



Haemoglobinopathy Co-ordinating Centres Advice on COVID-19 for Patients with Diamond Blackfan anaemia

This document is a collaboration between the Haemoglobinopathy Co-ordinating Centres in England, offering guidance to health professionals working with patients with Diamond Blackfan anaemia (DBA). It has been reviewed and agreed by representatives of the Haemoglobinopathy Co-ordinating Centres in England and the Clinical Reference Group for Haemoglobin disorders and DBA(UK).

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Background:

A novel coronavirus named currently SARS-CoV-2 of a zoonotic origin has emerged and the infection called Coronavirus Diseases 2019 (COVID-19) started spreading worldwide. The time from exposure to symptom development is between 2-14 days. The majority of the affected general population suffer from minor flu symptoms, but around 15% of the proven positive patients develop a severe form of lower airways infection and up to 10% of the affected individuals require admission to intensive care for ventilatory support. Overall mortality from COVID19 disease seems to be around 2-3% of the affected individuals, but those figures are not final. Avoiding exposure by adhering to recommended hygiene procedures, isolation of SARS-CoV-2 infected persons and social distancing are the only prevention strategies. There are no approved treatment options and there is no available vaccine. Whilst most of the patients developing severe disease seem to have a frank pneumonitic evolution, some cases develop a severe inflammatory component, which might be responsible of a clinical picture similar to secondary HLH.

The NHP group has carried out a real-time survey of confirmed and suspect COVID-19 cases and their outcomes. To the end of May, there have not been any reported patients with DBA in England affected by COVID19 and based on our data there is no good evidence that children with rare anaemias are at increased risk of severe complications of COVID-19. We also note the absence of reports of complications from other international groups. However, we remain guarded as the following features may indicate a potential higher risk in DBA:

- approximately a third of patients with DBA are known to have impairment of cellular and/or humoral immunity.
- patients experience increased toxicity and myelosuppression with standard chemotherapy and transplant conditioning
- approximately a third of the patients with DBA are on steroids.
- there is a risk of adrenal insufficiency.
- patients and parents may have concerns/anxiety about undertaking ionising radiation containing radiological investigations because of the increase risk of cancer in DBA.

The patients we support were originally classified have been classified as ‘clinically extremely vulnerable’ and advised to shield for twelve weeks, or as ‘clinically vulnerable’ and advised to socially isolate. As knowledge has accrued and the situation changed, there has been new guidance from NHSE, Public Health England and the work carried out by the HCC, NHP and CRG in relation to the classification of patients and advice provided.

PROCEDURE

General Guidance

Refer patients to up to date advice on the NHS-E and PHE websites:

- <https://www.nhs.uk/conditions/coronavirus-covid-19/>
- <https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults>

The British Society of Haematology is hosting the latest updated versions of all the documents produced by the NHP: <https://b-s-h.org.uk/about-us/news/covid-19-updates/>

All patients with DBA are advised to adopt Social Distancing Measures. In addition:

- Adopt remote consultations and postponement of routine monitoring tests and clinical consultations that are not essential.
- Patients to let their specialist teams know if they have symptoms or have to self-isolate or, if they access emergency services or are admitted to hospital.
- Delay steroid trials until resolution of COVID-19 and remain on transfusion programme.
- Delay planned BMT admission unless for MDS/AML or aplastic transformation, in which case assessment of risk:benefit ration needs to be applied.

Clinically Extremely Vulnerable Patients with DBA

Patients with DBA are classified as Clinically Extremely Vulnerable if they fall in any of the following categories:

- Patients on high doses of steroids sufficient to significantly increase the risk of infection, defined as prednisolone (or equivalent) ≥ 0.5 mg/kg/day or ≥ 20 mg per day. **Most patients with DBA responsive to steroids are on doses of prednisolone ≤ 5 mg/kg or ≤ 20 mg on alternate days and therefore do NOT fall in this group.**
- Patients with an associated cellular or humoral immunodeficiency, or if infants or too young to have their immune status assessed.
- Severe iron overload defined as cardiac T2* < 10 ms AND additional co-morbidity (diabetes, chronic liver disease).
- Patients who have had a BMT within 1 years or are still using immunosuppressive drugs

Clinically Extremely Vulnerable Patients with DBA should follow the advice on <https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19> and register online for support using the link even if no additional support is needed right now.

Clinically Extremely Vulnerable Patients are strongly advised to Shield. Advice on Shielding has been updated:

1. Patients should work from home and children/young people should not return to school/educational establishments when these reopened.
2. Shielding means staying at home as much as possible and keep visits outside to a minimum (for instance once per day):
 - If you wish to spend time outdoors (though not in other buildings, households, or enclosed spaces) you should take extra care to minimise contact with others by keeping 2 metres apart.

