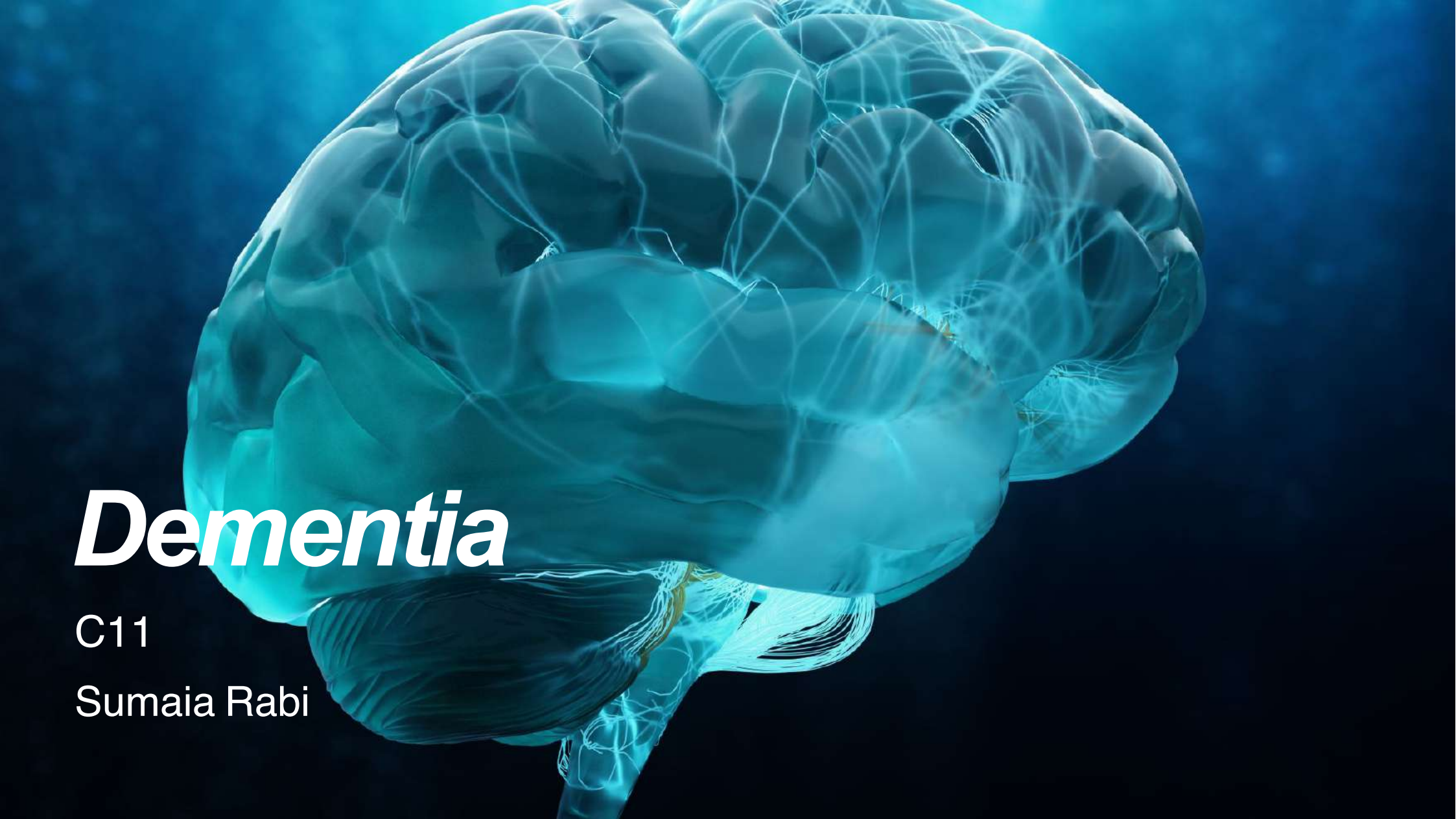


A glowing blue brain with visible neural pathways, set against a dark blue background. The brain is shown from a side profile, with the cerebral cortex and underlying white matter tracts highlighted in a bright blue, almost white, glow. The overall image has a futuristic, scientific feel.

Dementia

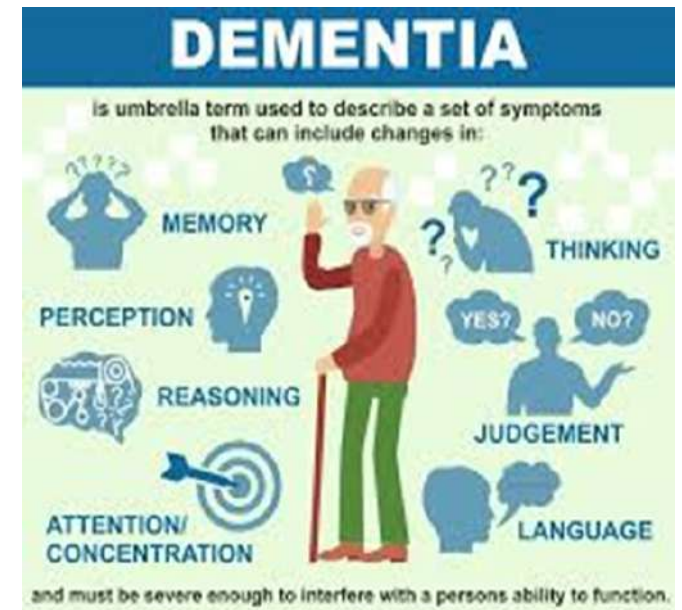
C11

Sumaia Rabi

Dementia

Intellectual and cognitive deterioration of sufficient severity with normal functioning , affect multiple aspects of cognitive function that include :

