



COVID-19 Literature Digest – 26/08/2020

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- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
25.08.2020	Antibody Responses and Clinical Outcomes in Adults Hospitalized with Severe COVID-19: A Post hoc Analysis of LOTUS China Trial	Clin Infect Dis / Article	<ul style="list-style-type: none">• Neutralizing antibodies (NAbs) 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

			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.
24.08.2020	An inflammatory cytokine signature predicts COVID-19 severity and survival	Nat Med / Article	<ul style="list-style-type: none"> • <i>This paper was previously included in the Digest as a preprint.</i> • 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 < 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).
22.08.2020	Potent anti-SARS-CoV-2 Antibody Responses are Associated with Better Prognosis in Hospital Inpatient COVID-19 Disease	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 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.
24.08.2020	SARS-CoV-2 infection of human ACE2-transgenic mice causes severe lung inflammation and impaired function	Nat Immunol / Article	<ul style="list-style-type: none"> • 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.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
20.08.2020	The COVID-19 XPRIZE and the need for scalable, fast, and widespread testing	Nat Biotechnol / Correspondence	<ul style="list-style-type: none"> • Authors present an online tool (http://www.resiliencehealth.com/tests) that profiles current and emerging virology tests for detecting SARS-CoV-2. • Plus COVID-19 XPRIZE competition, OpenCovidScreen (https://opencovidscreen.org/), to identify economically viable, high-quality, scalable testing options.
24.08.2020	Inactivation analysis of SARS-CoV-2 by specimen transport media, nucleic acid extraction reagents, detergents and fixatives	J Clin Microbiol / Article	<ul style="list-style-type: none"> • <i>This paper was previously included in the Digest as a preprint.</i> • 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

Publication Date	Title / URL	Journal / Article type	Digest
25.08.2020	COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing	Clin Infect Dis / Article	<ul style="list-style-type: none"> • 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.

Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
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	<ul style="list-style-type: none"> • 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.
25.08.2020	Prevalence of SARS-CoV-2 Infection in Children Without Symptoms of Coronavirus Disease 2019	JAMA Pediatr / Research letter	<ul style="list-style-type: none"> • Authors report the prevalence of positive SARS-CoV-2 test results in children without symptoms at 28 children's hospitals across the US - tested before surgery, clinic visits, or hospital admissions. • 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.
21.08.2020	Multisystem inflammatory syndrome in children in South Africa	The Lancet Child & Adolescent Health / Correspondence	<ul style="list-style-type: none"> • 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.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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/\text{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	<ul style="list-style-type: none"> • 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.
25.08.2020	Association between Body Mass Index and Risk of COVID-19: A Nationwide Case-Control Study in South Korea	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Study examining the association between BMI level and the risk of COVID-19 infection in a nationwide case-control study comprised of 3,788 COVID-19 patients diagnosed between 24 Jan and 9 Apr 2020, and 15,152 controls matched by age and sex who underwent health examinations between 2015-2017. • 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

			<p>association between higher BMI levels and higher risk of COVID-19 infection.</p> <ul style="list-style-type: none"> • 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.
18.08.2020	Clinical course and factors associated with outcomes among 1904 patients hospitalized with COVID-19 in Germany: an observational study	Clin Microbiol Infect / Article	<ul style="list-style-type: none"> • 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%. • Most prominent risk factors for death were male sex (hazard ratio [HR] 1.45; 95% CI 1.2-1.8), pre-existing lung disease (HR 1.61; 95% CI 1.20-2.16), and increased patient age (HR 4.1 [95% CI 2.6-6.6] for age >79 years versus <60 years).

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
21.08.2020	Empiric Antibacterial Therapy and Community-onset Bacterial Co-infection in Patients Hospitalized with COVID-19: A Multi-Hospital Cohort Study	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Authors determined prevalence and predictors of empiric antibacterial therapy and community-onset bacterial co-infections in randomly sampled cohort of 1705 patients hospitalized with COVID-19. • 56.6% were prescribed early empiric antibacterial therapy; 3.5% (59/1705) had a confirmed community-onset bacterial infection. • Prevalence of confirmed community-onset bacterial co-infections was low. Despite this, half of patients received early empiric antibacterial therapy. Antibacterial use varied widely by hospital.
15.07.2020	Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery	EClinicalMedicine / Article	<ul style="list-style-type: none"> • Study of long-term pulmonary function and related physiological characteristics of 55 COVID-19 survivors, 3 months after discharge: COVID-19 infection related symptoms detected in 35; radiological abnormalities in 39 patients. • Radiological and physiological abnormalities were still found in a considerable proportion of COVID-19 survivors without critical cases 3 months after discharge. Higher level of D-dimer on admission could effectively predict impaired DLCO after 3 months discharge.

03.08.2020	Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study	EClinicalMedicine / Article	<ul style="list-style-type: none"> • 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. • Findings revealed possible disruption to micro-structural and functional brain integrity in the recovery stages of COVID-19, suggesting the long-term consequences of COVID-19.
15.08.2020	SARS-CoV-2 has been circulating in northern Italy since December 2019: Evidence from environmental monitoring	Sci Total Environ / Article	<ul style="list-style-type: none"> • 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 5.6×10^4 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

Publication Date	Title / URL	Journal / Article type	Digest
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	<ul style="list-style-type: none"> • 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.

			<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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

Publication Date	Title / URL	Journal / Article type
25.08.2020	Household Composition May Explain COVID-19 Racial/Ethnic Disparities	JAMA / Health Agencies Update
24.08.2020	Not just antibodies: B cells and T cells mediate immunity to COVID-19	Nat Rev Immunol / Comment
24.08.2020	Vaccines targeting SARS-CoV-2 tested in humans	Nat Med / News
24.08.2020	Lifting the mask on neurological manifestations of COVID-19	Nat Rev Neurol / Perspective

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