Myopathy

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In medicine ,a **myopathy** is a muscular disease\ in which the muscle fibers do not function for any one of many reasons, resulting in muscular weakness. "Myopathy" simply means muscle disease (myo- "muscle", pathy-“suffering"). This meaning implies that the primary defect is within the muscle, as opposed to the nerves ("neuropathies" or "neurogenic" disorders) or elsewhere (e.g., the brain & neuromuscular junction.). .). Myopathies are a heterogeneous group of conditions with diverse etiologies. They usually affect muscle without involving the nervous system or any disorder of the neuromuscular junction.

Muscle cramps, stiffness, and spasm can also be associated with myopathy.

Muscular disease can be classified as neuromuscular or musculoskeletal in nature. Some conditions, such as myositis, can be considered both neuromuscular and musculoskeletal.

Abnormalities of muscle cell structure and metabolism lead to various patterns of weakness and dysfunction. In some cases, the pathology extends to involve cardiac muscle fibers, resulting in a hypertrophic or dilated cardiomyopathy.

Myopathies may be divided into two main categories: inherited and acquired. The temporal course, the pattern of muscle weakness, and the absence or presence of a family history of myopathy help distinguish between the two types

Acquired Myopathies & Inherited myopathies

Acquired myopathies:

Inflammatory Myopathy

Dermatomyositis and polymyositis

Primary polymyositis (idiopathic adult).

Dermatomyositis (idiopathic adult).

Childhood dermatomyositis (or myositis with necrotizing vasculitis).

Polymyositis associated with connective tissue disorder.

Polymyositis or dermatomyositis associated with neoplasia

Inclusion body myositis

Infection

Viral infections (HIV, influenza virus, Epstein-Barr virus)
Bacterial polymyositis (*Staphylococcus aureus* and streptococci are common organisms)
Spirochete (Lyme disease)
Parasitic infections such as trichinosis

Toxic Myopathy

- Medications causing myopathy

Steroids
Cholesterol-lowering medications: statins, fibrates, niacin, and ezetimibe
Propofol
Amiodarone
Colchicine
Chloroquine
Antivirals and protease inhibitors
Omeprazole
Tryptophan
Toxins

Alcohol

Toluene

Myopathy Associated with Systemic Diseases

Endocrine disorders

Thyroid

Parathyroid

Pituitary or adrenal dysfunction

Diabetes mellitus

Cushing’s diease

Systemic inflammatory diseases

Systemic lupus erythematosus

Rheumatoid arthritis

Scleroderma

Sjögren's syndrome

Mixed connective disease

Sarcoidosis

Electrolyte imbalance

Potassium or magnesium abnormalities

Hypophosphatemia

Critical illness myopathy

Nondepolarizing neuromuscular blocking agents

Steroids

Amyloid myopathy

Primary amyloidosis

Familial amyloidosis (TTR mutation)

Inherited Myopathies

Muscular Dystrophy

Dystrophinopathy (Duchene muscular dystrophy, Becker muscular dystrophy)

Myotonic dystrophy 1 and 2

Facioscapulohumeral muscular dystrophy

Limb girdle muscular dystrophy

Emery-Dreifuss muscular dystrophy

Rare forms of muscular dystrophy including:

- Distal muscular dystrophy.
- Oculopharyngeal muscular dystrophy.
- Congenital muscular dystrophy (CMD) - caused by genetic mutations and generally autosomal recessive disorders:
    - Extracellular matrix protein defects:
        - Laminin-alpha 2 deficiency.
        - Ulrich's CMD.
    - Integrin alpha 7 deficiencies.
    - Glycosyltransferases:
        - Walker-Warburg syndrome.
        - Muscle-eye-brain (MEB) disease.
        - Fukuyama CMD - quite common in Japan (7-12 per 100,000).
        - CMD with laminin deficiency (two types).
        - CMD with mental retardation.
    - Proteins of the endoplasmic reticulum:
        - Rigid spine syndrome.

- *Congenital myopathies* - these are rare (unknown incidence) conditions, in which gene defects lead to muscle protein defects:
    - Nemaline rod myopathy.
    - Central core disease.

    - Centronuclear myopathy.
    - Minimulticore myopathy.
    - Type 1 fiber predominance.
- *Metabolic myopathies*:
    - Hereditary muscle disorders caused by enzymatic defects (usually considered to be inborn errors of metabolism affecting the three major pathways of ATP supply) and relatively rare (much less common than the muscular dystrophies):
        - Glycogen storage diseases:
            - Pompe's disease - acid maltase deficiency (prevalence 1 in 40,000).[9]
            - McArdle's disease - (prevalence 1 in 100,000).
            - Other forms.
        - Lipid storage disease:
            - Carnitine palmitoyl transferase deficiency - (relative deficiency identified in as many as 1 in 150 patients).
            - Myopathic carnitine deficiency.
        - Disorders of purine nucleotide metabolism (affects replenishment of ATP).
        - Mitochondrial disorders.

Mitochondrial Myopathy

Myoclonic epilepsy and ragged red fibers (MERRF)
Mitochondrial myopathy, lactic acidosis, and strokes (MELAS)
Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE)
Progressive external ophthalmoplegia (PEO)

Presentation &clinical course

Type of myopathy	clinical presentation
Muscular Dystrophies	**early onset, chronic & progressive**
Metabolic myopathies	**occasionally precipitated acutely, may be progressive, fixed or recurrent. .**
Congenital myopathies	**Chronic, slowly progressive**
Systemic myopathy	**late onset, acute or sub acute**
Endocrine myopathies	**Adult onset, acute or sub acute**
Inflammatory &toxic	**Onset in any age, acute or sub acute**

General signs and symptoms of myopathy include the following:

- Symmetric proximal muscle weakness is typical.
- Pelvic muscles are more affected than the proximal muscles.
- Malaise, fatigue, cramps, stiffness and, exertional fatigue, impaired function in ADL are common symptoms.
- Difficulty rising from a chair, climbing stairs, changing a light bulb, or washing and combing their hair (weakness of proximal muscles).
- Weakness of distal muscles: Weak grasp, handwriting problems, and walking difficulties, (e.g., flapping gait).
- Metabolic myopathies present difficulty with exercise

- Dark colored urine (suggests myoglobinuria) and/or fever after intense exercise in metabolic myopathy associated with Rhabdomyolysis
- Absence of sensory complaints or paresthesias; however, deep tendon reflexes (DTRs) may be diminished/absent in hypokalemic paralysis
- Very late findings: Atrophy and hyporeflexia (early presence usually implicates neuropathies)
- Normal level of consciousness
- Gottron papules in dermatomyositis: Pink-to-violaceous scaly areas over knuckles, elbows, and knees
- Atypical distributions of weakness ininclusion body myositis, an inflammatory myopathy seen typically in older men that manifests with weakness in the finger flexors and quadriceps.

The acuity of symptom onset may aid in the diagnosis, as follows:

- Weakness progressing over hours: Possible toxic etiology or one of episodic paralyses
- Weakness developing over days: May be an acute dermatomyositis or Rhabdomyolysis
- Symptom development over a period of weeks: May be polymyositis, steroid myopathy, or myopathy resulting from endocrine causes (e.g., hyperthyroidism, hypothyroidism)

The most common forms of myopathy(muscular dystrophy) in a nutshell

Type	When it starts	Specific symptoms	Other body part involved
Duchenne Muscular Dystrophy(DMD)	Before 4 to 5 years of age	1. Weak hip and shoulder muscles. 2. Stops walking around the age of 10 to 12 years. 3. Kyphosis and scoliosis of spine. 4. Weak breathing muscles. 5. Affects males.	Cardiomyopathy(heart becomes big in size and weak in pumping action.)
Becker's muscular Dystrophy(BMD)	Early childhood to adult	1. Weak hip and shoulder muscles 2. Can walk even beyond the age of 15 years. 3. Breathing muscles also become weak but at a very later stage.	Same as above.
Limb Girdle Muscular Dystrophy(LGMD)	Early childhood to adult	1. Muscles of hip and shoulder become weak	Same as above.

		but slowly.	

Less common forms of myopathy(muscular dystrophy)in a nutshell

Type	**When it Starts?**	**Specific symptoms**	**Other body part involved**
4.Fascioscapulo Humeral Dystrophy(FSHD)	Before the age of 19 to 20	1. Weakness of shoulder, face and upper arm muscles but slowly.	None
5.Congenital Muscular Dystrophy	At birth or within First few months	1.Low tone or floppy 2.Contractures 3. Delayed milestones. 4. Weak breathing muscles.	Mentally retarded and problems with the eyes.
6.Myotonic Dystrophy	Starts between 11and 20 years of age	**1.** Weakness of shoulder, face and upper arm muscles but slowly.	Mental retardation, cataracts. Reduced size of testicles, heart problems.

7.Oculopharyngeal Dystrophy	Between 40 to 60 years	1. Slow weakness of the eye and throat muscles.	None
8.Emery Dreifuss Myopathy	childhood to adults	1. Weakness of shoulder and upper arm. 2. Contractures.	Cardiomyopathy
9.Distal Myopathy	40-50 years	1. Weakness of hand, arm and foot muscles.	None.

Clinical Features of Common Myopathies in a nutshell

Acquired Myopathies

Myopathy	**Epidemiology/**	**Distribution of Weakness**	**Other Systemic Manifestations**
Dermatomyositis	Female > male Peak incidence: children and ages 40–60 yr	Symmetrical proximal muscle weakness pelvic girdle > shoulder girdle muscles	Skin manifestations: heliotrope rash (purplish discoloration of the eyelids), Gottron's papules (erythematous scaling rash of extensor surfaces of fingers), shawl sign (erythematous rash over the shoulder and exposed areas of the back) Interstitial lung diseases Malignancy GI vasculitis
Polymyositis	Female > male predominance Peak incidence:	Symmetrical proximal muscle weakness Pelvic girdle >	Arthralgias

	20–50 yr	shoulder girdle muscles	
Inclusion body myositis	Men Peak incidence: >50 yr	Asymmetrical quadriceps muscle weakness and finger flexor muscle weakness	Dysphagia
Hypothyroid myopathy	Affects 30%–80% of patients with hypothyroidism	Proximal symmetrical pelvic > shoulder girdle weakness Pseudohypertrophy of muscles	Peripheral neuropathy Delayed relaxation of ankle jerks Myoedema (mounding of muscle when firmly palpated)
Hyperthyroid myopathy	Affects 52%–82 % of patients with hyperthyroidism	Symmetrical proximal weakness, atrophy, some distal muscle involvement	Peripheral neuropathy Graves' ophthalmopathy, extraocular muscle weakness
Sarcoidosis myopathy	Asymptomatic muscle involvement in ≤50% sarcoidosis patients	Symmetrical proximal muscle weakness Focal muscle weakness from sarcoid granuloma	Peripheral neuropathy CNS sarcoidosis Restrictive lung disease Heart failure
Critical illness myopathy	At least as prevalent as critical illness neuropathy Affects approximately 60% of patients	Symmetrical proximal >distal muscle weakness	Critical illness neuropathy Failure to wean off ventilation

	with prolonged ICU stay		
Amyloid myopathy	Rare	Proximal > distal muscle weakness Pseudohypertrophy of muscles Palpable muscle nodules	MacroglossiaPeripheral neuropathy Autonomic involvement Restrictive cardiomyopathy
Inherited Myopathies			
Duchenne muscular dystrophy	1 in 3500 male births Age of onset <13 yr	Symmetrical proximal girdle weakness Calf psedohypertrophy Ankle contractures	Cardiomyopathy Kyphoscoliosis Cognitive impairment
Limb girdle muscular dystrophy	1 per 15,000 population	Proximal pelvic >shoulder girdle weakness Calf hypertrophy Scapular winging	Different subtypes may have variable extent of cardiomyopathy or cardiac arrhythmias, respiratory muscle weakness
Myotonic dystrophy 1 and 2 (DM1, DM2)	Approximately 2.5–5.5 per 100,000 population	Distal muscle weakness predominates in DM1; proximal muscle weakness is common in DM2 Clinical myotonia (difficulty relaxing	Cataracts Diabetes mellitus Frontal balding Cardiac arrhythmias Cholecystitis Pregnancy- and labor-related complications Eyelid ptosis without

		after a forceful muscle contraction)	extraocular muscle weakness
Oculopharyngeal muscular dystrophy	Relatively rare	Rarely presents with distal muscle weakness	Mainly manifests with ophthalmoparesis and with bulbar weakness manifesting with dysarthria and dysphagia
Facioscapulohumeral muscular dystrophy	Approximately 4 per 100,000 population	Face and arm weakness, scapular winging, and later distal leg muscle weakness	Hearing loss Retinal telangiectasias
Mitochondrial myopathies	1 per 8000 population	Exercise intolerance Proximal girdle muscle weakness	Extraocular muscle weakness Peripheral neuropathy Migraine headaches Seizures Stroke Diabetes mellitus Cardiac arrhythmias
Acid maltase deficiency or glycogen storage disorder type 2	Approximately 1 in 40,000 newborns	Proximal girdle weakness	Macroglossia, hepatomegaly in infancy Severe ventilatory muscle weakness with adult presentation Cardiomyopathy

Common forms of myopathy(DMD)

Duchene muscular dystrophy (DMD) is easily the most common childhood-onset muscular dystrophy and affects 1 in 3,300 boys.[10] The prevalence of DMD is 63 cases per million. The prevalence of the Becker phenotype is 24 cases per million. Congenital muscular dystrophy (CMD) is approximately 50% as common as DMD.Dystrophies (or muscular dystrophies) are a subgroup of myopathies characterized by muscle degeneration and regeneration. Clinically, muscular dystrophies are typically progressive, because the muscles' ability to regenerate is eventually lost, leading to progressive weakness, often leading to use of a wheelchair, and eventually death, usually related to respiratory weakness.

