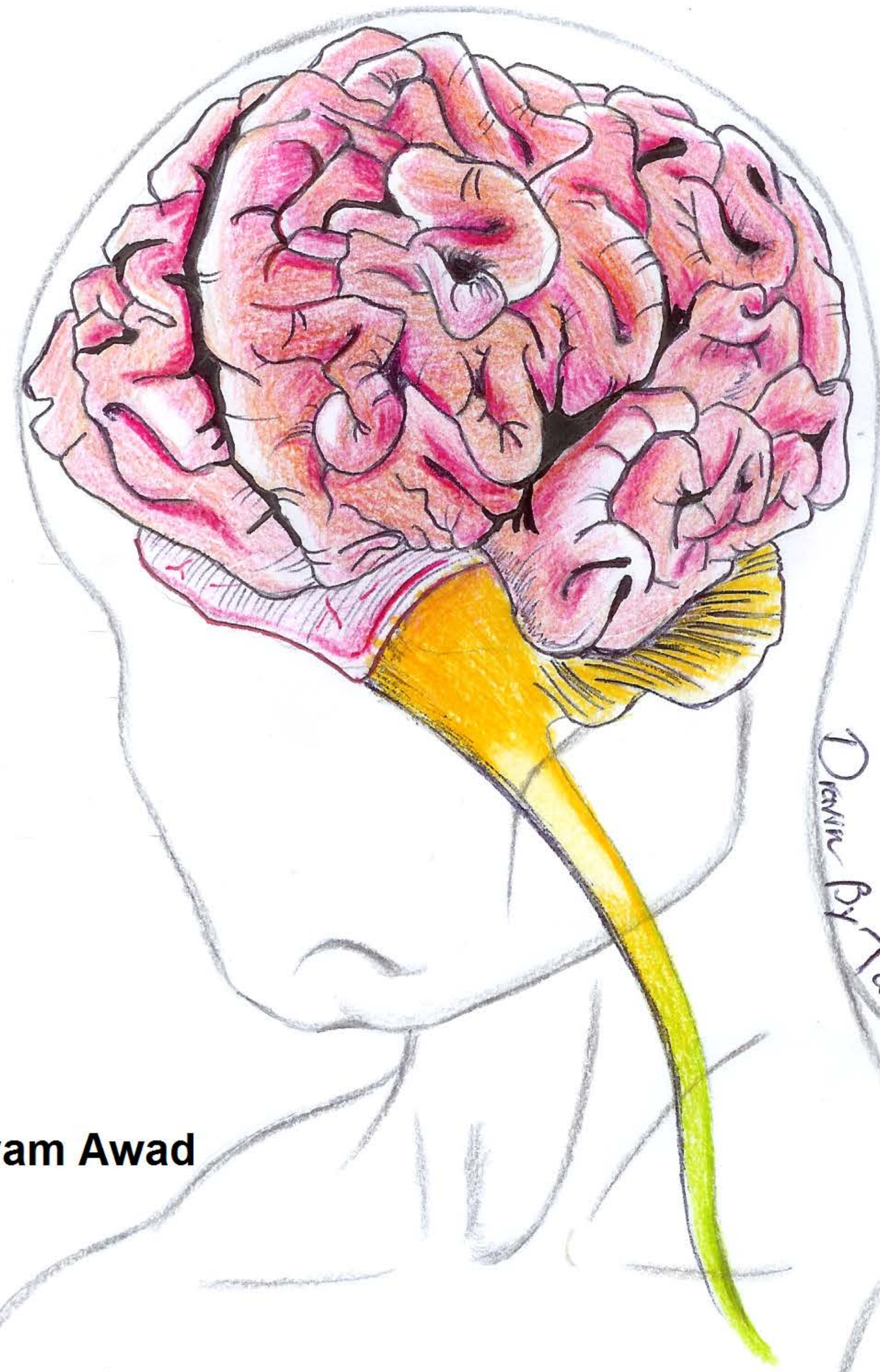
CENTRAL NERVOUS SYSTEM

- ○ Handout
- ○ Sheet
- ○ Slide

- ○ Anatomy
- ○ Physiology
- ● Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
- ○ PBL



Drawn By Tariq Bushnaq ...

Done By :

Dr. Name : **Heyam Awad**

Lec # : **6**

CNS lecture 6

Dr Heyam Awad
FRCPath

Neurodegenerative disorders 2

- Huntington disease
- Spinocerebellar ataxia
- Amyotrophic lateral sclerosis

Huntington disease

- Autosomal dominant
- Movement disorder which is chorieform =dancelike
- Degeneration of caudate and putamen

Choreiform movement

- Chorei = Greek word = circle dance

Chorieform movement

- Involuntary jerky movements of all parts of the body .

