



International EPI Cell Daily Evidence Digest – 26/06/2020

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
- Genomics
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
25.06.2020	Antibody tests for identification of current and past infection with SARS-CoV-2	Cochrane Database Syst Rev / Systematic Review	<ul style="list-style-type: none">• Review to assess the diagnostic accuracy of antibody tests to determine if a person presenting in the community or in primary or secondary care has SARS-CoV-2 infection, or has previously had SARS-CoV-2 infection, and the accuracy of antibody tests for use in seroprevalence surveys.• Found that the sensitivity of antibody tests is too low in the first week since symptom onset to have a primary role for the diagnosis of COVID-19, but they may still have a role complementing other testing in individuals presenting later, when RT-PCR tests are negative, or are not done.

			<ul style="list-style-type: none"> • Antibody tests are likely to have a useful role for detecting previous SARS-CoV-2 infection if used 15 or more days after the onset of symptoms. However, the duration of antibody rises is currently unknown, and they found very little data beyond 35 days post-symptom onset.
25.06.2020	Estimation of SARS-CoV-2 infection fatality rate by real-time antibody screening of blood donors	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Performed nationwide (in Denmark) real-time seroprevalence surveying among blood donors as a tool to estimate previous SARS-CoV-2 infections and the population based IFR. • The IFR was estimated to be slightly lower than previously reported from other countries not using seroprevalence data, and the IFR is likely several fold lower than the current estimate.
25.06.2020	Prevalence of serum IgG antibodies against SARS-CoV-2 among clinic staff	PLoS One / Article	<ul style="list-style-type: none"> • The authors' examined the SARS-CoV-2-IgG antibody status among clinic staff of a large neurological centre in Northern Germany. • Blood samples and questionnaires (demographic data, medical history) were collected pseudonymously, and in total, 406 out of 525 (77.3%) of the employees participated in the study. • The infection rate among the staff was as high as 2.7%. Including drop-outs (missing questionnaire but test result available), the infection rate was even higher (2.9%). • Only 36% of the positively tested employees suffered from flu-like symptoms in 2020.
24.06.2020	Seroprevalence of SARS-CoV-2 IgG significantly varies with age: results from a mass population screening (SARS-2-SCREEN-CdA)	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a mass screening involving 4174 out of about 4550 total inhabitants in Castiglione D'Adda, Lombardy, significant age-related differences in anti SARS-CoV-2 IgG seroprevalence were found, with the lowest prevalence in the youngest inhabitants.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
19.06.2020	Neutralization of SARS-CoV-2 by Destruction of the Prefusion Spike	Cell Host Microbe / Article	<ul style="list-style-type: none"> • SARS-CoV-2 binds host cells via a trimeric spike whose receptor binding domain (RBD) recognizes angiotensin-converting enzyme 2, initiating conformational changes that drive membrane fusion. • This study finds that the monoclonal antibody CR3022 binds the RBD tightly, neutralizing SARS-CoV-2, and report the crystal structure at 2.4 Å of the Fab/RBD complex. • CR3022 could have therapeutic potential alone or in synergy with a receptor blocker.

