COVID-19 Literature Digest – 26/08/2020

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
- 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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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

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<tr>
<th>Publication Date</th>
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<tbody>
<tr>
<td>25.08.2020</td>
<td>Antibody Responses and Clinical Outcomes in Adults Hospitalized with Severe COVID-19: A Post hoc Analysis of LOTUS China Trial</td>
<td>Clin Infect Dis / Article</td>
<td>• Neutralizing antibodies (NAb) and antibodies targeting nucleocapsid (N), spike protein (S), receptor-binding domain (RBD) in longitudinal plasma samples from the LOTUS China trial were measured - 576 plasma and 576 throat swabs were collected from 191 COVID-19 patients. After day 28 post symptoms onset, the rate of antibody positivity reached 100% for RBD-IgM, 97.8% for S-IgM, 100% for N-IgG, 100% for RBD-IgG, 91.1% for N-IgM and 91.1% for NAbs. IgM, IgG against N, S and RBD and NAbs developed in most severe</td>
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COVID-19 patients, and do not correlate clearly with clinical outcomes. The levels of IgG antibodies against N, S and RBD were related to viral clearance.

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<tr>
<th>Date</th>
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<th>Journal/Preprint Details</th>
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<tbody>
<tr>
<td>24.08.2020</td>
<td>An inflammatory cytokine signature predicts COVID-19 severity and survival</td>
<td>Nat Med / Article</td>
<td>This paper was previously included in the Digest as a preprint. A rapid multiplex cytokine assay was implemented to measure serum interleukin (IL)-6, IL-8, tumour necrosis factor (TNF)-α and IL-1β in hospitalized COVID-19 patients (n = 1,484) at a single centre in New York, with follow up no later than 41 days (median, 8 days). High serum IL-6, IL-8 and TNF-α levels at the time of hospitalization were strong and independent predictors of patient survival (P &lt; 0.0001, P = 0.0205 and P = 0.0140, respectively). Adjusting for disease severity, common laboratory inflammation markers, hypoxia and other vitals, demographics, and a range of comorbidities, IL-6 and TNF-α serum levels remained independent and significant predictors of disease severity and death. Findings were validated in a second cohort of patients (n = 231).</td>
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<td>22.08.2020</td>
<td>Potent anti-SARS-CoV-2 Antibody Responses are Associated with Better Prognosis in Hospital Inpatient COVID-19 Disease</td>
<td>medRxiv (non-peer reviewed) / Article</td>
<td>Antibody responses to the COVID-19 spike protein and nucleocapsid proteins were investigated in a UK patient cohort, using optimised immunoassays and a retrovirus-based pseudotype entry assay. In severe COVID-19 infections an early antibody response to both antigens was associated with improved prognosis of infection. Neutralizing potency of sera was found to be greater in patients who went on to resolve infection, compared with those that died from COVID-19. Viral genetic variation in spike protein was found to influence the production of neutralizing antibodies. Infection with the recently described spike protein variant 614G produced higher levels of neutralizing antibodies when compared to viruses possessing the 614D variant.</td>
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<tr>
<td>24.08.2020</td>
<td>SARS-CoV-2 infection of human ACE2-transgenic mice causes severe lung inflammation and impaired function</td>
<td>Nat Immunol / Article</td>
<td>Authors evaluate transgenic mice expressing the human angiotensin I-converting enzyme 2 (ACE2) receptor driven by the cytokeratin-18 (K18) gene promoter (K18-hACE2) as a model of SARS-CoV-2 infection. The K18-hACE2 model of SARS-CoV-2 infection shares many features of severe COVID-19 infection and can be used to define the basis of lung disease and test immune and antiviral-based countermeasures.</td>
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### Diagnostics

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| 20.08.2020       | The COVID-19 XPRIZE and the need for scalable, fast, and widespread testing | Nat Biotechnol / Correspondence     | • Authors present an online tool ([http://www.resiliencehealth.com/tests](http://www.resiliencehealth.com/tests)) that profiles current and emerging virology tests for detecting SARS-CoV-2.  
| 24.08.2020       | Inactivation analysis of SARS-CoV-2 by specimen transport media, nucleic acid extraction reagents, detergents and fixatives | J Clin Microbiol / Article          | • This paper was previously included in the Digest as a preprint.  
• Authors evaluated 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.  
• Study provides: critical data informing inactivation methods and risk assessments for diagnostic and research laboratories working with SARS-CoV-2; a framework for other laboratories to validate their inactivation processes and to guide similar studies for other pathogens. |

