



International EPI Cell Daily Evidence Digest – 13/07/2020

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- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
10.07.2020	SARS-CoV-2 antibody prevalence in blood in a large school community subject to a Covid-19 outbreak: a cross-sectional study	Clin Infect Dis / Article	<ul style="list-style-type: none">• A SARS-CoV-2 outbreak affecting 52 people from a large school community in Santiago, Chile was identified (March 12), nine days after the first country case.• Implemented a home-delivery, self-administered, IgG/IgM antibody test and survey to a classroom stratified sample of students and all staff from May 4-19, to determine overall seroprevalence rates by age group, reported symptoms, contact exposure and to explore dynamics of transmission.

			<ul style="list-style-type: none"> • Antibody positivity rates were 9.9% (95%CI: 8.2-11.8) for 1,009 students and 16.6% (95%CI: 12.1-21.9) for 235 staff. Among students, positivity was associated with younger age (P=0.01), lower grade level (P=0.05), prior RT-PCR positivity (P=0.03), and history of contact with a confirmed case (P<0.001). Among staff, positivity was higher in teachers (P=0.01) and in those previously RT-PCR positive (P<0.001). • Teachers were more affected during the outbreak and younger children were at higher infection risk, likely because index case(s) were teachers and/or parents from preschool.
08.07.2020	Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital	Nat Commun / Article	<ul style="list-style-type: none"> • This study (which was previously included as a pre-print) estimated the seroprevalence against SARS-CoV-2 in a random sample of HCW from a large hospital in Spain. • Of the 578 participants recruited from 28 Mar to 9 Apr 2020, 54 (9.3%, 95% CI: 7.1-12.0) were seropositive for IgM and/or IgG and/or IgA against SARS-CoV-2. • The cumulative prevalence of SARS-CoV-2 infection (presence of antibodies or past or current positive rRT-PCR) was 11.2% (65/578, 95% CI: 8.8-14.1). • Among those with evidence of past or current infection, 40.0% (26/65) had not been previously diagnosed with COVID-19. • A large proportion of HCW with past or present infection had not been previously diagnosed with COVID-19, which calls for active periodic rRT-PCR testing in hospital settings.
09.07.2020	Disappearance of antibodies to SARS-CoV-2 in a Covid-19 patient after recovery	Clin Microbiol Infect / Letter	<ul style="list-style-type: none"> • The authors' have estimated the longevity of specific antibodies against SARS-CoV-2, and reported antibodies disappeared in a moderate COVID-19 patient within 3 months after the onset of the symptoms.
09.07.2020	Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using sequential serum samples collected up to 94 days post onset of symptoms (POS) from 65 RT-qPCR confirmed SARS-CoV-2-infected individuals, this UK study shows seroconversion in >95% of cases and neutralizing antibody (nAb) responses when sampled beyond 8 days POS. • The magnitude of the nAb response is found to be dependent upon the disease severity, but this does not affect the kinetics of the nAb response. Declining nAb titres were observed during the follow up period. Whilst some individuals with high peak ID50 (>10,000) maintained titres >1,000 at >60 days POS, some with

