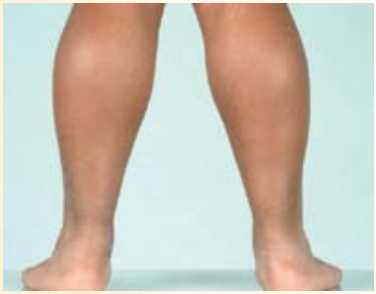
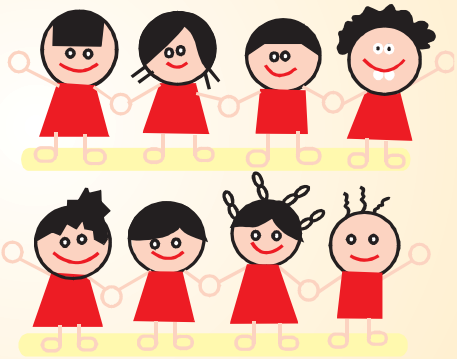
All you need to know about Duchenne muscular dystrophy !

Child Neurology Division
Department of Pediatrics, AIIMS, New Delhi

Parents/Patient Education Guide





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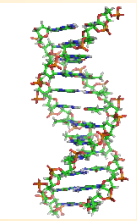
All you need to know about Duchenne muscular dystrophy (DMD) !

What is DMD ?

Duchenne muscular dystrophy (DMD) is a genetic disease characterized by progressive muscle wasting and weakness. It presents in early childhood and inevitably progresses. It affects only boys (with rare exceptions). Diagnosis is simple requiring few blood tests and sometimes muscle biopsy. There is currently no cure but early diagnosis and initiation of supportive management prolongs the survival of these boys. A lot of research is going on around the world to search for its cure.

What causes DMD ?

DMD is an inherited disorder of muscles which is caused by faulty genes (the units of inheritance that parents pass on to their children). This fault impairs the ability of the body to produce an important muscle protein called dystrophin. There is progressive muscle breakdown and loss leading to muscle wasting and weakness. Over time, children with DMD loose muscle control and strength which leads to the progressive inability to walk, stand, sit up, eat, and even breathe.



Who gets DMD ?

Only boys show the symptoms of this disease. It affects one in 3500 male births. Sometimes girls (who are carrier [see later]) may have mild symptoms.

Understanding the genetics of DMD !

DMD is an X-linked disease and thus affects only boys. Boys have only one X-chromosome which is faulty in this disease. Girls have 2 X-chromosomes of which one is normal and protects them against the disease.

In around 60% cases, there is a family history of similar illness. Mother is usually a carrier. This means that she has one normal gene and one faulty gene and does not have any symptoms of the disease. Each subsequent son of a carrier has a 50% chance of being affected and each daughter has a 50% chance of being a carrier herself.

In rest of the cases, there is no family history. This means that the faulty gene has arisen in the boy himself and no other member of the family carries it. There is no risk of the disease in the siblings.

The girls who are carriers do not manifest the disease or at most may have mild weakness. However, they might transmit the disease to their sons in future.

What are the early signs ?

Early signs of the disease may be non-specific. They may include :

- Delayed walking (beyond 16-18 months)
- Difficulty in running
- Difficulty in climbing stairs
- Inability to hop or jump
- Repeated falls while walking
- Walking on toes with back of ankle lifted up

What are the usual symptoms in DMD ?

In most of the patients, the weakness is not noticed till 5-7 years of age. But subsequently, walking becomes increasingly difficult with age with more problems in climbing stairs and getting up from the floor. The affected boys initially support themselves with hands on thighs as they get up from the floor. Time taken to do so progressively increases and finally they are unable to get up on their own. The parents may also notice abnormal enlargement and stiffness of calf muscles.

They also have difficulty in lifting head off the bed and turning around in bed. Gradually arms are also affected with difficulty in raising arms overhead. Hand functions like writing, buttoning/unbuttoning, mixing food and other fine activities may remain normal till late in the disease.

Over the next few years, weakness of the muscles gets progressively worse with many boys needing a wheelchair by around 12 years of age (if left untreated). Other problems, which occur in these boys at this stage, include breathing difficulties, heart problems (due to weakened heart muscles) and back deformities. Some boys also have learning and/or behavioural difficulties. Early treatment and supportive management may delay this stage.

