KFAS COVID-19 WEEKLY BRIEF
1st OF SEP. 2020
Executive Summaries

Infection Control and Prevention:
This week we will continue to explore new and creative innovations developed in infection control to combat the COVID-19 pandemic. We will discuss Self-Driving Disinfection Robots and ultra-low energy plasma technology for air disinfection.

Diagnosis and Testing:
This article reviews the latest development in testing: a saliva-based test recently approved by the Food and Drug Administration (FDA). Although four other saliva-based tests have previously been approved, this novel diagnostic technique uniquely reports accuracy similar to the current standard testing techniques while resolving many of the issues and disadvantages associated with reverse transcriptase polymerase chain reaction (RT-PCR) based testing methods. The test, named SalivaDirect, is affordable, quick, and does not require expensive saliva collection tubes typically associated with saliva assays. Another significant advantage to this technique is its methods are available to other labs as open source data and do not include any specialized reagents or instruments, making it easy to adopt by new labs.

Treatment and Therapies:
No vaccines have been approved for prevention of COVID-19. There are currently more than 137 candidates undergoing preclinical development and 23 in early clinical development, according to World Health Organization (WHO).

In April, Russia enacted a law which eliminated the need for a Phase 3 vaccine trial before approval. Approval now means the coronavirus vaccine can be distributed even as Phase 3 tests get underway, however, mass-manufactured doses are not expected to be ready for weeks. Russia is not alone when it comes to fast tracking. China approved an experimental coronavirus vaccine in June for members of its military. Russia’s vaccine data from Phase 1 and 2 trials are still to be published.

They are not as far ahead as other vaccines, noting that Moderna and Oxford’s vaccines have already begun Phase 3 trials.

Oxford University Vaccine ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.

In rhesus macaques, a single vaccination with ChAdOx1 nCoV-19 induced humoral and cellular immune responses, and protection against lower respiratory tract infection was observed in vaccinated non-human primates after high-dose SARS-CoV-2 challenge.

Moderna Vaccine currently being evaluated in Phase 3 clinical testing. The findings show that the investigational vaccine induced neutralizing antibodies in mice, and when challenged with SARS-CoV-2 virus they were found protected from viral replication in the lungs and nose.
Exit Strategies:
As schools start to open, with some focused on in person learning, there have been staggering increases in the number of infections and quarantined students, as well as staff. This has led to further speculations that perhaps the reopening of schools, with physical, in class learning, needs to be reconsidered across the US and globally, especially in communities where the pandemic is not well controlled. What remains to be understood is COVID-19 transmission in children, especially in relation to secondary transmission. Although studies continue to show that children are least likely to have severe complications if infected, their ability to transmit the virus to their households, can present a challenge, especially to persons of high-risk. Several studies have addressed transmission among children and household and non-household contacts. This section highlights the key findings of these studies and the potential implications for decision makers as the school year commences.
Russia’s approval of a COVID-19 vaccine is less than meets the press release Science

As Covid-19 cases in prisons climb, data on race remain largely obscured STAT

Can Air Conditioners Spread COVID-19? NPR

Coronavirus: Putin says vaccine has been approved for use BBC

Will Covid-19 vaccines be safe for children and pregnant women? The data, so far, are lacking STAT

Coronavirus vaccine: Australia rules out mandatory immunisations BCC

How Far Can A Urinal Spray Covid-19 Coronavirus? What This Toilet Study Says Forbes

The odds of catching Covid-19 on an airplane are slimmer than you think, scientists say CNN

Coronavirus research updates: An unprecedented map charts a key viral protein Nature

Covid-19 and common colds can both impair taste and smell, but study finds big difference CNN

Why ‘T Cell Immunity’ Won’t End The Coronavirus Pandemic Forbes

Study of More Than 55,000 COVID-19 Cases Reveals a Predictable Order of Symptoms Science Alert

Fitbit posts early findings showing its trackers can identify cases of COVID-19 before symptoms take hold Fierce Biotech

Pandemic on campus: tell us how your institution is coping Nature

Coronavirus in Scotland: Where have school pupils tested positive? BBC

Another existing drug shows promise against COVID-19 Medical News Today

Coronavirus Vietnam: The mysterious resurgence of Covid-19 BBC

Evidence lags behind excitement over blood plasma as a coronavirus treatment Nature

