COVID-19 - guidance for management of children admitted to hospital and for treatment of non-hospitalised children at risk of severe disease

Health Policy team

This best practice advice is focused on the management of confirmed or suspected SARS-CoV-2 infection in children admitted to hospital and on the currently available treatments for non-hospitalised children at risk of severe disease.

This has been produced with the British Paediatric Allergy, Immunity and Infection Group.

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It should be noted that policies cited within this guidance are rapidly evolving and services should ensure they are accessing the most up to date versions.

Summary

- Current diagnosis for SARS-CoV-2 infection is based on detection of viral RNA by PCR on nasopharyngeal and/or oropharyngeal swabs. Diagnosis of prior infection is on SARS-CoV-2 IgG serology in blood.
- Consider alternative diagnoses in children who are unwell, even in the presence of a positive SARS-CoV-2 PCR result
- Antibiotic prescribing should follow normal practice, considering the risk of sepsis and that an alternative diagnosis and focus of infection has been sought.
- Children with mild to moderate disease do not routinely need admission or investigations such as blood tests and radiology, unless otherwise clinically indicated
- Children with severe or critical disease (ie requiring oxygen, respiratory or cardiovascular support) as a minimum should have the following investigations:
    - Blood cultures, FBC, Coagulation, D-dimer, U+E, LFT, CRP, Troponin, ferritin, LDH and blood gas
    - Samples (respiratory and blood) should be sent for virology testing prior to initiating any antiviral or immunomodulatory treatment

- Dexamethasone (or equivalent dosing of alternative corticosteroid) should be considered for use in children > 5 years with severe or critical COVID-19 as per NICE recommendation. Use of corticosteroids in younger children and infants should also be considered on a case by case basis.
- Remdesivir should be considered for hospitalised children > 12 years and >40kg with COVID-19 requiring supplemental oxygen as per licensed indication, national policy for use of remdesivir and NICE recommendation.
- SARS-CoV-2 specific monoclonal antibody treatment or remdesivir should be considered for children >12 years and >40kg who develop hospital onset symptomatic COVID as per national policy.
- SARS-CoV-2 specific monoclonal antibody treatment or remdesivir should be considered for non-hospitalised children with additional risk factors for progression to severe disease or hospitalisation as per national policy and NICE guidelines. The specific paediatric considerations for non-hospitalised children are covered in the section **Treatment criteria for COVID–19 specific therapy** below and in Table 2. It is recommended that all potentially eligible patients are discussed with regional paediatric ID consultant to confirm whether to proceed with offering treatment.
- Consider chest x-ray in children who do not follow the expected clinical course, for example, those still requiring oxygen on day three of admission, those with worsening hypoxaemia or those requiring respiratory support
- Decision to escalate respiratory support to NIV should be made by a senior member of the paediatric team, in discussion with critical care and retrieval teams if necessary.
- Children admitted with suspected “severe” SARS-CoV-2 infection who have abnormal coagulation/D-dimer/fibrinogen results should be discussed with the local haematology team, in particular to consider the role of prophylactic low molecular weight heparin.
- Consider pulmonary embolism (PE) in the unwell patient with sudden worsening of hypoxaemia, BP or tachycardia
- It is recommended that all patients for which COVID-19 specific therapies are being considered should be discussed with a paediatric infectious diseases specialist and should be considered for entry into the RECOVERY trial.
- Where possible, all patients should only receive investigational treatments for COVID-19 within a treatment trial, but can be considered for compassionate use on a case-by-case basis on discussion with appropriate experts (eg paediatric infectious diseases/rheumatology/immunology)

- For children with clinical findings consistent with the recently defined Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) refer to RCPCH guidance.
- Follow usual discharge criteria as for other respiratory or infectious conditions. No guidelines exist to date regarding duration of follow up, or recommended investigations. As usual, parents should be provided with information on how and when to seek additional advice if children have new or persistent symptoms.

Key principles of good care of children admitted to hospital during the COVID-19 pandemic

Reassure: Compared with adults, children are much less likely to become severely unwell with the infection. Fatal infection is rare. Be aware that children and parents will have ascertained information (and misinformation) in mainstream and social media, and from friends and relatives.