Onset	**clinical features**	**Prognosis**
Childhood onset (3 to 5 yr)	Progressive weakness of the girdle muscles, bilateral symmetrical, proximal>distal. In the ambulatory phase, pelvic girdle>shoulder girdle Extensor group weaker than flexor group. Differential muscle weakness becomes more pronounced as the disease progresses.	Death usually occurs by age 25 typically from lung disorders.

- Difficulty running, jumping, hopping, unable to get up from the floor. Gower's maneuver, Toe walking is associated with lordotic posture.
- Pregnancy and birth are usually normal except some mothers report diminished movements.
- Timing of motor milestones often delayed (50 % of DMD babies fail to walk until 18 months.)

- Evidence of hypotonia during infancy.
- Although all skeletal muscles are involved, the Para axial & appendicular postural muscles first formed in the embryo are involved earliest and most severely.
- Facial and extra ocular muscles remain clinically intact, although macroglossia and hypertrophy of masseter muscles can be seen.
- Spurious improvement due to normal growth and increase in motor ability at age 5 to 8 years.

Early signs of DMD

- Flat feet
- Hesitance when ascending stairs.
- Poor standing jump.
- Poor balance.
- Wide base.
- Waddling run.
- Acceleration during final stage of sitting down.

Later signs of DMD

- Waddling gait(Hip abductor weakness)
- Lordosis(Hip extensor weakness accompanied by hip flexion contracture leading to increased lumbar lordosis)
- Frequent fall.
- Difficulty ascending stairs(more difficulty descending than ascending, the knees loaded with up to 7 times body wt when descending than ascending)
- Positive Gower's sign.(tripod sign)
- Weak neck flexion.
- Exercise cramping may occur.
- Deep tendon reflexes are depressed as muscles weaken. They tend to cease on the dominant side first. The non dominant Achilles reflex is usually the last to disappear; this is because the heel cord is the strongest tendon in the body.
- True muscle hypertrophy and later pseudo hypertrophy (substitution of fat and areolar tissue for muscle) seen in calves (occasionally in deltoids, triceps, serratus anterior and vastus lateralis muscle) Involved muscles have a doughy consistency on palpation. The specific gravity of this muscle is less than normal because of replacement by adipose and fibrous tissue.
- Sensation unaffected.
- Weakness accentuated by immobilization. Loss of ambulation between 9-12 years of age. Death (pulmonary or cardiac) in late teens.
- Significant number of patients is intellectually impaired.

Other Complications of myopathy

The most common complications seen in different muscular dystrophies are:

- **Breathing Complications**
- Patients with muscular dystrophy are at risk of breathing complications due to spinal muscle weakness & progression of spinal deformities.
- Breathing complications mostly occur only after the person stops walking. But in case of **congenital muscular dystrophy**, breathlessness is noticed even when the person is still walking.
- Shoulder weakness is the earliest sign indicating the onset of breathing muscle weakness.
- Breathing complications in muscular dystrophy majorly include reduced lung expansion leading to collapse of lung tissue, which in turn causes chest infections. It also causes difficulty in coughing which increases the accumulation of mucus in the lungs.
- In Myotonic dystrophy, there is combination of breathing muscle weakness and dysfunction of the breathing centers in the brain. Persons are at risk of aspiration pneumonia due to failure of swallowing muscle function.
- Difficulty in breathing at night may even cause breathing failure which can be fatal.

- In later stages of muscular dystrophy, the person may have to be put on a ventilator.
- Breathing complications are the major cause of death in 90% of Duchenne muscular dystrophy patients.

2. **Heart Complications**

- Involvement of the heart is very common in muscular dystrophy patients.
- Weakness of the heart muscle and replacement of muscle tissue with connective tissue or fat, results in complications of the heart.
- These complications are generally progressive leading to ECG abnormalities and poor ability of the heart to pump blood, which may be life threatening.
- Breathing problems & spine deformities may also affect the functioning of the heart.
- Approximately 70% of boys with Becker's muscular dystrophy have cardiac involvement by age 20.
- Heart problems in Becker's muscular dystrophy are worse than in Duchenne muscular dystrophy patients. Myotonic dystrophy type 1 has more than one system affected with prominent heart problems leading to an increased incidence of sudden death.

3. **Psychosocial complications:**

- People with muscular dystrophy may experience psychological & social difficulties due to their limited ability to participate in many activities when their friends are doing well.
- They may feel helpless as they become dependent on others.
- Social isolation or withdrawal, emotional disturbances like anger, depression, anxiety & reduced self-esteem are some of the psychosocial issues.
- Stopping schooling (due to difficulties in carrying the child and moving in the school building) has a huge impact on the psychosocial functioning of kids.

- Associated conditions such as ADHD, learning difficulties or autism spectrum disorders should be identified early to reduce psychological issues.
- A fear about the future may always worry them.

4**. Obesity**:

- People with muscular dystrophy often are overweight due to lack of physical activity.
- It adds strain to weak muscles due to which the person can approach non walking stage faster.

5. **SLEEP DISTURABNCE**

- As muscle weakness increases, the person with Muscular dystrophy will not be able to change his position on his own. Therefore the patient's & his caregivers sleep would be disturbed throughout the night.
- Breathing difficulties also may keep the person awake.

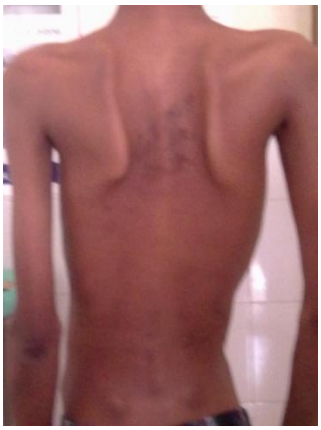
6. OSTEOPOROSIS:

- Osteoporosis is the thinning of the bone in which they lose calcium and become soft and brittle.
- These soft bones are more prone to fractures.
- Risk of osteoporosis increase with age and loss of walking as the bones are not subjected to normal weight bearing.
- Fractures in the walking phase lead long periods of bed rest which in turn could result in loss of walking.

7. SCOLIOSIS

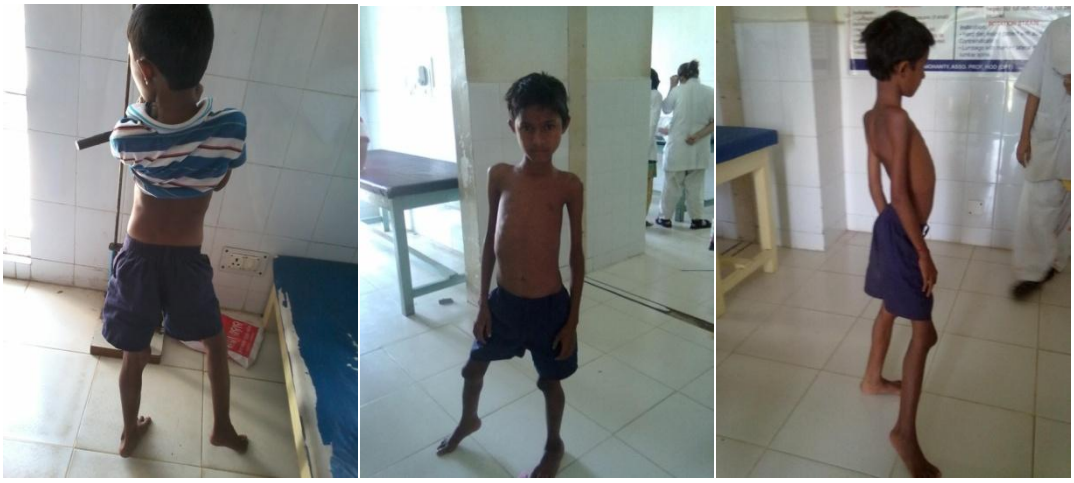
- Scoliosis is twisting in the spine (S shaped curvature) caused due to weakness in trunk muscles.

- It progresses when the child is unable to stand or walk.
- It results in poor sitting tolerance and balance, tightness of the trunk muscles and compression of lungs & heart.
- Restricted movement of the rib cage may cause difficulty in breathing & heart functions.



8. Contractures:

- Contractures are shortening and tightening of the muscle tissue due to which there is restriction in joint movements.
- Contractures occur due to weakening of certain groups of muscles.
- They are most commonly seen at hip, knees, ankles and elbows.
- Stretching of these contractures cause severe pain.



9. Pressure Sores

- Staying for long time in any particular position in muscular dystrophy could result in pressure or bed sore.
- Although sensation is generally not affected, person with MD are at risk of developing pressure sore as they are unable to reposition themselves on their own. Also, being overweight can increase the risk considerably.
- Pressure sores develop mainly on bony prominences including the spine, ankles, knees, shoulders and head depending upon the position of the patient.

10. Swallowing:

- Some children with MD have specific problems with swallowing. Food or drink may go down the wrong way (goes to breathing path instead of going to stomach). This is called aspiration.
- If this happens regularly, the child could be more prone to chest infections and find it hard to put on weight.
- Some may eat very slowly due to shape of their mouth or enlarged tongue (pseudohypertophy) or weakness in their chewing and swallowing muscles.

Also children may have weakness in their arms and upper limbs due to which they are unable to feed themselves

11. Complications due to prolonged steroid treatment include:

- Cataracts
- Cushingoid features(moon face)
- Obesity
- Short stature
- Constipation
- Hypertension
- Delayed puberty
- Behavioral changes (irritability, hyperactivity)
- Occasionally slight increase in body hair.

Laboratory diagnosis

a)Typical EMG

b) Typical biopsy

c) Markedly increased CPK (at least 10 times normal in early stages, though reduced later when walking ceases). Increased urinary excretion of 3-methylhistadine.

e) No dysphagia or sphincter difficulty.

Becker's muscular Dystrophy

1. X-linked. This variant constitutes 10% of DMD.

2. Later onset and patients are ambulatory into third decade with longer life expectancy than DMD.

3. Similar proximal distribution of muscle weakness as in DMD but asymmetrical; usually maintains **neck flexor** strength. May present with pes cavus, unusual hypertrophy (thenar eminence), or patellar subluxation secondary to quadriceps weakness.

a) **Triceps** power often greater than **biceps**.

b) May develop ambulatory scoliosis because of asymmetrical Para spinal muscle weakness.

4. Cardiac involvement less than in DMD.

5. Occasionally linked with deuteranopia (color blindness)

6. Mental retardation uncommon.

7. Laboratory diagnosis:

a) Increased CPK

b) Mixed pattern on EMG

c) Biopsy somewhat different than Duchenne Dystrophy (muscle fibers usually not rounded and hyaline fibers rare).

LIMB GIRDLE DYSTROPHY

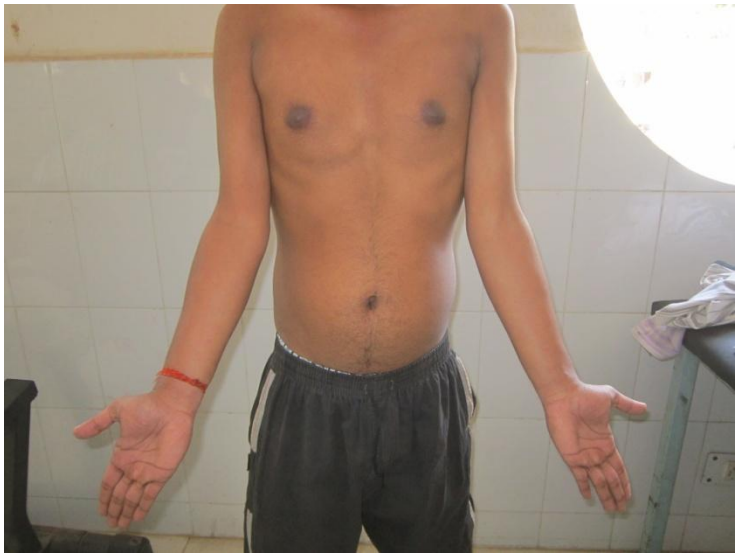
1. Autosomal recessive (many sporadic); consanguineous mating increases incidence (for e.g., first cousins, have one- eighth of their genes in common).

2. Onset usually in second or third decade.

3. Life expectancy reduced but variable.

4. - Usually pelvic girdle weakness is more than shoulder girdle with variable progression. Prognosis is better in patients who manifest shoulder weakness first.

a. Popeye arms"- muscles above elbow are atrophied, those below normal, Strong brachioradialis, but sometimes marked atrophy of biceps.