‘Silent spreaders’ of COVID-19: Kids who seem healthy may be more contagious than sick adults, study says USA Today

In Wuhan, crowds return as coronavirus fears fade Washington Post

South Korea tightens Covid-19 curbs amid warning of new ‘crisis BBC

Coronavirus: Spanish regions ban smoking over Covid-19 risk BBC
Ultraviolet Disinfection Robot:

An autonomous robot that emits ultraviolet C (UV-C) light and is currently used in hospitals to halt the spread of hospital-acquired infections and is being tested for its effectiveness against coronavirus. In 2014, a group of Danish hospitals identified the need for a far more effective way of reducing infection rates and led to collaboration between bacteriologists, virologists and hospital staff with Danish service robot manufacturer Blue Ocean Robotics. The UVD (Ultraviolet Disinfection) Robot uses high intensity UV-C light with a wavelength of 254nm to kill bacteria and viruses. This type of ultraviolet light does not usually penetrate the Earth’s ozone layer and is not naturally present on Earth. Hence, biological material is particularly vulnerable to the effects of UV-C radiation. ‘If a microorganism is hit by this, it penetrates into the cell membrane and destroys all the larger molecules inside the cell,’ said Claus Risager, chief executive of Danish professional robotics firm, Blue Ocean Robotics, who designed, developed and produced the robot. Studies have shown that it effectively limits the spread of coronavirus without exposing front-line hospital staff to the pathogen. The device is battery-powered and can move at 5.4 km/h and with an operating time of 2–2.5 hours. It can disinfect 9–10 rooms from a single charge in approximately 10–15 min per room. The device can be recharged in three hours. The first robots were shipped to hospitals in China in late February 2020 following an agreement between medical supplies company Sunay Healthcare Supply and UVD Robots. Through Sunay’s partners in China, the robots were deployed in all Chinese provinces to more than 2,000 hospitals.
The Sunburst UV Bots are being used in Singapore and are produced by local company PBA Group. More than 200 were rolled out in hospitals, shopping malls, and public transit. It uses advanced navigation technology and can detect when people are too close and automatically shuts off UV emission. It can operate for around 2.5 h on a single charge and is able to self-navigate to the charging stations. The company ultimately plans to deploy over 500 units in Malaysia, Thailand, and Hong Kong. In the USA, San Antonio-based Xenex produces the LightStrike UV disinfection robot. The mobile robot uses a patented system based on a pulsed xenon UV source operating at 200–315 nm which can deliver up to 4,300-times more germicidal pathogen-killing UV intensity than conventional UV-C mercury vapor sources and can disinfect an entire patient room in 20 min. These robots have been deployed in more than 500 hospitals worldwide in the USA, the UK, Italy, South America, Asia, the Middle East, and Africa. These numbers are increasing daily, according to the company. Although the cost is $125,000, the company estimates that this translates to about $2 to $8 per room depending on the number of rooms used each day.

In March 2020, the infection isolation area of the Third People’s Hospital of Hubei Province in China officially unveiled the mobile ARIS-K2 robot. Produced by Chinese robot manufacturer Youaizhihe Robot Technology, it has a high-definition visible light camera and a thermal camera that can identify people and measure their body temperature. Below the cameras, six UV lamps emit 270 μW/cm² of UV light, capable of killing more than 99.9% of viruses and bacteria within a six-metre radius within 10 min. During the day, the robot automatically cruises around the main entrance and exit of the hospital to detect people with abnormal body temperatures, and at night, it automatically implements a UV disinfection program in the hospital’s outpatient, emergency, and infection isolation areas.
As studies began confirming the transmission of SARS-CoV-2 spread via aerosol and of infectious particles light enough to move through entire rooms, small enough to slip through gaps in a surgical mask it became vital to find a way decrease air-borne transmission in high risk areas. A small Dublin-based company designed a device that would sterilize the air from airborne pathogens. Novaerus uses a patented atmospheric plasma discharge of the dielectric barrier discharge type. The plasma discharge comprises electrons and ions that cause extensive damage to microorganisms. Unlike other products, microorganisms are exposed directly to the plasma discharge as opposed to by-products of the discharge. Testing found the company’s technology can reduce airborne load of MS2 Bacteriophage, a virus used as a surrogate for SARS-CoV-2, by 99.99% in just 15 minutes. The company also states that the device is unique among air disinfection devices, as Novaerus’ units leave no harmful byproducts.