Involve parents: When parents / carers feel disempowered, they may become anxious and feel that their child is not being managed properly. The way healthcare professionals communicate with families is important.

1. When parents / carers have to stay in a room with a child for their entire hospital stay it can be daunting and claustrophobic. It is important that they are kept up to date, even more so than in normal circumstances, as their levels of anxiety will be heightened.
2. Furthermore, identify ways to actively involve parents / carers – in infection control procedures, entertaining and calming their child, supporting good nutritional intake, and asking questions on their child's behalf.

Personal Protective Equipment (PPE) for staff can look alarming to children, and it is important that parents and healthcare professionals proactively discuss the need for such measures and reassure children. These crucial aspects of care are best done by parents / carers.

Be vigilant: Some children will develop complications and comorbidities. Although the medical literature suggests that the majority of children will have self-limiting illness without any complications, it is important to follow local guidelines around sepsis, acute kidney injury, and respiratory failure.

Teamwork: The multidisciplinary team must work together to ensure the best outcome for the child. During times of viral pandemic, parents / carers and children want to see healthcare professionals adhere to the same guiding principles of practice. Deviation from the management plan is undermining to other professionals, and parents and children will pick up on differences in practice (however subtle). Written and verbal communication between professionals, and regular review of patients, is crucial to prevent this.

Minimising the spread of the virus in hospital is crucial. Be aware of local and national recommendations for doing this. In the ISARIC-WHO-CCP dataset, 55/651 (8.5%) of cases were hospital-acquired.[1]

Be careful with information and deal with misinformation. There is rapid spread of information through open access medical literature, via social media, and mainstream media outlets – this means the general public may find out new information as quickly as health professionals. In some ways, this can be very helpful. However, this information may be invalid or outdated. Medical literature prior to peer-review should be considered with caution. Decisions outside guidelines should be made as a team, to reach a consensus, with specialist input as needed.

Pathology of COVID-19

COVID-19 is caused by a novel coronavirus (SARS-CoV-2). The virus is extremely contagious, particularly where there is close contact between people indoors. The virus directly infects cells via the ACE2 and TMPRSS2 receptors, expressed in multiple organs including the lung. One proposed disease mechanism in adult severe cases is a 'cytokine storm'. This describes a cascade process whereby the virus leads to increased levels of cytokines that cause direct tissue damage, recruitment of neutrophils to tissues, and other pro-inflammatory effects. This damage can lead to organ failure including Acute Respiratory Distress Syndrome.

Extrapulmonary involvement and other organ failure have been identified in people with severe or fatal illness. Some patients develop cardiac dysfunction. This may be due to viral- induced direct damage, or hypoxic damage in people with respiratory failure. Liver damage and renal failure have been associated with severe infection.[2]

Clinical and laboratory features in children

In the ISARIC-WHO-CCP cohort, the most common presenting symptoms were fever (70%; 431/617), cough (39%; 233/599), nausea/vomiting (32%; 179/564), and dyspnoea (30%; 173/570).[1] In the NHS England/RCPCH audit of children who were admitted to hospital and tested positive for COVID-19, fever was the most common presentation (72%). Three clusters of presenting features were identified in the ISARIC-WHO-CCP cohort:

- A respiratory cluster in which children presented with a discrete respiratory episode of cough, upper and lower respiratory symptoms, and fever
- A mucocutaneous-enteric cluster of headache, myalgia, gastrointestinal symptoms, lymphadenopathy, fatigue, rash and conjunctivitis - and this cluster largely reflects the symptoms seen in children with PIMS-TS (see below)
- A rarer cluster of neurological features – particularly seizures and confusion

The common pattern of blood results seen in adults with severe COVID - 19 is not present in children to the same extent. Altered taste and smell are common features in adults with COVID-19, but there is little in the literature in children. One multicentre study evaluated smell and taste dysfunction in 10 children and found these symptoms to be present in all.[3] Presence of these symptoms should raise the index of suspicion for COVID-19 in children.

