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## Paediatric Anaesthetic implications of COVID-19 – A Review of Current Literature

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## **Summary**

Paediatric anaesthetists have an important role to play in the management of patients suspected or confirmed to have COVID-19. In many institutions, the COVID-19 intubation teams are staffed with anaesthetists as the proceduralists working throughout the hospitals also in the ICU and Emergency Departments. As practitioners who perform aerosol generating procedures involving the airway, we are at high risk of exposure to the virus SARS-CoV-2 and need to ensure we are well-prepared and trained to manage such cases. This article reviews the relevant paediatric literature surrounding COVID-19 and summarises the key recommendations for anaesthetists involved in the care of children during this pandemic.

## **Background**

In December 2019 a novel beta-coronavirus was identified in Wuhan, China after the presentation of a cluster of patients with atypical pneumonia. These initial cases had links to a “wet market” where a range of live or freshly slaughtered animals were sold.<sup>1</sup> The virus has since been named SARS-CoV-2 by the World Health Organisation (WHO) and the disease which it can cause is called Coronavirus Disease 2019 (COVID-19). The WHO declared a global pandemic on March 11, 2020. The virus particles have a diameter of 60-140nm and are round or oval shaped and studded with spike proteins.<sup>2</sup> The virus is highly contagious and gains entry to the host cell via the ACE-2 receptor on respiratory epithelia cells. A global response to the pandemic has included early publication of the pathogen genome, rapid development of diagnostic tests and co-ordinated research efforts to discover treatments and develop a vaccine.

## **Transmission and Epidemiology**

Cases of COVID-19 have spread rapidly around the world, demonstrating the highly contagious nature of the virus. Its main routes of transmission are respiratory droplets and contact with respiratory secretions. However, it is likely that there is also fomite spread via contaminated surfaces based on our knowledge of other coronaviruses.<sup>3</sup> In children there is also some evidence that the virus continues to shed in the stool for up to a month post infection.<sup>4</sup> This raises the possibility of faecal-oral transmission during the convalescence stage.

Another important route of transmission, particularly for healthcare workers, is aerosol particles. Anaesthetists, Intensive Care Physicians, Emergency Physicians and some surgical specialities (e.g. ENT) are involved in airway procedures that generate aerosols, such as bag-mask ventilation, intubation and extubation. This puts them at high risk of contacting the virus. By February 12<sup>th</sup> in Wuhan, 3.83% of all recorded infections were in healthcare workers (3019 of 78825 cases).<sup>5</sup> By March 22<sup>nd</sup> in Italy, 9% of all cases were in healthcare workers (4826 of 53578 cases) and many doctors and nurses had died from COVID-19.<sup>6</sup> In Spain it has been estimated that 14% of all cases are healthcare workers.<sup>7</sup> The high rate of infection amongst healthcare workers is most likely due to several factors; prolonged exposure to the virus, inadequate access to appropriate personal protective equipment (PPE), insufficient training with PPE and insufficient attention to careful application and removal of the PPE as well as preferential testing of health care workers in times when testing capacity is limited in supply. The loss of life and reduction in the health workforce puts a huge strain on an already overwhelmed system. Additionally, the diagnosis of one or more COVID 19 positive health care workers within a care team requires team members with close contact to self isolate leading to further reductions in available workforce leading to additional strain on the health care system.

A case study from Singapore describes how an asymptomatic but COVID-19 positive 6-month-old infant was cared for in a negative pressure isolation room. The baby was found to have a high viral load and the investigators took swabs of the healthcare worker's face shield, N95 mask and gown as well as the bedding, the cot rail and a table situated 1m away from the cot. The healthcare worker spent 15 minutes in the room and carried and fed the baby during this time. Interestingly, swabs were positive for SARS-CoV-2 on the bedding, cot rail and table, but not on any of the healthcare worker's PPE. The authors of this case report suggest that well infants with COVID-19 can contaminate the environment possibly through crying and drooling, however the contamination may have also occurred via the healthcare worker's hands and this reinforces the need for fastidious hand hygiene when caring for COVID-19 positive patients.<sup>8</sup>