Tens of thousands of the Novaerus devices are currently installed on shelves, mounted on walls above hospital beds, surgical gurneys, adjacent to dental chairs, on pharmacy walls, in school libraries, and hotel lobbies. This powerful technology has now been deployed in 58 countries to help prevent the spread of SARS-CoV-2. They are now fastened inside 80% of South Korea’s ambulance fleet.

Figure 5: Novaerus Devices (Image source: https://www.healtheuropa.eu)
NOVEL SALIVA TEST PAVES THE WAY TO MORE ACCESSIBLE TESTING

It's been seven months since Covid-19 was declared a global pandemic in March and testing strategies worldwide remain highly varied and in need of improvement. This publication has previously covered breakthrough innovations in testing techniques and strategies such as: antibody tests, antigen tests, smell tests, saliva tests, wastewater testing, sample pooling, and even dogs trained to sniff out infected individuals. Despite these leaps in progress, countries around the world continue to struggle in their efforts to improve testing while other countries intentionally slow their testing down to create the appearance that cases are decreasing.1 Disregarding the countries setting bad examples, testing and tracing remains a well-established and proven method for infection control.

This article reviews the latest development in testing: a saliva-based test recently approved by the Food and Drug Administration (FDA). Although four other saliva-based tests have previously been approved, this novel diagnostic technique uniquely reports accuracy similar to the current standard testing techniques while resolving many of the issues and disadvantages associated with reverse transcriptase polymerase chain reaction (RT-PCR) based testing methods. The test, named SalivaDirect, is affordable, quick, and does not require expensive saliva collection tubes typically associated with saliva assays. Another significant advantage to this technique is its methods are available to other labs as open source data and do not include any specialized reagents or instruments, making it easy to adopt by new labs.2

"This could be one the first major game changers in fighting the pandemic," tweeted Andy Slavitt, a former acting administrator of the Centers for Medicare and Medicaid Services in the Obama administration, who expects testing capacity to be expanded significantly. "Rarely am I this enthusiastic... They are turning testing from a bespoke suit to a low-cost commodity."3 Source: STATnews

SalivaDirect test offers similar sensitivity to standard RT-PCR techniques

The new test, developed by the Yale School of Public Health, relies on saliva samples while maintaining an accuracy rate comparable to RT-PCR-based nasal swab tests. The alternative testing method was granted an EUA from the US FDA on August 17, 2020 and if implemented could provide numerous advantages and resolve several issues associated with RT-PCR molecular-based tests.3 The SalivaDirect assay is currently being validated regarding its ability to identify asymptomatic individuals through a program that tests members of the US National Basketball Association (NBA); however, since the FDA authorization has already been granted, the method is currently available to any laboratories interested in adopting it.4 A preprint on the validation of SalivaDirect, recently published on MedRxiv, described a >94% agreement in test results when the novel method was compared with RT-PCR assay results from the same samples. The publication also notes that the new technique was found to be highly sensitive.5 A separate study from Yale University researchers published on MedRxiv examines the stability of SARS-CoV-2 viral genetic material in saliva at different temperatures and over extended durations of time (2-25 days). The study concludes that SARS-CoV-2 viral RNA is stable in saliva at room temperature for prolonged periods of time, indicating it would be a suitable alternate sample type to nasal swabs or nasopharyngeal swabs typically used, without requiring any reagents to stabilize the sample.6

Perhaps the most notable advantage to the SalivaDirect assay in comparison to other saliva-based tests we've reviewed in the past is its elimination of expensive saliva collection tubes. Samples can be collected in any sterile container and without the need for the specialized transport media or preservatives typically required for RT-PCR's nasopharyngeal swabs. Furthermore, the novel testing technique has been "validated with reagents and instruments from multiple vendors" ensuring the test can work through supply chain issues common throughout this pandemic.7 The SalivaDirect assay solves other problems as well. By cutting out a key step: nucleic extraction, the test distinctly avoids costly extraction kits and specialized reagents in short supply that are needed in this step with other tests.8 The assay can process about 90 samples in less than three hours in a lab and can be scaled up to larger numbers in larger labs. While other novel techniques include proprietary instruments or chemicals, this test requires neither and is easily implementable in new labs. Yale University aims to provide this "open source" testing protocol to labs around the US free of cost. The researchers behind this technique estimate each test should cost less than 5 US dollars in chemical reagents9 and rather than commercialize the test, the researchers want the method to help those most in need. Testing is an essential step to managing infection spread while reducing restrictions and this test has been hailed a game changer. SalivaDirect could allow a lab to double its testing capacity according to Professor Chen Liu, chair of Yale Pathology, and as the only saliva test to offer accurate results comparable to RT-PCR based techniques without the most common disadvantages, we think he may be right.10