- ▶ 1) memory loss
- ▶ 2) disorientation
- ▶ 3) language problems
- ▶ 4) impaired judgment
- ▶ 5) personality changes



Clinical manifestation

- ▶ 6) behavioral changes
- ▶ 7) loss of motivation
- ▶ 8) visuospatial impairment (problems with visual perception or understanding spatial relationships leading to difficulties in driving or navigating stairs)
- ▶ 9) delusions or hallucinations in some patients
- ▶ 10) decline in motor skills , difficulty with balance , coordination or fine motor tasks like writing

** Dementia differ from delirium , no loss of consciousness*

It is more common in elderly above age 85 years , but can occur at younger age specially in those with hereditary predisposition

Diagnostic Evaluation

Hamzah Abdallah / c11

DIAGNOSTIC EVALUATION OF DEMENTIA

- **Initial Recognition:**
 - Difficult due to similarities with normal aging.
 - Patients often unaware; families usually notice after months or years.
- **Subjective Cognitive Decline :**
 - Can be an early indicator of dementia.
 - Important even without objective cognitive dysfunction.
- **Diagnosis:**
 - Relies heavily on clinical history and detailed mental status examination.
 - Match patient's clinical features with known dementing illnesses.
- **Rule Out Depression :**
 - Depression can mimic dementia (pseudodementia).
- **Laboratory Studies:**
 - Useful for identifying reversible causes of dementia.

- **Hematologic Screening:**
 - Erythrocyte sedimentation rate
 - Vitamin B12 and folate
 - Blood calcium
 - Liver function tests, including ammonia
 - Electrolytes
 - Serum urea nitrogen and creatinine levels
- **Infection Workup:**
 - Syphilis, HIV, tuberculosis, etc.
- **Thyroid Function Tests**
- **EEG**
 - Not routinely ordered in dementia assessment.
 - Justified if cognitive status fluctuations suggest seizures.
 - Useful in initial presentation for suspected CJD.
- **Brain Imaging (CT or MRI) :**
 - Rules out structural abnormalities (tumor, subdural hematoma, hydrocephalus).
 - Evaluates cortical atrophy.
- **Neuropsychological Assessment:**
 - Useful in early stages to diagnose dementia.
 - Serves as a comparison tool for disease progression.
- **Brain Biopsy:**
 - Indicated in specific cases (CJD, HIV, CNS vasculitis).
 - Confirms diagnosis and identifies treatable causes

Causes of Dementia

Mohammad AlOtaibi / c11

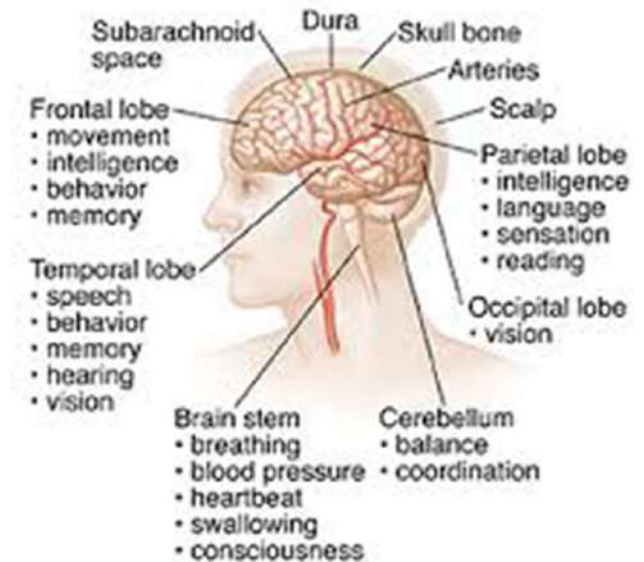
Definition of dementia

Dementia is chronic acquired impairment of intellect, memory and personality associated with many diseases (usually progressive, with no alteration of consciousness)

Defines as impairment of two or more areas of cognition; one must be the “memory “ the other being any of the following (language, praxis, visual-spatial skills, personality, social behavior, or abstract thought)

With the absence of delirium & psychiatric disease(e.g. schizophrenia)

Dementia occurs more commonly in the elderly than the middle-aged



Risk factors...



1.Age(>65y or older)

2.Hypertension



3.Diabetes mellitus

4.High BMI



5.Smoking

5.Too much alcohol



6.Sedentary lifestyle

7.depression

Dementia and it's causes

Primary neurodegenerative disorders (Alzheimer's disease, Huntington disease, Parkinson disease, diffuse Lewy body disease, frontotemporal degeneration)

Infection(prion, Creutzfeldt Jakob, AIDs, chronic meningitis, neurosyphilis)

Vascular &traumatic diseases(multi-infarct dementia, global hypoxic ischemic brain injury, chronic subdural hematoma)

Nutritional &Metabolic disorders (thiamine deficiency “wernickes-korsakoff syndrome “,vit b12 deficiency)

Miscellaneous (brain tumors, neuronal storage disease, toxic injury e.g. Mercury, lead)

Note...

Alzheimer is the most common cause of dementia.

Delirium vs dementia (delirium causes altered consciousness)

Neurodegenerative dementias are associated with movement disorder which are termed “subcortical dementia for example “Huntington disease “ characterized with slowing of cognitive function (Bradyphrenia), personality & mood change, absence of cortical deficits (e.g., Agnosia, dysphasia, dyspraxia) which are usually typical in Alzheimer



Alzheimer's disease

Is an illness with an insidious, progressive onset, that causes significant impairment of daily activity.

