**RECOMMENDATION OF ENDOCRINE & BONE MONITORING IN DUCHENNE MUSCULAR DYSTROPHY (DMD) IN THE UK NORTHSTAR NETWORK**

This UK NorthStar guidance on bone and endocrine monitoring of boys with DMD for use by neuromuscular clinicians in the clinic is adapted from recommendations laid out in the International Care Consensus of management of DMD (2018). This UK guidance was first developed in 2020 and has been revised in 2023.

**BONE**

- Annual screening with lateral thoracolumbar spine imaging and DXA for bone mineral density in all boys is recommended. Either lateral thoracolumbar spine x-ray or DXA based vertebral fracture assessment (ensure that imaging includes up to T4) can be used [1,2,3].
- Prescribe Vitamin D supplements to all boys with DMD.
- Blood monitoring of 25 hydroxy-vitamin D is recommended annually in all boys with DMD aiming for at least 50 nmol/L.
- Refer or discuss with paediatric endocrinology/bone specialist for consideration of the use of bone protective therapy (i.e. bisphosphonate) following:
  (a) Vertebral fracture with or without back pain, including mild vertebral fracture.
  (b) Low trauma long bone fracture.

**PUBERTY**

- Initiate conversation regarding likely pubertal delay and need for testosterone treatment in those treated with corticosteroid (Prednisolone and Deflazacort) during neuromuscular clinic follow-up at around 10-11 years of age. There is currently no clinical information on the impact of Vamorolone and puberty.
- Assess puberty in all boys aged 12 years and older. Formal assessment of pubertal status should be performed by a clinician with experience in assessment of puberty.
- Refer boys with no signs of puberty to the endocrine clinic for discussion about testosterone therapy (ideally before 14 years but should be considered from 12 years of age).
- Late or delayed puberty can be induced with gradually escalating doses of testosterone as utilised in the clinical trial of intramuscular testosterone for DMD [4], or from the guidance for management of boys with hypogonadism developed by the British Society for Paediatric Endocrinology and Diabetes (BSPED) https://www.bsped.org.uk/clinical-resources/guidelines/.

**ADRENAL**

- All boys prescribed Prednisolone, Deflazacort or Vamorolone, regardless of regimen, should be assumed to have adrenal insufficiency and therefore at risk of adrenal crisis during acute illness or significant stress (e.g. surgery, bisphosphonate infusion).
- All boys prescribed steroid therapy should have written documentation of an emergency sick day plan to be followed during acute illness.
- All families and boys should be educated about sick day plan and signs, symptoms and management of an adrenal crisis.
- Wearing of medical alert bracelet and carrying of a steroid card is strongly encouraged. A DMD steroid dependent bracelet is free to order https://dmdcareuk.org/emergency-support.
- The BSPED national steroid care plan card should be used BSPED steroid care plan.

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**Sick Days: When to give additional steroids**

- A plan for sick day dosing with oral steroids should be in place for moderate acute illnesses regardless of usual steroid regimen (continuous or intermittent). A paediatric steroid care plan for sick days and emergencies provides information on when to give additional oral sick day doses for illnesses as well as the management of an adrenal crisis: BSPED steroid care plan.
- Sick day dosing with steroids is recommended for the first bisphosphonate infusion, but may also be required for subsequent infusions as advised by treating bone specialist.

**For mild acute illness**

- Defined as mild infections (eg upper respiratory tract infection) but well enough to go to school.
- No extra oral sick day dosing is needed.

**For moderate acute illness**

- Defined as
  (a) Fever, flu, infection, childhood illnesses but usually not well enough to go to school
  (b) Vomiting and diarrhoea but able to keep oral medication.
- Extra oral steroids in the form of hydrocortisone on top of usual prescribed corticosteroids (i.e. Prednisolone, Deflazacort or Vamorolone) is our preferred recommendation.
- A simplified sick day dosing and schedules are provided below (Table 1) and adopts the dosing recommended by the UK national BSPED Paediatric Adrenal Insufficiency Guidance 2023 (BSPED Adrenal Insufficiency) [5].
- Prednisolone could be considered for sick day dosing (Table 1).
- We are unable to recommend the use of Deflazacort or Vamorolone for sick day dosing given the lack of published evidence and clinical experience.

