COVID-19 KIDS EVIDENCE UPDATE

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

Weekly Update No. 13
16th July 2020
HEAD OF DEPARTMENT
EDITORIAL

Professor Sarath Ranganathan - Stevenson Chair, Department of Paediatrics, University of Melbourne

Like me, you may have missed not having the report to rely on last week, but having published a dozen weekly reports back-to-back, our dedicated team of student and expert reviewers, editors and production gurus all took a well-deserved break to coincide with the Victorian school holidays. They needed a rest but, as can be witnessed from this report, have come back energised, resilient and resourceful. To read more about our remarkable team of student reviewers follow this link: https://medicine.unimelb.edu.au/mms/mms-staff-news/newsletter-issue-16-july-2020/covid-19-kids-research-updates-the-student-team

For the majority of school pupils in the state of Victoria the school holidays have been extended before schools are locked down again. Those in years eleven and twelve have scrambled back to their respective campuses in an effort to rescue some of their learning, but rumblings suggest a finite time for this activity. Case numbers are surging locally and adult hospitals and intensive care units are beginning to fill. A significant number of these new infections are in children and young people but so far none have led to severe symptoms.

At times like these we will need to ensure we keep abreast of all the information pertaining to children and young people so that we can provide the best care possible and identify the right questions for our researchers to tackle. We need to ensure that we all work together so that the best policies for children are introduced. It is not a time to withdraw from global health organisations or create fracture lines between policy makers and their scientific and medical advisors. In this regard, and from what I have witnessed, we should be grateful that we still live in the Lucky Country, even if the current surge in cases is partly due to bad luck! We should also continue to look at how we can support those in less lucky locales.

As always, a modicum of hope goes a long way and that may be found in the preliminary reports from the Phase 1, dose-escalation trial of Moderna’s mRNA vaccine that encodes the perfusion SARS-CoV-2 spike protein (https://protect-au.mimecast.com/s/sm_CROAEEnsv0gy7IS9DcT?domain=nejm.org). The vaccine induced immune responses in all 45 adult participants, with greater antibody produced with increasing doses of inoculant and after a booster. These were detected at one month, and neutralising activity correlated with that in convalescent samples. How long such responses are maintained is a critical issue. Another pre-print, reviewed by Dr Ryan Toh in the Immunology section of the current report (https://protect-au.mimecast.com/s/67eCCVAGLrskPz06UzDH1H?domain=medrxiv.org), suggests that after a peak at about thirty days, neutralising antibody response wanes in the majority. The Covid cup giveth (very little), the Covid cup taketh away (a lot). The phase 3 trial of the vaccine will recruit 30,000 adults and is due to commence by the end of July 2020. There are 23 vaccine trials involving human subjects currently. Fingers crossed that our T-cells come to the party!
One consideration in this regard is how T-cells affect pre-existing immunity to SARS-CoV-2. Existence of pre-existing immunity may have implications for disease severity, herd immunity, antibody-mediated disease enhancement and public health measures. An excellent paper on this is also reviewed in the Immunology section.

In this report are important data in relation to attack rates in children, clinical features of multi-inflammatory syndrome, the use of face masks and a superb section on perinatal health. As we have learnt repeatedly, two weeks is an extraordinarily long time in terms of a COVID-19 pandemic. The evidence curated in the current report is especially impactful and I urge you to have a considered browse.
HIGHLIGHTS

> The incidence of stillbirth has increased in the UK during the pandemic which may be related to indirect effects or possibly direct effects of COVID-19.

> Wearing a mask protects against COVID-19.

> A review suggests that children do not play a major role in transmission as compared to adults, although better epidemiological data from schools during periods of community transmission is needed.

> Adult-child transmission occurred in only 5.2% of households from a study in Singapore with young children < 5 years at lowest risk of infection (1.3%).

> Multicentre retrospective study from the UK suggests PIMS-TM may represent a post COVID-19 immunological disease that is clinically distinct from acute COVID-19 in children, given the high incidence of SARS-CoV-2 IgG antibodies in these patients.

> UK data suggests that viruses causing PIMS-TS in patients are representative of locally circulating SARS-CoV-2.

> A UK study challenges the idea that delayed presentations are a significant factor in paediatrics during the COVID-19 pandemic.

> Pre-existing immunity may have implications on disease severity, herd immunity and public health measures.

> The magnitude of the nAb response is dependent upon disease severity, but this does not affect the kinetics of the nAb response. For many individuals, nAb approach baseline after 50 days post onset of symptoms.

> As education becomes more digitised, the school system must be redesigned to support teachers and youth programmes in the identification and intervention of child abuse and neglect.

> Impact of COVID restrictions on mental health should also look at positive aspects, not just negative.

> Where adequate PPE is available, the risk of transmission of COVID-19 from patients to healthcare workers is low.

> mRNA-1273 vaccine is immunogenic and found no safety concerns in a phase one trial in health adults.
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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 health-care 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.

The Owners of this resource do not wish to use this resource as a means of communication with the general public (i) regarding questions or issues of a medical nature; (ii) to establish physician-patient relationships. Email communications regarding such matters will not be responded to and will be discarded unread.
The Epidemiology of Severe Acute Respiratory Syndrome Coronavirus 2 in a Paediatric Healthcare Network in the United States

Retrospective observational case series describing the prevalence of COVID-19 among tested individuals aged 21 and under, presenting to the CHOP Care Network in Pennsylvania and New Jersey. Indication, demographic features, and clinical characteristics were derived from electronic health record review.

In the 12 weeks from 9th March to 1st June, 7256 unique paediatric patients were tested and 424 (5.8%) tested positive for SARS-CoV-2 on PCR-assay.

The median age of tested children was 5.9 years. The highest test positive rate was in the 18-21 year age-group (11.2%) and the lowest in the 1-5 year age-group (3.9%). The percent of positive tests decreased with age, except in the <12 mth age group, which recorded 5.9% positive tests.

A higher percentage of black children tested positive (10.6%, 226/2132) compared with white children (3.3%, 117/3592).

