####  Distance Learning

#### Department of Paediatrics

#####  Medical College for Women and Hospital

 ( Teaching In the period of Gov. Declared Holidays for COVID 19 Pandemic )

####  TOPIC:

#### Duchenne and Becker Muscular Dystrophy

( RESPONSES)

Prepared by

Professor MOK Wahedi

FRCP(Edin), MRCPCH

Head, Paediatrics

Medical College for Women and Hospital

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##### British Paediatric Neurology Association

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Duchenne and Becker Muscular Dystrophy

**1. DUCHENNE MUSCULAR DYSTROPHY**

*Response to Activity 1:*

Diagnosis of Duchenne muscular dystrophy is based on clinical assessment of severity and correlating it with dystrophin immunocytochemistry on muscle biopsy and molecular studies of the dystrophin gene.

One of the common questions among paediatric neuromuscular clinicians is whether a muscle biopsy is essential for the diagnosis of Duchenne muscular dystrophy.

The multiple presentations of Duchenne muscular dystrophy:

Delay in onset of walking

Frequent falls

Abnormal gait

Speech delay

Global developmental delay

Failure to thrive

Myoglobinuric crisis to general anaesthetic

Raised “liver enzymes” (AST, ALT) in an young child investigated for an unrelated illness

 *Response to Activity 2:*

Your notes should make reference to inconvenience, attendant anxiety and discomfort for the child. However the information yield does offer confirmatory diagnostic information and does help more accurate guidance to be given to the family (within rather broad confines to complement the genetic studies). So let us now put these thoughts into practice.

 *Response to Activity 3:*

*Would you offer a muscle biopsy to this boy?* Yes.

The clinical presentation and CK is very suggestive of Duchenne Muscular dystrophy. We hope that from your reading, you will have been converted to the “yes camp”. Routine PCR screening of the Dystrophin gene will pick the mutations in only up to 70% of the cases. The other 30% will require screening for small gene rearrangements and point mutations, which require MLPA or full dystrophin gene sequencing, which can be performed on DNA from blood samples, but these studies may only be available in specialized labs, and may have long waiting times. Muscle biopsy will provide the diagnosis in all boys with DMD, allow quantitation of dystrophin, to allow prognostication in combination with the clinical picture, followed by dystrophin gene mutation testing which can then be used for genetic counselling and ante-natal diagnosis. Muscle biopsy also confers the advantage of simultaneously, excluding or diagnosing other conditions with a similar presentation, eg LGMD2I (Griggs and Bushby, 2005, Paper 5).

**2. NATURAL HISTORY OF DUCHENNE MUSCULAR DYSTROPHY**

*Response to Activity 4:*

Typical age of presentation with gait difficulties – 2 to 5 years

Loss of walking ability – mean 9.5 years

Development and progression of scoliosis – in early teenage years, following loss of ambulation

Sleep disordered breathing and respiratory failure – mid to late teenage years

Death – late teen to early twenties, in untreated cases

Data from non-randomized studies suggests that corticosteroids in DMD delay loss of walking and reduce the incidence and severity of scoliosis. Provision of non-invasive ventilation prolongs survival. Eagle et al 20021, reported that the mean age at death in ventilated patients in Northern England in the 1990s, was 25 years, and further increased to 30 years in the group of DMD individuals who had a combination of spinal surgery and ventilator support (Eagle, 2007).

Corticosteroids in Duchenne Muscular Dystrophy

There is now a general consensus on the role of corticosteroids in the ambulant child with Duchenne muscular dystrophy.

 *Response to Activity 5:*

A randomised trial of corticosteroids in young vs older DMD patients has not been published but analysis of subgroup of patients studied by Taylor suggests a more significant response in the younger patients (Dubowitz, 19912), and this was further highlighted by Dubowitz et al, 20023. The current consensus is to initiate this treatment before or at the time at which the boy’s physical performance plateaus. For practical purposes, this means between the ages of 4 and 6 years.

 *Response to Activity 6:*

The maximum available evidence for benefit is with daily dose corticosteroid regimes, listed as follows:

Prednisone 0.75 mg/kg/day

Or the equivalent

Deflazacort 0.9 mg/kg/day

 *Response to Activity 7:*

It is important to remember the possibility of Becker muscular dystrophy in a boy presenting with cramps on exercise, as the muscle weakness may be mild, and diagnosis not hitherto known.

Various presentations of Becker muscular dystrophy:

Motor difficulties – running, stairs

Leg pains

Exercise related cramps / myoglobinuria

Cardiac decompensation secondary to cardiomyopathy

Rarely, learning / behavioural difficulties

Rhabdomyolysis, hyperkalemia, myoglobinuria, or cardiac arrest in the course of general anesthetic including suxamethonium, or inhaled anaesthetics (Poole et al. Perioperative cardiac arrest in a patient with previously undiagnosed Becker's muscular dystrophy after isoflurane anaesthesia for elective surgery. Br J Anaesth. 2010;104:487-9)

 *Response to Activity 8:*

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| *Phenotype Characteristics*  | *Duchenne muscular dystrophy*  | *Becker muscular dystrophy*  |
| Typical age of presentation  | 2 to 5 years  | Usually 2nd decade and beyond. A minority may present between 5 – 10 yrs  |
| Loss of walking ability  | Mean age 9.5 years Range 7 to 12 years  | Majority maintain ambulation into 40s and beyond  |
| Incidence of scoliosis  | Over 90%  | Rare  |
| Learning difficulties  | Frequent  | Infrequent  |
| Sleep disordered breathing  | From late teens onwards, this is a constant finding  | Infrequent, but may occur in patients with FVC < 40%  |
| Serum CK  | Increased 10 fold or more \*CK level does not correlate with severity  | Increased 5 fold or more \*CK level, does not reliably differentiate between DMD and BMD  |
| Dystrophin in muscle biopsy  | Absent or severe reduction  | Variable patterns of decreased amount or molecular weight  |
| In-frame/Out of frame status of dystrophin gene mutation  | Out-of-frame  | In-frame  |