



International EPI Cell Daily Evidence Digest – 17/06/2020

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
- Infection control
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
15.06.2020	Systemically comparing host immunity between survived and deceased COVID-19 patients	Cell Mol Immunol / Correspondence	<ul style="list-style-type: none">• The kinetics of immune responses and their association with COVID-19 clinical outcomes remain poorly understood.• Here the characteristics of cellular immune responses in a total of 157 COVID-19 patients enrolled in Tongji Hospital between Feb and Mar 2020 are summarized, and the properties between 95 survived and 62 deceased patients with different onset time are compared.• Collectively, for the first time, data indicate that hypofunction, hyperaction, and anergy may represent the characteristics of immune

			responses in deceased COVID-19 patients in the early, middle, and late stage, respectively.
13.06.2020	Longitudinal immune profiling reveals distinct features of COVID-19 pathogenesis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK report from the Coronavirus Immune Response and Clinical Outcomes (CIRCO) study of hospitalised patients during the peak of the COVID-19 pandemic, showing the relationship between immune responses and severity of the clinical presentation. • Longitudinal analysis showed a very high neutrophil to T cell ratio and abnormal activation of monocytes in the blood, which displayed high levels of the cell cycle marker, Ki67 and low COX-2. These properties all reverted in patients with good outcome. • Unexpectedly, multiple aspects of inflammation were diminished as patients progressed in severity and time, even in ITU patients not recovering.
15.06.2020	Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium	JAMA / Research letter	<ul style="list-style-type: none"> • Belgium has a high burden of COVID-19, especially the region surrounding the Hospital East-Limburg, a tertiary care centre. • In this hospital-wide screening study for SARS-CoV-2 antibodies among hospital staff (n=3065), 197 staff (6.4%) had IgG antibodies for SARS-CoV-2. • Neither being directly involved in clinical care nor working in a COVID-19 unit increased the odds of being seropositive, while having a suspected COVID-19 household contact did. • The high availability of PPE, high standards of infection prevention, and PCR screening in symptomatic staff, coupled with contact tracing and quarantine, might explain a relatively low seroprevalence.
13.06.2020	Seroprevalence against COVID-19 and follow-up of suspected cases in primary health care in Spain	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study to measure the seroprevalence of antibodies against SARS-CoV-2 infection in a community sample of 311 asymptomatic individuals and among 634 symptomatic patients (without confirmed diagnosis) followed in a primary care setting. • 17 asymptomatic individuals were seropositive for IgM and/or IgG, resulting an overall prevalence of 5,47% (95% CI, 3.44-8.58), while 244 symptomatic patients (38.49%) were seropositive. • Results showed that the OR for a positive test was significantly increased in patients who had fever (>38°C), ageusia and contact with a patient diagnosed with COVID-19. • The seroprevalence of antibodies against SARS-CoV-2 among asymptomatic individuals in the general population was lower than expected.

13.06.2020	Prevalence of IgG antibodies to SARS-CoV-2 in Wuhan - implications for the ability to produce long-lasting protective antibodies against SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A study following four groups of individuals who received both COVID-19 IgM/IgG tests and RT-PCR tests for SARS-CoV-2, IgG (1470 hospitalized patients with COVID-19, 3832 healthcare providers without COVID-19 diagnosis, 19555 general workers, and 1616 other patients to be admitted to the hospital (N=26473)). • Prevalence was 89.8% in COVID-19 patients, 4.0% in healthcare providers, 4.6% in general workers, and 1.0% in other patients. IgG prevalence increased significantly by age among healthcare workers and general workers. • Prevalence of IgM antibodies to SARS-CoV-2 was 31.4% in COVID-19 patients, 1.5% in healthcare providers, 1.3% in general workers, and 0.2% in other patients. • Very few healthcare providers had IgG antibodies to SARS-CoV-2, though a significant proportion of them had been infected with the virus. After SARS-CoV-2 infection, people are unlikely to produce long-lasting protective antibodies against this virus.
16.06.2020	Coronavirus protective immunity is short-lasting	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The four seasonal human coronaviruses may reveal common characteristics applicable to all human coronaviruses. • Monitored healthy subjects over a time span of 35 years (1985-2020), providing a total of 2473 follow up person-months, and determined a) the time to reinfection by the same seasonal coronavirus and b) the dynamics of coronavirus antibody depletion post-infection. • Short duration of protective immunity to coronaviruses was found. Reinfections occurred frequently at 12 months post-infection and there was a substantial reduction in antibody levels for each virus as soon as 6 months post-infection. • Limitations: were not able to sequence the virus genome during infection, so strain variation could play a role in susceptibility to reinfection. All male, small sample size (n=10).

