INHERITED DISEASES IN CLINICAL NEUROLOGY

Prof. M. Gavriliuc

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
The hereditary metabolic diseases of early infancy	Tay-Sachs disease, Infantile Gaucher disease, Infantile Niemann-Pick disease, Infantile GM1 generalized gangliosidosis, Krabbe globoid-body Leukodystrophy, Farber lipogranuloma-Tosis, Pelizaeus-Merzbacher and other sudanophilic leukodystrophies, Spong degeneration (Canavan-Van Bogaert Bertrand), Alexander disease, Alpers Disease, Zellweger encephalopathy, Lowe oculorenalcerebral disease, Kinky-hair, or steely-hair, disease, Congenital lactic acidosis

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
The hereditary metabolic diseases of late infancy and early childhood	Milder disorders of amino acid metabolism, Metachromatic leukodystrophy, Late infantile GM1 Gangliosidosis, Late infantile Gaucher disease and Niemann-Pick disease, Neuroaxonal dystrophy, The Mucopolysaccharidoses, The mucolipidoses, Fucosidosis, The mannosidoses, Aspartylglycosaminuria, Ceroid lipofuscinosis (Jansky-Bielschowsky), Cockayne syndrome, Rett syndrome.

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Inherited metabolic encephalopathies of late childhood and adolescence	The progressive cerebellar ataxias of childhood and adolescence,The familial polymyoclonias and epilepsies, Extra-pyramidal syndromes of parkinsonian type, The syndrome of dystonia and generalized choreoathetosis, The syndrome of bilateral hemiplegia, cerebral blindness and deafness, and other manifestations of focal cerebral disorder, Strokes in association with inherited metabolic diseases, Metabolic Polyneuropathies, Personality changes and behavioral disturbances as manifestations of inherited metabolic diseases

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Adult forms of inherited metabolic diseases	Metachromatic leukoencephalopathy, Adrenoleukodystrophy, Globoid body leukodystrophy (Krabbe disease), Kufs form of lipid storage disease, GM2 gangliosidosis, Wilson disease, Leigh disease, Gaucher disease, Niemann-Pick disease, Mucopolysaccharide encephalopathy, Mucolipidosis type I, Polyneuropathies (Andrade disease, Fabry disease, porphyria, Refsum disease)

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Cromosomal Abnormalities	Down syndrome, *Trisomy 13. (Patau syndrome),* *Trisomy 18*, *Cri-du-chat syndrome*, *Ring chromosomes*, *Klinefelter syndrome,* *Turner syndrome*, *Colpocephaly*, *Fragile X syndrome*, *Williams syndrome*.

INHERITED AND DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
The muscular dystrophies	Facioscapulohumeral, Scapuloperoneal, Limb-girdle muscluar dystrophy, Distal myopathies, Oculopharingeal, Progressive external ophtalmoplegia

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of progressive dementia	A. Diffuse cerebral atrophy 1. Alzheimer disease 2. Diffuse cerebral cortical atrophy of non-Alzheimer type 3. Some cases of Lewy-body dementia B. Circumscribed cerebral atrophy 1. Pick disease (lobar sclerosis) 2. Mesolimbocortical dementia of non-Alzheimer type 3. Thalamic degeneration

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of progressive dementia in combination with other neurologic abnormalities	A. Huntington chorea B. Other (nonhuntingtonian) types of chorea and dementia C. Cortical-striatal-spinal degeneration (Jakob) and the dementia-Parkinson-amyotrophic lateral sclerosis complex (Guamanian and others) D. Cortical-basal ganglionic degeneration

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of progressive dementia in combination with other neurologic abnormalities	E. Dentatorubropallidoluysian degeneration F. Cerebrocerebellar degeneration (Greenfield) G. Familial dementia with spastic paraparesis or myoclonus H. Lewy-body disease I. Polyglucosan body disease

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of disordered posture and movement	A. Parkinson disease (paralysis agitans) B. Striatonigral degeneration with or without autonomic failure (Shy-Drager syndrome) and olivopontocerebellar atrophy (multiple system atrophy) C. Progressive supranuclear palsy (Steele-Richardson-Olzewski) D. Dystonia musculorum deformans (torsion spasm) E. Hallervorden-Spatz disease

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of disordered posture and movement	F. Restricted dystonias including spasmodic torticollis and Meige syndrome G. Familial tremors H. Multiple tic disease (Gilles de la Tourette syndrome) I. Acanthocytic chorea

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of progressive ataxia	A. Predominantly spinal forms of hereditary ataxia 1. Friedreich ataxia 2. Non-Friedreich ataxias (with retained reflexes, hypogonadism, or myoclonus) B. Pure cerebellar forms of hereditary ataxia 1. Holmes familial cortical cerebellar atrophy 2. Late cerebellar cortical atrophy of Marie-Foix-Alajouanine

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of progressive ataxia	C. Complicated cerebellar ataxias 1. Olivopontocerebellar degenerations with or without basal ganglia degeneration (multiple system atrophy) 2. Gerstmann-Straussler-Scheinker disease 3. Machado-Joseph disease 4. Other late-onset, autosomal dominant and sporadic ataxias D. Paraneoplastic and alcoholic-nuritional cerebellar degenerations

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of slowly developing muscular weakness and atrophy (nuclear atrophy)	A. *Without sensory changes*: motor system disease 1. Amyotrophic lateral sclerosis 2. Progressive spinal muscular atrophy 3. Progressive bulbar palsy 4. Primary lateral sclerosis 5. Hereditary forms of progressive muscular atrophy and spastic paraplegia

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of slowly developing muscular weakness and atrophy (nuclear atrophy)	B. *With sensory changes* 1. Hereditary sensory neuropathies 2. Hereditary sensorimotor neuropathies - peroneal muscular atrophy (Charcot-Marie-Tooth); hypertrophic interstitial polyneuropathy (Dejerine- Sottas); heredopathia atactica polyneuritiformis (Refsum); etc.

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome of spastic paraplegia without amiotrophy	A. Hereditary spastic paraplegia B. Primary lateral sclerosis

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

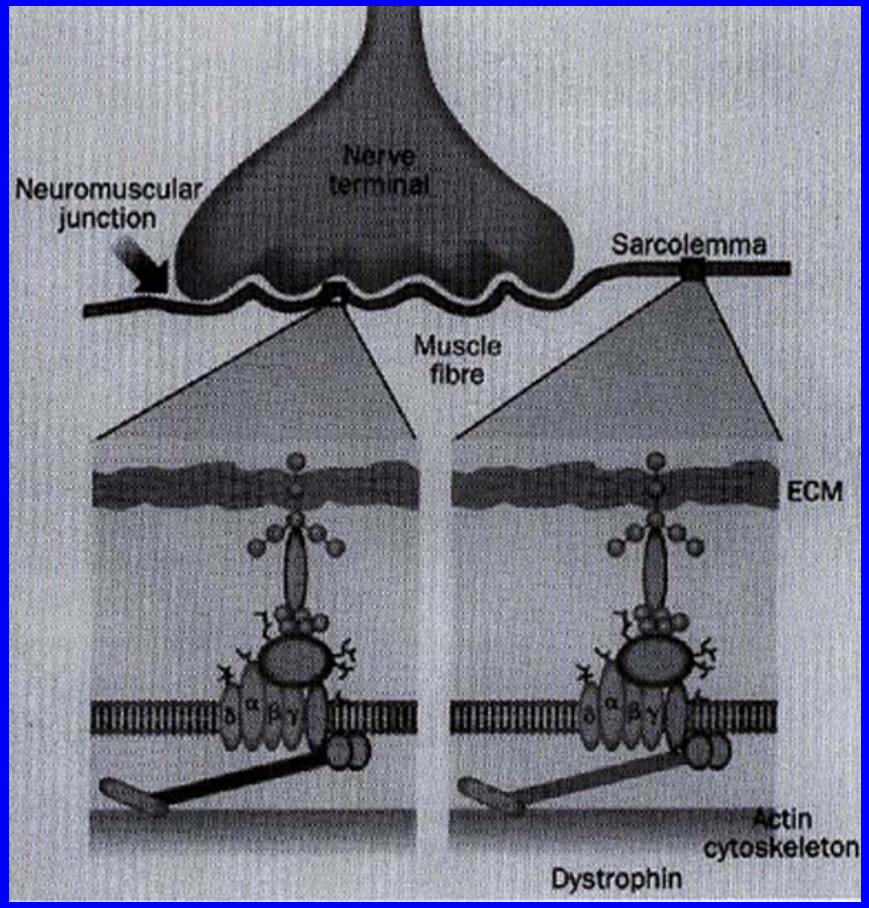
CATEGORY	THE NAME OF DISEASE
Syndrome of progressive blindness or ophtalmoplegia with or without other neurologic disorders	A. Hereditary optic neuropathy (Leber) B. Pigmentary degeneration of retina (retinitis pigmentosa) C. Stargardt disease D. Progressive external ophthalmoplegia with or without deafness or other system atrophies (Kearns-Sayre syndrome)

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

CLASSIFICATION

CATEGORY	THE NAME OF DISEASE
Syndrome characterized by neurosensory deafness	A. Pure neurosensory deafness B. Hereditary hearing loss with retinal diseases C. Hereditary hearing loss with system atrophies of the nervous system

Degenerative Muscular Disorders



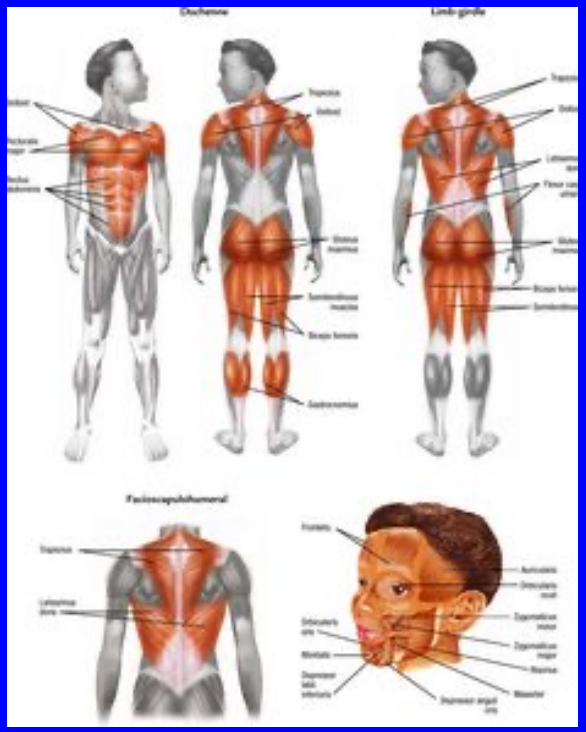
The muscular dystrophies are hereditary, degenerative dystrophinopathies and disorders of dystrophin-associated proteins.

Dystrophin is controlled by a very large gene, at least 2300 kb and 79 exons, that encodes a 3685 amino acid protein product with four distinct domains. It has an I-beam shape with globular domains at each end and a rodlike segment in the middle.

Degenerative Muscular Disorders

Dystrophinopathies

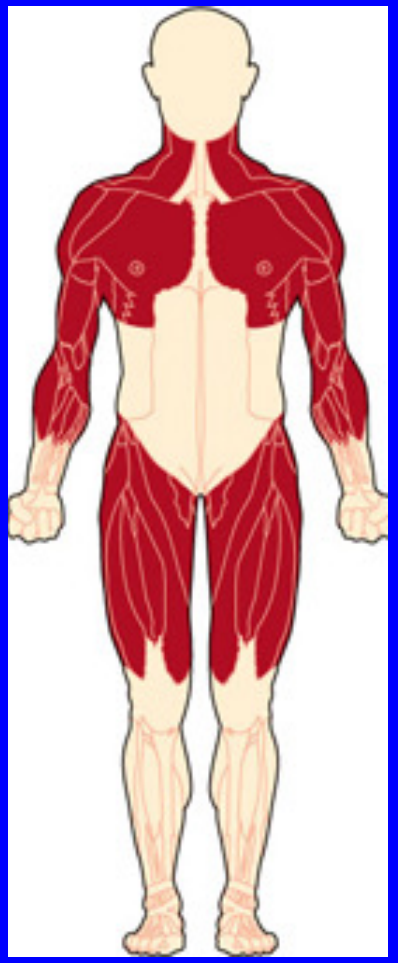
Different mutations in the dystrophin gene produce different allelic disorders, most commonly either the lethal Duchenne muscular dystrophy (DMD) or Becker muscular dystrophy (BMD), a milder myopathy.



