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A REVIEW ON DUCHENNE MUSCULAR DYSTROPHY

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Abstract: Duchenne Muscular Dystrophy is an inherited neuromuscular disorder caused by gene mutation i.e. dystrophin protein which is responsible for the structure and functions of the muscles. It is characterized by specific abnormalities in the muscle biopsy of the patients in which the muscles in the body weakens day by day and loosens its functions. DMD mostly occurs in the boys approximately 1/3500 male births worldwide, while females are normally carriers. The disease progression is fast as compare to other types of muscular dystrophy. Typically, symptoms start in early childhood. Children with DMD struggle to walk, stand up, and climb stairs. Many eventually require wheelchairs in order to move about. They may also experience heart and lung issues. The outlook for those who have DMD is brighter than it has ever been, despite the lack of a cure. Children with the condition used to typically not live past their adolescent years. They frequently live into their 30s and 40s today and live well into their 20s. There are treatments like gene therapy, physiotherapy, drug therapy that can reduce symptoms, and scientists are also exploring for new ones.

Keywords: DMD; Muscular dystrophy, Duchenne; Muscular dystrophy, progressive, Duchenne type; Duchenne Muscular Dystrophy; Dystrophinopathy; Dystrophin, heredity, chromosome, physiotherapy, corticosteroids, etc.

INTRODUCTION

Duchenne Muscular Dystrophy was firstly termed and elaborated by Dr. Guillaume Benjamin Amand Duchenne (Neurologist, French) in 1860. Duchenne muscular dystrophy is an inherited neuromuscular disorder caused by gene mutation i.e. dystrophin gene found on the X chromosome which is responsible for the structure and functions of the muscles. It is a severe condition of muscular dystrophy which is generally found in childhood because of deletion or alteration of dystrophin protein, which is encoded by DMD gene on Xp21 chromosome. It is characterized by specific abnormalities in the muscle biopsy of the patients in which the muscles in the body weakens day by day and loosens its functions. DMD mostly occurs in the boys approximately 1/3500 male births worldwide, while females are normally carriers. The disease progression is rapid as compare to other types of muscular dystrophy. The symptoms are not detectable at birth as well as up to the early childhood but as the age increases the symptoms start showing from age of 3 and the patient starts suffering from the loss of strength of the muscles. Because of the progressiveness of the disease, after some time interval in the teenage the patient is unable to do their daily work and needed the wheelchair for the movement. DMD causes the life-threatening condition as the growing age of the patient like heart problems and respiratory complications.

The majority of people with DMD pass away in their 20s. But with careful attention, some DMD sufferers reach their 30s. Most DMD patients will require full-time care as the disease progresses in order to maintain their quality of life.

PHYSIOPEDIA

The term "muscular dystrophy" refers to a variety of genetic conditions that cause a progressive, generalized disease of the muscle caused by insufficient or absent glycoprotein's in the plasma membrane of the muscle cell. DMD is a non-communicable illness with a wide range of manifestations. Each has a unique start period, inheritance pattern, and rate of muscle atrophy. Different manifestations of this disease are brought on by variations in particular genes. Progressive muscle atrophy and weakening are characteristics of muscular dystrophies. This type of muscular dystrophy results from dystrophin gene deletions or mutations. Over time, people with DMD lose the ability to do things like walk, sit upright, breathe easily, and move their arms and hands. The DMD condition is incurable. So that patients with DMD can live as actively and independently as possible, physiotherapists and other medical experts focus on enhancing muscle and joint function and decreasing muscle degradation.

Dystrophin forms an integral part of a muscle's cytoskeleton and links the contractile apparatus to the sarcolemma. Researchers identified the gene that, when damaged or faulty, causes Duchenne muscular dystrophy in 1986. The gene for this muscle protein was called dystrophin. With 79 exons, the dystrophin gene is the biggest in the human genome. Due to the dystrophin gene's huge size (>2 106 bases), it is prone to frequent spontaneous mutations. Inability to produce dystrophin by that gene results in Duchenne muscular dystrophy (DMD). Duchenne muscular dystrophy is a form of an inherited disease called X-linked disorders or genetic diseases that mothers can transmit to their sons even though the mothers themselves are unaffected by the disease.

Although there is no known treatment for muscular dystrophy, there are ways to manage the symptoms and enhance quality of life.

1. Medical Interventions : Anti-arrhythmic Anti-epileptics Anti-myotonic drugs Non-steroidal anti-inflammatory drugs (NSAIDs) Steroids
2. Surgical Interventions : Defibrillator or a cardiac pacemaker Contracture release Shoulder surgery Spinal correction
3. Other Interventions : Supportive physiotherapy, Supportive bracing, Supportive counseling, Genetic counseling

Physiotherapy: The goal of physical therapy is to improve strength in the large muscle groups and prevent scoliosis and contractures.

Exercises for range of motion can be a part of physical therapy for muscular dystrophy. Stretching Low-impact exercises like water exercise or swimming (aquatic therapy)

Supportive Bracing: This keeps normal function from deteriorating for as long as feasible. It's crucial to have proper wheelchair seats. For patients with foot drop, moulded ankle-foot orthoses aid stabilize gait. AFOs made of lightweight plastic that correct foot drop are very beneficial. AFOs make it simple to treat foot drop. Scapulohumeral muscular dystrophy patients can walk for 40 years or longer. Paraspinal muscle contractures can occasionally make it difficult to walk; in these situations, a wheelchair can help the person travel long distances. Bracing can be done to prevent tripping, for example, by using ankle-foot orthotics to result it in more effective the feet. Bracing can be done for comfort or for function, such as dorsiflexion of the feet with ankle-foot orthotics to prevent tripping. Children in schools may require physiotherapeutic interventions, such as: The use of assistive or adaptive technology in the classroom (such as a keyboard for writing) Wheelchair use or the use of joint braces Make use of a ventilator to breathe Due to physical therapy appointments, there should be special accommodations made for tardiness, absences, shorter school days, and missing assignments.

