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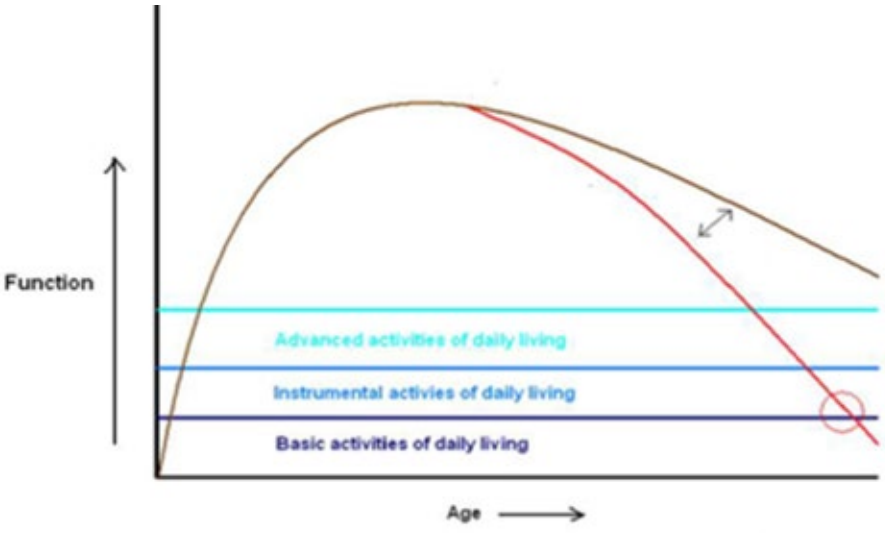
MEMORY LAPSES, MCI AND COGNITIVE ENHANCERS IN THE ELDERLY

Ageing incurs a gradual decline in our physiological and physical abilities and the erosion of our bodies' reserves. While about 70% of the elderly population is free from psychopathy, around 30% will require some form of psychopharmacological treatment at any given time. Ailments in the elderly may be co-morbid, transient, or persistent. This makes constant vigilance and frequent reviews of treatment all the more important.

Most people over 60 will recognise subjective memory loss themselves and a modest decline in cognition. Mild Cognitive Impairment (MCI) affects 20 to 30% of the elderly and a third of these will proceed to dementia. Statistics from the United Kingdom indicate that one in three patients will die from the condition. Mild Cognitive Impairment (MCI) is an intermediate between normal ageing and dementia. This provides clinicians and family a window of intervention to prevent or delay the progression of dementia. The earlier the treatment is, the better the prognosis will be.

The COVID-19 pandemic is having long-term effects on the elderly and patients in care. In addition to visiting restrictions and social/physical distancing rules that affect patients' sense of isolation, approximately 80 to 90% of elderly patients admitted to hospital with COVID-19 will experience long-term, ongoing pain, fatigue and shortness of breath.



Normal ageing is not associated with any functional impairment

THE RULE OF THUMB

When medicating an elderly patient, the procedures are similar to that of a younger patient so always start low, go slow, and review frequently. Elderly patients are more sensitive to side-effects and should be prescribed ½ to ⅓ of a standard adult dose. Polypharmacy is usually indicated. Medication regimes should be supervised and reviewed at least every three months.

MORBIDITY IN THE ELDERLY	
Sleep Disturbance	35%
Impaired ADL	34%
Somatic Complaints	27%
Decreased Subjective Cognition	25%
Depression	15%
Dementia	8%

CAUSES OF NEUROPSYCHIATRIC SYMPTOMS (NPS)	
Medical Disorders	Pain, constipation, infection, cardiac failure * the best laxative for elderly patients is Senna (Soflax) 1 – 4 tablets at 17:00
Psychiatric Disorders	Depression, dementia, delirium
Environmental Effects	A new caregiver, having hair washed
Medication Side-effects	Anti-cholinergic properties, benzodiazepines

CAREGIVER PSYCHO-EDUCATION

Taking the time to psycho-educate caregivers is crucial and enables further monitoring of patients' wellbeing. Elderly patients in care, with or without delirium, are fluctuating quite markedly due to COVID-19 restrictions. Psycho-educating caregivers so that they can identify mood fluctuations, times of the day that are more difficult for the patient as well as sleep and eating patterns is key to successful managed treatment.

