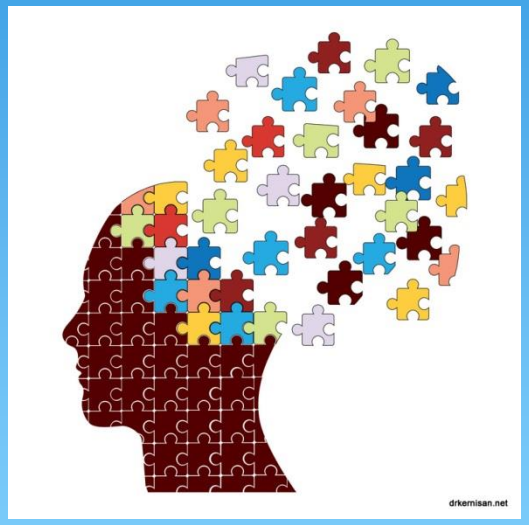
Dementia & Medications



&

Katherine Roper de Leake

NMP/ Clinical Lead

Intensive Older Persons Service

Norfolk

Draw a One Penny Coin Circa 1971-2008:

10 Points –

Face side

Queen

Facing right

Elizabeth II

D.C Reg .F.D/date

Dots

Rear side

One Penny

No.1

Portcullis

Chains

Dots

What is dementia?

* Dementia is a term that is used to describe a collection of symptoms including memory loss, problems with reasoning, perception and communication skills. It also leads to a reduction in a person's abilities and skills in carrying out routine activities such as washing, dressing and cooking.

(RCN March 2019)

Other symptoms; Disturbed behaviour, mood and or personality changes, psychosis.

Types of Dementia

* Alzheimers Disease - most common
* Vascular Disease – also known as multi-infarct
* Lewy Body Dementia – motor symptoms affected
* Fronto-Temporal Dementia – (Pick's)
* Others;
* Mixed Type – AD/Vas
* Parkinsons and dementia
* Huntingdon's Chorea
* Creutzfeldt-Jakob Disease (CJD)
* HIV related

Assessment (not in 10 mins)

- History of patient
- Cognitive assessment – ACEIII/MMSE
- Neuropsychiatric symptoms
- Depression
- Activities of daily living
- PMH
- Family history
- Medication
- Head injury

- General examination
- Other investigations –
  - FBC
  - ESR/CRP
  - Clinical chemistry profile (U&E, calcium, glucose)
  - Thyroid function
  - B12 and folate
  - Neuroimaging

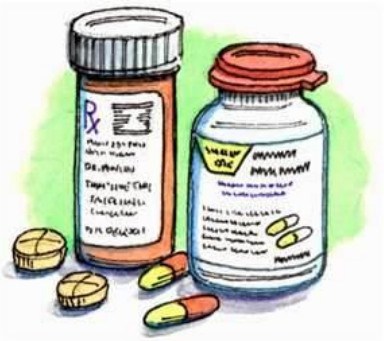
AD Symptoms overview

Activities of Daily Living	Behaviour	Cognition	Communication
showering/bath	agitation/ aggression	memory/ confusion	following conversation
being left alone	personality changes	concentration/ attention	comprehension of language
incontinence	irritability	orientation	irritability
finding belongings	wandering/ restlessness	recognising people	speaking
moving in general	depression		writing/reading
sleeping			