Complications Error creating thumbnail: Unable to save thumbnail to destination the complications of DMD. Some are mild, while others are serious and get worse very fast. Walking, breathing, swallowing, and speaking abilities can all be impacted by worsening muscle weakness.

Complications can include:

- Breathing problems - As breathing muscles weaken over time, it becomes more difficult to breathe (raising the risk for eg. lung infections such as pneumonia).
- Scoliosis, Heart problems - forms of muscular dystrophy can result in risky abnormalities to the heartbeat (a pacemaker may be needed). Cardiomyopathy from muscular dystrophy can also result in heart failure. Cardiopulmonary failure is the primary cause of death for most people before the age of 30.
- Difficulty in swallowing – The esophageal muscles are affected by the weakening, which makes chewing and swallowing difficult. Choking could result from this. Some muscular dystrophy sufferers will require a feeding tube.
- Contractures - Bracing and surgery to release a tendon can help prevent some contractures.
- Vision problems - Cataracts can develop in some cases of muscular dystrophy.
- Requirement for wheelchair - Some people with muscular dystrophy eventually need to use a wheelchair.

In combination with the best physiotherapy and cardio respiratory care, the use of corticosteroids has improved functional results in patients with Duchenne muscular dystrophy and increased the mean age at ambulation loss from less than 10 years to the early teenage years. As a result, patients now require ventilation around ten years later than they did in the past when respiratory comorbidity first requires ventilatory assistance.

PHARMACOLOGY

Each muscle fiber's cytoskeleton is joined to the basal lamina by a protein called dystrophin. The lack of dystrophin prevents calcium from passing through the cell membrane, which has an impact on how the cell signals. The mitochondria are then flooded with water, causing the cell to explode. Increased oxidative stress inside the cell destroys the sarcolemma, which leads to cell death in a multi-pathway complex cascading process. Necrosis causes muscle fibres to disappear, and connective tissue takes their place.

Additionally, the nerve cells (neurons) in some regions of the brain, notably the hippocampus, produce small amounts of dystrophin. The area of the brain responsible for learning, memory, and emotions is called the hippocampus. The loss of dystrophin in the neurons of the hippocampus and other areas of the brain where dystrophin is typically produced in modest levels is most likely responsible for the non-progressive memory and learning issues, as well as social-behavioral issues in some persons with DMD. However, research is being done to determine why this only affects a tiny percentage of people with DMD.

A mutation in the gene that codes for the 427-kDa cytoskeletal protein dystrophin, which has an impact on the muscles, is the cause of DMD. Muscles of people with DMD are deficient in dystrophin. Dystrophin deficiency causes muscle fibre injury and a progressive weakening of the muscles.

The 'proximal' muscles, or those close to the body's trunk and those around the hips and shoulders, are where the muscle weakness is most noticeable. The lower extremities are often where weakness begins proximally before spreading distally. Upper extremity weakness typically develops later. Fine motions like those made with the hands and fingers are therefore less influenced by this than larger movements like walking.

The symptoms usually start around age 1-3 years, and may include:

- Difficulty with stair climbing, running, leaping, and walking. A "waddling" gait may alter the appearance of walking. The boy may have a delayed onset of walking (although many children without DMD also walk late).
- The youngster may "slide through your hands" when you lift him up because the muscles around the shoulder are slack.
- Toe-walking, in this gait pattern, kids walk with their feet apart to help them stay balanced and have a more curved lower back.
- Repeated falls.
- As he grows, the youngster may use his hands to help him stand up, giving the impression that he is "climbing up his legs" even if his calf muscles are weak. This is called 'Gower's sign'.

Some guys who have DMD also struggle academically. Usually, this is not a serious issue.

A delay in development might occasionally be the first indication of DMD. The youngster may also have a delayed speech development. Consequently, a screening test for DMD may be provided to a youngster whose growth is delayed. DMD is simply one of many potential causes of developmental delay; there are other additional, unrelated causes as well.

Contractures are a common observation in DMD. Muscle fibres, which are typically elastic, are replaced by rigid, non-stretchable tissue as it matures. Since contractures restrict normal movement, they are considered a primary contributor to disability. Leg contractures, particularly in the calf and muscles around the hip and Progressive enlargement of heart muscles are common in children with DMD.

CAUSES

The DMD gene, which is found on the short arm (p) of the X chromosome, is what gives rise to DMD (Xp21.2). Human cells contain chromosomes, which contain the genetic material that makes each person unique. 46 chromosomes typically make up human body cells. The sex chromosomes are referred to as X and Y, and human chromosomal pairs are numbered from 1 to 22. Females have two X chromosomes, while males have one X and one Y chromosome. The short arm of each chromosome is denoted "p," and the long arm is designated "q." Chromosomes are further separated into numerous numbered bands. For example, band 21.2 on the X chromosome's short arm is referred to as "chromosome Xp21.2" in this instance. Each chromosome contains hundreds of genes, and the numbered bands identify their locations.

The dystrophin protein, which the DMD gene controls (encodes), is thought to be essential for maintaining the integrity of the cell membrane in skeletal (voluntary) and cardiac muscle cells. The inner side of the membrane that covers muscle fibres has dystrophin affixed to it. The dystrophin protein will not be present as a result of a mutation in the DMD gene, which would cause muscle fibre degradation. Some muscle fibres can be replaced (regenerated) by the body, but as time passes, more and more muscle fibres are lost. The DMD symptoms and results are brought on by such deterioration. Dystrophin is present in Becker muscular dystrophy, a similar condition, but it is truncated or merely present in insufficient levels to carry out its tasks.

Some boys with DMD may develop the disorders as a result of a spontaneous mutation of the dystrophin gene, which happens randomly for unidentified causes, despite the fact that most boys with DMD get the defective gene from their mothers (de novo or sporadic cases).

