



COVID-19 Literature Digest – 28/08/2020

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
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Modelling
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
21.08.2020	A cross-reactive human IgA monoclonal antibody blocks SARS-CoV-2 spike-ACE2 interaction	Nat Commun / Article	<ul style="list-style-type: none">• The authors characterize a cross-reactive human IgA monoclonal antibody, MAb362.• MAb362 binds to COVID-19 spike proteins and competitively blocks ACE2 receptor binding, by overlapping the ACE2 structural binding epitope.• Furthermore, MAb362 IgA neutralizes COVID-19 in 293 cells expressing ACE2.

			<ul style="list-style-type: none"> • When converted to secretory IgA, MAb326 also neutralizes authentic COVID-19 virus while the IgG isotype shows no neutralization.
26.08.2020	Sex differences in immune responses that underlie COVID-19 disease outcomes	Nature / Article	<ul style="list-style-type: none"> • <i>Previously included as a pre-print.</i> • The authors examine sex differences in viral loads, COVID-19-specific antibody titres, plasma cytokines, as well as blood cell phenotyping in COVID-19 patients with moderate disease (n=98). • Male patients had higher plasma levels of innate immune cytokines such as IL-8 and IL-18 along with more robust induction of non-classical monocytes. • Female patients mounted significantly more robust T cell activation than male patients during infection, which was sustained in old age. • A poor T cell response negatively correlated with patients' age and was associated with worse disease outcome in male patients, but not in female patients. • Higher innate immune cytokines in female patients was associated with worse disease progression, but not in male patients.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
26.08.2020	Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection	Cochrane Database / Syst Rev	<ul style="list-style-type: none"> • This review identifies early-stage evaluations of point-of-care tests for detecting SARS-CoV-2 infection, largely based on remnant laboratory samples. • The findings currently have limited applicability, as are uncertain whether tests will perform in the same way in clinical practice, and according to symptoms of COVID-19, duration of symptoms, or in asymptomatic people. • Rapid tests have the potential to be used to inform triage of RT-PCR use, allowing earlier detection of those testing positive, but the evidence currently is not strong enough to determine how useful they are in clinical practice.
26.08.2020	Pooling Upper Respiratory Specimens for Rapid Mass Screening of COVID-19 by Real-Time RT-PCR	Emerg Infect Dis / Dispatch	<ul style="list-style-type: none"> • To validate the specimen-pooling strategy for real-time reverse transcription PCR detection of SARS-Cov-2, the authors generated different pools including positive specimens, reflecting the distribution of cycle threshold values at initial diagnosis. • Cumulative sensitivities of tested pool sizes suggest pooling of <6 specimens for surveillance by this method.

28.08.2020	Notes from the Field: Universal Statewide Laboratory Testing for SARS-CoV-2 in Nursing Homes - West Virginia, April 21-May 8, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • For the period 8 May – 26 July, following completion of universal testing and under the new procedures, 18 COVID-19 outbreaks were identified in West Virginia nursing homes, 12 of which involved five or fewer cases. • Authors suggest that although universal testing is resource-intensive, it has proven essential to limiting COVID-19 transmission in nursing homes and has reduced the impact of the pandemic on this population in West Virginia.
26.08.2020	Clinical validation of a Cas13-based assay for the detection of SARS-CoV-2 RNA	Nat Biomed Eng / Article	<ul style="list-style-type: none"> • Authors report clinical validation of specific high-sensitivity enzymatic reporter unlocking (SHERLOCK) assay using the enzyme Cas13a from <i>Leptotrichia wadei</i> for detection of SARS-CoV-2 in 154 nasopharyngeal and throat swabs. • Within a detection limit of 42 RNA copies per reaction, SHERLOCK was 100% specific and 100% sensitive with a fluorescence readout, and 100% specific and 97% sensitive with a lateral-flow readout. For the full range of viral load in the clinical samples, the fluorescence readout was 100% specific and 96% sensitive. • The assay should facilitate SARS-CoV-2 detection in settings with limited resources.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
28.08.2020	Phylogenetic analysis of SARS-CoV-2 in the Boston area highlights the role of recurrent importation and superspreading events	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To investigate the introduction, spread, and epidemiology of COVID-19 in the Boston area, the authors sequenced and analysed 772 complete SARS-CoV-2 genomes from the region, including nearly all confirmed cases within the first week of the epidemic and hundreds of cases from major outbreaks at a conference, a nursing facility, and among homeless shelter guests and staff. • Studied two superspreading events covered by the data, events that led to very different outcomes because of the timing and populations involved. • The same two events differed significantly in the number of new mutations seen, raising the possibility that SARS-CoV-2 superspreading might encompass disparate transmission dynamics.

