Prioritising paediatric surveillance during the COVID-19 pandemic

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Children may represent only a small proportion of confirmed cases of coronavirus disease 2019 (COVID-19) in the current pandemic, but they are at the centre of every paediatrician's mind and the primary focus of their work. While much of the COVID-19 pandemic preparedness and response is rightly focused on adults, paediatricians should be reassured that children have not been forgotten. In the UK, the Royal College of Paediatrics and Child Health (RCPCH) has produced extensive guidance for paediatricians that are available online (https://www.rcpch.ac.uk/resources/covid-19-guidance-paediatric-services). At the same time, Public Health England (PHE) provides regularly updated guidance for healthcare professionals, focusing particularly on infection control and testing for COVID-19 (https://www.gov.uk/government/collections/wuhan-novel-coronavirus). PHE is also working with National Health Service (NHS) and academic colleagues to answer important questions about childhood COVID-19, including the course of illness and outcomes in neonates and children, the risk of vertical transmission during pregnancy and the role of children in infection and disease transmission in the community.

GLOBAL COVID-19 SITUATION

Coronaviruses typically cause mild upper respiratory tract infections, but they have been responsible for three major outbreaks associated with severe illness and death: severe acute respiratory syndrome (SARS) in 2002, Middle East respiratory syndrome (MERS) in 2012 and, now, COVID-19. Genomic analyses indicate that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, originated in bats[1] and was probably transmitted to humans through an intermediate host, most likely pangolins (scaly anteater-like mammals).[2] The illness was first recognised in Wuhan, Hubei Province, China, in early December 2019, and spread rapidly across the continents, leading the World Health Organization (WHO) to declare COVID-19 a public health emergency of international concern (PHEIC) on 30 January 2020 and then a global pandemic on 12 March 2020. By 28 April 2020, there were >3.2 million COVID-19 cases and >225 000 deaths worldwide (https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases).

COVID-19 IN THE UK

In the UK, imported COVID-19 cases were first diagnosed at the end of January 2020 and increased slowly because of the initial containment procedures involving rapid identification and isolation of symptomatic cases, with extensive contact tracing (https://www.gov.uk/guidance/high-consequence-infectious-diseases-hcid). On 4 March, there were only 85 cases but these increased rapidly to 456 on 11 March, 2626 on 18 March, 17 089 on 28 March, 25 150 on 31 March, 108 692 cases on 17 April and 161 145 cases with 21 678 deaths on 28 April 2020 (https://www.gov.uk/guidance/coronavirus-covid-19-information-for-the-public).

COVID-19 IN CHILDREN

In China, children under the age of 10 years (416 cases, no deaths) and 10–19 years (549 cases, one death) each represented <1% of the total number of 72 314 confirmed and suspected COVID-19 cases until 11 February,[3] a similar proportion to the SARS and MERS outbreaks.[4 5] In another case series of 2143 children with COVID-19, 94% of children had asymptomatic, mild or moderate disease (table 1).[6] Children were much less likely to develop severe or critical disease (5.9%) than adults (18.5%). Infants aged <1 year had the highest proportion with severe or critical cases (11%), which declined to 4% in individuals aged 11–15 years; only one teenager in this cohort died.[6] Overall, there have been very few deaths due to COVID-19 in individuals aged <50 years but case fatality rates increase exponentially after this age, reaching 15% among >80 years.[3]

Table 1 Diagnostic criteria used in a large paediatric series of 2143 childhood COVID-19 cases in China[6]

Severity of illness	Description of illness
1. Asymptomatic	Positive nose/throat PCR for SARS-CoV-2 in a child with no clinical symptoms or signs and with normal chest imaging if performed.
2. Mild	Symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing. Physical examination shows congestion of the pharynx and but no auscultory abnormalities. Some cases may present with no fever or have only gastrointestinal symptoms such as nausea, vomiting, abdominal pain and diarrhoea.
3. Moderate	Presentation with pneumonia, fever and cough (initially dry then productive), some may have wheezing or transmitted respiratory noises, but no obvious hypoxaemia such as shortness of breath. Some cases may have no clinical symptoms or signs, but chest CT shows lung lesions, which are subclinical.
4. Severe	Early respiratory symptoms such as fever and cough may be accompanied by gastrointestinal symptoms such as diarrhoea. Disease usually progresses around 1 week, and dyspnoea occurs, with central cyanosis. Oxygen saturations are less than 92% in air, with other hypoxia manifestations.
5. Critical	Rapid progression to acute respiratory distress syndrome or respiratory failure, with or without shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction and acute kidney injury. Organ dysfunction may be life threatening.