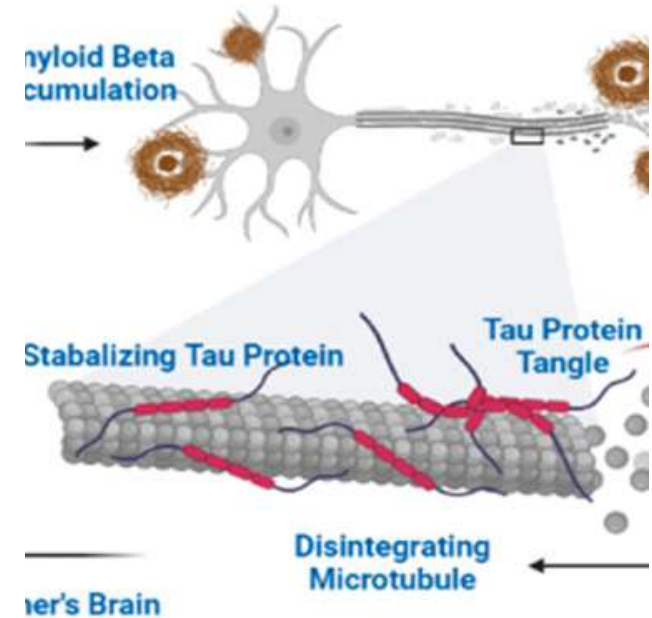
Most common cause of dementia in all age groups

Mostly sporadic.

Degenerative disease of grey matter of the cortex.

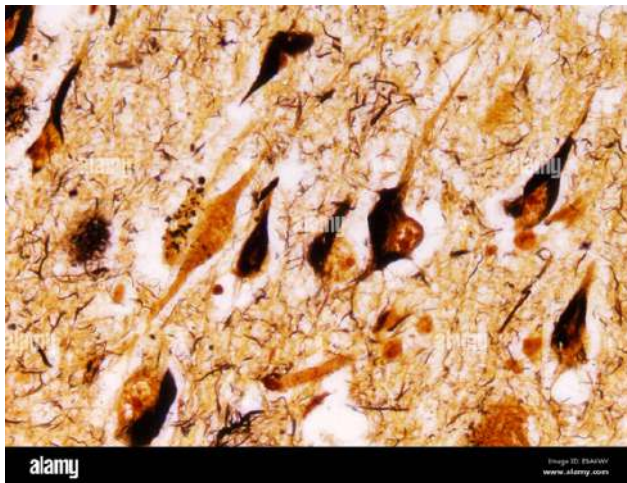
The end result is death of neurons in specific areas ,mainly the hippocampus, temporal neocortex.

Cholinergic neuron are also affected, so the cholinergic enhancing drug can improve memory in this disease

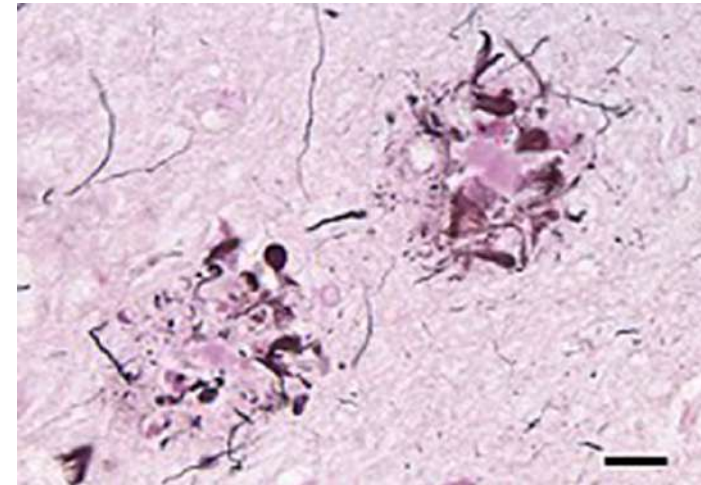


It is a neurodegenerative disorder characterized pathologically by

*Intracellular
neurofibrillary tangles
composed of paired
helical filament*



*Extracellular neuritic
plaques containing
amyloid core along with
neuronal loss*





Clinical features of Alzheimer's disease

Early(reflecting hippocampus dysfunction)

1-Immediate & short memory loss
new info

2-difficulty learning & retaining

Late(reflecting dysfunction of frontal & parietal lobe)

1-attention deficits.

2-Disorientation

3-hallucinations & delusions

4-Word-finding difficulties and loss of general knowledge

Final: 1-severe loss of cognitive function

2- amnesia, dyspraxia, dysphasia, agnosia

3-personality disintegration with behavioral disturbances(depression, anxiety, paranoia are common)

4-incontinence

5-death within 5-10 years

Cont.....

There is no specific test for **AD** , **Diagnosis** is currently done with clinical evidence, histological evidence, exclusion of other cause

Management:

(No curative treatment found so far)

1-treat any systemic illness, avoid sedative & alcohol

2-simple memory aids(diaries, labels)

3-combination of cholinergic-enhancing drugs(used to improve dementia)

NMDA receptor antagonist(memantine)

Cholinesterase inhibitors (rivastigmine)

Frontotemporal dementia(picks)

Disorder caused by slowly, progressive dementia(due to progressive neuronal loss in frontal, temporal lobes),more common in younger patients, caused by mutation in the gene encoding tau protein.

Frontal & temporal lobes atrophy present(vs diffuse atrophy in AD),with abnormal accumulation of tau protein.

Clinical features: similar to Alzheimer but more prominent personality &behavioral change.

Progressive non-fluent dysphasia.

Semantic dementia(loss of ability to match words or images to their meanings)

Spared memory but impaired learning, judgment, language.

No current treatment but SSRIs used to treat behavioral changes.



