Guidance for the clinical management of children admitted to hospital with proven COVID-19

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Scope and background:

This guidance outlines key principles for the medical management of children admitted to hospital with COVID-19 (caused by SARS-CoV-2 virus)

The guidance is based on literature review of published and unpublished data, expert opinion from teams at Alder Hey Children's Hospital, and national/international guidelines. It incorporates recommendations from the RCPCH. A list of relevant papers updated twice-weekly is shown in Appendix 1. The internal validity of the observational studies is generally low, and the results may not be directly generalisable to children in the UK, but there are common themes. This guideline will evolve as we learn more about this infection. The most up-to-date document will be hosted on the Alder Hey website.

Links:

RCPCH COVID-19 guidance page

Paediatric Intensive Care Society (PICS)

Alder Hey INFORMATION HUB

National advice

National advice for the public

Public Health England advice about preventing spread

Public Health England guidance on management of possible cases

Summary of the guidance:

Reassure parents and involve them in caring for their child, keep up-to-date using the evidence in Appendix 1 of this guidance, and communicate well with colleagues

Be extra-vigilant in children with pre-existing conditions but reassure parents that the risks of comorbidities is much greater in adults than children

Chest x-rays, bloods, and blood gases are not routinely indicated. Consider these only in children with persistent fever, altered fluid balance, signs of liver dysfunction, or respiratory failure

Although recommended in some adult papers, the following medical treatments are likely to have more side-effects than beneficial effects in children and are not routinely indicated: bronchodilators, systemic steroids, antibiotics, antivirals, and diuretics.

Escalate respiratory support as per the respiratory failure pathway – do not use high flow nasal cannula oxygen if the child is saturating adequately with low flow oxygen

Key principles for good practice during this pandemic:

Reassure: Most children will have mild symptoms - much milder than those seen in adults. Reassure children and parents, as they are likely to be concerned from information (and misinformation) in mainstream and social media. They may also know an adult with the infection, who may have been treated in a different way to how we manage children. This guidance explains the rationale behind the recommendations which may be useful in explaining clinical decisions.

Involve parents: When parents 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. Stress that active monitoring and supportive therapy as required is the best strategy, and that parents have a crucial role to play. Furthermore, it is important to identify ways in which the parents can be involved in care – being vigilant to infection control procedures, keeping their child calm and entertained, supporting good nutritional intake, asking questions on their child's behalf, and helping avoid unnecessary investigations and interventions. These crucial aspects of care are best done by parents.

Be vigilant: some children with COVID-19 will develop complications and comorbidities. Although the medical literature suggests that the vast majority of children will have self-limiting illness without complications, be aware of local sepsis guidelines, acute kidney injury guidelines, and respiratory failure guidelines. You must adhere to other trust guidance around infection control, and be aware that these may change over time.

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

Minimising spread of the virus in hospital is crucial. Guidance from RCPCH outlines standards around doing this.

Key principles of medical care:

History

The commonest features in the history of children with COVID-19 are fever and cough. Fever typically subsides within three days. Most children do not have respiratory problems. Ask about parental smoking and housing quality.

The information required for reporting to Public Health England is available here.

Comorbidities (avoid the term 'high risk' when talking to parents and children)

There is little evidence around COVID-19 in children with comorbidities. In adults, co-morbidities are an important risk factor for mortality but this is much less likely to be the case in children. As evidence is published, we will list this in Appendix 1.

Relevant pre-existing conditions include:

1. Long term respiratory conditions including:
Chronic lung disease of prematurity with oxygen dependency
Cystic fibrosis
Childhood Interstitial lung disease
Asthma
Respiratory complications of neurodisability

2. Immunocompromise (disease or treatment) including:
Treatment for malignancy
Congenital immunodeficiency
HIV
Immunosuppressive medication including long term >28 consecutive days of daily oral or IV steroids (not alternate day low dose steroid or hydrocortisone maintenance)
Post transplant patients (solid organ or stem cell)
Asplenia (functional or surgical)
Trisomy 21

3. Haemodynamically significant and/or Cyanotic heart disease

Type 1 Diabetes in itself is not a comorbidity associated with worse disease in children, although it may be in some adults. Diabetic control can worsen during times of intercurrent illness, so adhere to the guideline for managing this (link to diabetes guidance).