ANTIDEPRESSANTS

If there is even a hint of a mood condition, sadness – cognitive symptoms – rather prescribe an antidepressant with sedating agents.

Start low, go slow, and review frequently – always titrate upwards in small increments. It's important to note that there is an 80% relapse rate in elderly patients who don't stay on treatment for at least two years. Avoid the use of tricyclics, and benzodiazepines, in the elderly. Treating depression after a relapse is far more challenging. Venlapaxine XR (Effexor) in the morning is showing success in dosages of 150 to 225 mg.

ANTIDEPRESSANTS	
Sedating agents:	
Citalopram (Cipramil)	10 – 30 mg
Mirtazapine (Remeron)	15 – 30 mg
Agomelatine (Valdoxane)	25 – 50 mg
Escitalopram (Cipralex)	5 – 10 mg
Sertraline (Zoloft)	50 – 150 mg

ACUTE SEDATION AND BENZODIAZEPINES

While there are numerous methods and older combinations that work, the superior method overall is lorezapam. Ideally, patients should be medicated before bed so their circadian rhythms are not disrupted. Haloperidol is still frequently used but is far too strong for the elderly and wreaks havoc on circadian rhythms. Ziprasidone (10mg) works very well in private practice.

Among the hypnotics, benzodiazepines should, as a rule, be avoided. Elderly patients are sensitive to daytime somnolence, disruption of circadian rhythms, emotional lability, confusion, incoordination ataxia, and memory impairment. Elderly patients are already at high risk for falls and one in seven falls results in hip fracture. Of those, one in seven results in death.

It should take at least a year to wean an elderly patient off a benzodiazepine while converting to a different agent. Reduce dose by ¼ or ⅓ and maintaining that for several months before reducing again. Melatonin can be used for mild cases of sleep disturbance. The "Z medications" (zolpidem, zopliclone) are preferred for stronger cases. It's important to note that should you have an elderly patient with treatment-resistant psychosis, it's critical to refer to a specialist.

The COVID-19 pandemic and its resulting social constraints has seen many elderly patients in private practice "acting out". At times, an anxiolytic is required. However, these should be used with discretion as they act on the gabba system and the potential for addiction is similar to benzodiazepines.

NON-BENZODIAZEPINE
a. Melatonin Melatonin (Citcadin) 2mg – 60 to 90 minutes before sleep
b. Benzodiazepine-related Zolpidem (Stilnox) 5 – 10mg / Stilnox MR 12.5 mg Zopiclone (Imovane) 3.75 – 7.5 mh
c. Antidepressants Citalopram (Cipramil) 10 – 20 mg (1 in 20 will not be sedated) Mirtazepine (Remeron) 7.5 – 15 mg Agomelatine (Valdoxan) 25 mg at night
d. Neuroleptics Chlorpromazine (Largactil) 25 mg Olanzepine (Zyprexa) 24 mg given at 17:00 Quetiapine (Seroquel) 25 mg at night

NEUROLEPTICS

The use of antidepressants in Alzheimer's patients with a Mini-Mental State Exam (MMSE) of 22 and lower remains questionable. Patients with first-time onset of depression and/or anxiety in their 50s ultimately are diagnosed with Vascular Depression. Many people with dementia develop signs of depression, such as feelings of low self-esteem and confidence, tearfulness and appetite, concentration and memory problems. The apathy of depression should be treated with cognitive enhancers and neuroleptics rather than antidepressants in long-term, augmented treatment.

As a matter of course, elderly patients become emotionally depleted as the day wears on and at around 17:00 / 18:00 fall into a soft delirium, what we call 'sundowners'. In order to intercept this, evening doses of medication should be given at 17:00. Once an elderly patient is delusioning, a neuroleptic is required. Bear in mind

that phlegm and sputum build-up is more evident in elderly patients therefore agents like olanzapine can make swallowing as well as night coughing an issue.