### Genomics

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| 25.08.2020       | COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing | Clin Infect Dis / Article           | • Whole genome sequencing was performed directly on respiratory specimens collected during two episodes of COVID-19 in a patient. The second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient.  
• Viral genomes from first and second episodes belong to different clades/lineages.  
• Compared to viral genomes in GISAID, the first virus genome was phylogenetically closely related to strains collected in March/April 2020, while the second virus genome was closely related to strains collected in July/August 2020.  
• Another 23 nucleotide and 13 amino acid differences located in 9 different proteins, including positions of B and T cell epitopes, were found between viruses from the first and second episodes. |
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| 21.08.2020      | Implications of the school-household network structure on SARS-CoV-2 transmission under different school reopening strategies in England | medRxiv (non-peer reviewed) / Article          | • A modelled network of English schools, connected through pairs of pupils resident at the same address, was used to evaluate potential for COVID-19 transmission between schools and for long range propagation.  
  • Data suggests reopening only Reception, Year 1 and Year 6 resulted in the lowest risk of transmission between schools.  
  • However, the majority of schools present low risk of initiating widespread transmission through the school system.  
  • Reopening all secondary school years resulted in large potential outbreak clusters putting up to 50% of households connected to schools at risk of infection if sustained transmission within schools was possible. |
  • 250 of 33,041 children (0-18 years) without symptoms were positive, prevalence varied from 0% to 2.2%, with a pooled prevalence of 0.65% (95% CI, 0.47%-0.83%, with significant heterogeneity.  
  • Asymptomatic paediatric prevalence was significantly associated with weekly incidence of COVID-19 in the general population during the 6-week period over which most testing of individuals without symptoms occurred. |
<p>| 21.08.2020      | Multisystem inflammatory syndrome in children in South Africa              | The Lancet Child &amp; Adolescent Health / Correspondence | • Summarised the first 23 cases of MIS-C treated at The Red Cross War Memorial Children's Hospital, Cape Town, South Africa, and the Tygerberg Children's Hospital, Cape Town, South Africa, from June 4 to July 24, 2020. |</p>
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| 24.08.2020       | COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study | The Lancet Oncology / Article               | • The aim of this study was to investigate COVID-19 risk according to tumour subtype and patient demographics in patients with cancer in the UK.  
• Concluded that patients with cancer with different tumour types have differing susceptibility to SARS-CoV-2 infection and COVID-19 phenotypes.  
• The authors generated individualised risk tables for patients with cancer, considering age, sex, and tumour subtype. |
| 21.08.2020       | SARS-CoV-2 Community Transmission disproportionately affects Latinx population during Shelter-in-Place in San Francisco | Clin Infect Dis / Article                  | • In this study COVID-19 reverse transcription-PCR and antibody testing was offered to all residents (≥4 years) and workers in a San Francisco census tract (population: 5,174), regardless of symptoms, at outdoor, community-mobilized events over four days.  
• A total of 3,953 persons were tested: 40% Latino; 41% White; 9% Asian/Pacific Islander; and 2% Black.  
• Overall, 2.1% (83/3,871) tested PCR-positive: 95% were Latino and 52% asymptomatic when tested.  
• Risk factors for recent infection were Latino ethnicity, inability to shelter-in-place and maintain income, frontline service work, unemployment, and household income <$50,000/year.  
• Five COVID-19 phylogenetic lineages were detected. |
| 21.08.2020       | Epidemiology of COVID-19 Among Incarcerated Individuals and Staff in Massachusetts Jails and Prisons | JAMA Netw Open / Research letter           | • Among 14,987 individuals incarcerated across Massachusetts facilities, the rate of COVID-19 was 44.3 cases per 1000 persons—2.91 (95% CI, 2.69-3.14) times higher than the Massachusetts general population and 4.80 (95% CI, 4.45-5.18) times the US general population.  
• Overall, systems with higher testing rates had higher case rates. |
• Of the 18,940 study population, 11,755 (62.1%) were women, mean age was 53.7 years.  
• In multivariable logistic regression models there was a graded |
association between higher BMI levels and higher risk of COVID-19 infection.
  • Compared to normal weight individuals, the adjusted ORs in the overweight and obese individuals were 1.13 (95% CI, 1.03-1.25) and 1.26 (95% CI, 1.15-1.39), respectively.
  • This association was robust across age and sex subgroups.