			<p>lower peak ID50 had titres approaching baseline within the follow up period.</p> <ul style="list-style-type: none"> • The authors suggest that this transient nAb response is a feature shared by both a SARS-CoV-2 infection that causes low disease severity and the circulating seasonal coronaviruses that are associated with common colds.
10.07.2020	Clinical utility of targeted SARS-CoV-2 serology testing to aid the diagnosis and management of suspected missed, late or post-COVID-19 infection syndromes: results from a pilot service	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To determine indications and clinical utility of SARS-CoV-2 serology testing in adults and children, patient serum from 110 (72 adults, 38 children) vetted referrals was tested on CE marked and internally validated lateral flow immunoassay (LFIA) (SureScreen Diagnostics) detecting antibodies to SARS-CoV-2 spike proteins. • The LFIA was deemed suitable for clinical advice and decision making following evaluation with 310 serum samples from SARS-CoV-2 PCR positive patients and 300 pre-pandemic samples, giving a sensitivity and specificity of 96.1% and 99.3% respectively. • The study showed the benefit of introducing a serology service where there is a reasonable pre-test probability, and the result can be linked with clinical advice or intervention. Given recent evidence for a rapid decline in antibodies, particularly following mild infection, there is likely a limited window of opportunity to realise the benefit of serology testing for individuals infected during the first-wave before they potentially fall below a measurable threshold.
09.07.2020	Self-amplifying RNA SARS-CoV-2 lipid nanoparticle vaccine candidate induces high neutralizing antibody titers in mice	Nat Commun / Article	<ul style="list-style-type: none"> • Here, the authors' present a self-amplifying RNA encoding the SARS-CoV-2 spike protein encapsulated within a lipid nanoparticle (LNP) as a vaccine. • The study observes remarkably high and dose-dependent SARS-CoV-2 specific antibody titres in mouse sera, as well as robust neutralization of both a pseudo-virus and wild-type virus. • Upon further characterization the study also finds that the neutralization is proportional to the quantity of specific IgG and of higher magnitude than recovered COVID-19 patients. saRNA LNP immunizations induce a Th1-biased response in mice, and there is no antibody-dependent enhancement (ADE) observed.

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
08.07.2020	Inactivation analysis of SARS-CoV-2 by specimen transport media, nucleic acid extraction reagents, detergents and fixatives	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • PHE-led study to evaluate 23 commercial reagents designed for clinical sample transportation, nucleic acid extraction and virus inactivation for their ability to inactivate SARS-CoV-2, as well as seven other common chemicals including detergents and fixatives. • They also tested five filtration matrices for their effectiveness at removing the cytotoxic elements of each reagent, permitting accurate determination of levels of infectious virus remaining following treatment. • These data provide a framework for other laboratories to validate their inactivation processes and to guide similar studies for other pathogens.
09.07.2020	Saliva offers a sensitive, specific and non-invasive alternative to upper respiratory swabs for SARS-CoV-2 diagnosis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study to compare saliva as a non-invasive, equipment independent alternative to swabs, which analysed 145 paired saliva and nasal/throat (NT) swabs collected at diagnosis (day 0) and repeated on day 2 and day 7 and day 28 for study follow up. • Self-collected saliva samples were found to be consistent, and in some cases superior when compared to healthcare worker collected NT swabs from COVID-19 suspected participants.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
09.07.2020	Revealing COVID-19 transmission in Australia by SARS-CoV-2 genome sequencing and agent-based modeling	Nat Med / letter	<ul style="list-style-type: none"> • Here the authors' examine the added value of near real-time genome sequencing of SARS-CoV-2 in a subpopulation of infected patients during the first 10 weeks of COVID-19 containment in Australia and compare findings from genomic surveillance with predictions of a computational agent-based model (ABM). • The authors' report that the prospective sequencing of SARS-CoV-2 clarified the probable source of infection in cases where epidemiological links could not be determined, significantly decreased the proportion of COVID-19 cases with contentious links, documented genomically similar cases associated with concurrent

			<p>transmission in several institutions and identified previously unsuspected links.</p> <ul style="list-style-type: none"> • Only a quarter of sequenced cases appeared to be locally acquired and were concordant with predictions from the ABM. • These high-resolution genomic data are crucial to track cases with locally acquired COVID-19 and for timely recognition of independent importations once border restrictions are lifted and trade and travel resume.
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Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Severe refractory Kawasaki disease in seven infants in the COVID-19 era	The Lancet Rheumatology / Correspondence	<ul style="list-style-type: none"> • Describes a cohort of seven infants (aged ≤ 1 year) with severe Kawasaki-like disease who were diagnosed and treated at five hospitals in the UK between February and March, 2020.
10.07.2020	Change in the Incidence of Stillbirth and Preterm Delivery During the COVID-19 Pandemic	JAMA / Research letter	<ul style="list-style-type: none"> • High rates of preterm birth and caesarean delivery have been reported in women with SARS-CoV-2 infection. • However, studies have inadequate power to assess uncommon outcomes like stillbirth (foetal death ≥ 24 weeks' gestation). • The UK Obstetric Surveillance System reported 3 stillbirths among 247 completed pregnancies in women with confirmed COVID-19 vs the national rate (12.1 per 1000 births vs 4-5 per 1000 births). • The authors' assessed the change in stillbirth and preterm delivery rates during the pandemic.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
09.07.2020	Evolution and impact of COVID-19 outbreaks in care homes: population analysis in 189 care homes in one geographic region	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This study systematically examines care-home outbreaks of COVID-19 in a large Scottish health board. • 70 (37.0%) of care-homes experienced a COVID-19 outbreak, 66 of which were in care-homes for older people where care-home size was strongly associated with outbreaks. • There were 852 confirmed cases and 419 COVID-related deaths,