A change in the gene that produces the protein dystrophin, which is necessary for the healthy operation of our muscles, results in Duchenne. Muscles cannot effectively function or repair themselves without dystrophin. Strength and function are subsequently lost as a result of muscle loss.

Due to the fact that females have two X chromosomes and that only one of them has the faulty gene, carrier females typically do not show symptoms. Males inherit one X chromosome from their mother, and if that X chromosome carries a gene that causes the disease, the male will also get the sickness.

With each pregnancy, female carriers of X-linked disorders have a 25% chance of having a daughter who is also a carrier, a 25% risk of having a daughter who is not a carrier, a 25% chance of having a son who has the disease, and a 25% chance of having an unaffected son.

If a male with an X-linked illness is able to reproduce, all of his daughters who are carriers will receive the defective gene. Because males usually convey their Y chromosome rather than their X chromosome to male offspring, a male cannot pass an X-linked gene to his sons.

Some females with a single copy of the DMD gene (gene carriers or heterozygote's) may display specific of the disease's symptoms, such as weakening in some muscles, particularly the arms, legs, and back. Female carriers who experience DMD symptoms are also at risk for developing heart problems, which can lead to breathlessness or exercise intolerance. If left untreated, heart abnormalities can cause life-threatening complications in such affected females.

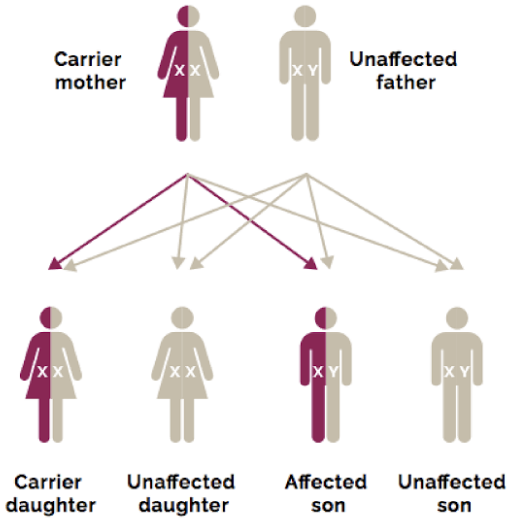

Fig. inheritance of the disease

SIGNS AND SYMPTOMS

Each DMD patient exhibits a unique set of signs and symptoms as they become older. DMD typically manifests itself early in childhood. The muscles nearest to the trunk (proximal muscles), such as those in the upper legs and pelvic region and upper arms and shoulder region, weaken and atrophy in affected children. A few other muscles, though, seem disproportionately large. Muscle atrophy and weakness spread as the illness worsens, affecting the neck, trunk, forearms, and lower legs. Although there may be some individual variance, the rate of advancement is generally very consistent from person to person.

Many DMD kids grow properly during infancy and the first few years of life. Once they are able to walk, they may stumble frequently and struggle to ascend stairs or get up from the floor. They might start to waddle or walk on their toes after a few years as well. DMD can harm the heart, lungs, and other body organs as well. Your kid may experience additional symptoms as they age, such as a curved spine (also known as scoliosis), shortened, tight muscles in their legs (also known as contractures), headaches, difficulties with learning and memory, shortness of breath, sleepiness, and difficulty concentrating.

Some common signs and symptoms as follows:

- Poor head control is frequently the first indication of muscle weakness. Due to hip muscular weakness and the tendency of affected toddlers to stand with their lower backs arched forward, many kids start walking at the right age.
- Children start to walk with a waddle and become unable to get up from a crouching position without pushing through their arms (Gower's sign) (Trendelenburg gait).
- Kids might stop being able to walk.
- By the time they are 10 to 12 years old, the majority will need to use a wheelchair.
- Parents or caregivers may observe weakening of the shoulder and pelvis, atypical clumsiness, and frequent falling in children. Children may have difficulties walking or getting up from a seated posture or from lying down.
- Trouble climbing stairs; inability to jump; balancing on one foot, Leg ache, weakness of the face, such as an inability to whistle or close one's eyes Heart issues can result in an irregular heartbeat and enlarged heart muscle. Breathing and lungs, a lack of motor skill development, exhaustion, and rapidly deteriorating weakness in the legs, pelvis, arms, and neck are all signs of a curved spine (scoliosis).

Children with DMD have less bone mass and are more likely to fracture particular bones, like the hips and spine.

DMD is generally not unpleasant, but occasionally cramps can be brought on by the muscle issues. The child will still be in charge of their bowels and bladder. Although some affected children have learning and behavioral issues, DMD doesn't impair a child's intelligence.

The late teens, DMD may also exhibit other potentially fatal consequences, such as heart muscle weakness and degeneration (cardiomyopathy). Heart failure, arrhythmias, and a reduction in the heart's capacity to pump blood can all be brought on by cardiomyopathy. The muscles in the rib cage are weak and deteriorating, which is another significant complication of DMD. As a result, one may be more vulnerable to respiratory infections (such as pneumonia), have trouble coughing, and finally experience respiratory failure.

Dysmotility, a disorder where the transit of food through the digestive tract is typically caused by slow and uncoordinated movements of the digestive tract muscles, may develop from the involvement of muscles within the gastrointestinal tract. Constipation and diarrhoea may be brought on by gastrointestinal dysmotility.

Progressive muscular wasting (weakness), poor balance, frequent falls, clumsiness, difficulty walking, difficulty standing, difficulty ascending stairs, waddling gait, restricted range of motion, breathing issues, drooping eyes, and back issues are some symptoms that may be present.