Georges et al, IJG Psychiatry 2008

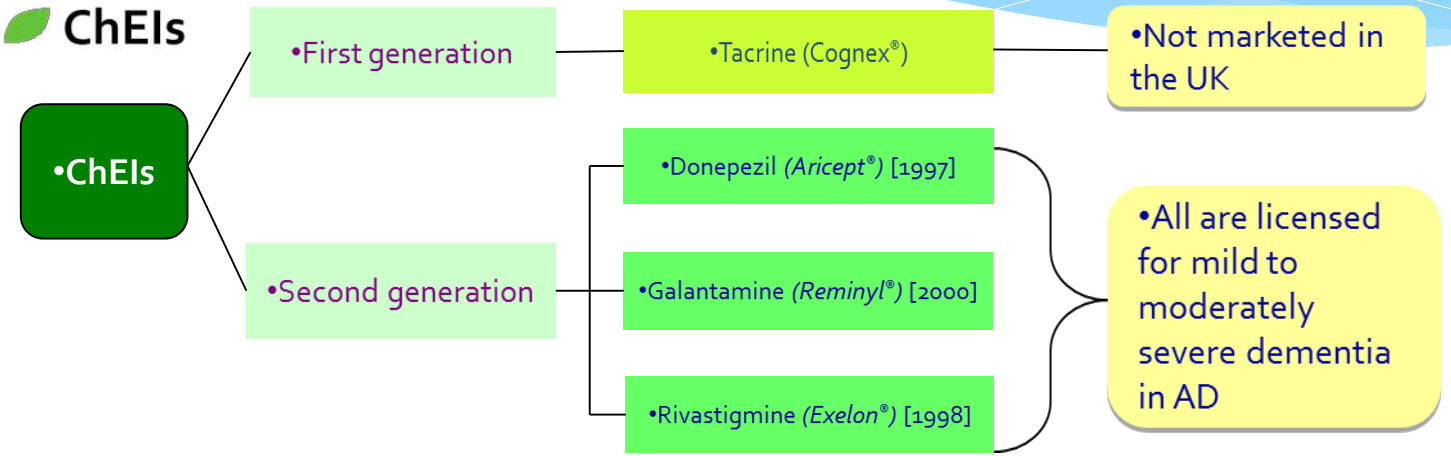
Treatment in AD, Role of medications:

- Do not change / modify the course of the disease deterioration
- Not a cure
- May slow down disease progression
- May improve memory and functioning in the short-term (?long-term)
- May have benefits with quality of life and behavioural disturbances
- ? May delay or reduce the need for nursing home placement or institutionalisation
- ? May reduce mortality