Degenerative Muscular Disorders

Dystrophinopathies

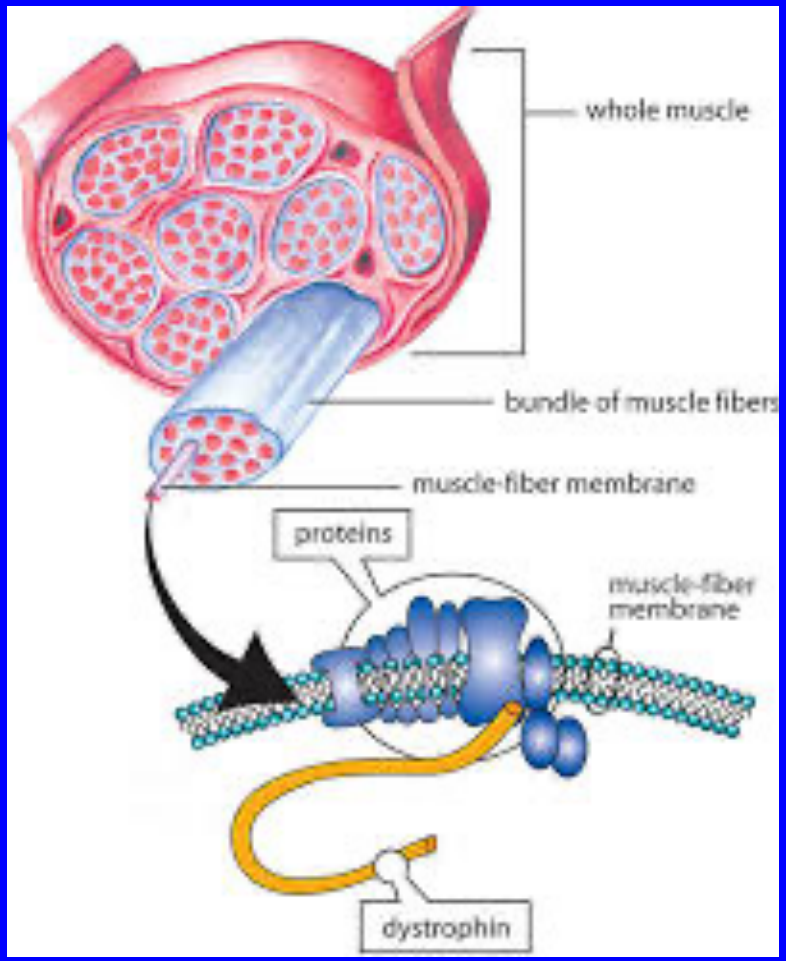
Very rarely, patients with cardiomyopathy with mild weakness, dilated cardiomyopathy without weakness, exercise intolerance associated with myalgias, muscle cramps, or myoglobinuria, and asymptomatic elevation of serum CK have also been identified.



Degenerative Muscular Disorders

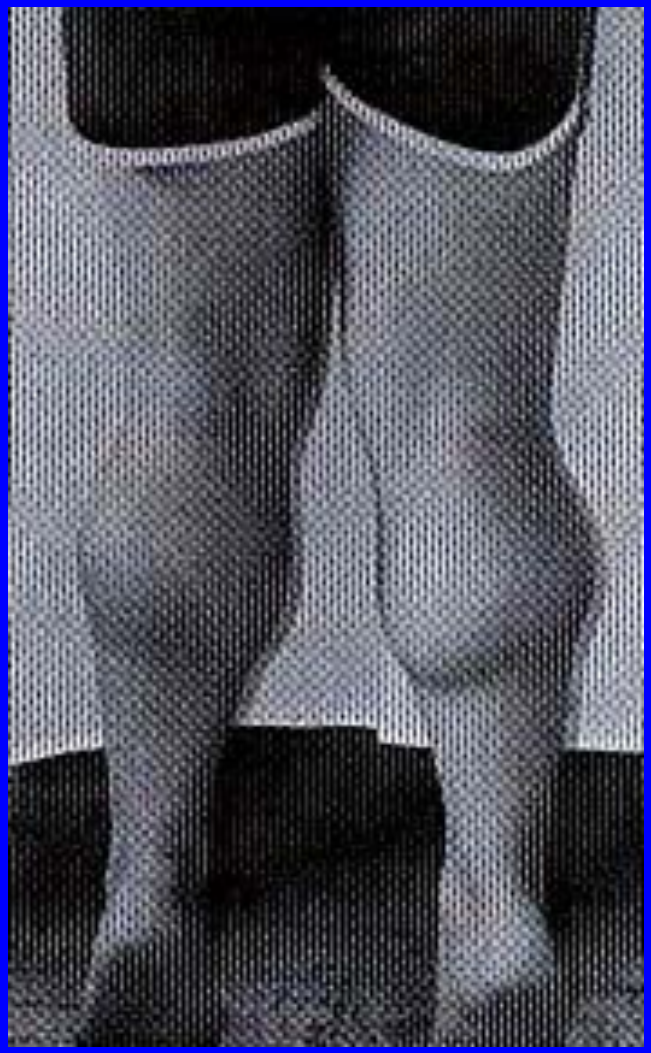
Dystrophinopathies

Pathogenesis and Pathophysiology. Large mutations in the dystrophin gene are identified in about 75 percent of patients with DMD and 87 percent of patients with BMD. Most large mutations are deletions, and they tend to occur in regions where the introns are longer.



DUCHENNE MUSCULAR DYSTROPHY

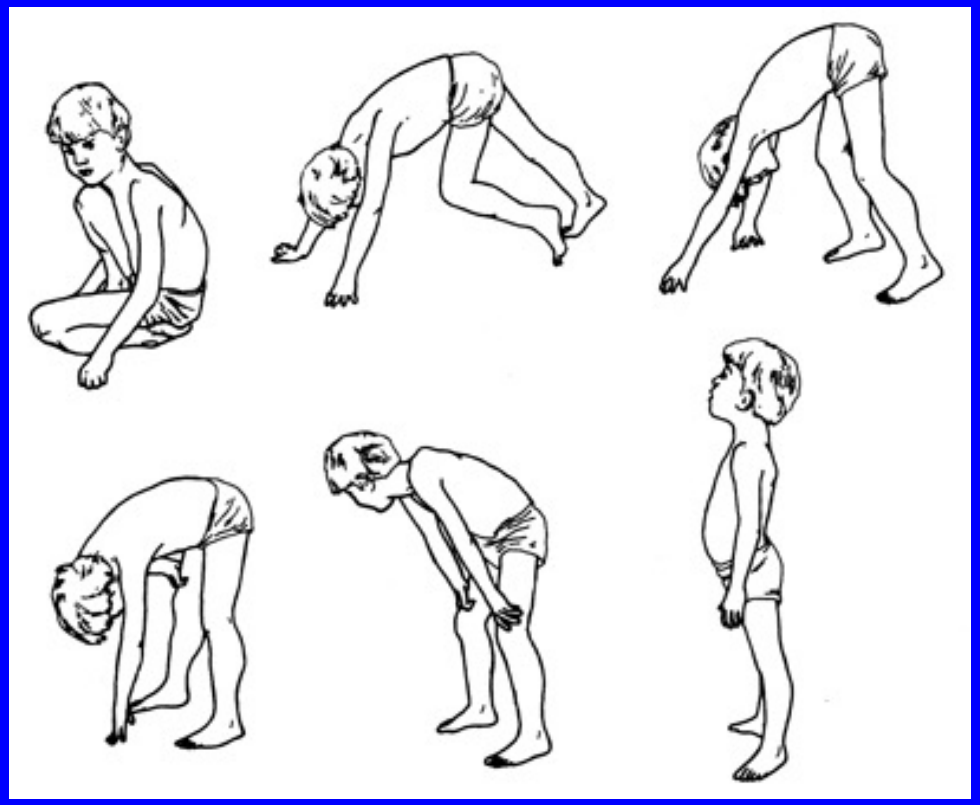
Clinical Features and Associated Disorders. The hallmarks of DMD are progressive proximal muscle weakness with pseudohypertrophy of the calves. The myocardium is involved, whereas bulbar muscles are spared. There may be mild mental retardation. DMD is universally fatal, usually either from respiratory or cardiac complications.



Enlarged calf muscles in a patient with Duchenne muscular dystrophy.

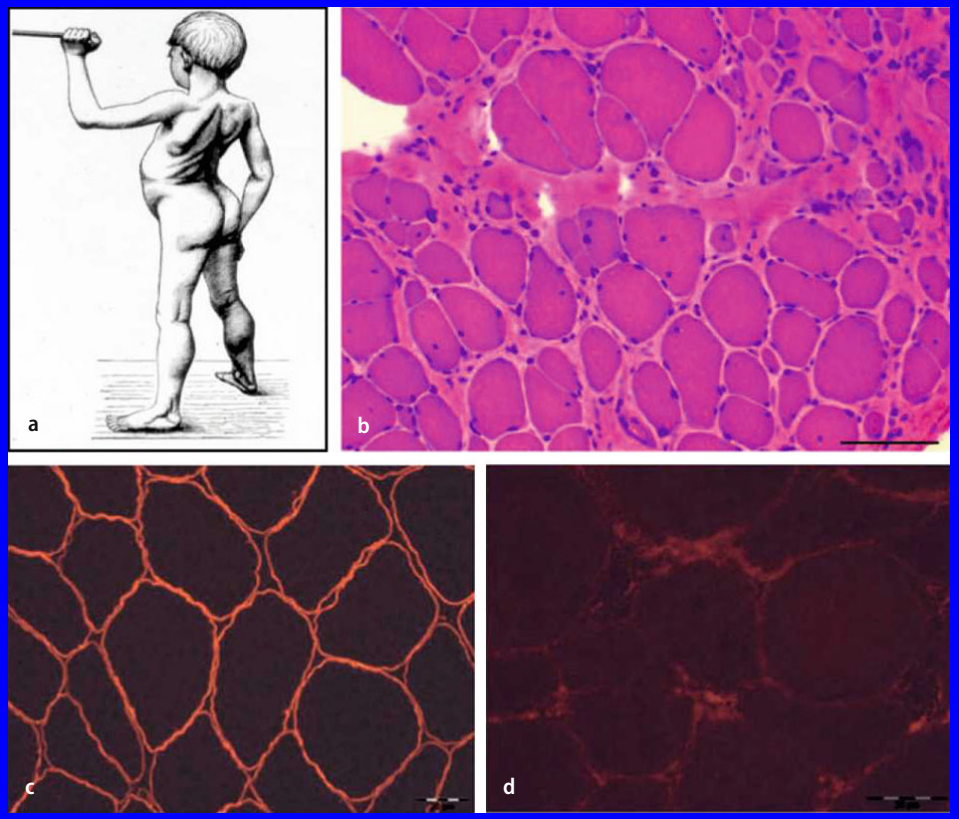
DUCHENNE MUSCULAR DYSTROPHY

Between the ages of 3 and 6, the gait becomes waddling and lordotic. Gowers' sign appears, in which the child stands from a prone position by a process of climbing up the legs, using the hands first on the knees and then on the thighs to support her- or himself.



DUCHENNE MUSCULAR DYSTROPHY

Usually by the age of 6 years, there is enlargement of calf, gluteal, lateral vastus, deltoid, and infraspinatus muscles, and weakness is readily apparent, with the proximal extremities more severely affected than the distal extremities, and lower extremities and torso more severely affected than the upper extremities .

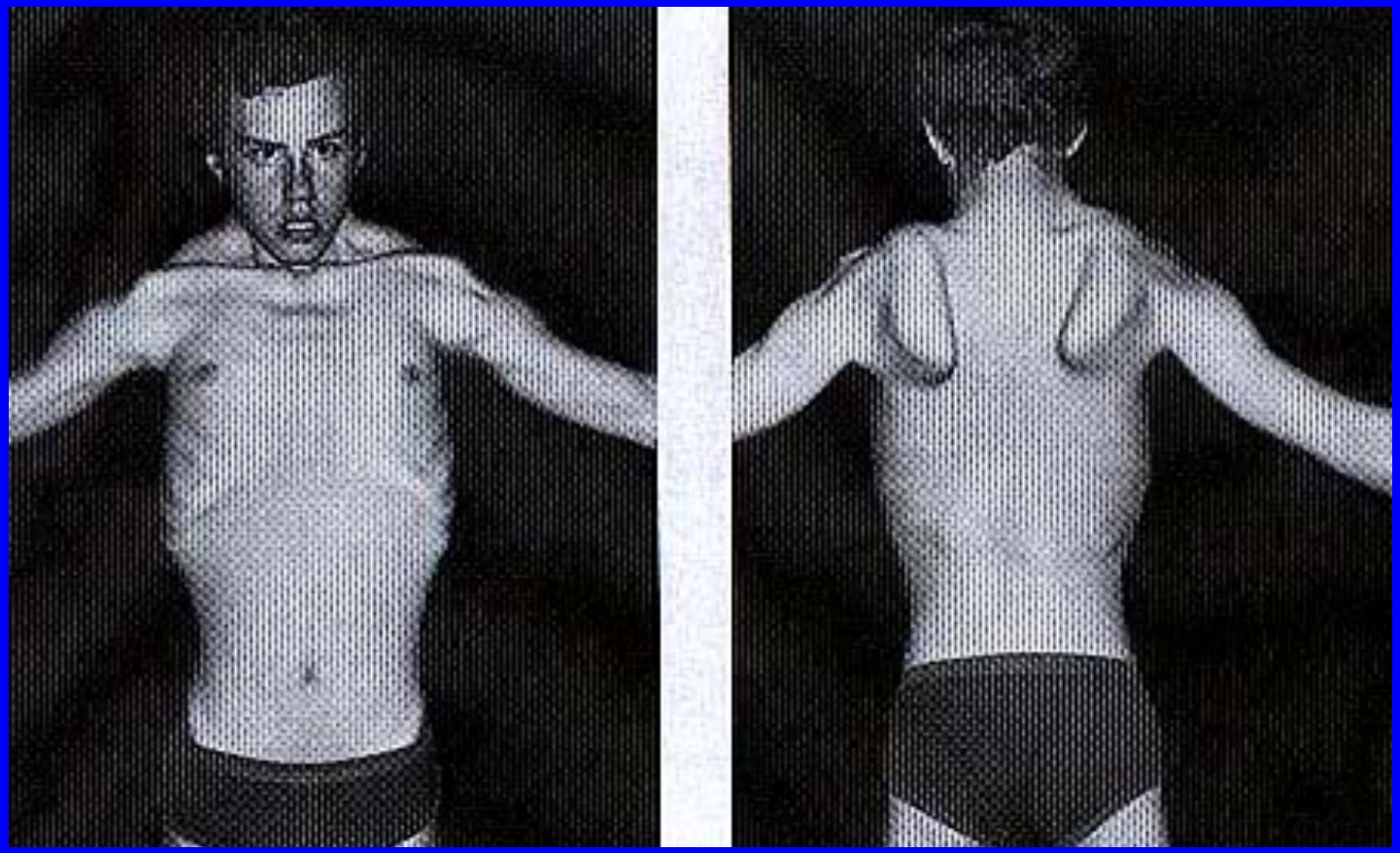


Duchenne muscular dystrophy. **a** Affected boy **b** H&E-stained section of a muscle biopsy : increase in connective tissue structures, pathological caliber variations of the muscle fibers, multiplication of central muscle fiber cores. **c** Regular sarcolemma dystrophin immunofluorescence labeling in normal muscle tissue. **d** Complete absence of the sarcolemmal dytrophin immunofluorescent label in muscular dystrophy type Duchenne. (Heinrich et al. 2014)