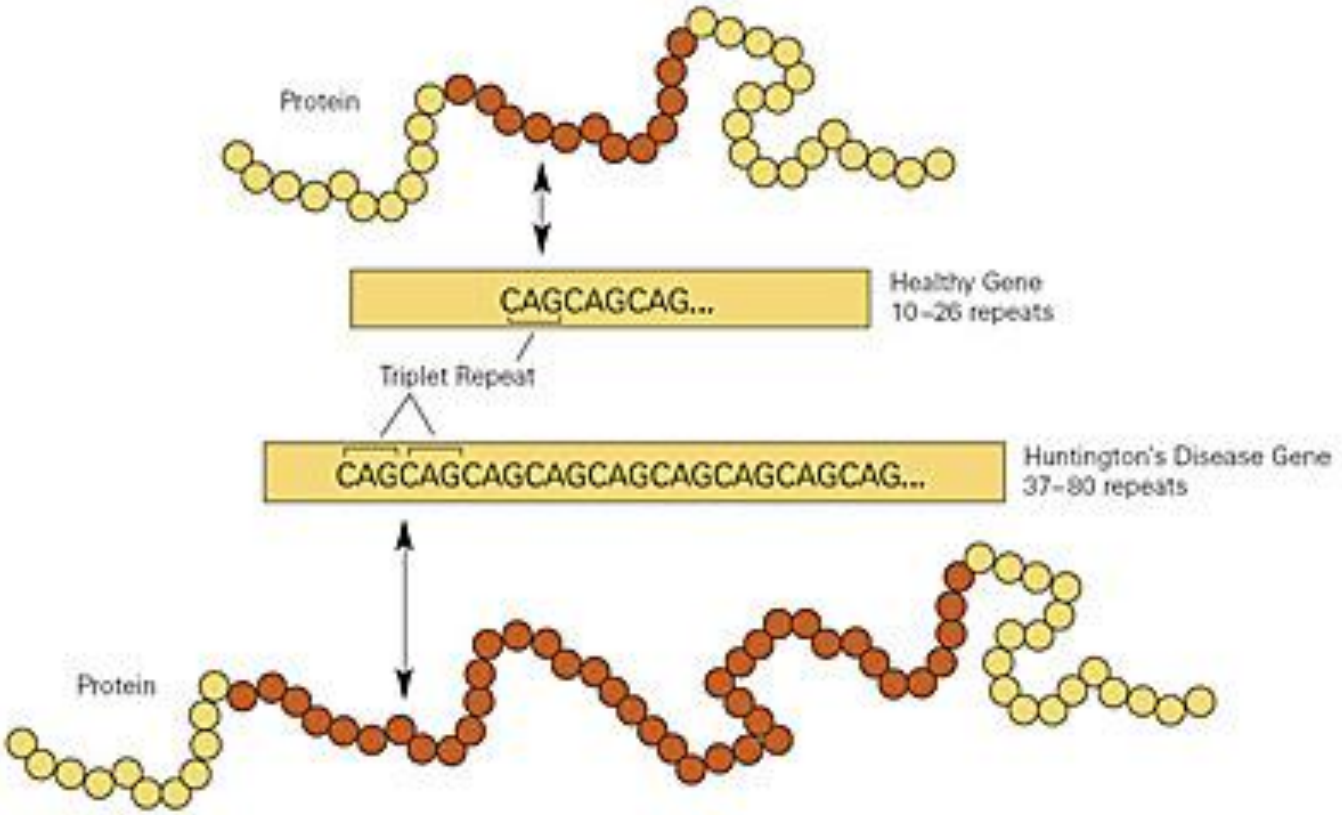
Clinical course

- Progressive
- Memory loss can develop and progresses to severe dementia
- Behavioural changes.. Risk of suicide

pathogenesis

- CAG(cytosine-adenine-guanine) trinucleotide repeat expansions in the gene that encodes huntingtin protein.
- CAG codes for glutamine

- Huntingtin protein is thought to play a role in long term memory storage


Protein
CAGCAGCAG...
Healthy Gene
10–26 repeats
Triplet Repeat
CAGCAGCAGCAGCAGCAGCAGCAGCAG...
Huntington's Disease Gene
37–80 repeats
Protein

- Normally CAG repeated between 11-35 times
- Huntington disease, repeats more than 35
- The more number of the repeats, the earlier the onset of symptoms
- Course of disease not affected by number of repeats

- The abnormal huntingtin protein.. Contains polyglutamine tract
- it forms large intra-nuclear aggregates
- These aggregates cause functional problems leading to the symptoms of Huntington disease

morphology

- Small brain
- Atrophy of caudate and putamen
- Severe loss of neurones

Spinocerebellar ataxia

- Ataxia; Greek = lack of order

Spinocerebellar ataxias

- Heterogeneous group of diseases
- Trinucleotide repeat expansion mutations.
- Group of diseases that differ in the mutation type, inheritance pattern, age of onset and clinical symptoms.
- Affects cerebellar cortex, spinal cord, other brain regions and peripheral nerves

- Affected areas: neuronal degeneration and gliosis
- Some types associated with CAG trinucleotide repeat expansion.