Investigations

Diagnosing SARS-CoV-2 infection

Tests to detect SARS-CoV-2 should be considered for symptomatic children, children admitted to hospital either electively or as an emergency, prior to surgical procedures or aerosol generating procedures, as part of screening in high risk areas (eg PICU, transplant or dialysis centres). Samples that can be collected to detect SARS-CoV-2 virus (nucleic acid or antigen) include nasopharyngeal/oropharyngeal swabs or saliva. Nucleic acid amplification testing (NAAT), most commonly with a reverse-transcription polymerase chain reaction (RT-PCR) assay, to detect SARS-CoV-2 RNA from the upper respiratory tract is the standard of care.

A positive RT-PCR confirms the diagnosis of SARS-CoV-2 infection. Patients may have detectable SARS-CoV-2 RNA for weeks after the onset of symptoms; however prolonged viral RNA detection does not necessarily indicate ongoing infectiousness. A single negative RT-PCR is sufficient to exclude the diagnosis of COVID-19 in the majority of children, however if there is high suspicion of COVID-19 (suggestive symptoms, clinical findings and investigations), a further test may be performed. It is usually recommended to repeat this test after at least 24 hours.

The interpretation of an inconclusive or indeterminate result depends on the specific nucleic acid amplification test (NAAT) performed; the clinician should confer with the performing laboratory about additional testing.

Diagnosis of prior SARS-CoV-2 infection

Serologic tests detect antibodies to SARS-CoV-2 in the blood and may identify patients who previously had SARS-CoV-2 infection or have developed immunity following immunisation. Detectable antibodies may be present within days of natural infection, but are usually present three to four weeks after the onset of symptoms, hence they are not used for diagnosis in the acute setting. IgG antibody is usually measured and sensitivity and specificity vary depending on which test is used. The duration of detectable antibody is uncertain but is known to wane over time.

Other tests including viral culture and other tests of SARS-CoV-2 immunity are not widely available currently.

Samples (respiratory and blood) should be sent for virology testing prior to initiating any antiviral or immunomodulatory treatment and it is recommended that all patients should be discussed with an infectious diseases team. Please also

refer to guidance on management of PIMS-TS.

Blood tests

The majority of children are expected to be asymptomatic or only have mild to moderate disease. No additional blood tests are required for these children who, if admitted requiring only supportive care, beyond those required to exclude alternative diagnoses. Given the relatively mild symptomatology of the majority of children with COVID-19, alternative diagnoses must be considered in unwell children presenting, following the same pathways in place prior to the outbreak.

Characteristic blood abnormalities have been associated with severe outcomes in adult COVID - 19. It is not currently known if they are applicable to children, however in unwell children with possible severe COVID-19, the following blood tests may have some diagnostic and prognostic value: blood cultures, full blood count, coagulation profile, D-dimer, renal function, liver function, bone profile, CRP, ferritin, LDH, troponin and pro-NT-BNP. Blood gases should be monitored in children with respiratory distress.

Radiology

Chest x-rays and CT scans may reveal findings even in asymptomatic children, and the individual relevance of these may be unclear. They should not be conducted routinely, even if children require a small amount of oxygen on admission, and should only be used to answer a specific question. Consider chest x-rays in children whose clinical course is not following an expected disease progression, or who deteriorate, for example those still requiring oxygen on day three of admission, those with worsening hypoxaemia or those requiring CPAP.

For children with proven COVID-19 infection but minimal or no respiratory symptoms chest CT is unlikely to be helpful. In adult COVID-19, with a crude in-hospital mortality rate of 30% in the UK, understanding the underlying lung pathology may be useful in determining prognosis or identifying appropriate strategies for respiratory support. However, most children with COVID-19 have self-limiting illness and mild disease progression, and knowing the changes on CT is unlikely to guide clinical decisions. Transferring infected children to the CT scanner unnecessarily puts other patients at risk. In addition, children with suspected COVID-19 but negative viral testing, chest CT is also unlikely to be of benefit, in one study nearly 10% of children had positive RT-PCR but negative CT.[4]

Supportive medical care

This section covers: admission, fluids, antipyretics, respiratory support, antibiotics, bronchodilators / treatment of children with asthma attacks, and COVID-19 related coagulopathy.