Clinical teams may have their own guidance around COVID-19 in children with these conditions, and where this is the case the links to these are included above. In general, have a lower threshold for treatments and investigations but adhere to the main guiding principles of this guideline where possible.

Medical treatments and investigations

Radiology: Chest x-rays should not be conducted routinely. There are well described chest x-ray findings, even in asymptomatic children, and these do not always reflect clinically relevant pneumonia. Most abnormal x-rays and CT scans showed non-specific findings in children, and this are not useful when conducted routinely. Be aware that it is crucial to isolate children and avoid movement around the hospital, so chest x-rays will be portable: they must only be done if there is a specific clinical question.

Lobar collapse due to bacterial pneumonia is more likely if the child has respiratory failure, and persistent temperature. Generally, chest x-rays should only be performed in children requiring HDU admission. Some children not on HDU may require a chest x-ray if they have worsening hypoxaemia, particularly if they have pre-existing conditions. No studies have described lobar collapse, pneumothorax, or effusion in children with COVID-19. A number of studies advocate for the use of CT scans, but these will not help with diagnosis or management and are not indicated. Transferring infected children to the CT scanner puts other children at risk.

Antipyretics: Paracetamol is the first line antipyretic. Avoid ibuprofen in children with poor fluid intake or suspected AKI.

Bronchodilators: Wheeze is not a common problem in children with COVID-19. In people with lung involvement, this tends to be in the alveoli rather than the small airways. 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 asthma who are wheezy, use bronchodilation via MDI/spacer rather than nebulisation where possible as this reduces the risk of side effects, and minimises droplet spread. For children having an asthma attack treat them as they usually would be treated but avoid nebulisation.

Systemic steroids: Systemic steroids should not be used. Some adult papers promote the use of steroids, and they were used in the outbreak in Wuhan. However they are likely to be harmful, immunosuppressive, and prolong viral shedding. They are unlikely to be beneficial. This is because there is no evidence of significant lung inflammation in children with COVID-19 so immunomodulation is not required. If children require ventilation and develop Acute Respiratory Distress Syndrome steroids may be useful (1) but there is no consistent and accurate way of identifying who will benefit.

Respiratory support: most children, even those with lung involvement, are unlikely to develop respiratory failure. It is important that children receive low flow nasal cannula (LFNC) oxygen if they are hypoxic, rather than high flow nasal cannulae (HFNC). This is to reduce droplet spread of the virus. If children are hypoxic despite LFNC, then HFNC can be tried. It should not routinely be used as a method of reducing work of breathing in children who are otherwise saturating adequately. There is no evidence in the literature about blood gases – these should not be done routinely. They can be used in children who despite administration of HFNC seem to require further respiratory support. In such children capillary blood gas (not venous) should be used to evaluate for pH and pCO2. Please note the v60 is an aerosol-generating ventilator, as are the portable ventilators used by the LTV service.

Antimicrobials: It is unclear how frequently bacterial co-infection occurs in children with COVID-19. One study has measured and reported this, and found that 20% of children admitted to hospital may have had co-infection with mycoplasma pneumoniae. This should be suspected in children with some combination of persistent fever, coughing discoloured sputum, and hypoxia. Although not described in the literature, bacterial coinfection may be more likely in children with severe disease, so antibiotics should be started in children admitted to HDU or PICU. These should be given enterally where possible. There should be a lower threshold for starting antibiotics in children with comorbidities. Chest x-ray is not always needed. There is no evidence that any antiviral treatment, or interferon, is beneficial. A number of papers in adults advocate the use of these therapies but they are not recommended in children. CRP should not be taken routinely. It is normal in the majority of children, and only slightly raised in those in whom it is abnormal.