Overall, only 45.6% of tests had an indication specified. When the indication was for symptoms or exposure to a confirmed case, 21.1% (371/1756) of tests were positive, whereas 3.5% (53/1410) of pre-procedural/preadmission tests were positive.

42.9% (182/424) of positive cases had no known comorbidities. The most common comorbidities were asthma (87, 20.5%) and obesity (55, 13.0%).

Symptomatology of positive cases included cough (221, 52.1%), fever (217, 51.2%) and shortness of breath (62, 14.6%), with 20.5% reporting none of these symptoms, and 12.7% asymptomatic.

A total of 77 (18.2%) SARS-CoV-2 positive patients were hospitalised, two-thirds of which were for symptoms associated with COVID-19. Twelve (15.6%) of the hospitalised patients required mechanical ventilation, and two patients died. One patient with relapsed leukaemia and gram-negative bacteraemia died of sepsis, the role of COVID-19 was unclearly defined in this death. The second deceased patient was an 18-year-old woman with obesity, cardiomyopathy, hypertension and type 2 diabetes mellitus who developed ARDS and myocarditis and died of a malignant arrhythmia.

The study supports the body of evidence suggesting clinical outcomes are less severe in children than adults.
Limitations included:
- Study did not conduct population-based sampling and the cohort was a composite of symptomatic/exposed patients tested from various sites. May not represent childhood infection with SARS-CoV-2 in other regions.
- Ability to characterise specific exposures and testing indications were limited.
- The study design relied on positive PCR-assay, thus was unable to assess associations with multisystem inflammatory syndrome in children (MIS-C).

Reviewed by: Dr Claire von Mollendorf

Jim Owens – 4th Year Medical Student, Department of Paediatrics, The University of Melbourne


> A small number of cases of shock and multisystem inflammation have been reported in children who have tested positive to SARS-CoV-2 or children who have had close epidemiological links to the virus. This illness has been termed paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).

> The exact pathogenesis is unknown, though the literature suggests that a component of the viral spike (S) protein may resemble a superantigen, and may trigger a cytokine storm in adults and the development of PIMS-TS in children.

> The polymorphic residues of the spike glycoprotein which are proposed to enhance binding affinity for the T-cell receptor the spike glycoprotein have been found circulating in Europe and North America and include:
  - A831V.
  - D839Y/N/E2.

> The authors sequenced SARS-CoV-2 from 61 children hospitalised from COVID-19 in London between late-March and mid-May 2020.
  - 36 were diagnosed with PIMS-TS.
  - 11 of these were positive for SARS-CoV-2 viral RNA.

> Full length SARS-CoV-2 genome sequences were obtained from five PIMS-TS children and eight non-PIMS-TS children.

> No single nucleotide polymorphisms (SNP) were unique to PIMS-TS or to other childhood cases, and there was no difference in the distribution of SNPs between PIMS-TS and community cases.

> All childhood cases were D839 and A831.

> The data suggests that viruses causing PIMS-TS in patients are representative of locally circulating SARS-CoV-2 and that no evidence for PIMS-TS to be associated with new or unusual sequence polymorphisms was found.

Reviewed by: Dr Wonie Uahwatanasakul
Natalie Commins - 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

**Incidence of arrhythmias and ECG abnormalities in symptomatic paediatric patients with PCR positive SARS-CoV-2 infection including drug induced changes in the corrected QT interval (QTc) (pre-proof)**

https://www.heartrhythmjournal.com/article/S1547-5271(20)30632-9/pdf

- Retrospective observational study looking at electrophysiologic findings and arrhythmias in paediatric patients being treated for COVID-19.

- Treatments for COVID-19, such as hydroxychloroquine and azithromycin, are known to cause QTc prolongation and can possibly predispose patients to ventricular arrhythmias.

- 36 hospitalised patients (0-21 years) on continuous telemetry were included in the study.

- 44% of patients received treatment with hydroxychloroquine, 25% of patients received hydroxychloroquine and azithromycin, and 31% patients received neither treatment.

- Six patients had significant arrhythmias.
  - Non-sustained ventricular tachycardia (five patients).
  - Sustained atrial tachycardia (one patient).

- Common abnormal ECG findings were (among others).
  - Low voltage QRS complexes (18%).
  - Left ventricular hypertrophy (4%).
  - Significant ST segment changes (4%).

- Elevated troponin levels were found in 28% of patients (8/29 patients).

- Treatment with hydroxychloroquine +/- azithromycin was associated with QTc prolongation but was not associated with a higher incidence of arrhythmia when compared to other COVID-19 patients.

- Arrhythmias are uncommon in paediatric patients with COVID-19 but occur at a higher rate when compared to the general population.

- The study has several limitations - sample size is small and only includes patients from one hospital (New York).

Reviewed by: Dr Wonie Uahwatanasakul
CO-INFECTION

Dr Lien Anh Ha Do - Virologist, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne

Community Acquired Co-infection in COVID-19: A Retrospective Observational Experience

This study reported the rates of community acquired coinfection among 321 hospitalised COVID-19 patients between 1st March 2020 and 11th April 2020 at University of Chicago Medical Center. The authors performed a retrospective observational analysis using patients’ medical records and five days’ time as a cut-off for the community acquired co-infection. Co-infection was defined by clinical signs and/or symptoms of infection and detection of a pathogen by diagnostic test.

> Main results:

- The mean age was 60 years (standard deviation 17 years), 155/321 (48%) were male.
- 17/321 (5%) were admitted to the ICU, and 22/321 (7%) died.
- 315/321 (98%) patients had at least one diagnostic test for co-infection.
- 12/321 (3.7%) patients had co-infection, seven (2.1%) were bacterial infection determined by PCR or bacterial cultures and four cases had S.pneumoniae urine positive.
- Significant high rate of co-infection found in ICU patients 7/17 (41%, p<0.005).
- 222/321 (69%) were given antibiotics.

> Significance: Highlighted low co-infection in SARS-CoV-2 infection.

