



International EPI Cell Evidence Digest – 15/07/2020

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- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
14.07.2020	An mRNA Vaccine against SARS-CoV-2 - Preliminary Report	N Engl J Med / Article	<ul style="list-style-type: none">• Here the authors' report interim results of a first-in-human phase 1 clinical trial in healthy adults to evaluate the safety and immunogenicity of mRNA-1273.• The mRNA-1273 vaccine induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified.• These findings support further development of this vaccine.

13.07.2020	Humoral and circulating follicular helper T cell responses in recovered patients with COVID-19	Nat Med / Letter	<ul style="list-style-type: none"> • Characterized humoral and circulating follicular helper T cell (cTFH) immunity against spike in recovered patients with COVID-19. • Overall, although patients who recovered from COVID-19 displayed multiple hallmarks of effective immune recognition of S, the wide spectrum of neutralizing activity observed suggests that vaccines might require strategies to selectively target the most potent neutralizing epitopes.
07.07.2020	Direct observation of repeated infections with endemic coronaviruses	The Journal of Infectious Diseases / Article	<ul style="list-style-type: none"> • This study used data from proactive sampling carried out in New York City from fall 2016 to spring 2018, and combined weekly nasal swab collection with self-reports of respiratory symptoms from 191 participants to investigate the profile of recurring infections with endemic coronaviruses. • This study provides evidence that re-infections with the same endemic coronavirus are not atypical in a time window shorter than 1 year and that the genetic basis of innate immune response may be a greater determinant of infection severity than immune memory acquired after a previous infection.
13.07.2020	Antibody kinetics in primary- and secondary-care physicians with mild to moderate SARS-CoV-2 infection	Emerg Microbes Infect / Letter	<ul style="list-style-type: none"> • 397 primary- and secondary-care physicians were tested for the presence of IgG (and IgA) antibodies against SARS-coronavirus-2 with a commercially available ELISA. • In 19 of 20 individuals with PCR-proven infection and only mild to moderate symptoms not requiring hospitalization positive IgG levels occurred within two to three weeks. • Among the remaining 377 persons without clear-cut evidence of infection, unequivocally positive IgG antibodies were found in only one, showing a surprisingly low prevalence (0.3%, 95% CI: 0.01-1.5) in physicians with likely contacts with infected patients in a region highly affected by the pandemic (Tyrol, Austria).

Diagnosics

Publication Date	Title/URL	Journal/ Article type	Digest
13.07.2020	At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR based tests?: A systematic review of individual participant data	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Individual participant data (IPD) systematic review of 32 longitudinal studies of RT-PCR test results in symptomatic SARS-CoV-2, with 1023 SARS-CoV-2 infected participants. • The highest percentage virus detection was from nasopharyngeal sampling between 0 to 4 days post-symptom onset at 89%, dropping to 54% after 10 to 14 days. On average, duration of detectable virus was longer

			<p>with lower respiratory tract (LRT) sampling than upper respiratory tract (URT).</p> <ul style="list-style-type: none"> • Duration of faecal and respiratory tract virus detection varied greatly within individual participants. In some participants, virus was still detectable at 46 days post-symptom onset. • They conclude that RT-PCR misses detection of people with SARS-CoV-2 infection; early sampling minimises false negative diagnoses.
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Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
13.07.2020	Neutralizing nanobodies bind SARS-CoV-2 spike RBD and block interaction with ACE2	Nat Struct Mol Biol / Article	<ul style="list-style-type: none"> • Using a naive llama single-domain antibody library and PCR-based maturation, the authors produced two closely related nanobodies, H11-D4 and H11-H4, that bind RBD (K(D) of 39 and 12 nM, respectively) and block its interaction with ACE2. • Single-particle cryo-EM revealed that both nanobodies bind to all three RBDs in the spike trimer. • Crystal structures of each nanobody-RBD complex revealed how both nanobodies recognize the same epitope, which partly overlaps with the ACE2 binding surface, explaining the blocking of the RBD-ACE2 interaction. • Nanobody-Fc fusions showed neutralizing activity against SARS-CoV-2 (4-6 nM for H11-H4, 18 nM for H11-D4) and additive neutralization with the SARS-CoV-1/2 antibody CR3022.
14.07.2020	Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: a prospective genomic surveillance study	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none"> • This study established real-time genomic surveillance of SARS-CoV-2 in a UK hospital and showed the benefit of combined genomic and epidemiological analysis for the investigation of health-care associated COVID-19. • This approach enabled the authors' to detect cryptic transmission events and identify opportunities to target infection-control interventions to further reduce health-care associated infections. • These findings have important implications for national public health policy as they enable rapid tracking and investigation of infections in hospital and community settings. <p><i>(This study was previously included as a pre-print)</i></p>