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
14.06.2020	Snapshot PCR Surveillance for SARS-CoV-2 in Hospital Staff in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Cross-sectional snapshot survey of HCWs recruited from six UK hospitals to study prevalence of SARS-CoV-2 carriage.

			<ul style="list-style-type: none"> • Point prevalence of SARS-CoV-2 carriage across the sites was 2.0% (23/1152 participants). Symptoms in the past month were associated with threefold increased odds of testing positive. SARS-CoV-2 virus was isolated from only one (5%) of nineteen cultured samples. 39% of participants reported symptoms in the past month. • The point-prevalence is similar to previous estimates for HCWs in April 2020, though a magnitude higher than in the general population. • Based upon interpretation of symptom history and testing results including viral culture, the majority of those testing positive were unlikely to be infectious at time of sampling.
11.06.2020	Multiple assays in a real-time RT-PCR SARS-CoV-2 panel can mitigate the risk of loss of sensitivity by new genomic variants during the COVID-19 outbreak	Int J Infect Dis / Article	<ul style="list-style-type: none"> • <i>Conflict of interest - authors are QIAGEN employees.</i> • 5 SARS-CoV-2 PCR assay panels were evaluated against the accumulated genetic variability of the virus to assess the effect on sensitivity of the individual assays. • As of week 21, 2020, the complete set of available SARS-CoV-2 genomes from GISAID and GenBank databases were used in this study. SARS-CoV-2 primer sequences from publicly available panels (WHO, CDC, NMDC, and HKU) and QIAstat-Dx were included in the alignment, and accumulated genetic variability affecting any oligonucleotide annealing was annotated. • A total of 11,627 (34.38%) genomes included single mutations affecting annealing of any PCR assay. • Stresses the importance of targeting more than one region in the viral genome for SARS-CoV-2 detection to mitigate the risk of loss of sensitivity due to the unknown mutation rate during this SARS-CoV-2 Outbreak.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
15.06.2020	Naturally mutated spike proteins of SARS-CoV-2 variants show differential levels of cell entry	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To investigate whether spike (S) protein mutations affect SARS-CoV-2 infectivity, the authors show that naturally occurring S mutations can reduce or enhance cell entry via ACE2 and TMPRSS2. • Among S variants, the D614G mutant shows the highest viral entry, as supported by structural observations. Nevertheless, the D614G

			<p>mutant remains susceptible to neutralization by antisera against prototypic viruses.</p> <ul style="list-style-type: none"> • Taken together, these data indicate that the D614G mutation enhances viral infectivity while maintaining neutralization susceptibility.
14.06.2020	The D614G mutation in SARS-CoV-2 Spike increases transduction of multiple human cell types	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors performed site-directed mutagenesis on a human codon-optimized spike protein to introduce the D614G variant and produce SARS-CoV-2-pseudotyped lentiviral particles (S-Virus) with this variant and with D614 Spike. • In multiple cell lines, including human lung epithelial cells, S-Virus carrying the recently emerged D614G mutation is up to 8-fold more effective at transducing cells than wild-type S-Virus, providing functional evidence that the D614G mutation in the Spike protein increases transduction of human cells. • Further, the G614 variant is more resistant to cleavage in vitro and in human cells, which may suggest a possible mechanism for the increased transduction. • Given that several vaccines in development and in clinical trials are based on the initial (D614) Spike sequence, this result has important implications for the efficacy of these vaccines in protecting against this recent and highly-prevalent SARS-CoV-2 isolate.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
16.06.2020	Beyond the data: Understanding the impact of COVID-19 on BAME groups	Public Health England / Review	<ul style="list-style-type: none"> • Review of disparities in the risk and outcomes of COVID-19 shows that there is an association between belonging to some ethnic groups and the likelihood of testing positive and dying with COVID-19. • Found that the highest age standardised diagnosis rates of COVID-19 per 100,000 population were in people of Black ethnic groups (486 F and 649 M) and the lowest were in people of White ethnic groups (220 F and 224 M). • Comparing to previous years, all-cause mortality was almost 4 times higher than expected among Black males for this period, almost 3 times higher in Asian males and almost 2 times higher in White males. Among females, deaths were almost 3 times higher in this