> Limitations: This is a retrospective study with several limitations in:

- Determining co-infection pathogens due to empirical use of antibiotics in 69% patients.
- Having a small sample size and limited age groups.
- Having a short study period that did not cover the high season of viral infections.
CRITICAL CARE

Samar Hikmat and Daniel Lamanna – 3rd Year Medical Students, Department of Paediatrics, The University of Melbourne

Intensive care admissions of children with Paediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 (PIMS-TS) in the UK

Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) was defined by the Royal College of Paediatrics and Child Health (RCPCH) as persistent fever, inflammation, and evidence of single or multi-organ dysfunction in a child, with exclusion of any other microbial cause, with or without PCR evidence of SARS-CoV-2. The definition came after a cluster of children presented to PICUs in the UK during the COVID-19 pandemic with unexplained multisystem inflammatory syndrome that had overlapping features with Kawasaki disease, toxic shock syndrome, haemophagocytic lymphohistiocytosis, and macrophage activation syndrome.

A multicentre observational study involving children (aged < 18 years), admitted to PICUs due to PIMS-TS in the UK was carried between 1st April and 10th May 2020 and found that:

- The rate of PICU admissions for PIMS-TS was at least 11-fold higher than that for similar inflammatory conditions in the past.
- Of the 78 cases of PIMS-TS that were reported:
  - Male patients (67%) and those from ethnic minority backgrounds (78%); including Afro-Caribbean and Asian were over-represented.
  - Common presenting features included: fever (100%), shock (87%), abdominal pain (62%), vomiting (63%), and diarrhoea (64%). Other features were rash (45%) and conjunctivitis (29%).
  - Laboratory markers (of only 36 patients who were still in ICU): over the first four days of admission, there was a reduction in C-reactive protein, D-dimer and ferritin towards normal levels and an abnormal increase in troponin. Children initially were lymphopenic but had increased lymphocyte count approaching normal levels.
  - A third of patients had coronary artery abnormalities (aneurysms or unusual echogenicity) on echocardiography.
  - Interventions/treatments: invasive ventilation (46%), extracorporeal membrane oxygenation (4%), vasoactive infusions (83%), steroids (73%), intravenous immunoglobulin (76%), biologic therapies (22%).
  - Two children died.
• There was a low incidence (22%) of positive SARS-CoV-2 PCR tests and high incidence (96%) of SARS-CoV-2 IgG antibodies in patients who were tested following a negative SARS-CoV-2 PCR. This along with the absence of significant respiratory involvement indicates that PIMS-TS might represent a post-COVID-19 immunological disease that is clinically distinct from acute COVID-19 in children.

> Further studies are needed to understand the long-term outcomes and treatments of PIMS-TS.

Reviewed by: Dr Wonie Uahwatanasakul
Children’s emergency presentations during the COVID-19 pandemic
[https://www.thelancet.com/pdfs/journals/lanchi/PIIS2352-4642(20)30206-6.pdf](https://www.thelancet.com/pdfs/journals/lanchi/PIIS2352-4642(20)30206-6.pdf)

> Changes were made to the NHS 111 (non-emergency) algorithms along with campaigns to highlight red- and amber-flag symptoms in children following early international reports of delayed paediatric emergency department presentations.

> A rapid, multicentre surveillance project in seven UK and Irish paediatric emergency departments over a two-week period within the overall period (27th April – 15th May 2020).

> 1349 usable entries from 1460 total entries.

- 93.5% patients felt there was not a delay in presentation.
- Uncertainty about potential delay in 2.7% of presentations.
- 11.8% of patients concerned about delayed presentation were admitted.
- Parental delay thought to be relevant in 3% of presentations.
- NHS or health-care professional advice possibly resulted in delayed presentation in 0.8% of presentations.
- Red-flag symptoms in 6% of patients with very few parents dismissing these, of which 2.5% had delayed presentation.

> There were low rates of delayed presentation and low rates of hospital admission in the delayed presentation group.

> Limitations:

- Unable to determine changes to delayed presentation due to no previous pre-pandemic studies.
- Unknown generalisability of data.
- Multifactorial nature of deterioration and disease outcome in paediatrics makes interpretation difficult.

> Despite its limitations, this article offers a rebuttal against the arguments that delayed presentations are a significant factor in paediatrics during the COVID-19 pandemic. This is important, as to date case reports about delayed paediatric ED presentations have dominated the discussion.

Reviewed by: Dr John Cheek
Epidemiology & Public Health

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

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31142-9/fulltext

> Until a vaccine or effective treatment is available, non-pharmacological public health interventions are crucial to controlling the spread of SARS-CoV-2.

> This systematic review and meta-analysis funded by WHO evaluated the effects of physical distancing, face masks and eye protection on the transmission of COVID-19 and other related viral diseases (SARS and MERS).

> Findings:

- Viral infection was lower with physical distancing of 1m or more, compared with less than 1m - Moderate certainty using the GRADE category of evidence; nine adjusted studies (n=7782) and 29 unadjusted studies (n=10736). The absolute risk of infection was 12.8% with short distance vs 2.6% with further distance. Meta-regression showed the risk of infection was lower with increasing distance (1m vs 2m) - for every 1m further away in distancing, the relative effect might increase 2.02 times.

- Face mask use was associated with a large reduction in risk of infection, compared with no use - low certainty using the GRADE category of evidence; ten adjusted studies (n=2647) and 29 unadjusted studies (n=10170). The absolute risk of viral infection was 17.4% with no face mask vs 3.1% with a face mask, with stronger association with protection shown with N95 or similar respirators (adjusted OR 0.04) compared with disposable surgical masks, 12-16 layer cotton masks or similar (adjusted OR 0.33). There were also stronger associations with reduction in risk in health care settings compared with non-health care settings (RR 0.30 in health care vs RR 0.56).

- Eye protection (goggles or face shields) was associated with lower risk of infection, compared with no use - Low certainty using the GRADE category of evidence; 13 unadjusted studies (n=3713). The absolute risk of infection was 16.0% without eye protection vs 5.5% with eye protection.