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Probable Vertical Transmission of SARS-CoV-2 Infection	The Pediatric infectious disease journal / Article	<ul style="list-style-type: none"> • Description of the probable vertical transmission of SARS-CoV-2 in a neonate born to a mother with COVID-19. • Following caesarean section, the neonate was kept in strict isolation. Molecular tests for SARS-CoV-2 on respiratory samples, blood, and meconium were initially negative, but positive on a nasopharyngeal aspirate on the third day of life. On day 5, the neonate developed fever and coryza, which spontaneously resolved. • Viral genomic analysis from the mother and neonate showed identical sequences except for 1 nucleotide.
10.07.2020	INTRAUTERINE TRANSMISSION OF SARS-COV-2 INFECTION IN A PRETERM INFANT	The Pediatric infectious disease journal / Article	<ul style="list-style-type: none"> • Case report of a preterm infant who developed a fever and mild respiratory disease on the second day of life. • Infant SARS-CoV-2 nasopharyngeal testing was positive at 24 and 48 hours of life. Placenta histopathology revealed SARS-CoV-2 infection by electron microscopy and immunohistochemistry.
13.07.2020	Vertical transmission of SARS-CoV-2 infection and preterm birth	Eur J Clin Microbiol Infect Dis / Brief report	<ul style="list-style-type: none"> • Describe a case of a known SARS-CoV-2-positive woman giving preterm birth to two fetuses with SARS-CoV-2 positive testing in placental tissue and amniotic fluid. • The placental histological examinations showed chronic intervillitis and extensive intervillous fibrin depositions with ischemic necrosis of the surrounding villi.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
14.07.2020	COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England	The Lancet / Article	<ul style="list-style-type: none"> • This study aimed to understand the scale, nature, and duration of changes to admissions for different types of acute coronary syndrome in England and to evaluate whether in-hospital management of patients has been affected as a result of the COVID-19 pandemic. • Compared with the weekly average in 2019, there was a substantial reduction in the weekly numbers of patients with acute coronary syndrome who were admitted to hospital in England by the end of March, 2020, which had been partly reversed by the end of May, 2020.

