Public Health England

International EPI Cell Daily Evidence Digest – 07/08/2020

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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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
02.08.2020	REGN-COV2 antibody cocktail prevents and treats SARS-CoV-2 infection in rhesus macaques and hamsters	bioRxiv (non-peer reviewed)	• Study evaluating the in vivo efficacy of a cocktail of two potent neutralizing antibodies (REGN10987+REGN10933), targeting non-overlapping epitopes on the SARS-CoV-2 spike protein, in both rhesus macaques and golden hamsters to demonstrate that REGN-COV-2 can reduce virus load in lower and upper airway and decrease virus induced pathological sequalae when administered prophylactically or

			therapeutically.
			• Authors suggest results provide evidence of the therapeutic potential of this antibody cocktail.
05.08.2020	[SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness](#)	Nature / Article	• Authors show investigational vaccine known as mRNA-1273 induces both potent neutralizing antibody responses to wild-type (D614) and D614G mutant(2) COVID-19 and CD8 T cell responses, and protects against COVID-19 infection in the lungs and noses of mice without evidence of immunopathology. • mRNA-1273 is currently in Phase 3 efficacy evaluation.
05.08.2020	[First-in-Human Trial of a SARS CoV 2 Recombinant Spike Protein Nanoparticle Vaccine](#)	medRxiv (non-peer reviewed)	• Presents the Day 35 primary analysis of a trial of NVX-CoV2373 recombinant nanoparticle vaccine with or without the saponin-based Matrix-M1 adjuvant in healthy adults (n=131). • There were no serious adverse events. • Reactogenicity was mainly mild in severity and of short duration (mean ≥ 2 days), with second vaccinations inducing greater local and systemic reactogenicity. • The adjuvant significantly enhanced immune responses and was antigen dose-sparing, and the two-dose 5µg NVX-CoV2373/Matrix-M1 vaccine induced mean anti-spike IgG and neutralizing antibody responses that exceeded the mean responses in convalescent sera from COVID-19 patients with clinically significant illnesses. • The vaccine also induced antigen-specific T cells with a largely T helper 1 (Th1) phenotype.
04.08.2020	[Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans](#)	Science / Research article	• SARS-CoV-2 reactive CD4+ T cells have been reported in unexposed individuals, suggesting pre-existing cross-reactive T cell memory in 20-50% of people. • Using human blood samples derived pre SARS-CoV-2 virus, authors mapped 142 T cell epitopes across the COVID-19 genome; demonstrate a range of pre-existing memory CD4+ T cells that are cross-reactive with comparable affinity to COVID-19 and common cold coronaviruses HCoV-OC43, HCoV-229E, HCoV-NL63, or HCoV-HKU1. • Variegated T cell memory to coronaviruses that cause the common cold may underlie at least some of the extensive heterogeneity observed in COVID-19 disease.
06.08.2020	[SARS-CoV-2 viral load predicts COVID-19 mortality](#)	The Lancet Respiratory Medicine / Correspondence	• Study on COVID-19 viral load at diagnosis as an independent predictor of mortality in a large hospitalised cohort (n=1145). • A Cox proportional hazards model adjusting for age, sex, asthma, atrial fibrillation, coronary artery disease, chronic kidney disease, chronic

| | | | obstructive pulmonary disease, diabetes, heart failure, hypertension, stroke, and race yielded a significant independent association between viral load and mortality (hazard ratio 1·07 [95% CI 1·03–1·11], p=0·0014), with a 7% increase in hazard for each log transformed copy per mL.
• A univariate survival analysis revealed a significant difference in survival probability between those with high viral load (defined as being greater than the overall mean log10 viral load of 5·6 copies per mL) and those with low viral load (p=0·0003), with a mean follow-up of 13 days (SD 11) and a maximum follow-up of 67 days. |
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Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
01.08.2020	Evidence for sustained mucosal and systemic antibody responses to SARS-CoV-2 antigens in COVID-19 patients	medRxiv (non-peer reviewed)	• While antibody response to COVID-19 has been extensively studied in blood, relatively little is known about the mucosal immune response and its relationship to systemic antibody levels.
• Authors developed enzyme linked immunosorbent assays to detect IgA and IgG antibodies to the COVID-19 spike protein (full length trimer) and its receptor binding domain (RBD) in serum (n=496) and saliva (n=90) of acute and convalescent patients with laboratory-diagnosed COVID-19 ranging from 3-115 days post-symptom onset (PSO), compared to negative controls.
• Anti-CoV-2 antibody responses were readily detected in serum and saliva, with peak IgG levels attained by 16-30 days PSO.
• Whereas anti-CoV-2 IgA antibodies rapidly decayed, IgG antibodies remained relatively stable up to 115 days PSO in both biofluids.
• IgG responses in saliva and serum were correlated, suggesting antibodies in saliva may serve as a surrogate measure of systemic immunity.
03.08.2020	Simply saliva: stability of SARS-CoV-2 detection negates the need for expensive collection devices	medRxiv (non-peer reviewed)	• Study investigated the stability of COVID-19 RNA over extended periods of time (2-25 days) and at temperatures representing at-home storage and elevated temperatures which might be experienced when cold chain transport may be unavailable.
• Found COVID-19 RNA in saliva from infected individuals is stable at 4°C, room temperature (~19°C), and 30°C for prolonged periods and found limited evidence for viral replication in saliva.
• Suggests that expensive saliva collection options involving RNA