- There was no one intervention that provided complete protection.
Conclusions:
- This systematic review and meta-analysis supports physical distancing of 1m or more.
- Optimum use of face masks, respirators and eye protection in public and health care settings should be informed by these findings and contextual factors.
- Robust RCTs are needed to better inform the evidence of these interventions.

Limitations:
- Studies included were non-randomised, not fully adjusted and potentially prone to recall and measurement bias.
- Many studies did not provide information on precise distances.
- Few studies assessed interventions in non-healthcare settings.
- Most evidence was reported on SARS or MERS, rather than COVID-19, however this data is better than comparing COVID-19 to influenza virus protection.

Reviewed by: Dr Claire von Mollendorf

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

Spotlight on child abuse and neglect response in the time of COVID-19
https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(20)30143-2.pdf

> 20% of child abuse and neglect reports in the USA are made by educational personnel.

> As the incidence of child abuse and neglect increased during the COVID-19 pandemic, the number of reported child maltreatment decreased by double digits.

> The long-term effects of child abuse and neglect, however short lived, include mental health disorders, sexually transmitted infections, unwanted pregnancies, and substance abuse.

> With increases in the distance learning model, teachers should be retrained to (i) identify at-risk individuals, (ii) use specific language and protocols to safely ask questions about home experience and (iii) report suspected abuse and neglect to appropriate personnel so as to direct specific resources to abused and neglected children.

> As education becomes more digitised, the school system must be redesigned to support teachers and youth programmes in the identification and intervention of child abuse and neglect.

Reviewed by: Professor Fiona Russell
GLOBAL HEALTH

Updates on Global COVID-19

IMAGING

Natalie Commins - 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

Brain MRI findings in severe COVID-19: A retrospective observational study
https://pubs.rsna.org/doi/10.1148/radiol.2020202222

- Retrospective study (16 French hospitals, over one month) evaluating MRI brain changes in patients with severe COVID-19 and neurological manifestations.

- 190 patients with neurological findings underwent a brain MRI, with positive findings in 30 men and 7 women (mean age 61 years) included in the study.

- Patients with MRI brain findings consistent with ischaemic stroke, cerebral venous thrombosis or chronic lesions were excluded.

- The mean duration of the time from onset of symptoms to MRI brain findings was 19 days (33 days for patients with haemorrhagic lesions).

- Altered consciousness was the most common neurological finding (73%), followed by pathological wakefulness when sedation was ceased (41%), confusion (32%) and agitation (19%).

- Markedly heterogeneous MRI findings with eight different neurological patterns found.

- 76% of patients’ scans were associated with one neuroimaging pattern, 19% with two patterns and 5% with three patterns.

- The most common patterns on MRI were:
  - Unilateral FLAIR and/or DWI hyperintensities in the mesial temporal lobes (43%) - similar to appearance of infectious or autoimmune limbic encephalitis.
  - Non-confluent multifocal white matter hyperintense lesions on FLAIR and DWI sequences, with variable enhancement and associated haemorrhagic lesions (30%) - ADEM-like - assumed immunologic parainfectious process/metabolic or toxic leukoencephalopathy or PRES.
  - Extensive, isolated white matter microhaemorrhages (24%) - uncertain pathophysiology, may reflect hypoxia or small vessel vasculitis.

- 54% of the patients had intracerebral haemorrhages which conferred a worse prognosis (high ICU admission rate, all developed ARDS).

- Most patients had lumbar puncture findings demonstrating markers of inflammation (21/31 patients) but only one patient had SARS-CoV-2 detected in their CSF (1/28 patients).

Reviewed by: Associate Professor Simone Mandelstam
IMMUNOLOGY

Dr Ryan Toh – Post doctoral researcher, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne

Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection (pre-print)

> The duration of antibody responses generated following SARS-CoV-2 infection remains unknown. This observational study in adults describes the longitudinal antibody responses (neutralising antibody, IgG, IgM and IgA) from 65 SARS-CoV-2 RT-qPCR confirmed individuals and 31 healthcare workers for duration of up to 94 days post onset of symptoms (POS).

> IgG and IgM responses against S, RBD and N proteins were observed in approximately 90-95% of the participants; IgA response to RBD and N was lower, with only 72.3% and 84.6% seropositive, respectively.

> Antibody response peaked at 20-30 days POS, followed by a decline in antibody concentration and neutralising activity for many individuals.
  - IgM and IgA declined to about baseline in several participants at >60 days POS.
  - IgG responses and neutralising antibodies remained detectable in most individuals, even up to 94 days.

> Disease severity impacted antibody response: significantly higher peak neutralising antibody responses were observed in participants with more severe disease, but the times taken to generate neutralising antibodies were similar regardless of disease severity.

> Several participants who were asymptomatic had low neutralising antibody response, and this response was no longer detectable after 50 days.

> Significance: Important implications when considering protection against reinfection with SARS-CoV-2. This transient nAb response is a feature shared by both a SARS-CoV-2 infection that causes low disease severity and the circulating seasonal coronaviruses that are associated with common colds.

> Limitations: Some important data were unavailable; limited sample size, particularly at the later time points.
Pre-existing immunity to SARS-CoV-2: the knowns and unknowns
https://www.nature.com/articles/s41577-020-0389-z

- A comment published in Nature discussing T cell reactivity to SARS-CoV-2 in unexposed individuals and the possible implications.
- Five studies have detected CD4+ T cell responses (and to a lesser degree CD8+ T cells) to both the spike protein of SARS-CoV-2 and non-spike proteins in blood samples of unexposed individuals.
- It is speculated this is due to circulating memory T cells present from exposure to ‘common cold’ coronaviruses.
- Precise specificites of these T cells are unknown.
- Speculations of the significance include:
  - Potential for reduced disease severity of COVID-19 in individuals with these T cells.
  - The differences in distribution of common cold coronavirus might correlate with the burden of disease of COVID-19 across the world.
  - Pre-existing immunity could influence vaccine outcomes, potentially providing a faster and better immune response. Or it may influence clinical trials of vaccines as presence of these T cells adds a confounding factor.
  - Pre-existing immunity might be detrimental due to ‘original antigenic sin’, where a potentially inferior immune response is elicited due to pre-existing immune memory to a similar pathogen or may contribute to antibody-mediated disease enhancement (ADE).
- Conclusion: the existence of pre-existing immunity may have implications on disease severity, herd immunity and public health measures, however actual data is needed to address this.

