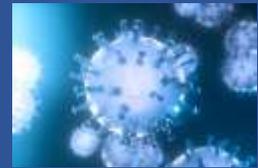


COVID-19

Jul 02-08, 2020



RESEARCH PUBLICATIONS

Publication Date: July 08, 2020

The emerging spectrum of COVID-19 neurology: Clinical, radiological and laboratory findings

Abstract

Preliminary clinical data indicate that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is associated with neurological and neuropsychiatric illness. Responding to this, a weekly virtual coronavirus disease 19 (COVID-19) neurology multi-disciplinary meeting was established at the National Hospital, Queen Square, in early March 2020 in order to discuss and begin to understand neurological presentations in patients with suspected COVID-19-related neurological disorders. Detailed clinical and paraclinical data were collected from cases where the diagnosis of COVID-19 was confirmed through RNA PCR, or where the diagnosis was probable/possible according to World Health Organization criteria. Of 43 patients, 29 were SARS-CoV-2 PCR positive and definite, eight probable and six possible. Five major categories emerged: (i) encephalopathies (n = 10) with delirium/psychosis and no distinct MRI or CSF abnormalities, and with 9/10 making a full or partial recovery with supportive care only; (ii) inflammatory CNS syndromes (n = 12) including encephalitis (n = 2, para- or post-infectious), acute disseminated encephalomyelitis (n = 9), with haemorrhage in five, necrosis in one, and myelitis in two, and isolated myelitis (n = 1). Of these, 10 were treated with corticosteroids, and three of these patients also received intravenous immunoglobulin; one made a full recovery, 10 of 12 made a partial recovery, and one patient died; (iii) ischaemic strokes (n = 8) associated with a pro-thrombotic state (four with pulmonary thromboembolism), one of whom died; (iv) peripheral neurological disorders (n = 8), seven with Guillain-Barré syndrome, one with brachial plexopathy, six

of eight making a partial and ongoing recovery; and (v) five patients with miscellaneous central disorders who did not fit these categories. SARS-CoV-2 infection is associated with a wide spectrum of neurological syndromes affecting the whole neuraxis, including the cerebral vasculature and, in some cases, responding to immunotherapies. The high incidence of acute disseminated encephalomyelitis, particularly with haemorrhagic change, is striking. This complication was not related to the severity of the respiratory COVID-19 disease. Early recognition, investigation and management of COVID-19-related neurological disease is challenging. Further clinical, neuroradiological, biomarker and neuropathological studies are essential to determine the underlying pathobiological mechanisms, which will guide treatment. Longitudinal follow-up studies will be necessary to ascertain the long-term neurological and neuropsychological consequences of this pandemic.

Reference

<https://academic.oup.com/brain/article/doi/10.1093/brain/awaa240/5868408?searchresult=1>

Sars-Cov-2 cell entry receptor Ace2 mediated endothelial dysfunction leads to vascular thrombosis in COVID-19 patients

Abstract

Several studies have described an unusually high incidence of vascular thrombosis in coronavirus disease-2019 (COVID-19) patients. Pathogenesis of the vascular thrombosis in COVID-19 is least understood for now and presents a challenge to the treating physicians. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the causative pathogen for COVID-19, has been shown to bind to angiotensin converting enzyme 2 (ACE2) protein in human epithelial cells which facilitates its entry in the organ and mediate tissue-specific pathogenesis. For ACE2 mediated cell entry of the SARS-CoV-2, co-expression of one more protein—Transmembrane protease serine 2 (TMPRSS2) is essential. Existing studies suggested a significant expression of ACE2 and TMPRSS2 in human vascular endothelium. Recently, in situ evidence has been presented that SARS-CoV-2 can infect cells in human vascular endothelium. Based on the circumstantial evidence present in the literature, we propose a SARS-CoV-2 cell entry receptor ACE2 based mechanism for vascular thrombosis in COVID-19 patients.

Reference

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3640259

Disease modifying therapies and COVID-19 severity in Multiple Sclerosis

Abstract

Background: Immunosuppressive and immunomodulatory therapies are a major issue during the current coronavirus disease 2019 (Covid-19) pandemic, and in anticipation of possible next waves.

Methods: In a nationwide study we retrospectively collected data of persons with Multiple Sclerosis (PwMS) with suspected or confirmed Covid-19. We assessed the association of therapies for MS with Covid-19 by comparing their observed frequency with the one expected in non-pandemic conditions (expressing the association by Odds Ratios [OR]). We evaluated baseline characteristics and MS therapies associated to a severe Covid-19 course by multivariate logistic models.