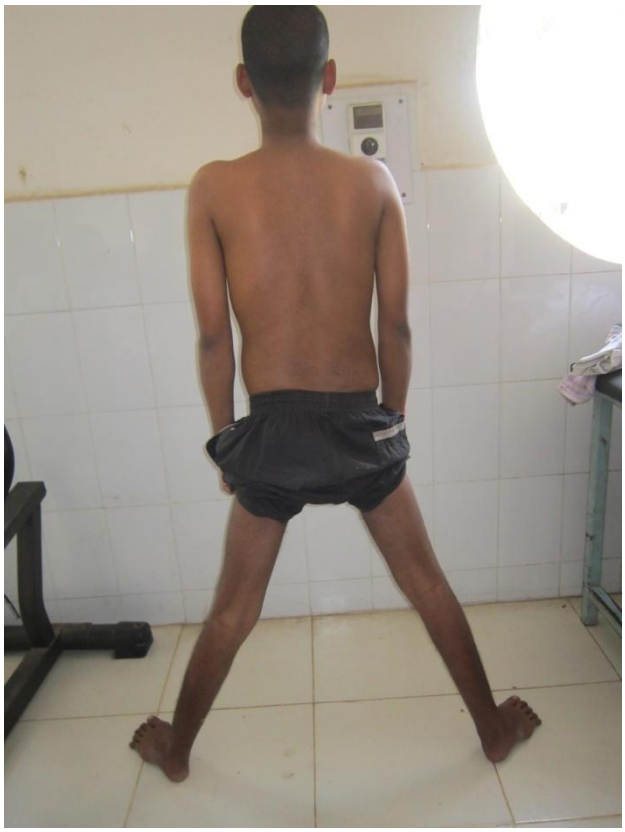


b. Occasionally severe atrophy in periscapular muscles. Upper extremities held in internal rotation during ambulation. May require thrown motion to move shoulder.

c. May have enlarged calves and can have hypertrophy of extensor digitorum brevis.

e. Diaphragm involved early, which leads to alveolar hypoventilation.

5. No cardiomyopathy.



6. Normal intelligence.

7. Laboratory workup.

    a. CPK modestly elevated.

    b. EMG and biopsy myopathic.

    c. Can be confused with Becker's Dystrophy,KugelbegWelanderdisease,metabolicmyopathies,congenital myopathies,Polymyositis and acid maltase deficiency

Facioscapulohumeral muscular dystrophy (landouzy-dejerine disease).

- Autosomal dominant—with variable expressivity (from patient to patient within a given pedigree, as well as from family to family).one parent always has at least sub clinical disease
- Onset usually in adolescence or early adult life with slow progression and normal life expectancy. But Childhood form is a more malign disease which runs a more rapidly disabling course. (May show inflammatory response in muscle biopsy). May be stationary for periods of time.

a) Weakness of face, shoulder girdle (particularly muscles of scapular fixation), and lower fibers of trapezius is often affected with high riding scapula. Deltoids often preserved.

b) Brachioradialis, dorsiflexor weakness of wrists & fingers produces "Praying mantis" posture.

- Positive bell's sign, accentuation of lateral lip "dimples," transverse smile, inability to whistle, inability to wrinkle forehead or puff cheeks, "tapir" mouth (lip eversion & protrusion).
- Lower limb usually affected 10-15 years after onset. Distal leg weakness of tibialis anterior and toe extensors causes foot drop and slapping gait. Back extensors, quadriceps, & tensor fascia often exempt.

a) Pelvic girdle weakness with increased lumbar lordosis. Occasionally cauda equina syndrome with leg paresthesias secondary to sway back may occur Involvement usually asymmetrical in distribution and degree..

- Cardiac involvement & intellectual impairment not characteristic.
- Lab workup.

a) CPK variably & slightly increased. Pyruvate kinase can be elevated (even with CPK normal).

b) EMG myopathic but can show some neuropathic elements.
c) Biopsy myopathic with an occasional inflammatory finding. Some cases show type 1 fibre predominance.

Scapulo peroneal muscular dystrophy (FSH minus the F)

- X-linked disease can often be characterised as Emery-Dreifuss muscular dystrophy
- Insidious onset in childhood and progression is slow without loss of ambulation.
- May be myopathic or neuropathic (in which case EKG abnormalities are observed) & hereditary pattern is variable.
- Muscle weakness mainly confined to scapular and peroneal groups of muscles.
- Achilles tendon & elbow flexion contractures as well as inability to fully flex the neck &spine.
- By mid adulthood, atrial conduction defects occur that can cause sudden death.

The syndrome of Facioscapulohumeral muscle weakness & wasting can be seen in such diverse conditions as myotubular myopathy, central core disease, nemaline myopathy, myasthenia gravis, polymyositis, adult acid maltase deficiency, & spinal muscular dystrophy.

Ocular (Oculopharyngeal) myopathy

Common in French Canadian families near Quebec & Spanish-American families in the south western united states. Regarded as a mitochondrial myopathy.. Usually autosomal dominant, onset in third to fourth decade, disease is Progressive with frequently asymmetrical distribution; women affected more than men.

a) Ptosis followed by external ophthalmoplegia with dysphasia.
b) Facial &upper limb muscles (late) may be involved.
c) CPK normal to slightly increased, EMG myopathic, ragged red fibbers on biopsy.

Oculo-cranio-somatic neuromuscular disease.

a) Onset in first decade.
b) Progressive external ophthalmoplegia plus:

Retinitis pigmentosa& optic atrophy.
Cardiomyopathy & heart block.
Cerebellar ataxia & spasticity.
Deafness.
Mental retardation.
Skeletal deformities.
Limb myopathy.
Peripheral neuropathy.
Pharyngeal weakness.

c) CPK slightly elevated, EMG myopathic, ragged red fibres on biopsy.

Distal Myopathy

- Inherited as a dominant character.
- Usually begins between 40-60 years of age.

- Affects small muscles of hands & peripheral leg muscles spreading slowly proximally.
- Comparatively benign condition found mostly in large Swedish kindreds.

Morphologically specific myopathies

(So called as benign or congenital myopathies)

- Major "structural" types—histological diagnosis.
    a) Central core disease(in which the nuclei are abnormally found in the centre of the muscle fibres).
    b) Nemaline Myopathy (rod diseases) –childhood & adult forms.
    c) Myotubular Myopathy.
    d) Mitochondrial Myopathy (which are due to defects in mitochondria, which provide a critical source of energy for the muscle).
    e) Minimulticore myopathy (characterised by multiple small cores or areas of disruption in the muscle fibres.)
    f) Congenital fibre type disproportion
- Similar clinical pictures for most types such as:
    a) Genetically determined (often autosomal dominant) but many sporadic cases.
    b) Hypotonia after birth. (floppy infants) or later development of muscle weakness.
    c) Delayed motor milestones.
    d) Commonly slowly progressive generalised muscle weakness more marked proximally; facial or extra ocular muscle weakness may be present. Occasionally rapid progression of disease

e) Can overlap with some of metabolic myopathies.

f) Dysmorphic features.

High arched palate.

Long-facies-dolichocephalic head.

Pectus carinatum or excavatum.

Absence of a single muscle (**Myotubular Myopathy**).

Long tapering fingers.

g) Skeletal abnormalities:

i. Congenital dislocation of hip, particularly in **central core disease**, Responds poorly to closed reduction because of muscle weakness, usually requires operative stabilization
ii. Pescavus.
iii. Scoliosis.

Lab diagnosis

i. CPK usually normal.
ii. EMG normal or myopathic.
iii. Biopsy reveals specific identifying histological abnormalities as seen by light or electron microscopy & in many cases type l fibre predominance.

Congenital muscular dystrophy

- Hypotonia at birth (with facial involvement).
- Motor milestones late but disease generally non progressive
- Progressive muscular contracture.
- Usually no cardiomyopathy or intellectual impairment.

- CPK modestly elevated; EMG myopathic; biopsy shows advanced dystrophic changes with early & extensive endomysial fibrosis.
  - Several kindred with dysplastic brain abnormalities & dystrophic involvement of skeletal muscles have been reported in Japan` (Fukuyama). These have markedly elevated CPK.
- Requires early aggressive orthopaedic attention.

Metabolic myopathies

- Myopathies of varying degree, secondary to biochemical defects of muscle metabolism.
- May be progressive, fixed or recurrent, difficulty with exercise.
- Fluctuating muscle power with exercise induced weakness, cramps, & sometimes myoglobinuria.
- Diagnosis is made on the basis of clinical findings (e.g., an unusual craving for salt can be associated with one of the mitochondrial myopathies),
- Enzyme assays, elevated CPK, ECG changes when heart is involved, typical histological findings (i.e., ragged red fibers in mitochondrial disease).
- EMG changes in some of conditions, special histochemical staining to identify specific metabolites, or lack of particular enzymes.

I. **Glycogenosis** the seven recognized type muscles disease associated with enzyme deficiency in the carbohydrate metabolism of muscles are outlined in table. The site of action (liver, heart, muscle, etc) of the deficient enzyme determines the format of the disease. Myopathy is present in types ll, lll, V & Vll. In types V & Vll, myopathic symptoms are the major manifestations.

II. Abnormalities of lipids metabolism. Myopathies are characterised by neutral lipid accumulation in muscle due to mitochondrial metabolic defects. Carnitine (synthesized in the liver & transported via the blood stream) facilitates the passage of free fatty acids

across the mitochondrial membrane. Diagnosis is by muscle biopsy (vacuolar [lipid] myopathy).

A. Carnitine deficiency.

1. Systemic: metabolic acidosis, encephalopathy, Hepatomegaly, cardiomyopathy
2. Muscle: progressive proximal Myopathy.
3. Secondary to genetic defects of intermediary metabolism or other conditions (e.g.cytochrome oxidase deficiency, glutaric aciduria, chronic renal failure treated by haemodialysis, cirrhosis with cachexia, renal fanconi syndrome).
4. Can be treated with diet.(Low in long chain fatty acids), steroid & oral L-Carnitine.

B. Carnitine palmityl transferase deficiency.post exertional or fasting pain with myoglobinuria, followed by weakness, tenderness or muscle swelling. Treat with high carbohydrate foods or medium chain fatty acids supplements.

lll. Periodic paralysis.

- Inherited as an Autosomal dominant trait having tendency towards remission & relapse.
- The primary defect for the many of the periodic paralysis is believed to be an increased membrane conductance to sodium ions resulting in membrane hypo excitability.
- Classified in to hypokalemic, normokalemic, & hypokalemic, depending on the level of venous blood potassium during an episode. This different form may occur at different times in the same patient (biphasic periodic paralysis).
- Clinical features overlaps. Episodic limb weakness usually occurring after exercise, typically spares muscles of respiration & disappear in an unpredictable manner. Clinical myotonia may be present.

Lab diagnosis

- Provocative testing with potassium may be helpful in making the diagnosis. Hypokalemic variety can often be induced by glucose & insulin, heavy exercise followed by rest, excessive alcohol, cold, trauma or stress. CPK can be raised during attacks. EMG changes may be present. Changes are apparent on biopsy if the specimen is taken during attacks.,

Treatment

- Hypokalemic variety can be treated with oral potassium, carbonic anhydride inhibitors, acetazolamide, sodium restriction, and high carbohydrate diet.. The norm kalmia type is best relieved with sodium infusion. Carbonic anhydride inhibitors may also help.

Glycogenoses

Type	Enzyme Deficiency	Eponymous or other names	Skeletal muscles affected	Clinical features	Other tissues affected
l	Glucose-6-phosphatase	Von Glerke's disease	No		
ll	α-1,4-glucosidase(acid maltase)	Pompe's disease	Yes	a) Severe form: Generalized; resembles infantile spinal muscular atrophy b) Mild form; resembles limb	Heart, nervous system, kidney, leukocytes ? Heart

				girdle dystrophy, may present as adult	
lll	Amylo- 1,6-glucosidase ("debranching enzyme")	Limitdextrinosis Forbe's Disease Cori's disease	Yes	Infantile hypotonia Mild Weakness	Hepatic Hypoglycaemia Ketosis Leucocytes
lV	α -1,4 – glucan: - α 1,4 – glucan 6 glycosyltransferase ("branching enzyme"; amylo (1,4 – 1,6) transglucosidase)	Amylopectinosis Anderson's disease	? Some cases only	Usually no muscle symptoms In some wasting or weakness	Hepatomegaly Cirrhosis Splenomegaly
V	Muscle Phosphorylase	McArdle's disease	Yes	Exercise intolerance Muscle cramps Fatigue Myoglobinuria Controlled with high glucose intake and avoiding strenuous	None

				activity	
Vl	Liver phosphorylase		No		
Vll	Phosphofructokinase	Tarui's disease	Yes	Exercise intolerance Muscle cramps Fatigue, Myoglobinuria	Erythrocytes

Malignant Hyperthermia

This is a syndrome initiated by a hyper metabolic state of skeletal muscle and characterized by rapid and sustained temperature rise during general anesthesia (surgical stress), accompanied by tachycardia, tachypnea, muscular rigidity, fever, muscle necrosis, cyanosis and severe metabolic and respiratory acidosis. Total body consumption of oxygen increases to two to three times normal and temperature can rise (as fast as 1^0C every five minutes) to as high as 43^0C.Serum CPK and potassium are markedly elevated. Muscle necrosis follows with myoglobinuria and sometimes renal shutdown.

l. Usually expressed as an autosomal dominant trait, but inheritance may be multifactorial. Patients with myopathy (including DMD and DMD carriers) are at increased risk, particularly central core disease. It is important to look for a history of similar problems with anesthesia in the family, though attacks may not necessarily occur with the first exposure to general anesthesia.

a) Incidence 1:15,000 anaesthetics in children; 1:50,000 in adults. Sexes affected equally in childhood; most post pubescent victims are males.
b) Halothane and Succinyl Choline are the most provocative anaesthetic agents, although any general anaesthetic can cause an incident.

c) Patients may have large muscle mass (they tend to be muscular and athletic) and a history of cramping (especially nocturnal, which tends to stop by the third decade), exercise intolerance in hot weather, and stress associated acrocyanosis. Musculoskeletal abnormalities such as Ptosis, clubfoot, scoliosis, pectus carinatum, and hernia are common.

d) The marked elevation of temperature is believed to be secondary to high calcium concentration in the myoplasm

ll. Lab diagnosis

a) Elevated CPK may be found during work up.
b) Muscle biopsy shows abnormal in vitro sensitivity to halothane, succinyl choline, or caffeine, which increases calcium efflux into the cell.

lll. Treatment

If Local or regional anaesthesia is not feasible, general anaesthesia can be accomplished with nitrous oxide, narcotics, barbiturates, ketamine or doperidol.

a) Stop anaesthesia and administer 100% $O_{2.}$
b) Cool the patient externally and internally (Gastric, rectal, peritoneal lavage) to combat hyperthermia.
c) Insert bladder and CVP catheters.