22.08.2020	A genetic barcode of SARS-CoV-2 for monitoring global distribution of different clades during the COVID-19 pandemic	Int J Infect Dis / Article	<ul style="list-style-type: none"> • Describe 11 major mutation events which defined five major clades (G614, S84, V251, I378 and D392) of globally-circulating viral populations. • Successfully developed a multiplexed sequencing-based, rapid genotyping protocol for high-throughput classification of major clade types of SARS-CoV-2 in clinical samples. • Several nonsynonymous mutations in the spike protein may have functional consequences: the G clade-defining mutation D614 G located in subdomain 1; the V367 F, G476S and V483A are localised in the receptor binding domain (RBD) of the spike protein.
25.08.2020	Origin and cross-species transmission of bat coronaviruses in China	Nat Commun / Article	<ul style="list-style-type: none"> • Authors use Bayesian statistical framework and large sequence data set from bat-CoVs (including 630 novel CoV sequences) in China to study macroevolution, cross-species transmission and dispersal. • Authors present a phylogenetic analysis suggesting a likely origin for SARS-CoV-2 in Rhinolophus spp. bats.
25.08.2020	The SARS-CoV-2 Spike mutation D614G increases entry fitness across a range of ACE2 levels, directly outcompetes the wild type, and is preferentially incorporated into trimers	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors developed a cell line with inducible ACE2 expression to confirm that D614G more efficiently enters cells with ACE2 levels spanning the different primary cells targeted by SARS-CoV-2. • Using a new assay for crosslinking and directly extracting Spike trimers from the pseudovirus surface, they found an increase in trimerization efficiency and viral incorporation of D614G protomers. • Findings suggest that D614G increases infection of cells expressing a wide range of ACE2, and informs the mechanism underlying enhanced entry.

Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
27.08.2020	Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study	BMJ / Research	<ul style="list-style-type: none"> • Prospective observational cohort study of 651 children and young people aged less than 19 years admitted to 138 hospitals in UK with confirmed covid-19; explore factors associated with multisystem inflammatory syndrome in children and adolescents temporarily related to COVID-19 (MIS-C). • Children and young people have less severe acute covid-19 than adults. A systemic mucocutaneous-enteric symptom cluster was also identified in acute cases that shares features with MIS-C. Ethnicity seems to be a factor in both critical care admission and MIS-C.

