



International EPI Cell Daily Evidence Digest – 11/06/2020

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
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Treatment
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
08.06.2020	SARS-CoV-2 virus and antibodies in front-line Health Care Workers in an acute hospital in London: preliminary results from a longitudinal study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• 200 front-line Healthcare Workers (HCWs) tested 26 Mar - 8 Apr 2020; twice-weekly self-administered nose and throat swabs, monthly blood samples.• During first month, 42/200 (21%) HCWs were PCR positive in at least one nose and throat swab. Of those, only 8/42(19%) had symptoms that met the current case definition.• 181 HCWs provided enrolment and follow-up blood samples: 82/181 (45.3%) were seropositive; 36/181 (19.9%) seroconverted during the study and 46/181 (25.4%) were seropositive at both time points. In 33

			<p>HCWs who had positive serology at baseline but were PCR negative, 32 remained PCR negative throughout follow-up.</p> <ul style="list-style-type: none"> • Extremely high seropositivity and RNA detection in this cohort of front-line HCWs who worked during the peak of the pandemic. Implications for planning for expected second wave and for future vaccination roll out campaigns in similar settings. Asymptomatic surveillance of HCWs is essential. • Study sets the foundations to answer pertinent questions around the duration of protective immune response and the risk of re-infection.
06.06.2020	Sex differences in immune responses to SARS-CoV-2 that underlie disease outcomes	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Examined sex differences in viral loads, SARS-CoV-2-specific antibody titres, plasma cytokines, and blood cell phenotyping in COVID-19 patients. Focused on patients with mild to moderate disease who had not received immunomodulatory medications. • Male patients had higher plasma levels of innate immune cytokines and chemokines including IL-8, IL-18, and CCL5, along with more robust induction of non-classical monocytes. • Female patients mounted significantly more robust T cell activation during SARS-CoV-2 infection, which was sustained in old age. • A poor T cell response negatively correlated with patients age and was predictive of worse disease outcome in male patients, but not female. Conversely, higher innate immune cytokines in female patients associated with worse disease progression, but not in male patients. • Possible explanation for observed sex biases in COVID-19; important basis for development of sex-based approach to treatment and care.

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Clinical and virological data were obtained from 129 hospitalized COVID-19 patients (89 intensive care, 40 medium care). • Infectious virus shedding detected in 23 patients (17,8%). Median duration of shedding was 8 days post onset of symptoms (IQR 5-11); probability of detecting infectious virus dropped below 5% after 15,2 days post onset of symptoms (95% confidence interval (CI) 13,4-17,2). • Patients with severe or critical COVID-19 may shed infectious virus for longer periods of time. Drops to undetectable levels below a viral RNA

load threshold and once serum neutralizing antibodies are present, which warrants the use of quantitative viral RNA load assays and serological assays in test-based strategies to discontinue or de-escalate infection prevention and control precautions.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	The hypothalamus as a hub for putative SARS-CoV-2 brain infection	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study targets and consequences of COVID-19 brain infection. Hypothalamic neural circuits play key roles in sex differences, diabetes, hypertension, obesity and aging, all risk factors for severe COVID-19, besides being connected to brainstem cardiorespiratory centres. • Human brain gene-expression analyses reveal that the hypothalamus and associated regions express angiotensin-converting enzyme 2 and transmembrane proteinase, serine 2, which mediate SARS-CoV-2 cellular entry, in correlation with several genes or pathways involved in physiological functions or viral pathogenesis. • Immunolabeling in human and animal brains suggests that the hypothalamus could be central to SARS-CoV-2 brain invasion through multiple routes, and that sex hormones and metabolic diseases influence brain susceptibility.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
04.06.2020	Severe and fatal forms of COVID-19 in children	Arch Pediatr / Research paper	<ul style="list-style-type: none"> • Retrospective, single-centre, observational study in a paediatric intensive and high-dependency care unit. 27 patients, 1 month to 18 years. • Comorbidities (n = 19, 70%) mainly neurological (n = 7), respiratory, (n = 4), sickle cell disease (n = 4). Respiratory involvement was observed in 24 patients (89%). • Supportive treatments were invasive mechanical ventilation (n = 9), catecholamine (n = 4), erythropoiesis (n = 4), renal replacement therapy (n = 1), and extracorporeal membrane oxygenation (n = 1). Five

children died, three without past medical history.