Vascular(multi-infarct dementia)

Non-degenerative disorder caused by recurrent thromboembolism in the brain ,dementia has “sudden” onset & stepwise progression (Alzheimer has an insidious & gradual progression)

Clinical features: presence of vascular disease elsewhere in the body

Focal neurological deficits(hyperreflexia, paresthesia)

Identical symptoms to Alzheimer (combined cortical, subcortical deficits)

Nocturnal confusion & fluctuating cognition

Diagnosed by MRI

Treatment is managing the vascular cause& controlling risk factors(smoking, HTN, DM)



Normal pressure hydrocephalus NPH

Is reversible cause of dementia, patients have enlarged ventricles with increased ICP(no papilledema).can be idiopathic or secondary to obstruction(trauma, chronic meningitis or subarachnoid hemorrhage)

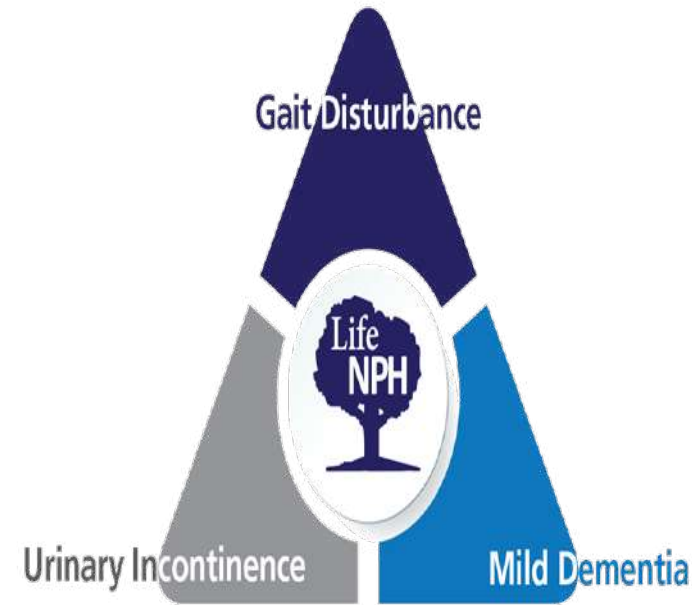
Diagnosis: is made with integration of clinical(no papilledema)+LP(normal opening & gait improvement)

MRI or CT(ventricular enlargement)

LP(normal opening pressure, observing clinical response of gait after high-volume LP)

NOTES: there are certain indicators of NPH(secondary causes present,<6 months of symptoms, gait disturbances>cognitive abnormality)

TREATMENT: is by ventriculo-peritoneal or ventriculo-atrial shunting



Dementia associated with Extrapyrarnidal features

Abeer Abdeljawad / c11

Quick Recap

PYRAMIDAL

TRAVEL THROUGH **PYRAMIDS OF THE MEDULLA**

RESPONSIBLE FOR **VOLUNTARY MUSCLE CONTROL**

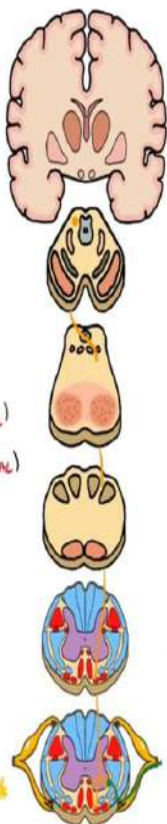
① CORTICOSPINAL TRACT

CEREBRAL CORTEX (BRAIN)
INTERNAL CAPSULE
CRUS CEREBRI (MIDBRAIN)
BASIS PONTIS (PONS)
PYRAMIDS (MEDULLA) 75% DECUSATE (LATERAL CORTICOSPINAL)
25% IPSILATERAL (ANTERIOR CORTICOSPINAL)
LOWER MOTOR NEURONS (VENTRAL HORN)

② CORTICOBULBAR TRACT

VOLUNTARY CONTROL OF FACE, HEAD AND NECK
CEREBRAL CORTEX
INTERNAL CAPSULE
LOWER MOTOR NEURONS (CRANIAL NERVE NUCLEI / BRAINSTEM)

* MOSTLY BILATERAL INNERVATION.
CN IX + LOWER CN VII ARE CONTRALATERAL *



EXTRAPYRAMIDAL

DO NOT TRAVEL THROUGH **PYRAMIDS OF THE MEDULLA**

RESPONSIBLE FOR **INVOLUNTARY CONTROL AND MODULATION (TONE, BALANCE)**
ORIGINATE IN BRAINSTEM

1) RUBROSPINAL TRACT

ORIGINATES FROM **RED NUCLEUS** (MIDBRAIN)
RESPONSIBLE FOR **FINE MOTOR CONTROL**
CONTRALATERAL INNERVATION

2) RETICULOSPINAL TRACT

MEDIAL - PONS, FACILITATES CONTRACTION AND INCREASES TONE
LATERAL - MEDULLA, INHIBITS CONTRACTION, DECREASES TONE, AUTOMATIC BREATHING

3) VESTIBULOSPINAL TRACT

ORIGINATES FROM **VESTIBULAR NUCLEI**
INVOLVED IN **BALANCE AND POSTURE**

4) TECTOSPINAL / COLLICULOSPINAL TRACT

ORIGINATES IN **SUPERIOR COLLICULUS**
HEAD AND EYE COORDINATION
CONTRALATERAL

PYRAMIDAL

- MAY BE DAMAGED AT ANY POINT ALONG THE SPINAL CORD
- **INTERNAL CAPSULE** OFTEN INVOLVED IN **HAEMORRHAGE AND STROKE**
- DEFICITS ARE MOSTLY **CONTRALATERAL**

TYPICAL MANIFESTATION OF UMN INJURY:

- 1) **INCREASED MUSCLE TONE**
- 2) **HYPERREFLEXIA**
- 3) **WEAKNESS**
- 4) **CLONUS**
- 5) **BABINSKI** (+) (UPWARD MOVEMENT OF BIG TOE ON SI STIMULATION)

HOFFMAN (+) (THUMB FLEXION ON FLICKING MIDDLE FINGER NAIL)



EXTRAPYRAMIDAL

MANIFESTATIONS OF EXTRAPYRAMIDAL TRACT INJURY:

- 1) **PARKINSONISM**
 - RIGIDITY
 - BRADYKINESIA
 - TREMORS
 - POSTURAL DEFICITS
- 2) **CHOREA**
- 3) **ATHETOSIS**
- 4) **DYSTONIA**

Extrapyramidal Features

This group of dementias includes a wide array of neurodegenerative syndromes, including but not limited to :

- ▶ Lewy body dementia (LBD),
- ▶ frontotemporal dementias (FTDs),
- ▶ progressive supranuclear palsy (PSP),
- ▶ corticobasal degeneration,
- ▶ striato-nigral degeneration, Huntington disease (HD),
and Wilson disease.

