

ENMC steroids in DMD material.

This document contains suggested material to help with the use of steroids in DMD. It was assembled at and following an ENMC sponsored workshop on gold standards of medical management in DMD in April 2004 when it was acknowledged that common information material for patients and parents and follow up protocols did not exist for standardised care or data collection. Such protocols might also be utilised as the basis for data collection for clinical trials, but should not be too unwieldy to use in clinical practise. The material consists of the following

1. Patient information sheet with questions and answers about the use of steroids in DMD
2. A checklist of investigations and discussions to have before starting steroids, based on the discussions at the meeting
3. A basic clinic assessment sheet for data collection
4. A table of the measures of the efficacy of steroids assembled at the workshop
5. A table of the side effects that might be experienced during the use of steroids, how to monitor them, prophylactic measures to prevent or minimise side effects and how the occurrence of side effects should be managed. This table was assembled by discussion and review of the evidence at the workshop
6. The Hammersmith motor ability score (HAMA)

Steroids and Duchenne Muscular Dystrophy (DMD) - some questions and answers

This leaflet has been produced to help you think about whether your child with Duchenne muscular dystrophy should have steroids or not. It includes some of the main questions people have asked in this situation and also gives you some further information to look up. It is not intended to replace discussion with your doctors and other professionals, so feel free to ask any questions, you may have after reading this.

Why are steroids used in DMD?

It has been known for a number of years now that steroids have an effect on muscle strength in DMD. If they are used in boys who are still walking, they may have an effect on stabilising or even improving muscle strength for a period of time. Not all boys respond to steroids and the way that steroids have this effect on slowing the dystrophic process is not known.

What steroids are used?

The main steroids that are used are corticosteroids called prednisolone, prednisone and deflazacort. Prednisone/ prednisolone and deflazacort are likely to be equally effective in improving muscle strength but may have different side effect profiles. Deflazacort is not available in some countries. We are **not** talking about “anabolic steroids” which is what athletes use illegally to build up muscle- this does not have an effect in DMD.

What are the possible beneficial effects?

The studies which are now being reported on steroids are showing that overall boys who are treated with steroids walk for longer than those who are not. This effect varies from child to child but there are some studies coming out which are showing that some boys may carry on walking for years longer than they otherwise would. These children also seem to develop other complications of the condition less frequently too - so they develop breathing difficulties later and fewer problems with their spines. There may also be a positive effect on the heart muscle.

What are the possible risks?

The down side of steroid treatment, and the reason that people are still very cautious about using them, is that they may have side effects. Steroids have many side effects, but the chances of getting these vary from person to person, and on the dosage and the regime used. There are also important things that you and your doctor can do to try and protect against some of these side effects.

The most common side effects reported in the studies of using steroids in DMD in the short term are weight gain and mood changes. Weight gain seems to be most of a problem just at the time that the boys start taking the steroids, so it is a really good idea to keep a close eye on food intake at that time to avoid running into problems. If you would like further information on this, please ask your doctor, or you may be able to have access to advice from a dietician. In the longer term (after many years of treatment) there may be growth suppression, the development of cataracts and thinning of the bones. The risk of these long-term effects cannot be measured, but it is likely that the risk of different side effects varies with the different steroids used. Deflazacort on average may be associated with less weight gain, but a higher risk of development of cataracts (though these do not usually require any treatment). Because children with DMD already have thin bones, it is very

important to look after bone health, and the best way to do this is by promoting a healthy diet with good intake of calcium and vitamin D and lots of sunshine and exercise.

You will have the opportunity to discuss these fully with your doctor. There are whole lists of other possible side effects, which include raised blood pressure, diabetes, thinning of the skin and poor wound healing and increased susceptibility to infection, but these have not commonly been reported in the studies on DMD. A rare side effect of taking steroids in DMD is stomach irritation. It is important not to take non steroidal anti inflammatory tablets or medicines like neurofen or aspirin while you are on steroids. If your son develops tummy pain, or there is any sign of bleeding, you should contact your GP. This may not mean that they have to stop taking the steroids but it is important that this is noted.