| | | | stabilization and virus inactivation buffers are not always needed, permitting the use of cheaper collection options. |

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
05.08.2020	[Intra- and intermolecular atomic-scale interactions in the receptor binding domain of SARS-CoV-2 spike protein: implication for ACE2 receptor binding](#)	Phys Chem Chem Phys / Article	• Reports details of the intra- and inter-molecular binding mechanism of RBD using density functional theory, including electronic structure, interatomic bonding and partial charge distribution. • Identifies five strong hydrogen bonds and analyzes their roles in binding. • This provides a pathway to a quantum-chemical understanding of the interaction between the S-protein and the ACE2 receptor with insights into the function of conserved features in the ACE2 receptor binding domain that could inform vaccine and drug development.
05.08.2020	[Unique SARS-CoV-2 clusters causing a large COVID-19 outbreak in Hong Kong](#)	Clin Infect Dis / Article	• After two months of relative quiescence, a large COVID-19 outbreak occurred in Hong Kong in July 2020 after gradual relaxation of social distancing policy. • Two unique COVID-19 phylogenetic clusters have been identified among locally-acquired cases, with most genomes belonging to cluster HK1 which is phylogenetically related to COVID-19 reported overseas.

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
06.08.2020	[COVID-19 in children and the role of school settings in COVID-19 transmission](#)	European Centre for Disease Prevention and Control / Report	Key report findings: •A small proportion (<5%) of overall COVID-19 cases reported in the EU/EEA and the UK are among children (18 years and under). When diagnosed with COVID-19, children are much less likely to be hospitalised or have fatal outcomes than adults. •Children are more likely to have a mild or asymptomatic infection. •When symptomatic, children shed virus in similar quantities to adults and can infect others in a similar way to adults.

			•While very few significant outbreaks of COVID-19 in schools have been documented, they do occur, and may be difficult to detect due to the relative lack of symptoms in children. •In general, the majority of countries report slightly lower seroprevalence in children than in adult groups, however these differences are small and uncertain. •Investigations of cases identified in school settings suggest that child to child transmission in schools is uncommon •If appropriate physical distancing and hygiene measures are applied, schools are unlikely to be more effective propagating environments than other occupational or leisure settings with similar densities of people. •Evidence from contact tracing in schools and observational data suggest re-opening schools has not been associated with significant increases in community transmission. •Available evidence also indicates that closures of childcare and educational institutions are unlikely to be an effective single control measure for community transmission of COVID-19 and such closures would be unlikely to provide significant additional protection of children's health, since most develop a very mild form of COVID-19, if any.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
05.08.2020	Cerebral Microbleeds and Leukoencephalopathy in Critically Ill Patients With COVID-19	Stroke / Research article	• Study to investigate the prevalence and distribution of cerebral microbleeds and leukoencephalopathy in hospitalized COVID-19 patients - retrospective chart review of 4131 patients identified subset of 115 patients who had an MRI of the brain performed • 35 (30.4%) of those patients had leukoencephalopathy and/or cerebral microbleeds. Findings included: these patients had longer hospitalizations (42.1 versus20.9 days; P<0.001), overall worse functional status on discharge (mRS 5 versus4; P=0.001), and higher mortality (20% versus9%; P=0.144). • The presence of leukoencephalopathy and/or cerebral microbleeds is associated with a critical illness, increased mortality, and worse functional outcome in patients with COVID-19.