EXAMPLE OF A NEUROLEPTIC REGIMEN	
Combination	
Risperidone (Risperdal)	0.25 – 0.5 mg twice daily
Increase the dose for daytime control	0.75, 1.0 and 1.5 mg twice daily
Together with:	
Quetiaine (Seroquel)	25 mg at night
Increase the dose for nocturnal control	50, 75 and 100 mg at night
Always wait a day or two between increases	
Single Medication	
Olanzapine (Zyprexa)	2.5 – 10 mg at 17:00
MAXIMUM DAILY DOSING	
Risperidone (Risperdal)	4 mg
Clozapine (Leponex)	300 mg
Quetiapine (Seroquel)	400 mg
Olanzapine (Zyprexa)	10 mg
Amisulpiride (Solian)	300 mg
Aripiprazole (Abilify)	10 mg
Ziprasidone (Geodon)	20 mg
Haloperidol (Serenace)	10 mg
Chlorpromazine (Largactil)	200 mg

MOOD STABILISERS / ANTICONVULSANTS

Unless the patient is a long-term Bipolar patient who is over 60, don't introduce mood stabilisers or anticonvulsants into their treatment regime. (Maintenance levels of lithium should be between 0.4 to 0.6 mmol/L). There is no convincing evidence that advocates the routine use of these medications in non-long-term Bipolar patients.

Patients in their late 50s who show signs of hypomania, severe psychosis and other key Bipolar symptoms, who have no history at all of Bipolar Disorder may have so-called 'Frontal Release Syndrome'. This is often misdiagnosed as a psychiatric issue or as Alzheimer's Disease and is almost always a sign of Vascular Dementia. These patients do not benefit from anticonvulsants and require treatment with neuroleptics. It's very important to educate and prepare caregivers and family for a diagnosis of Vascular Dementia which will generally be obvious once the medication has taken effect.

EFFICACY OF COGNITIVE ENHANCERS AND EARLY TREATMENT

Cognitive enhancers work for Mild Cognitive Impairment (MCI) and the earlier you begin treatment the better. Overseas, cognitive enhancers are registered for use in Vascular Dementia, Alzheimer's Disease, Lewy Body Dementia and Parkinson's Disease. In terms of the MMSE, as soon as a dementing illness is suspected, start treatment. On average, the MMSE score of a person with Alzheimer's declines about two to four points each year. When a patient reaches 8 or below on the 30 point scale, cognitive enhancers are no longer effective. The patient needs to be weaned off these medications over at least six months to prevent severe rebound effects.

Evidence shows that while cognitive enhancers don't extend life, they do improve functioning. Without these, patients need full nursing care three to four years earlier (at a starting cost of R14 000). Caregivers also report far more social and cognitive involvement. Only supplement when it's indicated and always test and treat early.

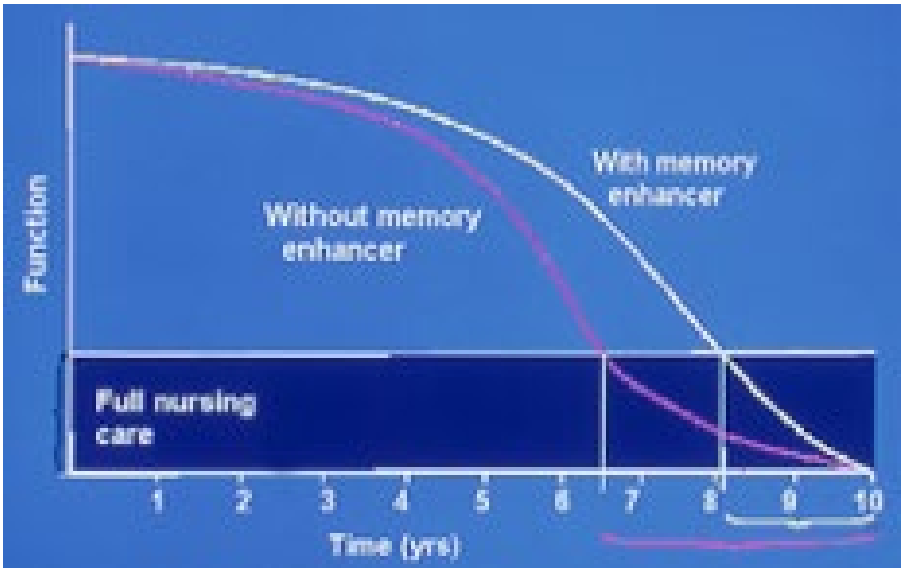
INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADL)

Functional decline and restriction of instrumental activities of daily living are critical to diagnose MCI and predict dementia. Most patients you see early on won't show any decline in MMSE score. There are subtle changes in IADLs over the 10 years preceding the clinical diagnosis of dementia and research has shown that patients who later developed dementia performed worse in complex activities of daily living.