24.06.2020	CoronaHiT: large scale multiplexing of SARS-CoV-2 genomes using Nanopore sequencing	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> The authors demonstrate that CoronaHiT, a method capable of multiplexing up to 95 small genomes on a single Nanopore flowcell, can multiplex up to 94 SARS-CoV-2 genomes per nanopore flowcell without compromising the quality of the resulting genomes while reducing library preparation complexity and significantly reducing cost.
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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
25.06.2020	COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study	The Lancet Child & Adolescent Health / Article	<ul style="list-style-type: none"> This study aimed to capture key data on children and adolescents with SARS-CoV-2 infection across Europe to inform physicians and health-care service planning during the ongoing pandemic. This multicentre cohort study involved 82 participating health-care institutions across 25 European countries. 582 individuals with PCR-confirmed SARS-CoV-2 infection were included, with a median age of 5.0 years (IQR 0.5–12.0) and a sex ratio of 1.15 males per female. This study found that COVID-19 is generally a mild disease in children, including infants, but a small proportion develop severe disease requiring ICU admission and prolonged ventilation, although fatal outcome is overall rare.
25.06.2020	Novel coronavirus 2019 transmission risk in educational settings	Clin Infect Dis / Article	<ul style="list-style-type: none"> Transmission risk of SARS-CoV-2 in schools is unknown. The authors' investigations especially in pre-schools could not detect SARS-CoV-2 transmission despite screening of symptomatic and asymptomatic children. The data suggests that children are not the primary drivers of SARS-CoV-2 transmission in schools and could help inform exit strategies for lifting of lockdowns.
26.06.2020	Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> During Jan 22–June 7, among 1,573,211 laboratory-confirmed cases of SARS-CoV-2 infection reported to CDC as part of national COVID-19 surveillance, a total of 326,335 (20.7%) occurred among women aged 15–44 years. Data on pregnancy status were available for 91,412 (28.0%) of these women; 8,207 (9.0%) were pregnant. Findings suggest that among women of reproductive age with COVID-19, pregnant women are more likely to be hospitalized and at increased risk for ICU admission and receipt of mechanical ventilation compared with nonpregnant women, but their risk for death is similar.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
24.06.2020	Determinants of COVID-19 disease severity in patients with cancer	Nat Med / Letter	<ul style="list-style-type: none"> • As of 10 April 2020, NY State had 180,458 cases of SARS-CoV-2 and 9,385 reported deaths. • Patients with cancer comprised 8.4% of deceased individuals. • Population-based studies from China and Italy suggested a higher COVID-19 death rate in patients with cancer, although there is a knowledge gap as to which aspects of cancer and its treatment confer risk of severe COVID-19. • Overall, COVID-19 in patients with cancer is marked by substantial rates of hospitalization and severe outcomes. • The association observed between ICI and COVID-19 outcomes in this study will need further interrogation in tumour-specific cohorts.
18.06.2020	Exploring the vulnerability to COVID19 between communities in England	The Place-Based Longitudinal Data Resource (PLDR) / Data analysis	<ul style="list-style-type: none"> • The authors' conducted a cross-sectional ecological analysis across the 6,791 Middle Super Output Areas (MSOAs) in England, using data provided by ONS on COVID-19 deaths of patients as occurred in England between 1 Mar and 31 May 2020. • The Isles of Scilly (E02006781) and City of London (E02006781) have been excluded due to missing data in these areas, leaving 6789 MSOAs for analysis. • The findings indicate high levels of vulnerability to COVID19 are clustered within the North West, West Midlands and North East regions. • Control measures and policies to shield certain groups need to take into account these factors targeting resources and proportionate to the greater needs experienced by some communities.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
25.06.2020	Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study	The Lancet Psychiatry / Article	<ul style="list-style-type: none"> • Investigated the breadth of complications of COVID-19 across the UK that affected the brain. 53 unique cases met the clinical case definitions by clinicians in the UK. • 77 (62%) of 125 patients presented with a cerebrovascular event, of whom 57 (74%) had an ischaemic stroke, nine (12%) an intracerebral

			<p>haemorrhage, and one (1%) CNS vasculitis. 39 (31%) of 125 patients presented with altered mental status, comprising nine (23%) patients with unspecified encephalopathy and seven (18%) patients with encephalitis.</p> <ul style="list-style-type: none"> • Found that altered mental status was the second most common presentation, comprising encephalopathy or encephalitis and primary psychiatric diagnoses, often occurring in younger patients.
26.06.2020	Potential Indirect Effects of the COVID-19 Pandemic on Use of Emergency Departments for Acute Life-Threatening Conditions - United States, January-May 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • In the 10 weeks following declaration of the COVID-19 national emergency, ED visits declined 23% for heart attack, 20% for stroke, and 10% for hyperglycaemic crisis. • Communication from public health and health care professionals should reinforce the importance of timely care for acute health conditions and assure the public that EDs are implementing infection prevention and control guidelines to ensure the safety of patients and health care personnel.
24.06.2020	A geotemporal survey of hospital bed saturation across England during the first wave of the COVID-19 Pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Describes the pattern of bed occupancy across England during the first wave of the pandemic, found that an adequate supply of all bed-types existed at a national level. • Due to an unequal distribution of bed utilization, many trusts spent a significant period operating above safe occupancy thresholds, despite substantial capacity in geographically co-located trusts; a key operational issue to address in preparing for a potential second wave.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
24.06.2020	Prolonged Infectivity of SARS-CoV-2 in Fomites	Emerg Infect Dis / Research Letter	<ul style="list-style-type: none"> • Evaluated the stability and infectivity of SARS-CoV-2 deposited on polystyrene plastic, aluminium, and glass for 96 hours at 45%–55% relative humidity and 19°C –21°C temperature range using a 106 50% tissue culture infectivity dose (TCID50)/mL inoculum. • Showed that a moderate protein concentration in droplets markedly increased the infectivity of SARS-CoV-2, suggesting that a protein-rich medium like airway secretions could protect the virus when it is expelled and may enhance its persistence and transmission by contaminated fomites. • Accordingly, it is plausible that fomites infected with SARS-CoV-2 play a key role in the indirect transmission of coronavirus.

