drugs

- ◆ Testosterone
- ◆ Statins
- ◆ Insulin sensitizers (used for Diabetes currently)
- ◆ Estrogen
- ◆ Doxycycline
- ◆ Metal chelators

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## Bottom Line

- ◆ FDA approved Anti-dementia drugs have a small (10%) but clinically significant role in treatment of AD.
- ◆ Is cost worth benefits?: generally yes for those who can afford.
- ◆ Brain memory fitness programs and other non-pharmacological interventions directed towards patients with dementia and their caregivers constitute 90% of the treatment and should receive more attention.

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## Suggested reading

- ◆ Lleo et al. Current pharmacotherapy for Alzheimer's disease. *Annu Rev Med.* 2006; 57: 7.1-7.21.
- ◆ Desai and Grossberg: Management of Alzheimer's disease. *J Gerontol Med Sci* 2003.
- ◆ Belgeri and Morley. *J Gerontol Med Sci.* 59A: 1025-1028, 2004.

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