Admission

Most children with COVID-19 do not require admission. Many people with confirmed COVID-19 may be managed at home. Paediatricians should consider the child's clinical presentation, requirement for supportive care, underlying medical conditions and the ability for caregivers to care for the child at home when deciding whether to admit a child with COVID-19, All children and young infants including those who are clinically extremely vulnerable should be considered on a case by case basis.

Fluids

Acute Kidney Injury (AKI) can complicate viral infections. Most children with mild illness do not require fluid restriction below normal maintenance values. Fluid restriction may be indicated in children with moderate to severe respiratory compromise as this may reduce the risk of acute respiratory distress syndrome (ARDS). Be aware that febrile children, and those who are tachypnoeic, may have increased insensible losses. Pharyngitis or anorexia may limit oral intake. Monitor fluid balance, and measure daily weight in those children in whom fluid intake is a concern.

Renal profile blood tests and urine dipstick are not required in all children but should be measured if there is a concern about fluid balance. Diuretics are not indicated routinely but should be considered in children with worsening respiratory failure requiring CPAP or NIV, particularly if there is evidence of pulmonary oedema on chest x-ray. Involve critical care and transport teams early in these cases and discuss with a paediatric infectious diseases team.

Antipyretics

Paracetamol is the first line antipyretic. Ibuprofen should be avoided in children with poor fluid intake or suspected AKI, but this is related to the risk of kidney damage rather than worsening COVID-19. RCPCH has recommended that parents treat symptoms of fever or pain related to COVID-19 with either paracetamol or ibuprofen.

Respiratory support

Most children, even those with lung involvement, are unlikely to develop respiratory failure. Children should initially receive low flow nasal cannula (LFNC) oxygen if they are hypoxic, rather than high flow nasal cannulae (HFNC). Guidance exists elsewhere on the rationale for use of HFNC during the pandemic (National guidance for the management of bronchiolitis during COVID-19). Decision to use HFNC should be made by a senior team member. There is no evidence in the literature about the benefit of blood gases – these should not be done routinely. They can be used in children who appear to require escalating respiratory support. In such children capillary blood gas (not arterial or venous) may be used to evaluate for pH and pCO2. Early use of CPAP and non-invasive ventilation may prevent deterioration requiring invasive mechanical ventilation.

Children with significant respiratory distress should be discussed early with a Critical Care Team, and strategies for respiratory support tailored around that child.

Antibiotics

Consider antibiotics if

- They are unusually sick at admission / day one (particularly fever and / or on oxygen) or if there is a clinical deterioration. Antibiotics should be prescribed

based on usual grounds and clinical judgement. Teams should ensure they have sought a focus of infection (urine, throat swab, blood culture +/- CSF as appropriate prior to starting antibiotics, as is best practice).

- Blood tests are suggestive of bacterial infection, e.g. raised CRP and neutrophil count.
- CXR changes reveal a pneumonic picture, e.g. lobar pneumonia and this is consistent with the clinical picture.
    - CXR changes should be mild in most children. Antibiotic choice may vary depending on findings, e.g. bilateral changes may indicate atypical infection and a macrolide may be indicated. However, bilateral CXR changes have been described in seemingly asymptomatic children, so should be interpreted in the context of the clinical picture.
- An alternative or co-incidental diagnosis is considered, e.g. sepsis, which may have overlapping clinical features.

Bacterial coinfection is uncommon in COVID-19. In a meta-analysis of observational studies-examining the risk of bacterial co-infection in people with COVID-19, 281/3338 (8.4%) had a reported bacterial infection (based on 24 studies, 3338 people with COVID-19 who were also evaluated for bacterial coinfection in respiratory, blood, or unspecified samples). In the three paediatric studies, 8/55 children (14.5%) had bacterial coinfection.[5]

Antibiotic choice should be based on local guidelines. A respiratory sample for microbiological culture should ideally be sent prior to starting antibiotics. For children with co- morbidities, such as cystic fibrosis, antibiotic choice should be based on known bacterial colonisation where available. Antibiotic choice, duration, route of administration should be reviewed daily in the context of clinical progression and microbiology results.