The basic reproductive number ( $R_0$ ) of SARS-CoV-2, which represents the number of secondary cases expected to develop from a single infected host, in a population that has no innate immunity has been estimated at between 2 and 3.5.<sup>4</sup> This number may change as more detailed data regarding infection rates becomes available. The  $R_0$  estimate for SARS-CoV-2 is higher than that of previous novel coronaviruses responsible for disease outbreaks in humans (Severe Acute Respiratory Syndrome and

Middle East Respiratory Syndrome) and much higher than seasonal influenza which has an  $R_0$  of 1.28 (IQR 1.19 to 1.37).<sup>9</sup> The average incubation period is 6.4 days (range 0 to 24 days).<sup>4</sup>

A retrospective epidemiological study of 2143 Chinese children who had confirmed (34%) or suspected (66%) COVID-19 found that the median age was 7 years and that 94.1% of all cases were mild to moderate in severity.<sup>10</sup> Those under 12 months of age were at highest risk of severe illness, however many of these were unconfirmed cases and may have had illnesses due to other pathogens such as Respiratory Syncytial Virus or Influenza. Another epidemiological paper from China found that of the first 72 312 cases recorded, 1% were aged 8 or under and 2% were aged 18 or under.<sup>11</sup> Data from Italy up until the 15<sup>th</sup> of March 2020 reveal 1.2% of cases were children under 18 years of age (270 of 22512 cases). Data from the Center for Disease Control (CDC) in the United States reveals 2572 of 149,760 cases between February 12 and April 2 were children <18 years of age (1.7%).<sup>12</sup> The median age was 11 years (range 0-17 years) with 57% male. Data on hospitalisation was not available for all cases, but the estimated rate of hospital admission for children in the US is between 5.7% and 20%. The corresponding adult estimates are between 10% and 33%. Intensive care admissions in children were between 0.58% and 2% of all paediatric cases and hospitalisation and ICU admission were more likely if an underlying medical condition was present or in patients <1 years of age.<sup>12</sup>

There have been published reports of clusters of SARS-CoV-2 infection within family groups. One family cluster involved a 10-year-old who was found to have bilateral ground-glass opacities on chest x-ray despite being asymptomatic. The second cluster involved a 3-year-old who had normal bloods, normal radiological findings and was asymptomatic. In both cases the index case was probably an adult.<sup>13,14</sup>

Another study has found an odds ratio of 6.3 (95% CI 1.5 to 26.3) for contracting the virus if living in the same household and an odds ratio of 7.1 (95% CI 1.4 to 34.9) if travelling together.<sup>15</sup>

The attack rate refers to the risk of becoming infected if exposed to someone positive for the virus. There are varying estimates for the attack rate in children that have been derived from data from different regions. The review from Wuhan Children's Hospital gives an estimate of 12.3%. 1391 children who had contact with someone with COVID-19 were tested and 171 cases were found.<sup>16</sup> Of these 171 cases, 27 (15.8%) were asymptomatic. However, data from Shenzhen indicates an attack rate in those under 10 years of 7.4%, which is similar to the rate estimated for the whole Shenzhen population (7.9%).<sup>15</sup> A study from Japan that looked at 2496 people who were exposed to the virus found 313 positive cases. The authors then looked at attack rates in various age groups and found that in children (under 19 years of

age) the attack rate in males was 7.2% (95% CI 3.0 to 14.3%) and in females was 3.8% (95% CI 0.8 to 10.6%). The highest attack rate was in those aged 50 to 59 (approximately 22%).<sup>16</sup>

The attack rate of SARS-CoV-2 appears to be lower in children meaning they are less likely to become infected when exposed. Based on the Chinese and Italian data, children represent between 1.2 and 2% of all cases. While it is certainly possible for infected children to transmit the virus, adults appear to be the primary vectors for SARS-CoV-2.