Findings: Of 784 PwMS with suspected (n=593) or confirmed (n=191) Covid-19 and a median follow-up of 84 days (range=30-135), 13 (1.66%) died: 11 of them were in a progressive MS phase, and 8 were without any therapy. Thirty-three (4.2%) were admitted to an Intensive Care Unit; 90 (11.5%) had a radiologically documented pneumonia; 88 (11.2%) were hospitalized. We found an excess of patients treated with Ocrelizumab (OR=1.84,95%CI=1.31-2.56, p<0.001) and a reduction of patients treated with Interferon (OR=0.47,95%CI=0.33-0.67, p<0.001) as compared to the frequency of use of these DMTs in the Italian MS population. After adjusting for region, age, sex, progressive MS course and recent methylprednisolone use, the therapy with an anti-CD20 agent (Ocrelizumab or Rituximab) was significantly associated (OR=2.59,95%CI=1.43-4.67, p=0.002) with an increased risk of severe Covid-19 course. Recent use (<1 month) of methylprednisolone was also associated with a worse outcome (OR=6.0,95%CI=2.2-16.5, p=0.007).

Interpretation: This study showed an acceptable level of safety of therapies with a broad array of mechanisms of action. However, the study detected elements of risk and protection with respect to Covid-19 in MS. These will need to be considered in countries where the pandemic is persisting and in preparation for post-pandemic scenarios.

Reference

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3631244

Four-step approach to efficiently develop capillary gel electrophoresis methods for viral vaccine protein analysis

Abstract

Vaccines against infectious diseases are urgently needed. Therefore, modern analytical method development should be as efficient as possible to speed up vaccine development. The objectives of the study were to identify critical method parameters (CMPs) and to establish a set of steps to efficiently develop and validate a CE-SDS method for vaccine protein analysis based on a commercially available gel buffer. The CMPs were obtained from reviewing the literature and testing the effects of gel buffer dilution. A four-step approach, including two multivariate DoE (design of experiments) steps, was proposed, based on CMPs and was verified by CE-SDS method development for: (i) the determination of influenza group 1 mini-haemagglutinin glycoprotein; and (ii) the determination of polio virus particle proteins from an inactivated polio vaccine (IPV). The CMPs for sample preparation were incubation temperature(s) and time(s), pH, and reagent(s) concentration(s) and the detection wavelength. The effects of gel buffer dilution revealed the CMPs for CE-SDS separation to be the effective length, the gel buffer concentration, and the capillary temperature. The four-step approach based on the CMPs was efficient for the development of the two CE methods. A four-step approach to efficiently develop capillary gel electrophoresis methods for viral vaccine protein analysis was successfully established.

Reference

<https://onlinelibrary.wiley.com/doi/10.1002/elps.202000107>

Changes in RT-PCR test results and symptoms during the menstrual cycle of female individuals infected with SARS-CoV-2: Report of two cases

Abstract

Background: The implications of the menstrual cycle for disease susceptibility, development, and severity of acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are largely unknown.

Case presentation: Here we describe two women infected with SARS-CoV-2 whose RT-PCR test results and symptoms changed during the menstrual cycle. The first patient developed a fever on the first day of her menstrual period, and again on the first day of her next menstrual period after hospital discharge. RT-PCR test results were positive during the first menstrual period before admission, but turned negative during hospitalization, and then were positive again during the second menstrual period after hospital discharge. Another one also developed a fever again on the first day of her menstrual period after hospital discharge. RT-PCR test results were negative before admission and during hospitalization, but turned positive during the first menstrual period after hospital discharge.

Conclusions: The cases indicate sex hormones may play an important role in SARS-CoV-2 infection. For women with history of exposure to SARS-CoV-2, the management protocol should include assessment of the menstrual status.

Reference

<https://onlinelibrary.wiley.com/doi/10.1002/jmv.26275>

Optimising benefits of testing key workers for infection with SARS-CoV-2: A mathematical modelling analysis

Abstract

Background: Internationally, key workers such as healthcare staff are advised to stay at home if they or household members experience coronavirus disease 2019 (COVID-19)-like symptoms. This potentially isolates / quarantines many staff without SARS-CoV-2, whilst not preventing transmission from staff with asymptomatic infection. We explored

the impact of testing staff on absence durations from work and transmission risks to others.

Methods: We used a decision-analytic model for 1,000 key workers to compare the baseline strategy of (S0) no RT-PCR testing of workers to testing workers (S1) with COVID-19-like symptoms in isolation, (S2) without COVID-19-like symptoms but in household-quarantine, and (S3) all staff. We explored confirmatory re-testing scenarios of repeating all initial tests, initially-positive tests, initially-negative tests; or no re-testing. We varied all parameters, including the infection rate (0.1%-20%), proportion asymptomatic (10%-80%), sensitivity (60%-95%), and specificity (90%-100%).