			<ul style="list-style-type: none"> • The reduced number of admissions during this period is likely to have resulted in increases in out-of-hospital deaths and long-term complications of myocardial infarction and missed opportunities to offer secondary prevention treatment for patients with coronary heart disease.
18.06.2020	Global evaluation of echocardiography in patients with COVID-19	Eur Heart J Cardiovasc Imaging / Article	<ul style="list-style-type: none"> • In a prospective international survey, the authors' captured echocardiography findings in patients with presumed or confirmed COVID-19 between 3 and 20 April 2020 (n=1216), and patient characteristics, indications, findings, and impact of echocardiography on management were recorded. • Cardiac abnormalities were observed in half of all COVID-19 patients undergoing echocardiography. Abnormalities were often unheralded or severe, and imaging changed management in one-third of patients.
13.07.2020	Pulmonary embolism in COVID-19 patients: a French multicentre cohort study	Eur Heart J / Article	<ul style="list-style-type: none"> • This study aimed to describe the risk factors and baseline characteristics of patients with pulmonary embolism (PE) in a cohort of COVID-19 patients. • Among 1240 patients (58.1% men, mean age 64 ± 17 years), 103 (8.3%) patients had PE confirmed by CTPA. • The ICU transfer and mechanical ventilation were significantly higher in the PE group (for both P < 0.001). In an univariable analysis, traditional venous thrombo-embolic risk factors were not associated with PE (P > 0.05), while patients under therapeutic dose anticoagulation before hospitalization or prophylactic dose anticoagulation introduced during hospitalization had lower PE occurrence.
12.07.2020	Blood type and outcomes in patients with COVID-19	Ann Hematol / Article	<ul style="list-style-type: none"> • This study aimed to determine if there is an association between ABO blood type and severity of COVID-19 defined by intubation or death as well as ascertain if there is variability in testing positive for COVID-19 between blood types. • All adult patients who tested positive for COVID-19 across five hospitals were identified and included from March 6th to April 16th, 2020 (n=1289). • Blood type was not associated with risk of intubation or death in patients with COVID-19. • Patients with blood types B and AB who received a test were more likely to test positive and blood type O was less likely to test positive. Rh+ patients were more likely to test positive.
13.07.2020	The National Early Warning Score (NEWS2) systematically underestimates the risk of in-hospital mortality in unplanned COVID-19 admissions to hospital	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of the performance of the UK National Early Warning Score (NEWS2) during the first phase of the COVID-19 pandemic, using discharge data on 6480 adult non-elective admissions to predict mortality at four time points (in-hospital, 24hours, 48hours, and 72hours) in COVID-19 versus non-COVID-19 admissions.

		<ul style="list-style-type: none"> • Out of 6480 non-elective admissions, 620 (9.6%) had a diagnosis of COVID-19. They were older, more often male, had higher index NEWS and NEWS2 scores and higher in-hospital mortality. • Increasing NEWS2 values reflected increased mortality, but for any given value the absolute risk was on average 24% higher (e.g. NEWS2=5: 36% vs 9%). NEWS2 is thus a valid predictor of the mortality risk but substantially underestimates the absolute mortality risk in COVID-19 patients.
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Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
14.07.2020	Outcomes of Universal COVID-19 Testing Following Detection of Incident Cases in 11 Long-term Care Facilities	JAMA Intern Med / Research letter	<ul style="list-style-type: none"> • Performed universal testing of untested residents across 11 Maryland long-term care facilities that (1) had previously undergone targeted testing through the local health department based on individual residents' symptoms and (2) had known positive cases. • Targeted symptom-based testing identified 153 cases prior to point-prevalence surveys at 11 facilities within 20 days of detection of the index case. Among the remaining 893 residents who were universally tested, 354 (39.6%) tested positive for SARS-CoV-2 RNA. Thus, universal screening increased the total number of detected COVID-19 cases across all sites from 153 to 507; of these, 281 (55.4%) were asymptomatic
14.07.2020	Serology-informed estimates of SARS-CoV-2 infection fatality risk in Geneva, Switzerland	The Lancet Infectious Diseases / Correspondence	<ul style="list-style-type: none"> • Estimated overall and age specific infection fatality risk (IFR) for the canton of Geneva, Switzerland, using age-stratified daily case and death incidence reports combined with population based seroprevalence estimates done each week for 5 consecutive weeks. • The results reveal that population-wide estimates of IFR mask great heterogeneity by age and point towards the importance of age-targeted interventions to reduce exposures among those at highest risk of death.
11.07.2020	Epidemiological characteristics of the COVID-19 outbreak in a secondary hospital in Spain	Am J Infect Control / Article	<ul style="list-style-type: none"> • The aim of this study is to describe the cases of COVID-19 at Infanta Sofia University Hospital (Madrid), a public secondary hospital that increased its hospital beds to provide assistance during the outbreak. • Of 1612 confirmed cases, 61,8% were hospitalised, 5,0% were admitted to the ICU. 52,2% were male. The median age was 63,2 years. 13,1% were nursing home residents. 19,0% were of Latin American origin of which 6,8% were admitted to the ICU, and overall case fatality was 14,6%.

