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MELBOURNE

Melbourne Medical School
Department of Paediatrics

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COVID-19 KIDS EVIDENCE UPDATE

WHAT THE MELBOURNE
CHILDREN'S CLINICIANS,
SCIENTISTS, EPIDEMIOLOGISTS,
AND MEDICAL STUDENTS HAVE
BEEN READING THIS WEEK

Weekly Update No.7

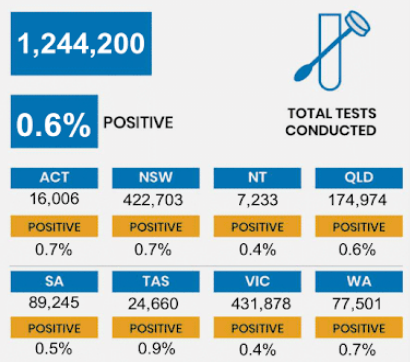
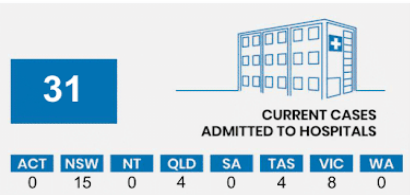
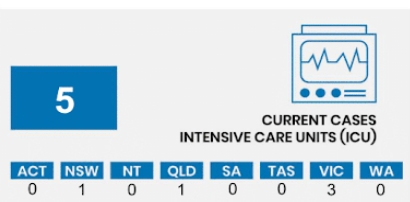
27 May 2020



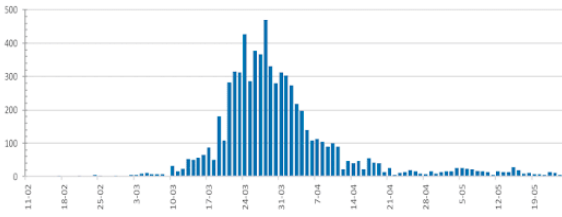
Australian Government
 Department of Health



CURRENT STATUS OF CONFIRMED CASES



DAILY NUMBER OF REPORTED CASES

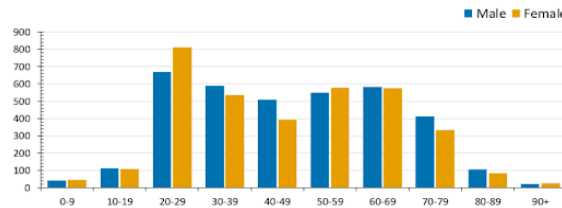


CASES IN AGED CARE SERVICES

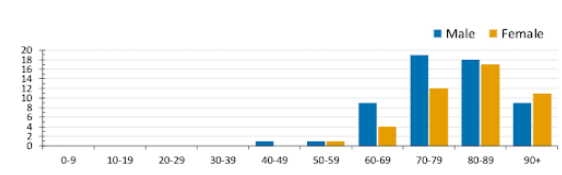
Confirmed Cases	Australia	ACT	NSW	NT	Qld	SA	Tas	Vic	WA
Residential Care Recipients	67 [25] (27)	0	61 [25] (25)	0	1 (1)	0	1 (1)	4	0
In Home Care Recipients	31 [27] (3)	0	13 [13]	0	8 [8]	1 [1]	5 [2] (2)	3 [3]	1 (1)

Cases in care recipients [recovered] (deaths)

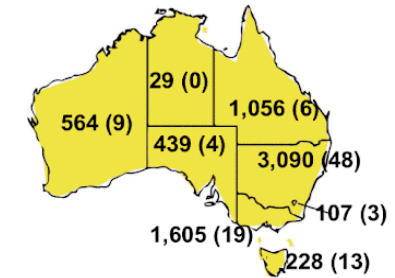
CASES BY AGE GROUP AND SEX



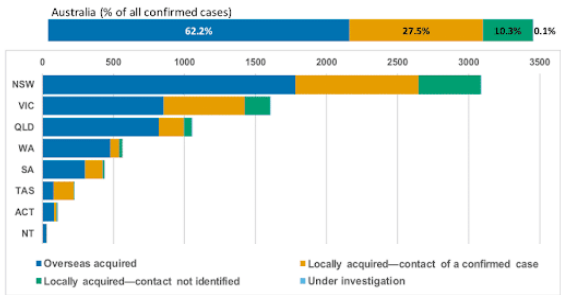
DEATHS BY AGE GROUP AND SEX



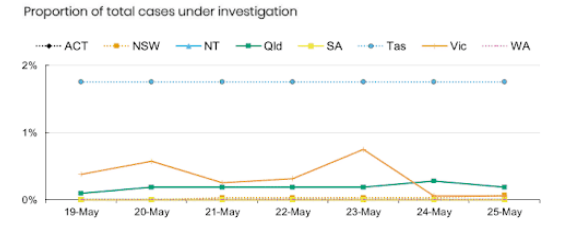
CASES (DEATHS) BY STATE AND TERRITORIES



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 25 May 2020

This infographic is updated every afternoon based on the data we receive by 3.00pm from states and territories

Source: Australian Government: Department of health [Internet]. 2020 [updated 2020 May 25; cited 2020 May 26]. Available from: <https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers#at-a-glance>

HIGHLIGHTS

- > Paediatric clinical manifestations: presentations mimicking appendicitis, septic shock in adolescents, chilblains.
- > Autopsy findings in adult COVID-19 lungs show severe vascular endothelial injury.
- > Storage of nasopharyngeal swabs at ambient temperature for 21 days sufficient for RT-PCR detection of SARS-CoV-2, but impact on load not tested.
- > Australian WGS and epidemiological study shows value in determining source of transmission in cases that the source is unknown through standard contact tracing.
- > Importance of maintaining public trust in public health intervention measures.
- > One billion people need to use shared toilets- highlighting the challenge of infection control in settings with poor sanitation and hygiene.
- > Directors of WHO, UNICEF, UNDP and Save the Children highlight that gains made in maternal and child health over decades, is likely to be reversed.
- > Six reasons why immunity passports are not recommended including: lack of a valid test; unfeasible to process the volume required; privacy issues; and potential for discrimination.
- > Differences in production of IgM Memory B cells may explain differences in disease severity in children vs adults.
- > Age dependent gene expression of ACE2 in nasal epithelium may explain differences in disease severity in children vs adults.
- > Two potential new antigen targets beyond the Spike protein.
- > Outcomes of remdesivir RCT: 11d vs 15d recovery time in treatment vs control group; but insufficient evidence to demonstrate mortality effect.
- > A large multi-site observational study found no clear benefit of hydroxychloroquine or chloroquine (+/- a macrolide) on in-hospital outcomes of COVID-19 patients. However, the study design and analysis has been extensively criticised.