(a) If using **Hydrocortisone** as oral sick day dose, give this four times a day for duration of illness [Table 1]. The usual *prescribed* steroid (Prednisolone, Deflazacort or Vamorolone) should continue.

(b) If using **Prednisolone** as oral sick day dose, give this two times a day for duration of illness [Table 1].
If usual *prescribed* Prednisolone dose is higher than the suggested Prednisolone *sick day* dose, split the *prescribed* Prednisolone and give in two doses (morning and evening).

- For example;
  1) Sick day steroid dose is Prednisolone 5 mg twice a day
  2) *Prescribed* Prednisolone dose is 20 mg daily
  3) In this case, simply split the usual *prescribed* Prednisolone dose and give Prednisolone 10 mg (morning) and Prednisolone 10 mg (evening).

***Table 1:*** *Suggested oral sick day dosing for moderate illness defined as* Fever, flu, infection, childhood illnesses but usually not well enough to go to school or vomiting and diarrhoea but able to keep oral medication

| **Weight** | **Hydrocortisone** | **Prednisolone** |
|---|---|---|
| 10 to 25 kg | 5 mg given four times a day | 2.5 mg given twice a day |
| 26 to 50mg | 10 mg given four times a day | 5 mg given twice a day |
| 51 to 90 kg | 15 mg given four times a day | 7.5 mg given twice a day<br>(or 10 mg am & 5mg pm) |

*The above is a simplified dosing plan for ease of implementation in the neuromuscular clinic with hydrocortisone dosing and equivalent Prednisolone dosing adapted from the UK national BSPED Paediatric Adrenal Insufficiency guidance (BSPED Adrenal Insufficiency).*
*If prescribed Prednisolone is higher than the suggested stress dose, split the prescribed Prednisolone and give in two doses (morning and evening). There is insufficient experience with the use of Deflazacort or Vamorolone for oral stress dosing.*

**For Severe Illness Or Vomiting Illness And Unable To Tolerate Oral Medication Or Fractures**

Hydrocortisone by intramuscular injection is required for emergencies (eg; fracture, recurrent vomiting). This could be given by the family or the attending emergency medical services.

| Age | Intramuscular Hydrocortisone dose |
|---|---|
| Less than 1 year | 25mg |
| 1 to 5 years | 50mg |
| 6 years and over | 100mg |

**For Minor Procedure Under Local Anaesthesia (Eg Tooth Extraction).**

- Give oral sick day dosing steroid for 24 hours.

**For Procedure Under General Anaesthesia**

- Please refer to the UK national BSPED Paediatric Adrenal Insufficiency Guidance 2022 (BSPED Adrenal Insufficiency).

***APPENDIX***

**Suggested Audit Targets**

Below are some suggested audit targets which each centre can use to evaluate clinical practise against the clinical recommendations. We have also provided results of a combined audit of all patients managed in Leeds and Glasgow in 2019 [6] for comparison for some of the audit standards.

1- What percentage of the boys with DMD in your clinic are on vitamin D supplements?
[88% Leeds and Glasgow audit]
2- What percentage of the boys with DMD in your clinic had 25 hydroxy vitamin D measured in a one year period?
[77% Leeds and Glasgow audit]
3- What percentage of boys with DMD in your clinic had 25 hydroxy vitamin D levels > 50 nmol/L?
4- What percentage of boys with DMD in your clinic had lateral thoracolumbar spine imaging to identify vertebral fracture in one calendar year?
[68% Leeds and Glasgow audit]
5- What percentage of boys with DMD in your clinic were initiated on bisphosphonates within six months of first low trauma long bone fracture?
6- What percentage of boys with DMD in your clinic were initiatied on bisphosphonates within six months of identification of vertebral fracture?
7- What percentage of boys with DMD in your clinic aged 12 years and older had an assessment of puberty?
[73% Leeds and Glasgow audit]
8- What percentage of boys with DMD aged 14 years or older with delayed puberty were initiated on testosterone before 15 years of age?

9- What percentage of steroid treated boys with DMD in your clinic have access to hydrocortisone for injection out of hospital with severe illness?
[93% Leeds and Glasgow audit]

**REFERENCES**


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