



International EPI Cell Evidence Digest – 27/07/2020

This 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
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - other
- Infection control
- Modelling
- Guidance, consensus statements and hospital resources (no digest)
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
24.07.2020	Point-of-care serological assays for delayed SARS-CoV-2 case identification among health-care workers in the UK: a prospective multicentre cohort study	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none">• Authors investigated the performance of point-of-care and laboratory serology assays and their utility in late case identification.• A good positive predictive value was observed with both lateral flow serological assays and ELISA, although only if the pre-test probability was modified by a strict clinical case definition.• Late development of lateral flow serological assay bands would preclude postal strategies and potentially home testing.• Identification of false-negative results among health-care workers

			<p>across all assays suggest caution in interpretation of IgG results at this stage.</p> <ul style="list-style-type: none"> • Suggests that testing is currently best delivered in a clinical setting, supported by government advice about physical distancing.
21.07.2020	Stringent thresholds for SARS-CoV-2 IgG assays result in under-detection of cases reporting loss of taste/smell	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • An assessment of IgG responses in asymptomatic healthcare workers with a high pre-test probability of Covid-19. • The proportion reporting anosmia/ageusia increased at antibody titres below diagnostic thresholds for both an in-house ELISA and the Abbott Architect chemiluminescent microparticle immunoassay. • Adjusting for the proportion of staff reporting anosmia/ageusia suggests sensitivity of both assays is lower than previously reported. • The sensitivity may be lower if some anosmia/ageusia in those with low-negative titres is Covid-19-associated. • Samples from individuals with mild/asymptomatic infection should be included in SARS-CoV-2 immunoassay evaluations.
24.07.2020	Estimated Community Seroprevalence of SARS-CoV-2 Antibodies - Two Georgia Counties, April 28-May 3, 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • The median model-based estimate of the prevalence of any of five underlying medical conditions associated with increased risk for severe COVID-19-associated illness among U.S. adults was 47.2% among 3,142 U.S. counties. The estimated number of persons with these conditions followed population distributions, but prevalence was higher in more rural counties.
23.07.2020	A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2-spike protein-protein interaction	Nat Biotechnol / Article	<ul style="list-style-type: none"> • Report a SARS-CoV-2 surrogate virus neutralization test that detects total immunodominant neutralizing antibodies targeting the viral spike (S) protein receptor-binding domain in an isotype- and species-independent manner. • Simple and rapid test is based on antibody-mediated blockage of the interaction between the ACE2 receptor protein and the receptor-binding domain. • The test, which has been validated with two cohorts of patients with COVID-19 in two different countries, achieves 99.93% specificity and 95–100% sensitivity, and differentiates antibody responses to several human coronaviruses.
23.07.2020	LY6E impairs coronavirus fusion and confers immune control of viral disease	Nat Microbiol / Article	<ul style="list-style-type: none"> • Show that lymphocyte antigen 6 complex, locus E (LY6E) potentially restricts infection by multiple CoVs, including SARS-CoV, SARS-CoV-2 and MERS-CoV. • Found that constitutive Ly6e directly protects primary B cells from

murine CoV infection. Results show that LY6E is a critical antiviral immune effector that controls CoV infection and pathogenesis.

Diagnostics

Publication Date	Title /URL	Journal / Article type	Digest
22.07.2020	Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection	JAMA Netw Open / Research letter	<ul style="list-style-type: none"> • A cross-sectional study compared unsupervised home self-collected swabs with clinician-collected nasopharyngeal swabs for COVID-19 diagnosis in 185 participants. • Unsupervised home mid-nasal swab collection was comparable to clinician-collected nasopharyngeal swab collection for detection of SARS-CoV-2 in symptomatic patients, particularly those with higher viral loads. • False-negative results in samples with low initial viral loads were observed. • Authors suggest a home-based strategy should be targeted toward individuals early in illness.
19.07.2020	Paired nasopharyngeal and deep lung testing for SARS-CoV2 reveals a viral gradient in critically ill patients: a multi-centre study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A study to evaluate SARS-CoV2 RNA loads between paired nasopharyngeal (NP) and deep lung (endotracheal aspirate or BAL) samples from 51 critically ill patients. • Data challenges assumption that SARS-CoV2 replicates more vigorously in the upper respiratory tract than SARS-CoV1. • Suggests patients with suspected severe COVID-19 should have virological samples obtained from the lower respiratory tract whenever possible, as upper respiratory samples have a significant negative rate.
23.07.2020	Scent dog identification of samples from COVID-19 patients - a pilot study	BMC Infect Dis / Article	<ul style="list-style-type: none"> • Eight detection dogs were trained for 1 week to detect saliva or tracheobronchial secretions of SARS-CoV-2 infected patients in a randomised, double-blinded and controlled study. • The dogs were able to discriminate between samples of infected (positive) and non-infected (negative) individuals with average diagnostic sensitivity of 82.63% (95% confidence interval [CI]: 82.02–83.24%) and specificity of 96.35% (95% CI: 96.31–96.39%). • During the presentation of 1012 randomised samples, the dogs achieved an overall average detection rate of 94% ($\pm 3.4\%$) with 157 correct indications of positive, 792 correct rejections of negative, 33

incorrect indications of negative or incorrect rejections of 30 positive sample presentations.