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Response to COVID-19 and any other medical condition at this time is based on science that is new, often uncertain, subject to change, and dependent on context.

Always seek the advice of your physician or another qualified health provider properly licensed to practice medicine or general healthcare in your jurisdiction concerning any questions you may have regarding any information obtained from this publication.

Never disregard professional medical advice or delay in seeking it because of something you have read in this publication. Information obtained in this publication is not exhaustive and does not cover all possible manifestations of COVID-19 nor its interaction with other conditions, diseases, ailments, or their treatment.

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ADULT MEDICINE

Professor Julie Bines - Paediatric Gastroenterologist, RCH; Lead Enteric Disease Group MCRI; Victor and Loti Smorgon Professor of Paediatrics, The University of Melbourne and Dr Celeste Donato- Virologist, Enteric Diseases Group, MCRI; Lecturer, Department of Paediatrics, The University of Melbourne

Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19 <https://www.nejm.org/doi/10.1056/NEJMoa2015432>

Progressive respiratory failure is the primary cause of death in patients with COVID-19.

- > This paper compared the morphological and molecular changes in the lung retrieved at autopsy from:
 - Patients who died from COVID-19 n=7.
 - Patients who died from acute respiratory failure secondary to Influenza A (H1N1).
 - Age and-matched, uninfected controls (n=10).
- > Features of the lung from COVID-19 patients.
 - Diffuse alveolar damage in the peripheral lung (also observed in influenza patients).
 - Distinctive vascular features in COVID-19 patients including severe endothelial injury associated with intracellular virus and disrupted cell membranes.
 - Pulmonary vessels widespread thrombosis with microangiopathy.
 - Alveolar capillary micro thrombi – 9 times more prevalent in COVID-19 compared with Influenza (p<0.001).
 - New vessel growth – predominantly through intussusceptive angiogenesis 2.7 times greater than in patients with influenza (p<0.001).
- > Summary: Vascular angiogenesis in the lung distinguishes COVID-19 from severe influenza infection.

CLINICAL PAEDIATRICS

Professor Fiona Russell - Director of Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research Group, MCRI

Gastrointestinal features in children with COVID-19: an observation of varied presentation in eight children

[https://www.thelancet.com/pdfs/journals/lanchi/PIIS2352-4642\(20\)30165-6.pdf](https://www.thelancet.com/pdfs/journals/lanchi/PIIS2352-4642(20)30165-6.pdf)

- > Case series of eight children in one centre in the UK with GI presentations of COVID-19.
- > Children had symptoms of atypical appendicitis before rapid deterioration requiring hospitalisation and, in some cases, intensive care support.
- > All children had imaging confirming terminal ileitis and no surgical intervention was required at the time of writing.
- > Authors recommend abdominal imaging and SARS-CoV-2 testing, in settings with high community transmission, when investigating for possible appendicitis.

Benjamin Watson – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Septic shock presentation in adolescents with COVID-19

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30164-4/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30164-4/fulltext)

- > There is a growing concern describing a paediatric multisystem inflammatory syndrome temporally associated with COVID-19.
- > This article describes three cases of adolescents (10-12 years) who presented in septic shock, showing signs of peritonitis and multiple organ dysfunction.
- > All three cases had BMI greater than 97th percentile for age – raising the question of obesity as a risk factor for severe disease.
- > Additionally – whether the preponderance of abdominal symptoms and the prevalence of cholestasis rather than liver injury are explained by a higher expression of ACE receptors on the GI epithelial cells on cholangiocytes rather than hepatocytes is yet to be confirmed.

Reviewed by: Dr John Cheek

Silent COVID-19: what your skin can reveal

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30402-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30402-3/fulltext)

- > Report of three young patients presenting with chilblain-like lesions who were diagnosed with SARS-CoV-2 infection (Two were asymptomatic and potentially contagious).
- > Previous studies have reported skin lesions in 20.4% of patients with COVID-19 (though these symptoms did not correlate with disease severity).
- > Lesions developed in acral sites (especially the dorsum of the digits of the feet) beginning as erythematous-violaceous patches that slowly evolved to purpuric lesions and then to blisters and ulceronecrotic lesions, with a final complete return to normal.
- > Burning and itching were also present with some of the lesions.
- > Acute acro-ischaemic manifestations along the course of SARS-CoV-2 infection seem to be different from classic acrocyanosis, erythema pernio, and vasculitis; however, they could represent a cutaneous expression of the typical thrombotic pattern of COVID-19 due to hyperinflammation and altered coagulation and endothelial damage.
- > In the Australian context, a higher index of suspicion for COVID-19 should be used when evaluating children and adolescents with “chilblains”, which we often see at this time of year.

Reviewed by: Dr John Cheek

CRITICAL CARE

Ha My Ngoc Nguyen – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne.

Virtual care practices transform the care delivery model in an intensive care unit during the coronavirus pandemic.

<https://catalyst.nejm.org/doi/full/10.1056/cat.20.0169>

- > Virtual connectivity has been implemented widely, particularly in the outpatient setting and recently in the inpatient units as well.
- > Neonatal intensive care unit at Abington Hospital-Jefferson Health implemented three practices - video monitoring, virtual rounds, and virtual handoffs. This has kept patients and providers safe, while still emphasising family-centered care.
 - Video monitoring: the hospital implemented livestream video monitoring using a small camera at every bedside, so that family members were able to see their baby from home. Bedside nurses can also take pictures of babies and send them to families through a secure digital app.
 - Virtual rounding: attending neonatologists still perform a physical exam on every patient. Rounds take place on Zoom with each member of the care team (nutritionist, bedside nurse, nurse practitioners, etc.) in a different location. Parents who are physically present at the bedside can also be involved to maintain the focus of family-centered rounds.
 - Virtual handoffs: all physician and nurse practitioner handoffs were done virtually on the phone or video conferencing, the same day as virtual rounds.
- > The majority of providers perceive virtual rounding as safe without compromising the quality of patient care.
- > These practices are relatively low-cost and can be implemented in inpatient units across the medical specialties.
- > There have been many examples of the use of virtual connectivity during the pandemic, including in adult ICU in North America where virtual rounds and virtual visiting by families have been used. These have been important tools for overwhelmed ICUs to deal with a larger than normal number of patients, to enable physical distancing, and reduce transmission to staff from patients and between staff. However, no-one has implied that this is effective without a physician being present at the bedside to do a proper examination in the critical care setting. The virtual hospital-in the home established in Sydney is also a successful model for monitoring non-critically ill ambulatory patients.