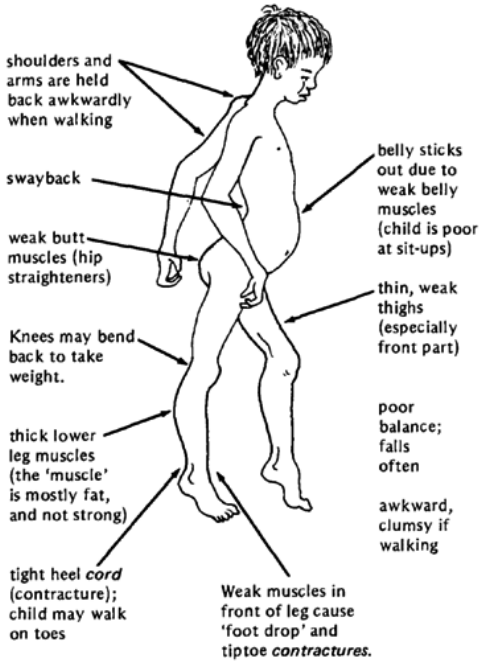

Fig. DMD patient physique

DIAGNOSIS

A thorough clinical assessment, a complete review of the patient's medical history, and a number of specialists testing, including molecular genetic tests, are used to make a diagnosis of DMD. Surgical excision and microscopic inspection (biopsy) of the damaged muscle tissue may reveal distinctive alterations to the muscle fibres if the genetic testing are inconclusive. There are also specialized blood tests (like creatine kinase) that assess the presence and concentrations of certain proteins in muscle (immunohistochemistry).

Deoxyribonucleic acid (DNA) is analysed in molecular genetic testing to look for specific genetic mutations, such as deletions, duplications, or single point mutations. Tests may be performed on blood or muscle cell samples. These methods can be used to identify DMD even before a baby is born (prenatally).

Creatine kinase (CK), an enzyme that is found at excessively high amounts when muscle is injured, may be detected in blood tests as higher levels. Although the presence of increased CK values, which are often in the thousands or tens of thousands, can support the presence of injured or inflamed muscle, it cannot support a DMD diagnosis.

In some circumstances, muscle biopsy samples can be subjected to a specialized test to determine the presence and concentrations of particular proteins within cells. There are numerous methods that can be utilized, including immunofluorescence, Western blotting, and immunostaining. Certain antibodies that react to specific proteins, such as dystrophin, are used in these testing. Creatine kinase (CK) levels in blood samples from muscle biopsies may be raised, and when tissue samples from muscle biopsies are subjected to these antibodies, the results might disclose if a particular muscle protein is present in the cells and, if so, in what quantity or size.

These tests confirm the diagnosis and determine the type of muscular dystrophy:

Physical examination: Gower's Sign is a physical finding that is particularly typical in people with Duchenne's disease. In order to stand up, they 'climb' up their legs with their hands. It results from the child's hip muscles being weak**.**

Blood testing: These can identify the gene mutation causing the absence of dystrophin in roughly two-thirds of boys with DMD. Genetic blood tests are one of these. To check for the dystrophin gene, blood DNA is examined. A creatine phosphokinase test was performed on the patient's blood in order to make this diagnosis. Creatine phosphokinase enzyme is released in significant quantities into the blood as muscles degrade. Muscle biopsies or genetic tests will identify the kind of DMD if the test shows elevated levels of creatine phosphokinase.

Muscle biopsy: A small sample of muscle tissue is examined under a microscope using specialized techniques to look at the muscle fibres and dystrophin protein in order to confirm the diagnosis for children who have clinical indications of DMD but do not have one of the frequent mutations.

Electromyogram (EMG): This test determines whether your child's muscle weakness is due to muscle tissue breakdown as opposed to nerve damage.

An electrocardiogram (ECG or EKG) is a test that monitors the electrical activity of the heart; it identifies damaged cardiac muscle and displays irregular rhythms (arrhythmias or dysrhythmias).

Outcome measures to quantify disease progression include:

The North Star Ambulatory Assessment scale, and the six-minute walking test time required to ascend four steps, time required to get up off the ground, operation of the upper limb.

The fact that the aforementioned measures only apply to ambulant or non-ambulant patients is one of their drawbacks. However, as the disease advances, the outcome measurements alter, making it challenging to examine the patient using only one end measure. Research is being done to develop a standardized measurement for muscular dystrophy disorders.

Other forms of muscular dystrophy, including Becker's Muscular Dystrophy, which is comparable but advances more slowly, are included in the differential diagnosis for DMD. Typically, the age of onset is later, and clinical involvement is less severe. The criterion for distinguishing between Becker's and Duchene's dystrophy is a muscle biopsy.

Creatinine Kinase levels are typically lower in other myopathies than in DMD. DNA analysis allows for the confirmation of the diagnosis by identifying relevant gene deletions or mutations.

Typical muscle biopsy findings of inflammation, such as mononuclear infiltration of non-necrotic muscle, CD8+ cytotoxic/suppressor T cells, macrophages, and the absence of perifascicular atrophy of dermatomyositis, are used to diagnose polymyositis. Typically, proximal and limb-girdle muscles are affected by polymyositis.

Muscle weakness can have neurological reasons, such as lesions in the spinal cord, spinal muscular atrophy, motor neurone disease, or multiple sclerosis. Additional symptoms including sensory loss, upper motor neuron lesion signs, or muscle fasciculation are probably present in these situations.

Higher transaminases (aspartate aminotransferase and alanine aminotransferase) which are produced by muscle as well as liver cells. Therefore, it is important to take into account the DMD diagnosis before liver biopsy in any male child with increased transaminases.

MANAGEMENT

Medical Management Although there is no known treatment for DMD, there are measures to increase the patient's quality of life and offer support for the stage they are at.

In order to enable the youngster be as autonomous as possible, mobility aids will be provided. These may start with a walker and eventually advance to a motorised wheelchair. When the caregivers require assistance transferring the child, in-home hoists are helpful. When a child is unable to stand up by themselves, standing frames are very helpful. Even if the youngster is unable to stand on their own, this enables them to benefit from standing, such as enhanced bone density and muscular stretching. Additionally, knee-ankle-foot orthoses (KAFOs) may be employed. KAFOs have been demonstrated to increase a child's ability to move independently. These ought to be used in conjunction with mobility aids like a zimmer frame. It is advised to keep as active as possible because prolonged bed rest might exacerbate muscle wasting.

