Spinocerebellar degenerations

Definition: Group of diseases affect cerebellum and nervous system

Distinguished from one another by:
1- Causative mutation
2- Patterns of inheritance
3- Age of onset
4- Signs and symptoms
** No distinctive histopathologic changes
Just mild gliosis

Examples:
**Autosomal dominant as spinocerebellar ataxia
**Autosomal recessive as
1- Friedreich ataxia
2- Ataxia telengectasia

Disease	Huntington disease	Friedreich ataxia	Amyotrophic lateral Sclerosis
General definition	An autosomal dominant Neurodegenerative disease leads to degeneration striatal neurons (Caudate and putamen)	An autosomal recessive spinocerebellar Neurodegenerative disease which manifests in first decade of life	The most common Neurodegenerative disease affect motor system, leading to: 1- loss of upper motor neurons in cerebral cortex (Betz cells) 2-loss lower motor neurons in (spinal cord) and brain stem
Pathogenesis	Accumulation of Huntington protein; due to "CAG" trinucleotide repeat expansion on chromosome number 4 **Normally there is (6-35) copies but in HD there will be more **There is strong genotype-phenotype correlation More repeats=earlier onset of disease (average 40-50) **Repeats occur during spermatogenesis	Decreased number of Frataxin protein; due to "GAA" trinucletide repeat expansion **Decreased protein level through transcriptional silencing **Decreased Frataxin leads to: 1- Mitochondrial dysfunction 2- Increase level of oxidative agents	Mutation in SOD1 gene on chromosome 21, leading to accumulation of misfolded form of SOD1 so it can't be removed and that will trigger apoptosis for cells due to "unfolded protein response" **Death of UMN= degeneration of descending corticospinal tracts **Death of LMN (AHCs)= atrophy of skeletal muscles **Nucleuses of cranial nerves will be affected

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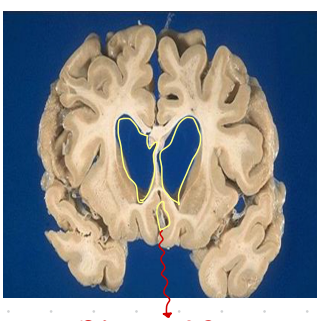
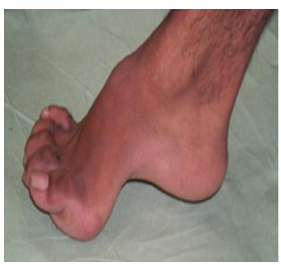
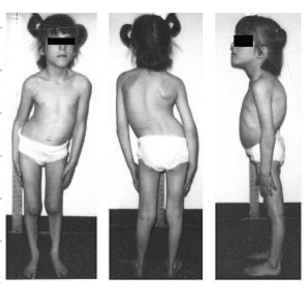
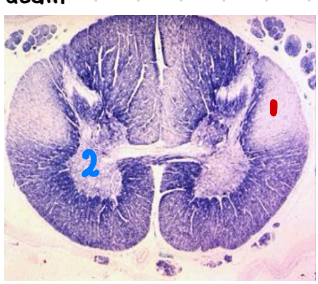
General features	1- Movement disorders "involuntary and jerky (dystonic sometimes)" this is called chorea 2- Dementia due to degeneration of neurons 3- No sporadic forms 4- Atrophy of caudate nucleus and putamen 5- Dilation of 3rd and lateral ventricles 6- Death may occur after an average 15 years	1- Gait ataxia followed by hand clumsiness and dysarthria 2- Pes cavus 3- Kyphoscoliosis 4- Cardiac diseases 5- Diabetes	1- More in males than females, 5th decade and later 2- More sporadic 80% than familial 3- Asymmetric weakness of hands leads to drop objects and difficulty doing tasks 4- muscle strength and bulk diminish 5- Involuntary contraction "fasciculation" 6- It may affect respiratory muscles which may cause death
	 5- Dilation of 3rd and lateral ventricles	 (Pes cavus)  (Kyphoscoliosis)	 1- Loss of color in lateral tract means degeneration of UMN 2- Atrophy in LMN  Attenuation (ضعف) in "anterior " motor roots compared with "posterior" sensory roots in spinal cord
	Note: In HD paternal transmission is associated with earlier onset of disease in next generation " Anticipation "	**Note:** Frataxin protein cellular iron levels in mitochondria	

Acquired metabolic diseases

** Brain has high metabolic demand

** Metabolic problems will disrupt brain function but no detectable morphological changes

Examples:

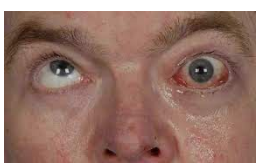
Hypoglycemia may cause necrosis

Hyperglycemia may cause confusion, coma and stupor

Thiamine deficiency (Vitamin B1)

Wernick encephalopathy

1- Psychotic symptoms and opthalmoplegia



If treated—>reversible

Untreated—>irreversible

Korsakoff syndrome

1- Short term memory and confabulation

بصير يختلق أحداث لم تحدث

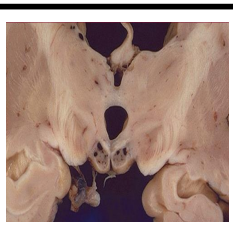
Causes of thiamine deficiency:

1- Chronic alcoholism

2- Gastric disorders as:

A-Carcinoma B-Chronic gastritis

C-Vomitting



Hemorrhage and necrosis in mammillary bodies and walls of third and lateral ventricles

Vitamin B12 deficiency

Subacute combined degeneration of spinal cord

Degeneration of ascending and descending spinal tracts due to defect in myelin formation

** Signs and symptoms:

Ataxia in lower extremities

NATS

- Numbness (Bilateral and symmetrical)
- Tingling
- Spasm and weakness in lower extremities

Lately will have paraplegia

Vitamin replacement—>clinically improvemen

Complete paraplegia—>recovery is poor

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