Bronchodilators / treatment of children with asthma attacks

Wheeze is not a common problem in children with COVID-19. Bronchodilators should not be used routinely unless there is strong suspicion of bronchoconstriction (wheeze, and prolonged expiratory phase). The side effects of bronchodilators include pro-inflammatory effects on the alveoli, worsening of V/Q mismatch, and tachycardia.

In children with acute wheeze or asthma attacks, prompt treatment with salbutamol and systemic steroids (within an hour of arrival) can reduce the risk of

hospitalisation, and further need for nebulisation.

Salbutamol given via Metered dose inhaler (MDI) is as effective as nebulisation, and less likely to lead to admission. There is insufficient evidence to recommend using concomitant ipratropium bromide if salbutamol is given via MDI, and no evidence for using intravenous magnesium sulphate earlier than it is usually given. If nebulisation is required because a child is hypoxic and tachypnoeic, salbutamol and ipratropium bromide may be given concomitantly, but there is no evidence to suggest that more than one such combined nebuliser should be given.

Nebulisation is not currently considered an aerosol generating procedure therefore normal droplet precautions should be made. Nevertheless, good practice would be to avoid nebulisation if at all possible and use MDI.

COVID-19 related coagulopathy

COVID-19 related coagulopathy observed in adults seems to be multifactorial in nature, and in adults, it is associated with poor outcome.6 Extrapolation from guidelines for management of COVID-19 coagulopathy in adults may be considered on a case by case basis.

Within this BTS guideline, recommendations are made about the management of potential venous thromboembolism (VTE) or pulmonary embolism (PE) which are relevant to children and young people:

"*PE should be considered if sudden worsening of hypoxaemia, blood pressure or tachycardia occurs, or if oxygen requirements are disproportionate to the severity of pneumonia on CXR. Compression ultrasonography should be performed if clinical signs suggestive of DVT develop. There should be a particularly high index of suspicion for VTE and a low threshold for investigating/treating for VTE in patients with high oxygen demands requiring CPAP or intubation*."

There are no specific guidelines for management of thrombosis in children with COVID-19, so early discussion with a paediatric haematologist is recommended, including for the interpretation of D-dimer and fibrinogen results and the role of prophylactic low molecular weight heparin.

Treatment criteria for COVID-19 specific therapy

All patients for which COVID-19 specific therapies are being considered should be

discussed with a paediatric infectious diseases specialist and hospitalised patients should also be considered for entry in to the RECOVERY trial.

Samples (respiratory and blood) should be sent for virology testing prior to initialising treatment and all patients should be discussed with microbiology/infectious diseases.

Treatments with specific criteria for consideration:

Corticosteroids (dexamethasone or equivalent dosing of alternative corticosteroid) should be considered for use in hospitalised children > 5 years with severe or critical COVID-19 as per NICE recommendation.

Dosing of dexamethasone should be 150 micrograms/kg IV or PO (maximum 6mg) once daily for 10 days or until day of discharge from hospital if this is before completion of 10 days.

Corticosteroids should also be considered for children aged between 44 weeks gestational age and 5 years with severe or critical COVID - 19 on a case by case basis following discussion with appropriate specialists in an MDT.

Remdesivir should be considered for hospitalised children > 12 years and >40kg with COVID-19 requiring supplemental oxygen as per licensed indication, national policy for remdesivir and NICE guidelines.

A shorter 3-day course of remdesivir can also be considered according to national policy for hospital onset symptomatic SARS-CoV-2 infection in children in clinical risk groups (see table 2) who or in hospital already for a non-COVID reason. Dosing should be as per SmPC. Use of remdesivir outside of the context of the licensed indication should ideally be in the context of a clinical trial but can be considered on a case-by-case basis on discussion with paediatric infectious diseases specialists.