Reviewed by: Professor Trevor Duke

DIAGNOSTICS & SAMPLING

Renee Cocks - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Extended Storage of SARS-CoV-2 nasopharyngeal swabs does not negatively impact results of molecular-based testing

<https://www.medrxiv.org/content/10.1101/2020.05.16.20104158v1>

- > With the demand for testing of COVID-19 quickly increasing and exceeding laboratory capacities, the understanding of the stability of viral RNA in swabs becomes important.
- > This was a laboratory study from New York.
 - Pooled 30 anonymised remnant positive nasopharyngeal swabs. Following heat-inactivation, the pool was divided into 126 aliquots that were stored at either ambient temperature (18-25°C) or refrigerated (2-8°C). For 102 aliquots, cycle thresholds (Ct) for the amplification of three automated real-time reverse transcriptase PCR platforms used in clinical testing were compared over 21 days. Some differences in Ct's were observed, but they were deemed not to be clinically significant.
 - Seven positive samples held at 4°C were re-tested at day 35 after collection on one platform. These remained positive.
- > Conclusion: Nasopharyngeal swabs can be stored under refrigeration or ambient conditions for 21 days without clinically impacting the results of real-time PCR testing.
- > Strengths: comparison of three testing platforms; study design testing extended storage which is likely important for overloaded testing centers.
- > Limitations: small numbers of samples; unclear how samples were selected and how many of the seven samples tested contained mucous; effect on samples with low viral loads was not determined; these samples may be more likely to be subject to delays in testing, but critical for determining community transmission.

Reviewed by: Associate Professor Catherine Satzke

Thomas Hill – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

What are the viral targets of the antibody response to SARS-CoV-2 beyond spike?
<https://www.medrxiv.org/content/10.1101/2020.04.30.20085670v1.full.pdf>

- > This study aimed to characterise the antibody response to 15 viral targets of SARS-CoV-2 for refinement of serological testing and for future therapeutics.
- > Convalescent sera of 15 patients infected with SARS-CoV-2 compared to healthy controls was used to assess the acute antibody response against open reading frames (ORF) and structural proteins (S, N, M and E) of the SARS-CoV-2 virus using the luciferase immunoprecipitation system (LIPS).
- > Significant antibody responses were seen to 11 of the tested antigens, of which only three, N, ORF3b and ORF8, were useful diagnostic targets with high sensitivity and specificity. When used alone, N, ORF3b and ORF8 had sensitivities of 93.3%, 86.6% and 100% respectively.
- > Using the LIPS technique, combining these three antigens achieved a high sensitivity and a specificity of 100% even at early time points of disease.
- > This study identified ORF3b and ORF8 as new and unique antigenic targets.
- > Further validation of the LIPS technique using the combination of antigens N, ORF3b and ORF8 for early detection of SARS-CoV-2 is needed in larger cohorts of COVID-19 patients.
- > Studies using serum from late convalescent and asymptomatic patients is also needed to investigate the validity of these targets for predicting disease in late and mild cases respectively.

Reviewed by: Dr Danielle Wurzel

EPIDEMIOLOGY & PUBLIC HEALTH

Professor Fiona Russell - Director of Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research Group, MCRI

Estimating the extent of true asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis (pre-print)

<https://www.medrxiv.org/content/10.1101/2020.05.10.20097543v1>

- > The prevalence of true asymptomatic COVID-19 cases is critical for considering the effectiveness of COVID-19 mitigation.
- > This is a systematic review on the asymptomatic rates and transmission rates.
- > Five studies from three countries (China, USA, Italy) that tested 9,242 at-risk people, of which 413 were positive and 65 were asymptomatic were included.
- > Asymptomatic prevalence ranged from 6% to 41%; meta-analysis (fixed effect) found that the proportion of asymptomatic cases was 16% (95% CI: 12% - 20%) overall; higher in non-aged care 19% (15% - 24%), and lower in long-term aged care 8% (4% - 14%).
- > Two studies provided direct evidence of forward transmission of the infection by asymptomatic cases but suggested lower rates than symptomatic cases.
- > These estimates of the prevalence of asymptomatic COVID-19 cases are lower than many highly publicised studies, but still substantial.
- > Further robust epidemiological evidence is urgently needed, including in sub-populations such as children, to better understand the importance of asymptomatic cases for driving spread of SARS-CoV-2.

Dr Claire von Mollendorf - Senior Research Officer, New Vaccines and Asia-Pacific Health Research Groups, MCRI and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne

What settings have been linked to SARS-CoV-2 transmission clusters?

<https://wellcomeopenresearch.org/articles/5-83/v1>

Systematic review to assess which situations have resulted in transmission of SARS-CoV-2 with resultant clusters. This information can advise countries regarding how to relax restrictions.

- > Identified 152 SARS-CoV-2 transmission clusters events from 18 different types of indoor or outdoor settings.
- > Largest cluster case numbers were from cruise ships and worker dormitories; followed by hospitals and aged care facilities.
- > A small number of clusters were linked to schools, with most of the cases identified in adults.
- > The highest number of SARS-CoV-2 transmission cluster reports were from households.
- > The review had a number of limitations based on issues related to cluster size and attack rate reporting:
 - Much of the available data regarding clusters was from media reports which resulted in missing data.
 - Cluster reports were often confounded by recall bias and limited by contact tracing and testing capacity.
 - In many settings only symptomatic and hospitalised cases are reported.
- > Settings linked to COVID-19 case clusters should be closely monitored and relaxation of restrictions in these places should be delayed. Improvements in surveillance capacity are required in many countries.

Alastair Weng – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Tracking the COVID-19 pandemic in Australia using genomics

<https://www.medrxiv.org/content/10.1101/2020.05.12.20099929v1.full.pdf>

- > The study aimed to investigate the transmission source of COVID-19 cases in Victoria, Australia by combining whole genome sequencing analysis of SARS-CoV-2 and epidemiological data from 1,333 confirmed COVID-19 cases from 6th January to 13th April 2020.
- > 62% (827/1,333) COVID-19 cases were identified in returning travelers, most commonly from north-west Europe and the Americas. 27%(360/1,333) in known COVID-19 contacts but 10.1% (134/1,333) cases were from an unknown source within Australia.