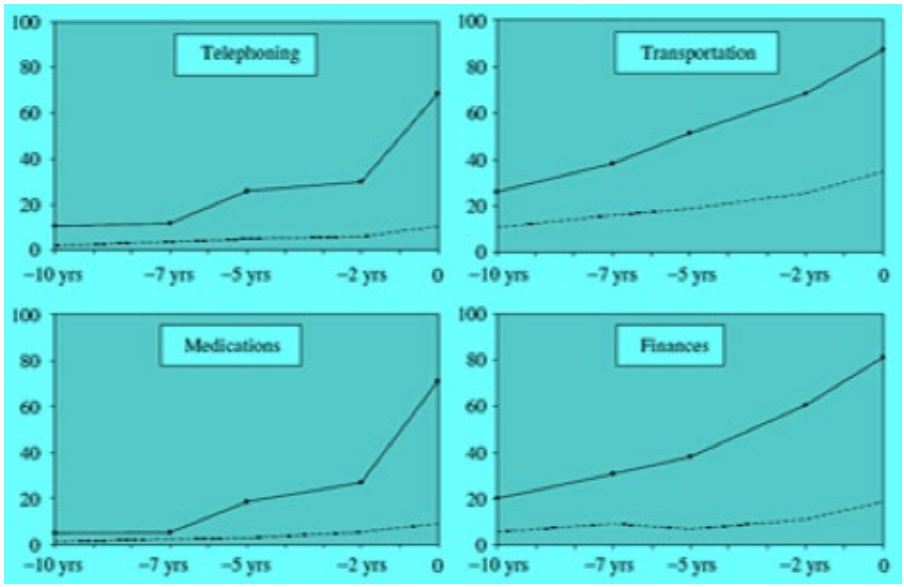
Problems with Communication (Telephoning): Issues with communication start 10 years before dementia is diagnosed.

Driving: This is heavily weighted as a pre-onset indicator. Be very aware of a patient's driving history – have they had repeated small incidents like reversing into walls or driving into gates, is there a history of accidents or near accidents?

Medication: Correctly taking medication is also an issue. Do patients need a pill dispenser to remember their medication regime, does a caregiver need to administer medication, does the patient consistently take the correct dosages?



Rate in functional decline: IADL over 10 years preceding dementia



N=986: >65yrs (104 =AD) Peres et al. J Am Geratr Soc 2008; 56:37 – 44a

Finance: This is a significant issue that is often overlooked. This is where the elderly are the most vulnerable. "Sudden" money mismanagement, irrational or over-the-top spending, accusations of theft are all warning signs.

ACETYLCHOLINESTERASE INHIBITORS (ACHEIS)

The first month of AChEI treatment is the most challenging because of the side-effects. Again, psychoeducation is crucial – prepare caregivers and the patient for what to expect and what to look out for. Donepezil must be titrated slowly upwards in the first month. Thereafter, AChEIs are always given in the mornings. The starting dose and subsequent mg dosage will be higher with Vascular Dementia, Parkinson's Disease, Dementia and Diffuse Lewy Body Dementia.

If a patient has chronic diarrheoa or rhinorrhoea, the medication must change to the other AChEI immediately. Monitor patients for vivid dreams, which they may act out. Ensure patients are taking the medication in the morning and either drop the dosage or change the medication if the dreams don't abate.

Memantine is an amantadine derivative so it will enhance L-dopa and is a dopaminergic agonist. This could be a benefit in Parkinson's Disease patients but always be aware of dosage. Alzheimer's patients tolerate 20 gm memantine, but be aware of the side-effects and co-effects. The most common side-effects are confusion during the day and excessive fatigue. Both of these are innate to the condition so it can be a challenge to identify those symptoms as a side-effect. Stop the medication for a couple of weeks if necessary.