An overview of drugs used for AD

ChEIs



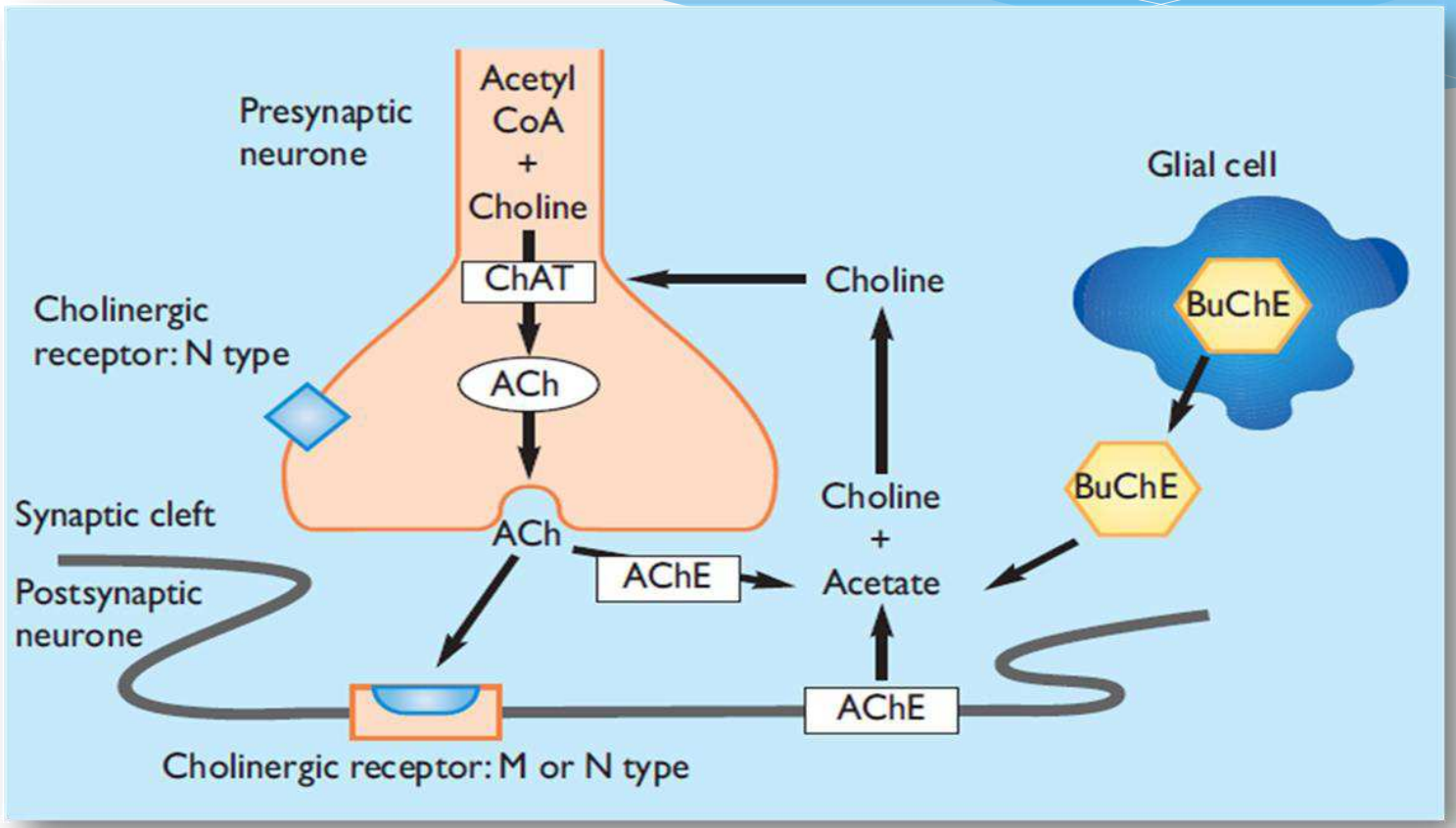
NMDA receptor antagonist

- Memantine *(Ebixa®)* [2002] – Licensed for moderately severe to severe AD

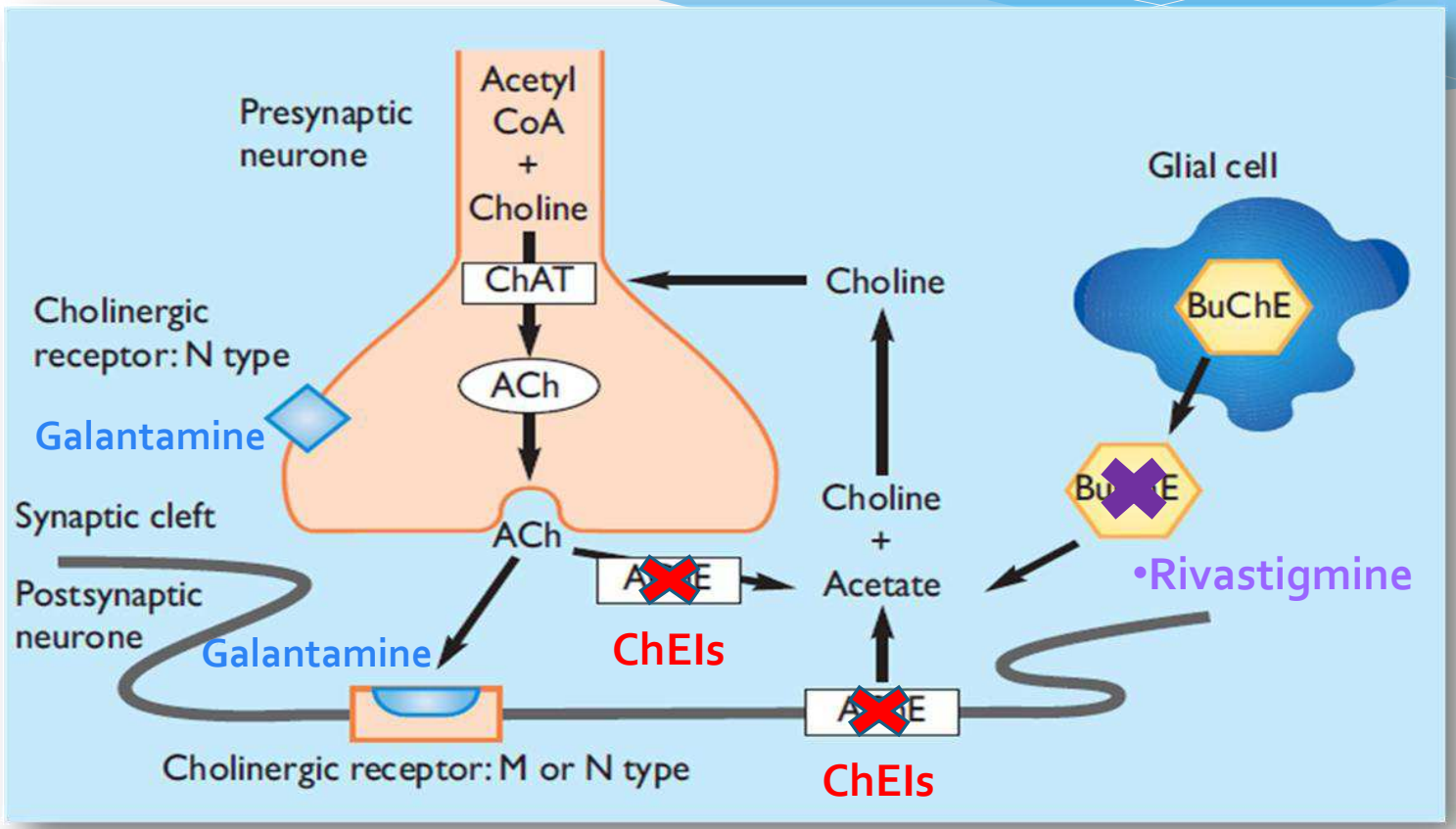
How does it work?