Administer:

1. Intravenous procaine or procainaminde(Avoidlidocaine) to combat rigidity. These drugs decrease intracellular calcium transport.
2. Intravenous steroids.
3. Bicarbonate to control metabolic acidosis.
4. Glucose and insulin infusion to treat hyperkalemia.

5. Dantrolene sodium (IV – 2.5 – 10 mg per kg) may avert an attack. Action: excitation – contraction uncoupling by decreasing release of calcium from sarcoplasmic reticulum.
6. Preanasthetic oral dantrolene loading (4 – 8 mg/kg for 2 days with final dose 2 hours before anaesthesia) may avert or lessen the severity of an episode.

d) Monitor for renal failure after recovery

Myotonic Disorder

- This is a group of conditions (Usually hereditary) having in common clinical myotonia(delay of muscular relaxation after contraction). This is best seen in the clenched fist or in the orbicularis oculi muscles. Myotonia in all myotonic diseases is often aggravated by cold. It can be improved (fatigues) by repetitive activities, but sometimes this increases its severity (myotonia paradoxica).
- Myotonia can be elicited by percussion. This is usually demonstrated in the tongue or thenar muscles.
- EMG is characterised by high frequency repetitive discharges that initially increase in frequency and amplitude then rapidly diminish (Dive-bomber effect).
- Myotonia is of muscular origin and independent of motor nerve activity. The repetitive activity persists even though the motor nerve is sectioned or the neuro muscular junction is blocked with curare. It is believed to be a membrane defect (Hyper excitability) related to one abnormality of chloride (Myotonia congenita) or calcium (dystrophia Myotonica) conductance.
- It can be induced by drugs (i. e., Clofibrate), may appear as a remote effect of lung carcinoma, maybe found in thyroid dysfunction or adult acid maltase deficiency. The major forms of myotonic disease are

1. **Myotonia congenita (Thomsen's disease)**

A. Generalised non progressive muscular hypertrophy with muscle stiffness and weakness, relieved by exercise, occurring in two forms.

i. Autosomal dominant; Mild nonprogressive myotonia diagnosed in infancy.

ii. Autosomal recessive; later onset with subsequent distal atrophy and weakness.

B. EMG myotonic; CPK slightly elevated: biopsy fibre hypertrophy. Increased creatine tolerance.

C. May present with complaints of garbled speech after eating iced foods (associated with tongue myotonia induced by cold)

2. **Dystrophia myotonica (Steinert's disease**)

A. Autosomal dominant multisystem disorder (linked with the secretor gene) with poor congruence in affected family members, the commonest form of which usually becomes apparent in early adulthood. Expression is variable, and the disease is characterised by

i. Stellate cataracts and retinal alterations.

ii. Gonadal atrophy.

A) Impotence in males, chronic abortion in females.

iii. Faulty tolerance to carbohydrate (diabetic glucose tolerance curve), Defective insulin metabolism.

1. Mild " diabetes " is common to many muscle diseases.

iv. Frontal and parietal alopecia(loss of hair) in males.

v. Thyroid dysfunction.

vi. Cardiac conduction defects sometimes requiring demand pacemakers. Stokes – Adams attacks are common.

vii. Impaired pulmonary function. Pickwickian syndrome. Alveolar hypoventilation (night sweats, nightmares)

viii. Progressive psychosocial deterioration with fall off of higher intellectual functions. Paranoid tendency. "belle indifference", " whining dependence" and depression (which may respond to tricyclic antidepressant treatment)

ix. Cerebral ventricular dilatation.

x. Skull abnormalities, including hyperostosis crania. Decrease in sella turnica size, prognathism, hyperostosis frontalis interna, and enlargement of the paranasal sinuses.
xi. Lugubrious facies with ptosis. Thin, haggard, expressionless face. Transverse smile, hollow temples and cheeks. Sternocleidomastoid(particularly clavicular head) weakening, leading to swan neck.
xii. Temporal muscle wasting; myotonic lid lag.
xiii. Distal muscle weakness, especially in the forearms and tibialis anterior muscles. Patient may trip because of weakness, and in attempting to regain balance, provoke a myotonic response that causes a fall. It is the weakness (dystrophy), not the myotonia that troubles these patients the most.
xiv. Percussion and effort myotonia.
    a. Hand (slowness in grip release)
    b. Tongue (dimpling on percussion)
    c. Thenar eminence (contracture on percussion)
    d. Spasm of globe elevators (after forced eyelid closure with sudden release).

NOTE: Myotonia persists after nerve section, block, or curarization. It is increased by cold, fatigue or sudden stress. It tends to lessen and sometimes disappear in the later stages of the disease as muscular weakness advances.

i.Dysphagia (late) because of pharyngeal myotonia and dysarthria secondary to tongue myotonia.

ii. Smooth muscle disorders of lower GI tract (megacolon).
iii. Increased incidence of gall bladder disease.
iv. Sometimes a high frequency hearing defect.
v. Neuronal heterotopias.
vi. Nasal speech (because of pharyngeal muscle weakness)
vii. CPK may be slightly elevated: EMG myotonic: Nerve conduction (Motor and sensory) may be slowed; muscle biopsy – many internal

nuclei appearing in long chains on longitudinal section, sarcoplasmic masses, ring fibres, selective type 1 fiber atrophy.

viii. Lab tests

a) Low igG level (hypercatabolized) : low urinary creatinine; may have low serum uric acid

b) ECG abnormalities

c) Low basal metabolic rate.

Treatment of myotonia.

1. Phenytoin, 100mg t.i.d, decreases sodium influx during membrane excitation.
2. Acetazolamide, 125 – 500mg/day, promotes kaluresis rendering muscle more resistant to depolarisation.
3. Quinine, grains 5 t.i.d, stabilizes membrane
4. Procainamide, 0.5 to 1 g q.i.d, stabilizes muscle membrane but may impair cardiac cinduction and can cause a lupus like syndrome.
5. Steroids.

A. Congenital (neonatal) dystrophia myotonica

1. Severe generalized hypotonia at birth.
2. Facial diplegia with sucking and breathing difficulty.
3. Bilateral talipes early and vigorous orthopaedic attention.
4. Frequent hydramnios in mother.
5. Mental retardation
6. Electrical and mechanical myotonia observed later.
7. Characteristic inverted V configuration to upper lip (Shark mouth)
8. Dismaturation almost always inherited from myotonic mother.
9. Muscle biopsy – maturational arrest at various foetal developmental stages.

3. **Paramyotonia congenita (VanEulenberg)**

a. Autosomal dominant condition manifest at birth by mild myotonia of face and hands, aggravated by cold, with tendency to muscle hypertrophy. Maybe due to temperature dependent anomaly in sodium conductance.
b. Patient muscle stiffness may be increased or reduced by exercise
c. May suffer episodes of flaccid weakness similar to the periodic paralysis.
d. Lid lag may be elicited (also found in myotonia congenita and in hyperthyroid myopathy).

NOTE: Clinical myotonia as an ancillary sign maybe found in Schwartz Jampel syndrome. It can also be seen in myxedma, hypokaelemic paralysis, and after treatment with a variety of drugs interfering with muscle membrane lipid metabolism. Electrical myotonia maybe noted in acid maltase deficiency and denervation.

Endocrine Myopathies

Myopathy can accompany a variety of endocrine disorders. These usually occur in adults. The onset of weakness is insidious. Proximal muscles are predominantly affected. CPK is elevated, creatine urea is present, and the EMG shows myopathic characteristics. However, there may be indications of neuropathic causation. Management of the primary disorder consists of organ specific treatment.

1. Thyroid myopathies.
   A. Hyperthyroidism
      I. Bulbar and EOM can be involved in severe thyrotoxicosis (this may be myasthenic). Lid lag may be seen.
   B. Hypothyroidism
      I. Muscle spasm and cramps can occur.
      II. Delayed relaxation of ankle reflex

III. May find electrical myotonia

2. Parathyroid disorder

A. Hypoparathyroidism

I. Tetany with carpopedal spasm.

B. Hyperparathyroidism and osteomalacia

I. Proximal weakness.

II. Muscle tenderness and aching.

III. EMG signs of denervation.

3. Pitutary and adrenal disorder

A. Hypoadrenalism(Addison's Disease).

I. Fatiguablility and muscle cramping

II. Proximal wasting

III. Periodic episodes of hypokaelemic weakness

B. Hyperadrenalism (Cushing's Syndrome)

I. Proximal weakness and wasting of insidious onset

4. Steroid myopthay.

I. This non specific proximal muscle weakness is seen with the administration of steroids, specially the halogenated compounds (triamcinolone, dexamethasone). May be due in part to epinephrine suppression, which blocks phoshporylase activation. Can prove difficult to diagnose, especially in the case of an inflammatory myopathy under treatment with glucocorticoids.

II. Lab diagnosis

A. CPK maybe normal

B. Increased creatineureas (in presence of normal or low serum enzyme level)

C. EMG – short duration polyphasic motor unit action potentials.

D. Type 2 atrophy on biopsy (versus inflammatory necrosis in polymyositis).

E. Weakness (usually in large antigravity postural muscles of lower extremities) may be dose related and develop rapidly.

F. Muscles often tender to palpation.

G. Other signs of hypersteroidism commonly present

i. Moon facies
ii. Increase in adipose tissue
iii. Acne vulgaris, diabetes.
iv. Osteoporosis (with vertebral compression fracture).
v. Hyper tension, psychiatric disorders.

H. Improvement with discontinuation of steroid medication.

5. Acromegaly

A. Early muscle hypertrophy followed by late proximal weakness

6. Hyperaldosteronism

A. Periodic attacks of hypokalemic weakness.

Nutritional and drug induced Mypoathies

2. Protein deprivation
3. Osteomalacia
4. Alcoholic myopathy

A. Acute

i. After heavy drinking bout
ii. Sudden onset of muscle pain with swelling and weakness, typically in the large appendicular postural muscles. CPK markedly increase (even modest alcoholic intake causes some increase in serum CPK.
iii. Muscle can be swollen and tender.
iv. Necrotizing myopathy (selective type II atrophy with excess lipid and glycogen in fibres suggesting a metabolic pathway inhibition) resulting in:
a) Myoglobinuria
b) Renal failure which requires supportive treatment.

B. Chronic

i. Slowly progressive limb-girdle weakness. Most of the effects of chronic alcoholism are due to vitamin deficiencies, particularly of vitamin B_1.

5. Other drugs that can cause neuromuscular pathology
    A. Vincristine – weakness.
    B. Diazacholesterol – myotonia
    C. Clofibrate –Cramping
    D. Penicillamine – inflammatory myopathy.
    E. Diuretics, licorice, purgatives – hypokalemic paralysis.
    F. Chloroquine, heroine – subacute painless myopathy.
    G. Cimetidine, lithium – mild weakness.

Inflammatory Myopathies

- These disorders are thought to be due to a viral or autoimmune mechanism.
- Characterized by symmetrical proximal muscle weakness often accompanied by muscular pain and tenderness.
- They occur more frequently in blacks.
- Dysphagia is sometimes present.
- Involvement of facial or EOM is rare.
- Pseudohypertrophy occasionally occurs.
- The deep tendon reflexes maybe absent, normal, hyperactive.
- The heart can be involved.
- Muscle atrophy with contracture and calcinosis are seen late in the course of the disease.
- CPK is raised as well as ESR and WBC (50% of the cases).
- Elevated ANA, positive latex test (50%), and increase in serum gamma globulins alpha 2, and IgM have also been reported.
- EMG shows polyphasic, brief, small motor action potentials with spontaneous fibrillations and positive sharp waves, insertional irritability, and bizarre high frequency repetitive discharges.

