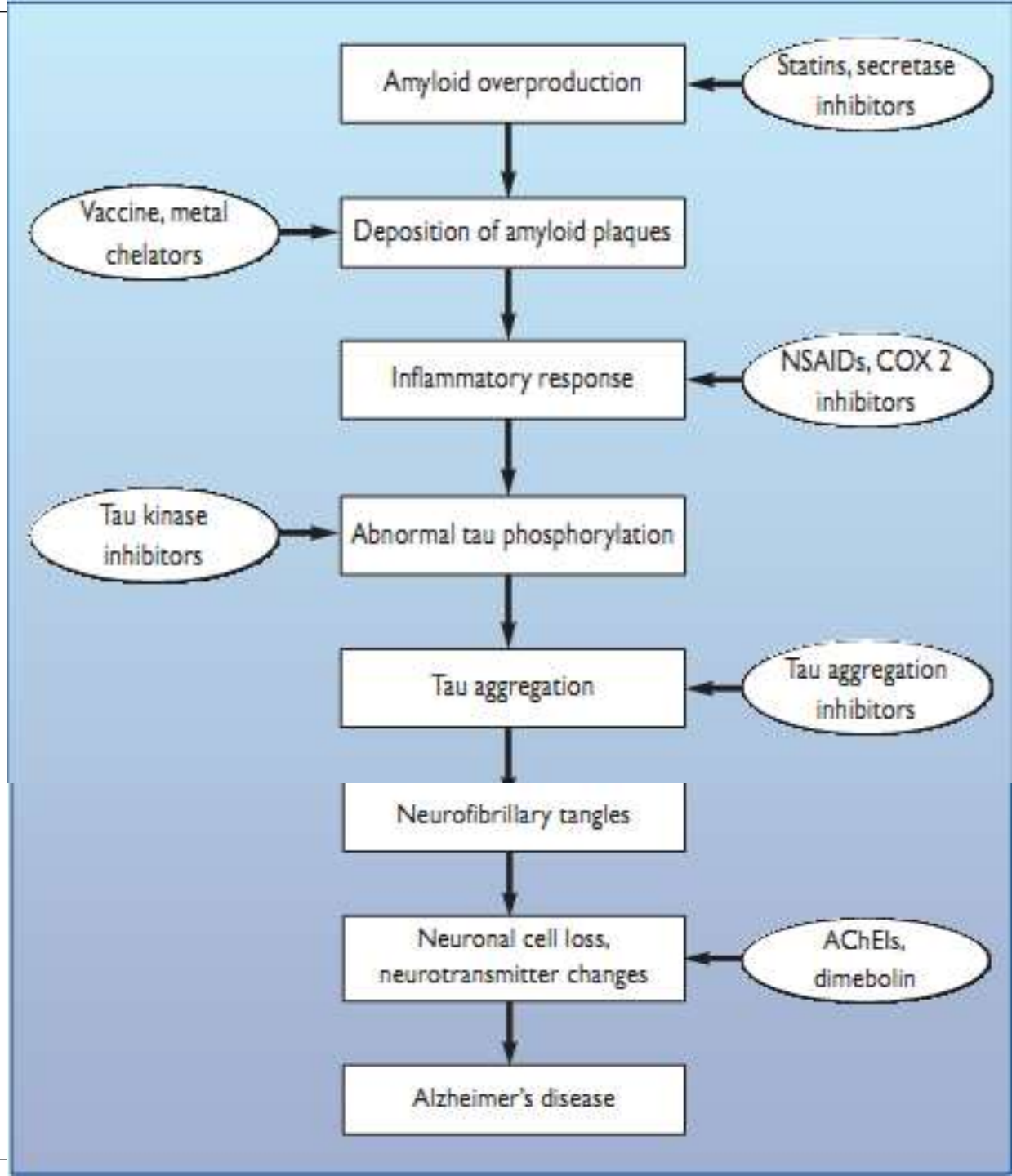
# Antidementia

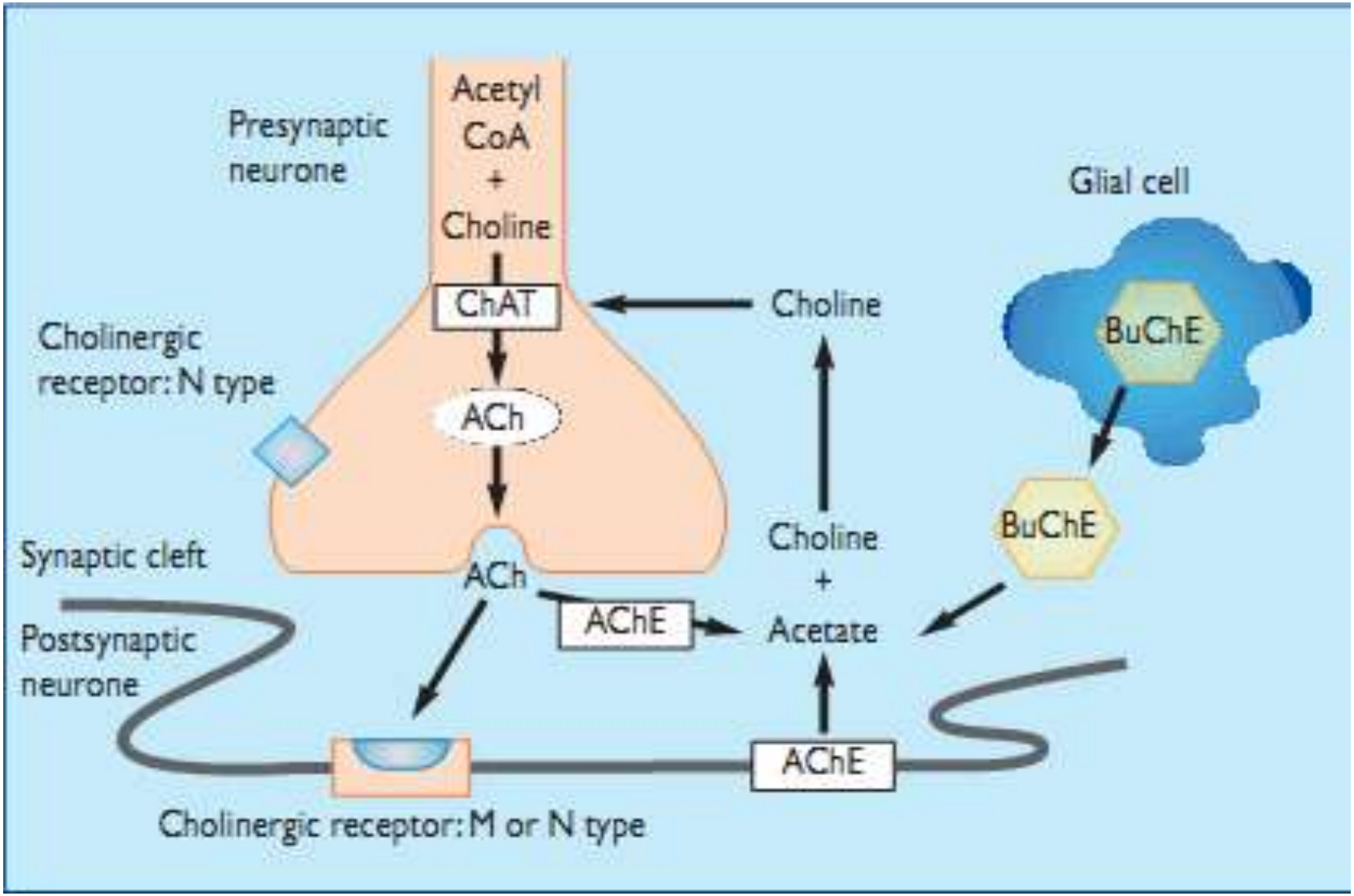
# Definisi

- Penyakit Alzheimer  (Alzheimer disease /AD) adalah jenis demensia paling umum yang awalnya ditandai oleh melemahnya daya ingat, hingga gangguan otak dalam melakukan perencanaan, penalaran, persepsi, dan berbahasa.
- AD=sindrom dengan apoptosis sel-sel otak pada saat yang hampir bersamaan sehingga otak tampak mengerut dan mengecil.
- ditandai dengan perubahan-perubahan yang bersifat degeneratif pada sejumlah sistem neurotransmiter, termasuk perubahan fungsi pada sistem neural monoaminergik yang melepaskan asam glutamat, noradrenalin, serotonin dan serangkaian sistem yang dikendalikan oleh neurotransmiter