* All ChEIs primarily work by enhancing the action of ACh
  - by inhibiting the enzyme AChE from breaking down ACh
* Relies on some intact cholinergic neurones to synthesise ACh. Hence, they are more beneficial in early stages of the disease
* Rivastigmine also a BuChE inhibitor (BuChEI)
* Galantamine also an allosteric modulator at nicotinic (N) cholinergic receptor

ACh synthesis and metabolism



ACh synthesis and metabolism



Memantine
Mode of action -

- Memantine blocks the NMDA receptor
- This reduces neuronal damage caused by excessive glutamate
  - Excess glutamate causes over stimulation of NMDA receptors, which allows the free flow of calcium (Ca^{2+}) into the cell
  - A rise in intracellular Ca^{2+} ions is believed to trigger the events that lead to neuronal cell death

* Memantine is thought to bind to NMDA receptor sites, thereby reducing the amount of calcium that gets into brain and nerve cells

Dementia Medications:

Donepezil:

Long duration of action (t½ = 70h)

- -Once daily dosing, preferably in the morning
- -Initial dose: 5mg/day
- -After 4 weeks, may increase dose to 10mg/day if tolerated
- -Maximum recommended daily dose is 10mg
- -Dose >10mg/day have not been approved in the UK

Patients with renal impairment - no dosage adjustment (as clearance is not affected)

Patients with mild to moderate hepatic impairment - dose escalation should be performed according to individual tolerability

Rivastigmine:

Capsules and solution:

- -BD dosing (t½=2h)
- -Starting dose 1.5mg BD
- -May increase to 3mg BD after at least 2 weeks, if tolerated
- -Maintenance dose 3 to 6mg BD (max: 6mg BD)

Moderate renal and mild to moderate hepatic impairment - dose escalation should be considered according to individual tolerability

Patches:

- -Starting dose 4.6mg/24h
- -May increase to 9.5mg/24h, after at least a minimum of 4 weeks, if tolerated
- -Recommended effective dose is 9.5mg/24h
- -May increase to 13.3mg/24h, after a minimum of 6 months, if tolerated

Galantamine:

Tablets and oral solution:

- -BD dosing (t½ = 7-8h)
- -Starting dose 4mg BD
- -May increase to 8mg BD after at least 4 weeks, if tolerated
- -A further increase to 12mg BD may be considered

XL capsules:

- -Once daily dosing (t½ = 8-10h)
- -Starting dose 8mg/day for 4 weeks
- -May increase to 16mg/day and maintain for at least 4 weeks
- -A further increase to 24mg/day may be considered

Renal impairment - no dosage adjustment if creatinine clearance is >9ml/min. Avoid if creatinine clearance <9ml/min

Moderate hepatic impairment – start with 4mg/daily in the morning for at least 1 week, then increase to 8mg/day for at least 4 weeks. Maximum daily dose 16mg/day. Avoid in severe hepatic impairment.