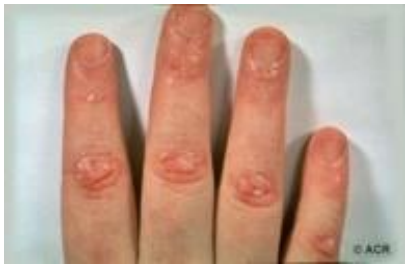
- The muscle pathology includes inflammatory cellular infiltrates (principally lymphocytes), segmental necrosis, de and re generation (necrosis, vacuolization and phagocytosis) and increase of endomysial connective tissue.
- Perifascicular atrophy of both type l&ll fibres is present. This pattern is probably related to ischaemic myopathy of fibres adjacent to perimysial collagenous septae and is more common in dermatomyositis. All of these biopsy findings are usually scattered.
- Polymyositis is the diagnostic label given to a non-hereditary inflammatory myopathy.
- Where a skin rash is present, the term dermatomyositis is used.
- These conditions can present acutely or run a subacute, relapsing, or chronic course.
- There are both childhood and adult forms.
- A bimodal age distribution between ages 5 and 15 and then between 50 & 60 years, has been reported.
- Polymyositis is as common as scleroderma, and half as common as systemic lupus erythematosus. Its incidence is 5 – 8 new cases per million people each year.
- Inflammatory myopathy in childhood can be confused with DMD.

1. **Idiopathic polymyosistis.**
    A. Pain and stiffness more marked in upper limbs, weaknesses in lower, but one third of patients present with a non muscular first symptom. May also mimic DMD almost completely.
    B. Cervical flexors involved early.
    C. Dysphasia, dysphonia, arthralgia, and Raynaud's phenomenon may occur. Arthritis, usually of the hands, may occur in the patients with chronic disease. Instability of the thumb and the interphalangeal joint may require fusion.
    D. Systemic symptoms (fever, weight loss, lethargy) are common
    E. Cardiac involvement has been reported.

2. Idiopathic dermatomyositis.

A. Female : male ratio 2:1

B. Less common than polymyositisin adults



C. More malign disease than polymyositis.

D. Myopathy similar to polymyositis but rash present.

a. Violaceous butterfly facial distribution.

b. Heliotrope rash of eyelids.

c. Periorbital oedema.

d. Erythema, scaly rash, or telangiectasia of forehead, neck, shoulder, chest, back, elbows or knees. Gottron's papules on the knuckles.

e. Late skin and subcutaneous nodular calcifications, mostly in children and correlated with a favourable outcome.

E. Childhood type.

a. Not associated with neoplasm.

b. Skin lesions can be florid or minimal

c. Severe malaise and listlessness

d. Usually insidious onset.

e. Systemic involvement

- Arthralgia also, calcinosis of subcutaneous tissue and interstitial tissues or muscle.
- Hepato and splenomegaly.
- Pneumonitis – pulmonary fibrosis.
- GI ulcerations secondary to vasculitis.

- Cardiac involvement.
- Renal involvement
- Necrozingvasculitis and other angiopathic features.
- Muscular contracture

f. C-reactive protein normal (elevated with infection), CPK maybe normal.

3. Polymyositis and collagen vascular disease. Both dermatomyositis and polymyositis may complicate other connective tissue disorder (" overlap syndrome "). Either maybe found in association with:
    a. Rheumatoid arthritis.
    b. Systemic lupus erythematosus.
    c. Scleroderma.
    d. PeriarthritisNodosa.

. **Inflammatory myositis associated with neoplasm**.

A. Many autoimmune diseases are associated with an increased incidence of neoplasia. Dermatomyositis with an onset after 40 years of age (particularly in a male) is often accompanied by a malignant disease.
B. All types of malignancy may occur. Carcinoma of lungs, breast, ovary, uterus, prostate, and stomach are most frequent.
C. In most cases, manifestations of inflammatory myopathy precede those of the tumor.
D. Treatment of the neoplasm may have favorable effect on associated muscle and skin lesions.

V. Miscellaneous diseases that can cause secondary inflammatory myopathy.

- Polymyalgia rheumatica.
- Eosinophilic fasciitis
- Trichinosis
- Sarcoid
- Cyscticercosis

Treatment

A. Steroids
    1. High doses for three months
        a. Avoid fluorinated steroid (dexamethasone and triamcinolone) as they more frequently induce steroid myopathy.
        b. Adults: 50-100 mg/kg/day.
        c. Children: 1-2 mg/kg/day
    2. Schedule
        a. Initial daily dose
        b. Can switch to alternate day dosage two to four weeks after initiating treatment
        c. Observe patient closely for complications.
            i. Acute complications
                1) Edema
                2) Weight gain
                3) Hypertension
                4) Diabetes
                5) GI hemorrhage
            ii. Chronic complications
                1) Cataracts and ocular hypertension
                2) Infection and poor wound healing
                3) Psychosis
                4) Osteoporosis (Fractures)
                5) Delayed growth
                6) Myopathy
                7) Cushinoid features
                    a) Moon facies
                    b) Central obesity
                    c) Buffalo hump
                    d) Facial hirsutism
                    e) Abdominal and thigh striae

8) Spontaneous tendon ruptures

a) Acne and thinning of skin

d. Necessary adjuncts to steroid therapy include:

i. Low sodium, high potassium intake.

ii. Antacids.

iii. High-protein, low carbohydrate diet.

e. Can reduce dose when clinical response has occurred.

1) Reduce very slowly.

2) Titrate treatment with serial CPK determination, but remember that CPK normalization or increase may precede clinical remission or exacerbation by at least several weeks. EMG can also be used to monitor disease activity (fibrillation potentials indicate active disease)

3) Increase dose slightly or return to daily dosage if symptoms worsen or CPK increases.

f. Recovery from dermatomyositis or polymyositis is slow (although spontaneous remissions can occur) and, although some patients recover completely (the overall survival rate of both treated and untreated patients is 80% after five years, although treatment seems to improve strength and lessen discomfort), minimal supportive steroid treatment maybe necessary for years in others. However, in children, tapering of the dose can usually begin earlier (persistence of skin rash is not indicative of active disease), and steroid treatment can often be discontinued within three to six months.

B. Immunosuppressive drugs

1. Initiate when no response to three to six months of steroid treatment. These drugs have teratogenic effects.

a) Methotrexate, 15-30mg/kg/day, may cause severe ulceration stomatitis and leukopenia

b) Azathioprine, 3mg/kg/day, can cause drug fever.

c) Cyclophosphamide, 2mg/kg/day, may produce hemorrhage cystitis.

2. Plasmapheresis has been used as an adjunct to immunosuppressive therapy.

C. Other measures
   1. Physical therapy to prevent or treat contractures
   2. Night splints as indicated
   3. Topical steroids and Burow's solution soaks for skin lesions.
   4. Diphosphonates for calcinosis in dermatomyositis.

D. Factors decreasing survivorship (most deaths occur in first two years after the diagnosis).
   1. Age greater than 50 years.
   2. Black race
   3. Extreme weakness (Dysphasia)
   4. Pneumonitis
   5. Neoplasm
   6. Associated collagen disease

MISCELLANEOUS

I. Prader-willi syndrome (H_3O syndrome-hypotonia, hypomentia, hypogonadism, obesity). Chromosome 15 breakage/translocation has been demonstrated in several cases.
   A. Patients present with typical appearance of fair hair, blue eyes, high forehead, small, almond-shaped eyes.
   B. Diabetes develops in adolescence.

C. CPK, AMG and biopsy are all normal.
D. Higher incidence in males.
E. Marked hypotonia at birth-floppy infant.
F. Compulsive eating beginning at early childhood.

II. Arthrogryposis (curved joints)

A. Symptom-complex, not a specific diagnostic entity.
B. Characterized by multiple joint contractures secondary to immobility of limbs in utero.
C. Maybe myopathic or neuropathic.
D. Must differentiate from congenital muscular dystrophy and spinal muscular atrophy.
E. Joint rigidity is secondary to fibrous ankylosis.
F. Fixed deformities can be surgically improved by aggressive soft tissue release.

III. Stiff man syndrome

A. Sustained repetitive activity of muscle fibers affecting both sexes, usually in adult life.
    1. Maybe produced by tightness of neck and chest muscles.
    2. Results in uncontrollable contractions, mostly of musculature of the limb girdles, but any and all voluntary muscles maybe involved.
    3. Dyspnea, dysphagia, and facial grimacing may occur.
    4. The limbs are held in rigid distorted position and the spasms are painful.
    5. Stiffness disappears during sleep (EEG shows less REM sleep than normal) and general anesthesia, and maybe elicited by a variety of stimuli (active or passive movement, emotional stress).
B. Physical examination reveals occasional hyperreflexia and extensor plantar response.
C. EMG shows a sustained interference pattern but is otherwise normal.
D. Muscle spasms are abolished by curare peripheral nerve block and spinal anesthesia.
E. Proposed etiology.

1. Gamma system overactivity.
2. Lack of inhibitory feedback to anterior horn cells.
3. Catecholaminergic- GABA system imbalance.

F. Treatment- high dose diazepam (upto 300 mg/day) or baclofen.

NOTE: Neuromyotonia (continuous muscle fiber activity) is yet another condition of an abnormal muscle activity. It is characterized by myokymia secondary to brief tetanic contractions of muscle fibers. This can be diagnosed by EMG. It may be simply annoying or severe enough to cause rigidity and deformity. Pathology is apparently in the peripheral nerve. Treatment is with diphenyldantoin or carbamazepine.

IV. Inclusion body myositis.

A. Progressive painless limb girdle weakness.
B. Normal mildly elevated CPK.
C. Unresponsive to steroids or immunosuppressive drugs.
D. Biopsy.
    1. Myopathic changes.
    2. Mononuclear inflammatory infiltrates.
    3. Vacuoles lined with basophilic granules in muscle fibres.

Myopathy may attend a variety of other diseases such as collagen vascular disorders (LE, rheumatoid arthritis, polyarteritis nodosa), sarcoid, carcinoma, Marfan's syndrome.

Differential diagnosis of systemic myopathy based on age of onset

Myopathies presenting at birth:- None as systemic causes; mainly hereditary

Myopathies presenting in childhood:-

Inflammatory myopathy – dermatomyositis, polymyositis (rarely)

Infectious myopathies

Endocrine and metabolic disorders – hypokalemia, hypocalcemia, hypercalcemia

Myopathies presenting in adulthood

Inflammatory myopathy – polymyositis, dermatomyositis, inclusion body myositis, viral (HIV)

Infectious myopathies

Endocrine myopathies – thyroid, parathyroid, adrenal, pituitary disorders

Toxic myopathies – alcohol, corticosteroids, narcotics, colchicines, chloroquine

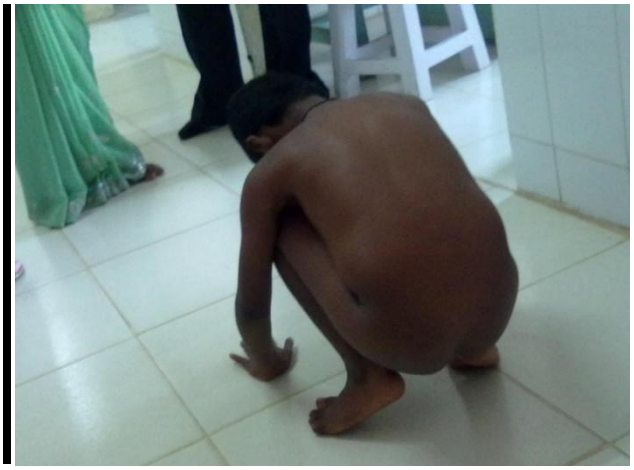
Critical illness myopathy

Metabolic myopathies

Para neoplastic myopathy

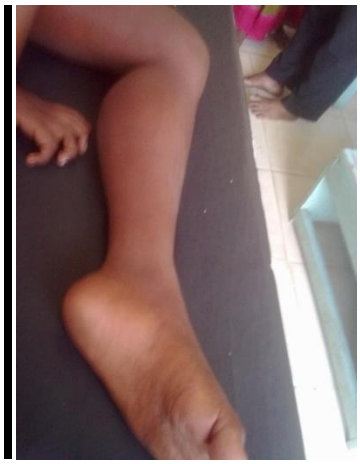
PATHOMECHANICS

Though specific therapy for a variety of neuromuscular conditions is covered, Duchenne muscular dystrophy with its rapidly progressive course and ultimate severe disability, is used as a model for analysis of those force imbalances that shape skeletal deformity. Comments concerning pathokinetic mechanisms as well as physiotherapeutic management can to a large degree ,be applied appropriately to any of the other muscular dystrophies.