- Highlights large spectrum of clinical presentation and time course of disease progression plus non-negligible occurrence of paediatric life-threatening and fatal cases of COVID-19 mostly in patients with comorbidities.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	Independent Correlates of Hospitalization in 2040 Patients with COVID-19 at a Large Hospital System in Michigan, United States	J Gen Intern Med / Concise research report	<ul style="list-style-type: none"> • Identified correlates for hospitalization in a large cohort of COVID-19 patients in Michigan. • Of 2040 COVID-19 positive patients, 1305 (64.0%) were hospitalized and 735 (36.0%) were evaluated in the Emergency Department (ED), discharged home, and did not require re-evaluation within 14 days. • Older age, medical comorbidities, obesity, ACE-I/ARB use, and male sex are independent correlates of hospitalization in COVID-19 patients presenting to the emergency department.
05.06.2020	Prevalence and Impact of Myocardial Injury in Patients Hospitalized with COVID-19 Infection	J Am Coll Cardiol / Original investigation	<ul style="list-style-type: none"> • Describe the degree of myocardial injury and associated outcomes in a large hospitalized cohort with laboratory-confirmed COVID-19. • Patients with COVID-19 admitted to one of five Mount Sinai Health System hospitals in New York City between Feb 27th and Apr 12th, 2020 with troponin-I (normal value <0.03ng/mL) measured within 24 hours of admission were included (n=2,736). • A total of 506 (18.5%) patients died during hospitalization. • Myocardial injury is prevalent among patients hospitalized with COVID-19 however troponin concentrations were generally present at low levels. Patients with CVD are more likely to have myocardial injury than patients without CVD. Troponin elevation among patients hospitalized with COVID-19 is associated with higher risk of mortality.
05.06.2020	Body temperature correlates with mortality in COVID-19 patients	Crit Care / Research letter	<ul style="list-style-type: none"> • Body temperature (BT) is a potential COVID-19 prognostic marker. Authors analyse how BT monitoring might inform mortality rate estimates, 7614 patients included. • One in three patients reaching a maximum BT above 39.5 °C died. Approximately 5-fold increase in mortality rate compared to patients whose temperature never broke 37 °C. In contrast, almost half of the patients initially presenting with low BT (< 35.5 °C) died.

			<ul style="list-style-type: none"> • A clear trend in increased mortality among patients with poor temperature control highlights usefulness of this non-invasively and easily obtained parameter for evaluating patients' prognoses.
08.06.2020	Non-febrile COVID-19 patients were common and often became critically ill: a retrospective multicenter cohort study	Crit Care / Letter	<ul style="list-style-type: none"> • To understand the prevalence of fever in COVID-19 and its correlation with other symptoms and outcomes, the authors conducted a chart review of 252 hospitalized patients from 15 participating hospitals in Guangdong, Hubei, and Jiangxi provinces, China, from Jan 19 to Mar 6, 2020. • No significant difference in any of the recorded comorbidities was observed between febrile and non-febrile patients. • Given the high proportion of non-febrile patients in COVID-19, and that 20% non-febrile patients became critically ill, heightened attention for this elusive group of patients may be required for a better containment of the pandemic.
10.06.2020	Hyperpyrexia in COVID-19 patients	J Med Virol / Short communication	<ul style="list-style-type: none"> • Hyperpyrexia is an elevation of body temperature (BT) above 106.7 °F (41.5 °C) due to an abnormally increased hypothalamic thermoregulatory set. • The authors present clinical features and outcomes of six COVID-19 patients who had developed hyperpyrexia during hospitalization. All patients died shortly after the onset of hyperpyrexia. The duration from the first occurrence of hyperpyrexia to death ranged between 3 to 45 hours (mean 17 hours, median 9.5 hours). • Hyperpyrexia seems to adversely impact the outcomes and mortality in patients with COVID-19.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
05.06.2020	Clinical characteristics of invasive pulmonary aspergillosis in patients with COVID-19 in Zhejiang, China: a retrospective case series	Crit Care / Letter	<ul style="list-style-type: none"> • The clinical characteristics and risk factors of invasive pulmonary aspergillosis (IPA) in patients with COVID-19 are not well defined. • Collected clinical data for 104 patients with COVID-19 between Jan and Mar 2020 in the First Affiliated Hospital of Zhejiang University, China. • The incidence rate of IPA among COVID-19 patients was lower than those among patients with influenza (7.7% vs 19%). Older age, initial antibiotic usage of β-lactamase inhibitor combination, mechanical ventilation, and COPD were the risk factors of IPA among patients with