How DMD can be diagnosed ?

All affected boys have very abnormally high levels of chemical called *creatine phosphokinase (CPK)* in their blood. This test is available in most laboratories. It is important to note that this test is only helpful for suspecting the diagnosis of DMD. The CPK may vary during various stages of the disease. It has no relation with the disease

progression or improvement and has no role in looking for response to therapy.

The diagnosis is confirmed by *genetic testing* (looking for the actual fault in the gene), which gives a positive result in almost 2/3rd of affected patients.

In the rest, a *muscle biopsy* is needed. The child is admitted for half a day. A minor operation is done where a small muscle piece is taken from the thigh. The biopsy is studied to look at the absence of the muscle protein called dystrophin.

Note : If the diagnosis is already established in another family member (e.g brother, maternal uncle), then no further testing is necessary for diagnosis. The clinical picture is sufficient for the doctor to make the diagnosis.

Can any carriers in the family be identified?

This task may be difficult but geneticists can identify from the family tree which women are at risk of being carriers. A combination of creatine kinase (CPK) and genetic tests allows the great majority of such women to be either identified as carriers or given a strong reassurance that their risk is very low. Specialised genetic counselling is now available to all families.

What other investigations need to be done ?

Besides tests needed for diagnosis, some others tests are usually advised to these children. They include :

- Tests to rule out underlying tuberculosis (as patients are given oral steroids for treatment which can worsen underlying tuberculosis)
- Heart evaluation to monitor heart function; this is done every 2 years in children < 10 years and every year in children > 10 years of age.
- Lung function tests to pick up any weakness of breathing muscles; these are done every year in children who are walking and every 6 months in children who are restricted to wheelchair/bed.
- Blood tests and a bone scan to assess the calcium status of the body (as patients are given oral steroids for treatment which can cause calcium deficiency and bone disease)

Is there any treatment?

Unfortunately no cure has yet been discovered. We do have ways to manage its complications. These have had a very important impact on the quality and length of life that can be expected with this condition. Intensive research like stem cell therapy and exon skipping are going on to find a cure in many centres around the world.

What medical help is required ?

Physical therapy : Encourage physical activities (like cycling, swimming) to prevent stiffness of muscles minimize tightness at the joints. Stretches for tight muscle groups and joints needs to be started under the guidance of a trained physiotherapist. Night time use of ankle splints may be needed when movement at the ankle joint is compromised. Stretching exercises of upper limbs, standing devices, breathing exercises and use of appropriate wheelchairs may be required at a later stage in the disease. Very rarely surgery may be required if a joint continues to be stiff or abnormal curvature of the spine persists despite adequate physiotherapy. This needs to be discussed with your doctor.

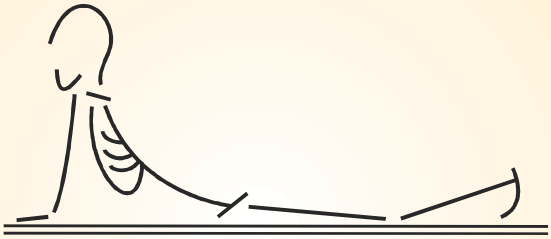
Home environment modification in form of specialised seating and equipment especially toilet seats may be beneficial, continued attention to weight control must be given as these boys are prone to gain weight in view of physical inactivity and medicines prescribed.

Management Of Child With Myopathy

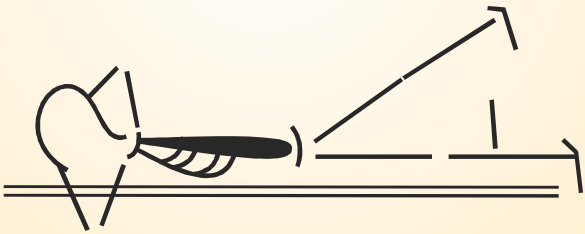
Prone Position i.e. Lying On Stomach

1. Hold hand behind your back. Lift head and shoulder up.

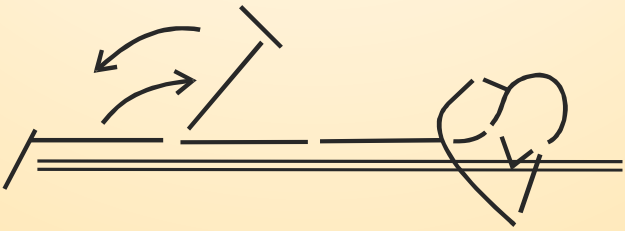
2. Raise head and shoulders with support of arms.



