



International EPI Cell Daily Evidence Digest – 10/06/2020

This Daily Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Serology and immunology
- Diagnostics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Miscellaneous
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	SARS-CoV-2 Infections and Serologic Responses from a Sample of U.S. Navy Service Members — USS Theodore Roosevelt, April 2020	Morbidity and Mortality Weekly Report / Article	<ul style="list-style-type: none">• Among a convenience sample of 382 young adult U.S. service members aboard an aircraft carrier experiencing a COVID-19 outbreak, 60% had reactive antibodies, and 59% of those also had neutralizing antibodies at the time of specimen collection.• One fifth of infected participants reported no symptoms.• Preventive measures, such as using face coverings and observing social distancing, reduced risk for infection.

			<ul style="list-style-type: none"> • Young, healthy adults with COVID-19 might have mild or no symptoms; therefore, symptom-based surveillance might not detect all infections.
08.06.2020	Seroprevalence of IgG antibodies against SARS coronavirus 2 in Belgium: a prospective cross-sectional study of residual samples	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A prospective serial cross-sectional seroprevalence study, stratified by age, sex and region, started with two collections in April 2020. • First collection: IgG antibodies detected in 100 out of 3910 samples. Second collection: 193 out of 3391 samples were IgG positive. Weighted overall seroprevalence increased from 2.9% (95% CI 2.3 to 3.6) to 6.0% (95% CI 5.1 to 7.1), reflected in a seroincidence estimate of 3.1% (95% CI 1.9 to 4.3). • Age-specific seroprevalence significantly increased in the age categories 20-30, 80-90 and ≥90. No significant sex effect was observed.
08.06.2020	A single-cell atlas of the peripheral immune response in patients with severe COVID-19	Nat Med / Article	<ul style="list-style-type: none"> • This paper was previously included in the Daily Digest as a preprint. • To elucidate pathways in peripheral immune cells that might lead to immunopathology or protective immunity in severe COVID-19, single-cell RNA sequencing (scRNA-seq) was applied to profile peripheral blood mononuclear cells (PBMCs) from seven COVID-19 patients and six healthy controls. • The authors identify reconfiguration of peripheral immune cell phenotype in COVID-19, including a heterogeneous interferon-stimulated gene signature, HLA class II downregulation and a developing neutrophil population that appears closely related to plasmablasts appearing in patients with acute respiratory failure requiring mechanical ventilation.
08.06.2020	Expansion of myeloid-derived suppressor cells in patients with severe coronavirus disease (COVID-19)	Cell Death Differ / Article	<ul style="list-style-type: none"> • Study of the pathogenesis of severe cases of COVID-19. Peripheral blood from 18 SARS-CoV-2-infected patients, 9 with severe and 9 with mild COVID-19 disease, was obtained at admission and analysed for T-cell activation profile, myeloid-derived suppressor cells (MDSCs) and cytokine profiles. • Massive expansion of MDSCs was observed, up to 90% of total circulating mononuclear cells in patients with severe disease, and up to 25% in the patients with mild disease; the frequency decreasing with recovery. • MDSCs suppressed T-cell functions, dampening excessive immune response. MDSCs decline at convalescent phase was associated to a reduction in TGF-β and to an increase of inflammatory cytokines in plasma samples. Substantial expansion of suppressor cells is seen in patients with severe COVID-19.