24.06.2020	Randomized Re-Opening of Training Facilities during the COVID-19 pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Randomised study of a total of 3,764 individuals in Oslo, Norway, to investigate SARS-CoV-2 virus transmission attributable to training facilities. • In the training arm, 81.8 percent trained at least once at the facilities. Out of 3,016 individuals who returned the SARS-CoV-2 PCR tests, there was one positive test, where contact tracing revealed the workplace as transmission source. There were no outpatient visits or hospital admissions due to COVID-19 in either group. • Provided good hygiene and social distancing measures, there was no increased COVID-19 spread at training facilities.
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Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
24.06.2020	Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: The GRECCO-19 Randomized Clinical Trial	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Evaluated the effect of treatment with colchicine on cardiac and inflammatory biomarkers and clinical outcomes in patients hospitalized with COVID-19. • In this prospective, open-label, randomized clinical trial (the Greek Study in the Effects of Colchicine in COVID-19 Complications Prevention), 105 patients hospitalized with COVID-19 were randomized in a 1:1 allocation from April 3 to April 27, 2020, to either standard medical treatment or colchicine with standard medical treatment. • Participants who received colchicine had statistically significantly improved time to clinical deterioration. • There were no significant differences in high-sensitivity cardiac troponin or C-reactive protein levels, but these findings should be interpreted with caution.
24.06.2020	Tocilizumab in patients with severe COVID-19: a retrospective cohort study	The Lancet Rheumatology / Article	<ul style="list-style-type: none"> • Assessed the role of tocilizumab in reducing the risk of invasive mechanical ventilation and death in patients with severe COVID-19 pneumonia who received standard of care treatment. • This retrospective, observational cohort study included adults (≥ 18 years) with severe COVID-19 pneumonia who were admitted to tertiary care centres in Bologna and Reggio Emilia, Italy, between Feb 21 and Mar 24, 2020, and a tertiary care centre in Modena, Italy, between Feb 21 and April 30, 2020. Of 1351 patients admitted, 544 (40%) had severe COVID-19 pneumonia and were included in the study. • Found that treatment with tocilizumab, whether administered

			intravenously or subcutaneously, might reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia.
24.06.2020	Pixatimod (PG545), a clinical-stage heparan sulfate mimetic, is a potent inhibitor of the SARS-CoV-2 virus	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study showing that pixatimod, a heparan sulfate mimetic with known anti-cancer, anti-inflammatory and also antiviral properties, inhibits binding of recombinant S1 RBD to Vero cells which express the ACE2 receptor. • In assays with three different isolates of live SARS-CoV-2 virus, pixatimod effectively inhibited viral infection of Vero cells. • Importantly, its potency is well within its safe therapeutic dose range.

Miscellaneous

Publication Date	Title/URL	Journal/ Article type	Digest
25.06.2020	SARS-CoV-2 does not replicate in embryonated hen's eggs or in MDCK cell lines	Eurosurveillance / Rapid Communication	<ul style="list-style-type: none"> • Investigated if SARS-CoV-2 could be propagated in embryonated hen's eggs or the most used mammalian cell lines that are currently used for propagating influenza viruses (in both the diagnostic laboratory and in vaccine production), MDCK cells and variants of this cell line. • Found that neither could support SARS-CoV-2 replication. • This finding will reassure influenza vaccine production staff and laboratory scientists who might be concerned about potential exposure to SARS-CoV-2 and also suggests that loss of potentially important influenza candidate vaccine viruses or final vaccine lots due to SARS-CoV-2 contamination is unlikely.
24.06.2020	The remaining unknowns: A determination of the current research priorities for COVID-19 by the global health research community	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • International mixed methods study, seeking the views of the global research community to build on the WHO's March 2020 Global Research Roadmap. • The WHO roadmap is globally relevant, however, new important priorities have emerged, in particular, pertinent to low and lower-middle income countries (less resourced countries), where health systems are under significant competing pressures. • They also found a shift from prioritising vaccine and therapeutic development towards a focus on assessing the effectiveness, risks, benefits and trust in the variety of public health interventions and measures, and they highlight the temporal nature of these research priorities, some of which can only be undertaken within the period of virus transmission.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
23.06.2020	Covid-19: Call for a rapid forward looking review of the UK's preparedness for a second wave-an open letter to the leaders of all UK political parties	Bmj / Letter
24.06.2020	Rapid roll out of SARS-CoV-2 antibody testing-a concern	Bmj / Letter
24.06.2020	Observational study of UK mobile health apps for COVID-19	The Lancet Digital Health / Comment
01.06.2020	Colchicine for the Treatment of Myocardial Injury in Patients With Coronavirus Disease 2019 (COVID-19)-An Old Drug With New Life?	JAMA Netw Open / Invited commentary
24.06.2020	Can tocilizumab calm the cytokine storm of COVID-19?	The Lancet Rheumatology / Comment
21.06.2020	Validity of the UK Early Access to Medicines Scheme Criteria for Remdesivir use in patients with COVID-19 disease	J Infect / Letter
21.06.2020	Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibodies in Pets in Wuhan, China	J Infect / Letter
23.06.2020	Pandemic publishing poses a new COVID-19 challenge	Nat Hum Behav / Comment

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