



## COVID-19 Literature Digest – 21/08/2020

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
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
18.08.2020	<a href="#">Evaluating the Association of Clinical Characteristics With Neutralizing Antibody Levels in Patients Who Have Recovered From Mild COVID-19 in Shanghai, China</a>	JAMA Intern Med / Key points	<ul style="list-style-type: none"><li>• In this cohort study of 175 patients who recovered from mild COVID-19, neutralizing antibody titres to SARS-CoV-2 varied substantially at the time of discharge. In addition, neutralizing antibodies were not detected in 10 patients.</li></ul>
14.08.2020	<a href="#">Detection, prevalence, and duration of humoral responses to SARS-CoV-2 under conditions of limited population exposure</a>	<b>medRxiv (non-peer reviewed) / Article</b>	<ul style="list-style-type: none"><li>• In an extensive serological study individuals with severe COVID-19 exhibited elevated authentic virus-neutralizing titres and antibody levels against nucleocapsid (N) and the receptor binding domain (RBD) and the S2 region of spike protein.</li><li>• Unlike disease severity, age and sex played lesser roles in serological</li></ul>

			<p>responses.</p> <ul style="list-style-type: none"> <li>• All cases, including asymptomatic individuals, seroconverted by 2 weeks post-PCR confirmation.</li> <li>• RBD- and S2-specific and neutralizing antibody titres remained elevated and stable for at least 2-3 months post-onset, whereas those against N were more variable with rapid declines in many samples.</li> <li>• In contrast to other reports, they conclude that immunity is durable for at least several months after SARS-CoV-2 infection.</li> </ul>
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### Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
18.08.2020	<a href="#">Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection</a>	Nat Med / Article	<ul style="list-style-type: none"> <li>• The authors performed peripheral leukocyte phenotyping in 25 children with MIS-C, in the acute (n = 23; worst illness within 72 h of admission), resolution (n = 14; clinical improvement) and convalescent (n = 10; first outpatient visit) phases of the illness and used samples from 7 age-matched healthy controls.</li> <li>• Among the MIS-C cohort, 17 (68%) children were COVID-19 seropositive, suggesting previous COVID-19 infections, and these children had more severe disease.</li> <li>• In the acute phase of MIS-C, high levels of interleukin-1<math>\beta</math> (IL-1<math>\beta</math>), IL-6, IL-8, IL-10, IL-17, interferon-<math>\gamma</math> and differential T and B cell subset lymphopenia were observed.</li> <li>• High CD64 expression on neutrophils and monocytes, and high HLA-DR expression on <math>\gamma\delta</math> and CD4(+)CCR7(+) T cells in the acute phase, suggested that these immune cell populations were activated.</li> </ul>
20.08.2020	<a href="#">SARS-CoV-2 in cardiac tissue of a child with COVID-19-related multisystem inflammatory syndrome</a>	The Lancet Child & Adolescent Health / Case report	<ul style="list-style-type: none"> <li>• Report the case of an (otherwise healthy) 11-year-old child with MIS-C related to COVID-19 who developed cardiac failure and died after 1 day of admission to hospital for treatment.</li> </ul>
17.08.2020	<a href="#">SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta</a>	EBioMedicine / Article	<ul style="list-style-type: none"> <li>• A study of 101 women who delivered between 7 Feb and 15 May 2020 provides first-time evidence for maternal-fetal transmission of SARS-CoV-2, likely propagated by circulating virus-infected fetal mononuclear cells.</li> <li>• Placenta infection was associated with recruitment of maternal inflammatory cells in the intervillous space, without villitis.</li> <li>• Authors suggest PD-L1 expression in syncytiotrophoblast and Hofbauer cells, together with limited production of NETs, may have prevented</li> </ul>

			immune cell-driven placental damage, ensuring sufficient maternal-fetus nutrient exchanges.
19.08.2020	<a href="#">Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women</a>	JAMA / Research letter	<ul style="list-style-type: none"> <li>• Between Mar 27 and May 6, 2020, the authors enrolled 18 women who had confirmed SARS-CoV-2 infection (77.7% White non-Hispanic, mean age 34.4 years [SD, 5.2 years]). Their offspring ranged in age from newborn to 19 months.</li> <li>• One breast milk sample had detectable SARS-CoV-2 RNA. The positive sample was collected on the day of symptom onset; however, 1 sample taken 2 days prior to symptom onset and 2 samples collected 12 and 41 days later tested negative for viral RNA. The breastfed infant was not tested. No replication-competent virus was detectable in any sample, including the sample that tested positive for viral RNA.</li> </ul>

#### Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
18.08.2020	<a href="#">Assessment of SARS-CoV-2 Transmission on an International Flight and Among a Tourist Group</a>	JAMA Netw Open / Research letter	<ul style="list-style-type: none"> <li>• This case series assessed a commercial airline flight (4 hrs 40 mins) from Tel Aviv, Israel, to Frankfurt, Germany, that occurred on Mar 9th, 2020.</li> <li>• Among 102 passengers were 24 members of a tourist group. Starting 7 days earlier, the group had contact with a hotel manager who later received a diagnosis of COVID-19. No member of the group had received a diagnosis of COVID-19 before the flight, and no measures to prevent transmission (e.g. wearing of masks) had been applied.</li> <li>• Discovered 2 likely SARS-CoV-2 transmissions on this flight, with 7 index cases. These transmissions may have also occurred before or after the flight. Both passengers with likely onboard transmission were seated within 2 rows of an index case.</li> </ul>
21.08.2020	<a href="#">Racial and Ethnic Disparities Among COVID-19 Cases in Workplace Outbreaks by Industry Sector - Utah, March 6-June 5, 2020</a>	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> <li>• Report on workplace outbreaks which occurred in 15 Utah industry sectors during 6 March 5 June 2020.</li> <li>• 58% of workplace outbreak-associated COVID-19 cases were in three sectors: Manufacturing, Wholesale Trade, and Construction.</li> <li>• Despite representing 24% of Utah workers in all affected sectors, Hispanic and non-white workers accounted for 73% of workplace outbreak-associated COVID-19 cases.</li> </ul>

20.08.2020	<a href="#">Risk factors for positive and negative COVID-19 tests: a cautious and in-depth analysis of UK biobank data</a>	Int J Epidemiol / Article	<ul style="list-style-type: none"> <li>• The authors explored the contribution of demographic, social, health risk, medical and environmental factors to COVID-19 risk using infection test data (n = 4509 tests; 1325 positive) from Public Health England, linked to the UK Biobank study.</li> <li>• Variables independently associated with the risk of being tested for COVID-19 with odds ratio &gt;1.05 were: male sex; Black ethnicity; social disadvantage (as measured by education, housing and income); occupation (healthcare worker, retired, unemployed); ever smoker; severely obese; comorbidities; and greater exposure to particulate matter (PM) 2.5 absorbance.</li> <li>• Of these, only male sex, non-White ethnicity and lower educational attainment, and none of the comorbidities or health risk factors, were associated with testing positive among tested individuals.</li> </ul>
21.08.2020	<a href="#">Disparities in Incidence of COVID-19 Among Underrepresented Racial/Ethnic Groups in Counties Identified as Hotspots During June 5-18, 2020 - 22 States, February-June 2020</a>	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> <li>• Examined county-level disparities in COVID-19 cases among underrepresented racial/ethnic groups in 205 U.S. counties (across 33 states) identified as hotspots.</li> <li>• Among these counties, race was reported for ≥50% of cumulative cases in 79 (38.5%) counties in 22 states; 96.2% of these counties had disparities in COVID-19 cases in one or more underrepresented racial/ethnic groups.</li> <li>• Hispanic/Latino persons were the largest group by population size (3.5 million persons) living in hotspot counties where a disproportionate number of cases among that group was identified.</li> <li>• This was followed by black/African American persons (2 million), American Indian/Alaska Native persons (61,000), Asian persons (36,000), and Native Hawaiian/other Pacific Islander persons (31,000).</li> </ul>
17.08.2020	<a href="#">Risk factors for detection of SARS-CoV-2 in healthcare workers during April 2020 in a UK hospital testing programme</a>	EclinicalMedicine / Article	<ul style="list-style-type: none"> <li>• Staff testing in their facility (County Durham and Darlington NHS Foundation Trust) commenced on the 1st April.</li> <li>• 991 individuals (mean age 42.6 years, 145 males) were tested over a 4 week period and overall 440/991 (43.4%) tested positive for SARS-CoV-2.</li> <li>• SARS-CoV-2 RNA detection rates were significantly higher in the first week of testing (59.0%) compared to week 2 (odds ratio 0.59), week 3 (odds ratio 0.32) and week 4 (odds ratio 0.23)(all p&lt;0.001).</li> <li>• No specific variables were identified that altered the risk of SARS-CoV-2 RNA detection including age, sex, occupation and ethnicity.</li> </ul>
19.08.2020	<a href="#">Characterization of Patients Who Return to Hospital Following Discharge from Hospitalization for COVID-19</a>	J Gen Intern Med / Article	<ul style="list-style-type: none"> <li>• Retrospective cohort study of COVID-19-positive patients with index hospitalization (n=2864) in New York City, with ≥ 14-day follow-up.</li> <li>• 103 (3.6%) returned for emergency care after a median of 4.5 days, with 56 requiring inpatient readmission. The most common reason for return</li> </ul>