- > 67.7% (903/1,333) COVID-19 cases were successfully obtained complete whole genome sequences (WGS). Only 7 single nucleotide polymorphisms (SNPs) (IQR 6-9) were observed (Wuhan-1 genome was used as reference) and these WGS were representative of global diversity.
- > 76 genomic clusters were identified. Genomic clusters were strongly concordant, 100% (IQR 85-100%), with epidemiological clusters that were defined as three or more cases with a common source exposure (e.g. healthcare facility). Large genomic clusters corresponded to cruise ships, healthcare facilities, and social venues.
- > For 81 cases with unknown epidemiological sources, 88% (71/81) of cases were identified within 24 genomic clusters providing potential sources of the transmission. Genomic cluster data also provided the evidence of community transmission or to exclude a putative transmission network involving four health services, an important implication of genomic data in nosocomial infection control.
- > Genomic analyses suggested the viral reproductive number R_0 was 1.63 prior to travel restrictions, but only 0.48 following social distancing measures.
- > Viral genomic data has shown to be a useful tool in public health responses and in COVID-19 contact tracing.

Reviewed by: Dr Lien Anh Ha Do

Julian Loo Yong Kee - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Public trust and controlling COVID-19

<https://pursuit.unimelb.edu.au/articles/public-trust-and-controlling-covid-19>

- > Australia has a good collective approach to public health which suggests a different attitude and behavior to other countries.
- > Reasoned persuasion with enforcement has gained prominence and acceptance in Australia with public health campaigns to convey importance to the community and research evidence to back legislation and enforcement.
- > Collective work of politicians, medical associations, and other major lobbying groups (eg. Motor vehicle companies in mandatory seatbelts) is important for successful public health intervention.
- > Trust and public health:
 - Trust is required to allow invoking of mandatory measures to ensure an individual's right does not compromise the collective health.
 - History facilitates trust: Lack of COVIDSafe tracing application uptake may reflect lack of positive experience with previous government technology.
 - Public health has greater trustworthiness than politicians.
 - Increased Australian Government trust due to actions during COVID-19 crisis.

- > COVID-19:
 - Australian public health measures and the collective Australian response has helped “flatten the curve”.
 - Dilemma of the more successful we are the harder it is to support collective measures that are burdening people.

Reviewed by: Associate Professor Margie Danchin

Batsho Mandlebe - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Reductions in commuting mobility predict geographic differences in SARS-CoV-2 prevalence in New York City

<https://dash.harvard.edu/handle/1/42665370>

- > New York City has been the epicentre of SARS-CoV-2 pandemic in the United States of America, however, there have been substantially different morbidity and mortality rates across its neighbourhoods.
- > This study compares prevalence of SARS-CoV-2 in each borough of New York City between 22nd March and 3rd May 2020 using 1746 SARS-CoV-2 test samples collected from pregnant women admitted for delivery during this time and high-volume mobility data from Facebook users.
- > Main outcomes
 - Prevalence of SARS-CoV-2 ranged from 11.3% (in Manhattan) to 26.0% (in South Queens) with lower rates associated with boroughs experiencing reduced outward-bound morning traffic and reduced inward bound commutes in the evening (Pearson R = -0.88).
 - Rates of SARS-CoV-2 peaked across New York City during the week of 30th March however temporal trends varied greatly within each borough.
 - Higher prevalence was in some boroughs likely to be associated with distribution of essential workers and of resources to support social distancing.
- > Limitations: biased representation of SARS-CoV-2 infection in pregnant women vs the rest of the population and failure to capture interpersonal contacts within boroughs.

Reviewed by: Associate Professor Margie Danchin

Sarah Jackson – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Considerations in adjusting public health and social measures in the context of COVID-19

https://apps.who.int/iris/bitstream/handle/10665/331773/WHO-2019-nCoV-Adjusting_PH_measures-2020.1-eng.pdf

- > The overarching goal of the WHO global COVID-19 response strategy has been to control the pandemic via slowing transmission and reducing mortality to reach a state of low-level or no mortality. Countries are at different stages in terms of public health measures based on their local epidemiology.
- > Public health and social measures such as personal protective measures, physical distancing, travel restrictions and lockdown/shutdown measures; have not yet had their public health impact assessed- which is needed.
- > Assessment will consider societal and economic costs of these measures and allow careful risk assessment and staged approach to adjusting these measures to minimise further outbreaks of COVID-19 until specific pharmaceutical interventions are available.
- > Decisions to alter restrictions should be based upon scientific evidence, real world experience, and critical factors such as the economy.
- > Four transmission scenarios have been defined: no reported cases, sporadic cases, clusters of cases, and community transmission. Each requires a tailored approach.
- > Adjustment of public health and societal restrictive measures should undergo risk assessment based upon epidemiological factors, health care and public health capacities, and availability of effective pharmaceutical interventions.
- > The nature and order of restrictions to be lifted should be based upon guiding principles of a controlled, slow and stepwise return, starting in areas of lowest incidence and population density. Protection of vulnerable populations should be central in decision making.
- > Large-scale changing of restrictions should rely on the following factors in order to minimise the risk of a resurgence of COVID-19 cases: controlled transmission, sufficient public health and health system workforce and capacities, minimisation of outbreak risk in high-vulnerability populations, preventative measures in workplaces, management of community transmission in areas with high risk of that, and full engagement of the community in this process.

Reviewed by: Associate Professor Margie Danchin

GLOBAL HEALTH

Rose Noble Kizhakekara - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Shared sanitation and the spread of COVID-19: risks and next steps
[https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196\(20\)30086-3/fulltext](https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(20)30086-3/fulltext)

- > Over a billion people in the world need to leave their homes to meet sanitisation needs. Live SARS-CoV-2 has been detected in faeces, and the virus remains viable for days on surfaces used for toilets and doors. Therefore, shared facilities could become sources of both airborne and contact exposures.
- > At increased risk: Countries with more shared sanitisation (e.g. urban sub-Saharan Africa, especially women due to more frequent use), migrant centres, prison inmates, refugee camps, homeless.
- > Suggestions: WHO guideline for shared sanitisation, handwashing resources and promotion, physical distancing in queues, cleaning of facilities (responsibility of both men and women).
- > Further research is needed to understand whether shared sanitisation contributes to risk of infection.