- If you choose to spend time outdoors, this can be with members of your own household. If you live alone, you can spend time outdoors with one person from another household (ideally the same person each time).
- You should stay alert when leaving home: washing your hands regularly, maintaining social distance and avoiding gatherings of any size.
- You should not attend any gatherings, including gatherings of friends and families in private spaces, for example, parties, weddings and religious services.
- You should strictly avoid contact with anyone who is displaying symptoms of COVID-19 (a new continuous cough, a high temperature, or a loss of, or change in, your sense of taste or smell).

Siblings and other members of the household are not required to adopt protective shielding measures for themselves but should avoid going to school and work where possible.

Clinically Vulnerable Patients with DBA

Patients with DBA are classified as Clinically Vulnerable if they fall in any of the following categories:

- Patients 50 years and above
- Severe cardiac iron overload $T2^* < 10$ ms, with no additional co-morbidities and adherent with therapy
- Severe cardiac iron overload ($T2^* > 10$ ms but < 12 ms).
- Severe - moderate iron overload ($LIC > 30$ mg/g DW and $T2^* > 12$ ms) AND additional comorbidity.
- Patients receiving steroid treatment.
- Patients with congenital heart disease as per British Congenital Cardia Association guidelines in https://www.bcca-uk.org/pages/news_box.asp?NewsID=19495710 (infants < 1 year with unrepaired congenital heart disease requiring surgery or catheter intervention, chronic cyanosis (oxygen saturations $< 85\%$ persistently), patients with severe cardiomyopathies requiring medication, and patients with congenital heart disease on medication to improve heart function).

This group should follow the Government guidance Staying alert and safe (social distancing) for the whole population about staying at home and staying away from others: <https://www.gov.uk/government/publications/staying-alert-and-safe-social-distancing/staying-alert-and-safe-social-distancing>.

Children and young people in the vulnerable group can attend school when schools re-open for their year group. Adults should continue to work from home if possible or alternatively placed in low risk environments. Give their potential for increased vulnerability; it is very important that patients still follow strict social distancing measures and good hand hygiene. Siblings and other household members should also all stay at home and stay away from others as much as possible.

DBA Treatment:

No changes to usual patient treatment are required, but avoid initiating new therapies unless essential.

- **Patients on regular transfusions** to remain on the same regimen. Routine blood tests monitoring for iron overload and for the effects of iron chelation should be continued. For patients on regular transfusions, outpatient review should be co-ordinated to take

place at the same time as transfusion. Clinicians should consider if routine MRI monitoring for iron overload can be postponed. If fever develops, all chelation agents should be stopped unless severe cardiac iron load is likely to cause decompensation and patients are advised to contact their clinical team.

- **Patients on steroid treatment** should remain on the same steroid regimen.
- **Patients in haematological remission** do not require additional monitoring.

Management of DBA Patients who are Unwell:

All DBA patients need urgent assessment if unwell or have fever to rule out non-COVID-19 causes (e.g. bacterial infections causing sepsis).

Stop all chelation treatment unless there is severe cardiac iron load with risk of decompensation (febrile or acute unwell patients have risk of AKI with both desferrioxamine and deferasirox, risk of severe tubular acidosis with deferasirox, risk of hyperammonaemic encephalopathy with deferasirox and risk of neutropenia in patients on deferiprone).

Patient on steroids:

In a DBA patients is steroid responsive and has suspected (or confirmed) coronavirus infection they should:

- if taking prednisolone <0.5 mg/kg (up to 15 mg a day) double the daily dose by taking the same dose of steroids twice a day.
- if taking prednisolone >0.5 mg/kg or >15 mg should continue their usual dose, but take it split into two equal doses of at least 10 mg every 12 hours.
- if on hydrocortisone replacement for adrenal insufficiency follow the usual advice for infections.
- if admitted to hospital very unwell we recommend there may be a need for a conversion to hydrocortisone IV continuous or every four hours.

Management of DBA Patients Fulfilling COVID-19 Criteria:

For a proportion of patients remote supervision following assessment will be sufficient:

- systems need to be in place for remote follow-up every 24 hours
- a clear pathway needs to be instituted for patients to seek help

- A. All DBA patients positive for SARS-CoV-2 should have a CXR despite lack of lower respiratory symptoms before ascribing them to remote supervision. Patients may need reassurance about the use of ionising radiation imaging because of the increased risk of cancer in DBA.
- B. Remote supervision is not appropriate if there are clinical symptoms of lower respiratory tract infection (shortness of breath, hypoxia and tachypnoea) despite the absence of radiological signs on the CXR. Further imaging should be considered: an MRI chest in preference to HCRT if possible to minimise ionising radiation.
- C. Co-infections should be evaluated and treated.
- D. Assess for possibility of adrenal insufficiency and if known adrenal insufficiency institute hydrocortisone replacement therapy.

Patients can take paracetamol or ibuprofen when self-medicating for symptoms of COVID-19, such as fever and headache, and should follow [NHS advice](#) if they have any questions or if symptoms get worse, as advised in the latest [CAS alert](#).

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