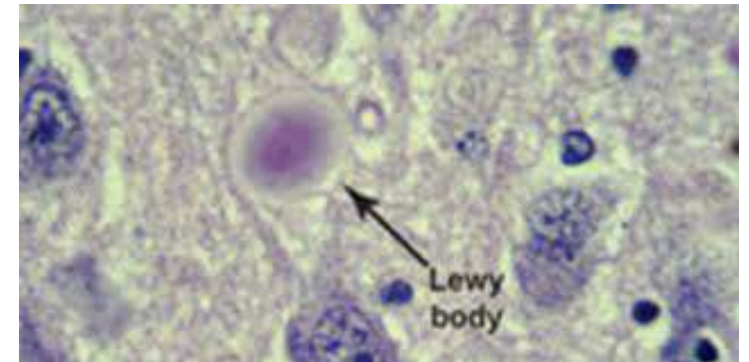
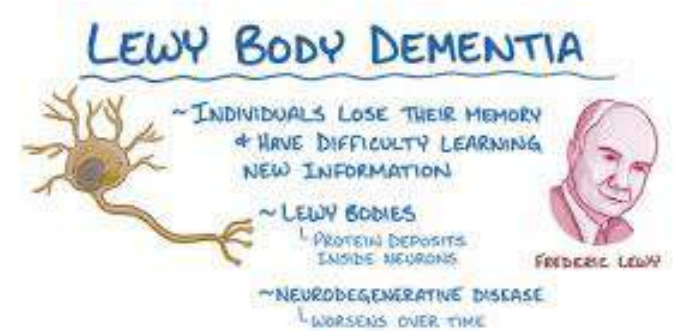
Some important examples of these diseases are discussed here .

DEMENTIA WITH LEWY BODIES

is a progressive neurological condition that affects cognitive function, movement, and behavior. It is characterized by the presence of abnormal protein deposits called Lewy bodies in the brain, which disrupt normal brain function.

LBD is now thought to be the second leading cause of dementia (rather than vascular dementia).

The clinical picture of LBD is that of a parkinsonian dementia syndrome; it is considered to be on a spectrum with PD dementia.



✦ CLINICAL MANIFESTATION

Early progressive cognitive decline, beginning after age of 55

Visual hallucination – manifesting small children, animals most commonly -.

Attention and visuospatial skills are typically affected earlier than memory difficulties.

+ Motor symptoms: “parkinsonian” Bradykinesia and gait impairment are more common than rest tremor.

Marked fluctuations of alertness, delusions, and an extraordinary sensitivity to neuroleptics (i.e., **marked worsening with drugs like haloperidol**) are **also key features of LBD.**

✦ DIAGNOSTIC EVALUATION

The pathologic hallmark of this disease is the Lewy body, an eosinophilic intracellular inclusion of the protein **alpha synuclein.**

In LBD and PD, widespread **limbic and cortical Lewy bodies are found,**

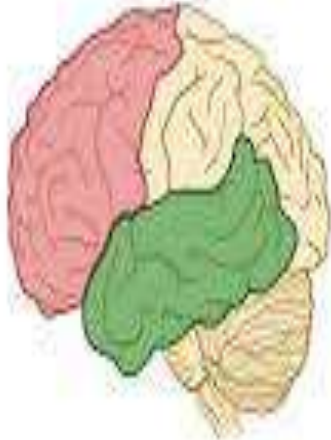
Other pathologic abnormalities can also be present, including varying degrees of AD-type abnormalities such **as NFTs and amyloid plaques.**

✦ Treatment

To treat behavioral symptoms low dose of *atypical neuroleptic* such as **Risperidone and Quetiapine** is used .

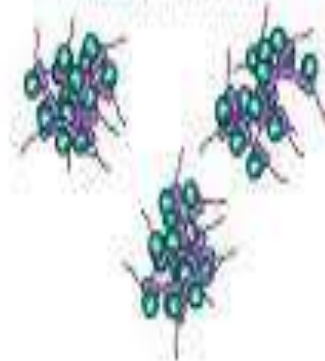
FRONTOTEMPORAL DEMENTIA (FTD)

* DEGENERATION of the **FRONTAL**
& TEMPORAL LOBES



* MISTAKEN for PICK DISEASE

- SUBSET of FTD
- PRESENCE of PICK BODIES
- TANGLES of TAU PROTEINS



FRONTOTEMPORAL LOBAR DEGENERATION (FTLD)

o(FTLD) is the underlying pathology associated with a **heterogeneous group of degenerative disorders** that collectively account for up to 20% of dementias.

oThese disorders are a leading cause of dementia in patients presenting before 65 years of age.

oFTLDs are pathologically notable for marked, preferential **degeneration of the anterior temporal and frontal lobes, with prominent tau accumulation.**

CLINICAL MANIFESTATIONS



-NEURODEGENERATION IS ASSOCIATED WITH A VARIETY OF SYMPTOMS, WHICH ARE LINKED TO DIFFERENT SUBTYPES

-THREE MAIN SUBTYPES ARE:

-BEHAVIORAL VARIANT FTLD

CHANGES IN BEHAVIOR, EMOTIONS, PERSONALITY, AND EXECUTIVE CONTROL

-SEMANTIC VARIANT PRIMARY PROGRESSIVE APHASIA(PPA)

-DEFICITS IN WORD COMPREHENSION, TROUBLE RECALLING CERTAIN WORDS, OTHER LANGUAGE DIFFICULTIES

-NONFLUENT VARIANT PRIMARY PROGRESSIVE APHASIA

DIFFICULTY PRODUCING FLUENT SPEECH (E.G., TROUBLE SPEAKING, PROBLEMS WITH THE USE OF THE GRAMMAR)

In addition, there are forms of FTD associated with parkinsonism and with motor neuron disease.