Memantine:

Once daily dosing interval (t½ = 60-100h) for tablets and oral pump solution, with or without food

Recommended dose titration regimen:

- Week 1: 5mg/day; week 2: 10mg/day; week 3: 15mg/day and week 4: 20mg/day

Recommended maintenance dose is 20mg/day

Maximum daily dose is 20mg/day

Dosage adjustment is required for patients with moderate to severe renal impairment

No dosage adjustment for mild to moderate hepatic impairment.

Avoid in severe hepatic impairment

Oral pump solution device

- Risk of medication errors and accidental overdose *[Drug Safety Update Nov.2010;4(4):A2]*
- One actuation of the pump device delivers 0.5ml of solution, corresponding to 5mg memantine.
- The max. daily dose is 20mg (four actuations)

Be vigilant regarding dose delivery for Memantine

Antipsychotic prescribing for BPSD

- Antipsychotic prescribing for BPSD is a 'hot topic'
- Over-prescribing of antipsychotic in BPSD is considered a huge problem
  - inappropriate prescription for management of behaviours
  - continued too long
  - risks not fully appreciated
- All antipsychotics are unlicensed in the UK for dementia-related behavioural disturbances except Risperidone and Haloperidol

10yrs ago it was estimated that 180,000 people with dementia were Px antipsychotics – but only 36,000 derived some benefit!

New Dementia Medication in 2020

Idalopirdine

- a potent and selective 5-HT6 receptor antagonist
- Lundbeck
- as an augmentation therapy for the treatment of cognitive deficits associated with Alzheimer's disease and schizophrenia

LMTM (Leuco-methylthioninium bis(hydromethanesulfonate)

- Stabilised form of methylene blue which is a first-in-class tau aggregation inhibitor
- TauRx Pharmaceuticals Ltd
- developed for the treatment of mild to moderate Alzheimer's disease and behavioural variant frontotemporal dementia

De-Prescribing
Dementia or medication side effects?

Patient Details:

- Alice is 81yrs old – not pregnant. Referred for a memory assessment - ?Dementia?
- PMH – Anxiety, Depression, Osteoarthritis, ID Anaemia, Parkinsons and Hiatus Hernia.
- CT Head 2014 - small vessel disease (SVD).
- Alice was born in Norfolk and left school at 14yrs, working in her parents chip shop. She is married and ran a grocery shop with her husband. She has two girls, both live near her and provide support.
- Currently experiencing depression following friends sudden death, anxiety, poor STM/confusion, auditory hallucinations, sleeping during the day, reduced ADL's and mobility.
- Non-smoker, no alcohol.

Calgary –Cambridge (1996)