Fluids: Acute Kidney injury (AKI) is a complication of viral infections. Most children do not require fluid restriction below normal maintenance values. Be aware that febrile children, and those who are tachypnoeic, will have increased insensible losses. A small proportion of children may have pharyngitis, but this is not reported as a common problem with this virus so should not in most children affect 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. The fluid guidelines are available here (link). Diuretics are not indicated routinely as there is no report of pulmonary oedema in the literature, and they increase the risk of AKI. In some children with worsening respiratory failure requiring CPAP or NIV, diuretics may be used under consultant guidance if there is evidence of pulmonary oedema on chest x-ray.

Liver: There are reports of raised liver enzymes in children and adults with COVID-19. It is unclear how significant this is. Children with viral infections do get transient derangement of liver function, but this is self-limiting. It is more likely that this would happen in children who are generally unwell, those with pneumonia, and those receiving medical treatments that we will not be using. If taking bloods because the child appears unwell, check and record any derangement in liver function. If the derangement persists, check clotting. Do not check LFT routinely.

Discharge from hospital: We will update this section when we understand the natural history of the infection better.

APPENDIX 2 – SOURCES OF EVIDENCE

This is a repository of published and unpublished literature around COVID-9 or SARS-CoV-2 infection in children. Note in version 1 quality appraisal is not complete, but all evidence is low quality.

Web of Science
You searched for: **TOPIC:** (co-vid or covid or coronavirus or MERS-CoV) *AND* **TOPIC:** (clinic* or radiolog* or manage* or treat* or therapy*)
Refined by: PUBLICATION YEARS: (2020)
Timespan: All years. **Indexes:** SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC.

Handsearching (daily) of:

General medical journals

NEJM
BMJ
Lancet
PLoS Medicine
JAMA
BMC

Open access journals

BMJ Open
BMJ Open paediatrics
Plos One

Paediatric journals

ADC
JAMA Pediatrics
Lancet Child and Adolescent medicine
BMC Pediatrics

Respiratory journals

Lancet Res Med
Thorax
Chest
BMC respiratory medicine

https://ourworldindata.org/coronavirus

https://www.arcgis.com/apps/opsdashboard/index.html - /bda7594740fd40299423467b48e9ecf6

Table 1 : studies relevant to COVID-19 in children (and selected adult studies – the adult studies will not be routinely added)

Study	Location	Patient population	Quality/ external generalisability	Summary findings
SELECTED ADULT STUDIES				
Xu BMJ	Zheijang Province	62 Adults and children (n=2 children)	Retrospective, multi-centre Selection: all relevant patients, but this is a short time frame so not all cases included Ascertainment: adequate. Methods around identifying respiratory complications not well described Generalisability: mainly adults in China, early in the epidemic. Treated with regimen not used in UK	20/62 (32%) had pre-existing comorbidity 21/62 (34%) were associated with familial clusters Median duration of symptoms 4 days Commonest clinical features: fever (77%), cough (81%) myalgia/fatigue (52%) Respiratory: 2/62 (3%) developed shortness of breath 1/62 (1.6%) ventilated Bloods: FBC: 19/62 (31%) leucopenic Renal: not reported LFT: AST increased in 10/62 (16%)
Huang Lancet	Wuhan	41 adults (no children were infected)	Retrospective multi centre Selection: all relevant patients, but this is a short time frame so not all cases included Ascertainment: adequate Generalisability: mainly adults in China, early in the epidemic. Treated with regimen not used in UK	13/41 (32%) had pre-existing comorbidity Median duration of symptoms 7 days Commonest clinical features: Fever (98%) Cough (76%) Myalgia/fatigue (44%) Respiratory: 22/41 (55%) developed dyspnoea (median at 8 days after onset) 13/41 (32%) required HFNC oxygen or more respiratory support 12/41 (29%) developed ARDS 4/41 (9%) required MV (2 of whom needed ECMO) Bloods: FBC: 10/41 (25%) leucopenic LFT: 15/41 (37%) raised AST AKI: 3/41 (7%)
Xu European Journal of Nuclear Medicine and Molecular Imaging	Guangzhou	90 adults		45/90 (50%) had comorbidities Commonest clinical features: Fever (78%) Cough (63%) Fatigue/weakness (21%) Respiratory: not reported Bloods: FBC: 19/90 (21%) leucopenic LFT: not reported AKI: not reported Radiology: 69/90 showed abnormalities (see radiology section)
Chen Lancet	Wuhan	99 Adults	Retrospective single centre Selection: all relevant patients, but this is a short time frame so not all cases included Ascertainment: adequate (?ARDS definition) Generalisability: mainly adults in China, early in the epidemic. Treated with regimen not used in UK	50/99 (51%) had pre-existing comorbidity Median duration of symptoms 7 days Commonest clinical features: Fever (83%) Cough (82%) Dyspnoea (31%) Respiratory: 81/99 (31%) developed dyspnoea 76% required oxygen 17% developed ARDS 4% required MV (3% needed ECMO) Bloods: FBC: 4% leucopenic (24% increased); 35% lymphopenic, 38% neutrophilic LFT: 35% raised AST AKI: 3%
PAEDIATRIC STUDIES				
Xia (2)	Wuhan	20 children	Retrospective single centre	Age: Median 2 years Sex: 13/20 (65%) male Comorbidities: 2/20 (10%) had previous cardiac surgery; 4/20 (20%) had known arrythmias; 1/20 (5%) had epilepsy