29.07.2020	Association of Coronavirus Disease (COVID-19) With Large Vessel Occlusion Strokes: A Case-Control Study	AJR Am J Roentgenol / Article	• Study sample of 329 patients for whom a code for stroke was activated (175 [53.2%] men, 154 [46.8%] women; mean age, 66.9 ± 14.9 [SD] years). • Among the 329 patients, 35.3% (116) had acute ischemic stroke confirmed with imaging; 21.6% (71) had large vessel occlusion (LVO) stroke; and 14.6% (48) had small vessel occlusion (SVO) stroke. • Among LVO strokes, the most common location was middle cerebral artery segments M1 and M2 (62.0% [44/71]). • Multifocal LVOs were present in 9.9% (7/71) of LVO strokes. • COVID-19 was present in 38.3% (126/329) of the patients. The 61.7% (203/329) of patients without COVID-19 formed the negative control group. • Among individual stroke-related risk factors, only Hispanic ethnicity was significantly associated with COVID-19 (38.1% of patients with COVID-19 vs 20.7% of patients without COVID-19; p = 0.001). • LVO was present in 31.7% of patients with COVID-19 compared with 15.3% of patients without COVID-19 (p = 0.001). • SVO was present in 15.9% of patients with COVID-19 and 13.8% of patients without COVID-19 (p = 0.632). • In multivariate analysis controlled for race and ethnicity, presence of COVID-19 had a significant independent association with LVO stroke (odds ratio, 2.4) compared with absence of COVID-19 (p = 0.011).
31.07.2020	Emergent Large Vessel Occlusion Stroke During New York City's COVID-19 Outbreak: Clinical Characteristics and Paraclinical Findings	Stroke / Research article	• Early data suggest higher rate of ischemic stroke in severe COVID-19 infection. Retrospective, observational case series of emergent large vessel occlusion (ELVO) and COVID-19 outbreak. • Forty-five consecutive ELVO patients presented during the observation period. Fifty-three percent of patients tested positive for COVID-19. • A 2-fold increase in the total number of ELVO was observed (estimate: 0.78 [95% CI, 0.47-1.08], P≤0.0001). • ELVO stroke patients with COVID-19 were younger, more likely to be male, and less likely to be White. Findings suggest an increase in incidence of ELVO stroke during peak of the COVID-19 outbreak.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
05.08.2020	Transient dynamics of SARS-CoV-2 as England exited national lockdown	medRxiv (non-peer reviewed)	• Describes results comparing rounds 1 and 2 of community-based sampling using, including asymptomatic individuals, carried out using nose and throat swab RT-PCR between approximately May and early July 2020 in 315 English local authority areas. • In round 1 there were 159 positive samples from 120,620 tested swabs while round 2 there were 123 positive samples from 159,199 tested swabs, indicating a downwards trend in prevalence from 0.13% (95% CI, 0.11%, 0.15%) to 0.077% (0.065%, 0.092%), a halving time of 38 (28, 58) days, and an R of 0.89 (0.86, 0.93). • The proportion of swab-positive participants who were asymptomatic at the time of sampling increased from 69% (61%, 76%) in round 1 to 81% (73%, 87%) in round 2. • Although health care and care home workers were infected far more frequently than other workers in round 1, the odds were markedly reduced in round 2. • Data suggests increased risk of infection in Black and Asian (mainly South Asian) ethnicities. • Age patterns of infection changed between rounds, with a reduction by a factor of five in prevalence in 18 to 24 year olds.
03.08.2020	Dying 'due to' or 'with' COVID-19: a cause of death analysis in hospitalised patients	Clin Med (Lond) / Rapid report	• Authors aim to provide an independent review of clinical features of COVID-19 patients who died during hospitalisation related to reported cause of death. • Between 23 March and 28 April 2020, 162 patients with a positive COVID-19 PCR died in this NHS trust. COVID-19 documented as direct cause of death in 150 (93%). • Review of the records revealed 138 (92%) patients had pulmonary infiltrates on chest radiography, and 146 (97%) required oxygen therapy. • Retrospective review of cause of death demonstrated that overwhelming majority of hospitalised patients with positive COVID-19 PCR died as a direct consequence of COVID-19 infection.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
