



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.

Data from China and Italy suggests that children have a milder form of the disease than adults, although we do not understand why this is the case. Only 2 in every 100 diagnosed cases of coronavirus in China have been in children and young people aged <18 years. The Italian experience in Milan and Turin (Prof Nica Capellini and Professor Antonio Piga) is that there has been limited impact in patients with thalassemia, as a model of a transfusion dependent anaemia in a high-risk area. Similarly, the Monza haematology, oncology and BMT paediatric service (Professor Adrianna Balduzzi) has seen limited impact in children with serious haematological disorders. Early data collected by this collaboration confirms limited incidence of serious disease in rare anaemias, but this may reflect the distancing and shielding measures taken. 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.

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, which includes being supported to work from home as per the current government guidance, even if the patient is a key worker.

- 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 ratio needs to be applied.

Shielding in Patients with DBA:

Follow 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>

DBA patients require Shielding if:

- on high doses of steroids defined as:
 - children: prednisolone (or equivalent) ≥ 0.5 mg/kg on alternate days or ≥ 0.25 mg/kg daily
 - adults: prednisolone (or equivalent) ≥ 30 mg on alternate days or ≥ 15 mg per day
- have an associated cellular or humoral immunodeficiency, or due to still being infants or too young to have their immune status assessed.
- have adrenal insufficiency on steroid replacement
- have iron overload defined as
 - cardiac T2* < 15 ms, previous or current impaired LV function or other cardiac complications due to the iron load or significant congenital heart disease due to DBA
 - severe hepatic iron overload LIC > 15 mg/g DW
 - Please note: the ferritin cannot be used as an assessment tool unlike other transfusion dependent anaemias as it often underrepresents the iron load.
- have had a BMT within 2 years or are still using immunosuppressive drugs

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. NHSBT are working to maintain the blood supply and will update clinical teams if problems develop, which has not been the case so far. If that were to be the case, there may be a need to lower the transfusion threshold from current recommendation of Hb ≥ 90 g/L to ≥ 80 g/L in the first instance. 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).

Red flag symptoms: patients should be encouraged to attend the Emergency Department (A+E) or call 999 if any of the following occur:

- Respiratory distress (new shortness of breath or increased breathlessness compared to baseline particularly at rest or on minimal exertion) +/- chest pain
- Persistent fever $\geq 38^{\circ}$ C (lasting for at least one hour).
- Severe headache, confusion or neurological changes.

Management of DBA Patients Fulfilling COVID-19 Criteria:

For a proportion of patients remote supervision 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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