DIAGNOSTIC EVALUATION



•the clinicopathologic correlations of FTDs vary significantly, likely because of the heterogeneity of the underlying cause of the FTLD.

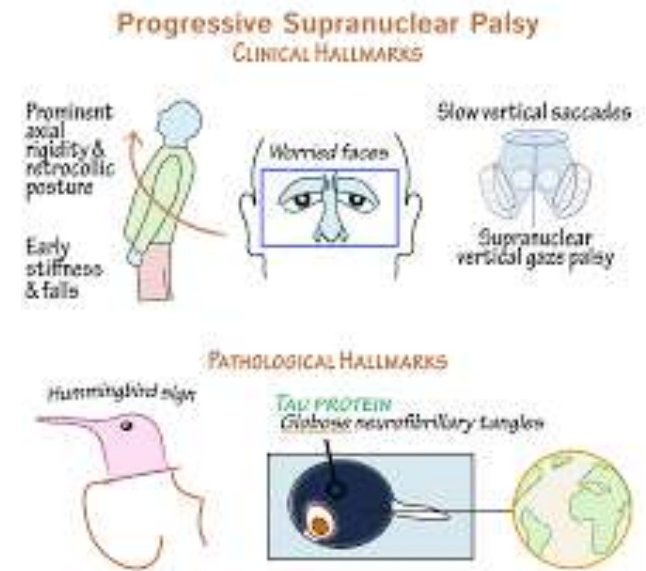
•There are multiple known genetic mutations associated with FTLD, and nearly 40% of patients with FTD have a first-degree relative with dementia.
INCLUDING :

- I. mutations in chromosome 9 open reading frame 72 (C9ORF72)
- II. microtubule-associated protein tau
- III. fused in sarcoma (FUS)
- IV. TAR DNA-binding protein-43 (TDP-43)
- V. Granulin

mutations in C9ORF72, FUS, and TDP-43 are also associated with inherited motor neuron disease amyotrophic lateral sclerosis (ALS) and FTD-ALS o

PROGRESSIVE SUPRANUCLEAR PALSY

- Progressive supranuclear palsy (PSP) is a rare neurodegenerative disorder that affects movement, balance, and eye movements. It's used to be classified as a type of parkinsonism, it shares some symptoms with Parkinson's disease but has been classified as a distinct disorder.
- PSP may account for 2% to 3% of dementias.
- No clear predisposing or genetic factors have been identified



CLINICAL MANIFESTATIONS

PSP typically presents in mid- to late adulthood.

Its main features are:

supranuclear gaze palsy, an impairment of vertical eye movement; prominent postural instability and falls. Additional features include dysarthria, dysphagia, extrapyramidal rigidity, gait ataxia, and dementia.

As such, there are many subtypes of PSP based on the prominent clinical abnormalities.

Dementia may occur early or develop later, and frontal lobe abnormalities predominate. Patients become apathetic. In early stages, PSP may be mistaken for AD.

DIAGNOSTIC EVALUATION

PSP remains a clinical diagnosis.

Similar to AD, PSP is a tauopathy,

but unlike the cortical accumulation of tau in AD, there is a predominantly subcortical disease burden in PSP, with atrophy of the dorsal midbrain, globus pallidus, and subthalamic nucleus.

The course is progressive, with a median survival of 6 to 10 years.

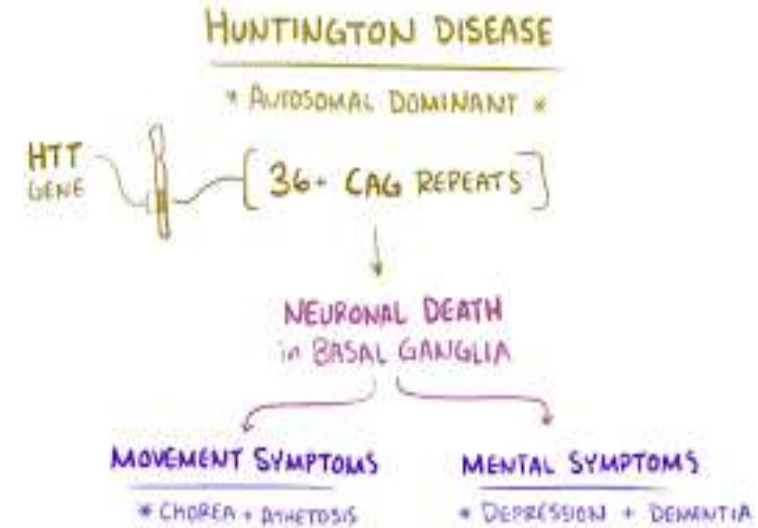
HUNTINGTON DISEASE

(HD) is an **autosomal dominant neurodegenerative disease** with typical clinical onset between the ages of 35 and 45 years. Key clinical manifestations

- • include: **chorea**, behavioral changes, personality changes (frequently obsessive-compulsive disorder), and dementia.

Diagnosis is by family history, clinical signs, **early caudate atrophy** (often very prominent) on brain imaging, and demonstration of **more than 40 CAG repeats in the HD gene on chromosome 4**.