			<p>401 (95.7%) of which occurred in care-homes with an outbreak, 16 (3.8%) in hospital, and two in the 119 care-homes without a known outbreak.</p> <ul style="list-style-type: none"> • For non-COVID related deaths, there were 73 excess deaths in care-homes with an outbreak, but no excess deaths in care-homes without an outbreak, and 24 fewer deaths than expected of care-home residents in hospital. A quarter of COVID-19 related cases and deaths occurred in five (2.6%) care-homes, and half in 13 (6.9%) care-homes.
08.07.2020	A case-control and cohort study to determine the relationship between ethnic background and severe COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To examine the relationship between ethnic background and (1) hospital admission for severe COVID-19; (2) in-hospital mortality, the authors conducted a case-control study of 872 inner city adult residents admitted to hospital with confirmed COVID-19 (cases) and 3,488 matched controls, along with a cohort study of 1827 adults consecutively admitted with COVID-19. • The 872 cases comprised 48.1% Black, 33.7% White, 12.6% Mixed/Other and 5.6% Asian patients. Black and Mixed/Other ethnicity were associated with higher admission risk than white. Asian ethnicity was not associated with higher admission risk. • In the cohort study of 1827 patients, 455 (28.9%) died over a median (IQR) of 8 (4-16) days. Age and male sex, but not Black or Mixed/Other ethnicity, were associated with in-hospital mortality. Asian ethnicity was associated with higher in-hospital mortality.
08.07.2020	COVID-19: Outcomes of patients with confirmed COVID-19 re-admitted to hospital	J Infect / Letter	<ul style="list-style-type: none"> • Investigated the clinical outcomes of patients with confirmed COVID-19 who were re-admitted to hospital, in order to identify risk factors for patients discharged and subsequent management of COVID-19 in clinical practice. • Of 729 positive patients (in North Middlesex University Hospital), 391 of whom were discharged, 39 patients re-presented to the hospital Emergency Department, with 25 then requiring re-admission. • Data suggests patients with COVID-19 who are re-admitted may be at increased risk of hypoxia and death.
08.07.2020	Clinical features and outcomes of adult COVID-19 patients co-infected with Mycoplasma pneumoniae	J Infect / Letter	<ul style="list-style-type: none"> • Describes the clinical features and outcomes of COVID-19 patients co-infected with <i>Mycoplasma pneumoniae</i> (MP). • Among a total of 874 patients with laboratory-confirmed COVID-19, the overall rate of MP co-infection was 2.5% (22 of the 874 patients). In this study, 88 patients with COVID-19 mono-infection were matched as the control group using the propensity score.