How do the benefits and risks balance out?

This is a difficult question to answer because long term controlled trials to look at this have not yet been done. The reason that it is important to consider using steroids is because the studies which are coming out now are showing some significant benefits. In some studies some boys with DMD are still walking at the ages of 14 or 15. But there is no doubt that there can be important side effects, and the worst of these include significant growth delay and weak bones. It is important to try to minimise the risk of side effects by checking for them when you come to clinic. If significant side effects were picked up then the dose of the steroids might need to be altered or tapered off completely. It would also make sense to do this if it seemed like they were not having a positive effect. It is important to realise that if you do decide to use steroids this is not an “all or nothing” decision, but that the regime would be carefully worked out on an individual basis and changed if required.

What dose would be used and how often?

There are many regimes which have been suggested to be used.

All of the studies that have shown a useful benefit of steroids have given them on a daily basis, either prednisone/ prednisolone 0.75mg/kg/day or deflazacort 0.9mg/kg/day. However, some clinics believe that it is possible that using steroids intermittently (i.e. not all the time) or at a slightly lower dose could be effective while reducing the risk of side effects. The kinds of regimes in use include using steroids on every second day instead of every day, for 10 days on/ 10 days off, or at the weekends only. If you were particularly worried about the side effects one of these regimes might be a good alternative, also depending on the experience and advice of your local doctor. However, it has not been proven in controlled studies that these regimes are as effective as using steroids every day.

At what age would it be considered to start and stop using steroids?

There is some experience now that suggests that starting steroids before boys start to lose significant muscle function leads to better results. All boys with DMD achieve a plateau of their motor function when they are no longer improving but not yet deteriorating. The age at which this occurs varies from child to child but is commonly around the age of 4-5 years.

Later on, when more function has been lost, there may still be benefits of starting steroids in improving strength and particularly the strength of the breathing muscles. There is no evidence as yet for benefit of starting steroids in boys who have already lost ambulation, but studies looking at this are being done.

The age to stop steroids needs to be decided individually. It may be necessary to change or stop the steroids because of side effects. In other situations, they can be used for many years, beyond the age at loss of ambulation.

What happens if we decide to use steroids?

If you do decide that you want your son to use steroids, then there will be some extra checks that are necessary to make sure that they are having the desired effect and not causing any problems.. It will be very important that you attend these appointments. Your son will need to have some blood and urine tests to check everything is OK to use the steroids, and to check that he is immune to chicken pox (if not he will need to be immunised against it as chicken pox can be very serious in children who are on steroids). He will also need a scan of his bones and an eye check (these will need to be repeated at intervals while he is on the steroids), and a good assessment of how he is getting on at the moment.

Once the steroids have been started, it will be important to see your son regularly to check for any side effects and see if there is any difference in your son's physical performance and discuss with you if the dose seems right.

It is very important that steroids are not stopped suddenly but tapered off as the body becomes used to their effect and needs time to adjust if they are withdrawn. So if you decide you want to stop the steroids, that is fine, but he must do this under the guidance of a doctor. The dose has to be lowered gradually over several weeks to allow his own adrenal glands time to start making the steroids again themselves.

You need to get in touch with your doctor, either your GP or paediatrician, if he is sick and can't take his steroid for more than 24 hours, as he may need to have it by injection.

It is useful if your son wears a medi-alert bracelet or similar device when he is taking steroids. This should state that he is on prednisolone or deflazacort. If he is sick or has an accident this will ensure that the doctor who is treating him knows about the treatment and that he might need to have steroids given to him.

What happens if we decide not to use steroids?

The follow-up of your son will carry on in the usual way and all other options will be discussed as they become relevant. If you change your mind and want to think about steroids again in the future, you just need to mention this at one of your routine appointments.

Where can I find out more?

There are lots of sites on the web that discuss the use of steroids in DMD.

Here are a couple of examples, but you will be able to find more. Not all of them are completely up to date and it is important to realise that some of the most recent studies have not been formally published yet.