			<p>COVID-19.</p> <ul style="list-style-type: none"> • Early intervention with bronchoscopy, observation of changes in the bronchial mucosa, and obtaining evidence of fungal microbiology were important in patients with severe/critical COVID-19.
Sept 2020	Guillain-Barré syndrome: The first documented COVID-19-triggered autoimmune neurologic disease: More to come with myositis in the offing	Neurol Neuroimmunol Neuroinflamm / Article	<ul style="list-style-type: none"> • Eleven Guillain-Barré syndrome (GBS) cases in four key COVID-19 hotspots discussed presenting symptoms, response to therapies, cross-reactivity of COVID spike proteins with nerve glycolipids. • Emerging cases of COVID-19–triggered autoimmune necrotizing myositis (NAM) and encephalopathies also reviewed in context of viral invasion, autoimmunity and ongoing immunotherapies. • COVID-19 can trigger not only GBS but other autoimmune neurological diseases necessitating vigilance for early diagnosis and therapy initiation.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	Characteristics of registered clinical trials assessing treatments for COVID-19: a cross-sectional analysis	BMJ Open / Original research	<ul style="list-style-type: none"> • Characterises registered clinical trials on WHO’s International Clinical Trials Registry Platform. 201 registered for testing therapeutic benefits of 92 drugs or plasma for COVID-19, including 64 in monotherapy and 28 different combinations. Only eight (8.7%) products or combinations involved new molecular entities. • Many trials lack features to optimise their scientific value. Global coordination and increased funding of high-quality research may help to maximise scientific progress.
06.06.2020	ICON (Ivermectin in COvid Nineteen) study: Use of Ivermectin is Associated with Lower Mortality in Hospitalized Patients with COVID19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Retrospective cohort study of consecutive COVID-19 patients to see if ivermectin associated with lower mortality rate: 280 patients, mean age 59.6 years [standard deviation 17.9], 45.4% female), of whom 173 were treated with ivermectin and 107 were usual care were reviewed • Ivermectin associated with lower mortality during treatment (25.2% versus 15.0%, OR 0.52, 95% CI 0.29-0.96, P=.03), especially in patients who required higher inspired oxygen or ventilatory support, but there was no significant difference in successful extubation rates (36.1% vs 15.4%, OR 3.11 (0.88-11.00), p=.07).

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
07.06.2020	Depression, Anxiety and Stress during COVID-19: Associations with Changes in Physical Activity, Sleep, Tobacco and Alcohol Use in Australian Adults	Int J Environ Res Public Health / Article	<ul style="list-style-type: none"> • Examined the associations between psychological distress and changes in selected health behaviours since the onset of COVID-19 in Australia. • An online survey was distributed in April 2020 and included measures of depression, anxiety, stress, physical activity, sleep, alcohol intake and cigarette smoking. The survey was completed by 1491 adults (mean age 50.5 ± 14.9 years, 67% female). • Negative change was reported for physical activity (48.9%), sleep (40.7%), alcohol (26.6%) and smoking (6.9%) since the onset of the COVID-19 pandemic. • Significantly higher scores in one or more psychological distress states were found for females, and those not in a relationship, in the lowest income category, aged 18–45 years, or with a chronic illness. • Ongoing evaluation of the impact of lifestyle changes associated with the pandemic is needed.
02.06.2020	Mental health outcomes of quarantine and isolation for infection prevention: A systematic umbrella review of the global evidence	Epidemiol Health / Review paper	<ul style="list-style-type: none"> • Review aimed to synthesize available evidence on mental health outcomes of quarantine and isolation for preventing infectious diseases. • Eight reviews included. Report high burden of mental health problems among patients, informal caregivers, and healthcare providers. Include depression, anxiety, mood disorders, psychological distress, posttraumatic stress disorder, insomnia, fear, stigmatization, low self-esteem, lack of self-control, and other adverse mental health outcomes.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
08.06.2020	Using socioeconomics to counter health disparities arising from the covid-19 pandemic	Bmj / Analysis
09.06.2020	Covid-19: Test and trace system is not fit for purpose, says Independent SAGE	Bmj / News
10.06.2020	Hydroxychloroquine side-effects raise concerns for rheumatology patients	The Lancet Rheumatology / News
05.06.2020	Implications of antibody-dependent enhancement of infection for SARS-CoV-2 countermeasures	Nat Biotechnol / Correspondence
08.06.2020	Dissecting antibody-mediated protection against SARS-CoV-2	Nat Rev Immunol / Comment
08.06.2020	COVID 19: Frontline experience at a tertiary care hospital in UK	J Glob Health / Viewpoint