https://pediatrics.aappublications.org/content/pediatrics/early/2020/03/16/peds.2020-0702.full.pdf.
SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Data on childhood COVID-19 from other countries are slowly emerging. In the US, between 12 February and 02 April 2020, children aged <18 years accounted for 1.7% (2572/149 082) of cases where age was reported; 20% were hospitalised, 23% had ≥1 comorbidity and three died.[7] The main comorbidities were chronic lung disease including asthma, cardiovascular disease and immunosuppression; such children were more likely to be hospitalised and admitted to intensive care units.[7]

Many questions, however, remain unanswered. It is still not clear why children have a lower risk of COVID-19 and develop milder disease. The answer is likely to be related to both exposure and host factors. Unlike most other infectious diseases, children primarily acquire SARS-CoV-2 from adults, usually a family member; this mode of transmission may be less efficient and result in a lower infecting dose. Alternatively, the maturity, function and/or avidity of the human receptor for SARS-CoV-2, the ACE 2,[8] may be lower in children than adults. Children are also more likely to have been recently exposed to other coronaviruses (four strains are identified: HCoV 229E, NL63, OC43 and HKU1) that are endemic worldwide and cause mild respiratory illnesses,[9] which could provide some cross-protection against COVID-19. The immune response of children to SARS-CoV-2 is also likely to be different to adults. A less mature immune system does not explain the increased severity in infants compared with older children,[6] but the smaller airways and immature respiratory tract could potentially contribute to more severe disease.

The role of children in the COVID-19 transmission chain remains unclear.[10] So far, reports of asymptomatic children who are PCR positive for SARS-CoV-2 are mainly from contact tracing after a confirmed case, and they account for a small proportion of reported childhood cases. We urgently need population screening, seroincidence and seroprevalence studies to estimate age-specific asymptomatic infection rates in the community, which is critical for modelling and predicting disease transmission, as was done with influenza A (H1N1).[11] Such studies are currently underway (box 1), and their results will be important for informing policy decisions about school closures, lockdown and social distancing measures.

Whether pregnant women are at increased risk of COVID-19—as with influenza A(H1N1)—is not clear. Neither is the risk of vertical transmission in utero

Box 1 Ways in which Public Health England is working with National Health Service and academic partners to answer important questions about SARS-CoV-2 transmission and COVID-19 disease in children

Clinical follow-up of laboratory-confirmed COVID-19 cases in children aged 29 days to <16 years (paed COVID)

Public Health England receives electronic notifications of all confirmed COVID-19 cases from National Health Service hospital laboratories through the Second Generation Surveillance System. Notified childhood cases in the surveillance age group are followed up with their general practitioners and hospital to determine whether they were hospitalised and, if so, the responsible paediatric consultant is then contacted to complete a short online clinical questionnaire for each case. Information collected includes clinical presentation, underlying comorbidities, investigations, intensive care requirements, treatment and outcome at hospital discharge.

In order to speed up data collection, paediatricians in England can directly report cases to PHE by emailing phe.paedcovid@nhs.net. If you would like more information about the surveillance, please contact Dr Shamez Ladhani at shamez.ladhani@phe.gov.uk.

Confirmed COVID-19 cases in children are also followed up using the same online clinical questionnaire in Wales (Jennifer.Evans7@wales.nhs.uk) and Northern Ireland (Sharon.Christie@belfasttrust.hscni.net).