<http://www.dmdforum.org/information/steroids.html>

<http://www.dmdoptions.com/query247.htm>

<http://www.parentprojectmd.org/aboutdmd/treatment/supplements.html>

<http://www.enmc.org/workshops/reports.cfm?p=157>

<http://journals.elsevierhealth.com/periodicals/NMD/content/workshop>

<http://www.cochrane.org/cochrane/revabstr/ab003725.htm>

Baseline assessment

Name:

Date of birth:

Hospital number:

Date:

Weight:

Height:

Blood pressure:

Urine dipstix testing

Blood tests

Full blood count (FBC)

Random glucose

Electrolytes, urea, creatinine

Vitamin D

Patient information sheet- to be provided and discussed in advance of starting treatment

Functional, strength measures as per follow up assessment sheet

Dietary advice

- Discuss risk of weight gain, dietary measures at initiation of steroids, to include adequate dietary intake of calcium and vit D
- Consider dietician referral

Behavioural advice

- Record current behavioural issues
- Discuss behavioural management techniques

Immune status

- History of chicken pox OR varicella antibodies requested
- If there is history of active TB in a family member, this would be a contra-indication for steroid use. Boys from communities with high incidence of TB should be offered Mantoux testing and BCG as indicated, with parental consent prior to joining the trial; such children should not be started on prednisolone until 4 months following the BCG vaccination.

Bone Health

- History of fracture: frequency, site, trauma
- Request bone mineral density assessment by Dual X-ray Absorptiometry (DXA) scan (using DXA scan software with age appropriate normative bone density data from paediatric population to define normal ranges and to calculate z scores)

Ophthalmologic review

- Check for cataracts
- Visual acuity

Cardiac review

Steroid alert card- to be provided for each child

ENMC steroids in DMD material 3: clinical record

Name
 Date of birth
 Record number
 Date started steroids
 Regime

	Assessment 1	Assessment 2	Assessment 3	Assessment 4
Date				
Steroid dose				
Weight (centile)				
Height (centile)				
Blood pressure				
Urinalysis				
FUNCTION				
Run time				
Stairs time				
Gowers time				
HAMA score				
MRC score				
FVC (% predicted)				
SIDE EFFECTS				
Behaviour report				
Visual acuity/ red reflex				
GI symptoms				
Fracture				
Bone/ back pain				
Others				
Parent/ child report				
Action				

ENMC steroids in DMD material 4: recommended assessment of efficacy

Effect	Measure	Frequency	Adaptation for long term follow up
Function (1)	Milestones of disease progression - can do, age lost (hop, jump, get up from floor, stand on one leg, step up, step down, walk, stand)	0,3,6,12 months etc....	Needs no adaptation. Can be gathered by history and observation at long term follow up and has high clinical relevance.
Function (2)	Timed testing (time to get up from floor, to run defined distance)	0,3,6,12 months etc....	Timed tests will become impossible as milestones of disease progression are reached
Function (3)	Hammersmith motor ability score	0,3,6,12 months etc....	Scale may be less sensitive as children become less ambulant. May need adaptation or additional scale to accommodate changes in upper limb function
Muscle strength (1)	MRC score 34 muscle groups	0,3,6,12 months etc....	Applicability may be limited in long term
Muscle strength (2)	Quantitative muscle testing 6 muscle groups , Citec dynamometer http://www.citec.nu/frm/uk.htm	0,3,6,12 months etc....	Grip strength may remain useful measure in long term follow up.
Respiratory capacity	Forced vital capacity	0,3,6,12 months etc....	Will need additional respiratory investigation as FVC drops
Cardiac status	Echocardiography, electrocardiology	0,12 months etc....	Will need to be continued in long term as part of best practise monitoring [20}
Quality of life	CHQ-PF50, CHQ-CF87	0,3,6,12 months etc....	Annual administration in long term.