Management is usually with **dopaminergic antagonists**, including neuroleptic drugs, for the chorea. Despite these therapies, the clinical decline is relentless. Genetic counseling for the family is fundamental.



PARKINSON DISEASE



:progressive neurodegenerative disorder that primarily affects movement. It results from the loss of dopamine-producing neurons in a part of the brain called the substantia nigra

Motor symptoms:

(bradykinesia + rigidity + resting tremors)

Non-motor symptoms:

Cognitive Changes: Some individuals may develop dementia or experience difficulties with memory and attention.

Etc...

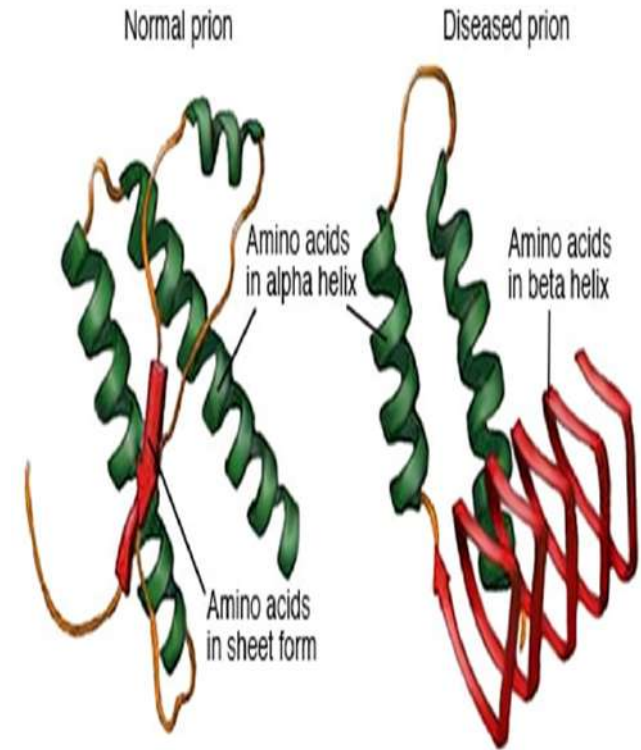
PD may produce subcortical dementia. Cognitive impairment develops in about 30% of patients with idiopathic PD. The distinction from other types of dementia is based on the natural history and the presence of associated symptoms. The clinical manifestations include those of subcortical dementia, with marked psychomotor involvement

Dementia caused by infectious agents

Marah Nahiah / c11

Prion Diseases

- Prion diseases are a group of rare neurodegenerative disorders affecting both animals and humans. Examples include bovine spongiform encephalopathy (mad cow disease) and Creutzfeldt-Jakob disease (CJD) most common in humans.
- The causative protein > prion protein (PrP), may undergo a conformational change from its normal shape (PrP^c) to an abnormal conformation called PrP^{sc}



Creutzfeldt-Jakob disease (CJD)

- neurocognitive disorder due to prion disease
- It is characterized by rapidly progressive dementia, pyramidal signs (motor abnormalities), myoclonus (muscle twitching) and Cerebellar or extrapyramidal signs (coordination and movement problems)
- Types of CJD:
 1. Sporadic CJD: most common
 2. Familial CJD: (10-15%) as autosomal dominant due point mutation, peak incidence in the 7th decade.
 3. Variant CJD: likely by consuming meat from a cow that had BSE.
 4. Iatrogenic: Acquired. It is transmitted through medical procedures including surgery, transplantation, and blood transfusion

- Diagnosis:

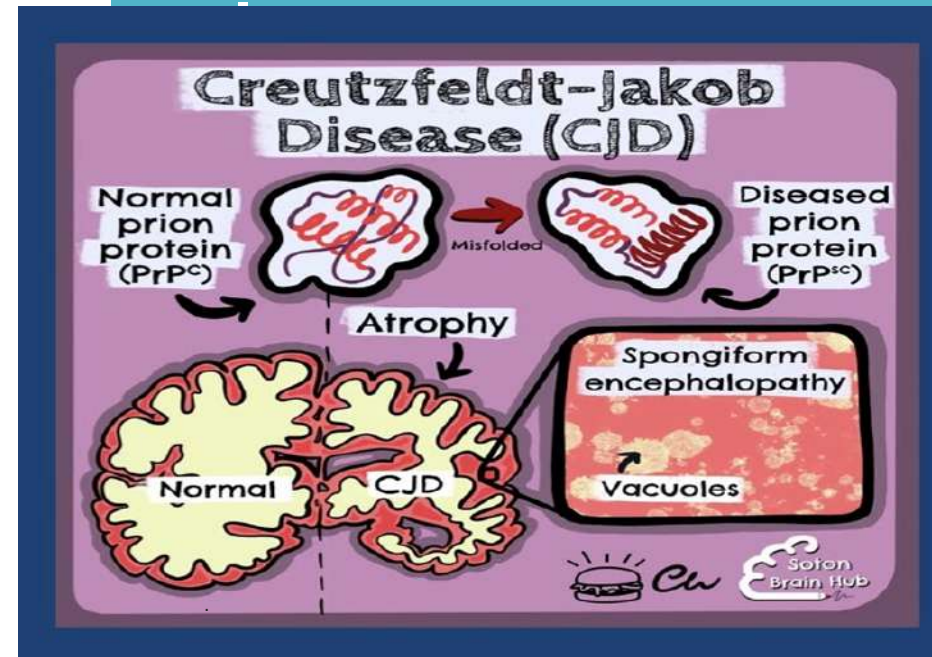
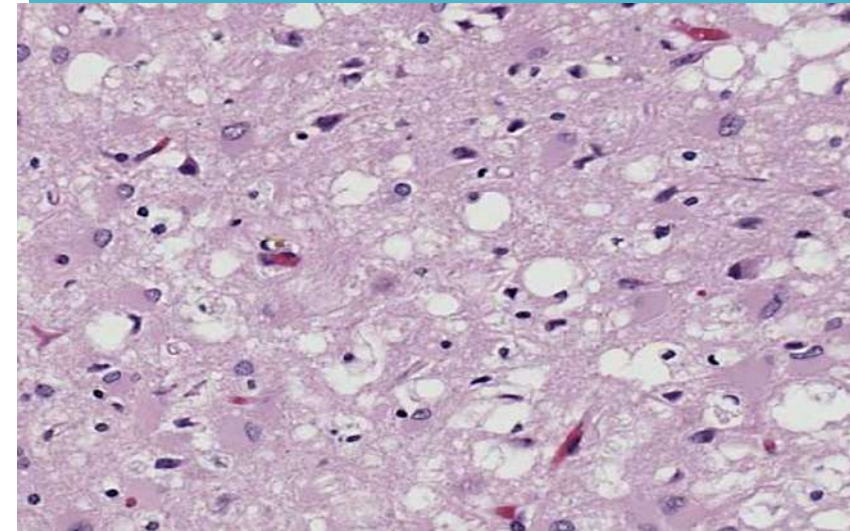
Suggested by clinical features.

