

Alzheimers Dementia

History of Presenting Illness :

To qualify as demented, you must →

Differential Diagnoses

- Aphasia
- Cortical Basal Ganglionic Degeneration
- Dementia in Motor Neuron Disease
- Dementia with Lewy Bodies
- Frontal and Temporal Lobe Dementia
- Lyme Disease
- Multiinfarct Dementia
- Neurosyphilis
- Parkinson Disease
- Parkinson-Plus Syndromes
- Prion-Related Diseases
- Thyroid Disease
- Wilson Disease

Findings on History

Mainly interested in the above criteria, thus:

- determine **progression (CHRONIC)**
- determine **degree of impairment**
- personality change?
- Inappropriate behaviours?
- **LATER CHANGES:**
 - **apathy,**
 - **decreased speech output,**
 - **failure to recognize family members,**
 - **incontinence.**
- **RULE OUT DIFFERENTIALS :**
diagnosis is by exclusion

Findings on Examination

- **LISTEN TO THE LUNGS AND HEART!**
(These patients die of pneumonia and CHF)
- **MMSE score of 24 or lower? = DEMENTED!**
Standard rate of decline is ~ 3 points every 6 months
- **LOOK FOR GLOVE AND STOCKING SENSORY LOSS**
(could it all stem from B12/folate deficiency?)
- **LOOK FOR FOCAL NEURO SIGNS**
(could it all stem from a massive temporal lobe tumour?)
- **LOOK FOR ANAEMIC PALLOR**
(could it all stem from cerebral hypoxia?)
- **LOOK FOR JAUNDICE** (hepatic encephalopathy?)
- **LOOK FOR ATRIAL FIBRILLATION** (multi-infarct dementia?)
- **LOOK FOR CLAUDICATION + Hypertensive Retinopathy**

Evaluating delirium: Delirium is the impairment of attention.

It is tested by repetition of digits, or spelling "world" backwards.

Do what you like- the patient will have an **INCOMPLETE MEMORY** of these episodes

Cognitive/behavioural deficits: due in part to the deficit in attention.

...**paranoia, aggression, PERSEVERATION, persecutory delusions**

Acute/subacute time course: onset is typically over hours or days.

Fluctuations in the clinical state: frequently worse at night (sun-downing).

UNSTABLE VITAL SIGNS, due to autonomic involvement

PROGRESSIVE CHANGES:

MEMORY IMPAIRMENT AND...

Either

- **Aphasia**
 - **Apraxia**
 - **Agnosia**
 - **Loss of executive function**
eg. planning, organizing, sequencing, abstracting
 - **NOT RESULTING FROM**
Delirium or a Psychiatric or Neurological disease
- *Early Onset: if onset is at age **65 years or below**

commonest cause of dementia is

Alzheimer's disease, = 60-80 % of

The next commonest is

vascular dementia. = 10-20%

Third commonest =
Lewy Body disease

Findings which **exclude Alzheimers**

Finding	Explanation
Sudden onset of dementia	Consider systemic disease, drug effect, cerebrovascular disease, infection, or tumor
Normal memory	Consider psychiatric disease, cerebrovascular disease, or early frontal lobe dementia
Plateaus in course	Alzheimer's disease is usually relentlessly progressive; consider stroke, amnesic syndrome
Depression	Consider pseudodementia secondary to depression
Personality change	If personality change is an early sign with minor memory loss, consider frontal lobe dementia
Seizures	Uncommon in early Alzheimer's disease, but do occur in late Alzheimer's disease; consider stroke, mass lesions

MINI MENTAL STATE EXAM= 30 points

Orientation (10 points)

Year, Season, Date, Day of week, and Month
State, County, Town or City

Hospital or clinic, Floor

Registration (3 points)

Name three objects: Apple, Table, Penny

Each one spoken distinctly and with brief pause

Patient repeats all three (one point for each)

Repeat process until all three objects learned

Record number of trials needed to learn all 3 objects

Attention and Calculation (5 points)