			<ul style="list-style-type: none"> • Study provides evidence for refining the WHO MIS-C preliminary case definition. Children meeting the MIS-C criteria have different demographic and clinical features depending on whether they have acute SARS-CoV-2 infection (PCR positive) or are post-acute (antibody positive).
18.08.2020	SARS-CoV-2 Infections Among Children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective cohort study of 382 children and adolescents (<21 years of age) with a SARS-CoV-2-infected close contact. 293 (77%) were SARS-CoV-2-infected. • Infected children more likely to be Hispanic ($p<0.0001$), less likely to have asthma ($p=0.005$), more likely to have an infected sibling contact ($p=0.001$) • Children 6-13 years were frequently asymptomatic (39%) and had respiratory symptoms less often than younger children (29% vs. 48%; $p=0.01$) or adolescents (29% vs. 60%; $p<0.0001$). • Despite the age-related variability in symptoms, no differences in nasopharyngeal viral load by age or between symptomatic and asymptomatic children was found.
28.08.2020	Limited Secondary Transmission of SARS-CoV-2 in Child Care Programs - Rhode Island, June 1-July 31, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • On 1 June 2020, child care programs in Rhode Island state reopened after a nearly 3-month closure implemented as part of COVID-19 mitigation efforts. • A total of 101 possible child care-associated COVID-19 cases were reported during 1 June – 31 July. Among them, 49 (49%) symptomatic persons were excluded after receiving negative laboratory test results, 33 persons (33%) had confirmed cases, and 19 (19%) were classified as having probable cases. Possible transmission routes are discussed.
26.08.2020	Ocular Manifestations and Clinical Characteristics of Children With Laboratory-Confirmed COVID-19 in Wuhan, China	JAMA Ophthalmol / Original investigation	<ul style="list-style-type: none"> • In this cross-sectional study of 216 children hospitalized with COVID-19 in Wuhan, China, 49 (22.7%) had ocular manifestations, including conjunctival discharge, eye rubbing, and conjunctival congestion. • Children with systemic symptoms or cough were more likely to develop ocular symptoms, which were mild, and recovered or improved with minimal eye drops or self-healing.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
24.08.2020	UK prevalence of underlying conditions which increase the risk of severe COVID-19 disease: a point prevalence study using electronic health records	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A study described the population at risk of severe COVID-19 due to underlying health conditions across the United Kingdom in 2019 using anonymised records from Clinical Practice Research Datalink GOLD. • On 5 March 2019, 24.4% of the UK population were at risk due to a record of at least one underlying health condition, including 8.3% of school-aged children, 19.6% of working-aged adults, and 66.2% of individuals aged 70 years or more. • 7.1% of the population had multimorbidity. • The size of the at-risk population was stable from 2014 to 2019.
24.08.2020	Risk factors for outbreaks of COVID-19 in care homes following hospital discharge: a national cohort analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A study examined the number of hospital discharges to all Welsh adult care homes and the subsequent outbreaks of COVID-19 occurring over an 18 week period from 22 Feb 2020. • Of 1068 care homes, 330 homes experienced an outbreak of COVID-19, and 511 homes received a discharge from hospital. • Exposure to discharge from hospital was not associated with a significant increase in the risk of a new outbreak, after adjusting for care home size, which was by far the most significant predictor. • Hazard ratios (95% CI) in comparison to homes of <10 residents were: 3.4 (2.0, 5.8) for 10-24 residents; 8.3 (5.0, 13.8) for 25-49 residents; and 17.3 (9.6, 31.1) for homes of 50+ residents.
27.08.2020	Excess all-cause mortality during the first wave of the COVID-19 epidemic in France, March to May 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Through a weekly all-cause mortality surveillance system, the authors observed in France a major all-cause excess mortality from Mar to May 2020, concomitant with the COVID-19 epidemic. • The excess mortality was 25,030 deaths, mainly among elderly people. Five metropolitan regions were the most affected, particularly Île-de-France and the Grand-Est regions. • Assessing the excess mortality related to COVID-19 is complex because of the potential protective effect of the lockdown period on other causes of mortality.
27.08.2020	Reduced vitamin K status as a potentially modifiable risk factor of severe COVID-19	Clin Infect Dis / Article	<ul style="list-style-type: none"> • A study compared 135 hospitalized COVID-19 patients with 184 historical controls to examine whether vitamin K may be implicated in COVID-19, linking pulmonary and thromboembolic disease.