## **Clinical Features**

### *Symptoms*

The most common clinical features of COVID-19 in children are fever and upper respiratory tract symptoms such as cough, sore throat and coryza. Gastrointestinal symptoms are also possible, including diarrhoea, vomiting and abdominal discomfort. Some children are asymptomatic. A review of 171 children with COVID-19 from China found that 83/171 (48.5%) had cough, 79/171 (46.2%) had sore throat, 71/171 (41.5%) had fever, 15/171 (8.8%) had diarrhoea and 13/171 (7.6%) had rhinorrhoea. Tachypnoea was present in 49/171 (28.7%) and tachycardia was present in 72/171 (42.1%).<sup>17</sup> Numerous smaller case series have found the same types of symptoms occurring at similar rates.<sup>18-20</sup> A series of six children from Wuhan in China found all six had fever and four of the six had vomiting. Median recovery time was 7.5 days and one of the six children required admission to intensive care.<sup>21</sup> In the United States, data from 291 paediatric cases showed 56% had fever, 54% had cough and 13% had shortness of breath. A total of 73% of children had at least one of these symptoms compared to 93% of adults during the same period. Fifty-three (18%) of children had no reported symptoms, however data from these children is incomplete so may not be a true representation of the asymptomatic rate in children particularly in the light of currently limited wide spread testing capacity in many areas.<sup>12</sup>

### *Laboratory Findings*

A number of case series from China have been combined to examine the typical laboratory findings in SARS-CoV-2 positive children. Eight studies with a range of 6 to 171 cases (total n=286) were included.<sup>22</sup> Two studies showed low lymphocyte counts (10 of 214 cases, 4.7%), whilst two studies reported elevated lymphocyte counts (18 of 43 cases, 41.9%). C-Reactive protein was reported in six of the studies and was elevated (>5mg/L) in 70 of 271 cases (25.8%).

### *Radiological Findings*

The most common abnormalities reported on chest x-ray and chest computed tomography (CT) scans are unilateral or bilateral opacities or ground-glass opacities. Combined results from eight case series from China have been examined to determine the rates of radiological changes in children with COVID-19.<sup>22</sup> The chest x-ray findings were reported in three of eight studies and showed no abnormalities in 24 of 46 cases (52.2%), unilateral changes in 15 of 46 cases (32.6%) and bilateral changes in 7 of 46 cases (15.2%). CT findings were normal in 89 of 267 cases (33.3%), showed unilateral changes in 63 of 267 cases (23.6%) and bilateral changes in 112 of 267 cases (41.9%). In one case series of 20 children with COVID-19 from Wuhan Children's Hospital, all 20 children had sub-pleural changes on chest CT. Consolidation with a halo was seen in 50% of cases, which is an atypical finding in children. This series suggests that an early CT scan in children is necessary, as some children in this study were treated on the basis of their CT alone until laboratory confirmation was obtained.<sup>18</sup>

### **Clinical Course and Severity**

The available evidence suggests that children experience less severe symptoms of COVID-19 than adults. Most cases are mild to moderate with the rate of asymptomatic infection estimated to be 4.4%, 15.8% and 28% in three different Chinese studies.<sup>10,17,23</sup> The true figure of asymptomatic infection may actually be higher than the current estimates, and it will not be fully known until widespread antibody testing is completed in community cohorts. In the observational study that found an asymptomatic rate of 28%, nearly all cases (32 of 36) were transmitted to the child by close contact with a family member.<sup>23</sup> The combined rate of asymptomatic, mild and moderate cases was 94.1% in the Wuhan series,<sup>17</sup> severe cases made up 5.3% of all cases and critical cases, defined as Acute Respiratory Distress Syndrome, shock or organ failure accounted for 0.6%. In contrast, data from the WHO suggest that in adults 80% of cases are mild to moderate, 15% are severe and 5% are critical requiring ventilation. The median duration of fever has been reported at 2 days with a range of 1 to 9 days<sup>24</sup> and one case series from Wuhan reported the average length of stay in hospital was 12.9 days.<sup>18</sup> Other data from Wuhan reveals that 3 of 171 (1.8%) children required admission to intensive care. All three had co-morbidities, two recovered but one infant with intussusception eventually died.<sup>17</sup>