The only palliative treatment for DMD in children is the frequent prescription of steroids. It has been demonstrated that steroids improve the child's functional capacity and muscle strength. Steroids may delay the child's dependence on a wheelchair, but they also carry a risk of negative side effects. Beta-Blockers are a different class of drugs that have been demonstrated to be beneficial. These medications are used to assist manage the steady decrease in the children's heart and respiratory systems.

Some families might think about having surgery for their kid. Children with DMD frequently need foot surgery, the placement of a feeding tube, and spinal procedures to treat scoliosis, which can develop as a result of being wheelchair-dependent. A number of factors need to be taken into account before surgery, such as how general anesthesia would affect the respiratory and cardiac systems, which are already weakened in children with DMD. Before making a choice, families must compare the benefits of the procedure with the danger. For instance, it has been demonstrated that scoliosis surgery improves the child's comfort and looks as well as their respiratory function.

Improved survival into adulthood has been made possible by proactive symptom-based multidisciplinary team (MDT) therapy and non-invasive ventilation access. A multidisciplinary care team, which may include a neurologist, cardiologist, orthopaedic surgeon, pulmonologist, medical geneticist, physical therapist, and occupational therapist, may be involved in the treatment for

the patient to ensure the best possible management. With the right management and intervention, men with DMD can now be expected to live into their 30s and 40s.

Age of Preschool: The child will usually be healthy and not require much therapy at this point. Managing involves: provided details about patient support organisations and DMD. To monitor a child's health, a professional team (such as a paediatrician or neurologist, a physiotherapist, and a specialist nurse) may be referred advice on the appropriate intensity of exercise and about genetics for the family.

Ages 5-8 years Management: Muscle strength gradually decreases between the ages of 6 and 11; by the time they are 12, the majority of kids are wheelchair-bound. Children who depend on wheelchairs have additional challenges, such as scoliosis and respiratory issues. It may be necessary to provide some support for the legs and ankles using knee-ankle-foot orthoses or nighttime ankle splints. There is no proof that any intervention to increase ankle range of motion is significantly beneficial.

The child's muscle strength can be preserved with the use of corticosteroid therapy. This entails taking medication for a lengthy period of time, either continuously or in several courses, such as prednisolone or deflazacort.

Management from 8 through late adolescence: After becoming 8 years old, the child's leg muscles start to get much weaker. As walking becomes increasingly challenging, a wheelchair is required. Depending on the individual, this typically occurs between the ages of 9 and 11 years old.

Some DMD patients on corticosteroid therapy can walk for longer. An RCT in children with Duchenne muscular dystrophy aged 6 to 10 years shows that a physical therapy treatment programme combined with bicycle ergometer and treadmill training significantly improves functional walking capacity (measured by the 6-minute walk test) and balance (measured on Biodex Stability System). The physical therapy programme includes instruction in gait and balance exercises as well as moderate stretching, isometric muscular contraction (of the quadriceps, hamstrings, anterior tibial group, calf muscles, biceps, and triceps muscles), and gait analysis. In addition, the study's findings showed that treadmill training significantly increased children with Duchenne muscular dystrophy's walking ability and balance compared to bicycle ergometer training.

It is important to manage the child's health and treat any issues as soon as they arise because complications usually start once the child gets dependent on a wheelchair. Wheelchairs and modifications to the child's home and school will be needed at this point, along with practical help and equipment. It may also be beneficial for the child and family to receive counselling and emotional support.

Management from Late Adolescence to Early Adulthood: Muscle sluggishness now poses more of an issue. It is necessary to provide assistance and make changes to homes and communities. More medical surveillance and treatment are necessary since complications like chest infections are likely to rise.

Rehabilitation Management: The management of Duchenne's disease requires physical therapy. Physiotherapists collaborate with parents and other caregivers, giving them knowledge and practical skills that will benefit the kid. Physical therapy can help the youngster remain active for as long as possible while also helping to monitor the physical signs of the disease.

One of the major side effects that is addressed by a stretching exercise plan is contractures. The parents can also learn it.

Parents are sent to a paediatricorthotist by physiotherapists who also advise them on the necessity of orthoses like AFOs or KAFOs. Additionally, they will assist parents in deciding what equipment and mobility aids the child may require.

The physical therapist will assist in keeping the child active in the initial stages of the ailment. Respiratory problems are addressed as the illness progresses.

The child's posture while standing, lying down, and sitting will be observed by physiotherapists. They can explain to the parents how to use splints or pillows to help the child sit, stand, or lie in the best postures. To support the child's posture for an extended length of time, a sleep system and night splints may be advised.

The North Star Ambulatory Assessment is frequently used by physiotherapists to objectively track the child's development. It was created in 2003 with children with DMD in mind and asks them to execute up to 17 different movements, such as standing, raising their heads, hopping, and running. Only kids who can still walk are subjected to this evaluation. Each child receives the identical instructions for this standardized test, and the results are graded on a scale of 0 to 2. It just takes around 10 minutes to administer, and it is simple. These are helpful for determining the physical status of the child and for consultation with other medical professionals.

Patients with DMD experience difficulty with a variety of daily activities due to the muscular atrophy brought on by the absence of dystrophin. Physiotherapists can assist with the management of neuro-musculoskeletal issues that are currently present. They can work to enhance gait pattern, posture/alignment, and reduce the decline of muscle strength, range of motion, and everyday function. The patient's pain may also be treated by physical therapy. A standing programme may be implemented by the physiotherapist as the patient's ability to walk and stand declines.