3. Raise leg straight up hold for a count of 3-5

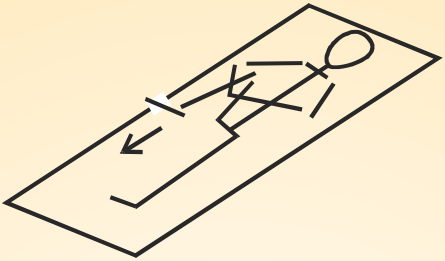


4. Bend one knee at a time.

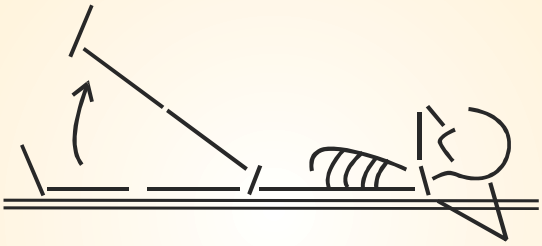


Supine Posture i.e. Lying on back

5. Bend one knee at a time



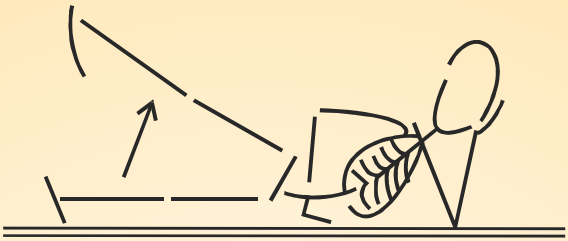
6. Lift one leg straight up. Hold for a count of 3-5



7. Knees bend. Lift your lower back up.

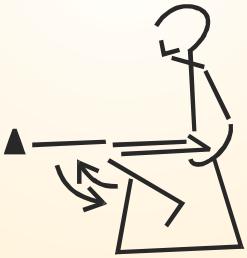
8. Knees bend and holding hands in fornt, lift head and shoulders up.

9. Lying on side. Lift one leg straight up. Hold for a count of 3-5.



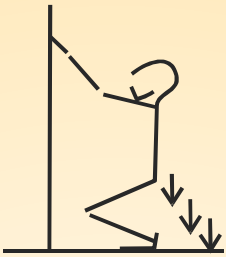
10. Sitting. Rotate legs in and out

11. Sitting. Straighten up one knee. Hold for a count of 8-10

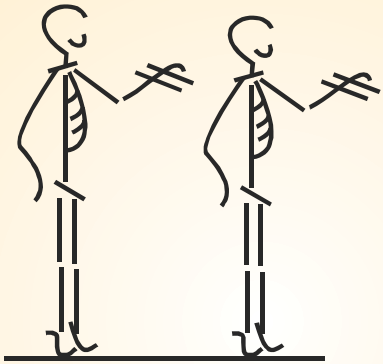


12. Crouch position

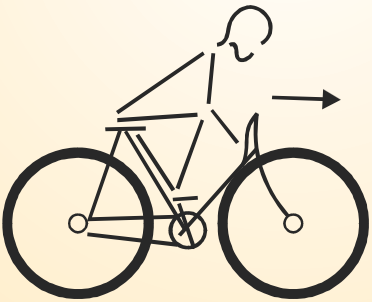
13. Holding onto some support, both knees bending and stretching.



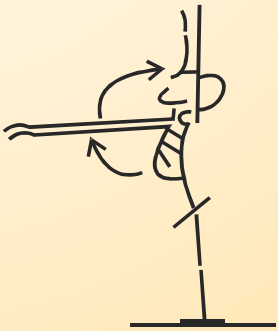
14. Standing alternately on heels and toes.