Friedreich ataxia

- Autosomal recessive
- Manifests in the first decade of life
- Gait ataxia and hand clumsiness and dysarthria
- High incidence of cardiac disease and DM
- Due to GAA repeat expansion.. Coding for frataxin; a protein that regulats cellular iron level

Friedreich ataxia

- Frataxin… important in iron levels especially in the mitochondria
- The repeat mutation causes transcription silencing.. Decreased frataxin.. Causes mitochondrial dysfunction and increased oxidative damage

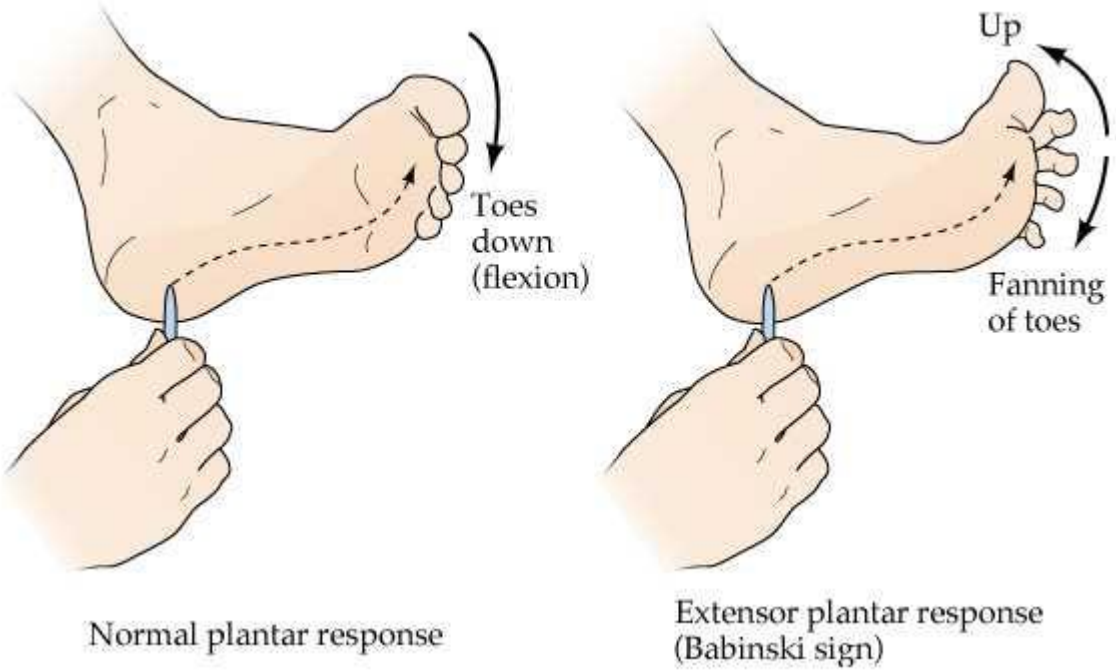
Amyotrophic lateral sclerosis (ALS)

- Due to death of **lower** motor neurons in the spinal cord and brain stem and of **upper** motor neurons in the motor cortex.

ALS

- Loss of lower motor neurones… denervation of muscle , muscle atrophy (amyotrophic)and weakness.
- Loss of upper motor neurones… paresis, hyperreflexia, , spasticity and Babinski sign, along with degeneration of corticospinal tracts in lateral portion of spinal cord (lateral sclerosis)

Babinski sign



ALS

- Sensation NOT affected.
- Cognitive impairment occurs.
- Males slightly more than females
- Majority sporadic
- 5-10% inherited; autosomal dominant
- familial cases: earlier onset but disease progression similar

How to remember neurodegenerative disorders?

- Make a table and compare!!!

Acquired metabolic and toxic disturbances

- Nutritional disorders
- Metabolic disorders
- toxins

Nutritional disorders

- Thiamine (B 1) deficiency
- Vitamin B12 deficiency

Thiamine deficiency

- Thiamine def. causes Wernicke encephalopathy :

1. Confusion
2. Abnormal eye movements
3. Ataxia

-Treatment: thiamine.. Things go back to normal

-If thiamine def. untreated: irreversible memory disturbances: Korsakoff syndrome.

Wernicke- Korsakoff

Causes:

-Alcoholism

-Gastric disorders affecting thiamine absorption: tumors, chronic gastritis

- Chronic vomiting

morphology

- Foci of haemorrhage and necrosis mainly in mammillary bodies

Vitamin B12 def

- Subacute combined degeneration of the spinal cord
- Combined: ascending and descending tracts affected
- Ataxia, lower extremity numbness and tingling
- Can progress to lower limb weakness

Metabolic disorders

1. **Hypoglycaemia**: effect similar to global hypoxia…hippocampal neurones and Purkinje cells first affected.
2. **Hyperglycaemia:** ketoacidosis or hyperosmolar coma: confusion then coma
3. **Hepatic encephalopathy**: decreased consciousness and coma due to increased ammonia, inflammation and hyponatremia.

Toxic disorders

- Alcohol
- Ionizing radiation
- Pesticides
- Carbon monoxide

- And many other toxic agents can affect the brain function

We’ll be back after the mid!!