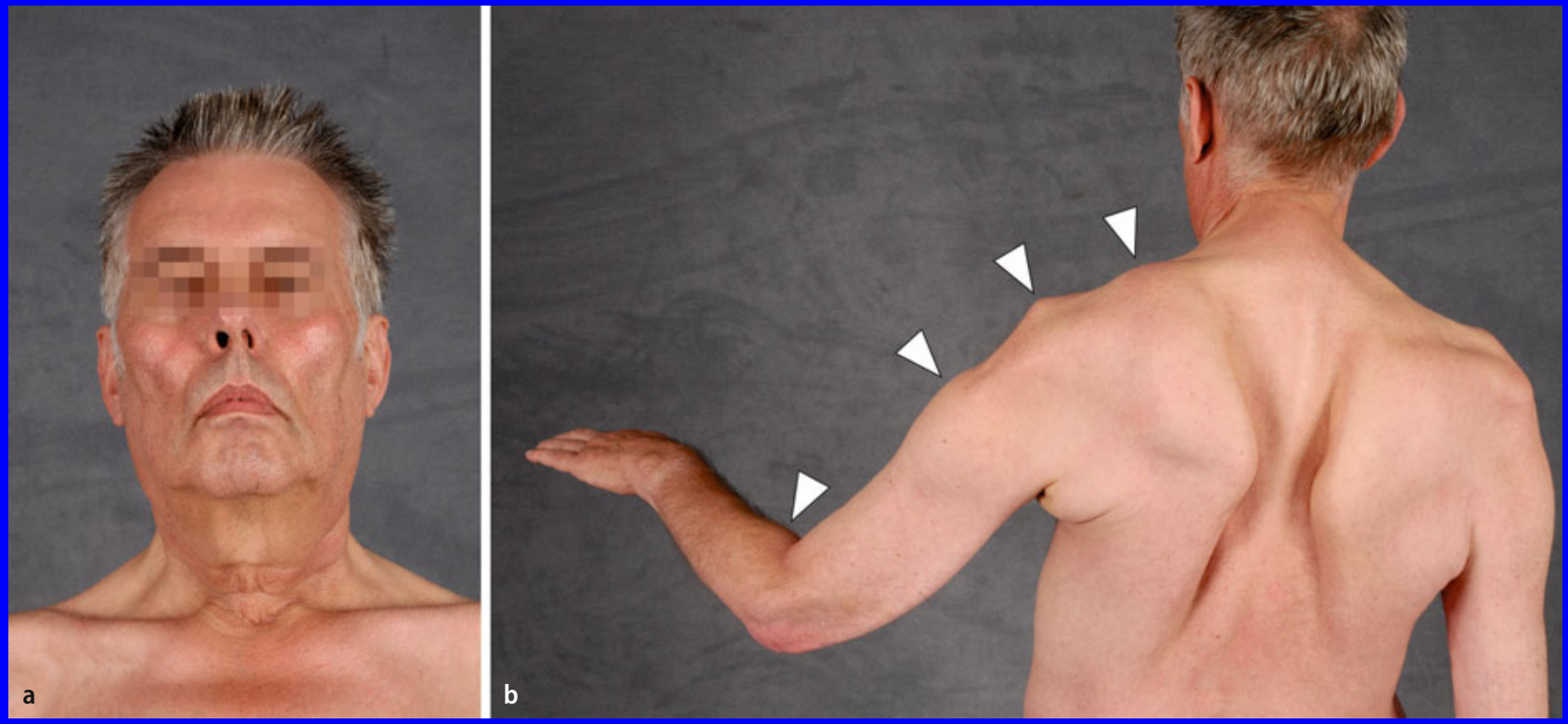
Degenerative Muscular Disorders

Scapuloperoneal Syndromes

The scapuloperoneal syndromes (SPSs) are heterogeneous disorders characterized by weakness of both shoulder girdle and peroneal muscles.



Fazio-scapulo-humeral muscular dystrophy



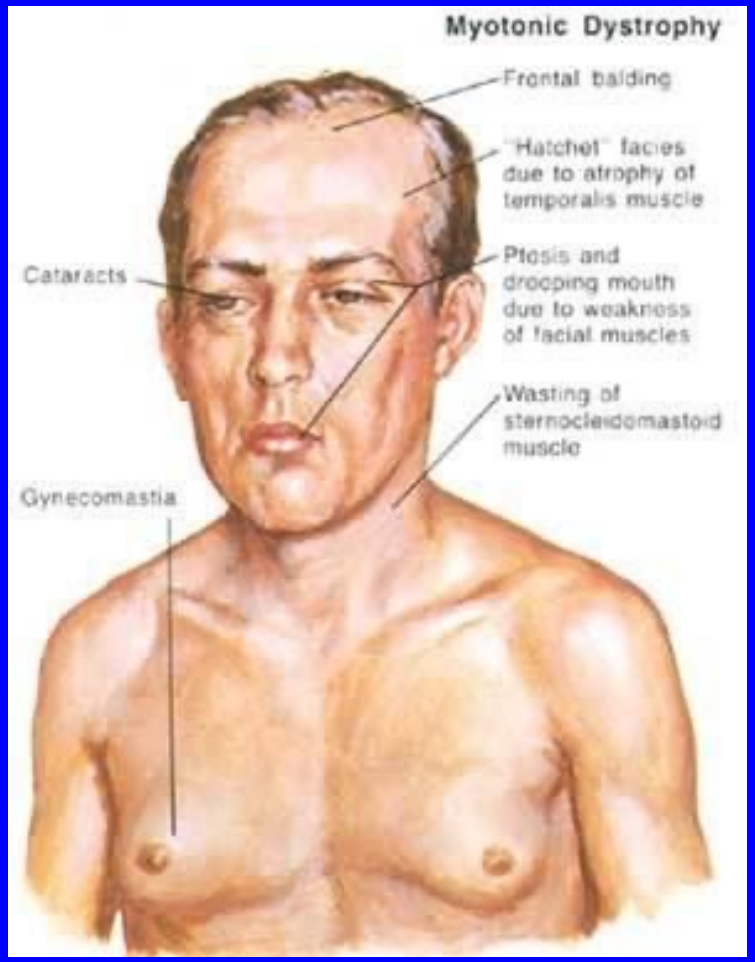
a Facies myopathica with bilateral ptosis and atrophy of the facial muscles.

b Atrophy of the scapulo-humeral muscles with scapula alatae on both sides and »poly-hill sign« (arrowheads)

Degenerative Muscular Disorders

Myotonic Dystrophy

Myotonic dystrophy (DM), or Steinert's disease, is an autosomal dominant multisystem degenerative disease characterized by myotonia, progressive muscular weakness, gonadal atrophy, cataracts, and cardiac dysrhythmias.



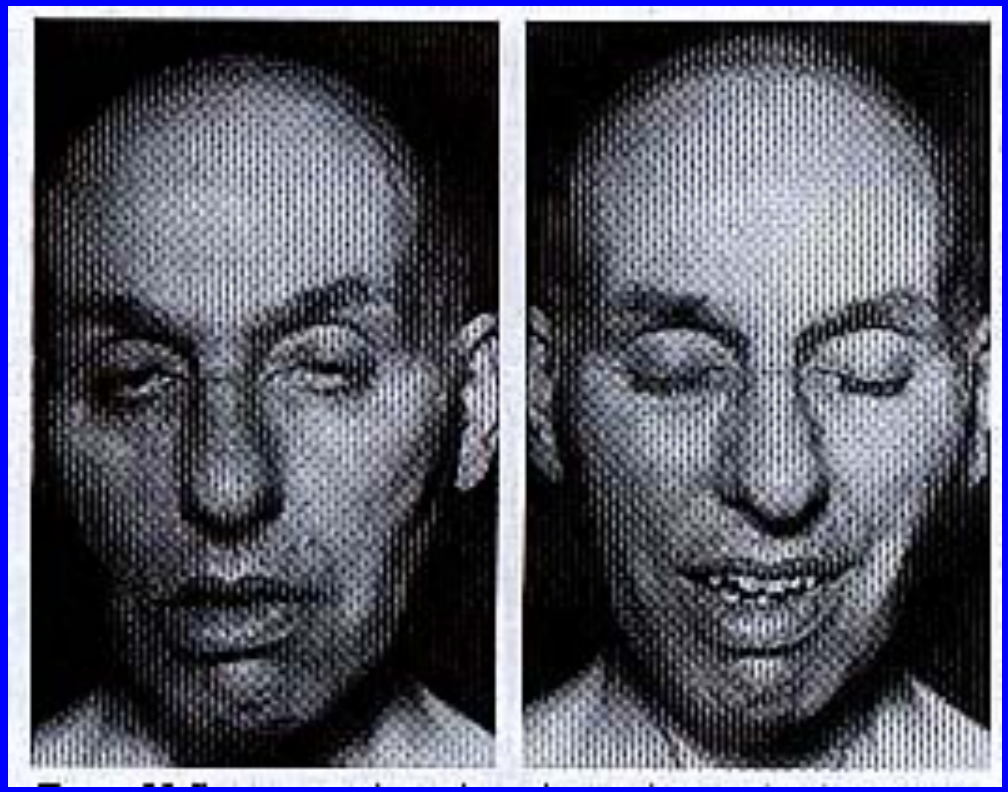
Degenerative Muscular Disorders

Myotonic Dystrophy

Pathogenesis and Pathophysiology. The molecular basis of DM is an unstable trinucleotide repeat sequence, cytosine, thymine, and guanidine (CTG) in the protein kinase-encoding gene (DMK), located at 19q13.3.

Myotonic Dystrophy

<u>Clinical Features and Associated Findings.</u> The classic presentation of noncongenital DM, which is well described by Harper, includes marked weakness in the face, jaw, and neck muscles and milder distal extremity weakness.

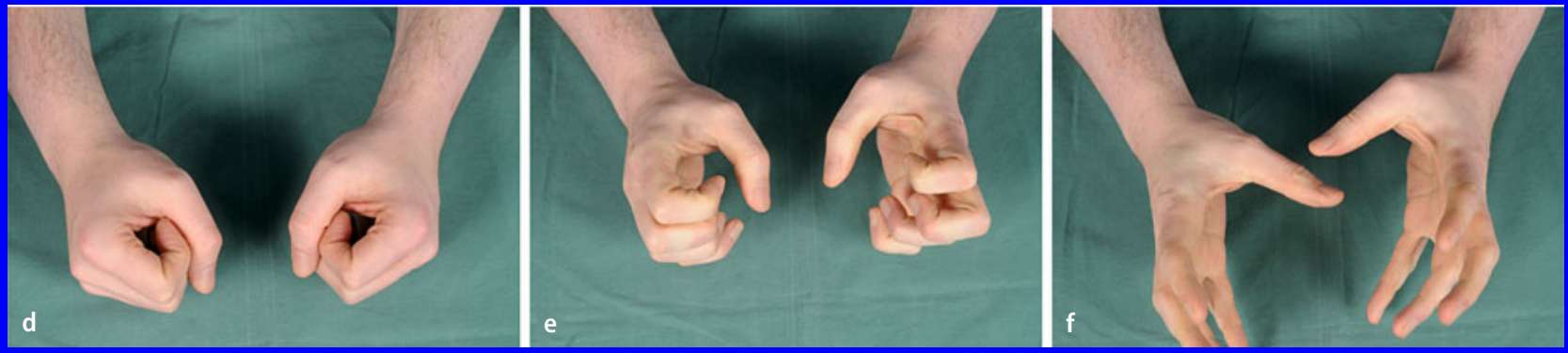


Myotonic dystrophy with typical myopathic facies, frontal balding, and sunken cheeks.

Degenerative Muscular Disorders

Myotonic Dystrophy

Clinical Features and Associated Findings. **Weakness of the extremities is often the first problem perceived by the patient, even when a careful evaluation may reveal a clear history of myotonia (sometimes termed muscle stiffness or cramping by patients), facial weakness, and nasal speech. Patients frequently seem unaware of their illness and symptoms, both in themselves and in family members.**



Grasping myotonia. After tight fist clenching for several seconds (d) the hands can be opened only with a delay (e, f).