Fig. Multidisciplinary approach to management and complications of DMD.
ABG=arterial blood gas. ACE=angiotensin converting enzyme. DMD=Duchenne muscular dystrophy. Echo=echocardiogram. ECG=electrocardiogram. GC=glucocorticoids. GI=gastrointestinal. MEP=maximum expiratory pressure.MIP=maximum inspiratory pressure. PCF=peak cough flow. ROM=range of motion

COMPLICATIONS

Anaesthesia: Those who have DMD require special attention if they get a general anaesthetic. People with DMD may experience adverse effects from some anaesthetic medications. Additionally, the chest and respiration require additional attention. Preoperative evaluations and anesthesia care should be administered by a senior anaesthetist.

Osteoporosis: People with DMD who are immobile or who take steroids frequently may become osteoporotic. Osteoporosis must be avoided for as long as feasible. Calcium and vitamin D consumption should be enough. A blood test to measure vitamin D levels is occasionally suggested, and vitamin D supplements might be recommended.

Joint and Spinal Complications: It might be brought on by muscle weakness. The Achilles tendon and ankle joint are frequently tightened in DMD. Both orthotic devices and surgical tendon release can be used to treat this.

Scoliosis: It may be brought on by weakened muscles. After the patient has lost the ability to walk, this typically occurs at the start of the second decade of life. Scoliosis can be uncomfortable and has negative effects on breathing and posture. The recommended treatments include spinal surgery or a brace. There is evidence that surgery enhances both function and quality of life. When putting the patient under anesthesia, surgery should be performed while the patient still has adequate lung function and before cardiomyopathy becomes a significant risk factor.

Nutrition and Digestion: Some DMD children are prone to obesity, particularly if receiving steroid therapy. Due to the decrease of muscular mass, adolescents and adults with DMD may also be underweight. Dietary guidance may be useful in certain circumstances.

Constipation: Anyone who is immobile may experience constipation. Laxatives and a diet high in fibre can be used to treat this.

Complications with Chewing and Swallowing: People with DMD who are older or in the later stages of the disease may experience problems with chewing and swallowing meals. These people require a thorough evaluation and dietary counselling or supplementation. A gastrostomy can be required if the issue is severe.

Chest and Breathing Problems: During adolescence, the respiratory muscles deteriorate, resulting in shallow breathing and a less potent coughing reflex, which can result in chest infections. Restrictive lung disease will be present in all DMD patients. Techniques for clearing the area and non-invasive ventilation might be helpful.

There may be a decrease in blood oxygen levels when the respiratory muscles deteriorate. While sleeping, lowered oxygen levels become considerably more severe. Because it happens gradually, the symptoms might not be immediately apparent. Low oxygen levels can cause fatigue, irritability, headaches in the morning, nighttime awakening, and vivid dreams.

Up until the age of ten, vital capacity will expand as it would in a typical person. An individual's vital capacity will decline by roughly 8–12% annually after the age of ten.

Early detection and treatment of respiratory issues are beneficial. When patients with DMD begin to experience severe muscle weakness, regular lung function tests are frequently administered to them.

Cardiac (Heart) Complications: Teenagers and adults with DMD may develop cardiomyopathy, which is a cardiac (heart) complication. By the time they are 18 years old; all people with DMD will have cardiomyopathy, which typically begins to develop around the age of 10. The heart's ability to pump blood to the body is compromised by dilated cardiomyopathy because the heart's chambers have enlarged and the heart wall has thinned.

Cardiomyopathy typically does not produce many symptoms in DMD patients. Shortness of breath, swollen legs, fatigue, and an erratic heartbeat are all potential signs. It is possible to treat cardiomyopathy with medicine, which seems to work best when it is started before symptoms become apparent. Therefore, starting in early childhood, persons with DMD are typically provided with regular cardiac exams that include an ECG.

TREATMENT

A series of hereditary illnesses known as muscular dystrophy (MD) cause gradual muscle atrophy and weakening. All forms of DMD are now incurable, although there are treatments that can reduce symptoms and improve patients' quality of life. These include surgery, pharmacological therapies, respiratory therapy, occupational therapy, speech therapy, and physical therapy.

Physical Therapy:

Physical therapy can help muscles affected by DMD become stronger and help prevent contracture. A patient's individualised exercise programme can be carried out initially in a physiotherapist's office and afterwards at home. In addition to increasing muscle strength and range of motion, these activities help boost patients' wellbeing and sense of self-worth.

In order to avoid joint stiffness for as long as possible, physiotherapy will assist preserve muscle strength and flexibility. Specialized neurological physiotherapists will also offer assistance and guidance on mobility-preserving physical aids like wheelchairs or braces. Improve posture and lessen the severity of back problems; Increase fitness and energy levels; Improve mood; Prevent joint stiffness; Promote independence; Improve muscle endurance and strength; Improve balance; Stretch and warm muscles; Facilitate daily tasks like as walking;

Physiotherapy treatment will include:

Stretching to release muscle tension and prevent contractures. Additionally, stretching and strengthening exercises will reduce back issues; improving comfort and adjusting position to avoid pressure sores; exercise to improve endurance and lessen weariness; balancing exercises that will help you adapt on different surfaces like hills, slopes, kerbs, gravel, and grass; recommendations for mechanical assistance, such as wheelchairs, walking aids, and orthotics, to enhance functional abilities; To soothe painful muscles, use hydrotherapy and massage; control over breathing and, if necessary, assistance with coughing to keep the chest free.

Recommending adapted seating, mobility aids, and other equipment; following a fracture or injury, rehabilitation. The aim of therapy in Duchenne is to maintain range of motion (a person's flexibility).

Stretching: Patients should include it into their regular routines under the direction of a physiotherapist. Regular stretching of joints like the hip, ankle, knee, shoulder, elbow, and wrist should start young and continue into maturity. Potential advantages of stretching include: Continuing motion across the joint's complete range of motion; Temporary increase in tolerance to stretch; Temporary decrease in muscle stiffness; Temporary improvement in blood flow to the muscle; Decrease in report of discomfort; a feeling of wellness.

Example - Ambulatory Stretching, Mobility devices, Non ambulatory stretching, etc.