Spell WORLD backwards: DLROW

Points given up to first misplaced letter

Example: DLORW scored as 2 points only

Recall (3 points)

Recite the 3 objects memorized in Registration above
Language (9 points)

Patient names two objects when they are displayed

Example: Pencil and Watch (1 point each)

Repeat a sentence: 'No ifs ands or buts'

Follow three stage command

Take a paper in your right hand

Fold it in half

Put it on the floor

Read and obey the following

Close your eyes

Write a sentence

Copy the design (picture of 2 overlapped pentagons)

Tests and Investigations

- **B12, folate, thiamine levels** (vitamin deficiency)
- **Blood glucose** (hypoglycemia)
- **Complete blood count** (anemia)
- **Drug screen** (drug toxicity)
- **Electrolytes** (hypercalcemia, hypermagnesaemia, hypernatremia, uraemia)
- **Liver function** (liver disease, hepatic encephalopathy)
- **Lumbar puncture** (normal-pressure hydrocephalus, encephalitis, meningitis)
- **Thyroid function** (hypothyroidism)
- **VDRLT** (syphilis and HIV infection)

From the clinician's mouth:
ONLY EVER NEED 2 BLOOD TESTS:

1. **B12, Folate**
2. **Thyroid function (TSH, T4)**

IMAGING STUDIES eg. CT and MRI : needed to exclude anatomical brain lesions eg. tumour.
OTHERWISE on CT/MRI all you will see is **DILATED VENTRICLES and WIDENED SULCI**

How is this diagnosis made?

→ in **AUTOPSY**

Alzheimers is diagnosed by exclusion of everything else, until a brain biopsy is performed:

THEN → characteristic degenerative changes are witnessed

Management Of dementia:

MILD

- TRAIN the patient to help with their ADLS
- Treat their anxiety, depression, social phobia
- Refer them to social services
eg. meals on wheels, community nursing etc.
- At this stage it is wise to address issues of will-making and enduring guardianship

PREVENTION OF DEMENTIA:

Avoid head injury!
Dont drink Alcohol or smoke!
Control diabetes and cholesterol!
Control atrial fibrillation!
DRINK COFFEE!!

MODERATE

- in-house assessment: are they able to continue living where they currently live?
- Informal support: engage neighbours, family etc.
- FORMAL SUPPORT eg. nursing if they live alone

WHO WILL CARE FOR THE CARE-GIVER?

Proven: improved care-giver mental health →
→ improved QOL of demented patient
!! BETTER and FEWER SYMPTOMS !!

SEVERE

- Time to cart them off to a home.
- Residential care with help eating, dressing, hygiene
- This improves continence and nutrition
- Review their comorbidities (is it time to take them off some of their drugs, or put them on more)
- Socialize them to improve mental state (happy demented inmate = happier care-giver)

“RAGING”

- uncommon, because most commonly the end-stage is **APATHY and DEPRESSION**
- **EARLY FORM:** depressed anxiety,
- **MIDDLE FORM:** vivid hallucinations and delusions
- **LATE FORM:** inappropriate behaviour, “wandering”, “pacing”, repetitiveness, “shadowing”, nudity.
- **AGGRESSION IS RARELY SPONTANEOUS!!** The staff usually deserve it

THUS: do not jump directly to the major sedatives and neuroleptics.

EDUCATE THE CARE-GIVERS AND MODIFY THEIR BEHAVIOUR

TERMINAL DEMENTIA:

- Bedbound,
- Incontinent,
- Not swallowing
- **THERE IS NO BENEFIT IN ANTIBIOTICS AND ARTIFICIAL FEEDING:**

→ **DEATH from:**

**pressure sores, contracture (muscle shortening),
Infections eg. pneumonia, dehydration, malnutrition**

They do not seem to improve survival

~ALZHEIMERS DRUGS~

SYMPTOM CONTROL

Cholinergics, eg precursors (choline, lecithine)

→ weak long term effects

CHOLINESTERASE INHIBITORS: like neurotoxin Sarin:

→ **Donepezil** is the best one: dose = once per day
(hard to forget even for a demented patient)

FOR ACUTE EXACERBATIONS

- **ANXIOLYTICS** (but **NOT BENZO-based**)
- **NEUROLEPTICS** in low doses
Eg. **olanzepine + haloperidol**
- **ANTIDEPRESSANTS** or **MOOD STABILISERS**
Eg. **prozak or lithium**

Management Of acute delirium:

Neuroleptics if you absolutely have to. **NO BENZOS!** → will make it much worse

Prognosis

The lifetime risk of developing Alzheimers == 1:4
14% of individuals older than 65 years have AD
40% in individuals older than 80 years have AD

WOMEN ARE MORE AT RISK.

**RISK DECREASES AFTER YOU REACH
90-100 y.o (good genes!)**

DELIRIUM CONFERS A POORER OUTCOME:

No matter what your condition, it will be worse

Otherwise... DELEIRIUM IS REVERSIBLE:

If the cause of the delirium can be successfully treated, the recovery phase usually begins in 10-14 days, most recovering within 4 weeks;

BUT: in 10% of patients confusion may last for up to 6 months

Epidemiology

RISK FACTORS FOR DEMENTIA

- A. **Age**
 - 1. Risk increases with age over 65 years
- B. **Apo E4 Allele**
 - 1. Confers 8% risk if two alleles
- C. **Family History of Alzheimer's Disease**
- D. FAD gene
- E. Female gender
- F. Low education
- G. Head Trauma
- H. Myocardial Infarction
- I. Combined CV factors in middle age (odds ratio 3.5)
 - 1. Hyperlipidemia
 - 2. Hypertension (increased systolic Blood Pressure)