			<ul style="list-style-type: none"> • There were no significant associations between MP co-infection and major complaints on admission, but an approximate of 4 days increase in the length of cough was reported. Importantly, the already elevated risk of thrombosis in COVID-19 patients is significantly increased by the co-infection with MP
10.07.2020	Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study	The Lancet Haematology / Article	<ul style="list-style-type: none"> • Changes in haematological characteristics in patients with COVID-19 are emerging as important features of the disease, and this article explores the haematological characteristics and related risk factors in patients with COVID-19. • Of 466 patients admitted to hospital from Jan 23 to Feb 23, 2020, 380 patients with COVID-19 were included in this study. • The incidence of thrombocytopenia (platelet count <100 × 10⁹ cells per L) in patients with critical disease (42 [49%] of 86) was significantly higher than in those with severe (20 [14%] of 145) or moderate (nine [6%] of 149) disease (p<0.0001). • Rapid blood tests, including platelet count, prothrombin time, D-dimer, and neutrophil to lymphocyte ratio can help clinicians to assess severity and prognosis of patients with COVID-19. • The sepsis-induced coagulopathy scoring system can be used for early assessment and management of patients with critical disease.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Community prevalence of SARS-CoV-2 virus in England during May 2020: REACT study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The REal-time Assessment of Community Transmission (REACT) study is a nationally representative prevalence survey of SARS-CoV-2 virus swab-positivity in the community in England, which found 159 positives from 120,610 swabs giving an average prevalence of 0.13% (95% CI: 0.11%,0.15%) from 1st May to 1st June 2020. • Results showed decreasing prevalence with a halving time of 8.6 (6.2, 13.6) days, implying an overall reproduction number R of 0.57 (0.45, 0.72). Adults aged 18 to 24 yrs had the highest swab-positivity rates, while those >64 yrs had the lowest. • Symptoms strongly associated with swab-positivity were: nausea and/or vomiting, diarrhoea, blocked nose, loss of smell, loss of taste, headache, chills and severe fatigue. Recent contact with a known

			<p>COVID-19 case was associated with odds of 24 (16, 38) for swab-positivity.</p> <ul style="list-style-type: none"> • Compared with non-key workers, odds of swab-positivity were 7.7 (2.4, 25) among care home workers and 5.2 (2.9, 9.3) among health care workers.
10.07.2020	Characteristics and transmission dynamics of COVID-19 in healthcare workers at a London teaching hospital	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To examine the characteristics and transmission dynamics of SARS-CoV-2 in HCWs in a university teaching hospital in London, staff sickness and COVID-19 rates from Mar to Apr 2020 were compared with staff professional groups, department of work and ethnicity. • COVID-19 rates in HCWs largely rose and declined in parallel with the number of community cases. White and non-white ethnic groups among the HCWs had similar rates of infection. Clinical staff had a higher rate of laboratory-confirmed COVID-19 than non-clinical staff, but total sickness rates were similar. • Doctors had the highest rate of infection, but took the fewest sickness days. Critical Care had lower rates than the Emergency Department (ED), but rates in the ED declined once all staff were advised to use PPE.
10.07.2020	Diagnostic value of skin manifestation of SARS-CoV-2 infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using data collected on a subset of 336,847 eligible UK users of the COVID Symptom Study app, it was observed that 8.8% of the swab positive cases (total: 2,021 subjects) reported either a body rash or an acral rash, compared to 5.4% of those with a negative swab test (total: 25,136). Together, these two skin presentations showed an odds ratio (OR) of 1.67 for being swab positive. • Skin rashes were also predictive in the larger untested group of symptomatic app users (N=54,652), as 8.2% of those who had reported at least one classical COVID-19 symptom, i.e., fever, persistent cough, and/or anosmia, also reported a rash. • Data from an independent online survey of 11,546 respondents with a rash showed that in 17% of swab positive cases, the rash was the initial presentation. Furthermore, in 21%, the rash was the only clinical sign.
09.07.2020	Persistent Symptoms in Patients After Acute COVID-19	JAMA / Research letter	<ul style="list-style-type: none"> • Italian study assessed persistent symptoms in patients who were discharged from the hospital after recovery from COVID-19, finding that in patients who had recovered from COVID-19, 87.4% reported persistence of at least 1 symptom, particularly fatigue and dyspnoea. • Limitations include lack of information on symptom history before acute COVID-19 illness, lack of details on symptom severity, single-