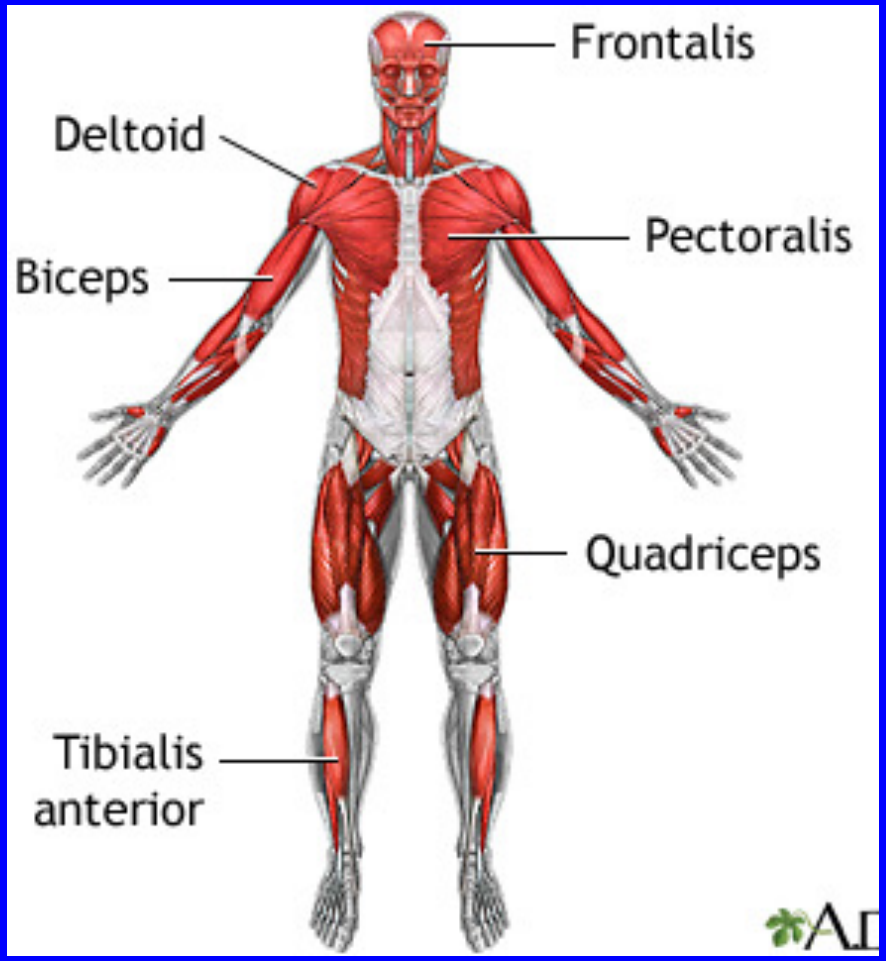
Degenerative Muscular Disorders

Myotonic Dystrophy

Clinical Features and Associated Findings. Using a percussion hammer, myotonia can be elicited in patients with DM with a brisk tap on the thenar muscle, causing flexion-opposition of the thumb with slow relaxation.

Chloride Channelopathies

Autosomal Dominant Myotonia Congenita (Thomsen's Disease)

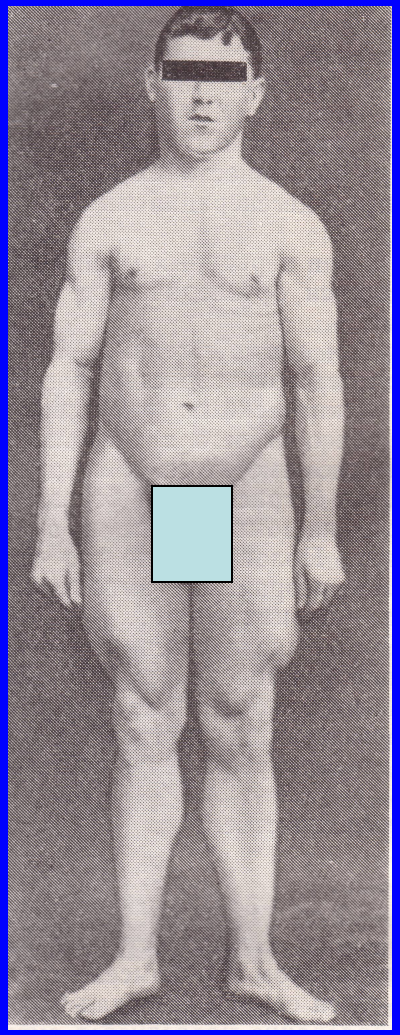


The main symptom in this disorder is painless generalized myotonia, which is perceived as muscle stiffness. It usually appears in the first and second decades of life and is provoked by exertion following rest. It may be demonstrated by asking the patient to rise from a chair after a period of quiet sitting. This myotonia improves with exercise.

Chloride Channelopathies

Autosomal Dominant Myotonia Congenita (Thomsen's Disease)

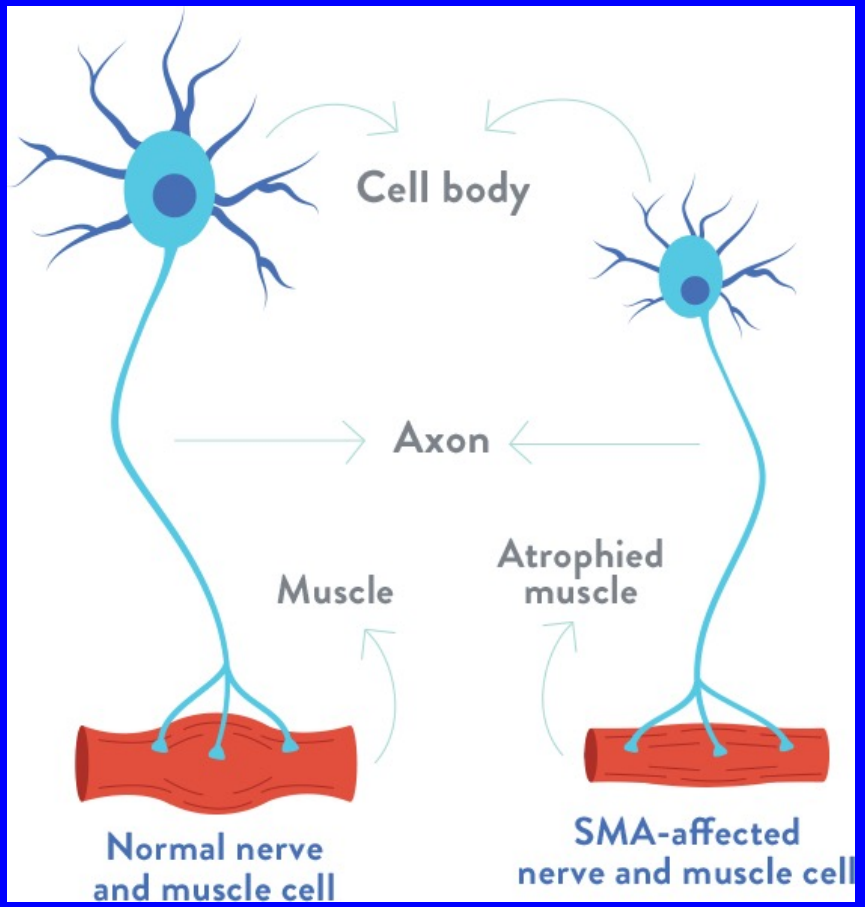
Patients have well-developed muscles with particular hypertrophy of the lower limbs, giving them an athletic appearance. Muscle strength may be normal, or possibly even stronger than normal. This attribute results in an advantage in power sports in which speed is not a requisite. The patients have normal reflexes, and eyelid, grip, and percussion-induced myotonia can usually be demonstrated.



Membrane-stabilizing drugs such as *Mexitil*, *Phenytoin*, *Carbamazepine* or *Quinine sulfate* can improve the symptoms.

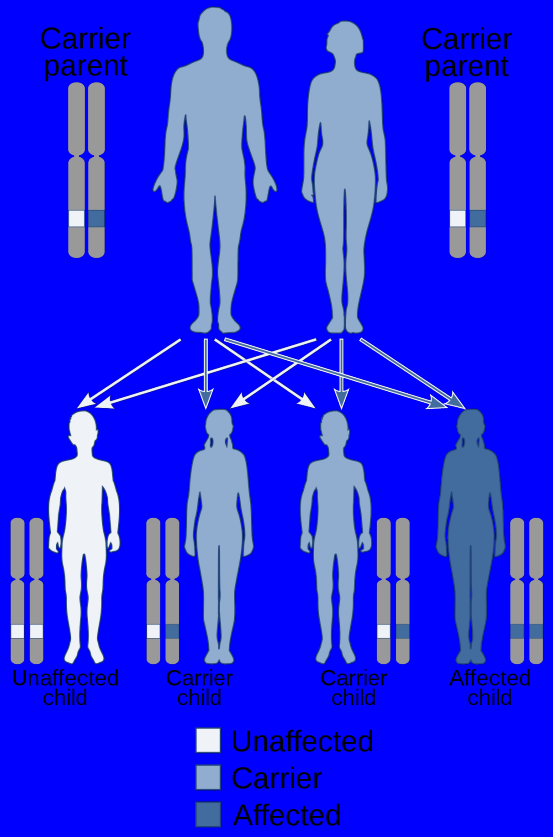
Spinal Muscular Atrophy

- The SMAs are a family of selective lower motor neuron diseases of early onset.



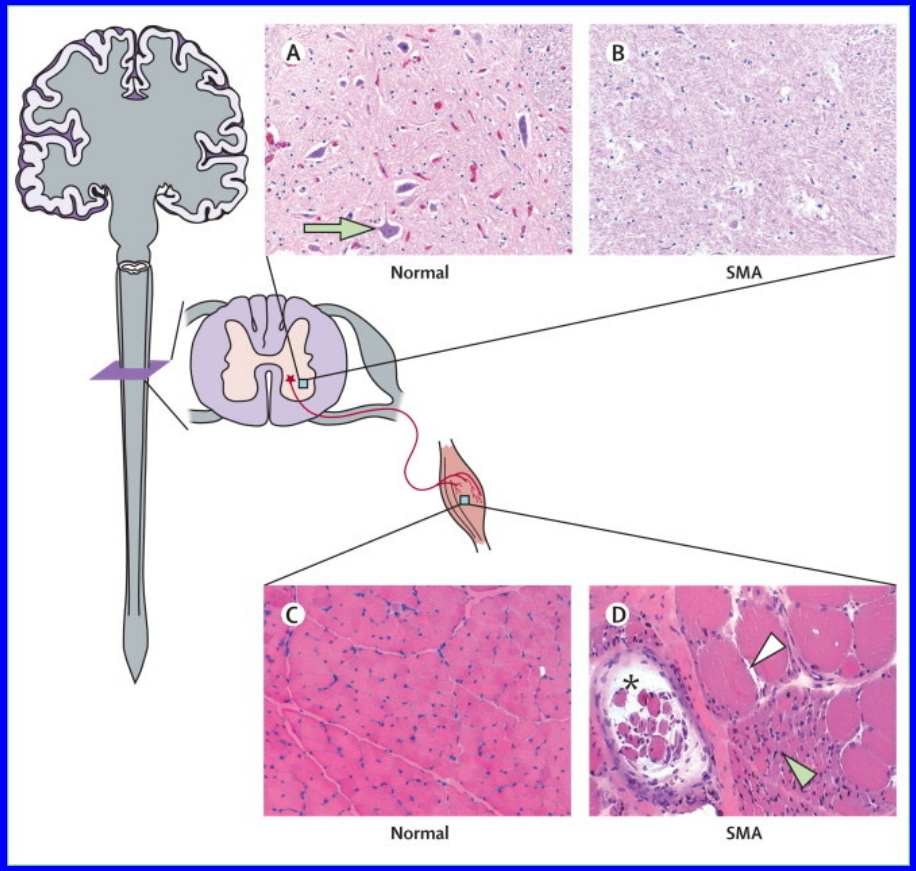
Spinal Muscular Atrophy

- The defect in the majority of families with SMA maps to a locus on chromosome 5 encoding a putative motor neuron survival protein



Spinal Muscular Atrophy

- Neuropathologically these disorders are characterized by extensive loss of large motor neurons; muscle biopsy reveals evidence of denervation atrophy.



Spinal Muscular Atrophy

- Several clinical forms exist.

(1) Infantile SMA (SMA I,Werdnig-Hoffmann disease)

(2) Chronic childhood SMA (SMA II)

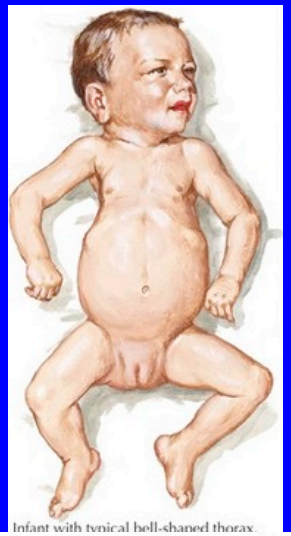
(3) Juvenile SMA(SMA III, Kugelberg-Welander disease)

Infantile SMA (SMA I,Werdnig-Hoffmann disease)

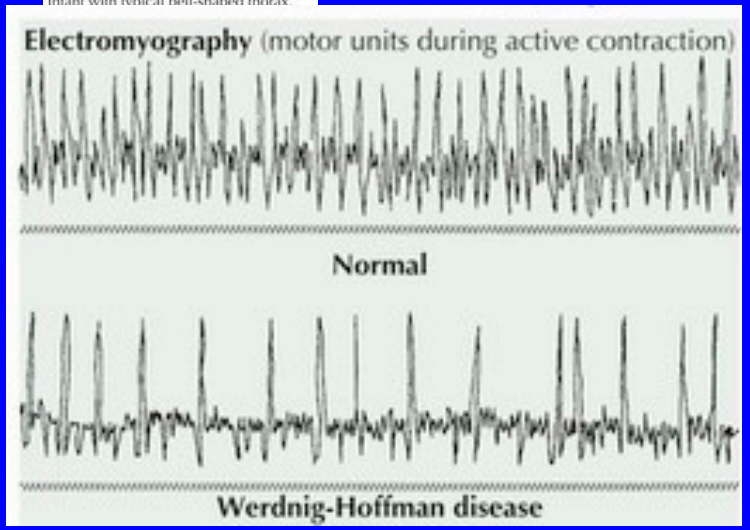
Has the earliest onset and most rapidly fatal course. In some instances it is apparent even before birth, as indicated by decreased fetal movements late in the third trimester.

A baby with spinal muscular atrophy, showing the flaccid head lag in the supine position.

Infantile SMA (SMA I,Werdnig-Hoffmann disease)



Infant with typical bell-shaped thorax



Although alert, afflicted infants are weak and floppy (hypotonic) and lack muscle stretch reflexes. Death generally ensues within the first year of life.