			<ul style="list-style-type: none"> • Inactive vitamin K-dependent MGP (dp-ucMGP) was elevated in COVID-19 patients compared to controls ($p < 0.001$), with even higher dp-ucMGP in patients with poor outcomes ($p < 0.001$). • Suggests a mechanism of pneumonia-induced extrahepatic vitamin K depletion leading to accelerated elastic fibre damage and thrombosis in severe COVID-19 due to impaired activation of MGP and endothelial protein S, respectively.
27.08.2020	COVID-19 and rheumatic autoimmune systemic diseases: report of a large Italian patients series	Clin Rheumatol / Article	<ul style="list-style-type: none"> • Authors investigated 1641 autoimmune systemic disease Italian patients during Covid-19 pandemic. • Covid-19 is more frequent in the subgroup of autoimmune systemic diseases patients without ongoing conventional synthetic disease-modifying anti-rheumatic drugs, mainly hydroxyl-chloroquine and methotrexate, which might play some protective role against the most harmful manifestations of Covid-19.
27.08.2020	EXPRESS: Cerebrovascular events and outcomes in hospitalized patients with COVID-19: The SVIN COVID-19 Multinational Registry	Int J Stroke / Article	<ul style="list-style-type: none"> • Summarize the findings of a multinational observational cohort of patients with SARS CoV-2 and cerebrovascular disease. • Retrospective observational cohort of consecutive adults evaluated in the emergency department and/or admitted with coronavirus disease 2019 (COVID-19) across 31 hospitals in four countries. • Of the 14,483 patients with laboratory-confirmed SARS-CoV-2, 172 were diagnosed with an acute cerebrovascular event 68/171 (40.5%) were female and 96/172 (55.8%) were between the ages 60-79 years. • Concluded that COVID-19 is associated with a small but significant risk of clinically relevant cerebrovascular events, particularly ischemic stroke.
26.08.2020	Clinical Characteristics and Outcomes of 821 Older Patients with SARS-Cov-2 Infection Admitted to Acute Care Geriatric Wards	J Gerontol / Article	<ul style="list-style-type: none"> • A multicentric retrospective cohort study in 13 acute COVID-19 geriatric wards, from March 13 to Apr 15, 2020, in Paris area. All consecutive patients aged ≥ 70 years, with confirmed COVID-19, were enrolled ($n=812$). • This study provides new information about older patients with COVID-19 who are hospitalized. A quick bedside evaluation at admission of sex, functional status, systolic arterial pressure, consciousness, respiratory rate and asthenia can identify older patients at risk of unfavourable outcomes.
26.08.2020	Association of Troponin Levels With Mortality in Italian Patients Hospitalized With Coronavirus Disease 2019: Results of a Multicenter Study	JAMA Cardiol / Brief report	<ul style="list-style-type: none"> • In this multicentre, cross-sectional study of 614 White Italian patients hospitalized with coronavirus disease 2019, elevated troponin values were associated with higher mortality and a greater risk of cardiovascular and non-cardiovascular complications.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
27.08.2020	Pathophysiology of COVID-19-associated acute respiratory distress syndrome: a multicentre prospective observational study	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none"> Examined the functional and morphological features of COVID-19-associated ARDS to compare these with the characteristics of ARDS unrelated to COVID-19. Between Mar 9 and Mar 22, 2020, 301 patients with COVID-19 met the Berlin criteria for ARDS at participating Italian hospitals. Concluded that patients with COVID-19-associated ARDS have a form of injury that, in many aspects, is similar to that of those with ARDS unrelated to COVID-19.
27.08.2020	Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: a prospective observational study	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none"> In this exploratory analysis of 39 patients, ARDS due to COVID-19 was not associated with higher systemic inflammation and was associated with a lower prevalence of the hyperinflammatory phenotype than that observed in historical ARDS data. This finding suggests that the excess mortality observed in COVID-19-related ARDS is unlikely to be due to the upregulation of inflammatory pathways described by the parsimonious model.
24.08.2020	Clinical, immunological and virological characterization of COVID-19 patients that test re-positive for SARS-CoV-2 by RT-PCR	EBioMedicine / Research paper	<ul style="list-style-type: none"> Among 619 discharged COVID-19 cases, 87 re-tested as SARS-CoV-2 positive in circumstances of social isolation. All re-positive cases had mild or moderate symptoms at initial diagnosis and were younger on average (median, 28). Re-positive cases (n = 59) exhibited similar neutralization antibodies (NAbs) titre distributions to other COVID-19 cases (n = 218) tested here. No infectious strain could be obtained by culture and no full-length viral genomes could be sequenced from re-positive cases.
24.08.2020	Twelve out of 117 recovered COVID-19 patients retest positive in a single-center study of China	EClinicalMedicine / Article	<ul style="list-style-type: none"> Retrospectively analysed a cohort of 117 discharged patients and analysed the differences between retest positive and negative patients in terms of demographics, clinical characteristics, laboratory findings, chest computed tomography (CT) features and treatment procedures. Twelve out of 117 recovered COVID-19 patients retested positive. Patients with COVID-19 who met discharge criteria could still test positive for SARS-CoV-2 RNA. Longer hospital stay and lymphopenia could be potential risk factors for positive SARS-CoV-2 retest in COVID-19 patients after hospital discharge.