Clinical follow-up of laboratory-confirmed cases in neonates up to 28 days of age

PHE is working with colleagues at the National Perinatal Epidemiology Unit and Imperial College London to conduct clinical surveillance of COVID-19 in neonates from birth up to 28 days of the through the British Paediatric Surveillance Unit (www.bpsu.org.uk). Paediatricians across the UK and Ireland will receive weekly emails from the BPSU team to report whether they have managed a case of neonatal COVID-19 in the previous week. Those confirming a case will be asked to complete a short clinical questionnaire. Further information about the BPSU surveillance is available online: https://www.rcpch.ac.uk/bpsu-study-neonatal-complications-coronavirus-disease-covid-19#lead-investigators. For more information about the BPSU surveillance, please contact: Dr Jenny Kurinczuk or Dr Chris Gale at bpsu-covid@ndph.ox.ac.uk

At the end of the surveillance, cases will be linked to a similar surveillance of COVID-19 in pregnant women and their babies, which is in progress through the UK Obstetric Surveillance System (UKOSS). Further information about the UKOSS surveillance is available online: https://www.npeu.ox.ac.uk/ukoss/current-surveillance/covid-19-in-pregnancy. For more information about the UKOSS surveillance, please contact Dr Marian Knight

Risk of vertical transmission during pregnancy (peri-COVID)

Public Health England is working with St. George's University of London to assess the risk of vertical transmission in pregnant women with confirmed COVID-19. This surveillance will aim to collect blood, throat swab, urine and stool samples from the pregnant women and, after childbirth, from the baby. Obstetricians and Neonatologists across England are asked to contact the peri-COVID team when they have a pregnant woman with COVID-19 who hasn't yet delivered. More information including the protocol, the Participant Information Leaflet and the Consent Form are available online: www.pericovid.com. The peri-COVID team can be contacted at: pericovid@sgul.ac.uk

Serosurveys in children

PHE is conducting several seroprevalence surveys that include children, using blood samples from a number of different sources. For more information, contact Dr Gayatri Amirthalingam at: gayatri.amirthalingam@phe.gov.uk

i. PHE Seroepidemiology Unit (SEU): the SEU archive is an opportunistic collection of residual sera samples from routine microbiological testing, submitted voluntarily each year from hospital laboratories throughout England; PHE has contacted all NHS trusts requesting their support by providing 10 serum samples per week to the PHE SEU.
ii. Royal College of General Practitioners Research and Surveillance Centre: residual sera are collected from children over 10 years of age and adults from approximately 100 GP practices across England participating in primary care research mainly for influenza surveillance.
iii. *What's The Story COVID-19*: this serosurvey will build on an existing national research network and ethically approved NIHR-funded study to collect childhood and teenage serum samples for near real-time monitoring of increases in paediatric SARS-CoV-2

Continued

Box 1 Continued

seropositivity rates across the UK in 2020. Paediatric hospitals can support the serosurvey by agreeing to provide residual serum samples from children having routine blood tests; this will ensure sufficient numbers of samples are collected across the childhood age groups.

nor during childbirth. There have been several reports of severe disease in pregnant women, including maternal deaths,[12] as well as intrauterine deaths, stillbirths and neonatal deaths.[13] So far, there is no clear evidence of vertical transmission from infected mothers to the newborn,[14] despite reports of SARS-CoV-2 positivity in neonates within 36 hours of birth,[15] Larger, more detailed studies are needed, and these, too, are currently underway (box 1).

CHILDHOOD COVID-19 IN THE UK

On the frontline, paediatricians have been working hard to prepare for an influx of cases, developing and implementing new guidelines, agreeing treatment options, restructuring emergency departments, wards and isolation units—all this while supporting adults services that are already overwhelming hospitals nationally. In children, COVID-19 cases and hospitalisations increased rapidly since the second half of March although with smaller numbers than in adults. Currently, paediatricians are receiving multiple requests for providing data on the same children with COVID-19. Some requests are important for managing healthcare resources and capacity, while others merely duplicate data that PHE is collecting as part of national surveillance. Given the relatively small number of childhood COVID-19 cases, the importance of centralised national reporting, data collection and dissemination is critical for establishing the true burden of disease in UK children and will allow more robust collaboration and comparisons with international cohorts in the future. PHE receives electronic notifications for all laboratory-confirmed COVID-19 cases in England and continues to contact paediatricians to request clinical information for hospitalised cases. Paediatricians in the UK can facilitate the surveillance by proactively reporting cases to PHE by email (box 1). PHE is working to provide paediatricians with childhood COVID-19 data as quickly as possible. In addition to providing surveillance data, paediatricians are encouraged to get involved with research and clinical trials to better understand the immunopathophysiology and identify effective treatments for COVID-19 in children (https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/).

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