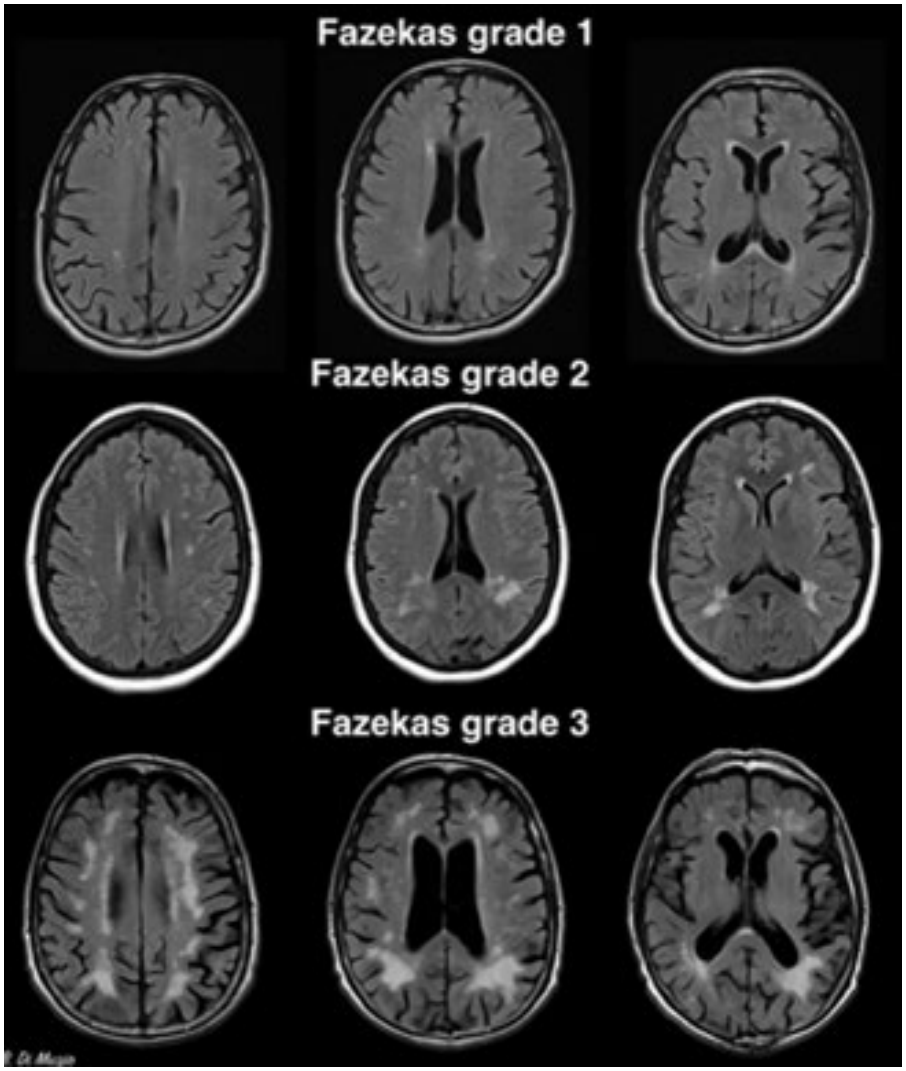
ACHEI RX: VASCULAR DEMENTIA, PARKINSON'S DISEASE DEMENTIA, DIFFUSE LEWY BODY DEMENTIA	
Donepezil dose titration (1 tab = 5, 10 mg)	
Month 1	2.5 mg at night (GIT)
Month 2 onwards	5 mg in the morning
OR	
Galantamine dose titration (1 tab = 8, 16, 24 mg)	
Month 1	8 mg in the morning
Month 2 onwards	16 mg in the morning
MEMANTINE RX: VASCULAR DEMENTIA, PARKINSON'S DISEASE DEMENTIA, DIFFUSE LEWY BODY DEMENTIA	
N-methyl-D-aspartate (NMDA) receptor antagonist half-life: 60- 100 hours Amantadine derivative enhances L-dopa and dopaminergic agonists	
Dose titration for Altzheimer's (1 tab = 10 mg)	
Month 1	½ tablet (5 mg) at night
Month 2 onwards	1 tab (10 mg) at night
If renal glomerular filtration rate (GFR) falls below 30 mL/min, reduce daily dose to 10 mg or less	