Chronic childhood SMA (SMA II)

begins later in childhood and evolves with a more slowly progressive course.

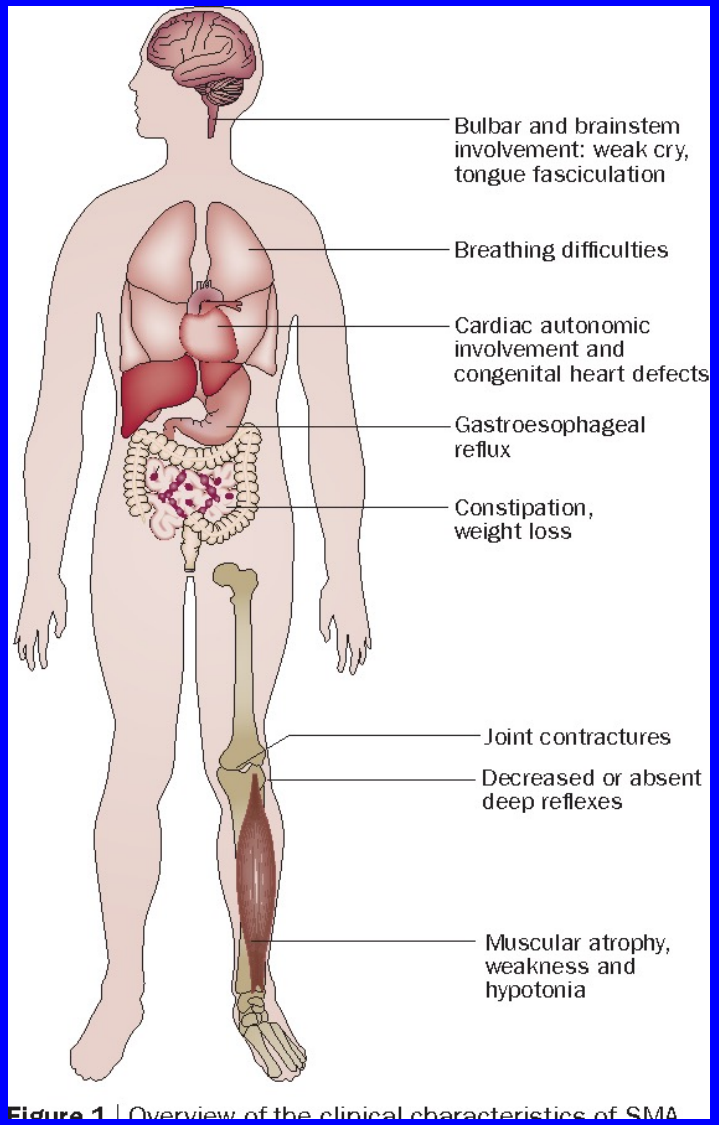
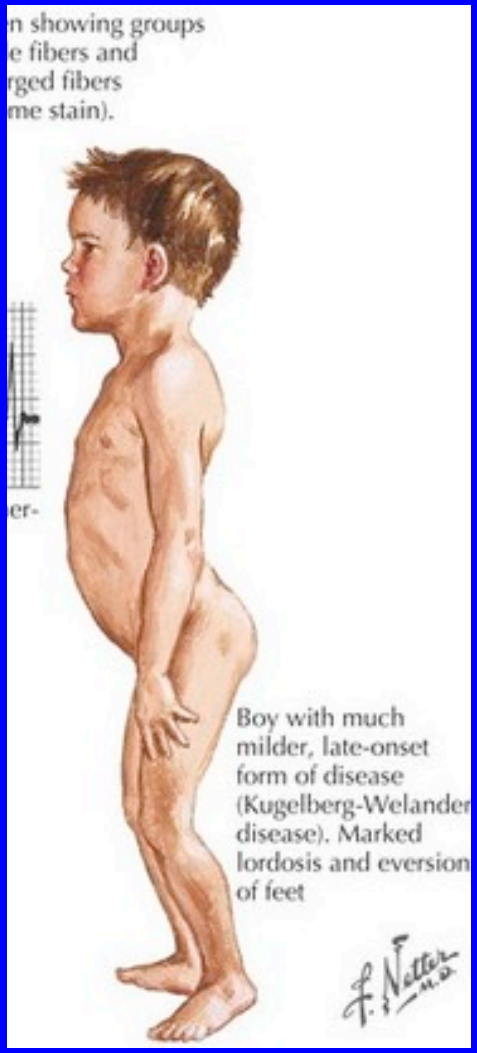


Figure 1 | Overview of the clinical characteristics of SMA

Juvenile SMA(SMA III, Kugelberg-Welander disease)

- Manifests during late childhood and runs a slow, indolent course.
- Weakness is greatest in the proximal muscles.
- Electrophysiologic and muscle biopsy evidence of denervation distinguish SMA
- III from the myopathic syndromes.

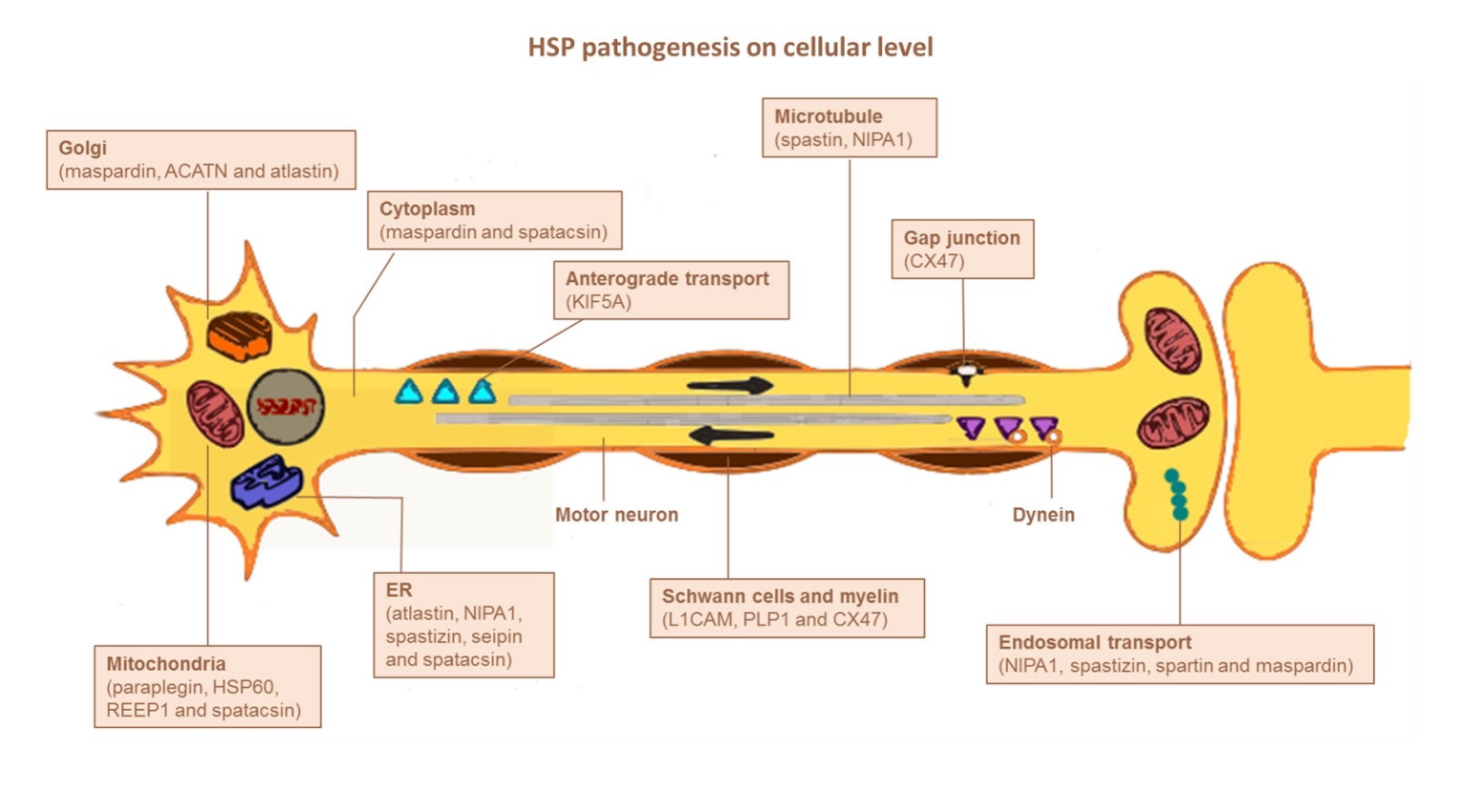


Spinal Muscular Atrophy

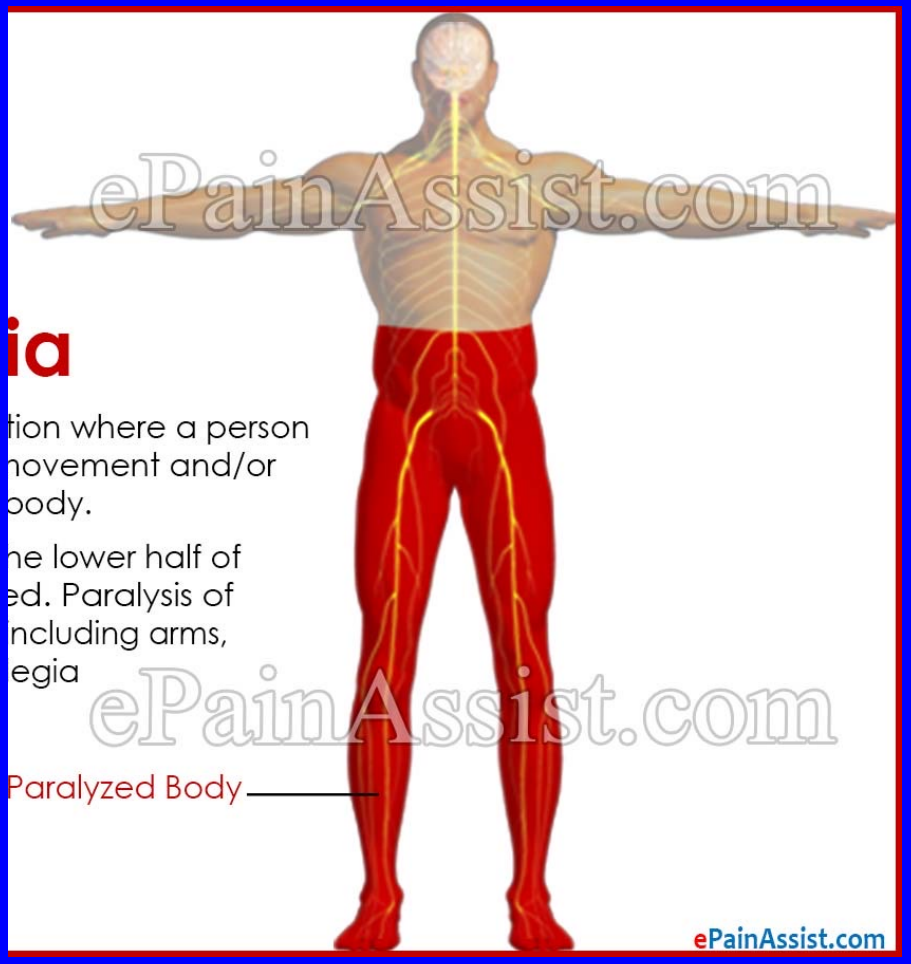
Management and Future Prognosis. There is no specific treatment for any of the SMAs. A multidisciplinary approach aimed at preventing contractures, skeletal deformities, respiratory complications, and social isolation is imperative. Genetic counseling of parents of young SMA patients or SMA patients approaching childbearing age is appropriate

Familial Spastic Paraplegias

The FSPs, also known as Strumpell-Lorrain syndrome and hereditary spastic paraplegias, are a broad group of genetically and clinically diverse disorders characterized by lower extremity spasticity and weakness. Generally, they are classified according to mode of inheritance and symptoms.



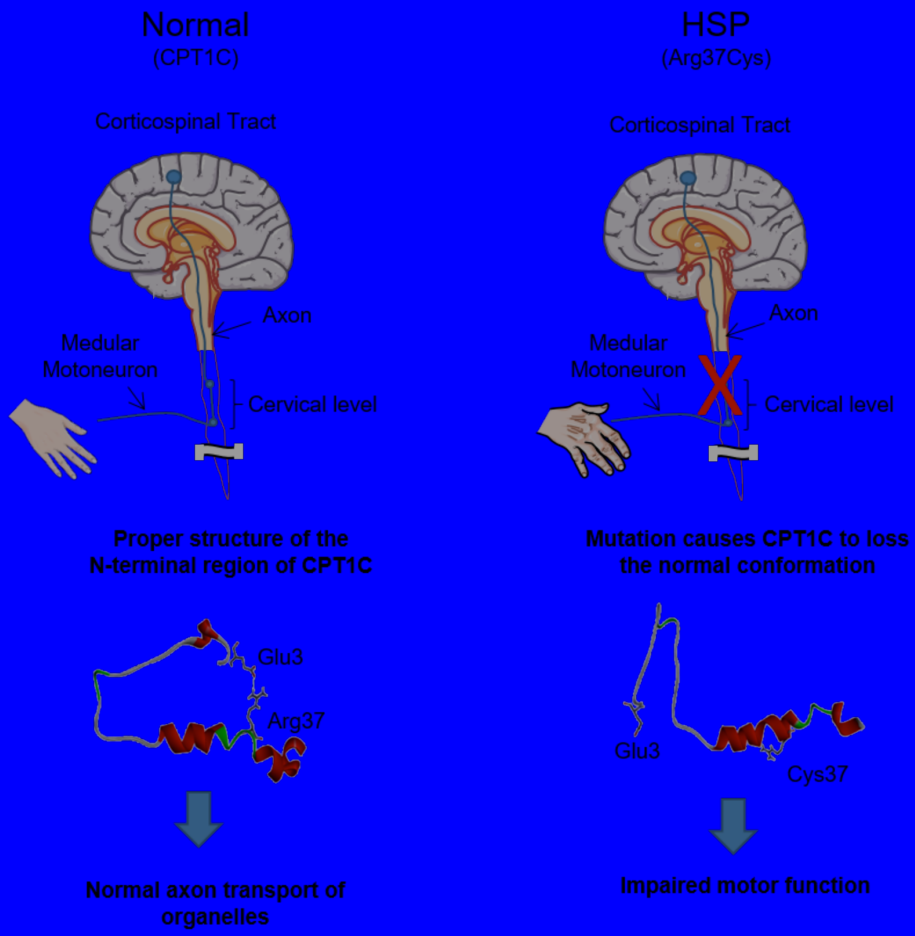
Familial Spastic Paraplegias



The more common uncomplicated or so-called pure FSP indicates progressive spasticity of the lower extremities that may be accompanied by a mild decrease in proprioception and urinary sphincter dysfunction, whereas complicated FSP denotes the presence of other neurological problems.