The case fatality rate (CFR), which is the number of deaths from confirmed cases, is lower in children than in adults, and particularly elderly adults. Data from China showed the CFR in the 0-19 year age group to be 0.1% compared to the overall CFR of 2.3% and a CFR of 6% in those over 60 years.<sup>25</sup> In the US the CFR in children is 0.1% (3 of 2572), however data is not complete on all cases included in the analysis.<sup>12</sup> In Italy, only one child fatality has been recorded out of 16,654 COVID-19 deaths until April 9, 2020 giving a CFR of 0.006%.<sup>26</sup> It is important to note that the CFR will be higher in countries that have limited testing as they are only testing the patients with the most severe symptoms. In countries that conduct widespread testing the CFR becomes closer to the infection fatality rate, which is the number of deaths from the total number of cases.

Although deaths in children from COVID-19 are rare, they have been reported – and in some cases deaths have occurred in otherwise healthy children. Reports of fatalities in children include a 12-year-old girl from Belgium, a 13-year-old and a 5-year-old from the UK, a 16-year-old girl from France, a 14-year-old from Portugal, a six-week-old baby from Connecticut in the US and another infant from Illinois.

### **Anaesthesia and Airway Management in COVID-19 Children**

Paediatric anaesthetists will be required to perform airway procedures in children suspected or confirmed of having COVID-19. This may be for children with critical COVID-19 infection who require ventilation, or it may be for COVID-19 positive children who require surgery. It is important that all departments develop policies and procedures for the management of these scenarios to ensure best possible outcomes for patients and for healthcare workers.

Airway procedures such as laryngoscopy, intubation, bronchoscopy, gastroscopy, head and neck procedures using drills and front of neck procedures are high risk for producing aerosols that can infect healthcare workers.<sup>27</sup> Important factors in protecting healthcare workers are meticulous planning, correct use of appropriately fitted PPE and good communication. Guidelines from the Australian and New Zealand College of Anaesthetists (ANZCA), recommend all staff undergo a formal fit-test of N95/P2 masks to comply with the International Organisation for Standardisation (ISO) standard for use.<sup>28</sup> If this is not possible, then at a minimum, staff need to be fit-checked by a trained staff member. In cases where a staff member fails a fit-test/check, or stocks of N95/P2 masks are inadequate, alternative PPE should be used such as Powered Air-Purifying Respirators (PAPRs) or full-face respirators. Care must be taken to ensure

correct donning, doffing and cleaning of this equipment. Care should be taken to limit the number of staff exposed to only those who are essential for patient care particularly during aerosol generating procedures.

Anaesthetic departments need to rapidly develop policies and protocols for managing suspected or confirmed COVID-19 patients. Anaesthetists will be expected to be team leaders in these situations and other healthcare workers will look to anaesthetists to provide leadership during these times. The development of protocols should be in consultation with infectious disease specialists, intensive care, emergency department, surgical, nursing and patient transport staff. An important aspect of planning and training for COVID-19 patients is the use of simulation. All staff need to understand their roles and responsibilities and be comfortable with patient flow, PPE use and specific procedures. Simulation is an excellent way to achieve this safely in a relatively short timeframe.

#### *Preoperative management*

Once a decision has been made to bring a child with COVID-19 to the operating theatre, there should be a team huddle with anaesthetists, anaesthetic assistants, surgeons, scrub-scout nurses, patient transport staff and theatre assistants. All team members need to be clear on their roles and the management plan. A theatre specially designated for COVID-19 patients should be used where possible and this theatre should be a negative pressure room or at least neutral pressure. If unavailable consider intubating in a negative care room in the ICU before transporting the patient to theatre. All equipment that will be required for the procedure should be available in the room and any unnecessary equipment removed. A clear transport path from the isolation ward to the operating theatre needs to be created and the child should ideally wear a surgical mask during transport. Given that the child in this special circumstance often needs to be separated from the parent for the induction of anaesthesia in order to reduce the number of people exposed, strong consideration should be given to administration of a premedication. A crying or screaming child will increase the risk of droplet or aerosol spread of the virus. Usual policies surrounding parental presence may need to be reviewed as it is important to limit the number of people involved or exposed.