			<p>period in Black, Mixed and Other females, and 2.4 times higher in Asian females compared with 1.6 times in White females.</p> <ul style="list-style-type: none"> • These analyses did not account for the effect of occupation, comorbidities or obesity.
16.06.2020	Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • In this study of patients (n=463) infected with SARS-CoV-2 in the metropolitan Detroit area, 76.7% of the patients who were infected were hospitalized and most of these patients were African American. • The high prevalence of comorbidities and severe obesity in the population likely contributed to the disparities in morbidity associated with COVID-19.
12.06.2020	COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study	Lancet Oncol / Article	<ul style="list-style-type: none"> • Studied the effect of SARS-CoV-2 infection on patients with thoracic malignancies. • Between Mar 26 and Apr 12, 2020, 200 patients with COVID-19 and thoracic cancers from 8 countries were identified and included in the TERAVOLT registry; median age was 68.0 years (61.8-75.0) and the majority were current or former smokers (159 [81%] of 196), had non-small-cell lung cancer (151 [76%] of 200), and were on therapy at the time of COVID-19 diagnosis (147 [74%] of 199), with 112 (57%) of 197 on first-line treatment. • Data suggest high mortality and low admission to intensive care in patients with thoracic cancer. Whether mortality could be reduced with treatment in intensive care remains to be determined.
13.06.2020	Electrocardiographic Findings in COVID-19: Insights on Mortality and Underlying Myocardial Processes	J Card Fail /Article	<ul style="list-style-type: none"> • 756 patients who presented to a large New York City teaching hospital with COVID-19 underwent an ECG. The mean age was 63.3 ± 16 years, 37% were women, 61% of patients were non-white, and 57% had hypertension; 90 (11.9%) died. • The study found that patients with ECG findings of both left sided heart disease (APCs, IVB, repolarization abnormalities) and right sided disease (RBBB) have higher odds of death. ST elevation at presentation was rare.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
14.06.2020	Bloodstream infections in critically ill patients with COVID-19	Eur J Clin Invest / Article	<ul style="list-style-type: none"> • Little is known about the incidence and risk of ICU-acquired bloodstream infections (BSI) in critically ill patients with COVID-19.

			<ul style="list-style-type: none"> • This retrospective, single-centre study was conducted in Northern Italy, and the primary study objectives were: (i) to assess the incidence rate of ICU-acquired BSI; (ii) to assess the cumulative risk of developing ICU-acquired BSI. • Overall 78 critically ill patients with COVID-19 were included in the study. • The incidence rate of BSI was high, and the cumulative risk of developing BSI increased with ICU stay. Further study will clarify if the increased risk of BSI detected in COVID-19 patients treated with anti-inflammatory drugs is outweighed by the benefits of reducing any possible proinflammatory dysregulation induced by SARS-CoV-2.
16.06.2020	Bacterial Pneumonia in COVID-19 critically ill patients: a case series	Clin Infect Dis / Correspondence	<ul style="list-style-type: none"> • This correspondence reports on bacterial pneumonia in critically ill patients with COVID-19 diagnosed by bacterial cultures of blind bronchoalveolar lavage (BBAL). • A prospective single-centre study was conducted including every patient admitted to Saint-Louis surgical ICU (Paris) for respiratory failure related to COVID-19. • BBALs were performed in 45 patients during ICU stay; all were mechanically ventilated and suspected of bacterial pneumonia. Bacterial cultures of BBAL grew with significant amount of bacteria (i.e. $\geq 10^4$ CFU/mL) in 37% (n=20) of patients. • A significant rate of bacterial pneumonia was reported, mostly late-onset VAP, in critically ill patients with COVID-19 in this unit.
16.06.2020	Brain MRI Findings in Severe COVID-19: A Retrospective Observational Study	Radiology / Article	<ul style="list-style-type: none"> • Describes the neuroimaging findings (excluding ischemic infarcts) in patients with severe COVID-19 infection. • This was a retrospective study of patients evaluated from Mar 23th, 2020 to Apr 27th, 2020 at 16 hospitals. • Thirty men (81%) and 7 women (19%) met inclusion criteria, with a mean age of 61+/- 12 years. • Patients with severe COVID-19 and without ischemic infarcts had a wide range of neurologic manifestations that were be associated with abnormal brain MRIs. • Eight distinctive neuroradiological patterns were described.
14.06.2020	Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication	BMJ Case Rep / Case report	<ul style="list-style-type: none"> • A 57-year-old man presented with a progressive flaccid symmetrical motor and sensory neuropathy following a 1-week history of cough and malaise. • He was diagnosed with Guillain-Barré syndrome secondary to