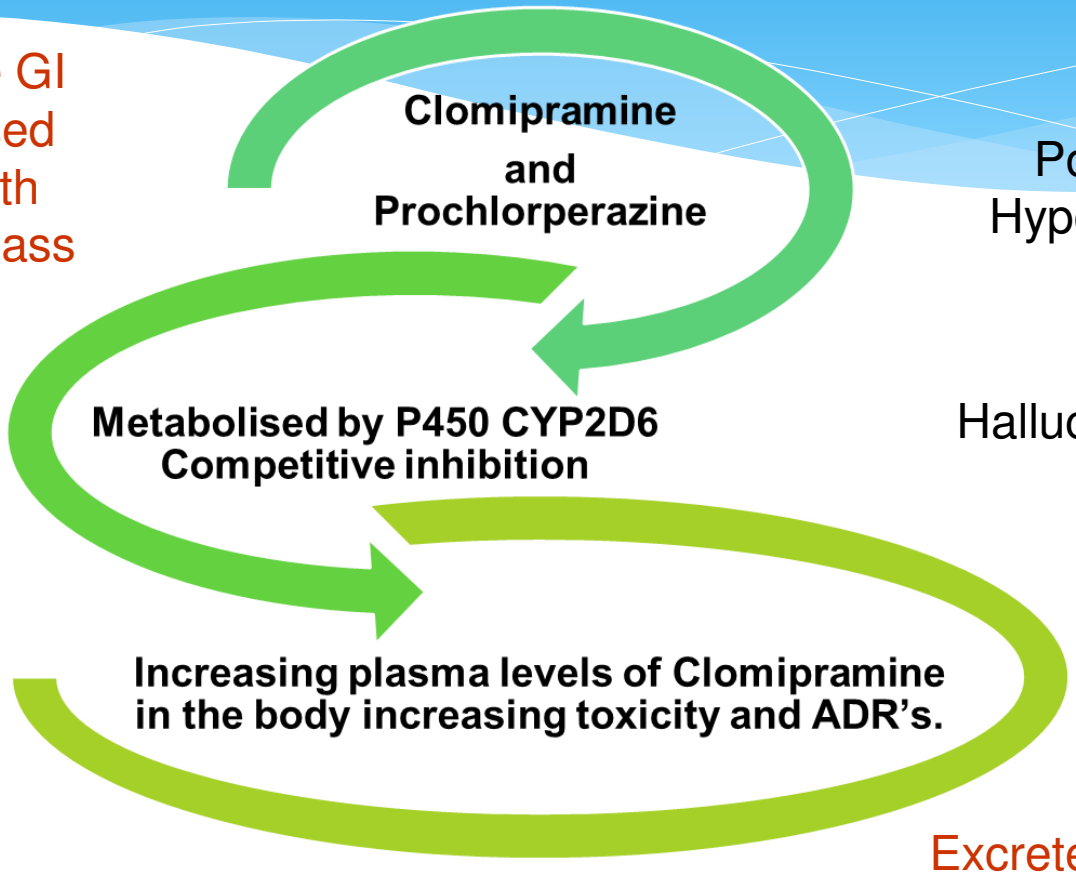
Medications/Presentation

Medication	Indication	Comments
Clomipramine 35mg at night and 25mg in morning	Depression	Increased at Christmas by GP
Prochlorperazine 5mg twice daily (reduced from 5mg three times a day)	Nausea	Parkinson's team recommended reduction in 2014
Sinemet 12.5/50mg 2 tabs three times a day	Parkinson's	Started 2014
Lorazepam 1mg three times a day	Anxiety	
Lansoprazole 30mg daily	Hiatus hernia	
CosmoCol™ 6.9g sachet daily	Constipation	

Nil OTC medications

Pharmacokinetics, Metabolism…

Absorbed in the GI tract, metabolised by the Liver with significant first pass effect.



Postural Hypotension

Hallucinations

Dystonia – Parkinsonian symptoms

Confusion

Excreted in bile but mainly through kidneys.

Actions:

- Further bloods to rule out physiological reasons for confusion - Folate, VitB12.
- **Stop Prochlorperazine prescription, due to contraindication with Parkinsons and interaction with Clomipramine. (Alice did not want to – as did not want to vomit due to HH, however did eventually agree).**
- Reduce with view to stop Lorazepam – reducing titration over 6/52 – reduce over sedation.
- Request ECG to review cardiac rhythm (Assessed prior to memory medications being prescribed).
- Request MRI brain, Diagnostic tool: Vas/Alz dementia?
- If diagnosed with a dementia, possibly prescribe Memantine (due to SVD).
- **Informed GP, Follow up – 6/52.**

Outcome:

* Alice reduced and stopped the Prochlorperazine over the 6 weeks.
* She managed to reduce the Lorazepam to 0.5mg three times a day, halving the dose.
* Presentation: more alert, no evidence of hallucinations, spontaneous in speech, stated mood had improved although she was still upset about losing her friend. Alice was also able to walk more – short distances.
* Review in 3 months (following MRI) and repeat the ACEIII.

ANY QUESTIONS?

The Patient Experience. . .

V