Dementia

Gradual onset

Patients → conceal cognitive deficits
→ give near-miss answers
→ recent memory : WORSE
→ Sundown common

Causes:

Alzheimer's D 50-80%

Multi-infarct dementia 10%

Alcoholism

Trauma

Reversible **d**ementia 5-15%

Pick's D
Huntington's
Parkinson's

— intracranial : meningioma
⊖-I hydrocephalus

sys : anaemia

def : vit B_{12}, thiamine

endocrine : Hthy

heavy metal poison : Pb

Infect : neurosyphilis
Chr TB

autoimm : SLE

drug toxicity : Br^-

Dx (DSM-III-R criteria):

(A) Impairment short-term memory → forgetful, difficulty learn new material
→ X remember 3 objects 5mn
long- " "
→ past personal info (birthplace, job)
facts' common knowledge (Prime Minister, footy)

(B)
(i) ↓ abstract thinking
(ii) Impaired judgement → temporal orientat° ? year ? month ? season
(iii) Higher cortical funct° → X copy 3D figures
→ calculat°s
(iv) Personality △ → labile
shallow affect
dis⊖ : tell obscene jokes
(E) ↓ insight

Alzheimer's D

Commonest cause ` dementia (50-80%)
Age-related

→ Acq decline in higher mental funct²

Progressive
Irrev
: Mental impairment
memory
intellectual fct
↓
Speech
↓
Fine motor movements
↓
Δ personality
↓
↓ self-care : poor nutrit² de H₂O
↓
Bed-ridden
↓
DEATH · resp infect²
accidents

Riskfactors :

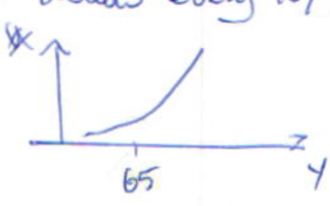
① Familial/Genetic
↓
3%

Chr **21** (APP mutat²) ← clott process, wound repair → serproteases in coag cascade
19 (Apolipo Pr E)
14 (?. gene product)

≡ nexin II protease
↓
binds NGF EGF
↓
++ FB in culture

② Down syndrome (Trisomy 21)
↑ gene dosage
↓
βA4/APP

③ Age → double every 10Y < 50



→ younger-onset
Familial

Pathology

Sites: Ⓣ esp hipp → memory fct, temporo orientat²
Ⓟ
Ⓕ
(X in occipital & motor cx
Spares 1° somato sens areas)

Ⓗ : Intra© — Neurofibrillary tangles < paired helical fil, single straight "
↳ tau
Extra© — Amyloid plaques
Para-" "
— Amyloid congophilic angiopathy
↳ rupture

Mech ` amyloidogenesis

↑ exp ` APP 695, 751, 770 res (brain, kidney, blood platelets) → βA4 (brain only) 42/43 res
↓ degradat² ` mem bound APP — persists
Mutat²s in APP gene — affect degradative P(W)
Δ in ratio ` splice products
Proteases — kallikrein-like serine ~
Calpain
prolyl-endopeptidase

Rx :

① Anti-amyloidogenesis
anti-fibrillogenesis
reg ` APP gene
vs APP/βA4

② Cholinergic → ACh & AChE ↓↓ > 50%, NA & Somatostatin ↓
ACh ` precursors — Choline, lecithine
M-ago — Arecoline
Anti-ChE — Physo-stigmine
Tacrine
↳ also K+ channel anta
↓

③ Neurotrophic
NGF
NT3
BDNF
bind ` p75 (low-aff), TrkA (high ")
↓
stop © death signal
gen CNS ⊕

④ Anti-inflamm
vs microglia

⑤ ApoE (protective effect)

Rx: Parkinson's D

Transplantat ↔ open microsurgery → head of Caud
↔ stereotactic inject → putamen + head of Caud

- ↓reliance on drugs
  ↓S/E
  slow progress
- X complete cure

① Ad- medulla implants
→ poor results < X NGF, crude tech
improvements for host response

② Foetal mesencephalic DA implants
→ ✓ some success ↔ growth of DA Nr
host: sprout (↓ bind in Cx, [^{3}H]-marked)
↑ On' phase
↓ rigidity & hypokinesia in Off'
(X Δ in tremor)
>1Y : ✓ improve
Graft survival