			centre study with a relatively small number of patients and without a control group of patients discharged for other reasons.
09.07.2020	BCG vaccine protection from severe coronavirus disease 2019 (COVID-19)	PNAS / Research article	<ul style="list-style-type: none"> • This epidemiological study assessed the global linkage between BCG vaccination and COVID-19 mortality. • Signals of BCG vaccination effect on COVID-19 mortality are influenced by social, economic, and demographic differences between countries. • After mitigating multiple confounding factors, several significant associations between BCG vaccination and reduced COVID-19 deaths were observed.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review	Cochrane Database Syst Rev / Review	<ul style="list-style-type: none"> • The authors aim to continually assess, as more evidence becomes available, whether convalescent plasma or hyperimmune immunoglobulin transfusion is effective and safe in treatment of people with COVID-19. • Included 20 studies (1 RCT, 3 controlled NRSIs, 16 non-controlled NRSIs) with 5443 participants, of whom 5211 received convalescent plasma, and identified a further 98 ongoing studies evaluating convalescent plasma or hyperimmune immunoglobulin, of which 50 are randomised. They did not identify any completed studies evaluating hyperimmune immunoglobulin. • In conclusion the authors' are very uncertain whether convalescent plasma is beneficial for people admitted to hospital with COVID-19.
10.07.2020	What are the risk factors and effectiveness of prophylaxis for venous thromboembolism in COVID-19 patients?	Oxford COVID-19 Evidence Service / COVID-19	<ul style="list-style-type: none"> • This study identified a paucity of evidence for both the risks factors of VTE and the effectiveness of prophylactic strategies to prevent VTE in COVID-19 patients. • Potential risk factors which were identified for thrombotic events include older age and higher levels of D-dimer, though the actual threshold for a high level D-dimer varied between studies • Commonly encountered prophylactic strategies which were; low molecular weight heparin (LMWH) or unfractionated heparin, nadroparin and enoxaparin. • A number of studies found that despite prophylaxis there was still a

high incidence of thrombolytic complications in COVID-19 patients, which led a number of reviews to suggest earlier prophylaxis and in higher doses.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Using simulation to assess the potential effectiveness of implementing screening at national borders during international outbreaks of influenza, SARS, Ebola virus disease and COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • PHE study utilising epidemiological data and Monte Carlo simulation to calculate the potential success rate of deploying border screening for a range of diseases (including the current COVID-19 pandemic) in varying outbreak scenarios. • Primary results showed that in the best-case scenario, screening has the potential to detect 46.4%, 12.9% and 4.0% of travellers infected with influenza, SARS and Ebola respectively, while screening for COVID-19 could potentially detect 12.0% of infected travellers.
09.07.2020	Transmission dynamics and control measures of COVID-19 outbreak in China: a modelling study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • PHE-supported modelling study to understand the COVID-19 outbreak in China and provide potential lessons for other parts of the world. • Before 29th Jan 2020, the ascertainment rate is 6.9% (95%CI: 3.5 – 14.6%); then it increased to 41.5% (95%CI: 30.6 – 65.1%). The basic reproduction number (R0) was 2.23 (95%CI: 1.86 – 3.22) before 8th February 2020; then it dropped to 0.04 (95%CI: 0.01 – 0.10). This estimation also indicates that the effect on transmissibility of control measures taken since 23rd January 2020 emerged about two weeks late. • The confirmed CFR is estimated at 4.41% (95%CI: 3.65 – 5.30%). This shows that SARS-CoV-2 virus is highly transmissible but less severe than SARS-CoV-1 and MERS-CoV. They found that at the early stage, the majority of R0 comes from the undetected infected people. • Implies that the successful control in China was achieved through decreasing the contact rates among people in general populations and increasing the rate of detection and quarantine of the infected cases.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
10.07.2020	Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review	Jama / Review
10.07.2020	Extrapulmonary manifestations of COVID-19	Nat Med / Review article
10.07.2020	Covid-19: Many trusts have not done risk assessments for ethnic minority staff, BMJ investigation finds	Bmj / News
13.07.2020	Exposed, silenced, attacked: failures to protect health and essential workers during the COVID-19 pandemic	Amnesty International / Report
09.07.2020	David Oliver: Covid-19 should increase our commitment to publicly funded and provided healthcare	Bmj / Views and reviews

Produced by the PHE COVID-19 Literature Digest Team