04.08.2020	Safety of hot and cold site admissions within a high volume urology department in the United Kingdom at the peak of the COVID-19 pandemic	medRxiv (non-peer reviewed)	• A study of patients (n=611; male=73.8%) admitted to a single surgical department in London under the care of the urology team from 1st March to 31st May 2020, to determine the safety of continuing surgical admissions and procedures during the height of the COVID-19 pandemic using hot (n=101) and cold (n=510) surgical sites. • Surgical procedures were performed in 495 patients of which 8 (1.6%) contracted COVID-19 post-operatively with 1 (0.2%) post-operative mortality due to COVID-19. • Overall, COVID-19 was detected in 20 (3.3%) patients with 2 (0.3%) deaths. • On multivariate analysis, length of stay was associated with contracting COVID-19 (OR 1.25, 95% CI 1.13-1.39). • Suggests continuation of surgical procedures using hot and cold sites throughout the COVID-19 pandemic is safe practice, although risk of COVID-19 remained. Reduced length of stay may reduce risk of infection.
03.08.2020	Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients	medRxiv (non-peer reviewed)	• Air samples were collected in the room of two COVID-19 patients, one of whom had an active respiratory infection with a nasopharyngeal (NP) swab positive for COVID-19. • The genomes of COVID-19 collected from the air, isolated in cell culture from air sampling, and from a NP swab from a newly admitted patient in the room were sequenced. • Viable virus was isolated from air samples collected 2 to 4.8m away from the patients. • The genome sequence of the SARS-CoV-2 strain isolated from the material collected by the air samplers was identical to that isolated from the NP swab from the patient with an active infection. • Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
04.08.2020	Plasma exchange in critically ill COVID-19 patients	Crit Care / Research letter	• Case study of 5 patients who had received at least one plasma exchange (PE) until May 15, 2020, were considered for analysis with clinical follow-up until June 15, 2020. • Three of the 5 most critically ill patients are alive; a 71-year-old male and a 76-year-old female patient died after the therapy was limited due to persistent severe ARDS. • PE improved inflammation, microcirculatory clot formation, and hypotension, thereby improving clinical outcomes. • Further studies to test whether (repeated) PE can alter the course of critically ill COVID-19 patients are clearly indicated.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
06.08.2020	Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: results from multiple mathematical models	The Lancet HIV / Article	• An article using five models of HIV epidemics to estimate the effect of potential disruptions to HIV prevention/treatment services in sub-Saharan Africa caused by COVID-19 • A 6 month interruption of antiretroviral supply due to COVID-19 across the whole population would be expected to result in approximately 2-fold increase in HIV-related deaths, as well as a 2-fold increase in mother to child transmission of HIV. • Changes including interruptions to supply of other drugs such as cotrimoxazole, suspension of HIV testing, condom supply and peer education are discussed, with social distancing measures (and resultant reductions in risky sex) being acknowledged.
04.08.2020	An improved methodology for estimating the prevalence of SARS-CoV-2	medRxiv (non-peer reviewed)	• Article presenting an improved methodology for estimating COVID-19 prevalence and applying it to 166 countries (or individual states of the USA). • The methodology takes cases and deaths (together with population size) as raw prevalence for the population, applies an age-adjustment to influence the case-fatality rate and the proportion of asymptomatic cases, and finally calculates the likely underreporting factor for the population and uses this to adjust prevalence estimate.

			• The results of this study may be used to understand the risk between different geographical areas and highlight regions where the prevalence of COVID-19 is increasing most rapidly. • Authors suggest the methodology is quick and easy to implement. Prevalence estimates should be updated on a regular basis to allow for rapid fluctuations in disease patterns.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
03.08.2020	SARS-CoV-2 (COVID-19) serology: implications for clinical practice, laboratory medicine and public health	Cmaj / Review
06.08.2020	COVID-19, asthma, and return to school	The Lancet Respiratory Medicine / Comment
06.08.2020	Elimination of COVID-19: what would it look like and is it possible?	The Lancet Infectious Diseases / Comment
01.08.2020	Anosmia and hyposmia in health-care workers with undiagnosed SARS-CoV-2 infection	The Lancet Microbe / Correspondence
01.08.2020	Cross-reactivity towards SARS-CoV-2: the potential role of low-pathogenic human coronaviruses	The Lancet Microbe / Correspondence
01.08.2020	The use of dexamethasone in the treatment of COVID-19	Ann Med Surg (Lond) / Correspondence
05.08.2020	Immunity passports to travel during the COVID-19 pandemic: controversies and public health risks	J Public Health (Oxf) / Letter

Produced by the PHE COVID-19 Literature Digest Team

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