15. Cycling-15-20 mins/day

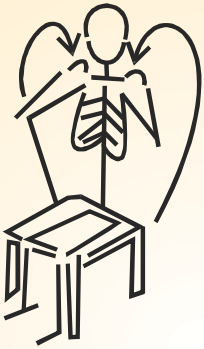


16. Forward and upward movement of arms.



17. Sideways and upward movement of arm.

18. Bending and stretching of elbows.



19. Squeezing the ball

20. Breathing Exercises.

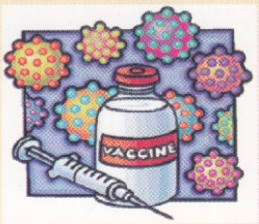
(i) Take a deep breath through your nose and blow out through mouth 10-15 repetitions every two hours.

(ii) Blowing whistle and balloons.

(iii) Making bubbles with soap water.

Immunization : The routine immunization as per the national schedule must be completed. As these children are prone to develop pneumonia and are immunocompromized (i.e. decreased ability of the body to fight infections) secondary to use of steroids, the following additional vaccines are usually recommended:

- **Pneumococcal Vaccine :**



  - If affordable, PCV (protects against 7 types of a germ called pneumococcus which causes pneumonia) should be given first. A single dose is recommended in children > 2 years of age.
  - Susequently, a single dose of PPV23 (protects against 23 types of the germ called pneumococcus which causes pneumonia) must be given. At least there should be a gap of 2 months between PCV and PPV23. The repeat dose of PPV 23 may be given after 3-5 years if the child is less than 10 years of age and after 5 years if child is aged more than 10 years of age.
  - In non-affordable patients, PPV23 is sufficient.
- Influenza vaccine should also be given yearly to protect against pneumonia caused by influenza virus.
- Chicken pox immunization should be given as single dose in children < 13 years of age prior to starting steroids.

Steroid treatment : Steroids are the only medicines which have been shown to delay the progression of DMD. There is no doubt that they are beneficial for boys with DMD. The goal of steroid use is to help the child walk independently for longer, to allow enhanced participation in routine activities and to later minimize breathing, heart and orthopedic problems. They can also reduce the abnormal sideward curvature of the spine (also called scoliosis) which produces back deformity.

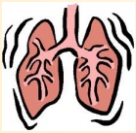
The optimal time for starting steroid treatment is when motor function is in a plateau phase when the boy has stopped gaining any further motor skills, but have not yet started to get worse. This is normally sometime between the age of 4-6 years. They may also be started in boys who have stopped walking after discussion with the parents.

They are taken orally usually in the morning in doses advised by the doctor. Few precautions that need to be observed while taking steroids include :

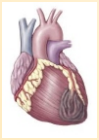
- The child has been screened for tuberculosis or any active infection.
- The immunization of the child has been done adequately after discussion with the doctor.
- Observe for any side effects that the children taking steroids may have. Report them to your doctor at each visit. These side effects may include weight gain, increased body hair, Heartburn/acidity, pimples, increased frequency of urination/thirst, headache, blurring of vision, etc.

- In case of any suspected infection, immediately report to your doctor.
- The child should not suddenly stop taking steroids. Always consult your doctor in case of any problem.
- Ensure the child is getting adequate physiotherapy as advised.
- Ensure the child is getting adequate calcium tablets/syrups as advised by the doctor.
- Keep an eye on the weight gain of the child. Always consult the dietician at every visit.
- Besides the routine tests (as already described). These children on steroids should also undergo following tests periodically :
  - Weight/Height/BMI monitoring
  - Blood pressure monitoring at each visit
  - Blood/Urine sugar monitoring
  - Annual eye check up

Respiratory support : This may be required in later stages. Important points to remember are :



- Periodic lung function tests should be done every year in children who are walking and every 6 months in children who are restricted to wheelchair/bed. Sleep studies may also be required at later stages.
- Encourage wind instruments, blowing bubbles and singing etc. Encourage young people to maintain an active lifestyle within their capabilities.
- Adequate vaccination as advised by the doctor.
- Early treatment of any chest infection.
- Special techniques to improve chest function : breath stacking, glossopharyngeal breathing, lung volume recruitment technique and chest clearance technique. Discuss about these with your doctor/ physiotherapist.