08.06.2020	The inhibition of IL-2/IL-2R gives rise to CD8(+) T cell and lymphocyte decrease through JAK1-STAT5 in critical patients with COVID-19 pneumonia	Cell Death Dis / Research article	<ul style="list-style-type: none"> • In 54 patients who were enrolled and divided into three groups, among which 34 were common, 14 were severe, and 6 were critical, the constitution of peripheral blood mononuclear cells (PBMC) in patients was analysed by CyTOF. • The count and percentage of lymphocytes were significantly decreased in critical patients compared to common and severe patients with COVID-19. • The count of T cells, B cells, and NK cells was remarkably decreased in critical patients compared to normal controls. The percentage of CD8(+) T cells was significantly lower in critical patients than that in common and severe patients with COVID-19 pneumonia. • The expression of IL-2R, JAK1, and STAT5 decreased in PBMC of common, severe, and critical patients, but IL-2 level was elevated in severe patients and decreased in critical patients with COVID-19 pneumonia.
07.06.2020	Dynamics of IgG seroconversion and pathophysiology of COVID-19 infections	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Report dynamics of seroconversion to SARS-CoV-2 infections in 177 individuals. • 2-8.5% of individuals do not seroconvert even weeks after infection. They are younger than seroconverters who have increased co-morbidity and higher inflammatory markers such as C-Reactive Protein. • Higher antibody responses are associated with non-white ethnicity. Antibody responses do not decline during follow up almost to 2 months. • Serological assays increase understanding of disease severity. Their application in regular surveillance will clarify duration and protective nature of humoral responses to SARS-CoV-2.
03.06.2020	Magnitude and kinetics of anti-SARS-CoV-2 antibody responses and their relationship to disease severity	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Sera (n=533) from COVID-19 patients (n=153) tested using a high-throughput quantitative IgM and IgG assay that detects antibodies to the spike protein receptor binding domain and nucleocapsid protein. • Patterns of SARS-CoV-2 antibody production varied considerably. Among 52 patients with 3 or more serial specimens, 44 (84.6%) and 42 (80.8%) had observed IgM and IgG seroconversion at a median of 8 and 10 days, respectively. • Compared to those with milder disease, peak measurements significantly higher for ICU-admitted patients for all time intervals between 6 and 20 days for IgM, and all intervals after 5 days for IgG. • IgM and IgG responses were significantly higher in patients with severe than mild disease. These differences may affect strategies for seroprevalence studies, therapeutics and vaccine development.

08.06.2020	A consensus Covid-19 immune signature combines immuno-protection with discrete sepsis-like traits associated with poor prognosis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors identify a consensus peripheral blood immune signature across 63 hospital-treated Covid-19 patients who were otherwise highly heterogeneous • The core signature conspicuously blended adaptive B cell responses typical of virus infection or vaccination with discrete traits hitherto associated with sepsis, including monocyte and dendritic cell dampening, and hyperactivation and depletion of discrete T cell subsets.
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Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Clinical Performance of SARS-CoV-2 Molecular Testing	J Clin Microbiol / Article	<ul style="list-style-type: none"> • Study providing estimates of the clinical performance of SARS-CoV-2 molecular assays and suggesting time frames for appropriate repeat testing, namely 15 to 20 days after a positive test and the same or next 2 days after a negative test in patients with high suspicion for COVID-19 (27,377 SARS-CoV-2 molecular assays from 22,338 patients.).
08.06.2020	An analysis of SARS-CoV-2 viral load by patient age	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • RT-PCR threshold cycle data from 3303 patients tested positive for SARS-CoV-2 analysed to examine the relationship between patient age and estimated viral load. • A considerable percentage of infected people in all age groups, including those who are pre- or mild-symptomatic, carry viral loads likely to represent infectivity. • There is little evidence from the present study to support suggestions that children may not be as infectious as adults.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Systematic Review	Obstet Gynecol / Systematic review	<ul style="list-style-type: none"> • Systematic review of 13 articles including 538 pregnancies complicated by SARS-CoV-2 infection, with reported outcomes on 435 (80.9%) deliveries. • Maternal ICU admission occurred in 3.0% of cases and maternal critical disease in 1.4%. No maternal deaths were reported.