"Using SalivaDirect, our lab can double our testing capacity." - Professor Chen Liu, Chair of Yale Pathology; Source: Yale News
The investigational vaccine known as mRNA-1273 protected mice from infection with SARS-CoV-2, the virus that causes COVID-19, according to research published on 5th Aug 2020 in Nature. Scientists at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC) worked with investigators from the University of Texas at Austin to identify the atomic structure of the spike protein on the surface of the novel coronavirus. This structure was used by VRC and Moderna in the development of the vaccine candidate.

The findings show that the investigational vaccine induced neutralizing antibodies in mice when given as two intramuscular injections of a 1-microgram (mcg) dose three weeks apart. Additional experiments found that mice given two injections of the 1-mcg dose and later challenged with SARS-CoV-2 virus either 5 or 13 weeks after the second injection were protected from viral replication in the lungs and nose. Importantly, mice challenged 7 weeks after only a single dose of 1 mcg or 10 mcg of mRNA-1273 were also protected against viral replication in the lung.

The investigational vaccine also induced robust CD8 T-cell responses in mice. It did not induce the type of cellular immune response that has been linked to vaccine-associated enhanced respiratory disease (VAERD). This rare, allergic-type inflammation was seen in individuals vaccinated with a whole-inactivated respiratory syncytial virus (RSV) vaccine in the 1960s. VAERD can occur when a vaccine induces an immune response that is not strong enough to protect against infection. The investigators vaccinated mice with sub-protective doses of mRNA-1273 and then challenged the mice with SARS-CoV-2. The mice showed no evidence of enhanced lung pathology or excessive mucus production, indicating the vaccine did not cause enhanced disease, the authors write1.

The authors note that the data from these studies, combined with data from studies in nonhuman primates and phase 1 clinical testing, support the evaluation of mRNA-1273 in clinical efficacy trials2. They also explain how their prior research on a candidate MERS-CoV vaccine paved the way for a rapid response to the COVID-19 outbreak. “This is a demonstration of how the power of new technology-driven concepts like synthetic vaccinology facilitates a vaccine development program that can be initiated with pathogen sequences alone,” the authors write.

1 https://www.nature.com/articles/s41586-020-2622-0
An ideal vaccine against SARS-CoV-2 would be effective after one or two vaccinations; would protect target populations such as older adults and those with comorbidities, including immunocompromised individuals; would confer protection for a minimum of 6 months; and would reduce onward transmission of the virus to contacts. Replication-deficient viral vectored vaccines have been used in immunocompromised individuals with no safety concerns and Oxford university ChAdOx1 vaccines are immunogenic in older adults and can be manufactured at large scale, making this platform technology a promising candidate to develop a vaccine for the prevention of COVID-19.

Oxford University is working with the UK-based global biopharmaceutical company AstraZeneca for the further development, large-scale manufacture and potential distribution of the Covid-19 vaccine, with plans for clinical development and production of the Oxford vaccine progressing globally. The project has been further spurred by £84 million of Government funding to help accelerate the vaccine’s development.

Oxford and AstraZeneca are collaborating with clinical partners around the world as part of a global clinical programme to trial the Oxford vaccine. The global programme is made up of a Phase III trial in the US enrolling 30,000 patients, a paediatric study, as well as Phase III trials in low-to-middle income countries including Brazil and South Africa which are already underway.

AstraZeneca remain committed to fulfilling their commitment for broad and equitable access to the vaccine, should late-stage clinical trials prove successful. So far, commitments to supply more than 2 billion doses of the vaccine have been agreed with the UK, US, Europe’s Inclusive Vaccines Alliance (IVA), the Coalition for Epidemic Preparedness (CEPI), Gavi the Vaccine Alliance and Serum Institute of India.