Bracing: By supplying a sustained, extended stretch, it aids in maintaining joint alignment as well as flexibility and function. Braces can be worn on the hands, wrists, and lower extremities (ankle-foot orthosis (AFO) and knee-ankle-foot orthosis (KAFO). A skilled occupational therapist or orthotist will custom fit braces for each person, which are frequently constructed of plastic.

Due to the shortening of the calf muscle and strain on the Achilles tendon, as we indicated earlier, tightness first appears in the ankles in Duchenne. The ankle and foot joints can be stretched for many hours by wearing braces at night (also known as "night splints" or "moon boots"). To increase tolerance and duration spent using night splints, most kids are urged to begin wearing them at or shortly after diagnosis. "AFOs" are the name for these braces (ankle, foot orthoses). Your physical therapy team will place an order for the precise brace you require. This kind of splint should not be worn during the day as they tend to exacerbate falls and put more strain on the quadriceps (thigh) muscle. It is important that the patient is evaluated by a PT who is familiar with Duchenne.

Serial Casting: It is the process of covering a person's joint with a series of stiff casts, usually made of plaster (most often used for heel cords at the ankle). The purpose of the casts is to gradually develop range of motion at a particular joint over the course of many weeks with frequent cast changes. With each fresh cast placement—typically 1-2 times per week—the joint is "slightly" stretched further. Not all centres do this operation, and those who do should be acquainted with both Duchenne and the procedure. Success depends on careful supervision by a PT with knowledge of Duchenne and serial casting.

Positioning: As mobility aids are required, the physical therapy staff will also need to evaluate these. The apparatus must provide the best possible support and be positioned correctly, and it must be used carefully (always buckle your seatbelt and use a chest strap if necessary). It's important to follow your physical therapist's recommendations about when particular mobility aids are required. The patient's physical therapy team will assist them in getting access to the equipment that will best improve their function and quality of life.

Use Wheelchair Inserts and Support: Use bolsters, rolls, or cushions to support or position a body part in a proper alignment when using a wheelchair. Muscles and joints stiffen more quickly in people who spend an increasing amount of time sitting or lying down. To maintain their comfort and range of motion, it's crucial to place them in a comfortable position. Ideally, boys should sit with their feet flat on the ground or on a footrest, knees bent at a 90-degree angle, back straight, and pelvis aligned with the hips.

Keep legs out of the frog posture for short periods of time (splayed out). The hips and feet should be in alignment with the knees. Changes in the chair's proportions during growth aid in maintaining the best upright posture without leaning.

Small adjustments to posture when using a wheelchair may signal potential spine modifications. The inserts on wheelchairs should allow patients to sit up straight and keep your entire body supported and in the optimal position. A back brace might be helpful if your back pain is becoming worse and patient are not having spinal surgery.

Standing Devices: Standers are specialized pieces of equipment that can be used to assist someone in standing for a lengthy period of time. Children who are unable to stand independently, have trouble standing, or have lost their ability to walk may qualify as standers. Several possibilities exist for standing gadgets: Allows a person to go from a sitting to a standing position. Support the back of the body using a supine stander as the youngster is brought to standing from a supine position.

Safety: Fall prevention will significantly aid in maintaining ambulation. Making ensuring areas inside are as clear of debris, slick surfaces, and fall hazards as possible is beneficial. Outside, keeping an eye out for slick or uneven surfaces can also assist to prevent falls. Additionally, if the sufferer is using a mobility aid, fasten your seatbelt!

Physical Activity and Exercises: Physical therapy professionals have a significant role in prescribing, overseeing, and directing exercise. Low-impact or no-impact aerobic activity should involve little resistance. The ideal workout is typically

swimming since the water environment puts less strain on the muscles that support posture. It's critical to take breaks and avoid overexerting oneself. Ask your physical therapist and the rest of your rehabilitation staff what is safe.

Additional Daily Reminders: In addition to stretching daily and bracing at night, there are a number of smaller actions you should keep in mind to do each day to help maintain the flexibility, strength, and functionality of your skeletal muscles. These actions include sitting up straight with good support, keeping your knees together, moving your hands and wrists frequently, keeping your tongue in your mouth, working your jaw muscles, staying safe, and more. Keeping in mind to take breaks as necessary

Occupational Therapy: Occupational therapy can support people with DMD in carrying out everyday tasks as independently as feasible. Additionally, it can instruct patients on how to use wheelchairs and other adjustments to make daily life simpler.

To guarantee that programmes designed to the needs of each patient are carried out, occupational therapists might collaborate with medical teams. To aid patients in realising their full potential and preserving their freedom, they can also collaborate with the patient's school or place of employment.

Speech Therapy : The muscles used for swallowing and speaking can be impacted by DMD. Dysphagia and dysarthria may result from this. Through articulation treatment, oral motor therapy, and language intervention exercises, speech therapy can help improve speech. 4 Speech therapists can provide augmentative and alternative communication support for patients in advanced stages of MD.

Respiratory Therapy : As DMD worsens, respiratory muscles are affected. This results in respiratory dysfunction and frequently occurs lung infections.

Lung function tests and sleep studies can be done by respiratory therapists to evaluate a patient's respiratory health. They can provide manual and mechanical coughing assistance, regulate lung volume recruitment, and give advice on noninvasive ventilation with associated interfaces, tracheostomies, and mechanical ventilators.

Surgery : Scoliosis and cardiomyopathy are two consequences of DMD. Different sorts of surgery are necessary depending on the type of DMD a patient has. To address their scoliosis, some people may require spine surgery, but others may require tendon release surgery to treat contracture. Patients with muscular dystrophy may also require orthopaedic procedures on the hip, knee, and ankle (lengthening or tenotomy of the Achilles tendon).

To treat their irregular heart rhythm disorders, some people may require cataract surgery, while others may require a pacemaker or cardiac defibrillator.