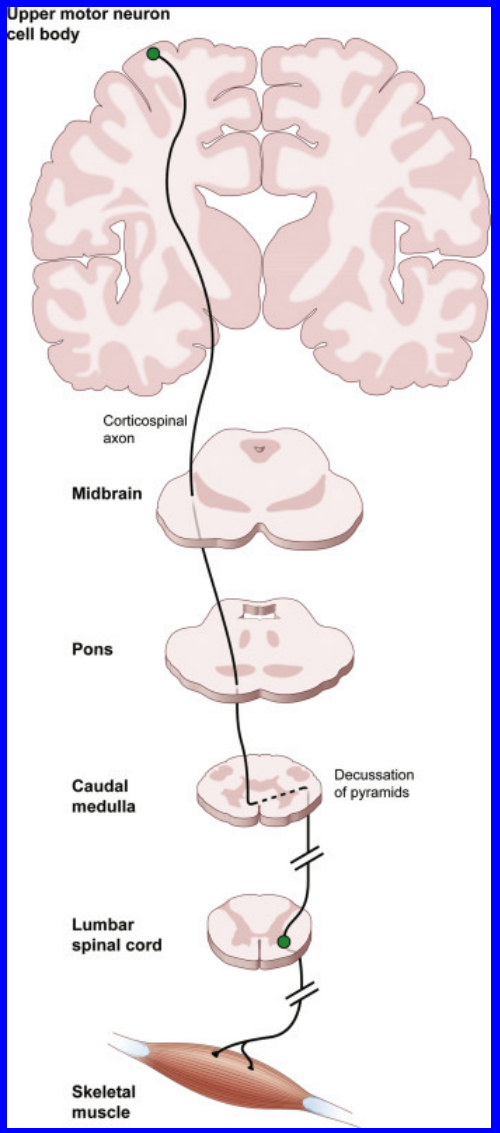
Familial Spastic Paraplegias

Pathogenesis and Pathophysiology. Information about the genetic basis for these disorders is mushrooming. It has been established that uncomplicated autosomal dominant, autosomal recessive, and X-linked FSPs are heterogeneous disorders.



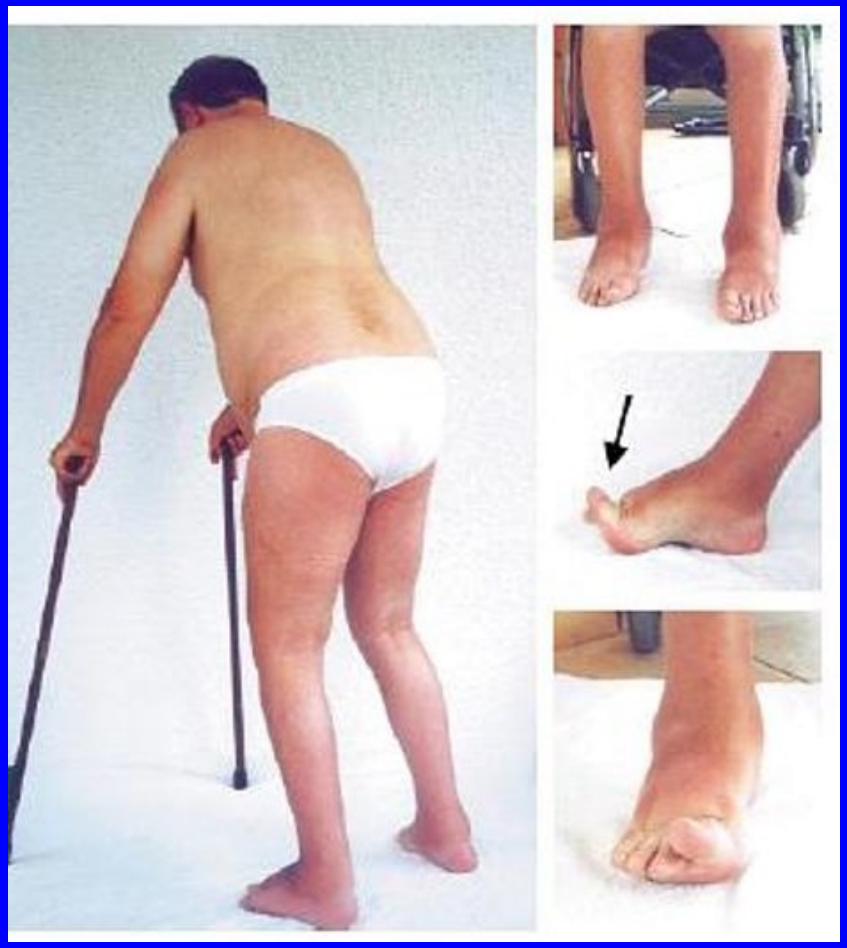
Familial Spastic Paraplegias

Pathogenesis and Pathophysiology. There may be various points of disturbance in a common biochemical pathway that leads to degeneration of the most distal portions of the longest ascending and descending central nervous system axons, particularly the corticospinal tracts from the motor cortex to the legs, the fasciculus gracilis fibers, and the spinocerebellar fibers. Genetic penetrance is age dependent and nearly complete.



Familial Spastic Paraplegias

Clinical Features and Associated Disorders. The patient generally presents with leg stiffness, weakness in the hip flexors, and impaired foot dorsiflexion in the second through fourth decades, although symptoms may be apparent in infancy or not until late adulthood.



Familial Spastic Paraplegias

Clinical Features and Associated Disorders. The gait disturbance progresses insidiously and continuously. Patients may also have paresthesia and mildly decreased vibratory sense below the knees, and urinary urgency and incontinence late in the disease.

Familial Spastic Paraplegias

Familial Spastic Paraplegias

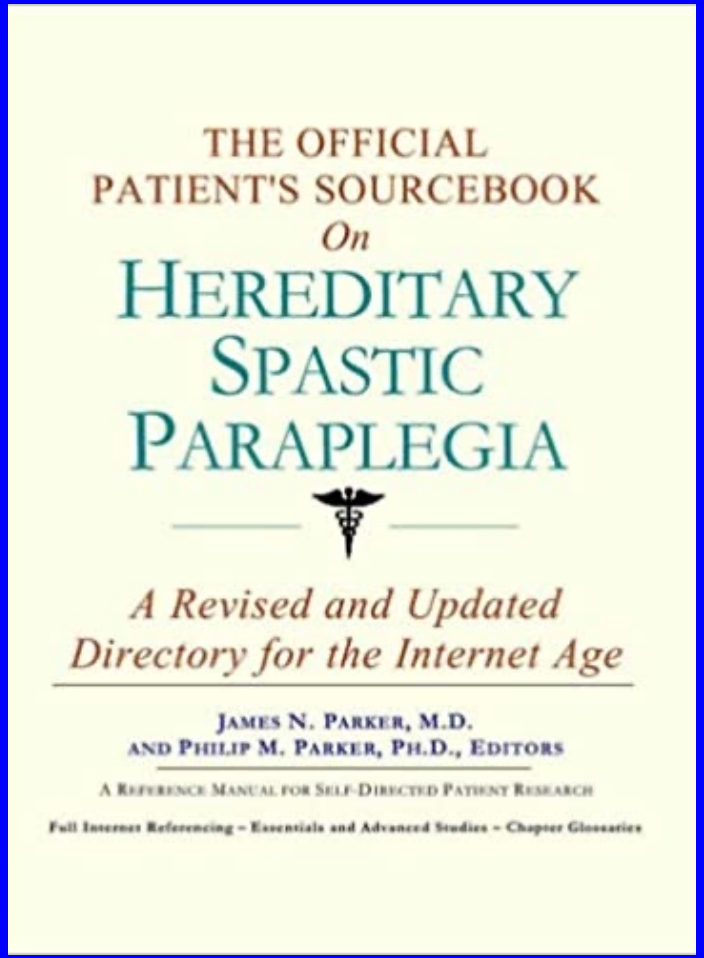
Clinical Features and Associated Disorders.

In the lower extremities, deep tendon reflexes are pathologically increased and there is decreased hip flexion and ankle dorsiflexion. Crossed adductor reflexes, ankle clonus, and extensor plantar responses are present. Hoffman's and Tromner's signs, as well as pes cavus, may be present. Occasionally, slight dysmetria may be seen on finger-to-nose testing in patients with longstanding disease.

Familial Spastic Paraplegias

Management and Prognosis.

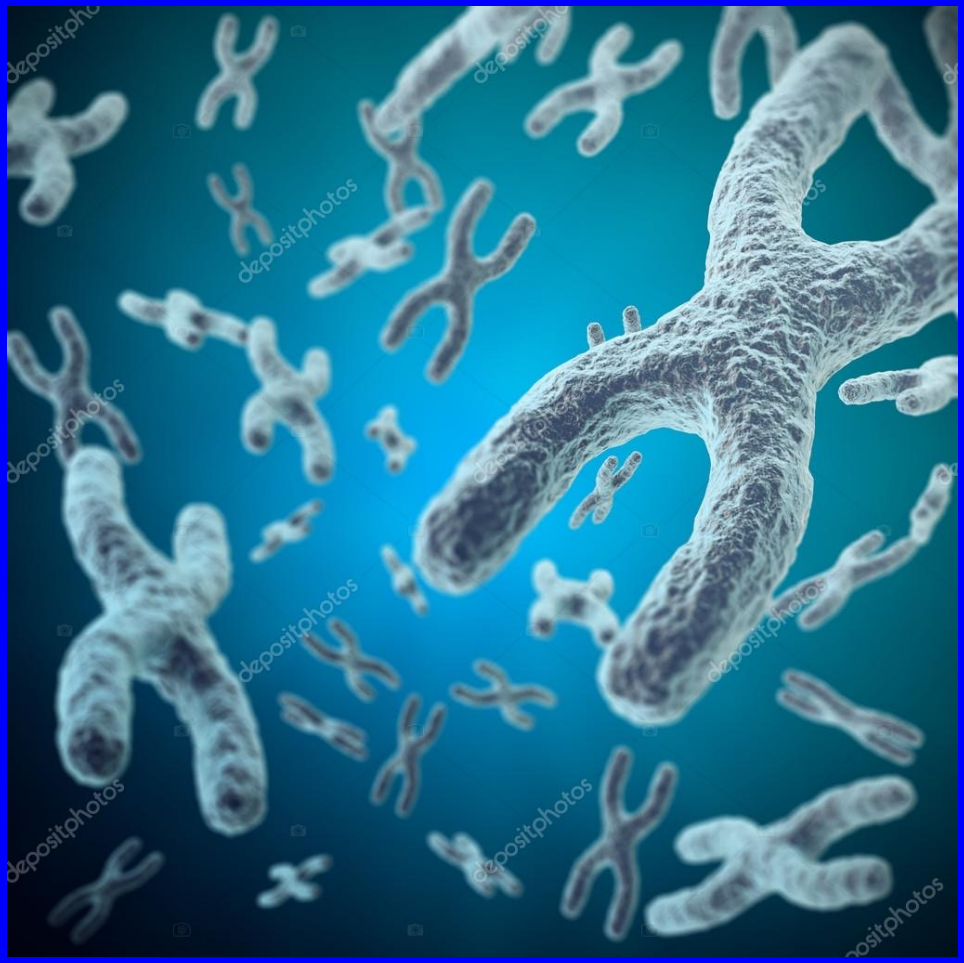
There is no treatment available to address the underlying process in FSP. Treatments to combat the problems associated with chronic paraplegia can be helpful, particularly oral or intrathecal baclofen or oral dantrolene for the lower extremity spasticity, and oxybutynin for bladder spasticity. Caution should be exhibited in counseling regarding the course of the disease because there is variation in severity of phenotype reported.



The hereditary metabolic diseases

WILSON'S DISEASE

Wilson's disease is due to the homozygous state for a mutation or mutations in the Wilson's disease locus on the long arm of chromosome 13. The gene has been recently cloned and appears to be a copper-binding, membrane-associated, ATPase protein. The Wilson's disease gene has been mapped to chromosome 13q14.3.



The hereditary metabolic diseases

WILSON'S DISEASE

As a result of the mutation in the Wilson's disease gene, the liver is not capable of excreting the regulatory copper into the bile, and a positive copper balance, averaging about 0.25 mg/d, is established. This copper accumulates over time, first in the liver and then in other parts of the body, such as in the brain.