During the study participants who received the vaccine had detectable neutralising antibodies, which have been suggested by researchers as important for protection, and these responses were strongest after a booster dose, with 100% of participants blood having neutralising activity against the coronavirus. The next step in studying the vaccine is to confirm that it can effectively protect against SARS-CoV-2 infection.

The results of the Phase I/II trial published at the end of July 2020 in the scientific journal, The Lancet, indicate no early safety concerns and induces strong immune responses in both parts of the immune system.

The Phase I/II data for coronavirus vaccine shows that the vaccine did not lead to any unexpected reactions and had a similar safety profile to previous vaccines of this type. The immune responses observed following vaccination are in line with what previous animal studies have shown are associated with protection against the SARS-CoV-2 virus, although we must continue with our rigorous clinical trial programme to confirm this in humans,’ says Professor Andrew Pollard, Chief investigator of the Oxford Vaccine Trial at Oxford University and co-author of the study.

The vaccine provoked a T cell response within 14 days of vaccination (white blood cells that can attack cells infected with the SARS-CoV-2 virus), and an antibody response within 28 days (antibodies are able to neutralise the virus so that it cannot infect cells when initially contracted).

1 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31604-4/fulltext
2 www.cnn.com
3 www.sputnikvaccine.com
Dr. Scott Gottlieb, former commissioner of the US Food and Drug Administration (FDA), said that the number of people the vaccine had been tested on so far was the equivalent of a Phase 1 trial, which typically involves a small group and studies the safety of the vaccine.

Is the Russian vaccine safe? The short answer is that it is unknown. Russia has released no scientific data on its vaccine testing. But Russia says the vaccine has passed through Phase 1 and Phase 2 trials which were completed on August 1.

A Phase 1 study typically focuses on whether a vaccine is safe and whether it elicits an immune response in a small number of people. Russia claims that volunteers in the Phase 1 and 2 trials felt well after taking the vaccine and exhibited no unforeseen or unwanted side effects.

Is the vaccine effective? Without data and completed Phase 3 trials, Russia has not proven to the world Sputnik V works. Russia has said that its vaccine is an adenoviral vector one. Adenoviruses cause the common cold, but in Covid-19 vaccines they are weakened and modified to deliver genetic material that codes for a protein from the novel coronavirus. The body then produces that protein and may produce an immune response against it, but the method can cause problems.

Sputnik V's makers say the vaccine induced a "strong antibody and cellular immune response," in trial volunteers, according to the official website for the vaccine.

"Not a single participant of the current clinical trials got infected with Covid-19 after being administered with the vaccine," the statement adds.

Russia's Health Ministry has said the country's frontline medical staff and teachers will be the first vaccinated. The country plans to begin mass vaccination of citizens in October, Kirill Dmitriev, CEO of the RDIF told CNN on 11th Aug 2020.

"We will start massive vaccination of Russians in October. This vaccine will be available to other countries around November," Dmitriev told CNN's Anderson Cooper and Dr. Sanjay Gupta.

Russia plans to mass produce the vaccine by September 2020.

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4 www.cnn.com
5 www.sputnikvaccine.com
In the last two weeks of July, in the United States alone, there have been 97,000 positive cases of COVID-19 among school aged children. As some schools reopened in late July/early August, and resumed in-person classes, with an attempt to mark the beginning of some sense of normalcy, a grim start was observed. In Cherokee County, a school district in the state of Georgia, more than 900 students and staff had to be quarantined because of potential exposure to the virus. Although the Centers for Disease Control and Prevention’s Morbidity and Mortality Weekly Report showed that children are still considered to be at a lower risk for developing severe complications from COVID-19, health officials continue to warn that multisystem inflammatory syndrome in children has presented itself to be a challenge based on the analysis of pediatric COVID-19 hospitalization data from 14 states. Furthermore, data has also shown that one in three children are admitted to an intensive care unit. These staggering numbers have led to further speculations that perhaps the reopening of schools, with physical, in class learning, needs to be reconsidered across the US and globally, especially in communities where the pandemic is not well controlled.

What remains to be understood is the correlation between COVID-19 transmission and children. Several studies have addressed this, through testing and tracing. The following paragraphs highlight the key findings of these studies and the potential implications for decision makers as the school year commences.