# Patofisiologi AD



# AChE inhibitor



# AChE inhibitor

| Characteristic | Donepezil | Rivastigmine | Galantamine | Memantine |
|---|---|---|---|---|
| Starting dose | 5mg daily | 1.5mg twice daily | 4mg twice daily<br>(or 8mg XL daily) | 5mg daily |
| Usual treatment dose (max dose) | 10mg daily | 6mg twice daily<br>9.5mg/24 hrs (patch) | 12mg twice daily<br>(or 24mg XL daily) | 10mg twice daily or<br>20mg daily |
| Recommended minimum interval between dose increases | 4 weeks<br>(increase by 5mg daily) | 2 weeks<br>(increase by<br>1.5mg twice daily) | 4 weeks<br>(increase by 4mg<br>twice daily) | 1 week<br>(increase by 5mg<br>daily) |
| Adverse effects<br>* very common:<br>≥ 1/10;<br>or common:<br>≥ 1/100 | nausea*<br>headache*<br>diarrhoea*<br>vomiting<br>insomnia<br>muscle cramps<br>fatigue | nausea*<br>vomiting*<br>diarrhoea*<br>dizziness*<br>anorexia*<br>agitation<br>confusion | nausea*<br>vomiting*<br>diarrhoea<br>abdominal pain<br>dyspepsia<br>anorexia<br>fatigue | headache<br>dizziness<br>constipation<br>somnolence<br>hypertension |
| Management of adverse effects | Stop treatment if the following adverse effects occur: bradycardia, gastrointestinal ulceration<br>Reduce dose or discontinue if intolerable if the following adverse effects occur: nausea, vomiting, diarrhoea, muscle cramps, insomnia, fatigue | | | |

# Perkembangan Tx AD

| Agent(s) | Mechanism of action | Evidence |
|---|---|---|
| NSAIDs<br>Cyclo-oxygenase (COX-2) inhibitors | Anti-inflammatory: plaque-associated inflammation causes cellular damage | Results from prospective studies were disappointing |
| HMG-CoA reductase inhibitors (statins)[33] | Cholesterol depletion strongly inhibits β-amyloid secretion and amyloid precursor protein processing, although exact mechanism for this is not known | Two RCTs suggested that statins slow cognitive decline in AD. Promising results but further studies needed |
| Secretase inhibitors[34,35] | Secretase enzymes are involved in β-amyloid processing. β-amyloid is generated from amyloid precursor protein by β- and γ-secretases | Phase II and Phase III studies underway |
| Metal chelators | Dissolve amyloid plaques<br>Copper and zinc are implicated in the formation of amyloid plaques | More data on safety and efficacy are required |

# Perkembangan Tx AD

| | | |
|---|---|---|
| Immunisation (vaccine) | Production of β-amyloid antibodies<br>Lowering of amyloid burden | Phase II of vaccine suspended following cases of meningoencephalitis |
| Antibiotics, eg tetracyclines, rifampicin | Reduce inflammatory cytokines<br>Interfere with plaque development | More data on efficacy are required |
| Tau kinase inhibitors,[36] eg lithium | Reduce tau hyperphosphorylation<br>Prevention of tangles | No data published as yet; however, preliminary data were not positive |
| Tau aggregation inhibitors[37] | Facilitate the proteolytic degradation of tau aggregates | |
| Oestrogens | Possibly neurotrophic and enhances neurotransmission | Conflicting evidence showing both benefit and harm |
| Curcumin (extract of turmeric)[38] | Anti-inflammatory and anti-oxidant properties.<br>May inhibit the formation of β-amyloid fibrils and induce dissociation of pre-formed ones | Clinical trials sponsored by the National Institutes of Health are underway |
| Dimebolin[39] | Weak inhibitor of butyrylcholinesterase and acetylcholinesterase. Also weakly blocks NMDA receptor signalling pathway | Studies have shown significant benefits.<br>Further RCTs underway |