Genomics

Publication Date	Title /URL	Journal / Article type	Digest
24.07.2020	Presence of Genetic Variants Among Young Men With Severe COVID-19	JAMA / Article	<ul style="list-style-type: none"> • In this case series of 4 young male patients with severe COVID-19, rare putative loss-of-function variants of X-chromosomal TLR7 were identified that were associated with impaired type I and II IFN responses. • These preliminary findings provide insights into the pathogenesis of COVID-19.
23.07.2020	Evolution and epidemic spread of SARS-CoV-2 in Brazil	Science / Report	<ul style="list-style-type: none"> • Sequencing of 427 new genomes and analysis of a geographically representative genomic dataset identified >100 international virus introductions in Brazil. • Estimate that most (76%) of the Brazilian strains fell in three clades that were introduced from Europe between 22 Feb and 11 Mar 2020.
23.07.2020	Structure-based design of prefusion-stabilized SARS-CoV-2 spikes	Science / Report	<ul style="list-style-type: none"> • Characterized 100 structure-guided spike designs and identified 26 individual substitutions that increased protein yields and stability. • Testing combinations of beneficial substitutions resulted in the identification of HexaPro, a variant with six beneficial proline substitutions exhibiting ~10-fold higher expression than its parental construct and the ability to withstand heat stress, storage at room temperature, and three freeze-thaw cycles. A 3.2 Å-resolution cryo-EM structure of HexaPro confirmed that it retains the prefusion spike conformation. • High-yield production of a stabilized prefusion spike protein will accelerate the development of vaccines and serological diagnostics for SARS-CoV-2.
24.07.2020	Structural basis of RNA cap modification by SARS-CoV-2	Nat Commun / Article	<ul style="list-style-type: none"> • Reports here the high-resolution structure of a ternary complex of SARS-CoV-2 nsp16 and nsp10 in the presence of cognate RNA substrate analogue and methyl donor, S-adenosyl methionine (SAM). • Observed large conformational changes associated with substrate

			<p>binding as the enzyme transitions from a binary to a ternary state.</p> <ul style="list-style-type: none"> • This induced fit model provides mechanistic insights into the 2'-O methylation of the viral mRNA cap. • Also discovered a distant (25 Å) ligand-binding site unique to SARS-CoV-2, which can alternatively be targeted, in addition to RNA cap and SAM pockets, for antiviral development.
24.07.2020	Structural analysis of the SARS-CoV-2 methyltransferase complex involved in RNA cap creation bound to sinefungin	Nat Commun / Article	<ul style="list-style-type: none"> • Structural comparisons reveal low conservation of the MTase catalytic site between Zika and SARS-CoV-2 viruses, but high conservation of the MTase active site between SARS-CoV-2 and SARS-CoV viruses. • These data suggest that the preparation of MTase inhibitors targeting several coronaviruses - but not flaviviruses - should be feasible. Together, this data adds to important information for structure-based drug discovery.

Epidemiology and clinical - children and pregnancy

Publication Date	Title /URL	Journal / Article type	Digest
24.07.2020	COVID-19 in children with chronic kidney disease: findings from the UK renal registry	Arch Dis Child / Letter	<ul style="list-style-type: none"> • Between 26 March and 15 July 2020, five UK children with CKD who tested positive for SARS-CoV-2 infection were reported; none have died.
25.07.2020	Multi-Inflammatory Syndrome in Children related to SARS-CoV-2 in Spain	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Describes the epidemiological and clinical features of children with MIS-C in Spain. • By June 1st, 312 patients had been attended in the 49 hospitals, and 252 participants were hospitalized. Of them, 181 (72%) were admitted due to causes directly or likely related to SARSCoV-2. The remaining 71 (28%) were admitted due to causes not related with SARS-CoV-2, but were screened and found to be infected with SARS-CoV-2. • A total of 31/252 (12%) children were diagnosed as MIS-C and/or Kawasaki disease by their physicians.
25.07.2020	Systematic SARS-CoV-2 screening at hospital admission in children:a French prospective multicenter study	Clin Infect Dis / Article	<ul style="list-style-type: none"> • To assess the relevance of systematic SARS-CoV-2 screening of all children admitted to hospital, the authors conducted a prospective multicentre study including 438 consecutive hospitalized children. • A symptom-based SARS-CoV-2 testing strategy failed to identify 45% (95%CI [24; 68]) of hospitalized children infected by SARS-CoV-

2.
 - To limit intra-hospital transmission, a systematic screening of children admitted to hospital should be considered.