		<p>COVID-19 and started on intravenous immunoglobulin.</p> <ul style="list-style-type: none"> • He proceeded to have worsening respiratory function and needed intubation and mechanical ventilation. • This is the first reported case of this rare neurological complication of COVID-19 in the UK, but it adds to a small but growing body of international evidence to suggest a significant association between these two conditions.
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Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
12.06.2020	Contamination of personal protective equipment by SARS-CoV-2 during routine care of patients with mild COVID-19	J Infect / Correspondence	<ul style="list-style-type: none"> • A total of 133 surface swab samples were collected from PPE worn by 19 HCWs caring for the two patients. • Of them, 15 (11%) revealed positive SARS-CoV-2 PCR results in the following areas: top of the head (26%), foot dorsum (26%), sole (16%), wrist (5%), and abdomen (5%). No SARS-CoV-2 RNA was detected on the neck and back. The top of the head, foot dorsum, and sole were more frequently contaminated than the neck, wrist, abdomen, and back (23% [13/57] vs. 3% [2/76], $P < 0.001$ by Fishers' exact test). • Data showed contamination of SARS-CoV-2 on the head, foot dorsum, and sole of the HCWs, even when caring for patients with mild COVID-19 who did not undergo aerosol generating procedures.
15.06.2020	What Has Been the Impact of Covid-19 on Safety Culture?	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Safety culture during Covid-19 at a large UK teaching hospital was compared with data from 2017, using the Safety Attitudes Questionnaire (SAQ). • Significant increases were seen in SAQ score for doctors and AHPs from baseline. A decrease in SAQ was found in the nursing group, largely due to perception of management and safety climate subscales. • During Covid-19, female gender, age 40-49 years, non-white ethnicity, nursing job role were all associated with lower SAQ scores. Training and support for redeployment were associated with higher SAQ scores.

- A significant decrease was seen in error reporting after the onset of the Covid-19 pandemic.

Miscellaneous

Publication Date	Title/URL	Journal/ Article type	Digest
14.06.2020	Publish or perish: Reporting Characteristics of Peer-reviewed publications, pre-prints and registered studies on the COVID-19 pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Comparison of the amount and reporting characteristics of COVID-19 related peer-reviewed and pre-prints publications and the amount of ongoing trials and systematic reviews. • To May 20, 2020, the authors found 3635 peer-reviewed publications and 3805 pre-prints, of which 8.6% (n=329) were published in indexed journals. • Peer-reviewed and pre-print publications amount both increased significantly over time (p<0.001). • Case reports and letters accounted for a greater share of the peer-reviewed compared to pre-print publications. In turn, randomized controlled trials and systematic reviews accounted for a significantly greater share of the pre-print publications, which have been promoted as rapid responses to give direct and prompt access to scientific findings in this pandemic.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
16.06.2020	Dexamethasone reduces death in hospitalised patients with severe respiratory complications of COVID-19	University of Oxford / News
15.06.2020	Covid-19: NHS Test and Trace releases first figures, with experts calling for improvements	Bmj / News analysis
15.06.2020	COVID-19 and the other pandemic: populations made vulnerable by systemic inequity	Nat Rev Gastroenterol Hepatol / Comment
16.06.2020	Seroepidemiologic Study Designs for Determining SARS-COV-2 Transmission and Immunity	Emerg Infect Dis / Perspective
15.06.2020	Biobanks could identify medically actionable findings relevant for COVID-19 clinical care	Nat Med / Correspondence