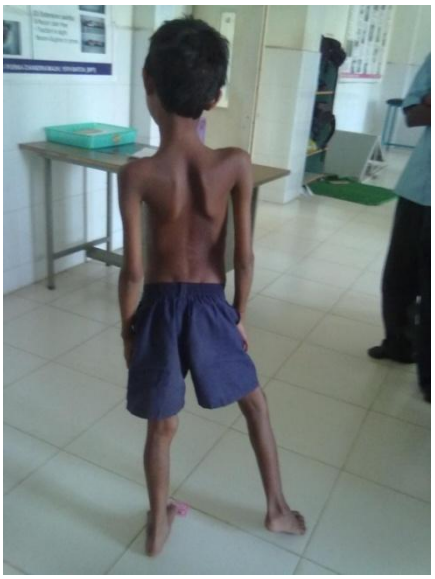


- The mechanical efficiency of the skeleton probably doubles as the body matures. From the new born to the adult skeletal mass increases 20 times and muscle mass increases 40 times.
- The axial musculature, and that of the limb girdle muscles which are first formed in the embryo, are initially and most severely involved in DMD.

- Most major axial or appendicular musculature loose at least 30%-40% of their original strength before clinical weakness manifest.
- Some patients from 5-7 years of age show some improvement which can be explained by the process of normal development outstripping progression of the disease during this period.
- Spurt muscles, such as the biceps brachii, tend to atrophy earlier in myopathy than shunt muscles, such as the brachioradialis.
- Mal alignment of weight-bearing joints can aggravate the effect of muscle weakness on ambulation.
- Muscles shortened by contracture develop less maximal tension than they could otherwise, they also fatigue more rapidly.



- All skeletal muscles are affected in DMD.
- Weakness is first noted and most severe in those antigravity muscles serving a postural role. The work density of a muscle determines its rate and degree of degeneration. Those muscles requiring the longest periods of sustained activity degenerate first. Musculature developing first phylogenetically, even if its original function is lost, is the earliest to degenerate in disease, which leads to alteration of the dynamics of postural maintenance.



- "Hanging onto" ligaments requires little more energy than a properly aligned position. It may be effective, but it is hardly efficient because it is a posture that can cause pain due to stress. It is not a position from which one is able to move with dispatch. It leaves a narrow margin of safety, since joints are forced and held at their limit in one direction.

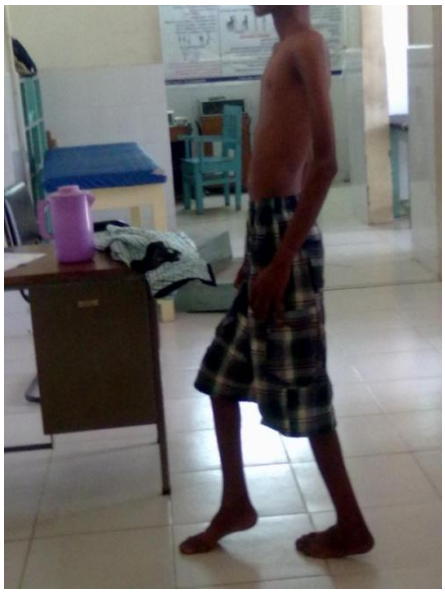
- As weakness progresses, gravity, always in force, causes contracture, fatigue, and eventually inhibits the upright posture.
- Although physiologically at rest, muscle is physically in a state of tonic stretch. Muscle spindles protect against overstretch. Loss of its deep tendon reflex marks the regression of a muscle from a kinetic to a static stretch.

POSTURAL DYNAMICS

Wasting in DMD bears a direct relationship to muscular function. The skeletal segments of the body are moving levers, powered by muscles monitored through feedback system. Vertical bodily displacements are against gravity and as a rule require more energy and superimpose more stress than horizontal movements.

- Work hypertrophy is seen in the antigravity muscles maintaining postural alignment. Such postural overwork (hypertrophy) weakens the dystrophic muscle.For e.g **Psoas**(postural) is more severely involved than iliacus(non postural),Clavicular head of **sternocliedomastoid** suffers more than the sternal component.
- Normally the muscle spindles protect muscles against overstretch. As the disease advances, reflex function is lost (the muscle spindle becomes “detuned”) which marks the regression of a muscle from kinetic to a static state and makes the muscle vulnerable to ordinary strain.

- Finally , the muscle sub serves only a passive supportive role,
    a) Thus, dynamic (kinetic) stability degenerates to passive (static) stability, which finally weakens to instability.
    b) With decline in elasticity and reflex contractility, muscle is now vulnerable to deforming forces imposed by postural or supportive traumatic stress. Such stress can be active, such as that put upon gastrocnemius during overwork, and like the stretching of pectoralis major in maintaining torso balance.



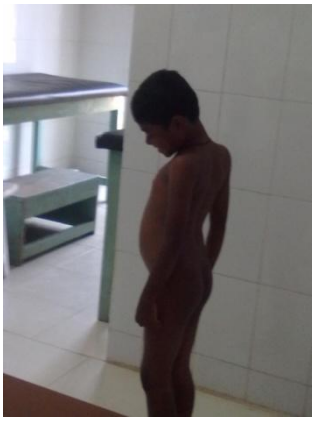
- The Duchenne dystrophic cannot control momentary imbalance imposed by competing demands for both knee and hip stability. Such adjustments are increasingly difficult as weakness and contracture progresses. The trunk represents 70% of the body's weight. Steadying it over the pelvis becomes a progressively difficult task. Postural status regresses from stability to merely balance and finally to imbalance and instability.
- Muscular dystrophy patients lose the ability to control the momentary imbalances that occur in normal locomotion. This is due to progressive (a) weakness (b) Contracture (c)

and loss of muscle spindle proprioceptive function, resulting in an attempt to preserve as minimal a level of energy expenditure as possible through exaggerations of motion at unaffected, or less affected body levels.

- Three processes contribute to the deformities of muscular dystrophy-
    a) Muscle weakness
    b) Muscle imbalance
    c) Specific muscle contractures secondary to gravity and compensatory postural habitus. Often contracture is asymmetrical and less in dominant limb because of relative increased activity.

BIOKINETICS- Clinical Correlation

- In DMD ,hip flexors, TFL, and triceps surae develop ambulation limiting contractures.
- Contractures are seldom symmetrical and seem to be greater on the non dominant side.
- Quadriceps insufficiency is the key factor in gait deterioration.
- The earliest postural change in the lower extremities is an increase in lumbar lordosis secondary to gluteus maximus weakness. Hip extension at this time is largely performed by the hamstrings muscle.
- Some changes in joint lever systems occur. For instance, the hip is a first class lever with force exerted by the abductors over the fulcrum of the articulated femoral head to balance body weight. As hip abductors weaken, hip hikers (quadratuslumborum) are called upon to elevate the hip during swing, thus creating a third class lever, where power is sacrificed for a wider arc of movement.



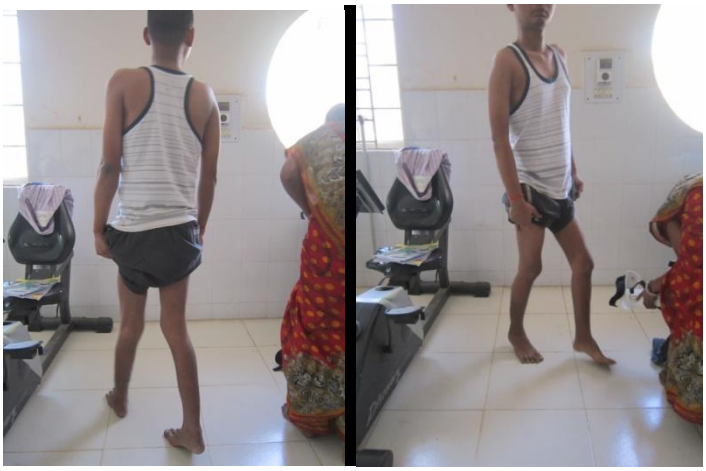
- With progression of quadriceps weakness, hip adductors are called upon to assist knee extension. As contracture increases, the base of support decreases, pelvic femoral balance is unstabilized, and the patient can no longer utilize normal postural mechanism for efficient balance. He must walk with a wide base characterized by:
    - Equinus posturing caused by forward shift of the COG ,which now falls anterior to a point 60% of foot length as contrasted with 40% in the normal.
    - Heel varus
    - Knee flexion, in an effort to lower the COG for better balance, aggravated by both tensor fascia and hip flexion contractures.
    - Hip flexion
    - Hip abduction.

Exaggerated lumbar lordosis and widened base

- Exaggerated lumbar lordosis is a functional deformity noted early as the patient attempts to compensate for pelvic force imbalance secondary to weakened hip extension, accompanied by hip flexion contracture. Abdominal muscle weakness allows the pelvis to drop anteriorly, augmenting this deformity.

- In lordosis, the COG is shifted posteriorly. The child adjusts by rising on the balls of his feet and ultimately onto his toes. Some equinus is necessary to compensate for the displacement of the CG as well as weakness of the quadriceps.

- Abdominal and low back extensor weakness contribute to this awkward and effortful posture as loss of scapular stabilizer strength draws the shoulders forward, requiring exaggerated lumbar lordosis to achieve torso balance.



- Hips are further abducted in an effort to widen the BOS so that the line of gravity will fall within the BOS.

- Several biarticular muscles of the lower extremity, functioning within a closed kinetic chain, may reverse their usual roles in response to the antigravity needs of this postural crisis.
- As the ankle is held in plantar flexion, the narrow portion of the talus is brought into the mortise, rendering this joint vulnerable to those forces shaping a rotatory deformity.
- The centre of hip rotation shifts medially during standing. Psoas major functions as an external hip rotator in swing phase and an internal rotator during stance. As the disease progresses, the lower extremities are progressively externally rotated to widen the BOS. A small subset of children instead of rotating hip out, exhibit hip joint valgus and ante version with internal rotation of legs. This effectively medially rotates the knee joints out of the plane of flexion buckling, and the hip extensor force of the adductor magnus and hamstrings can assist knee extension. The adductor-hamstring extensor response is apparently facilitated through reflexes of the gait pattern rather than being called on as prime movers.
- Ultimately the head is used as an adjustment force. As the trunk is maintained in extension, the neck is held flexed.
- Hip extension ability finally determines whether or not a patient will walk.

Diagnosis of muscular dystrophy

The clinical history is essential in identifying the presence of a myopathy and narrowing down the differential diagnosis. In particular, the patient should be questioned about medication and recreational drug history (especially alcohol), chemical exposures, exercise intolerance, childhood development, and family history of muscle disease or developmental motor delay.

- **Clinical examination**:

Done by doctor/physician. Child will be asked to run, jump and climb stairs and after this he will be asked to sit or get up from floor. If he puts his hands on the knees and pushes himself up, it is a sign of muscular dystrophy known as Gower's sign.

Laboratory Testing

The following laboratory tests may be used to evaluate patients with myopathies:

- **Blood test**:

Blood sample is taken and checked for CPK level (Creatine PhosphoKinase is a chemical substance released in blood by a damaged muscle. Usually in muscular dystrophy, the level is 10 times more than the normal.This testing, which can indicate muscle damage, includes elevations in aldolase, lactate dehydrogenase (LDH), and liver function enzymes. A screening panel of laboratory tests may also be obtained to rule out more common causes of myopathy, which are listed in Box 2. In cases suspected to be a primary inflammatory myopathy, specific autoantibodies can be considered to determine the prognosis and rule out associated conditions. For example, the presence of anti-Jo antibody in **dermatomyositis** predicts a superimposed interstitial lung disease. In addition, these patients should also be evaluated for an underlying systemic autoimmune disease with an extensive autoimmune panel and angiotensin-converting enzyme (ACE) levels. In myopathies that are accompanied by polyneuropathy, renal involvement, and a restrictive cardiomyopathy, immunofixation electrophoresis studies in the serum and urine should be considered to rule out the possibility of **amyloid** disease.

Normal CPK levels:

Males: 38 – 174 units/L

Female: 96 – 140 units/L

- **Genetic testing**

Genetic testing is available for some inherited myopathies. These are listed in Table 2. . Genetic testing for DMD/BMD is commonly available in India. For LGMD or FSHD it is available in very few centers. It is important for several reasons to have the genetic confirmation of the diagnosis as it will help to determine if the patient is eligible for any clinical trials and also helps the family to take decision regarding prenatal diagnosis and future planning of pregnancies.

- Carrier analysis: In few cases, the mother is the carrier of the faulty genes which means that the mother must have passed the faulty gene or disease to the child. However, the mother is not always a carrier. It could be a fresh mutation. If mother is found to be the carrier, genetic counseling should be advised for other female relatives of the child.

    - **Muscle biopsy**

    Under anesthesia, a small piece of muscle is taken from the bulkiest muscle and examined under a microscope. Histopathologic examination of muscle may be helpful in determining the specific type of muscle disease, especially in patients with a suspected inflammatory or infectious myopathy. Selecting the optimal muscle to biopsy is very important because factors such as severe weakness and technical artifacts can hamper an accurate histologic diagnosis. The ideal muscle that should be sampled is one that is clinically involved but still antigravity in strength, because more-severe weakness can lead to unhelpful, nonspecific findings of fibrosis. Also avoid muscles that have been examined by an EMG should be avoided because the needle portion of the electrical study might have caused local damage, which can result in spurious findings. Common biopsy sites include the **biceps** and **deltoid** muscles in the upper extremity and the **quadriceps** and **gastrocnemius** muscles in the lower extremity.