The hereditary metabolic diseases

WILSON'S DISEASE

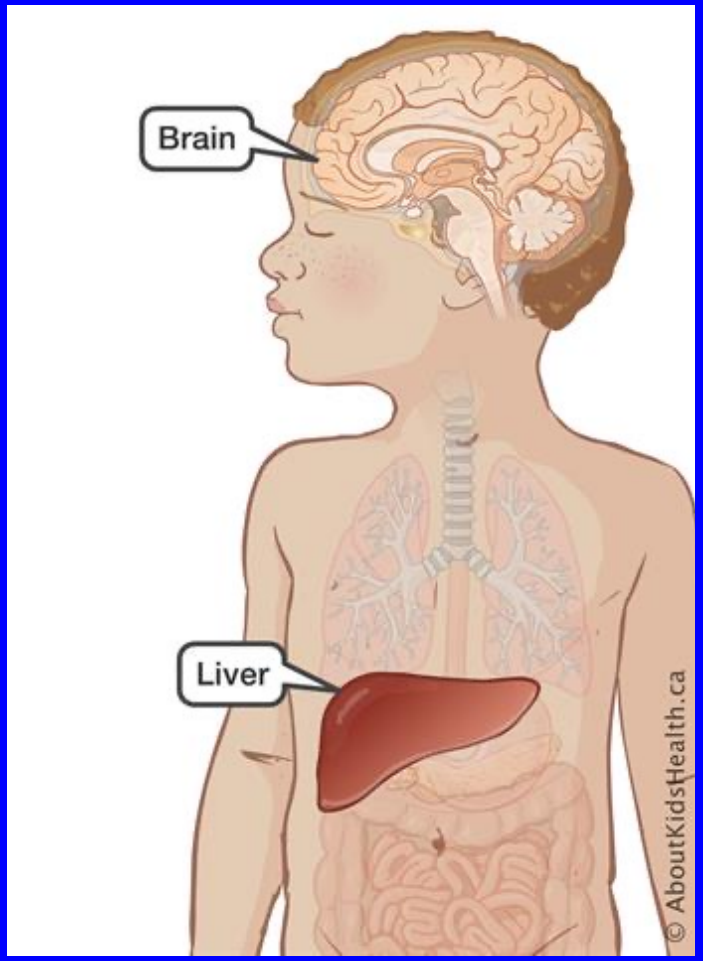
Researchers have postulated that the liver's packaging mechanism involves the secretion of ceruloplasmin into the bile because ceruloplasmin is a protease-resistant package for copper.

CERULOPLASMIN

WILSON'S DISEASE

Clinical manifestation

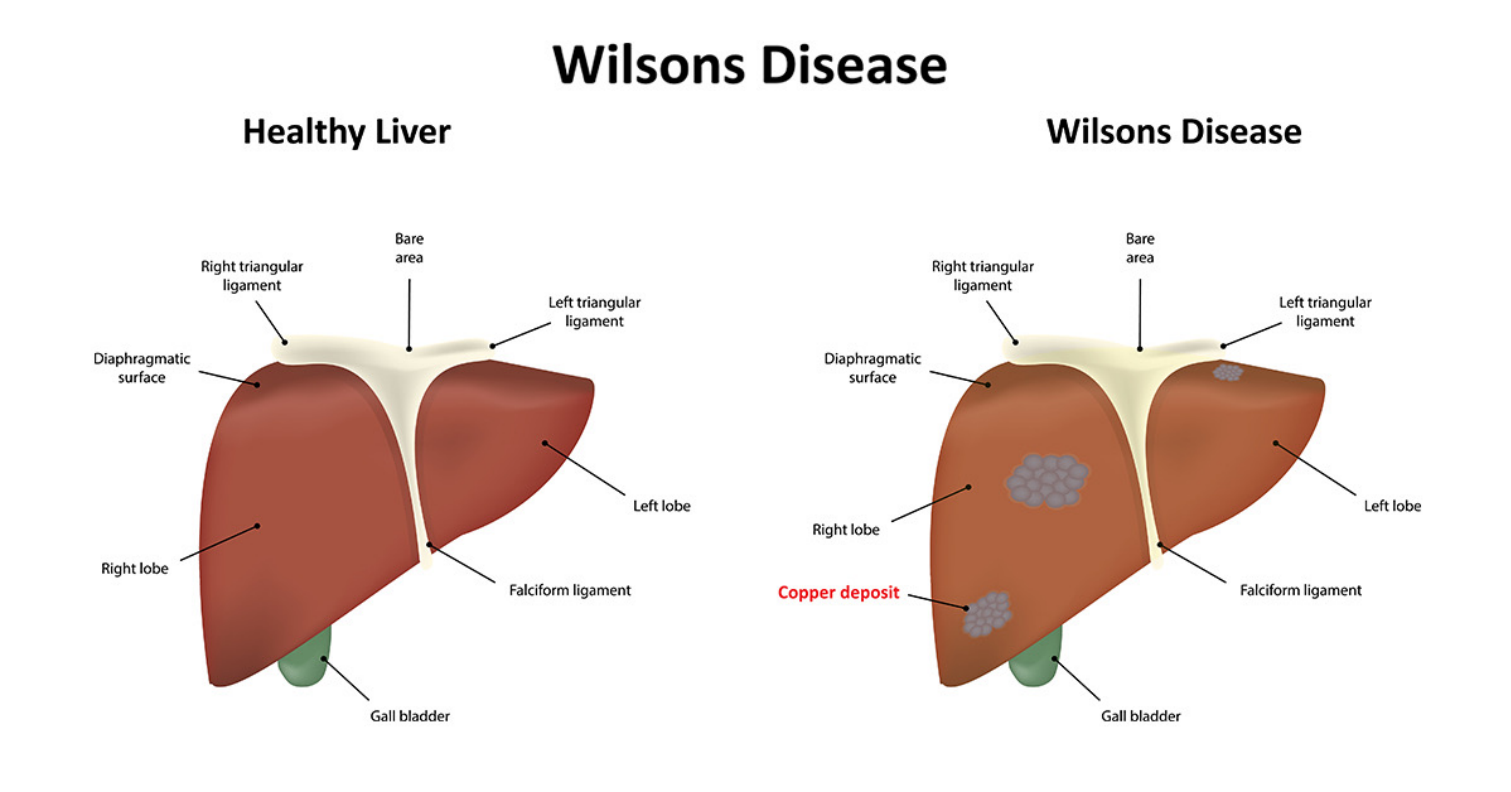
During early life, the patient is presymptomatic, but accumulating copper, which invariably causes subclinical liver disease. Then, between early childhood and the fifth or sixth decade of life, but with a peak incidence of around 21 years, the patient presents with hepatic, neurologic, and psychiatric manifestations, occurring in roughly equal proportions.



WILSON'S DISEASE

Clinical manifestation

The hepatic presentation can vary in its onset from insidious, appearing much like chronic active hepatitis or alcoholic cirrhosis, to acute fulminant hepatic failure. Clinically, separating chronic active hepatitis due to Wilson's disease from that due to other etiologies is impossible.

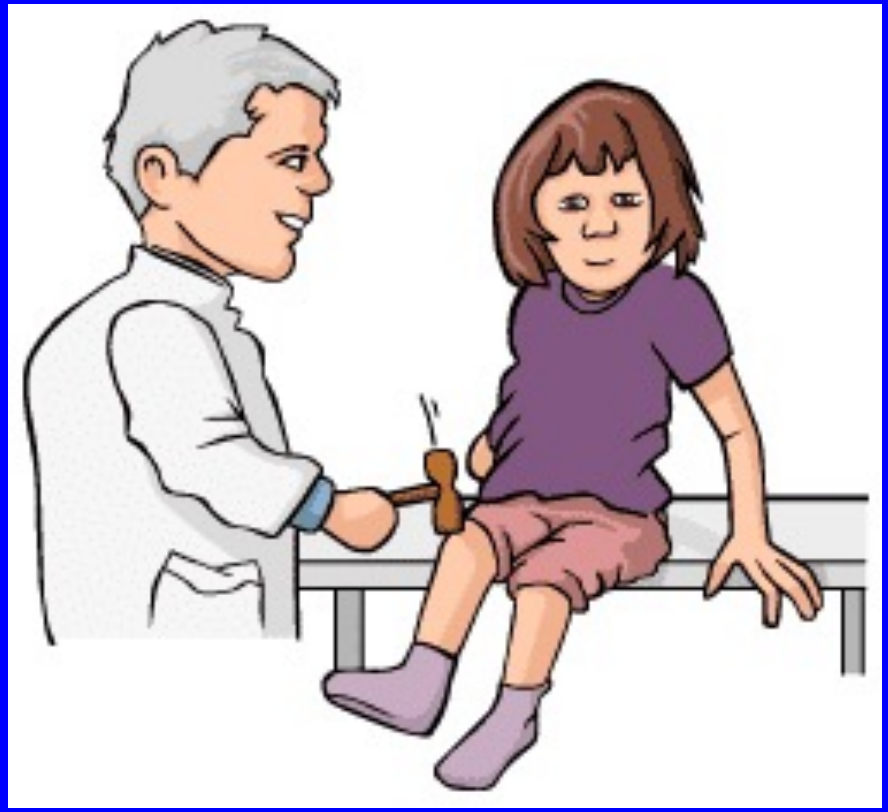


The hereditary metabolic diseases

WILSON'S DISEASE

Clinical manifestation

Some patients present with neurologic disease rather than liver disease. These patients almost invariably have subclinical liver disease, usually a mild-to-moderate cirrhosis. The onset of the neurologic symptoms and signs is usually insidious and gradually progresses.

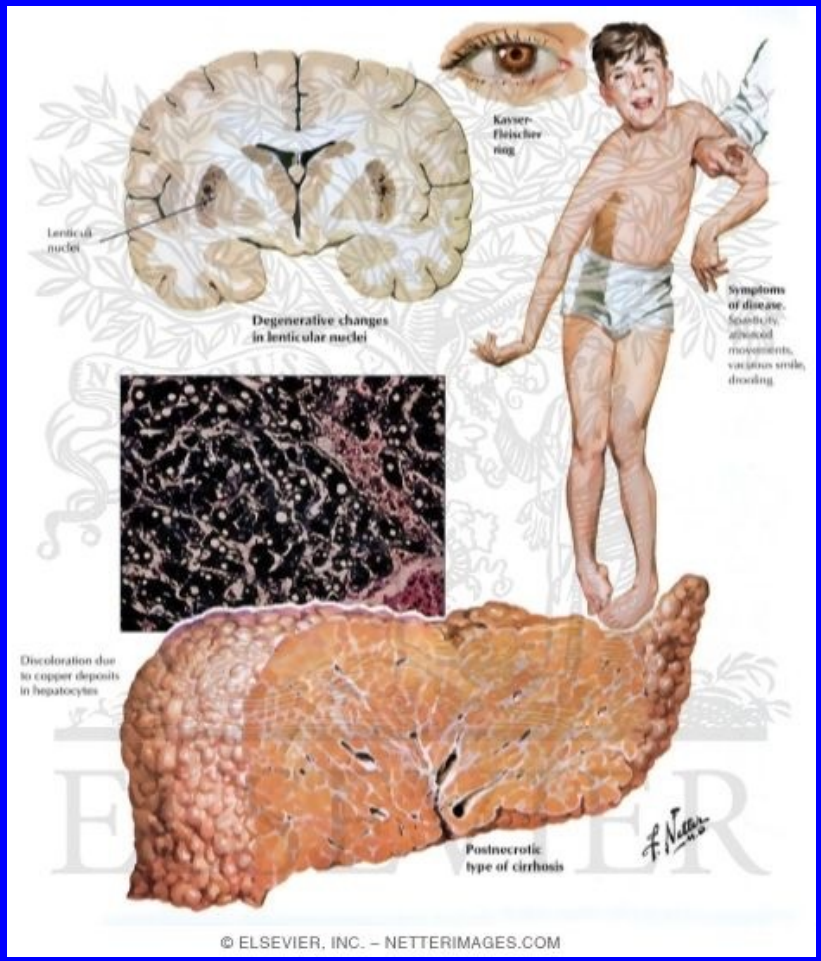


The hereditary metabolic diseases

WILSON'S DISEASE

Clinical manifestation

Dysarthria is extremely common, as are dystonia, rigidity, abnormalities of posture, gait, and facial expression. Tremor occurs in up to half of the patients. Because of poor control of facial muscles, drooling is common, and usually as the disease progresses, dysphagia becomes a problem. Intellect and sensory perception are spared.



The hereditary metabolic diseases

WILSON'S DISEASE

Clinical manifestation

Approximately one third of the patients present initially with psychiatric symptoms, which can take any number of forms. Irritability and loss of temper control are common. The patient may be depressed, almost catatonic, or may exhibit manic behavior. Often a loss of sexual inhibition leads to exhibitionism. Invariably, performance at work or school suffers, often resulting in the inability to continue in school and/or job loss.

Clinical manifestation

Because these patients are young, usually with a normal psychiatric history, these behavior changes are often attributed to substance abuse. Patients with these unspecific behavioral abnormalities should be screened for Wilson's disease, unless the etiology is clear. Unfortunately, patients with psychiatric abnormalities are usually not diagnosed at this stage, but go on to develop neurologic signs or symptoms and are then referred to a neurologist where the diagnosis is usually made.

The hereditary metabolic diseases

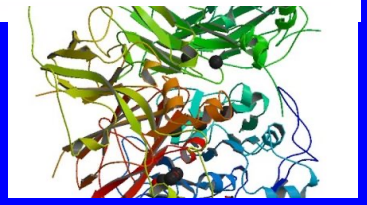
WILSON'S DISEASE

The hereditary metabolic diseases

WILSON'S DISEASE

Diagnostic Workup

The most common screening method for Wilson's disease is a blood ceruloplasmin determination, although this is inadequate for either ruling in or ruling out Wilson's disease. The ceruloplasmin value is usually low in Wilson's disease, but in approximately 10% of patients it may be normal or near normal. Further, about 10% of heterozygous carriers who will never have clinical problems have low ceruloplasmin values.