Definitive diagnosis can be made only by brain biopsy or autopsy: the pathognomonic finding is a spongiform transformation of the cerebral cortex & deep gray matter structures.

The EEG in classical CJD may show a characteristic abnormality, 'periodic complexes'.

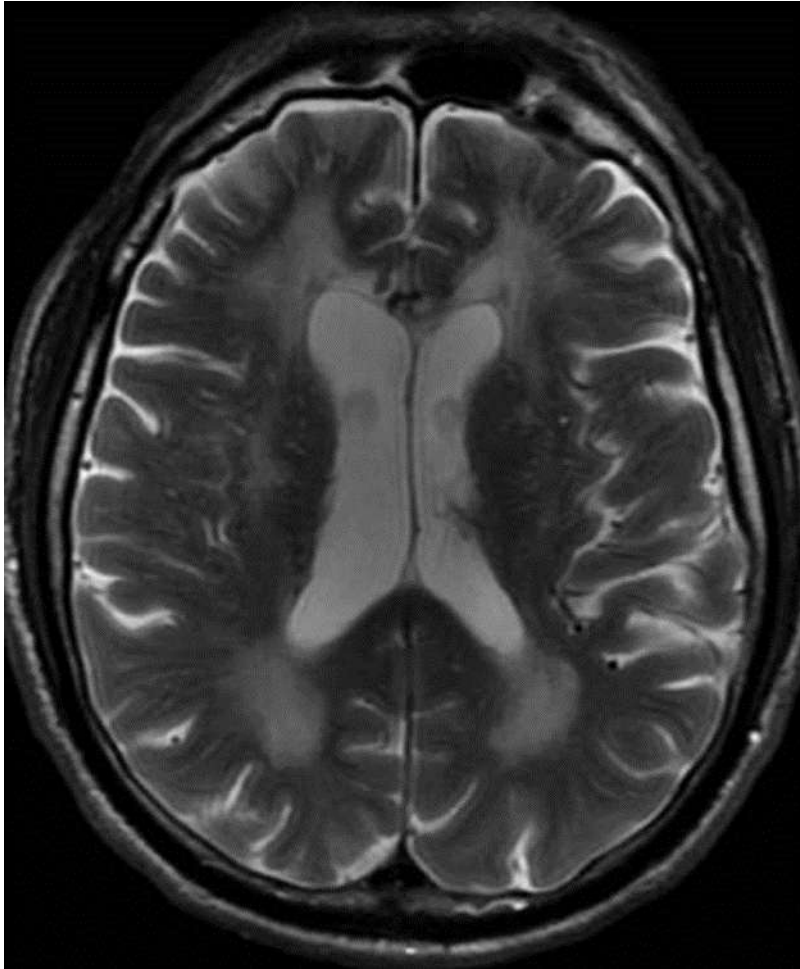
Neuroimaging is relatively normal.

The CSF may contain elevated levels of neuronal proteins



HIV-Associated Dementia (HAD)

- In many patients with HIV (Human Immunodeficiency Virus), dementia occurs due to involvement of the central nervous system (CNS). HIV can lead to encephalitis and makes individuals more vulnerable to CNS infections like toxoplasmosis, tuberculosis, and syphilis, which can also result in dementia. HIV-associated dementia is typically observed in patients with low CD4 cell counts and is marked by a gradual deterioration in cognitive abilities.
- Clinical Manifestations:
 - Memory problems
 - Difficulty with concentration and attention
 - Cognitive deterioration



- **Diagnostic Evaluation:**

MRI may show cortical and subcortical atrophy, with white matter changes being common.

- **Treatment:**

Highly active antiretroviral therapy (HAART) should be administered to reduce the incidence of HIV-associated dementia.

Metabolic Causes of Dementia

Nayef Alajmi / c11

METABOLIC CAUSES OF DEMENTIA

Vitamin B12 deficiency may present as a progressive dementing illness. Usually, however, there are many other neurologic features and signs on physical examination, including dysfunction of the spinal cord (subacute combined degeneration) and peripheral nervous system, such that the diagnosis becomes evident even prior to the development of dementia. The most common neurologic symptoms are those of neuropathy (paresthesias in hands and feet, sensory ataxia, visual loss, orthostatic hypotension) and memory loss. Other systemic manifestations include anemia and a sore tongue. Appropriate replacement of .vitamin B12 should suffice in the treatment



Thank You

ANY QUESTIONS?

REFERENCES :
Blueprint 5th Edi.
osmosis