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<td>18.08.2020</td>
<td>Clinical course and factors associated with outcomes among 1904 patients hospitalized with COVID-19 in Germany: an observational study</td>
<td>Clin Microbiol Infect / Article</td>
<td>Nationwide retrospective cohort study of 1904 COVID-19 patients (median age 73 years, 48.5% (924/1904) female) admitted to hospital in Germany. Mortality rate was 17%, rate of admission to ICU 21%, and the rate of invasive mechanical ventilation 14%.</td>
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### 03.08.2020

**Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study**

**EClinicalMedicine / Article**

- To identify the existence of potential brain micro-structural changes related to COVID-19, diffusion tensor imaging (DTI) and 3D high-resolution T1WI sequences were acquired in 60 recovered COVID-19 patients (56.67% male; age: 44.10 ± 16.00) and 39 matched non-COVID-19 controls (56.41% male; age: 45.88 ± 13.90).
- Neurological symptoms were presented in 55% COVID-19 patients at follow up.

### 15.08.2020

**SARS-CoV-2 has been circulating in northern Italy since December 2019: Evidence from environmental monitoring**

**Sci Total Environ / Article**

- The authors analysed 40 composite influent wastewater samples collected in Northern Italy between Oct 2019 and Feb 2020, using both nested RT-PCR and real-time RT-PCR assays.
- A total of 15 positive samples were confirmed.
- The earliest dates back to 18 Dec 2019 in Milan and Turin and 29 Jan 2020 in Bologna.
- Virus concentration in the samples ranged from below the limit of detection (LOD) to $5.6 \times 10^4$ genome copies (g.c.)/L, and most of the samples (23 out of 26) were below the limit of quantification of PCR.
- Suggests that COVID-19 was already circulating in Northern Italy at the end of 2019, and in different geographic regions simultaneously.

### Infection control

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| 20.08.2020       | **Environmental contamination in the isolation rooms of COVID-19 patients with severe pneumonia requiring mechanical ventilation or high-flow oxygen therapy** | J Hosp Infect / Article | • Environmental swab samples and air samples were taken from the isolation rooms of three COVID-19 patients with severe pneumonia.  
• Patient 1 and Patient 2 received mechanical ventilation with a closed suction system, while Patient 3 received high-flow oxygen therapy and non-invasive ventilation.  
• Of the 48 swab samples collected in the rooms of Patient 1 and Patient 2, only samples from the outside surfaces of the endotracheal tubes tested positive for COVID-19 by rRT-PCR.  
• However, in Patient 3’s room, 13 of the 28 environmental samples (fomites, fixed structures, and ventilation exit on the ceiling) showed positive results. |
• Air samples were negative for COVID-19.
• Viable viruses were identified on the surface of the endotracheal tube of Patient 1 and seven sites in Patient 3’s room.

21.08.2020 Quarantine and testing strategies in contact tracing for SARS-CoV-2 medRxiv (non-peer reviewed) / Article

• Adapting a simulation model for contact tracing, the authors find quarantine periods of at least 10 days combined with a PCR test on day 9 may largely emulate the results from a 14-day quarantine period in terms of the averted transmission potential from secondary cases (72% (95%UI: 3%, 100%) vs 75% (4%, 100%), respectively), assuming delays in testing and contact tracing are minimised to no more than 4.5 days.
• Concluded that the use of PCR testing is an effective strategy for reducing quarantine periods for secondary cases, while still reducing transmission of SARS-CoV-2, especially if delays in the test and trace system can be reduced, and may improve quarantine compliance rates.

Overviews, comments and editorials

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<td>25.08.2020</td>
<td>Household Composition May Explain COVID-19 Racial/Ethnic Disparities</td>
<td>JAMA / Health Agencies Update</td>
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<td>24.08.2020</td>
<td>Not just antibodies: B cells and T cells mediate immunity to COVID-19</td>
<td>Nat Rev Immunol / Comment</td>
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<tr>
<td>24.08.2020</td>
<td>Vaccines targeting SARS-CoV-2 tested in humans</td>
<td>Nat Med / News</td>
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<tr>
<td>24.08.2020</td>
<td>Lifting the mask on neurological manifestations of COVID-19</td>
<td>Nat Rev Neurol / Perspective</td>
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Produced by the PHE COVID-19 Literature Digest Team

To sign-up, email COVID.LitDigest@phe.gov.uk

A selection of previous digests can be found here