Reviewed by: Associate Professor Paul Licciardi
INFECTION CONTROL

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

Complete protection from COVID-19 is possible for health workers
https://www.bmj.com/content/370/bmj.m2641

- Liu and colleagues found that none of 420 doctors and nurses reallocated to frontline work at Wuhan hospitals from 24th January to 7th April 2020 contracted COVID-19.

- The staff received training in proper use of PPE before their assignment and were provided with appropriate PPE: protective suits, isolation gowns, gloves, face shields or goggles, hair covers, boots, and shoe covers as well as N95 respirators or surgical masks (both being used at the same time during aerosol generating procedures).

- Hefei and Wuhan that also reported that none of 420 frontline healthcare workers provided with appropriate access to PPE contracted COVID-19.

- In accordance with WHO guidelines, there is reasonable evidence suggesting droplet and contact precautions provided by a surgical face mask, eye protection, a gown, and gloves offer adequate protection in most circumstances when caring for patients with COVID-19.

- Apart from providing training in proper use of, and robust access to appropriate PPE, implementing control measures to prevent spread of infection between healthcare workers may increase safety even further.

Reviewed by: Dr Wonie Uahwatanasakul

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

Pandemic peak SARS-CoV-2 infection and seroconversion rates in London frontline health-care workers
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31484-7/fulltext


- Recruited 200 patient-facing health care workers (HCWs) between 26th March and 8th April and followed for three months.

- Self-collected nose/throat swabs tested for SARS-CoV-2 by RT-PCR twice per week; symptom diary completed twice a week; monthly blood samples for serology (ELISA and flow cytometry for IgG, IgA, IgM).
Main results:

- 87 of 200 (44%) HCWs had evidence of SARS-CoV-2 infection at any time point during the study, either by RT-PCR or serology.
- 46 of 181 (25%) HCWs were already seropositive at study entry and a further 13% showed evidence of infection during the study.
- Of the 42 HCWs that ever tested positive for SARS-CoV-2 by RT-PCR, 20 (48%) had symptoms consistent with COVID-19 and 16 (38%) did not report any symptoms.
- Trend towards higher infection rate in HCWs <30 years old (55%) compared to >50 years old (33%).

These high rates of HCW infection in London frontline health care workers (higher than the general population) highlight the need for a strong focus on PPE policies and adequate supply of PPE to ensure HCW safety.

Reviewed by: Dr Vanessa Clifford
MENTAL HEALTH

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

Is isolation beneficial for the mental wellbeing of some children and adolescents? (Letter)  

> Most research has focused on the negative impact of the pandemic on the mental health of children and adolescents.

> Clinical reports have suggested that some children and adolescents may be benefiting from a reduction in the sensory and social pressure of modern life while living in lockdown.

> Potential positive effects include, reduction in stress, improved sleep and relaxation, loss of social pressure, more time to think and improved affect.

> Research agendas could also include understanding the perspective of children and families who are benefiting from the societal change.

> The pandemic provides an opportunity for child and adolescent psychiatrists to understand how our social and economic environment interacts with mental health and mental wellbeing.

> Reviewers note: It will be important to properly study the positive as well as negative impacts of isolation. The same individual may, for example, experience both at the same time.

Reviewed by: Professor David Coghill

Paediatric mental and behavioural health in the age of quarantine and social distancing (pre-print)  
https://preprints.jmir.org/preprint/19867/accepted

> Social distancing existing over a long period as a consequence of the pandemic has become a new reality.

> Children and adolescents are at risk of negative psychological and behavioural changes from prolonged stress.

> A warm family unit is at the centre of the mental well-being of children and adolescents. Schools and community groups also play a role in facilitating online learning and interaction.

> From a clinical perspective, digital technologies such as telehealth services have been an essential adaptation to continue to provide necessary care.
The author proposes a call to use innovative digital technologies to engage young people. Research may be directed towards developing cutting edge technologies to provide children and young people with accessible interactive health services.

Suggestions include using mobile technology to monitor mental and behavioural health and using augmented and virtual reality platforms as part of psychological support services.

Reviewers note: Although much of what is said has a good face validity there is very little research evidence to determine the efficacy of the proposed approaches and as pointed out by the author much further research is required.

Reviewed by: Professor David Coghill

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

**Mental health status of pregnant and breastfeeding women during the COVID-19 pandemic: A call for action**


- Conducted an online survey in Belgium, using the Edinburgh Depression Scale and Generalised Anxiety Disorder 7-item Scale.
- Of 5866 women (2421 pregnant and 3445 breastfeeding), 25.3% self-reported major depressive symptoms in pregnancy and 23.6% postpartum, which is higher than seen prior to the pandemic.
- 40% of women scored ≥5 on the EDS scale of anxiety and 14% scored ≥10 on the GAD-7, indicating high anxiety.
- Routine mental health screening should be conducted to ensure optimal mental health of mothers and infants.

Reviewed by: Professor David Coghill
PERINATAL HEALTH

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

Change in the Incidence of Stillbirth and Preterm Delivery During the COVID-19 Pandemic
https://jamanetwork.com/journals/jama/fullarticle/2768389

> So far, studies have had inadequate power to assess uncommon outcomes like stillbirth (foetal death ≥24 weeks’ gestation).

> This study assessed the change in stillbirth and preterm delivery rates during the pandemic.

> Pregnancy outcomes were compared at St George’s University Hospital, London in two epochs: from October 1st, 2019 to 31st January 2020 (preceding the first reported UK cases of COVID-19), and from 1st February, 2020, to 14th June 2020.

> The incidence of stillbirth was higher during the pandemic period (n = 16 [9.31 per 1000 births]; none associated with COVID-19) than during the prepandemic period (n = 4 [2.38 per 1000 births]).