			<ul style="list-style-type: none"> • The preterm birth rate was 20.1%, the caesarean delivery rate was 84.7%, the vertical transmission rate was 0.0%, and the neonatal death rate was 0.3%. • The preterm birth rate of 20% and the caesarean delivery rate exceeding 80% seems related to geographic practice patterns.
09.06.2020	Cardiac MRI of Children with Multisystem Inflammatory Syndrome (MIS-C) Associated with COVID-19: Case Series	Radiology / Article	<ul style="list-style-type: none"> • In four children and adolescents admitted to intensive care for multisystem inflammatory syndrome and Kawasaki disease-like features related to COVID-19, acute myocarditis occurred less than 1 week after onset of fever and gastrointestinal symptoms. • SARS-CoV-2 RT-PCR was negative on nasopharyngeal, stool, and respiratory samples and was positive on serology. • Cardiac MRI showed diffuse myocardial edema on T2-STIR sequences and native-T1 mapping, with no evidence of late gadolinium enhancement suggestive of replacement fibrosis or focal necrosis. • These findings favour post-infectious myocarditis in children and adolescents with COVID-19.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Are there risk factors and preventative interventions for acute respiratory distress syndrome (ARDS) in COVID-19?	Oxford COVID-19 Evidence Service / Rapid review	<ul style="list-style-type: none"> • 17 studies were included in this rapid review, with older age, diabetes, certain blood tests and African American ethnicity amongst the most evidenced risk factors for ARDS. • Assessments of risk associated with other comorbidities, symptoms or exposure to medications pre-admission were more inconsistent. • Found a lack of robust data regarding risk factors or prevention of COVID-19 ARDS and identified an urgent need for high quality research in this area.
09.06.2020	Risks to healthcare workers following tracheal intubation of patients with COVID-19: a prospective international multicentre cohort study	Anaesthesia / Cohort study	<ul style="list-style-type: none"> • Prospective international multicentre cohort study recruiting healthcare workers participating in tracheal intubation of patients with suspected or confirmed COVID-19, with the primary endpoint being the incidence of laboratory-confirmed COVID-19 diagnosis or new symptoms requiring self-isolation or hospitalisation after a tracheal intubation episode. • Between 23 Mar and 2 June 2020, 1718 healthcare workers from 503 hospitals in 17 countries reported 5148 tracheal intubation episodes.

			<ul style="list-style-type: none"> • The overall incidence of the primary endpoint was 10.7% over a median follow-up of 32 days. The cumulative incidence within 7, 14 and 21 days of the first tracheal intubation episode was 3.6%, 6.1%, and 8.5%, respectively. • The risk of the primary endpoint varied by country and was higher in females, but was not associated with other factors.
09.06.2020	Addressing COVID-19 Among People Experiencing Homelessness: Description, Adaptation, and Early Findings of a Multiagency Response in Boston	Public Health Rep / Article	<ul style="list-style-type: none"> • Description of a citywide COVID-19 care model for people experiencing homelessness who are at high risk of COVID-19. • Components included symptom screening at shelter front doors, expedited testing at pop-up sites, isolation and management venues for symptomatic people under investigation and for people with confirmed disease, quarantine venues for asymptomatic exposed people, and contact investigation and tracing. • Adaptations to the care model to better respond to the local epidemiology of illness are described. • During the first 6 weeks of operation, 429 of 1297 (33.1%) tested people were positive for COVID-19; of these, 395 people were experiencing homelessness at the time of testing, representing about 10% of the homeless adult population in Boston.
08.06.2020	Adverse Outcomes and Mortality in Users of Non-Steroidal Anti-Inflammatory Drugs tested positive for SARS-CoV-2: A Danish Nationwide Cohort Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Population based cohort study on safety of non-steroidal anti-inflammatory drug (NSAID) use during SARS-CoV-2 infection • Treatment with NSAIDs not associated with 30-day mortality (RR 1.02, 95% CI 0.57 to 1.82; RD 0.1%, -3.5% to 3.7%), increased risk of hospitalisation (RR 1.16, 0.87 to 1.53; RD 3.3%, -3.4% to 10%), ICU-admission (RR 1.04, 0.54 to 2.02; RD 0.2%, -3.0% to 3.4%), mechanical ventilation (RR 1.14, 0.56 to 2.30; RD 0.5%, -2.5% to 3.6%), or renal replacement therapy (RR 0.86, 0.24 to 3.09; RD -0.2%, -2.0% to 1.6%).
09.06.2020	COVID-19 related mortality and spread of disease in long-term care: first findings from a living systematic review of emerging evidence	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Review identified 30 studies reporting primary data on COVID-19 related mortality and incidence of disease among long-term care (LTC) users and staff. • Outbreak investigations in LTC facilities found COVID-19 incidence rates of between 0.0% and 71.7% among residents and between 1.5% and 64.0% among staff. • Mortality rates varied from 0.0% to 9.9% of all residents at outbreak facilities, with case fatality rates between 0.0% and 33.7%. In included studies, no LTC staff members had died. • LTC residents accounted for between 0% (Hong Kong) and 82% (Canada) of COVID-related deaths, according to official figures.