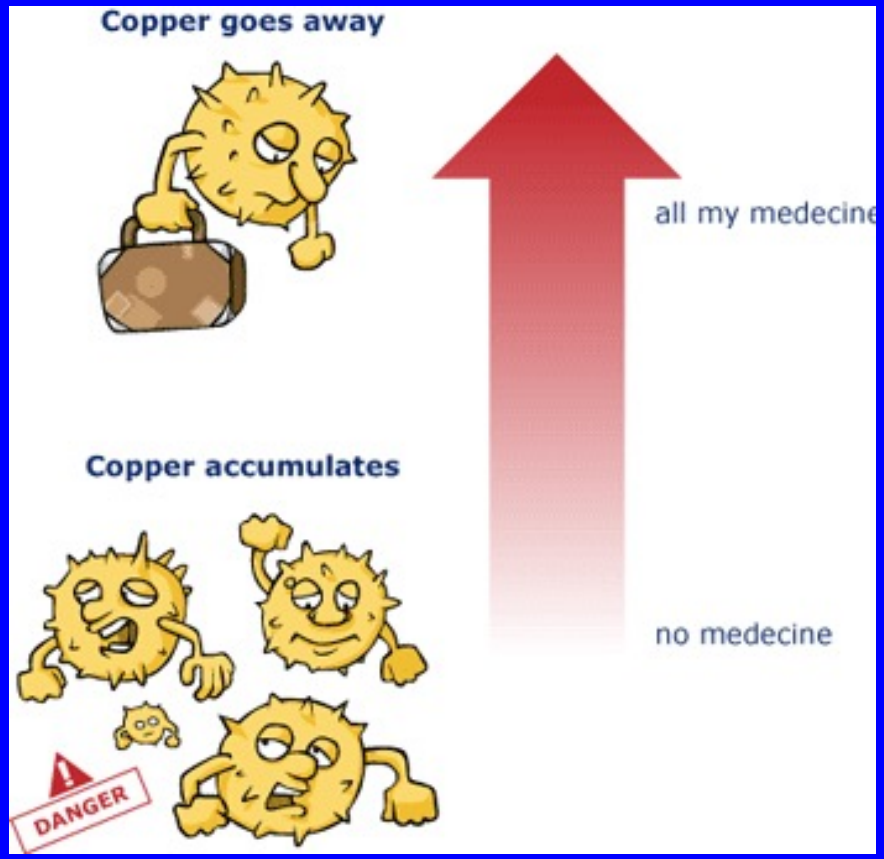


Ceruloplasmin

WILSON'S DISEASE

Diagnostic Workup

The most useful screening procedure is a 24-hour urine copper test. The 24-hour urine copper is always elevated to a value of 100 µg per 24 hours (normal is 50 or less) in symptomatic Wilson's disease. The 24-hour urine sample must be collected in a container free of trace elements. A laboratory that is capable of measuring copper in low concentrations is required to do the assay. If these difficulties can be overcome, this test is quite reliable in screening for Wilson's disease.



WILSON'S DISEASE

Diagnostic Workup

Another common screening procedure is a slit-lamp examination for Kayser-Fleischer rings. Visual inspection is not adequate. Kayser-Fleischer rings are invariably present in the psychiatric and neurologic presentations; however, they are present in only about 50% of patients who present with liver disease.

Kayser-Fleischer ring

The hereditary metabolic diseases

WILSON'S DISEASE

Diagnostic Workup

Various brain scans may be somewhat useful in the diagnosis. MRI scans are generally positive in patients who have neurologic or psychiatric symptoms but are often negative in patients with only liver disease.

In neurologically involved patients the most common findings are T-2 high signal areas in the lentiform and caudate nuclei, thalamus, brain stem, and white matter.

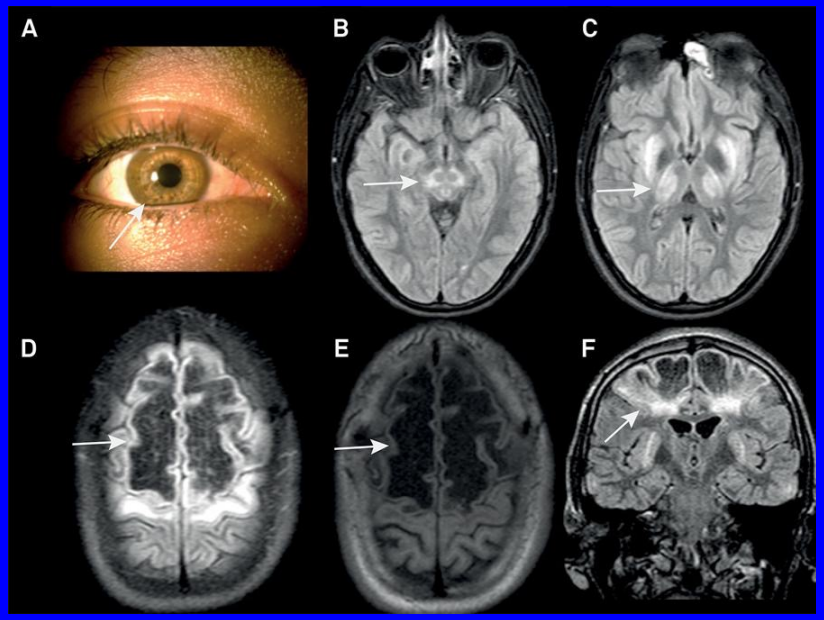


Figure. A. Kayser-Fleischer ring (arrow). B and C: Axial FLAIR-weighted brain MRI shows a giant Panda sign and hyperintense signs in the basal ganglia. D, E and F: marked bilateral frontal leukoencephalopathy with cystic lesions.

WILSON'S DISEASE

Management

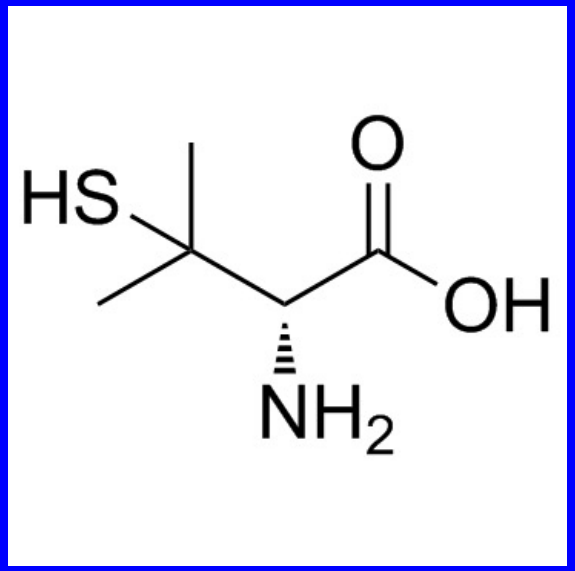
Wilson's disease is a condition that can be effectively treated.

Available pharmacologic agents include two chelator-type drugs, penicillamine and trientine, zinc acetate, which blocks copper absorption, and tetrathiomolybdate .

WILSON'S DISEASE

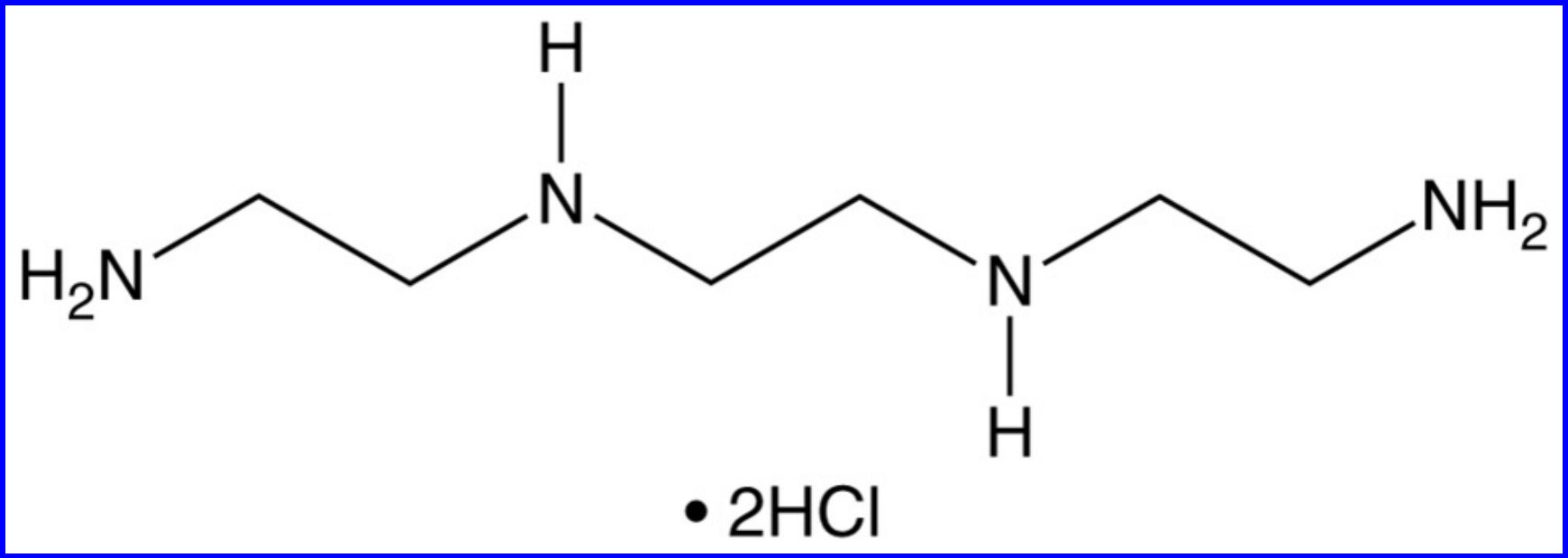
Management

The standard starting dose of penicillamine is 250 mg four times a day or 500 mg twice a day. When initiated, the patient should be carefully monitored for various kinds of toxicities including bone marrow and kidney. An acute hypersensitivity reaction occurs in about 25% of patients, which can be dealt with either by corticosteroid therapy or withdrawal of the drug and readministration in very low doses.



Management

Trientine is generally used in similar doses to penicillamine. Both drugs should be separated from food to be effective. As with penicillamine, trientine therapy should be carefully monitored during early therapy for signs of any kind of toxicity.

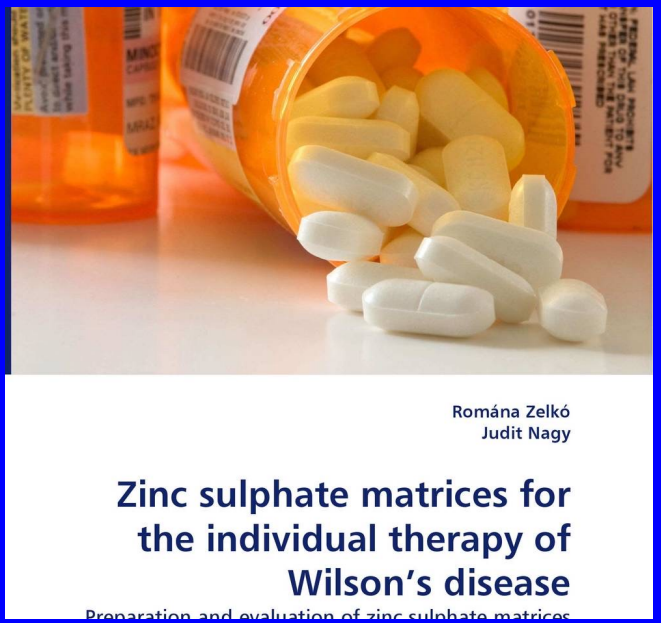


The hereditary metabolic diseases

WILSON'S DISEASE

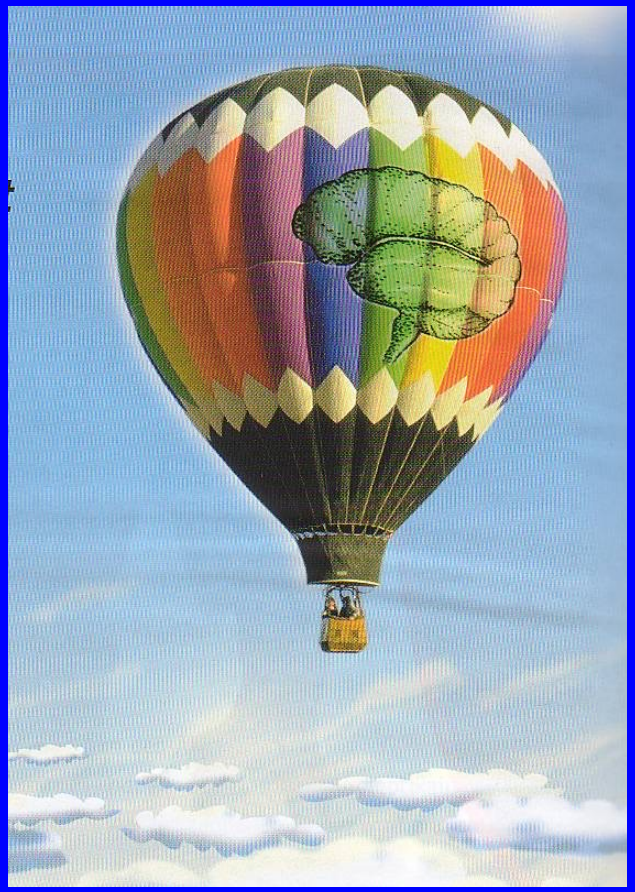
Management

Zinc is given to induce hepatic metallothionein and allow that metallothionein to complex copper in the liver in a nontoxic form. This combination is used for 4 months and then the trientine is discontinued.



QUESTIONS?

NEUROLOGY



"Knowledge is of two kinds. We know a subject ourselves, or we know where we can find information on it."
-- *Samuel Johnson*