Reviewed by: Dr Wonie Uahwatanasakul

Alastair Weng – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Winning the war against maternal and child deaths
<https://www.project-syndicate.org/commentary/covid19-defend-progress-on-maternal-child-mortality-by-tedros-adhanom-ghebreyesus-et-al-2020-05>

- > The authors Tedros Adhanom Ghebreyesus (Director General, WHO), Henrietta H. Fore (Executive Director, UNICEF), Natalia Kanem (Executive Director, UNPF), Kevin Watkins (CEO, Save the Children UK) discuss the importance of maternal and child health in the face of coronavirus.
- > The current situation
 - Maternal and child (<5y) mortality have plummeted since 1990, primarily due to international co-operation and health system transformation in developing nations.
 - Five million children and 300,000 mothers still die every year of preventable disease and complications, far higher than expected tracking for SDG3.

- The COVID-19 pandemic has further detracted from our fight to prevent maternal and child deaths, including delay in immunisation, decreased antenatal visits, and poor access to routine healthcare.
- > The fight forward
 - Government and aid organisations must ensure funding for community health services to ensure progress is not lost.
 - Health systems need to address weaknesses exposed by COVID-19 eg. oxygen, ventilators, PPE.
 - Universal health coverage must be a reality across the world to ensure safe access by the poorest populations.
 - Financial resources must be directed towards healthcare and invested into child and maternal health.
 - We are united by our shared values and hold our pledge to end preventable deaths by 2030.

Reviewed by: Professor Fiona Russell

IMMUNOLOGY

Professor Fiona Russell - Director of Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research Group, MCRI

Ten reasons why immunity passports are a bad idea

<https://www.nature.com/articles/d41586-020-01451-0>

- > Restricting movement on the basis of biology threatens freedom, fairness and public health.
- > On 24th April 2020, WHO cautioned against issuing immunity passports because their accuracy could not be guaranteed.
- > Author states that “6 ethical issues add up to one very bad idea”:
 - It is unknown whether COVID-19 immune response confers long lasting protection
 - Serological tests are unreliable:
 - Low specificity means the test measures antibodies other than those that are specific to SARS-CoV-2 (false positives).
 - Low sensitivity requires a person to have a high concentration of SARS-CoV-2 antibodies for them to be measured effectively. This causes false negatives in people who have few antibodies, leading to potentially immune individuals being incorrectly labelled as not immune.
 - Testing is unfeasible due cost and amount of testing whole populations, even if enough reliable testing kits were available, and even if limited to health care workers.
 - Too few survivors to boost the economy: low disease prevalence (estimated to be 2-3% of global population) combined with limited testing capacity and unreliable tests, means that only a small fraction of any population would be certified as free to work and free to shop etc.
 - Breach of privacy.
 - Marginalised groups will face more scrutiny: with increased monitoring comes increased policing, and with it higher risks of profiling and potential harms to racial, sexual, religious or other minority groups.

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Why are children less susceptible to COVID-19 compared to adults? The immune system may be the answer (a comment)

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30135-8/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30135-8/fulltext)

- > Since SARS-CoV-2 is a new pathogen, there is no pre-existing immunity to it, and everyone is susceptible to infection and developing COVID-19 disease.
- > However, children's immune systems are more equipped to deal with new pathogens compared to adults and the elderly. The reason for this could be due to children being capable of producing large numbers of Innate or IgM Memory B-cells (MBCs).
- > MBCs come in two subtypes:
 - CD27dull produce non-specific IgM antibodies that can recognize different novel pathogens and help to contain the infection during the two weeks necessary for the production of high-affinity antibodies that will eventually clear the virus and prevent reinfection.
 - In children, most MBCs are CD27dull
 - CD27bright produce highly antigen specific antibodies that can mainly recognise their targets but are incapable of adaptations to new antigens.
 - In the elderly, most MBCs are CD27bright
 - These two MBC populations work together to maintain the MBC pool following encounter with pathogen.
 - B cells also secrete regulatory cytokines such as IL-10 that might also help suppress immune-mediated pathology in the lung.

Reviewed by: Associate Professor Paul Licciardi

INDIGENOUS HEALTH

Isabella Overmars - 2nd Year Master of Public Health Student,
The University of Melbourne

Voluntary collective isolation as a best response to COVID-19 for indigenous populations? A case study and protocol from the Bolivian Amazon

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31104-1/fulltext?utm_campaign=tlcoronavirus20&utm_content=129573089&utm_medium=social&utm_source=twitter&utm_channel=tw-27013292](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31104-1/fulltext?utm_campaign=tlcoronavirus20&utm_content=129573089&utm_medium=social&utm_source=twitter&utm_channel=tw-27013292)

- > Indigenous communities worldwide share common characteristics, such as higher rates of respiratory and other health conditions, and limited access to medical services, that place them at higher risk of complications and death from COVID-19.
- > Teenagers from industrialised countries have exhibited minimal risk of death from COVID-19, but children with an indigenous background with history of respiratory illness are at a greater risk. For example, 3/7 positive cases from the Yanomami tribe in South America died from COVID-19, among the dead was a 15-year-old boy.
- > Potential threats arising from COVID-19 transmission, such as death of Elders leading to loss of language and cultural traditions, has caused many indigenous communities to restrict or close their own borders, with action aimed largely at preventing viral transmission.
- > The Tsimane Health and Life History Project worked with Tsimane peoples in the San Borja municipality with a two-phased approach to help prevent SARS-CoV-2 from reaching Tsimane communities.
 - Phase One: Awareness and Prevention. Involved coordination of tribal leaders, education and awareness, collective decision making, coordination with government and public health efforts, purchasing and training in use of PPE, and delivering medical care for non-COVID-19 diseases to prevent exposure to hospital environment.
 - Phase Two: Containment and Patient Management. Involved case reporting to the Tsimane population and local authorities, tracking spread by linking cases to geographic information systems, coordinating isolation responses within affected and unaffected communities, testing and contact-tracing, and patient management.
- > There are many indigenous communities who have not benefited from advanced preparation for this pandemic, and whose needs might be excluded from regional plans because of scarce resources and insufficient logistical and cultural support. The paper offers advice for adapting these prevention strategies to other indigenous populations, to mitigate the effects of the COVID-19 pandemic on their communities.