    - **The electromyogram** (EMG)

    EMG is an electrical study of the nerves and muscles that plays an important role in confirming the presence, duration, and severity of a myopathy. A thin-needle is inserted through the muscle to be tested and electrical activity is studied. This also can give a

clue whether the muscle is damaged or not.The study can also disclose special findings such as myotonic potentials. This is the electrical equivalent of clinical myotonia, which is manifested as impaired relaxation of muscles after forceful contraction; for example, patients cannot release objects from their grip. Myotonic potentials have the characteristic sound of a dive bomb on EMG and can help point toward the diagnosis of myotonic dystrophy when found in the appropriate muscles.Although integral in the evaluation of a myopathy, the EMG can be normal in mild myopathies, steroid myopathies, and a number of metabolic myopathies. Therefore, it is important to remember that a normal EMG does not exclude the presence of a myopathy.

- ***Ischemic Forearm Test***

A traditional test used in the evaluation of a suspected **metabolic myopathy** is the ischemic forearm test. This is performed by obtaining baseline serum ammonia and lactate levels taken from the forearm. The patient then exercises that arm for 1 minute, after which repeat serum lactate and blood ammonia levels are measured. This is repeated at several intervals (1, 2, 5, and 10 minutes). In normal muscle, the resultant ischemia causes a 3- to 5-fold rise in lactate levels. In contrast, patients with glycogen storage disorders demonstrate no change in lactate levels after exercise.

- **MRI or Magnetic Resonance Imaging**:

MRI is a painless and non surgical procedure which is done to examine the muscle quality, size or any abnormalities in the size. It monitors the fatty replacement of the muscle tissue as well as progression of the disease.

Box 2 Laboratory Evaluation for Suspected Myopathy

Confirm the Presence of Muscle Disease

Creatine phosphokinase
Aldolase
Liver function tests
Lactate dehydrogenase levels

Identify Etiology

Complete blood count with differential
Complete metabolic panel
Thyroid function tests
Parathyroid hormone level
Sedimentation rate
C-reactive protein and antinuclear antibody panel

Suspected Inflammatory Etiology

Myositis-specific autoantibodies
Anti–double stranded DNA antibody
Anti-Scl 70 antibody
Anti-SSA and SSB antibodies
Anti-ribonucleoprotein antibody
Rheumatoid factor
Anti-PM1 antibody
Angiotensin-converting enzyme levels

Suspected Mitochondrial or Metabolic Myopathy

Serum lactate, pyruvate, ammonia, coenzyme Q10 , myoglobin levels
Ischemic forearm lactate test
Carnitine levels

Urine analysis: Myoglobinuria indicated by positive urine analysis with few red blood cells on microscopic evaluation levels of electrolytes, calcium, and magnesium

Suspected Amyloid Myopathy

Immunofixation electrophoresis of monoclonal proteins in serum and urine

Table 2 Commercially Available Genetic Tests in Diagnosis of a Myopathy

Myopathies with Known Genetic Defects	Gene Abnormalities	Pattern of Inheritance
Duchenne muscular dystrophy	Dystrophin gene	X-linked recessive
Becker muscular dystrophy	Dystrophin gene	X-linked recessive
Emery-Dreifuss muscular dystrophy	Emerin gene	X-linked recessive
Limb girdle muscular dystrophy	Lamin A/C Calpain Dysferlin Fukutin related protein	Some are autosomal dominant and others are recessive
Facioscapulohumeral muscular dystrophy	*D4Z4* deletion	Autosomal dominant
Oculopharyngeal muscular dystrophy	GCG repeat expansion in poly A binding protein 2 gene	Autosomal dominant
Myotonic dystrophy 1 and 2	*DMPK* gene for type 1	Autosomal dominant

	CNBP (ZNF9) gene for type 2	
Mitochondrial myopathy	Specific point mutation analysis for diseases like MELAS *POLG1* sequencing for MERRF available Southern blot analysis for mtDNA deletions and mtDNA sequencing	Maternally inherited. But other can be inherited as autosomal dominant or recessive disease
Amyloid myopathy from familial causes	Transthyretin mutation	Autosomal dominant
Statin myopathy (predictor of increased susceptibility)	*SLCO1B1* gene	Unknown

MELAS, mitochondrial myopathy, lactic acidosis, and strokes; MERRF, myoclonic epilepsy and ragged red fibers; mtDNA, mitochondrial DNA.

What next after the diagnosis?

Once the diagnosis is confirmed it is important that the patient/ parents approach an appropriate team of specialists who can guide in the management of the condition. The team may comprise of a physician, neurologist, pediatrician, orthopedic surgeon, neurosurgeon, physiotherapist, occupational therapist, speech therapists, social worker, dietician and psychologist. These specialists can give proper advice regarding the outcome and treatment options.

Management

The treatment of a myopathy is dependent on its etiology and can range from supportive and symptomatic management to therapy for specific conditions. Such treatments may include the following:

- Supportive: Management of airway, breathing, circulation; hydration; intensive care management may be needed in some cases. Patients should also be monitored over time for complications related to kyphoscoliosis or involvement of cardiac, respiratory, or bulbar muscles.

- Drug therapy(Steroids are the mainstay of the treatment, the most commonly used steroid is Prednisolone,this has a beneficial effect on muscle strength and functioning over short term especially in the ambulatory phase). In patients with mitochondrial myopathy, small studies have shown some benefit with creatine monohydrate (5-10 g/day), but no consistent benefit was seen with coenzyme Q10 replacement. Myopathies that result from **systemic diseases** are best treated by correcting the underlying endocrine or electrolyte abnormality. In patients with **drug- or toxin-induced rhabdomyolysis**, withdrawal of the offending agent is key. Control of the underlying infection is important for bacterial, parasitic, or spirochete-related myopathies as well as postinfectious inflammatory myositis. In HIV-related myositis, treatment with the combination of highly active antiretriviral therapy (HAART) and steroids may be beneficial.

In patients with **inflammatory myopathies** or those related to underlying autoimmune diseases, a number of immune-modulating medications may be used for treatment. Oral and intravenous steroids are most commonly used, with favorable results in most cases. Regimens of daily prednisone at a dose of 1.5 mg/kg per day or intravenous methylprednisolone at 500 to 1000 mg for 3 to 5 days are often used. Intravenous immune globulin (IVIg), methotrexate, azathioprine, and cyclophosphamide may also be helpful. Unfortunately, inclusion body myositis, though classified as an inflammatory myopathy, is typically refractory to immunosuppressant treatment and continues to progress, with prominent dysphagia and more generalized weakness over time. For patients who present with **rhabdomyolysis,** treatment is aimed at preventing kidney failure in the acute setting. Vigorous hydration with close monitoring of kidney function and electrolytes are paramount. In patients with an underlying **metabolic myopathy**, education about following a more moderate exercise program and avoiding intense exercise and fasting is necessary in preventing recurrent episodes. Measures that have been suggested to be helpful

include sucrose loading before exercise in some glycogen storage disorders and a low-fat, high-carbohydrate diet in patients with lipid storage disorders.

- Additives or nutritional supplements(Vitamin E ,coenzyme Q ,omega 3 fatty acid,etc have general protective effects, act as antioxidants,have effect on strengthening the cell wall.studies show that they support formation of new muscle cells to repair the injured muscle.However evidence is not clear on its protective effects in muscular dystrophy.

- Physical therapy
- Assistive devices and alternative techniques.(Equipment to help in eating ,drinking ,grooming, home modifications, orthoses and night splints make the persons more independent.
- Bracing

- Surgery, Tendon release surgery - for example, to prolong the ability to walk.

- Stem cell Therapy (The usefulness of this therapy has been proved in terms of functional improvements and slowing down the disease progression).
- Prognosis

This depends on the specific diagnosis. The primary disorders are incurable conditions with varied prognosis. Secondary myopathy may be corrected by treating the underlying cause.

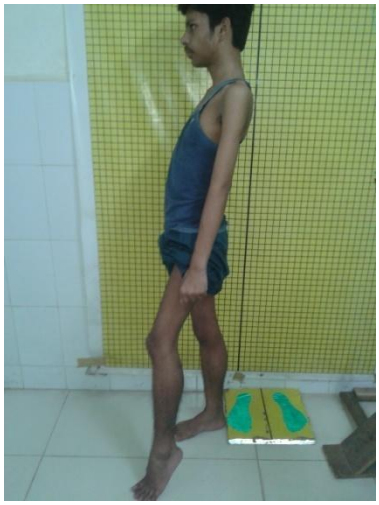
- Prevention

Genetic counselling is, in some of the most common myopathies such as Duchenne muscular dystrophy (DMD), the only intervention that can prevent disease. In general:

- ✓ Give genetic counselling early.
- ✓ Test early for carrier status where appropriate.
- ✓ Consider prenatal diagnostic testing where appropriate.
- ✓ Advances in molecular genetics may help in the future.

PHYSICAL THERAPY

UNDERSTANDING ENERGETICS



- As long as the patient can maintain the line of gravity behind his hips, in front of the knees , and within his base of support, he can stand upright.
- Gait requires body unbalancing through the coordinated activity of tibialis anterior, quadriceps, hip abductors and peroneal muscles, a process the Duchenne dystrophic patient finds difficult to perform.
- To execute the swing phase of gait, the hip must extend and the extensor muscles unload.
- The most severe contractures occur in postural muscles spanning two joints.
- Muscular weakness, tendon contracture, and mechanical mal posture contribute to ultimate deformity.

An outline of the biomechanical sequence

- leading to the typical dystrophic posture is as follows:

a) Hip extensor and shoulder stabilizer weakness
b) Hip flexor contracture, thrusting the trunk forward
c) Compensatory lumbar lordosis
d) Forward shift of centre of mass forcing patient to rise on toes, thus shortening ankle-to-toes lever arm and shifting centre of gravity forward.

e) Hip abduction to increase equilibrium by widening body's BOS.
f) Secondary TFL contractures.
g) External tibial torsion; thus, ankle and knee axes are no longer in the same plane.
h) Ankle varus.
i) Mild knee flexion to lower centre of mass and gain balance.
j) Progressive quadriceps weakness requiring to lock knees for stability.
k) With foot fixed in equinus and knee flexed, gastrocnemius and soleus can now act to extend knee.
l) True overwork exercise hypertrophy of calves.

- Generalized weakness makes it increasingly difficult to attain alignment stability when the trunk is balanced over unstable lower extremities.
- Propriceptive abilities are also affected.
- A slight weight gain or a period of several days of bed rest can decrease strength enough to impair ambulation. In its later stages DMD is a brittle disease, and the transition from moderately to severely impaired ambulation may be abrupt.
- Because of individual differences in weakness, contracture, weight, and motivation, age alone is a poor index of disease progression.
- The more disabled the patient, the more determinants of gait are lost, the more energy is required for ambulation, and the less efficient is the gait.

PHYSICAL THERAPY - ASSESSMENT

THE roles that the physical therapist plays in the management of the patient with muscular dystrophy are several.

The therapist monitors the assessment of specific muscle weakness, imbalance and contracture.

ASSESSMENT

Strength and range of motion: shoulders, hips, knees.

Contractures: hip flexors, TFL, and heel cord

Function: rising stairs, walking, etc.

- Muscle testing grades key muscles as to strength and range of motion of activated joints against gravity
- The patient's ability to perform a number of standard tasks is assessed, measuring time required and observing method employed to complete the task. Subtle alterations in method as well as slight changes in time needed for any given task objectively reflect changes in strength.
- The patient can be rated on a functional 10 point –step scale.

a) *Stage 1*, walks and climbs stairs without assistance(it takes 15 times as much energy to ascend a flight of ordinary stairs as to walk a level distance equal to the vertical height of the stairs).
b) *Stage2*, walks and climbs stairs easily with aid of railing
c) *Stage3* walks and climbs stairs slowly with aid of railing.
d) *Stage4* walks but cannot climb stairs.
e) *Stage5*, walk unassisted but cannot climb chair or get out of chair.
f) *Stage6*, walks only with assistance or only with braces
g) *Sage7*, in wheelchair, sits erect and can roll chair and perform bed and wheelchair activities of daily living.
h) *Stage8*, in wheelchair, sits erect but is unable to perform bed and chair activities without resistance.
i) *Stage9, in wheelchair, sits erect only with support, and able to do only minimal activities of daily living.*
j) *Stage10*, in bed, cannot perform activities of daily living without resistance.