			<p>was respiratory distress (50%).</p> <ul style="list-style-type: none"> <li>• There were higher proportions of COPD (6.8% vs 2.9%) and hypertension (36% vs 22.1%) among those who returned vs those who did not.</li> <li>• Patients who returned had shorter median length of stay (LOS) during index hospitalization (4.5 [2.9,9.1] vs 6.7 [3.5, 11.5] days; P(adjusted) = 0.006), and were less likely to require intensive care on index hospitalization (5.8% vs 19%; P(adjusted) = 0.001).</li> <li>• A trend towards association between absence of in-hospital treatment-dose anticoagulation on index admission and return to hospital was observed (20.9% vs 30.9%, P(adjusted) = 0.06).</li> <li>• On re-admission, rates of intensive care and death were 5.8% and 3.6%, respectively.</li> </ul>
17.08.2020	<a href="#">Risk of stroke in hospitalized SARS-CoV-2 infected patients: A multinational study</a>	EBioMedicine / Article	<ul style="list-style-type: none"> <li>• A multinational observational study (99 tertiary centres in 11 countries) aimed to better depict short-term risk of stroke and its associated factors among COVID-19 hospitalized patients.</li> <li>• Among 17,799 patients included in meta-analyses, 156 (0.9%) patients had a stroke: of these, 123 (79%) were ischaemic stroke, 27 (17%) intracerebral/subarachnoid haemorrhage, and 6 (4%) cerebral sinus thrombosis.</li> <li>• Subsequent stroke risks were 0.5% among all centres in all countries, and 0.7% among countries with higher health expenditures.</li> <li>• The need for mechanical ventilation (OR: 1.9, 95% CI:1.1-3.5, p = 0.03) and the presence of ischaemic heart disease (OR: 2.5, 95% CI:1.4-4.7, p = 0.006) were predictive of stroke.</li> </ul>
20.08.2020	<a href="#">Obesity doubles mortality in patients hospitalized for SARS-CoV-2 in Paris hospitals, France: a cohort study on 5795 patients</a>	Obesity / Article	<ul style="list-style-type: none"> <li>• A prospective cohort study of 5795 adult patients aged 18-79 years, hospitalized from 1 Feb to 30 April 2020 in the Paris area.</li> <li>• A total of 891 deaths occurred at 30 days.</li> <li>• Mortality was significantly raised in people with obesity with the following OR in BMI 30-35, 35-40 and &gt;40 kg/m(2) : 1.89 (95%CI 1.45-2.47), 2.79 (1.95-3.97) and 2.55 (1.62-3.95), respectively (18.5-25 kg/m(2) , as the reference class). This increase holds for all age classes.</li> </ul>
19.08.2020	<a href="#">Circulating Endothelial Cells as a Marker of Endothelial Injury in Severe COVID -19</a>	J Infect Dis / Article	<ul style="list-style-type: none"> <li>• The authors investigated whether increased levels of circulating endothelial cells (CEC) might be associated with severe forms of COVID-19 in a retrospective study of 99 patients.</li> <li>• Patients in intensive care units (ICU) had significantly higher CEC counts than non-ICU patients and the extent of endothelial injury was correlated with putative markers of disease severity and inflammatory cytokines.</li> </ul>

04.08.2020	<a href="#">Humidity is a consistent climatic factor contributing to SARS-CoV-2 transmission</a>	Trans and Emg Dis / Short communication	<ul style="list-style-type: none"> <li>• The relationship between climatic factors and COVID-19 cases in New South Wales, Australia was investigated during both the exponential and declining phases of the epidemic in 2020, and in different regions.</li> <li>• Increased relative humidity was associated with decreased cases in both epidemic phases, and a consistent negative relationship was found between relative humidity and cases.</li> <li>• Overall, a decrease in relative humidity of 1% was associated with an increase in cases of 7–8%. Overall, they found no relationship with between cases and temperature, rainfall or wind speed. Authors conclude that information generated in this study confirms humidity as a driver of SARS-CoV-2 transmission.</li> </ul> <p>Included as is receiving a lot of media attention.</p>
16.08.2020	<a href="#">Air pollution, SARS-CoV-2 transmission, and COVID-19 outcomes: A state-of-the-science review of a rapidly evolving research area</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A scoping review of epidemiologic research on the link between short- and long-term exposure to air pollution and COVID-19 health outcomes.</li> <li>• 27 studies of the 28 reported evidence of statistically significant positive associations between air pollutant exposure and adverse COVID-19 health outcomes.</li> <li>• All studies included various confounders, spatial and temporal resolutions of pollution concentrations, and COVID-19 health outcomes.</li> <li>• Several such as data quality issues, ecological study design limitations, and geographic variability in testing are highlighted.</li> </ul>

#### Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
20.08.2020	<a href="#">Three infection clusters related with potential pre-symptomatic transmission of coronavirus disease (COVID-19), Shanghai, China, January to February 2020</a>	Eurosurveillance / Outbreaks	<ul style="list-style-type: none"> <li>• Report three clusters related with potential pre-symptomatic transmission of COVID-19 between Jan and Feb 2020 in Shanghai, China. Investigators interviewed suspected COVID-19 cases to collect epidemiological information.</li> <li>• The interval between the onset of illness in the primary case and the last contact of the secondary case with the primary case in their report was 1 to 7 days.</li> <li>• In Cluster 1 (five cases), illness onset in the five secondary cases was 2 to 5 days after the last contact with the primary case. In Cluster 2 (five cases) and Cluster 3 (four cases), the illness onset in secondary cases occurred prior to or on the same day as the onset in the primary cases.</li> </ul>

			<ul style="list-style-type: none"> <li>• The study provides empirical evidence for transmission of COVID-19 during the incubation period and indicates that pre-symptomatic person-to-person transmission can occur following sufficient exposure to confirmed COVID-19 cases.</li> </ul>
11.08.2020	<a href="#">Association Between Antecedent Statin Use and Decreased Mortality in Hospitalized Patients with COVID-19</a>	Res Sq (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A retrospective analysis of patients (n=2626) admitted with COVID-19 sought to determine whether antecedent statin use is associated with lower in-hospital mortality.</li> <li>• A total of 951 (36.2%) were antecedent statin users.</li> <li>• Among 1296 patients (648 statin users, 648 non-statin users) identified with 1:1 propensity-score matching, demographic, baseline, and outpatient medication information were well balanced.</li> <li>• Conclude that antecedent statin use in patients hospitalized with COVID-19 was associated with lower inpatient mortality.</li> </ul>
20.08.2020	<a href="#">Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study</a>	The Lancet Microbe / Article	<ul style="list-style-type: none"> <li>• Describe the histopathological findings and viral tropism in patients (n=10) who died of severe COVID-19.</li> <li>• Findings supports clinical data showing that the four dominant interrelated pathological processes in severe COVID-19 are diffuse alveolar damage, thrombosis, haemophagocytosis, and immune cell depletion.</li> <li>• Additionally, they report here several novel autopsy findings including pancreatitis, pericarditis, adrenal micro-infarction, secondary disseminated mucormycosis, and brain microglial activation, which require additional investigation to understand their role in COVID-19.</li> </ul>

## Infection control

Publication Date	Title / URL	Journal / Article type	Digest
19.08.2020	<a href="#">Automated and partly automated contact tracing: a systematic review to inform the control of COVID-19</a>	The Lancet Digital Health / Review	<ul style="list-style-type: none"> <li>• A systematic review of automated or partly automated contact tracing.</li> <li>• Of the 4036 studies identified, 110 full-text studies were reviewed and 15 studies were included in the final analysis and quality assessment.</li> <li>• No empirical evidence of the effectiveness of automated contact tracing (regarding contacts identified or transmission reduction) was identified. This paper was previously included in the Digest as a preprint.</li> </ul>
18.08.2020	<a href="#">Influenza A virus is transmissible via aerosolized fomites</a>	Nature Communications / Article	<ul style="list-style-type: none"> <li>• This paper is not directly related to SARS CoV 2 but findings may be of interest.</li> <li>• In the guinea pig model of influenza virus transmission, the authors</li> </ul>

show that the airborne particulates produced by infected animals are mainly non-respiratory in origin. Surprisingly, they find that an uninfected, virus-immune guinea pig whose body is contaminated with influenza virus can transmit the virus through the air to a susceptible partner in a separate cage. They further demonstrate that aerosolized fomites can be generated from inanimate objects, such as by manually rubbing a paper tissue contaminated with influenza virus.

- The data suggest that aerosolized fomites may contribute to influenza virus transmission in animal models of human influenza, if not among humans themselves, with important but understudied implications for public health.

### Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
14.08.2020	<a href="#">Covid-19: breaking the chain of household transmission</a>	Bmj / Editorial
20.08.2020	<a href="#">What Happens When COVID-19 Collides With Flu Season?</a>	JAMA / Medical News & Perspectives
19.08.2020	<a href="#">Face coverings for covid-19: from medical intervention to social practice</a>	Bmj / Analysis
20.08.2020	<a href="#">Clinical trials of disease stages in COVID 19: complicated and often misinterpreted</a>	The Lancet Global Health / Comment
17.08.2020	<a href="#">The National COVID Cohort Collaborative (N3C): Rationale, Design, Infrastructure, and Deployment</a>	J Am Med Inform Assoc / Article

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