				Symptoms: Asymptomatic: 0 (0%) Fever: 12/20 (60%) Cough 13/20 (65%) Respiratory: 2/20 (10%) tachypnoeic Examination: Crackles 3/20 (15%), recession 1/20 (5%), cyanosis 1/20 (5%). Support required: not reported (suspect 0/20 required ICU) Bloods: FBC: 4/20 (20%) leucopenia; 2/20 (10%) leucocytosis LFT: 5/20 (25%) raised ALT AKI: not reported CRP: >3 in 7/20 (35%) Cardiac enzymes: CK-MB >25 in 5/20 (25%) Radiology: CXR not reported CT (20 children): Pulmonary - normal 4/20 (20%), Consolidation with halo sign 20/20 (50%) Ground glass 12/20 (60%) Nodules 3/20 (15%) Microbiology: Bacterial coinfection: 4/20 (20%) - mycoplasma
Chen (3)	Shenzen	31 children	Prospective single centre All received interferon, ribavirin, lpoanivir, ritonavir	Age: Median 6.8 years (range 1.5-17) Sex: 13.31 (42%) male Comorbidities: 2/31 (6.5%) – one asthma, one 'delicate kidneys' Symptoms: Asymptomatic 12/31 (38.7%) Fever: 14/31 (45%) duration median 2 days IQR 1-3 Cough: Respiratory: Not reported Bloods: FBC: 12/31 (38.7%) leucopenia; 17/31 (55%) lymphycytosis; 2/31 (6.5%) neutrophilic LFT: 2/31 (6.5%) Raised ALT AKI: 0/31 (0%) (creatinine) CRP: >8 in 4/3 (12.9%) Cardiac enzymes: not raised (though LDH abnormal in 39%) Radiology: Normal 19/20 (95%) CT showed ground glass changes, subpleural shadows and 'hazy pathces'
Tang (4)	Shenzen	26 children	Low quality evidence Retrospective single centre Selection: unclear if all cases included Ascertainment: definition of Covid19 as per national guidance Not yet peer-reviewed Methodology not clear	Age: mean 6.9 (0.7) years (1-13) Sex: 9/26 male (35%) Comorbidities: 0/26 (0%) Symptoms: Asymptomatic 9/26 (35%) Fever 11/26 (42%) Cough 12/26 (46%) Median duration before attendance at hospital unknown Respiratory: None (0%) developed ARDS or 'acute lung injury' Bloods: FBC: 50% leucopenia; 96% lymphocytosis LFT: 3/26 (12%) raised AST and/or ALT AKI: not reported CRP: >5 in 5/26 (19%) Myocardial enzymes: normal, except 6% had raised LDH Radiology (CXR/CT) Normal: 8/26 (31%) Unilateral changes: 11/26 (42%) Bilateral changes: 7/26 (27%)
Henry (5)	International	82 children	Low quality evidence Multicentre database No standardisation Ascertainment – unclear of case definition	Age: median 10 years (IQR 5-15). 27/82 (33%) adolescents Sex: 52.4% male Comorbidities: Symptoms (available in 25 children): 2/25 (8%) asymptomatic Fever 17/25 (68%) Cough 9/25 (36%) Median duration of symptoms: 3 days