SARS-CoV-2 specific monoclonal antibodies should be **considered** for patients with hospital onset COVID as per current national clinical commissioning policy. Currently, sotrovimab is commissioned for use in hospitalised children and young people aged 12-17 years, weighing at least 40kg, with certain additional considerations relating to underlying clinic risk and comorbidity as well as timing of symptom onset and reason for hospitalisation. It is recommended that decision on eligibility and risk benefit of administration should be urgently discussed on a

case by case basis with a paediatric infectious diseases specialist and other specialists involved in the child or young person's care.

Table 1

Suggested additional general criteria for consideration of specific therapies for COVID-19 for hospitalised children and young people

General treatment criteria		
Mild to moderate disease No O2 requirement Mild upper airway infection	All groups Risk group*	Supportive care NB Currently only for hospital onset COVID: Consider SARS-CoV-2 specific monoclonal or remdesivir as per national policy
Severe disease Mild - moderate ARDS**: 1. Unventilated requiring FiO2 >40% to maintain saturation 88-97% 2. Ventilation: • Oxygenation index: 4 ≤ 16 • Oxygenation saturation index: 5 ≤ 12.3	All groups Risk group*	Supportive care Consider dexamethasone as per above Consider remdesivir as per above Consider SARS-CoV-2 specific monoclonal antibody in eligible patients as per above Consider RECOVERY trial Treatment with investigational immunomodulatory therapy may be considered on a case by case basis especially in a risk groups* and especially if evidence of hyperinflammation (raised CRP, ferritin, IL6, sCD25)

Critical disease Severe ARDS**: • Oxygenation index ≥ 16 • Oxygenation saturation index: ≥ 12.3 Septic shock Altered consciousness Multi-organ failure	All groups	Supportive care Consider dexamethasone as per above Consider remdesivir as per above Consider SARS-CoV-2 specific monoclonal antibody in eligible patients as per above Consider RECOVERY trial Treatment with immunomodulatory therapy may be considered especially if evidence of hyperinflammation (raised CRP, ferritin, IL6, sCD25)

***Risk group:** See table 2

**ARDS as defined by the PARD criteria: Pediatric Acute Lung Injury Consensus Conference Group.7

For children with clinical findings consistent with Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2 (PIMS-TS), please also refer to guidance.

SARS-CoV-2 specific monoclonal antibodies or short course (3 days) remdesivir should be considered for non-hospitalised patients with SARS-CoV-2 infection as per national commissioning policy.

In children and young people (aged < 18yr), risks of hospitalisation or death from COVID are very low. Current evidence suggests those in the listed risk groups in the national policy (see table in appendix of national policy) do not have equivalent risk to older adults with the same conditions.

Studies of pre-hospital nMAbs and/or anti-virals have largely been in adults and there are minimal data to assess benefit of nMAbs to those <18yr, even in symptomatic inpatients. Due to low numbers of severely unwell children and young people, it is challenging to estimate the risks vs benefit, or number needed to treat to prevent hospitalisation, severe disease. Administration of an

intravenous or sub-cutaneous drug to children and young people in hospital brings its own burden, and requires specialised paediatric teams. Nevertheless, equity of care for those deemed to be at risk is vital.

All children and young people who potentially are eligible through the national policy should therefore be discussed with regional paediatric infectious diseases service to confirm eligibility and to consider the risk benefit and whether to proceed with offer of treatment.

The following should also be taken in to account when considering pre-hospital treatment:

- It is generally accepted that comorbidities are additive in terms of risk of hospitalisation or severe disease
- Additional comorbidities (not included in the current main national policy) that, according to current evidence, should be taken in to account in decision making include:
    - Complex neuro-disability
    - High BMI
    - Severe pre-existing respiratory disease
    - Complex genetic or metabolic conditions associated leading to comorbidity
    - Multiple congenital abnormalities

This preliminary guidance will be updated regularly.

Table 2 provides guidance on the clinical risk factors that should be considered when recommending treatment to non-hospitalised symptomatic, SARS-CoV-2 PCR positive children and young people under 18 years. Neutralising monoclonal antibodies or ambulatory remdesivir should be administered in an age-appropriate paediatric/adolescent facility. Concerned clinicians should refer for regional MDT case discussion through local established pathways.