Results: Testing all staff (S3) changes the risk of workplace transmission by -56.9 to +1.0 workers per 1,000 tests (with reductions throughout at RT-PCR sensitivity of $\geq 65\%$), and absences by 0.5 to +3.6 days per test but at heightened testing needs of 989.6-1995.9 tests per 1,000 workers. Testing workers in household-quarantine (S2) reduces absences the most by 3.0-6.9 days per test (at 47.0-210.4 tests per 1,000 workers), while increasing risk of workplace transmission by 0.02-49.5 infected workers per 1,000 tests (which can be minimised when re-testing initially-negative tests).

Discussion: Based on optimising absence durations or transmission risk our modelling suggests testing staff in household-quarantine or all staff, depending on infection levels and testing capacities.

Reference

<https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa901/5868532?searchresult=1>

Neurological immunotherapy in the era of COVID-19 — looking for consensus in the literature

Abstract

The coronavirus disease 2019 (COVID-19) pandemic is concerning for patients with neuroimmunological diseases who are receiving immunotherapy. Uncertainty remains about whether immunotherapies increase the risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or increase the risk of severe disease and death upon infection. National and international societies have developed guidelines and statements, but consensus does not exist in several areas. In this Review, we attempt

to clarify where consensus exists and where uncertainty remains to inform management approaches based on the first principles of neuroimmunology. We identified key questions that have been addressed in the literature and collated the recommendations to generate a consensus calculation in a Delphi-like approach to summarize the information. We summarize the international recommendations, discuss them in light of the first available data from patients with COVID-19 receiving immunotherapy and provide an overview of management approaches in the COVID-19 era. We stress the principles of medicine in general and neuroimmunology in particular because, although the risk of viral infection has become more relevant, most of the considerations apply to the general management of neurological immunotherapy. We also give special consideration to immunosuppressive treatment and cell-depleting therapies that might increase susceptibility to SARS-CoV-2 infection but reduce the risk of severe COVID-19.

Reference

<https://www.nature.com/articles/s41582-020-0385-8>

Immunological and inflammatory profiles in mild and severe cases of COVID-19

Abstract

COVID-19 is associated with 5.1% mortality. Although the virological, epidemiological, clinical, and management outcome features of COVID-19 patients have been defined rapidly, the inflammatory and immune profiles require definition as they influence pathogenesis and clinical expression of COVID-19. Here we show lymphopenia, selective loss of CD4+ T cells, CD8+ T cells and NK cells, excessive T-cell activation and high expression of T-cell inhibitory molecules are more prominent in severe cases than in those with mild disease. CD8+ T cells in patients with severe disease express high levels of cytotoxic molecules. Histochemical studies of lung tissue from one fatality show sub-anatomical distributions of SARS-CoV-2 RNA and massive infiltration of T cells and macrophages. Thus, aberrant activation and dysregulation of CD8+ T cells occur in patients with severe COVID-19 disease, an effect that might be for pathogenesis of SARS-CoV-2 infection and indicate that immune-based targets for therapeutic interventions constitute a promising treatment for severe COVID-19 patients.

Reference

<https://www.nature.com/articles/s41467-020-17240-2>

BCG vaccination policy and preventive chloroquine usage: Do they have an impact on COVID-19 pandemic?

Abstract

Coronavirus disease 2019 (COVID-19) is a severe acute respiratory syndrome caused by Coronavirus 2 (SARS-CoV-2). In the light of its rapid global spreading, on 11 March 2020, the World Health Organization has declared it a pandemic. Interestingly, the global spreading of the disease is not uniform, but has so far left some countries relatively less affected. The reason(s) for this anomalous behavior are not fully understood, but distinct hypotheses have been proposed. Here we discuss the plausibility of two of them: the universal vaccination with Bacillus Calmette–Guerin (BCG) and the widespread use of the antimalarial drug chloroquine (CQ). Both have been amply discussed in the recent literature with positive and negative conclusions: we felt that a comprehensive presentation of the data available on them would be useful. The analysis of data for countries with over 1000 reported COVID-19 cases has shown that the incidence and mortality were higher in countries in which BCG vaccination is either absent or has been discontinued, as compared with the countries with universal vaccination. We have performed a similar analysis of the data available for CQ, a widely used drug in the African continent and in other countries in which malaria is endemic; we discuss it here because CQ has been used as the drug to treat COVID-19 patients. Several African countries no longer recommend it officially for the fight against malaria, due to the development of resistance to Plasmodium, but its use across the continent is still diffuse. Taken together, the data in the literature have led to the suggestion of a possible inverse correlation between BCG immunization and COVID-19 disease incidence and severity.