ENMC steroids in DMD material 5: side effect recording and action

Adverse event group	Measure	Prophylactic measures	Events to be recorded/ treated without dose alteration	Events as criterion for dose reduction	Events as criterion for drug withdrawal	Long term monitoring
Behaviour changes	CHQ-PF50, CHQ-CF87	Advice on behaviour modification	Change in behaviour from baseline. Psychology input as necessary	Behaviour changes disrupting family/ school life	Severe behaviour changes disrupting family/ school life	As for QOL issues
Weight	Weight for age/ height/ BMI 0,3,6, 12 Months etc	Dietary advice	Change in weight centile from baseline. Reinforced dietetic input as necessary	25% or 3 centile increase from baseline	Weight gain unacceptable to child/ family despite dietetic input/ dose reduction	Continue annually in long term
Height	Standing height or arm span in non ambulatory children 0,3,6, 12..... months etc		Change in height compared to predicted centiles	Failure to gain height that is unacceptable to child/ family	Failure to gain height that is unacceptable to child/ family despite dose reduction	Arm span necessary for assessment of respiratory function in non-ambulant patients
BD	DEXA baseline and annually, recording of fracture history 0,3,6 ... months etc	Vit D, calcium dietary advice, sunshine, exercise	Fracture, site, trauma. Limb fracture to be treated with early mobilisation. Vertebral fracture to be treated with iv bisphosphonates			Long term risk of vertebral fractures needs to be addressed by history. Careful checking of X rays obtained for other reasons for vertebral fracture.
Glucose tolerance	Blood, urine glucose 0,3,6, 12... months	Dietary advice		fasting blood sugar >110 <126mg/dl after dietary modification or blood glucose two hours after meal >140<200mg/dl	Diabetes mellitus as defined as fasting blood sugar >126 mg/dl or blood glucose 2 hours after a meal <200mg/dl	Urinalysis
Blood pressure	Blood pressure	Advice about dietary sodium		Consistent increase in systolic blood	Confirmed hypertension as defined as an increase	

	compared to age norms, measured 0,3,6, 12.... months	intake		pressure 15mmhg over the 97 th centile or diastolic blood pressure of 10mmHg over 97 th centile for age after sodium restriction	in systolic blood pressure of 15-30mmHg over the 97 th centile or diastolic blood pressure increased 10-30mmHg over 97 th centile for height	
Immune/ adrenal suppression	History of infection. Measure adrenal axis at start, midpoint and end of trial	Ensure prior exposure/ immunisation to chicken pox. Advise on steroid cover for surgery/ injury	Infectious diseases Abnormal response to stress	Unusually high frequency of infection/ unusual organisms- seek guidance from immunology expert.		
Gastrointestinal symptoms	History 0,3,6, 12 ... months etc	Advise to avoid NSAIDs	Abdominal pain/ peptic ulceration- treat with gaviscon, zantac	Persistent GI symptoms despite treatment		History, also history for other GI symptoms in long term eg constipation
Cataract	Ophthalmology/ visual acuity examination yearly for cataracts and intraocular pressure		Cataracts- if symptomatic, surgery. Increased IOP- follow ophthalmological advice			Visual acuity assessment
Skin changes	History and examination at 0,3,6,12 months for atrophy, easy bruising, fragility, striae, cutaneous/ oral infections		Skin changes, type and extent. Treat infections as indicated			

ENMC steroids in DMD material 6- HAMA (score of 2 denotes normal performance, 1 can do but not normally and 0 unable to perform)
The Hammersmith motor ability score (HAMA)

MOTOR ABILITY	Score 2,1,0	Comments
Lifts Head		
Supine to prone over ®		
Supine to prone over (L)		
Prone to supine over ®		
Prone to supine over (L)		
Gets to sitting		
Sitting		
Gets to standing		
Standing		
Standing on heels		
Standing on toes		
Stands on ® leg		
Stands on (L) leg		
Hops on ® leg		
Hops on (L) leg		
Gets off chair		
Climbing step ® leg		
Descending step ® leg		
Climbing step (L) leg		
Descending step (L) leg		
TOTAL OUT OF 40		