#### *Intraoperative management*



All personnel involved in patient care need to don appropriate PPE in a designated area such as an antechamber or induction room. Specific donning check lists should be developed and visual aids should be available in the room, and a buddy system is recommended to reduce cognitive load and ensure compliance with correct selection and order of donning. The recommended level of PPE for various clinical scenarios is outlined in the ANZCA consensus statement on personal protective equipment during the SARS-CoV-2 pandemic.<sup>28</sup> Entry and exit points to the room need to be tightly controlled and door opening kept to a minimum. It is important to recognise that these cases are associated with high levels of stress and it is vital to remember to adhere to usual surgical safety procedures, such as a team time-out, to ensure correct patient, correct site and correct surgery. The induction of anaesthesia and airway management are times of high risk and specific recommendations and guidelines have been published by the Safe Airway Society and the Australian Society of Anaesthetists<sup>27,29</sup> The key principles include having a consultant anaesthetist and a highly trained anaesthetic assistant. Additionally, the team should have a very low threshold to add a second anaesthetist if a difficult airway or other potential challenges may be expected. The anaesthetic technique should aim to minimise the risk of aerosolisation by avoiding coughing and positive pressure ventilation. This can be achieved by a modified rapid sequence induction with deep paralysis, no bag-mask ventilation or two provider bag and mask ventilation and ensuring the endotracheal tube cuff is inflated prior to commencing controlled ventilation. Depending on the air circulation in the room / theatre, the surgical team should wait before entering the room. Based on the ANZCA guidelines, this should be after 3 to 5 room air changes.<sup>28</sup>

The principles of airway management in children are broadly the same as adults, however a number of differences exist and these have been highlighted in consensus guidelines published by a collaboration of numerous British anaesthetic and intensive care associations and societies.<sup>30</sup> Some of the issues outlined in this document include: paying careful attention at extubation when complications such as laryngospasm and the need for reintubation are more common, taking extra care that the endotracheal tube is not displaced or blocked and ensuring those managing the airway are suitably experienced, even at the height of a crisis when there may be staff managing children who do not routinely do so.<sup>30</sup>

#### *Postoperative management*

Extubation is a high-risk procedure and careful attention should be paid to avoidance of coughing. Where possible patients should be recovered in the operating room to reduce transport and minimise the number of staff exposed. After the patient has been safely returned to the ward the room needs to be

thoroughly cleaned and staff need to safely remove PPE. The doffing of PPE is a high-risk time for infection and, once again, a buddy should guide the removal of each item of PPE in the correct sequence, paying particular attention to hand hygiene between each step. A Canadian simulation study that used a dye solution sprayed from a mannequin found that aerosolised particles can end up on a healthcare worker's exposed neck area and below their gown on the lower legs and shoes.<sup>31</sup> For this reason, it is recommended that shoes be disinfected and healthcare workers shower after an episode of care with a COVID-19 patient. At the completion of the procedure the entire team should meet for a debrief where lessons can be learnt on how to improve for subsequent patients.

## **Conclusion**

Paediatric anaesthetists have an important role to play during the COVID-19 outbreak. Good organisation, communication and remaining calm in a crisis are common attributes of anaesthetists and these are the attributes required for healthcare leaders during a pandemic. Children seem to be less susceptible to infection if exposed to SARS-CoV-2 and only represent between 1 and 2% of all cases of COVID-19 and generally have less severe symptoms than adults. However, some children will still need airway management or surgery and systems need to be in place to deal safely with these children. Preventing healthcare workers from infection is vital and maintaining the physical and mental health of the hospital workforce is essential to best serve the health needs of the community. Careful planning and training, including simulation, are the cornerstones of safe management of COVID-19 children.

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