26.08.2020	Correlates of critical illness-related encephalopathy predominate postmortem COVID-19 neuropathology	Acta Neuropathol / Article	<ul style="list-style-type: none"> • A report on autoptic neuropathological findings for a cohort of seven COVID-19 patients, and comparison with a negative control autopsy cohort comprising individuals with non-septic and systemic inflammatory/septic clinical courses.
24.08.2020	Evidence of SARS-CoV-2 transcriptional activity in cardiomyocytes of COVID-19 patients without clinical signs of cardiac involvement	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • An investigation of COVID-19 presence in heart tissue autopsies of 6 consecutive COVID-19 patients deceased for respiratory failure showing no signs of cardiac involvement and with no history of heart disease. • Suggests the need of cardiologic surveillance even in survived COVID-19 patients not displaying a cardiac phenotype, in order to monitor potential long-term cardiac sequelae.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
25.08.2020	Two metres or one: what is the evidence for physical distancing in covid-19?	BMJ / Analysis	<ul style="list-style-type: none"> • Authors argue current rules on safe physical distancing are based on outdated, dichotomous notion of respiratory droplet size - propose more nuanced model. • Distribution of viral particles is affected by numerous factors, including air flow. • Evidence suggests SARS-CoV-2 may travel more than 2 m through activities such as coughing and shouting. • Rules on distancing should reflect the multiple factors that affect risk, including ventilation, occupancy, and exposure time.
26.08.2020	Experimental survival of SARS-CoV-2 on an insect-repellent-treated surface	Defence Science and Technology Laboratory / Research and Analysis	<ul style="list-style-type: none"> • Defence Science and Technology Laboratory (DSTL) study to determine the level of anti-viral activity of Mosi-guard Natural® spray against Covid-19 virus. • One minute liquid suspension tests indicated that Mosi-guard Natural® has anti-viral activity against SARS-CoV-2 England-2 isolate if mixed with the virus in the liquid phase. Viral studies on latex indicated that Mosi-guard Natural had antiviral activity against SARS-CoV-2 England-2 isolate. • This research paper demonstrates preliminary findings on the effectiveness of Citriodiol against COVID-19.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
25.08.2020	Lung transplantation for COVID-19-associated acute respiratory distress syndrome in a PCR-positive patient	The Lancet Respiratory Medicine / Case Report	<ul style="list-style-type: none"> • Authors report first case of lung transplantation for a patient (44 year old female) with a persistently positive SARS-CoV-2 real-time RT-PCR test result. • Case Report shows that lung transplantation should be added to the armamentarium of therapies for patients with COVID-19-related ARDS. The criteria for patient selection and timing of lung transplantation need to be validated in future studies.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
26.08.2020	The geography of COVID-19 spread in Italy and implications for the relaxation of confinement measures	Nat Commun / Article	<ul style="list-style-type: none"> • Describes a spatially explicit model capable of estimating the expected unfolding of the Italian COVID-19 outbreak under continuous lockdown (baseline trajectory), assessing deviations from the baseline should lockdown relaxations result in increased disease transmission, and calculating the isolation effort required to prevent a resurgence of the outbreak. • The authors provide an ex-post assessment based on the epidemiological data that became available after the initial analysis and estimate actual disease transmission that occurred after weakening the lockdown.
24.08.2020	Age-specific mortality and immunity patterns of SARS-CoV-2 infection in 45 countries	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a study using age-specific death data from 45 countries the authors found that relative differences in the number of deaths by age amongst individuals aged <65 years old are highly consistent. • When combined with data from 15 seroprevalence surveys it demonstrates how age-specific infection fatality ratios (IFRs) can be used to reconstruct infected population proportions. • Found notable heterogeneity in overall IFR estimates as suggested by individual serological studies. • Suggests age-specific COVID-19 death data in younger individuals can provide a robust indicator of population immunity.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
27.08.2020	Timely monitoring of total mortality associated with COVID-19: informing public health and the public	Eurosurveillance / Editorial
27.06.2020	Physiological and biological heterogeneity in COVID-19-associated acute respiratory distress syndrome	The Lancet Respiratory Medicine / Comment
26.08.2020	Type 1 Diabetes in People Hospitalized for COVID-19: New Insights From the CORONADO Study	Diabetes Care / Article
26.08.2020	Emerging preclinical evidence does not support broad use of hydroxychloroquine in COVID-19 patients	Nat Commun / Comment
26.08.2020	Developing Safe and Effective Covid Vaccines — Operation Warp Speed's Strategy and Approach	New England Journal of Medicine / Perspective
26.08.2020	Making ordinary decisions in extraordinary times	BMJ / Analysis

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