			Not yet peer reviewed	Respiratory: not reported Bloods: not reported Radiology: not reported
Cai (6)	Shanghai	10 children	Low quality evidence Single centre retrospective Not yet peer reviewed	Mean 6 years range 3 months – 11 years Sex: male:female 1:1.5 Comorbidities: Symptoms: 0/10 (0%) asymptomatic Fever 8/10 (80%) – resolved after 24 hours Cough 6/10 (60%) Median duration of symptoms: 2.5 days Respiratory: 0 children had dyspnoea, 0 required oxygen Bloods: FBC: 3/10 leucocytosis, 1/10 leucopenia, 1/10 neutrophilia CRP: >10 in 3/10 (max 33) LFT: ALT raised in 1/10 (100U/l) AKI: 0/10 Radiology: CXR: 4/10 (40%) bilateral patchy infiltrate, 6/10 normal Microbiology: Bacterial coinfection: not reported
Wang (7)	Shenzhen	34 children	Abstract only Low quality evidence Single centre retrospective review	Median age 8 years 1 months Sex: 14/34(42%) male Comorbidities: not reported Symptoms: Fever 17/34 (50%) Cough 13/34 (38%) Respiratory: "no severe cases were identified" Bloods: FBC: 1/10 leucopenia CRP: 'elevated' in 1 case LFT: not reported AKI: not reported Radiology: "bilateral multiple patchy or nodular ground-glass opacities and/or infiltrating shadows in middle and outer zone of the lung or under the pleura." Numbers nor rpeorted
Wang (8)	Northern China (6 provinces)	31 children	Abstract only Low quality evidence Retrospective multicentre review	Mean age 7 years Symptoms: Fever 20/31 (65%) Cough 14/31 (45%) Respiratory: Bloods: FBC: leucopenic in 2/31 (6%) CRP: 'elevated' in 3/30 (10%) LFT: 6/27 (22%) – unsure of which enzyme AKI: none Radiology: abnormal in 14 cases unsure how many had CT) – ground glass, patchy, nodules, subpleural, lower lobes
Wei (9)	China	9 infants <1 year	Letter Retrospective review Low quality	Median age 7 months Sex: 2/9 male Symptoms: Fever 4/9 URT symptoms 2/9 Asymptomatic: 1/9 Median duration of symptoms 1 day Respiratory: None required ICU or mechanical ventilation Family clustering in all infants
Liu (10)	Wuhan	6 children	Letter; 6 children (early in Wuhan outbreak) Low quality evidence	Median age 3 years (range 1-7) Sex: 3/6 (50%) male Comorbidities: none Symptoms: Fever >39 in 6/6 Cough in 6/6

			Used treatments we are not recommending (antiviral, steroids, Ig)	Respiratory: 1 required oxygen and also admission to ICU Bloods: FBC: leucopenia in 4/6, neutropenia 4/6 CRP: not reported LFT: not reported AKI: not reported LOS 5-13 days (median 7.5) Radiology: 4/6 had pneumonia on CT
Studies with adults and children, but did not report paediatric data separately – listed but data not extracted				
Chang (11)				

Appendix 2: Summary data from Cheshire and Mersey Network – all confirmed admitted cases of COVID-19

Age
Gender

Comorbidities

Clinical outcome

Length of stay

Needed oxygen y/n; duration of oxygen

HFNC
CPAP/NIV
PICU for MV

Bronchodilators
Antibiotics
Chest x-rays

Appendix 3: Contributors, advisors, and reviewers

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