Heart problems : These problems may arise at a later stage due to progressive weakness of heart muscles, problems with rhythm of beating of heart, increased blood pressure or susceptibility to develop clot. Early referral to a heart specialist is important. The symptoms can be non-specific and may include fatigue, abdominal pain, sleep disturbances, inability to tolerate daily activities, palpitations, etc. Heart evaluation to monitor heart function should be done every 2 years in children < 10 years and every year in children > 10 years of age.

Schooling : The child must be sent to school. Make sure the school is fully informed about your childs condition. The school personnel need to be sensitized about the special needs of your child, and they may need to arrange minor special equipment. A special individualized education plan should be developed to address potential learning problems and to modify activities that might otherwise prove harmful to the childs muscles (e.g. physical education), reduced energy/fatigue (e.g. walking long distances to/from lunch), safety (e.g. playground activities) and accessibility issues. Computers offer a real route to help children with DMD develop their talent to the best of their abilities.

Follow up: This should happen atleast every 6 months or before if need arises.

Can DMD be diagnosed before birth?

Once a child with DMD has been born in a family, it is often possible to offer prenatal (meaning before the birth of the child) diagnosis in future pregnancies, either for the mother or for other women who are found to be at risk of being carriers. This is normally possible when genetic studies give positive results in the child.

The test is performed on a tiny piece of the developing placenta usually at about the 11th-12th week of pregnancy and studying its genetic make up to locate the faulty gene. For further details, parents should talk to a geneticist, a doctor who specializes in these issues.

How does steroid treatment in DMD help?

Steroids in DMD help in various ways

(a) Stabilize muscle strength & function

(b) Prolong independent ambulation

(c) Delay progression of Scoliosis(sideways bending of spine)

(d) Delay the progression of cardiomyopathy

Can Steroids still be given after loss of ambulation?

Yes continued treatment of steroids after loss of ambulation is beneficial.

What are the side effects of steroids?

The common steroid-related side effects include weight gain,short stature, cataracts and increased propensity for skeletal fractures

Is alternative treatment like Yoga beneficial for DMD?

Yoga is a wonderful option for self-stretching, core/trunk stabilization, respiratory health and circulation to add to home exercise program. However the program should avoid “power poses” which may require a great deal of energy and strength.

What constitutes an ideal healthcare team for a patient with DMD?

An ideal healthcare team for a patient with DMD would consist of a Neurologist who commonly is the head of multi-disciplinary Duchenne healthcare teams along with a Cardiologist, Pulmonologist,

Can contractures be reversed in a patient with DMD?

A contracture is when a joint is no longer able to move through the full range of motion due to a severe muscle, tendon or joint fibrosis which means that there is significant fibrosis. This leads to loss of range of motion if necessary aggressive interventions are not done. But many times, stiffness is incorrectly referred to as a “contracture.” Tightness or stiffness don't feel as rigid and can actually be changed or reversed by less invasive treatments such as stretching and positioning. Therefore range of motion program must be specific, prolonged, frequent and consistent to improve range of motion and prevent tightness from becoming a true contracture

Do stem cells have any role in the treatment of DMD?

Though Stem cells based therapies for the treatment of DMD appear lucrative & promising ,as of now there is no role of Stem cells in the management of DMD and this kind of therapy is still considered experimental and there currently no stem-cell-based therapies for muscular dystrophy. A lot of work is still needed to determine whether these treatments will be safe and effective in humans.

What are the newer future therapies that may be available for DMD in the years to come?

New emerging treatment includes viral-mediated microdystrophin gene replacement and Exon skipping to allow translation and production of a modified dystrophin protein. However these drugs have been used only in clinical trials which have shown limited success in delaying disease progression.

Child Neurology OPDs	**Tuesday & Friday 9 a.m. onwards**	**Room No.4, 5, 14**
Development Clinic	**Monday 2 p.m. onwards**	**Room No.5**
Neurocysticercosis Clinic	**Monday 2 p.m. onwards**	**Room No.11**
Pediatric Neurology Clinic	**Wednesday 2 p.m. onwards**	**Room No.3, 4, 5**
Autism Clinic	**Thursday 9 a.m. onwards**	**Room No.12, 13, D**
Neuromuscle Disorders Clinic	**Friday 2 p.m. onwards**	**Room No.3, 4**

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