			<ul style="list-style-type: none"> • 60 to 79 year old males were admitted and deceased more often than women, and Latin Americans were admitted more often to the ICU.
15.07.2020	Comparing dynamics and determinants of SARS-CoV-2 transmissions among health care workers of adult and pediatric settings in central Paris	Clin Infect Dis / Article	<ul style="list-style-type: none"> • This prospective study compared a 1,500-bed adult and a 600-bed paediatric setting of a tertiary-care university hospital located in central Paris. • From Feb 24th until April 10th, 2020, all symptomatic HCW were screened for SARS-CoV-2. • Among 1344 HCW tested, 373 were positive (28%) and 336 (90%) corresponding questionnaires were completed. • Residual transmissions were related to persistent exposures with undiagnosed patients or colleagues and not to contacts with children attending out-of-home care facilities.
13.07.2020	Clusters of 2019 coronavirus disease (COVID-19) cases in Chinese tour groups	Transbound Emerg Dis / Article	<ul style="list-style-type: none"> • This study describes clusters of COVID-19 cases within Chinese tour groups travelling in Europe Jan 16-28, and compares characteristics of cases and non-cases to determine transmission dynamics. • The index case travelled from Wuhan, China, to Europe on Jan 16, 2020, and to Shanghai, China, on January 27, 2020, within a tour group (group A). • Tour groups with the same outbound flight (group B) or the same tourism venue (group D), and all Chinese passengers on the inbound flight (group C) were investigated. • The outbreak involved 11 confirmed cases, 10 suspected cases, and 6 tourists who remained healthy. • There was less pathogenicity with propagative transmission than with familial transmission, and the disease was transmitted in shared outbound flights, shopping venues within Europe, and inbound flight back to China.
14.07.2020	Absence of in-flight transmission of SARS-CoV-2 likely due to use of face masks on board	J Travel Med / Article	<ul style="list-style-type: none"> • The authors describe a 14 hour flight of 11 passengers and 4 crew members in which 2 positive SARS-COV-2 were on board. • No new viral acquisitions found in this flight, probably due to the use of masks.
14.07.2020	Clinical and Pathological Findings in SARS-CoV-2 Disease Outbreaks in Farmed Mink (Neovison vison)	Vet Pathol / Article	<ul style="list-style-type: none"> • SARS-CoV-2 caused respiratory disease outbreaks with increased mortality in 4 mink farms in the Netherlands. • The most striking post-mortem finding was an acute interstitial pneumonia, which was found in nearly all examined mink that died at the peak of the outbreaks. • Acute alveolar damage was a consistent histopathological finding in mink that died with pneumonia. • SARS-CoV-2 infections were confirmed by detection of viral RNA in throat swabs and by immunohistochemical detection of viral antigen in nasal

			<p>conchae, trachea, and lung.</p> <ul style="list-style-type: none"> • Clinically, the outbreaks lasted for about 4 weeks but some animals were still PCR-positive for SARS-CoV-2 in throat swabs after clinical signs had disappeared.
14.07.2020	Detection of SARS-CoV-2 RNA in commercial passenger aircraft and cruise ship wastewater: a surveillance tool for assessing the presence of COVID-19 infected travelers	Journal of Travel Medicine / Article	<ul style="list-style-type: none"> • Study to investigate the possible use of SARS-CoV-2 RNA wastewater surveillance from airline and cruise ship sanitation systems and its potential use as a COVID-19 public health management tool. • Airline and cruise ship wastewater samples (n = 21) were tested for SARS-CoV-2 RNA which was detected in samples from both aircraft and cruise ship wastewater; however, concentrations were near the assay limit of detection. • The study indicates that surveillance of wastewater from large transport vessels with their own sanitation systems has potential as a complementary data source to prioritize clinical testing and contact tracing among disembarking passengers. Importantly, sampling methods and molecular assays must be further optimized to maximize sensitivity.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
14.07.2020	Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers	JAMA / Research letter	<ul style="list-style-type: none"> • This study assessed the association of hospital masking policies with the SARS-CoV-2 infection rate among HCWs. • Of 9850 tested HCWs, 1271 (12.9%) had positive results for SARS-CoV-2. • During the preintervention period, the SARS-CoV-2 positivity rate increased exponentially from 0% to 21.32%, with a weighted mean increase of 1.16% per day and a case doubling time of 3.6 days (95% CI, 3.0-4.5 days). • During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46%, with a weighted mean decline of 0.49% per day and a net slope change of 1.65% (95% CI, 1.13%-2.15%; P < .001) more decline per day compared with the preintervention period. • Decrease in HCW infections could be confounded by other interventions inside and outside of the health care system, such as restrictions on elective procedures, social distancing measures, and increased masking in public spaces.