RISK FACTORS FOR DELIRIUM

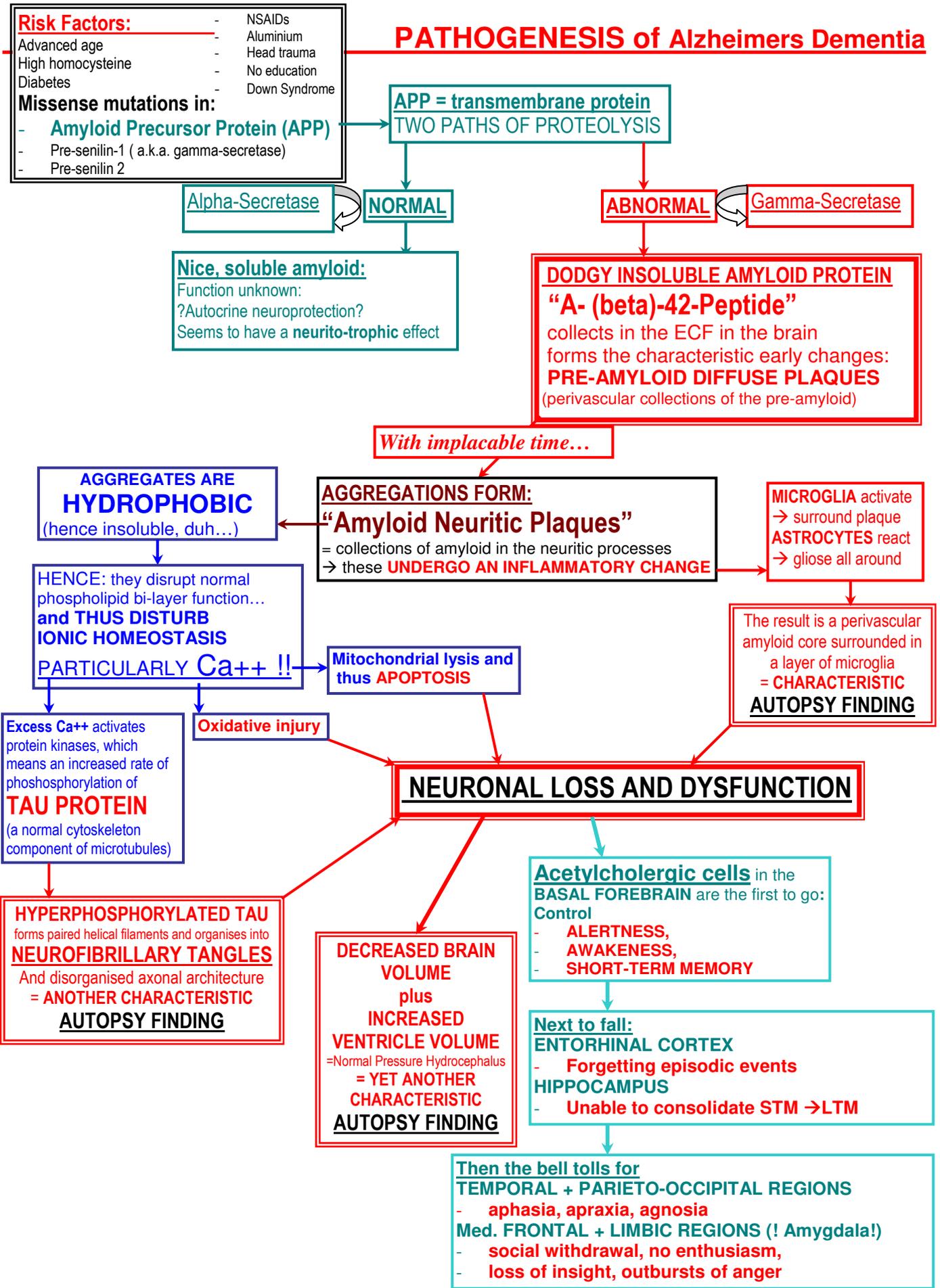
- J. Age over 60 years
- K. Drug or alcohol addiction and withdrawal
- L. Prior brain injury (vascular or traumatic injury)
- M. Hearing Loss or decreased Visual Acuity
- N. Insomnia or other sleep deprivation
- O. Polypharmacy
- P. Hospitalization or post-surgery
- Q. Multiple comorbid conditions
- R. Poor nutritional status
- S. Hepatic failure
- T. Chronic Renal Failure
- U. Poor nutritional status

- **3% of 65 – 74 year olds**
- **20% of 75-84**
- **45% of 85+**
- **... are DEMENTED**

Pathophysiology : Age-associated brain changes:

1. **Brain Atrophy: decrease in size and weight** (! Male brains are normally 100g heavier)
 - !! SECULAR ATROPHY !! is a normal difference: people in the beginning of the 20th century were born WITH SMALLER BRAINS therefore comparison is slightly off.
2. **Neurofibrillary tangles**
 - Discussed below → see mechanism
3. **Neuronal Loss**
 - controversial- may not exist
4. **Cognitive Decline**
 - its no secret: old people have poor memories.
 - There is a **LONG PRE-CLINICAL PERIOD** in Alzheimers: steady decline with stable deficits.

PATHOGENESIS of Alzheimers Dementia



Anatomy and Physiology of Memory (a'la Mitrofanis)

Thing to know:

MEMORY IS NOT AN ACTUAL BRAIN PROPERTY

More like something we infer from behaviour

CATEGORIES OF MEMORY:

PROCEDURAL vs DECLARATIVE:

PROCEDURAL is unconscious, automated eg.

remembering how to write, what language to speak

→ VIA BASAL GANGLIA + CEREBELLUM (climbing fibres of cerebellum)

+ Red nucleus and Olive of medulla

DECLARATIVE MEMORY is the conscious variety

= its facts and events

separated into **SHORT and LONG TERM**

according to no real criteria, eg

Short Term Memory means about 5 minutes

SHORT TERM MEMORY:

Based in the secondary cortex of each sense (i.e visual memories are all kept together for a while in the occipital lobe)

The Pre-Frontal Cortex pools these together; somehow the Basal Forebrain is involved in their storage and distribution (Acetylcholine cells with widespread connections)