> The incidence of stillbirth was higher when late terminations for foetal abnormality were excluded during the pandemic period (6.98 per 1000 births vs 1.19 in the prepandemic period).

> There were no differences over time in births before 37 weeks’ gestation, births after 34 weeks’ gestation, neonatal unit admission, or caesarean delivery.

> During the pandemic period, 19 patients with COVID-19 were hospitalised in the study site maternity department.

> None of the pregnant women who experienced stillbirth had symptoms suggestive of COVID-19, nor did the post-mortem or placental examinations suggest SARS-CoV-2 infection. Universal testing for SARS-CoV-2 started on 28th May 2020, and only one pregnant woman, who had a live birth, tested positive.

> This increase may be the direct consequence of SARS-CoV-2 although none of the stillbirths in the pandemic period were among women with COVID-19. Surveillance studies in pregnant women reported that as much as 90% of SARS-CoV-2–positive cases are asymptomatic. Alternatively, the results may be from indirect effects such as reluctance to attend hospital when needed (e.g., with reduced foetal movements), fear of contracting infection, or not wanting to add to the health system burden.
Grace Newman – 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

The clinical course of SARS-CoV-2 positive neonates
https://www.nature.com/articles/s41372-020-0715-0

> This is a literature review evaluating the clinical course, prognosis, and transmission routes of SARS-CoV-2 positive newborns.

> 25 reported neonates affected by SARS-CoV-2.

- Gestational age 37.4 +/- 4 weeks (range 26.57 – 41.28) and birth weight 3041.6 +/- 866 g (range 960-4440 g).
- Male to female ratio hospitalised was 2.8, suggesting males were more susceptible to SARS-CoV-2.
- Clinical signs in the neonates at onset included fever (28%), vomiting (16%), cough or shortness of breath (12%), diarrhoea, lethargy or respiratory difficulty (8%) or cyanosis, feeding intolerance, hyperpnoea, mild intercostal retractions, mottling, sneezing, nasal stuffiness, paroxysmal episodes (4%).
- Only 4/25 newborns had no clinical signs.
- The age at disease onset was 8.2 ± 8.5 days of life (range: 1–25 days).
- 76% did not show other signs during clinical course.
- Intensive care required for 32%; 20% required mechanical ventilation.
- Major complications included pneumonia (12%), respiratory distress (8%) and sepsis or pneumothorax (4%).
- No deaths.
- The swabs became negative within 10.3 ± 4.5 days (range: 6–17 days). Serology was patchy.
- Radiological findings included thickening of lung structure (32%), opacity of the ground lobe glass (8%), and mild lung infection, bilinear opacities or bilateral nonspecific striated lung infiltrates (4%), no lung lesions in 48% of symptomatic cases.
- 68% of cases the mothers were affected by SARS-CoV-2; 20% both mothers and fathers, other cases grandparents were infected.

> Conclusions:

- SARS-CoV-2 positive newborns show good prognosis, with low rate of severe complications and without deaths, with symptomatic or supportive treatment.
- Vertical transmission remains unproven with horizontal transmission the most likely source of infection in newborns.
- High quality studies needed to better understand clinical manifestations, clinical course, and prognosis of SARS-CoV-2 positive newborns.

Reviewed by: Professor Suzanne Garland
Disappearance of SARS-CoV-2 Antibodies in Infants Born to Women with COVID-19, Wuhan, China

https://wwwnc.cdc.gov/eid/article/26/10/20-2328_article

> Positive IgM in early infants could be potential evidence of intrauterine vertical transmission as maternal IgM does not cross placental barrier intact. IgG is transferred passively from mother to foetus via the placenta, however the duration of passive immunity is still unclear.

> Study population: 64 infants admitted to neonatal unit Tongji Hospital Wuhan.

- 24 born to women with PCR confirmed COVID-19 – gestational age range 31 weeks to 41+2.

> Method: assay for SARS-CoV-2 specific antibodies, and SARS-CoV-2 nucleic acid test (RT-PCR) from throat and anal swabs.

- Timing of antibody testing in infants inconsistent due to introduction of antibody testing in March (ranged day 0 to day 75 of life, some tested at various time points).

> Of 24 born to COVID-19 PCR positive women.

- 15 had detectable IgG (62%), 6 had detectable IgM (25%), nucleic acid test negative in all.

- 11 had antibody titres detected at birth, IgG detectable in all and IgM detectable in five (using a Chemiluminescence Immunoassay).

- No infants had complications related to pneumonia.

- IgG levels declined more slowly in infants with positive IgM compared to those without.

> Findings not sufficient to confirm SARS-CoV-2 vertical transmission, as no infants had positive nucleic acid testing. However, some had positive IgM titres at birth.

- Infants showed rapid rate of decline in antibody titres, indicating a lack of protective passive immunity in infants and decline of likely passively acquired maternal antibodies.

- It is unknown what level of antibody titre is considered protective against infection.

- More work is needed to understand immunity to SARS-CoV-2 in infants and may be important in informing vaccination efforts.

> Limitation: Study limited by small sample size.

Reviewed by: Professor Suzanne Garland
Rose Noble Kizhakekara – 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

Clinical Implications of SARS-CoV-2 Infection in the Viable Preterm Period

> Objectives: To determine the rate of preterm birth (PTB) during hospitalisation among women diagnosed with SARS-CoV-2 infection between 23 and 37 weeks of gestation, and whether this rate differed by gestational age at diagnosis.

> Method: retrospective, cross-sectional multicentre study in New York over a six-week period.

- 65 total patients included: 36 (53.7%) diagnosed in the early preterm period (230/7 to 336/7 weeks) and 29 (46.3%) diagnosed in the late preterm period (34 to 366/7 weeks). Baseline demographics were similar between the two groups.

- Preterm delivery is less likely among women diagnosed in the early preterm compared with late preterm (7/36 [19.4%] vs. 18/29 [62%], p-value = 0.001).

- Most women infected in the early preterm period recovered and were discharged home undelivered.