3 https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e3.htm
A population-based contact tracing study on transmission in schools in Australia was published in the Lancet, which focused on prospectively examining COVID-19 transmission among children and adults in educational settings. The goal of the study was to provide real-time evidence for decision making on school-based policies. The study was done in New South Wales (NSW), where in a population of 8.1 million, 23% are 18 years or younger. The study period was from the end of January (25th) to the beginning of April (9th) during the 10-week school period.

As of May 1st, NSW had 3,033 confirmed COVID-19 cases, in which most were acquired overseas and 54 (1.8%) of 3033 cases were contracted in NSW. Roughly 3% of those cases were found in patients 18 years or younger. Of those, 9% were admitted to the hospital and one was admitted to the intensive care unit. Furthermore, only 25 of 7,700 NSW educational facilities showed infection, and the primary COVID-19 cases were observed mainly among staff in 56% of the facilities.

The study also considered the impact of secondary transmission. They showed that secondary transmission occurred in three out of 15 schools and one of ten early childhood education and care (ECEC) settings. There was one incidence of an outbreak in an ECEC setting, following the of a staff member; thus, 13 of the 37 contacts in the ECEC center were infected. Of those, three children were infected, all below the age of three. The children were asymptomatic and the others had mild disease. Excluding this single ECEC setting outbreak, the rate of secondary transmission was observed to be 0.4%, or one in every 282 contacts.

One important aspect of the study was the continuous follow-up with a subset of educational facilities, including those with both asymptomatic and symptomatic adult and child contacts. Two-thirds of close contacts were tested using serology testing, which identified four additional secondary cases, including an asymptomatic student and staff member, increasing the number of secondary infections detected. By contrast, in Ireland, of the six COVID-19 cases, detected in three schools, suggested no secondary transmission to close contacts. However, the study did not include data on children 10 years or younger. Thus, the transmission rate, despite being low (1.3% across schools), appeared to be occurring between staff and from staff to children, but not between child to child and/or child to staff. Furthermore, delays in diagnosis, because of the testing eligibility criteria, as well as the mixing of children and staff, along with the use of shared physical spaces, likely contributed to the several generations of transmission. Overall their findings suggest children are unlikely to initiate or propagate outbreaks, in line with previous studies that have led to similar conclusions.

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7 Within the time frame of the study, from March 22, 2020, children were encouraged to stay home for distance learning until the end of the term; however, schools were still open if children could not be home schooled.
9 Zhu Y, Bloxham CJ, Hulme KD, et al. Children are unlikely to have been the primary source of household SARS-CoV-2 infections. medRxiv. 2020; (published online March 30.) (preprint); Viner RM, Russell SJ, Croker H et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. Lancet Child Adolesc Health. 2020; 4: 397-404
It is important to note that there are some limitations to the study. First, only close, symptomatic contacts were tested; therefore, infected contacts with no or mild symptoms might have been missed. Enhanced surveillance of the schools and ECEC centers were limited based on those that were willing to participate. The transmission rates reported might be impacted by the sensitivity and specificity of the tests, since they were not adjusted for test performance. There were various factors that could not be controlled, such as differences in the definition of “close contacts” and the declining school attendance rates. Furthermore, at the time that the study was conducted, the national public health definition of the infectious period for cases was considered to be 24 hours. This was later extended to 48 hours, and had that parameter been in place during the study, it might have allowed for additional close contacts to be identified. Lastly, the study was unable to assess the effect of hygiene or physical distancing within the educational settings, in relation to transmission, which progressively increased over the study period.

Figure 6: Onset date of total (A) and pediatric (B) confirmed COVID-19 cases in NSW, Jan 13–May 1, 2020, relative to control measures and school attendance. Adopted from Reference 4.

South Korea

In South Korea, a study that traced and tested nearly 60,000 people who had contact with the infected people, showed some interesting patterns in relation to transmission. Contacts of individuals considered high risk, such as household contacts, were routinely tested. For the contacts in the non–high-risk groups, testing was only done for symptomatic individuals, and non–high-risk asymptomatic contacts were asked to quarantine for 14 days. For each infected patient, a household and a non-household contact person was identified. Patients were indexed based on different age groups, as indicated in Table 1.