Reviewed by: Associate Professor Margie Danchin

INFECTION CONTROL

Dr Vanessa Clifford - Infectious Diseases physician and Microbiologist, RCH/RWH; Honorary Research Fellow in the Infection and Immunity Group, MCRI; and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne

Detection of SARS-CoV-2 in human breast milk

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2931181-8>

- > German study reporting clinical follow up and testing of a cluster of two breastfeeding mothers and infants with COVID-19 infection. Breast milk was tested at several time points using qPCR for SARS-CoV-2 (N and ORF1b-nsp14 genes).
- > SARS-CoV-2 was detected in breast milk at 4 time points (approximately six-nine days after onset of symptoms) from one mother with mild symptomatic COVID-19.
- > The mother was reported to have worn a surgical mask since the onset of symptoms and followed safety precautions when handling or feeding the neonate (including proper hand and breast disinfection).
- > Her infant became symptomatic approximately four days after the mother developed symptoms (and 24 hours after SARS-CoV-2 was detected in breast milk). The infant tested positive for SARS-CoV-2, and was co-infected with RSV, requiring hospitalisation and respiratory support.
- > This is the second case report of SARS-CoV-2 detected in breast milk from a mother with COVID-19 (other recent case series have not reported SARS-CoV-2 in milk). Presence of viable virus was not confirmed by viral culture. A possible alternative explanation for SARS-CoV-2 detected in breast milk is retrograde transmission from infant saliva to the breast during breastfeeding.
- > This study does not provide direct evidence of transmission of SARS-CoV-2 via breast milk. Droplet or contact transmission from the mother remains the more likely mode of transmission. Further detailed studies of SARS-CoV-2 in breast milk are warranted.

PERINATAL HEALTH

Jenny Pham - 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection

<https://www.cmaj.ca/content/cmaj/early/2020/05/14/cmaj.200821.full.pdf>

This case represents probable congenital infection of SARS-COV-2.

- > 40y G2P1 woman, with a background of familial neutropaenia, gestational diabetes and frequent bacterial infections, presented with common symptoms of COVID-19 and tested positive.
- > The neonate was not in contact with vaginal secretions and membranes were intact prior to birth.
- > The neonate's nasopharyngeal swabs (birth, day two, day seven) were all positive. Neonatal plasma tested positive on day four, and stool was positive on day seven. All neonatal samples were collected prior to contact with the mother.
- > Limitations: lack of evidence for SARS-CoV-2 in umbilical cord tissue, lack of cord blood for testing, potential contamination of breast milk, maternal familial neutropaenia may have contributed to dissemination of the virus.
- > Implications: neonates born to mums with suspected or confirmed SARS-CoV-2 infection should be thoroughly cleaned and investigated (nasopharynx, placenta, cord blood) for the disease as soon as possible. This will guide neonatal management and enable health workers to adopt appropriate precautions.

Reviewed by: Dr Wonie Uahwatanasakul

Benjamin Watson – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Effects of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcomes: a systematic review

<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.22088>

- > Systematic review of 24 studies including a total of 324 women with COVID-19 met the criteria – comprising nine case series and 15 case reports.
- > The most common symptoms at presentation were: fever, cough, dyspnoea/shortness of breath, fatigue and myalgia.
- > The rate of severe pneumonia reported amongst the case series ranged from 0-14% with the majority of the cases requiring admission to intensive care – and almost all cases having positive Ct chest findings.

- > Only four cases of spontaneous miscarriage or abortion were reported.
- > In the 155 neonates that had nucleic acid testing in throat swab, all except three cases were SARS-CoV-2 negative.
- > From the case reports, two maternal deaths, one neonatal death and two cases of neonatal SARS-CoV-2 infection were reported.
- > Despite the increasing number of published studies on COVID-19 in pregnancy, there are insufficient good-quality data to draw unbiased conclusions with regard to the severity of the disease or specific complications of COVID-19 in pregnant women, as well as vertical transmission, perinatal and neonatal complications.
- > Need for better data in pregnancy.

Reviewed by: Professor Fiona Russell

THERAPEUTICS

Nicholas Baxter – 3rd Year Medical Student,
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Remdesivir for the treatment of COVID-19 – preliminary report

<https://www.nejm.org/doi/full/10.1056/NEJMoa2007764>

- > This is a report of the NIAID trial conducted in ten countries, the second trial of remdesivir.
- > Double blind, randomised, placebo-controlled trial of intravenous remdesivir in 1059 patients evaluating the efficacy of remdesivir (200_{mg} loading dose + 100_{mg} per day for up to ten days) compared to placebo.
- > The primary endpoint was changed from day 15 status (on the WHO ordinal scale) to time to recovery (not requiring medical care/supplemental O₂) as external data suggested recovery times were longer than initially expected.
- > Patients in the remdesivir group had a shorter time to recovery than patients in the placebo group (median, 11 days, as compared with 15 days; rate ratio for recovery, 1.32; 95% confidence interval [CI], 1.12 to 1.55; P<0.001).
 - The benefit seemed to be greater in those with moderate severity illness (requiring oxygen), than critical illness (HFNP, ventilation/ECMO) although a statistical test of interaction was negative reflecting small numbers in other groups. There were no obvious differences in those treated early (<10 days) vs later.
 - Mortality was numerically lower in the remdesivir group than in the placebo group, but the difference was not significant (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04; 1059 patients). 28 day follow up was not yet complete in 28%.
 - On an ordinal scale, the odds of improvement were higher in those on remdesivir (proportional OR 1.5, 95% CI: 1.2 to 1.9).
- > Serious adverse events occurred in 114 patients (21.1%) in the remdesivir group and 141 patients (27.0%) in the placebo group; four events (two in each group) were judged by site investigators to be related to remdesivir or placebo. There were 28 serious respiratory failure adverse events in the remdesivir group (5.2% of patients) and 42 in the placebo group (8.0% of patients).
- > This trial is larger than the previously reported Chinese trial of remdesivir that did not show differences in time to improvement.
- > It appears that remdesivir results in more rapid clinical improvement.
- > There is a suggestion that it may improve early mortality but there is insufficient evidence against the null hypothesis of no effect; antivirals alone may not have a large impact on outcome, particularly in severe disease.