- The majority of PTB were indicated and not due to spontaneous preterm labour (64%, 16/25).

- There were no deliveries prior to 33 weeks of gestation for worsening COVID-19. Furthermore, severity of disease did not alter the likelihood of delivery during hospitalisation with SARS-CoV-2 infection.

> Limitations: There is a higher likelihood of preterm delivery with increasing gestational age. However, there is no control group in this study, making it unclear whether SARS-CoV-2 infection further increases this risk. The actual PTB rate is unknown (only the PTB rate during hospitalisation). At the end of the study, several of the pregnancies were ongoing. It is not clear whether the obstetric indications for preterm delivery, such as preeclampsia and PPROM, may have been related to the SARS-CoV-2 infection or an independent complication.

Reviewed by: Professor Fiona Russell

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

Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study

> As COVID-19 cases rose, obstetrics units in New York City implemented universal testing for all pregnant women admitted to Labour and Delivery wards.

> This is a prospective cohort study of 675 pregnant women beyond 20 weeks gestation across three New York City hospitals investigating the prevalence and outcomes of maternal COVID-19, obstetrics & neonatal complications, and placental pathology.
> 70 (10.4%) pregnant women were SARS-CoV-2 PCR positive on admission; 55 of the 70 (78.6%) were asymptomatic.

> Significant differences in sociodemographics and comorbidities were observed between women with symptomatic vs. asymptomatic vs. no COVID-19.

> Clinical presentation: Cough (46.7%) and fever (33.3%) were the most common symptoms reported on admission.
  - New symptomatology or clinical worsening was observed in 13% of SARS-CoV-2 positive women within the first 7 days postpartum.
  - Three cases of maternal hypoxia were reported during admission, none requiring mechanical ventilation.

> Obstetric complications:
  - Median gestation of delivery was 39 weeks with 100% (n=15) live births amongst women with symptomatic COVID-19, 98.2% (n=54) in asymptomatic women and 99.0% (n=599) in women without COVID-19.
  - Six stillbirths between 20-25 weeks’ gestation occurred in women without COVID-19 and preterm birth rates were similar across the three groups (symptomatic, asymptomatic, and negative).
  - Caesarean delivery rates were 7 (46.7%), 25 (45%) and 187 (30.9%) with symptomatic, asymptomatic COVID-19 positive and no COVID-19, respectively (p=0.044).
  - Postpartum fever was 33% in symptomatic women with COVID-19, 5.5% of asymptomatic women with COVID-19, and 17 (2.8%) of women without COVID-19.
  - No maternal deaths were recorded.

> Neonatal outcomes: n=71 (100%) infants of SARS-CoV-2 positive mothers were SARS-CoV-2 negative within 24 hours of birth, with no differences in birth weight, Apgar score or location of neonatal readmissions.

> Placental pathology: Foetal vascular malperfusion and higher rates of meconium staining were noted in placentas of women with COVID-19 versus without (p<0.001) and (p=0.004). No differences in histologic chorioamnionitis or chronic villitis by group were noted.

> Limitations: miscategorisations of self-reported symptoms, limited laboratory findings to distinguish symptomatic and asymptomatic pregnant women, misclassification of patients.

Reviewed by: Professor Suzanne Garland
TRANSMISSION

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

Role of children in the transmission of the COVID-19 pandemic
https://bmjpaedsopen.bmj.com/content/bmjpo/4/1/e000722.full.pdf

- A rapid scoping review was undertaken.
- 14/1099 identified articles were included.
- Studies included cases from China (n=9 to 2143), China and Taiwan (n=536), Korea (n=1), Vietnam (n=1), Australia (n=9), Geneva (n=40), the Netherlands (n=116), Ireland (n=3) and Spain (population-based study of IgG, n=8243).
- Although no complete data were available, between 15% and 55%-60% were asymptomatic, and 75%-100% of cases were from family transmission.
- Studies analysing school transmission showed children as not a driver of transmission.
- Prevalence of COVID-19 IgG antibody in children <15 years was lower than the general population in the Spanish study.
- Results suggest that children are as likely to be asymptomatic as frequently as adults, and that a high percentage of reported cases in children came from family transmission. Although there are still many uncertainties, it does not appear that children are transmitters to a greater extent than adults.
- Limitations: there needs to be better epidemiological data from schools during periods of community transmission to solve current uncertainties.

SARS-CoV-2 antibody prevalence in blood in a large school community subject to a COVID-19 outbreak: a cross-sectional study

- A SARS-CoV-2 outbreak affecting 52 people from a large school community in Santiago, Chile was identified (12th March), nine days after the first country case.
- The school was closed on 13th March, and the entire community was placed under quarantine.
- A classroom stratified random sample of students and all staff was included from 14th - 19th May.
- The study aimed to determine the overall seroprevalence rates (self-administered finger-prick chromatographic-based IgM/IgG antibodies test) by age group, reported symptoms, contact exposure and to explore dynamics of transmission.
Antibody positivity rates were 9.9% for 1,009 students and 16.6% for 235 staff.

Among students, positivity was associated with younger age, lower grade level, prior RT-PCR positivity, and history of contact with a confirmed case.

Among staff, positivity was higher in teachers and in those previously RT-PCR positive.

Excluding RT-PCR positive individuals, antibody positivity was associated with fever in adults and children, abdominal pain in children, and chest pain in adults.

Within antibody positive individuals, 40% of students and 18% of staff reported no symptoms.

Teachers were more affected during the outbreak and younger children were at higher infection risk, likely because index case(s) were teachers and/or parents from preschool.

Self-administered antibody testing, supervised remotely, could be a suitable and rapid tool.

Limitations: rapid test not confirmed by ELISA.

Chan Ying Zhen Charissa – 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study
https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30471-0.pdf

Retrospective cohort study.

Traced 195 unrelated close contacts who travelled to or resided in Wuhan or nearby cities (215 primary, 134 secondary or tertiary cases, 1964 uninfected close contacts.

Mean incubation period five days: maximum infectious period of 13 days.