The study showed that out of the 59,073 contacts of 5,706 COVID-19 indexed patients, 11.8% of the household contacts (10,592 contacts) had COVID-19. Rates were higher for children than in adults. 18.6% of the household contacts that contracted COVID-19 were from 10 to 19 year old patients that had been infected, the highest among the other age groups (Table 2). Their findings suggest that children in this age group may spread the coronavirus more frequently than adults. In comparison, 1.9% of the 48,481 non-household contacts, had contracted the virus.

Children below the age of 10 had the lowest rate of transmission (5.3%), but nevertheless showed some transmission patterns. These numbers could be biased because of school closures, but the authors note that these children might still have had contact during this time. In Wuhan, a contact survey showed that school closures and social distancing reduced the transmission of COVID-19 among contacts of school-aged children. Furthermore, as observed with the flu, or other respiratory viruses, children that attend school or daycare are at a higher risk for transmission; thus the low detection rate for household contacts of preschool kids in South Korea could be due to the social distancing measures in place during the study period. Therefore, higher transmission rates might be observed once schools are opened.

The authors note that there are several limitations to their study, some overlapping with the ones outlined in the Australian study. For one, the number of cases might be underestimated due to asymptomatic patients, and some of the household cases observed could have resulted from outside contacts. The testing policy is also a limitation in assessing transmission, and that a comparison of symptomatic patients of both groups, would be more reflective.


From the index-secondary case pairs, the exposure time between the child index and the secondary case was three days, unless if the indexed case was symptomatic, in which case the exposure time was one day.

It had been previously shown that the almost half of the secondary transmission cases were infected during the presymptomatic phase, in situations where households were clustered together.

Presymptomatic pediatric cases are likely to expose other household members to a high level of infection.

Given the low-level community transmission in Korea, most cases will arise from travel. Due to the crowded living conditions, there is some concern on transmission among household contacts during home quarantine after a flight.

Recently, based on additional data, a new study was published where the transmission dynamics of households for the first 107 pediatric patients indexed were assessed.12 In looking at the secondary transmission rate, they were able to see that the transmission from children to adults was relatively low, taking into consideration the mitigation (i.e. social distancing) measures in place. There is also no evidence that children are the main cause of transmission, although, it is important to note that the study was again conducted in the context of lockdown. What the authors concluded is that transmission is likely determined by various parameters, such as viral kinetics, presence of symptoms, contact rate and duration.13 In relation to these factors, the following conclusions were made:

- From the index-secondary case pairs, the exposure time between the child index and the secondary case was three days, unless if the indexed case was symptomatic, in which case the exposure time was one day.

- It had been previously shown that the almost half of the secondary transmission cases were infected during the presymptomatic phase, in situations where households were clustered together.

- Presymptomatic pediatric cases are likely to expose other household members to a high level of infection.

- Given the low-level community transmission in Korea, most cases will arise from travel. Due to the crowded living conditions, there is some concern on transmission among household contacts during home quarantine after a flight.

### Table 2. Rates of coronavirus disease among household and non-household contacts, South Korea, January 20–March 27, 2020; Source: Adopted from Reference 10.

<table>
<thead>
<tr>
<th>Index patient age, y</th>
<th>No. Contacts positive/no. Contacts traced</th>
<th>% Positive (95% c1)</th>
<th>No. contact positive/no. contact traced</th>
<th>% Positive (95% C1)</th>
</tr>
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<tbody>
<tr>
<td>0-9</td>
<td>3/57</td>
<td>5.3 (1.3-13.7)</td>
<td>2/180</td>
<td>1.1 (0.2-3.6)</td>
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<tr>
<td>10-19</td>
<td>43/231</td>
<td>18.6 (14.0-24.0)</td>
<td>2/226</td>
<td>0.9 (0.1-2.9)</td>
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<td>20-29</td>
<td>240/3,417</td>
<td>7.0 (6.2-7.9)</td>
<td>138/12,393</td>
<td>1.1 (0.9-1.3)</td>
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<tr>
<td>30-39</td>
<td>143/1,229</td>
<td>11.6 (9.9-13.5)</td>
<td>70/7,407</td>
<td>0.9 (0.7-1.2)</td>
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<tr>
<td>40-49</td>
<td>206/1,749</td>
<td>11.8 (10.3-13.4)</td>
<td>161/7,960</td>
<td>2.0 (1.7-2.3)</td>
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<td>50-59</td>
<td>300/2,045</td>
<td>14.7 (13.2-16.3)</td>
<td>166/9,308</td>
<td>1.8 (1.5-2.1)</td>
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<td>60-69</td>
<td>177/1,039</td>
<td>17.0 (14.8-19.4)</td>
<td>215/7,451</td>
<td>2.9 (2.5-3.3)</td>
</tr>
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<td>70-79</td>
<td>86/477</td>
<td>18.0 (14.8-21.7)</td>
<td>92/1,912</td>
<td>4.8 (3.9-5.8)</td>
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<td>&gt;80</td>
<td>50/348</td>
<td>14.4 (11.0-18.4)</td>
<td>75/1,644</td>
<td>4.6 (3.6-5.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,248/10,592</strong></td>
<td><strong>11.8 (11.2-12.4)</strong></td>
<td><strong>921/48,481</strong></td>
<td><strong>1.9 (1.8-2.0)</strong></td>
</tr>
</tbody>
</table>