Gene-Based Therapies : Additionally, the US Food and Drug Administration (FDA) has recently approved a number of gene-based medicines for the treatment of Duchenne muscular dystrophy (DMD). These exon-skipping treatments include Amondys 45, Vyondys 53, and Exondys 51 (eteplirsen) (casimersen). Exon skipping restores the reading frame of a gene by masking some exons with antisense oligonucleotides. Point mutations or large-scale deletions of the DMD gene, which both alter the reading frame of the gene and prevent the production of dystrophin, are two possible causes of DMD. Exon skipping can guarantee that cells produce a shortened but still useful dystrophin protein. Depending on the underlying mutation, different exons must be skipped in order to restore the gene's reading frame, hence not all DMD patients respond to exon-skipping medications.

There are further gene-based treatments for treating muscular dystrophy that are presently undergoing clinical testing. These include treatments that use an adeno-associated virus to deliver a healthy copy of the disease-causing gene to the body, such as TranslarnaTM (ataluren), a stop codon read-through therapy that reverses the effects of nonsense mutations and is already approved for use in the EU to treat some patients with DMD (AAV).

Drug Therapy: In order to slow the disease's progression and prolong patients' ability to walk, corticosteroids may be recommended for some kinds of MD.

Corticosteroids: Corticosteroids, also known as glucocorticoids, are frequently recommended to MD patients. They may help to retain muscular tissue by lowering inflammation and immune system assaults on it. They might also hasten the procedures needed to repair cell membranes. For DMD, a variety of corticosteroid kinds may be administered.

Drugs approved by the FDA for the treatment of Duchenne muscular dystrophy (DMD) are :

- ***Amondys 45 (casimersen)*** **Injection :**

FDA Approved: February 25, 2021 Company: Sarepta Therapeutics	Amondys 45 is an antisense oligonucleotide used to treat Duchenne muscular dystrophy (DMD) patients with genetic abnormalities that allow exon 45 of the Duchenne gene to be skipped.

- ***Viltepso (viltolarsen)*** **Injection :**

FDA Approved: August 12, 2020 Company: NS Pharma, Inc.	Viltepso is an antisense oligonucleotide prescribed to treat Duchenne muscular dystrophy (DMD) in people with a confirmed DMD gene mutation that can tolerate exon 53 skipping.

- ***Vyondys 53 (golodirsen)*** **Injection :**

FDA Approved: December 12, 2019 Company: Sarepta Therapeutics	An antisense oligonucleotide called Vyondys 53 is recommended for the treatment of DMD in people with a verified mutation of the DMD gene that can be treated by skipping exon 53.

- ***Emflaza (deflazacort)*** **Tablets and Oral Suspension :**

FDA Approved: February 9, 2017 Company: PTC Therapeutics, Inc.	A glucocorticoid called emflaza is recommended for patients with DMD who are 2 years of age or older. Another glucocorticoid used in the treatment of DMD is prednisone. Prednisone is a derivative of deflazacort.

- ***Exondys 51 (eteplirsen)*** **Injection :**

FDA Approved: September 19, 2016 Company: Sarepta Therapeutics	In patients with a verified mutation of the DMD gene amenable to exon 51 skipping, exondys 51 is an antisense oligonucleotide that is prescribed for the treatment of DMD.

Ayurvedic Approach :

Scientific research is being done to determine the potential benefits of some Ayurvedic herbs utilized for their Rasayana effects in the treatment of muscular dystrophy, including:

1. ***Curcuma longa:*** Prior research has demonstrated the clinical relevance for the pharmaceutical management of individuals with muscular dystrophy.
2. ***Withania somnifera:*** This plant produces withanolide, which significantly promotes the regeneration of axons, dendrites, pre-synapses, and post-synapses in neurons. It also inhibits the production of free radicals and improves neuronal dysfunction. Emaciation in children (when given with milk, it is the finest tonic for youngsters), vata-vitiated diseases, mental breakdown, induced immunomodulatory activities, and longevity in users are all circumstances where it is frequently utilized.
3. ***Terminalia Arjuna:*** Cardiomyopathy and arrhythmias are the main causes of cardiac manifestation in DMD, and death happens as a result of both cardiomyopathy and respiratory insufficiency, which is why. Due to its cardio-protective qualities, Terminalia Arjuna is utilized in the treatment of DMD.
4. ***Tinospora cordifolia:*** Used as a Rasayana, it is one of the most significant plants for immunomodulation in Ayurveda (that which promotes health, provides defence against disease and promotes longevity). It also has immunomodulatory properties. Physical therapy and regular exercise should be combined.
5. ***Ashwagandha:*** Ashwagandha's revitalising and regenerating capabilities can aid in maintaining lean muscle mass. It may encourage muscle cell renewal, eventually regaining muscular mass.
6. ***Giloy:*** Has anti-inflammatory properties and lessens muscular injury. Additionally, it can have an antioxidant effect and defend the muscular tissues from oxidative stress.
7. ***Brahmi:*** This herb aids in increasing muscular mass and improving nerve activity. It functions as an antioxidant and prevents oxidative damage to the muscular tissues.

CONCLUSION

DMD is an incurable disease which cause by mutation in dystrophin gene. It is very important to understand the disease so we can avoid miss-guidance, wrong judgment and wrong treatment. In this review article, we have presented every basic information about the Duchenne Muscular Dystrophy including its hereditary characteristics, physiopedia, pharmacology, its causes, signs & symptoms, diagnosis, management & complications and various types of treatment or preventive measures like gene therapy, drug therapy, physiotherapy, ayurvedic approach, etc.

The challenge of DMD treatment is the discovery of safe, effective and potent molecule which can not only prevent but cure duchenne muscular dystrophy. Currently there are only corticosteroid, stem cell and gene therapy treatments available but they are not that effective.

The main aim of this review was to promote the awareness about the disease and disease condition so no one can receive false treatment which can threaten once life. It is one of the rare disease condition which still does not have any definite treatment which can state that there is still hope and a vast world of research is awaiting for new researchers.

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