SIDE-EFFECTS OF ACHEIS	
Mild sedation (initially)	Dizziness / postural hypotension
Abdominal discomfort	Anxiety, insomnia **Vivid dreams**
Anorexia, nausea, vomiting	Depression
Diarrhoea Rhinorrhoea (discontinue) Sexual dysfunction	Increased salivation Sweating Cramps
SIDE-EFFECTS OF MEMANTINE	
Amantadine derivative:	
Confusion	Dizziness
Headache	Fatigue
Enhances L-dopa and dopaminergic agonists	

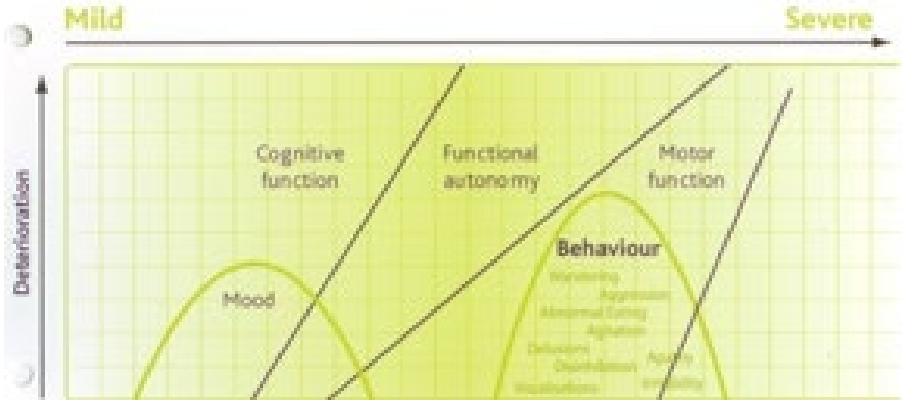
URGENCY INCONTINENCE

An overactive bladder is a criteria of Vascular Dementia and is present is 30 to 60% of Alzheimer's patients and in 10 to 20% of MVI patients. Overactive Bladder Syndrome (OBS) occurs both day and night but nocturnal urinary frequency (urinating up to six times a night) is highly disruptive. Patients often nap, or fall asleep, during the day which completely disrupts the day/night cycle.

Dosage of quetiapine (or chlorprozamine) controls the bladder and helps the patient sleep better. Dosage requires 25 mg per two nocturnal urinary cycles.



Presentation of Alzheimer's Disease (Stahl)



Progression of Alzheimer's Disease

PREVENTION & SLOWING DOWN ONSET OF ALZHEIMER'S DISEASE

The South African Society of Psychiatrists (SASOP) guidelines, 2012, there are a number of factors that can slow down the onset of Alzheimer's Disease. Medical treatments include Hormone Replacement Therapy (oestrogen), anti-inflammatories, Apolipoprotein E2 or E3, supplementation with Vitamins B, C, D and Calcium with or without NSAIDs, and control of cardiovascular risk factors. Lifestyle factors include red wine (resveratrol), intellectual stimulation, healthy eating, coffee, chocolate, as well as sleep and exercise.

The Cache County Study (Norton et al, JAGS, 2010) found that spouses of patients with dementia have a 6 times greater risk of dementia themselves. Husbands of women with dementia have an even greater risk – they are 12 times more likely to develop dementia.

In conclusion, ageing involves a gradual decline in our physiological and physical abilities. Up to 30% of elderly patients will suffer Mild Cognitive Impairment (MCI). Patients with MCI show a modest decline in cognition, behaviour and function, and their social and occupational abilities are disrupted. MCI marks a transition between normal ageing and dementia and, therefore, is an ideal time to recognise, prevent or delay the onset on dementia. As in many areas, the earlier treatment begins, the better the prognosis is. MHM

References available upon request