Epidemiology and clinical – other

Publication Date	Title /URL	Journal / Article type	Digest
24.07.2020	Characteristics and outcomes of patients with COVID-19 at a district general hospital in Surrey, UK	Clin Med (Lond) / Article	<ul style="list-style-type: none"> • This retrospective cohort study aimed to define the clinical findings and outcomes of every patient admitted to a district general hospital in Surrey with COVID-19 in March 2020, providing a snapshot of the first wave of infection in the UK. • 108 patients were included. 34 (31%) died in hospital or were discharged for palliative care. 43% of patients aged over 65 died. The commonest comorbidities were hypertension (49; 45%) and diabetes (25; 23%). • This study identifies older patients with frailty as being particularly vulnerable and reinforces government policy to protect this group at all costs.

Infection control

Publication Date	Title /URL	Journal / Article type	Digest
23.07.2020	Effective Contact Tracing for COVID-19: A Systematic Review	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Systematic review examined contact tracing effectiveness in the context of COVID-19. • Authors suggest public health practitioners have 2-3 days from the time a new case develops symptoms to isolate the case and quarantine at least 80% of contacts, and that once isolated, cases and contacts should infect zero new cases. • Delays of 4-5+ days or less than 60% of contacts quarantined with no further transmission may not contribute meaningfully to control of COVID-19.

Modelling

Publication Date	Title /URL	Journal / Article type	Digest
23.07.2020	Evolution of spray and aerosol from respiratory releases: theoretical estimates for insight on viral transmission	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Modelling study to assess the evaporation and settling of droplets emitted during respiratory releases and using previous measurements of droplet size distributions and SARS-CoV-2 viral load. • Settling times of a droplet cloud and its suspended viral dose are significantly affected by droplet composition. • Aerosol from 30 seconds of continued speech was higher than from a short cough. • Time-of-flight to reach 2m is only a few seconds, resulting in a viral dose above the minimum required for infection and implying physical distancing in the absence of ventilation is not sufficient. • Suspended aerosol emitted by continuous speaking for 1 hour in a poorly ventilated room gives 0.1-11% infection risk, decreasing to 0.03-3% for 10 air changes per hour by ventilation.
24.07.2020	Strategies to reduce the risk of SARS-CoV-2 re-introduction from international travellers	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Combined strategies of self-quarantine and active testing of air travellers arriving in the UK were evaluated using a simulation model. • Quarantine period of 8 days with a PCR test on day 7 can reduce the number of infectious arrivals released into the community by median 94% compared to a no quarantine, no test scenario. • This reduction is similar to that achieved by 14-day quarantine period (median 99% reduction). • All strategies in which travellers spend at least 5 days in quarantine and have at least one negative test before release are highly effective.
23.07.2020	Herd immunity thresholds for SARS-CoV-2 estimated from unfolding epidemics	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors used epidemiological models with inbuilt distributions of susceptibility or exposure to SARS-CoV-2 outbreaks to estimate R numbers alongside coefficients of individual variation (CV) and the effects of containment strategies. • Suggests herd immunity thresholds at around 10-20%, considerably lower than the minimum coverage needed to interrupt transmission by random vaccination. • Authors state the classical formula, $1-1/R_0$, remains applicable

			to describe herd immunity thresholds for random vaccination, but not for immunity induced by infection.
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Guidance, consensus statements

Publication Date	Title / URL	Journal / Article type
24.07.2020	Excess weight and COVID-19: insights from new evidence	Public Health England / Report
27.07.2020	COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services	NICE / Guideline
27.07.2020	COVID-19: EU guidance for cruise ship operations	European Centre for Disease Prevention and Control / Technical guidance

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
24.07.2020	UK government's work to tackle health disparities of covid-19	BMJ / Letter
22.07.2020	Covid-19 and Health Equity - Time to Think Big	N Engl J Med / Perspective
22.07.2020	Pooling Data From Individual Clinical Trials in the COVID-19 Era	JAMA / Viewpoint
24.07.2020	Public perceptions on data sharing: key insights from the UK and the USA	The Lancet Digital Health / Comment
24.07.2020	Need for sustainable biobanking networks for COVID-19 and other diseases of epidemic potential	The Lancet Infectious Diseases / Personal view
24.07.2020	The time to do serosurveys for COVID-19 is now	The Lancet Respiratory Medicine / Comment
24.07.2020	Particle sizes of infectious aerosols: implications for infection control	The Lancet Respiratory Medicine / Viewpoint
24.07.2020	Molecular Underpinnings of Severe Coronavirus Disease 2019	Jama / Editorial

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