Table 2

Non-hospitalised patient cohorts in the 12-17 years age range considered at highest risk from COVID-19 and to be prioritised for consideration of treatment with neutralising monoclonal antibodies when symptomatic and SARS-CoV-2 PCR positive

CYP at significant risk

Neuro-disability

- Complex life-limiting neuro-disability with recurrent respiratory infections/ compromise

CYP at significant risk if 2 or more of these risk factors are present

Primary immunodeficiency

- Common variable immunodeficiency (CVID)
- Primary antibody deficiency on immunoglobulin (or eligible for immunoglobulin replacement)
- Hyper-IgM syndromes
- Good's syndrome (thymoma plus B-cell deficiency)
- Severe Combined Immunodeficiency (SCID)
- Autoimmune polyglandular syndromes /autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- Primary immunodeficiency associated with impaired type I interferon signalling
- X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

Secondary immunodeficiency

- HIV CD4 count <200 cells/mm3
- Solid organ transplant
- HSCT within 12 months, or with GVHD
- CAR-T therapy in last 24 months
- Induction chemotherapy for acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma, chemotherapy for acute myeloid leukaemia (AML), relapsed and /or refractory leukaemia or lymphoma

Immunosuppressive treatment

- Chemotherapy within the last 3 months
- Cyclophosphamide within the last 3 months
- Corticosteroids >2mg/kg/day for 28 days in last 4 weeks
- B cell depleting treatment in the last 12 months

Other conditions

- High BMI (>95th Centile)
- Severe respiratory disease (e.g. CF or bronchiectasis with FEV1 <60%)
- Tracheostomy or long term ventilation
- Severe asthma (PICU admission in 12 months)
- Neurodisability and/or neurodevelopmental disorders
- Severe cardiac disease
- Severe chronic kidney disease
- Severe liver disease
- Sickle Cell disease or other severe haemoglobinopathy
- Trisomy 21
- Complex genetic or metabolic conditions associated with significant comorbidity
- Multiple congenital anomalies associated with significant comorbidity

Investigational therapy

Our recommendation is that, as far as possible, all patients in the UK should only receive investigational treatments for COVID-19 within a treatment trial.

Criteria for antiviral and immunomodulatory treatment
As highlighted above, apart from corticosteroids, neutralising monoclonal antibodies and tocilizumab there is currently relatively limited published evidence of efficacy of specific therapies for COVID -19 in adults, and very limited high quality evidence in children. The decision to start specific treatment should therefore be made carefully on a case by case basis.

We recommend discussion within already established internal review pathways, but also suggest discussion with a Paediatric Infectious Disease Specialist prior to

starting antiviral therapy and/or a clinician with experience in the use of immunomodulatory therapy if these are being considered (immunology, haematology, bone marrow transplant, rheumatology).

Antiviral treatment is likely to have the most benefit in the first phase of illness. Immunomodulatory therapy may only be indicated if clear evidence of hyperinflammation, or in the second phase of the illness, and evidence is currently extremely limited in children.

Clinical trials and observational studies for COVID-19 and paediatric patients

The following interventional clinical trials and national/international observational studies are active in the UK for recruitment for hospitalised paediatric patients:

- RECOVERY trial
- ISARIC
- Diamonds
- BATS
- BPSU

Discharge

NHS England has guidance on discharge.

There is no specific guidance currently around who requires follow-up, but parents should be told to seek medical advice if the child has persistent symptoms after discharge. As the results of longitudinal follow-up studies become available, it will be possible to give more structured advice around this. Chronic symptoms related to SARS-CoV-2 infection have been described in adults (Long COVID), but data is lacking in children; research studies are underway.

Further information

For children with clinical findings consistent with the recently defined Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) please also refer to guidance available here.

For guidance around management of bronchiolitis this winter, please refer to RCPCH national guidance on the management of children with bronchiolitis during COVID-19.

The British Association of Perinatal Medicine has produced frequently asked questions within neonatal services during the pandemic.

NHS England has produced general guidance on the clinical management of COVID-19. Please note that this is not specific to paediatric patients.

NICE has produced rapid guidelines for COVID-19. This includes guidance for the management of immunocompromised children and young people and general COVID-19 treatment guidelines.

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