Reviewed by: Professor Allen Cheng

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

The benefits and safety of Hydroxychloroquine or chloroquine with or without a macrolide for the treatment of COVID-19

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2931180-6>

- > Method: A multinational registry analysis was conducted to evaluate the safety and benefit of four regimens for the treatment of COVID-19.
 - Data from 671 hospitals in six continents was used. A total of 96,032 patients hospitalized between Dec 20th, 2019 and April 14th, 2020 with PCR-confirmed SARS-CoV-2 infection were included.
 - Patients who received one of the treatments of interest within 48 hours of diagnosis were included in one of four treatment groups: chloroquine alone (n=1868), chloroquine with a macrolide (3783), hydroxychloroquine alone (3016), or hydroxychloroquine with a macrolide (6221), and patients who received none of these treatments formed the control group (81144).
 - Two outcomes were studied: in-hospital mortality and occurrence of de-novo ventricular arrhythmias.
- > Findings: Each of the four treatment regimens was associated with an:
 - Increased risk of hospital mortality compared to the control group:
 - Control (9.3%), chloroquine alone (16.4%), chloroquine with a macrolide (22.2%), hydroxychloroquine alone (18%), or hydroxychloroquine with a macrolide (23.8%)
 - Increased risk of de-novo ventricular arrhythmias:
 - Control (0.3%), chloroquine alone (4.3%), chloroquine with a macrolide (6.5%), hydroxychloroquine alone (6.1%), or hydroxychloroquine with a macrolide (8.1%)
- > Conclusion: There is no clear therapeutic benefit of hydroxychloroquine or chloroquine (when used either alone or with a macrolide) on in-hospital outcomes of patients with COVID-19. Instead, each of these regimens could be associated with increased risk of ventricular arrhythmia and in-hospital death with COVID-19.
- > Limitations: Observational study. A cause-and-effect relationship between drug therapy and survival cannot be inferred. Survivor bias is substantial in this study as only the more severe cases were exposed (received the therapeutic) and achieved the outcome (death). Even though severity was adjusted for in the analysis, this is insufficient to account for substantial bias in treatment allocation. Additionally, there has been a lot of criticism about this study in terms of the definition of severity outcome; the likely heterogeneity in clinical care across sites and dosage used; the variability in the duration of symptoms prior to treatment. Open access to data is not yet available to be able to check some potential inconsistencies in the number of patients treated and outcomes reported. Only well designed randomised clinical trials can determine whether Hydroxychloroquine or chloroquine is effective.

Reviewed by: Dr Amanda Gwee, Professor Fiona Russell and Professor Allen Cheng

Further critique of the study can be found here:

<https://statmodeling.stat.columbia.edu/2020/05/26/last-post-on-hydroxychloroquine-perhaps/>

https://twitter.com/jwato_watson/status/1264793409618935809

TRANSMISSION

Julian Loo Yong Kee - 3rd Year Medical Student,
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Infectious SARS-CoV-2 in faeces of patient with severe COVID-19

https://wwwnc.cdc.gov/eid/article/26/8/20-0681_article?deliveryName=USCDC_333-DM28664

A research letter reporting the isolation of SARS-CoV-2 from the faeces of COVID-19 patients in China

- > Case:
 - 78-year-old male admitted with seven days of coughing and intermittent fever in the context of recent travel to Wuhan, China on 17th January 2020
 - Ct-chest: Multiple, ground-glass opacities
 - Nasopharyngeal and oropharyngeal swab positive for SARS-Cov-2 RNA (qRT-PCR)
 - Patient intubated 22nd January and died 20th February
 - Faeces samples obtained: 27th & 29th January, 1st & 7th February
 - All faecal samples positive for viral RNA (qRT-PCR)
 - Viral RNA loads higher in faeces than in respiratory specimens (17-28 days after symptom onset)
 - On electron microscopy: Spiral viral particles with distinct surface spike proteins projections (similar to SARS-CoV-2 image)
 - Isolation of SARS-Cov-2 from RNA-positive stool at early time points only
 - Viral antigen detected in gastrointestinal epithelial cells of a biopsy sample
 - High levels of IgG against spike protein with levels of nucleocapsid protein-specific antibodies being relatively lower
- > 28 patients (including this case):
 - 12/28 patients positive for viral RNA at ≥ 1 -time point
 - SARS-CoV-2 Virus isolated from two of three patients that were viral RNA positive
- > Summary:
 - Confirmation of infectious SARS-CoV-2 virus in faeces
 - Potential for faecal-oral or faecal-respiratory transmission
 - Further studies are warranted

Reviewed by: Professor Julie Bines

Renee Cock - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Cluster of coronavirus disease associated with fitness dance classes, South Korea
https://wwwnc.cdc.gov/eid/article/26/8/20-0633_article#tnF1

- > Fitness dance classes to Latin rhythms have been gaining popularity in South Korea because of the high intensity of exercise.
- > This research letter identified 112 COVID-19 cases associated with fitness dance classes at 12 different sports facilities in South Korea by 9th March. Instructors and students met only during classes which were 50 minute classes twice a week. The instructors had attended a four hour training workshop for fitness dance on 15th February.
- > Characteristics that might have led to transmission from instructors include large class sizes (5-22), small spaces (60m²) and high intensity of workouts, as the moist atmosphere in sports facilities along with turbulent airflow potentially causes a denser transmission of droplets.
- > Interestingly, in one facility where transmission during fitness dance classes was found, one instructor positive for SARS-CoV-2 taught Pilates and yoga but none of her students (class size seven-eight) tested positive for the virus. This supports the hypothesis of the high intensity exercise increasing risk of infection.
- > Limitations: complete rosters of visitors to sports facilities were unavailable
- > Conclusion: Intense physical exercise in densely populated sports facilities could increase the risk of infection, so it is recommended by the authors that vigorous exercise in confined spaces be minimised during outbreaks. This reinforces the “three Cs” - “conversation” (proximity and types of respiratory activity), crowds and confined spaces - as important factors contributing to transmission.