Estimated secondary attack rate among household contacts was 12.4% (95% CI 9.8–15.4) when household contacts were defined on the basis of close relatives and 17.1% (13.3–21.8) when household contacts were defined on the basis of residential address.

Compared with the oldest age group (>60 years), the risk of household infection was lower in the youngest age group (<20 years; odds ratio [OR] 0.23 [95% CI 0.11–0.46]) and among adults aged 20–59 years (OR 0.64 [95% CI 0.43–0.97]).

Suggests greater infectivity during the incubation period than during the symptomatic period, although CI crossed the null value (OR 0.61 [95% CI 0.27–1.38]).

Estimated local reproductive number (R) based on observed contact frequencies of primary cases was 0.5 (95% CI 0.41–0.62).

Conclusion: SARS-CoV-2 more transmissible in households than SARS-CoV or MERS. Older individuals are most susceptible.

Recommendation: timely tracing and quarantine of close contacts should be implemented to prevent onward transmission during viral incubation period.

Reviewed by: Professor Fiona Russell
Household Transmission of SARS-CoV-2 from Adults to Children (Singapore)

https://www.jpeds.com/article/S0022-3476(20)30852-0/pdf

> Attack rate among 213 children in 137 households to be 6.1% in households with a confirmed adult COVID-19 case.

> Transmission from an adult to a child occurred in only 5.2% of households.

> Young children < 5 years were at lowest risk of infection (1.3%).

> Children were most likely infected if index case was mother.

> Limitations: limited generalisability to other settings or with another strain of SARS-CoV-2.

Reviewed by: Dr Wonie Uahwatanasakul
VACCINES

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

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

> A phase 1, dose-escalation, open-label trial was undertaken in 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25μg, 100μg, or 250μg. There were 15 participants in each dose group.

> The mRNA-1273 vaccine induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified.

> These findings support further development of this vaccine.

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

Ensuring Uptake of Vaccines against SARS-CoV-2

This multidisciplinary Stanford group suggest six criteria that must be met to justify a mandatory vaccination program for COVID-19.

> These include:

- The COVID-19 must not be adequately controlled in the state.

- The ACIP must have identified and recommended vaccination for groups being considered for mandatory vaccination.

- There must be adequate supply of a well-evidenced vaccine for the population groups being considered.

- Available evidence about the safety and efficacy of the vaccines has been transparently communicated.

- The state must ensure access to vaccination without financial or logistic barriers, compensation to workers who have adverse effects from the vaccine and real-time surveillance of vaccine side effects.

- Voluntary uptake of the vaccine amongst high-priority groups has fallen short to prevent epidemic spread.
What a mandatory vaccination program might look like is discussed, emphasising the importance of public trust in such a program.

The authors suggest that careful deliberation about the state vaccination policy needs to start now, whilst we have time on our side.

Reviewed by: Associate Professor Margie Danchin
Primary exposure to SARS-CoV-2 protects against reinfection in rhesus macaques

https://science.sciencemag.org/content/early/2020/07/01/science.abc5343/ta b-pdf

This study reported a primary exposure to SARS-CoV-2 can protect against early reinfection in rhesus macaques’ model. Seven adult Chinese-origin rhesus macaques (M0 to M6, 3–5 kg, 3–5 years of age) were modelled for challenge and rechallenge observations. M1-M6 were initially intratracheally challenged with SARS-CoV-2 at 1 × 106 50% tissue-culture infectious doses (TCID50).

Four macaques (M3 to M6) were rechallenged intratracheally with the same dose of the SARS-CoV-2 strain at 28 days post-initial challenge (dpi). M1 and M2 macaques were the negative control of the rechallenge group. M0 was healthy control for initial challenge group and was “infectious control” for the rechallenge group as M0 was also exposed to SARS-CoV-2 at the second challenge. Body weight, rectal temperature, viral detections in nasal/throat/anal swabs, haematological measurement, chest X-ray, and the analysis of immune cells, as well as binding and neutralizing antibodies were analysed during the post-challenge and post-rechallenge periods. Necropsy was performed for M0 at 5 dpi and M1 at 7 dpi) and M3 and M5 (at five days post rechallenge, or 33 dpi).

In the initial challenge group, all monkeys were successfully infected with SARS-CoV-2 and that the pathogenicity in monkeys is similar to that reported in recent studies. Those monkeys required about two weeks to transition into the recovery stage.

In the re-challenged group, the rechallenged monkeys exhibited a transient increase in temperature, which was not observed during the primary infection; but did not have indications (viral detection, abnormal X-ray, histological modifications) that suggest a re-infection status of SARS-CoV-2.

Comparison of viral and immunological traits between the primary-challenge stage and the rechallenge stage in four monkeys (M3-M6) suggested potential factors that could influence the host response in re-challenged monkeys:

- activated CD8+ T cells in peripheral blood.
- increased percentage of central memory CD4+ T cells.
- high titre of specific antibody levels against the SARS-CoV-2 spike.

Limitations: Short-term infection rechallenge model would not reflect the reality of SARS-CoV-2 infection; lack of immunological explorations on detailed phenotypes of immune cells.
OTHER RESOURCES

Burnet Institute research findings, policy and technical reports
https://www.burnet.edu.au/covid-19//36_know_c19_hub

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

Lancet COVID-19 papers

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects

All COVID-19 literature

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/1FAlpQL5OxCoAuLV0aJdf_z2uWV7r3FaPzAOIr86q9ZXBcT21QcCE_Nw/formResponse

Victorian Department of Health and Human Services

Australian Government

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

University of Birmingham COVID-19 Research Briefing

Australian Government Department of Health Webinars on the COVID-19 response for primary care practitioners

Global summary, identifying changes in the reproduction number, rate of spread, and doubling time during 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

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)
https://www.covid19-hpc-consortium.org/

Introduction to Coronavirus: free, online course aimed at teenagers and young adults: scientists and experts from the London School of Hygiene & Tropical Medicine explain research to understand the virus and guide the global response to coronavirus
https://www.open.edu/openlearncreate/course/view.php?id=5319
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