The kinetic sequence of the above scale provides a treatment format for the physical therapy program.

a) In stages 1-3, the patient is ambulating independent. Passive stretch of early lower extremity contracture may be necessary by stage3. Functional activities of daily living and ambulation are sufficient active exercise for stages 1-3.
b) Between stages 5-6, lower extremity surgery is indicated because contracture leads to increased difficulty with anti gravity activities. Where contracture is minimal or absent, orthotic modifications or bracing alone may be sufficient to augment weakened knee extension and keep the patient ambulating. With fair quadriceps strength, the knee flexion moment can be decreased by an anteriorly places cushion(SACH) heel, or converted to an extension moment with an equinus(floor reaction) AFO
c) Ambulant patients in stage 5 and 6 should not avoid activity and use wheelchair, except when absolutely necessary and then for only brief periods of time.
d) Stage 7 should not be skipped as the patient is thus condemned to stage 10 immediately.
e) When stage 7 is reached, routine conditioning exercises are prescribed to retard disuse atrophy and maintain independence in wheelchair activities. Prophylactic treatment of scoliosis is also initiated at this time as well as a full program of respiratory therapy.
f) Obesity is usually a problem after stage 6.
g) The closer a patient is to stage 10, the more assistive devices he requires.

Explanation of the testing procedures

1. **Run 25 feet**

   Both feet off the ground at one time.

2. **Walk 25 feet**
   a. Independent – no assistance from mechanical aids
   b. Short leg braces- test items 3, 4 and 5 with braces also.
   c. Long leg braces – test items 3, 4, and5 with braces also.

d. Crutches, walker or cane.

Stair measurements: Depth-11", height -7", railing height- 36"

3. Climb 8 stairs

a. Independent- foot over foot- no assistance such as pushing on knee. Using rail
b. Independent- one step at a time
c. Hands on knees- assistance from rail
d. Railing- one hand
e. Railing and hand on knee- patient pulls on rail with one hand, pushes on knee with the other.
f. Railing- two hands, some patients may use two rails

4. Walk down 8 stairs

a. Independent- No assistance from rail. May go foot over foot or one step at a time
b. Railing- One hand , often used for safety but not for support
c. Railing- Two hands, or rail and therapists hand for safety.

5. Rise from chair

Care must be taken to seat the patient in a chair which places his feet flat on the floor and his knees in 90°flexion. This is particularly important with children as a higher chair would give them mechanical advantage.

a. Independent- rising without pushing on chair or knees, arms folded across chest or extended.
b. Gower's sign- includes pressure on knees or pressure on seat of chair or both.
c. Turn to side, and then push up- patient turns sideways in chair to sit on one hip, with feet on floor pushes with arms to 90° hip flexion and pushes off to upright position or climbs up chair to upright position.

d. Pull up with aid of table-patient takes support from table with hips flexed while extending knees. Once knees are locked, patient extends hip by pushing up on table.

6. Roll over from supine to prone

Contractures may inhibit this activity.

7. Roll over from prone to supine

Contractures may inhibit this activity.

8. Get to all four position from prone

Push up to hands and knees

9. Sit up from supine

a. Independent-no aids other than having ankles held down by therapist which is within the range of normal; must achieve sitting balance.
b. Pull up- patient holds on to leg or clothing to pull him up.
c. Pull and push on elbow- begins to pull up, then pushes on at least one elbow.
d. Turn to side, and then push up-patient will roll to side, and then push up with both arms to achieve sitting balance.
e. To hands and knees and then sit up-roll to prone, to hands and knees, and then to side sit or other sitting balance.

10. Rise up from floor from prone position

a. Independent- no assistance required
b. Gower's sign- can bring himself to his feet but must push on knees to assume erect posture.
c. Chair to standing-patient pulls himself to feet with aid of chair, then pushes on chair to achieve upright position
d. Chair to sitting, then to standing- patient pulls himself to sitting position in chair, then pushes himself to upright position, using chair. Patient should be placed on edge of table with thighs fully supported and knees flexed to 90°.

11. Sitting balance

a. Stable
b. Unstable- Patient sits erect but cannot recover balance if it is lost. Or, patient is unable to maintain his balance without support of his arms.

12. Vital capacity

Measured sitting, taking highest of two readings. Take weight and height into consideration.

13. Height

14. Weight

15. Hand grip

Measured with hand grip dynamometer taking highest of two readings for left and right hands. Keep arms at side during measuring.

PHYSICAL THERAPY TREATMENT

Physical therapy includes **stretching** (preventing and correcting contractures), **muscular strengthening** and **gait training**, thus increasing efficiency in the functional activities of daily living, including ADL and transfer.

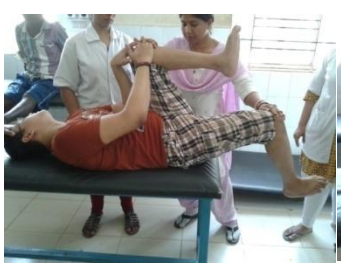
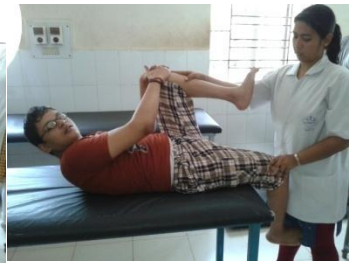
- Strengthening deforming muscles by prompting the patient to fight the passive force by an active effort of his own.
- Disability from weakness must be distinguished from that caused by contracture. The essential tenodesis effect of contracure in the face of severe loss of muscular support should be monitored by the therapist. Initially such compensating mechanism help maintain proper body alignment. Eventually they contribute to ambulatory loss.

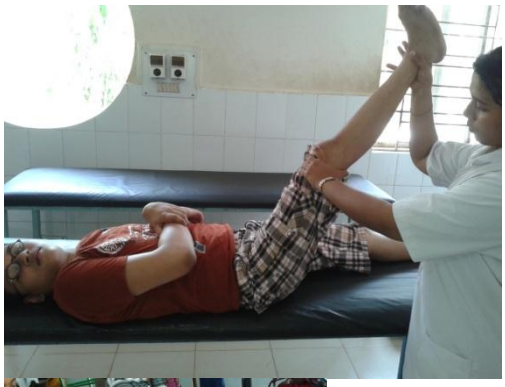
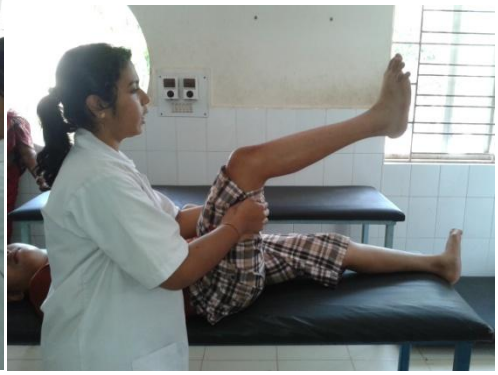
Stretching of tight muscles and prevention of contractures

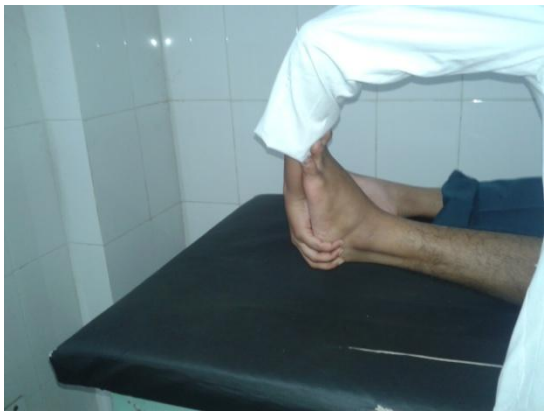
- Overenthusiastic stretching of contractures should be avoided because it produces pain ad stimulates the stretch reflex.

- Maintaining dynamic flexibility by an active effort of the muscle is a good way of controlling contractures.
- Passive stretching of contractures (particularly hip flexors, TFL, and heel cords) can prolong function and decrease the energy cost of muscular activity to the patient by balancing agonists against antagonists.
- Stretch positioning (prone) to stretch hip flexors and daily active assisted exercises can significantly lengthen the period of functional ability.
- If a patient is having heel cord contracture with quadriceps and gluteus weakness then stretching the heel cord may affect his ambulation and should be checked cautiously before giving a stretching program.

PICTURES FOR STRETCHING KEY MUSCULATURE

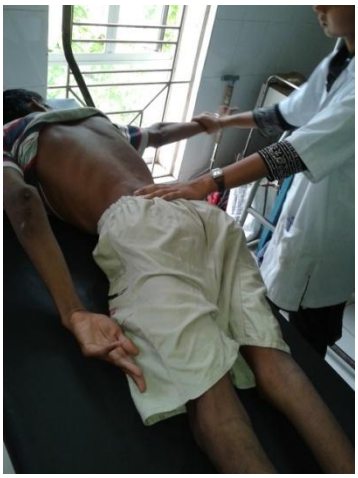





STRENGTHENING EXERCISES

- Muscular activity enhances contractile protein synthesis.
- At complete rest strength is lost at a rate of 3% - 5% a day. To maintain normal strength, the maximal daily tension exerted must be greater than 20% of maximal muscular strength.

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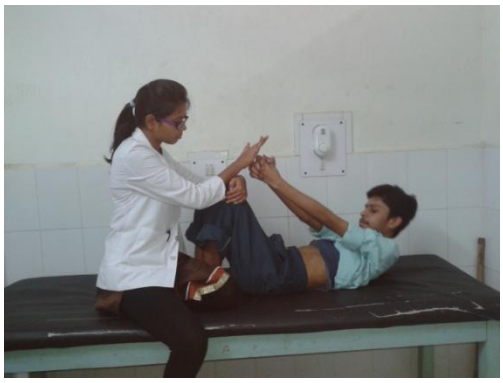
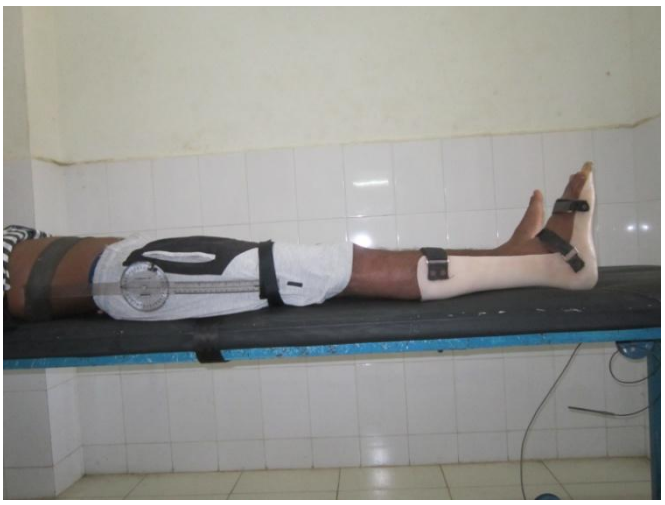
- DMD, LGD and FSH have demonstrated definite but limited increase in muscle strength with exercise. But heavy exercise may potentially accelerate weakness leading to metabolic bankruptcy.
- For improved performance overload is also required.
- Endurance training is required to increase the oxidative capacity of the muscle.
- Physical function can be maintained through an aggressive program of physical therapy.
- Potential for increasing muscle strength is related to the pre- exercise strength of the muscle.
- For maximum salutary effect exercise programs in DMD should be initiated early in the course of the disease.

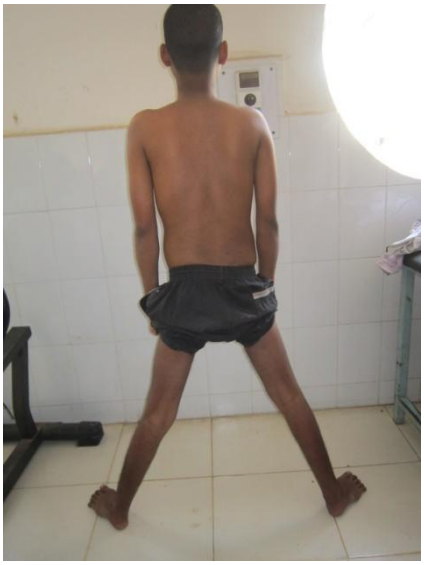
Functional exercises



- Non exhausting functional exercise may be helpful in maintaining strength.
- Patients with DMD suffer severe disuse atrophy when immobile:
    a. Bed or chair confinement should be for no more than a day at most.
    b. Alternate haunch standing is encouraged to avoid heel cord contracture
    c. Although weakening is symmetric in many of the muscular dystrophies, joint contractures are not so.

- The patient with muscle disease should be kept orthograde for as long as possible. Standing and walking are the best functional physical therapy for accomplishing this.
- Two to three hours a day of such activity is encouraged.
- Night splints are sometimes also effective in preserving joint posture.
- Where lower extremity night splints are used, KAFO are advised as AFO night splints may initiate or increase knee flexion contracture because of the tendency of patients to flex their knees in order to relieve discomfort from heel cord tightness.





Summary

- Myopathy refers to skeletal and cardiac muscle dysfunction from various inherited, metabolic, inflammatory, infectious, or toxic etiologies.
- Patients typically present with proximal muscle weakness of legs more than arms, with no sensory involvement.
- Age of presentation, duration of illness, and distribution of weakness are helpful in determining the classification and etiology of myopathy.
- Serologic testing, electromyography, muscle biopsy, and genetic testing are helpful tools in identifying the presence of myopathy and determining the etiology.
- Management is largely supportive for an inherited myopathy. In acquired myopathies, treatment is targeted toward the underlying cause.
- Treatment of statin myopathies is dependent on creatine phosphokinase levels and degree of muscle symptoms. Consider lower doses when initiating statin therapy.