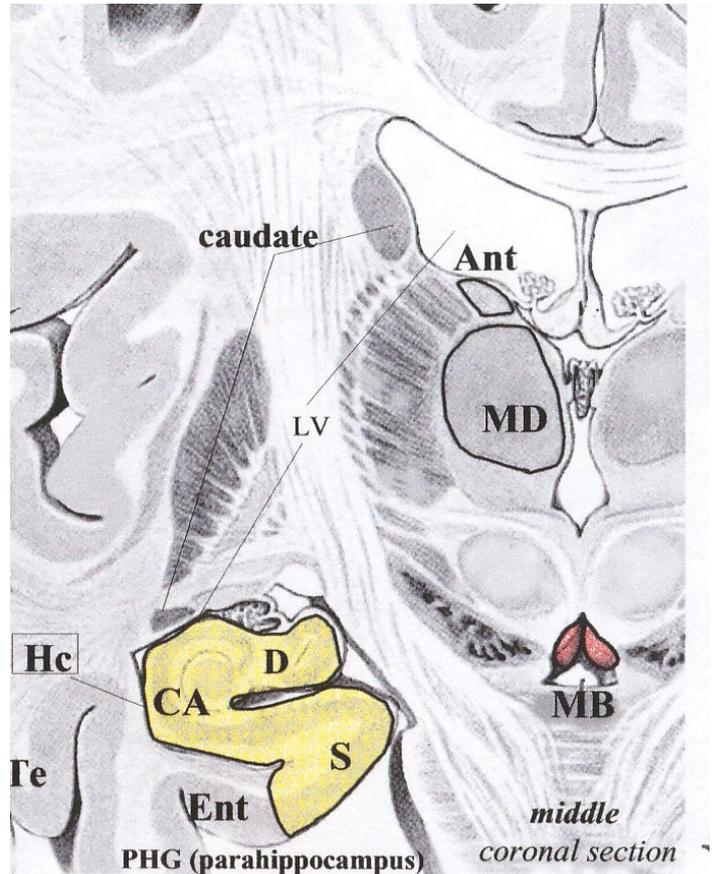
LONG TERM MEMORY: permanent storage with HUGE capacity

Mediated by the MIGHTY HIPPOCAMPUS

→ IT DOES EVERYTHING

Long term memories are stored in the NEOCORTEX, vaguely associated with the sensory area of their origin

* **AMYGDALA** is involved in the emotional tagging of memories



MD= medial dorsal nucleus of thalamus
 HC = Hippocampus
 D = dentate nucleus
 CA = cornu ammonis
 Ent =Entorhinal
 MB = mamillary body
 LV = left ventricle
 Te = temporal cortex
 S= subiculum

ATTENTION and DELIRIUM

Delirium is the impairment of attention.
 is tested by repetition of digits,
 or spelling "world" backwards

USEFUL RULE OF THUMB:

SEDATION = REDUCES MEMORY-MAKING
AROUSAL = INCREASES MEMORY-MAKING

Attention comes in 2 flavours: **GLOBAL** and **SPECIFIC**

GLOBAL ATTENTION:

is stimulated by all systems;

works via the Brainstem Reticular Formation → via Thalamus → to the cortex

runs on **Acetylcholine**;

Ach from basal forebrain WAKES US UP

Serotonin determines HOW AWAKE and ALERT

SPECIFIC ATTENTION

Unimodal, i.e ONE THING AT A TIME

The Components:

Parietal cortex (filters relevant from irrelevant)

Sup. Colliculus of Midbrain (motor reflex avoidance of incoming missiles)

Pulvinar Thalamus, (Pulvinar prioritises eye movements upon orders from sup. colliculus)

How attention is gathered on one target:

The **THALAMOCORTICAL PATHWAY** (of thalamic reticular nucleus → cortex) does this:

It **AMPLIFIES ONE INPUT** and
INHIBITS ITS SURROUNDINGS
 THUS, attention is focussed.