Reviewed by: Professor Allen Cheng

VACCINES

Dan Lindholm - 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

WHO - Key criteria for the ethical acceptability of COVID-19 human challenge studies

https://apps.who.int/iris/bitstream/handle/10665/331976/WHO-2019-nCoV-Ethics_criteria-2020.1-eng.pdf?ua=1

- > Human challenge studies have been proposed as one method of speeding up COVID-19 vaccine development, as well as providing a number of other potential benefits discussed in this paper.
- > Here, the WHO proposes an ethical framework for scientists, research ethics committees, funders, policy-makers and regulators to guide decision making around the ethical acceptability of such studies.
- > The below criteria are discussed in detail, and recommended to ensure ethical justifiability, minimise harm to participants, and maintain high levels of public trust in research:
 - Any human challenge study with COVID-19 must have strong scientific justification.
 - The potential benefits of a COVID-19 challenge study must be reasonably expected to outweigh the risks.
 - COVID-19 research programmes must be informed by consultation with the public, in addition to experts and policy-makers.
 - Coordination between researchers, funders, policy-makers and regulators is essential for such challenge studies.
 - Human challenge studies with COVID-19 must only be situated at centres where the highest scientific, clinical and ethical standards can be achieved, including the provision of high-quality supportive treatment where necessary.
 - Participants must only be selected where they will experience minimal and limited risk.
 - All such studies should be reviewed by a specialised and independent committee.
 - As ever, human challenge studies with COVID-19 must involve rigorous informed consent.
- > If this is of particular interest, the National Paediatric Bioethics E-Conference (2nd - 4th September), held by the Children's Bioethics Centre at the Royal Children's Hospital, will focus on "Ethical Reflections on COVID-19 in Paediatric Healthcare"

Reviewed by: Associate Professor Margie Danchin

VIROLOGY

Daniel Lamanna - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Nasal gene expression of angiotensin-converting enzyme 2 in children and adults

https://pubmed.ncbi.nlm.nih.gov.ezp.lib.unimelb.edu.au/32432657/?from_term=Nasal+Gene+Expression+of+Angiotensin-Converting+Enzyme+2+in+Children+and+Adults&from_pos=1

Children account for <2% of identified cases of COVID-19 - it is hypothesized that the lower risk is attributable to differential expression of angiotensin-converting-enzyme 2 (the receptor that SARS-CoV-2 uses for host entry).

- > Retrospective study examining gene expression in the nasal epithelium from individuals aged 4 - 60 years from 2015 - 2018 within the Mount Sinai Health System (New York, New York).
- > Age-dependent ACE2 expression in nasal epithelium was found; expression was lowest in younger children (4-9 years of age) and increased with age.
- > Lower ACE2 expression in children relative to adults may explain why COVID-19 is less prevalent in children, however, the nasal and lung environments are distinct with known differences in gene expression.
 - ACE2 expression in the nasal epithelium does not reflect ACE2 expression in the pulmonary epithelium.
- > A limitation of this study was that individuals over 60 years of age were not included.

Reviewed by: Dr Celeste Donato

Nasal ACE2 levels and COVID-19 in children

<https://jamanetwork.com/journals/jama/fullarticle/2766522>

After adjustment for comorbidities, age has been independently associated with increased mortality due to COVID-19 - to date little attention has been given to children who appear to have a lower risk of SARS-CoV-2 infection and mortality.

- > Older children, young adults, and adults all demonstrated higher expression of ACE2 in the nasal epithelium compared to younger children.
- > Analysis from close contacts of index cases in China found that infection rates in children were comparable with or perhaps slightly higher than in younger adults, but were significantly lower than older patients (aged > 60 years) - this suggests that children presumably have similar rates of becoming infected compared to middle aged adults following close contact to an infected individual.

- > Previous studies show that ACE2 may play a protective role in severe lung injury, however, ACE2 has also been identified as a receptor for viral entry.
 - In the nasal epithelium of the upper airway decreased ACE2 expression could be helpful in reducing the acquisition of SARS-CoV-2 infection.
 - In the lower respiratory tract decreased ACE2 expression could potentiate a higher risk of developing severe acute respiratory distress and lung injury.

Reviewed by: Dr Celeste Donato

Benjamin Watson – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Symptomatic infants have higher nasopharyngeal SARS-CoV-2 viral loads but less severe disease than older children

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa608/5841161>

- > Previous studies have demonstrated a correlation between viral load and disease severity, however this is not consistent across the paediatric age spectrum.
- > Report suggests that symptomatic infants have higher nasopharyngeal viral loads at presentation but develop less severe disease compared to older children and adolescents (severe disease defined as requiring ICU admission or mechanical ventilation).
- > This may be attributed to slightly earlier presentation to clinical care or host biology – further studies are required.

Reviewed by: Dr Lien Anh Ha Do

OTHER RESOURCES

National COVID-19 clinical evidence taskforce: continually updated evidence-based clinical guidelines
<https://covid19evidence.net.au/>

Lancet COVID-19 papers
https://www.thelancet.com/coronavirus?utm_campaign=tlcoronavirus20&utm_content=126383502&utm_medium=social&utm_source=twitter&hss_channel=tw-27013292

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects
<https://dontforgetthebubbles.com/evidence-summary-paediatric-covid-19-literature/>

All COVID-19 literature
<https://www.ncbi.nlm.nih.gov/research/coronavirus/>

Oxford COVID-19 Evidence Service
<https://www.cebm.net/oxford-covid-19/>

Daily updates on COVID-19 literature compiled by Canadian medical students
https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuLV0aJdf_z2uWV7r3FaPzAOr86q9ZXBcTZ1QcCE_Nw/formResponse

Victorian Department of Health and Human Services
<https://www.dhhs.vic.gov.au/coronavirus-covid-19-daily-update>

Australian Government
<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers>
<https://www.health.gov.au/resources/publications/management-and-operational-plan-for-people-with-disability>

COVID-19 and the kidney, which is currently the recommended US resource
<http://www.nephjc.com/covid19>

University of Birmingham COVID-19 Research Briefing
<https://www.birmingham.ac.uk/university/colleges/mds/Coronavirus/COVID-19-research-briefing.aspx>

Australian Government Department of Health Webinars on the COVID-19 response for primary care practitioners
<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-advice-for-the-health-and-aged-care-sector/webinars-on-the-coronavirus-covid-19-response-for-primary-care-practitioners>

Global summary, identifying changes in the reproduction number, rate of spread, and doubling time during the course of the COVID-19 outbreak whilst accounting for potential biases due to delays in case reporting both nationally and sub-nationally
<https://epiforecasts.io/covid/posts/global/>

WHO Rolling updates on COVID-19
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)
<https://www.scimex.org/info/2019-20-coronavirus>
<https://www.covid19-hpc-consortium.org/>

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