Therefore, their conclusions show that some of the household members, who were thought to be infected by children between the ages of 10 and 19 from the previous study\textsuperscript{10}, were probably exposed to the virus at the same time as the children; hence they may have been infected by contacts they shared. Furthermore, their original findings that children below the age of 10 are less likely to lead to secondary transmission still holds true, but that older children are, at least, unlikely to transmit more than adults.\textsuperscript{12}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure7.png}
\caption{A family of household transmission by a child index. Adopted from Reference 12.}
\end{figure}
Is the lower transmission in children related to a lower amount or presence of viral particles when infected? A study by Heald-Sargent et al. considered the various levels of viral nucleic acids in children, in comparison to adults. Reverse transcriptase–polymerase chain reaction (PCR) assays were performed on nasal swabs gathered from patients at various testing sites in Chicago, Illinois. The cohort of 145 samples collected were of patients ranging from one month old to 65 years of age, but in analyzing the data, the researchers compared three main groups: children below the age of 5 (n=46), older children between 5 and 17 years of age (n=51) and adults from 18 to 65 years old (n=48). In comparing the amplification cycle threshold (CT values from the PCR tests), which is used to assess the viral particles present, the findings showed similar median CT values for older children and adults, but younger children had significantly lower median CT values. This suggests that children younger than 5 years old, with moderate to high symptoms, have high viral nucleic acid in their nasopharynx compared with older children and adults. Therefore, in terms of viral particles, the difference in the amount might suggest that this age group may be important drivers of SARS-CoV-2 spread in the general population.

Potential Reasons for Lower Transmission and Susceptibility in Children


Inpatient, outpatient, emergency department, and drive-through testing sites

There are, however, other hypotheses currently being explored that might explain provide some insight into the differences in transmission and susceptibility to COVID-19 among the different age groups. Some are related to differences in immunity, or the expression of angiotensin converting enzyme 2 (ACE2) virus receptor.\(^\text{17}\) For example, when the nasal expression of the ACE2 receptor was assessed in the epithelium, models showed a positive correlation between ACE2 gene expression and age, where lower ACE2 expression was observed in children relative to adults.\(^\text{18}\) The study did not, however, include patients above 60 years of age, and are contrary to findings that showed no correlation between the ACE2 protein activity and age in bronchoalveolar lavage fluid.\(^\text{19}\) This might be attributed to the different environments in relation to the expression of ACE2 between the lung and nasal, which have been shown to be distinct.\(^\text{20}\) These findings might help explain why COVID-19 is less likely to cause severe infection in children.


There is no doubt that policymakers, educators, administrators, and decision makers have the difficult task of weighing the possible benefits of school closures in relation to the transmission of COVID-19 with the adverse effects of these closures on the development of children, as well as their mental and emotion wellbeing, and the exacerbation of inequalities. As highlighted by these studies, the key is ensuring that transmission is managed based on the evidence provided, and kept low through stringent mitigation efforts to ensure that schools can open and remain open safely. This involves ensuring that an adequate testing and tracing platforms are developed nationally, as well as within each school, to continuously gather real-time data to guide policies. School policies surrounding personal hygiene, social distancing, as well as other infection control measures can further reduce, not only spread in schools, but also household spread, especially amongst family members considered high risk. Finally, the importance of seroprevalence studies are needed on a local level to understand the state of the pandemic, and evaluate the public health benefit of school closures as a part of national mitigation strategies.

Policy Implications and Recommendations