			<ul style="list-style-type: none"> • Wide variation in spread of disease and mortality rates between outbreaks at individual LTC facilities. Further research into factors determining successful prevention and containment of COVID-19 outbreaks is needed to protect long-term care users and staff.
08.06.2020	Longitudinal Surveillance for SARS-CoV-2 RNA Among Asymptomatic Staff in Five Colorado Skilled Nursing Facilities: Epidemiologic, Virologic and Sequence Analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors sampled workers weekly at five SNFs (skilled nursing facilities such as rehabilitation centres and nursing homes) in Colorado using nasopharyngeal swabs, determined the presence of viral RNA and infectious virus, and sequenced 48 nearly complete genomes. • Data reveal high degree of asymptomatic infection, strong correlation between RNA detection and presence of infectious virus in NP swabs, persistent RNA in a subset of individuals, and declining incidence over time. • Data suggests that asymptomatic individuals infected by SARS-CoV-2 may contribute to virus transmission within the workplace.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
10.06.2020	Mobile applications in support of contact tracing for COVID-19 - A guidance for EU EEA Member States	European Centre for Disease Control and Prevention / Technical report	<ul style="list-style-type: none"> • This document is intended to facilitate the dialogue between public health authorities and app developers to ensure that the main epidemiological and operational considerations are taken into account, while also understanding the technological limitations. • Mobile applications can help trace and alert more contacts as they do not rely on the memory of the infected case. • Apps can also trace contacts unknown to the case and can notify contacts quickly and can facilitate cross-border contact tracing.
08.06.2020	Preliminary analysis of SARS-CoV-2 importation & establishment of UK transmission lineages	Virological (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Provide estimates of trends through time on the number and sources of SARS-CoV-2 introductions into the UK. • Obtained these estimates by combining data on the numbers of inbound travellers to the UK, estimated numbers of infections worldwide, and large-scale virus genome sequencing undertaken by the COG-UK consortium. • Preliminary analysis provides a platform for evaluating future trends in virus introduction, however it does not attempt to measure the relative contributions to the UK epidemic of importation versus local

			transmission, nor model the possible impact of public health interventions on virus introduction.
08.06.2020	Genomic epidemiology of SARS-CoV-2 spread in Scotland highlights the role of European travel in COVID-19 emergence	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors investigated first four weeks of SARS-CoV-2 virus in Scotland. Obtained full genome sequences from 452 individuals, 20% of all cases until 1st April 2020 (n=2310). • From combined phylogenetic and epidemiological analysis, authors estimated at least 113 introductions of SARS-CoV-2 into Scotland during this period. • A shift from travel-associated to sustained community transmission was apparent after only 11 days. Undetected introductions occurred prior to the first known case of COVID-19. • Earlier travel restrictions and quarantine measures might have resulted in fewer introductions; high number and transmission rates likely impacted on national contact tracing efforts.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	COVID-19 infection prevention and control for primary care, including general practitioner practices, dental clinics and pharmacy settings	European Centre for Disease Control and Prevention / Technical report	<ul style="list-style-type: none"> • This document provides guidance on infection prevention and control to healthcare providers in the EU/EEA in order to prevent COVID-19 infection.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Hydroxychloroquine inhibits trained immunity - implications for COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In this study of 13 patients, authors demonstrate that hydroxychloroquine inhibits trained immunity at the functional and epigenetic level and is accompanied by profound changes in the cellular lipidome as well as reduced expression of interferon-stimulated genes. • Trained immunity comprises a functional adaptation induced by epigenetic reprogramming which facilitates the anti-viral innate immune response. These findings suggest that hydroxychloroquine

may not have a beneficial effect on the anti-viral immune response to SARS-CoV-2.

Miscellaneous

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	Using mHealth to support COVID-19 education, self-assessment, and symptom monitoring: An observational study in The Netherlands	JMIR Mhealth Uhealth / Research article	<ul style="list-style-type: none"> • Observational cohort study to assess people's usage of an app that provides COVID-19 education, self-assessment and health monitoring for a 7-day period, and how this data would be useful for healthcare providers and policymakers. • The study demonstrated the successful implementation and use of an app with COVID-19 education, self-assessment, and a 7-day symptom diary. Overall, users were satisfied with the information supplied through the app and appreciated its functionality. • Data collected with the app were successfully applied to an interactive map displaying postal code specific demographics, health status, and healthcare consumption.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
09.06.2020	Update Alert: Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers	Annals of Internal Medicine / Letter
09.06.2020	Addressing the public mental health challenge of COVID-19	The Lancet Psychiatry / Comment
08.06.2020	Covid-19: PHE review has failed ethnic minorities, leaders tell BMJ	Bmj / News analysis

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