26.06.2020	Face masks and coverings for the general public: Behavioural knowledge, effectiveness of cloth coverings and public messaging	Royal Society and British Academy / Pre-print Rapid review	<ul style="list-style-type: none"> • Cloth face coverings are effective in reducing source virus transmission, i.e., outward protection of others, when they are of optimal material and construction (high grade cotton, hybrid and multilayer) and fitted correctly and for source protection of the wearer. • Socio-behavioural factors are vital to understanding public adherence to wearing face masks and coverings, including public understanding of virus transmission, risk perception, trust, altruism, individual traits, perceived barriers. • Face masks and coverings cannot be seen in isolation but are part of 'policy packages' and it is imperative to review interrelated non-pharmaceutical interventions in tandem including hand hygiene, sanitizers and social distancing when maintaining the 2 metre or 1 metre+ distancing rule is not possible. • Consistent and effective public messaging is vital to public adherence of wearing face masks and coverings. Conflicting policy advice generates confusion and lack of compliance. Populations without a previous history of mask wearing have rapidly adopted face coverings during the COVID-19 period.
12.07.2020	COVID-19 incidence and R decreased on the Isle of Wight after the launch of the Test, Trace, Isolate programme	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study using COVID-19 daily case data to infer incidence of new infections and estimate the reproduction number R for each of 150 Upper Tier Local Authorities in England, and at the National level, before and after the launch of the Test, Trace, Isolate programme on the Isle of Wight in May 2020. • They observed significant decreases in incidence and R on the Isle of Wight immediately after the launch, with results showing that the sub-epidemic on the Isle of Wight was controlled significantly more effectively than the sub-epidemics of most other Upper Tier Local Authorities, changing from having the third highest reproduction number R (of 150) before the intervention to the tenth lowest afterwards. • The data is not yet available to establish a causal link.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
12.07.2020	The effect of international travel restrictions on internal spread of COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • LSHTM study to inform decisions about international travel restrictions, by comparing the ratio of expected COVID-19 cases from international travel (assuming no travel restrictions) to the expected COVID-19 cases arising from internal spread on an average day in May 2020 in each country. • With May 2019 travel volumes, imported cases account for <10% of total incidence in 103 out of 142 countries, and <1% in 48. • If we assume that travel would decrease compared to May 2019 even in the absence of formal restrictions, then imported cases account for <10% of total incidence in 109-123 countries and <1% in 61-88 countries (depending on the assumptions about travel reductions). • In most countries imported cases likely contribute little to local COVID-19 epidemics.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
14.07.2020	Preparing for a challenging winter 2020/21	The Academy of Medical Sciences / Report
10.07.2020	Perceived Challenges of COVID-19 Infection Prevention and Control Preparedness: A Multinational Survey	J Glob Antimicrob Resist / Short Communication
13.07.2020	Covid-19: excess all cause mortality in domiciliary care	BMJ / Letter
14.07.2020	Universal Masking to Prevent SARS-CoV-2 Transmission-The Time Is Now	Jama / Editorial
13.07.2020	Airborne Transmission of SARS-CoV-2: Theoretical Considerations and Available Evidence	Jama / Viewpoint
13.07.2020	A perspective on potential antibody-dependent enhancement of SARS-CoV-2	Nature / Article
13.07.2020	Immune-mediated approaches against COVID-19	Nat Nanotechnol / Review article
14.07.2020	Review: The safe handling of a corpse (suspected) with COVID-19	J Forensic Leg Med / Article