Reference

<https://www.nature.com/articles/s41419-020-2720-9>

Sex differences in SARS-CoV-2 infection rates and the potential link to prostate cancer

Abstract

The recent outbreak of infections and the pandemic caused by SARS-CoV-2 represent one of the most severe threats to human health in more than a century. Emerging data from the United States and elsewhere suggest that the disease is more severe in men. Knowledge gained, and lessons learned, from studies of the biological interactions and molecular links that may explain the reasons for the greater severity of disease in men, and specifically in the age group at risk for prostate cancer, will lead to better management of COVID-19 in prostate cancer patients. Such information will be indispensable in the current and post-pandemic scenarios.

Reference

<https://www.nature.com/articles/s42003-020-1088-9>

Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital

Abstract

Health care workers (HCW) are a high-risk population to acquire SARS-CoV-2 infection from patients or other fellow HCW. This study aims at estimating the seroprevalence against SARS-CoV-2 in a random sample of HCW from a large hospital in Spain. Of the 578 participants recruited from 28 March to 9 April 2020, 54 (9.3%, 95% CI: 7.1–12.0) were seropositive for IgM and/or IgG and/or IgA against SARS-CoV-2. The cumulative prevalence of SARS-CoV-2 infection (presence of antibodies or past or current positive rRT-PCR) was 11.2% (65/578, 95% CI: 8.8–14.1). Among those with evidence of past or current infection, 40.0% (26/65) had not been previously diagnosed with COVID-19. Here we report a relatively low seroprevalence of antibodies among HCW at the peak of the COVID-19 epidemic in Spain. A large proportion of HCW with past or present infection had not been previously diagnosed with COVID-19, which calls for active periodic rRT-PCR testing in hospital settings.

Reference

<https://www.nature.com/articles/s41467-020-17318-x>

Publication Date: July 07, 2020

A one-step, one-tube real-time RT-PCR based assay with an automated analysis for detection of SARS-CoV-2

Abstract

Early diagnosis of SARS-CoV-2 infected patients is essential to control the dynamics of the COVID-19 pandemic. We develop a rapid and accurate one-step multiplex TaqMan probe-based real-time RT-PCR assay, along with a computational tool to systematically analyse the data. Our assay could detect to a limit of 15 copies of SARS-CoV-2 transcripts—based on experiments performed by spiking total human RNA with in vitro synthesized viral transcripts. The assay was evaluated by performing 184 validations for the SARS-CoV-2 Nucleocapsid gene and human RNase P as an internal control reference gene with dilutions ranging from 1-100 ng for human RNA on a cohort of 26 clinical samples. 5 of 26 patients were confirmed to be infected with SARS-CoV-2, while 21 tested negative, consistent with the standards. The accuracy of the assay was found to be 100% sensitive and 100% specific based on the 26 clinical samples that need to be further verified using a large number of clinical samples. In summary, we present a rapid, easy to implement real-time PCR based assay with automated analysis using a novel COVID qPCR Analyzer tool with graphical user interface (GUI) to analyze the raw qRT-PCR data in an unbiased manner at a cost of under \$3 per reaction and turnaround time of less than 2h, to enable in-house SARS-CoV-2 testing across laboratories.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)31249-4](https://www.cell.com/heliyon/fulltext/S2405-8440(20)31249-4)

Longitudinal isolation of potent near-germline SARS-CoV-2-neutralizing antibodies from COVID-19 patients

Abstract

The SARS-CoV-2 pandemic has unprecedented implications for public health, social life, and world economy. Since approved drugs and vaccines are not available, new options for COVID-19 treatment and prevention are highly demanded. To identify SARS-CoV-2 neutralizing antibodies, we analysed the antibody response of 12 COVID-19 patients from 8 to 69 days post diagnosis. By screening 4,313 SARS-CoV-2-reactive B cells, we isolated 255 antibodies from different time points as early as 8 days post diagnosis. Of these, 28 potentially neutralized authentic SARS-CoV-2 (IC₁₀₀ as low as 0.04 µg/ml), showing a broad spectrum of V genes and low levels of somatic mutations. Interestingly, potential precursors were identified in naïve B cell repertoires from 48 healthy individuals that were sampled before the COVID-19 pandemic. Our results demonstrate that SARS-CoV-2 neutralizing antibodies are readily generated from a diverse pool of precursors, fostering the hope of rapid induction of a protective immune response upon vaccination.

Reference

Kreer, Christoph, Matthias Zehner, Timm Weber, Cornelius Rohde, Sandro Halwe, Meryem S. Ercanoglu, Lutz Gieselmann *et al.* "Longitudinal isolation of potent near-germline SARS-CoV-2-neutralizing antibodies from COVID-19 patients." *bioRxiv* (2020).

SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study

Abstract

Background: In December, 2019, a novel zoonotic severe acute respiratory syndrome-related coronavirus emerged in China. The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became pandemic within weeks and the number of human infections and severe cases is increasing. We aimed to investigate the susceptibility of potential animal hosts and the risk of anthrozoönotic spill-over infections.

Methods: We intranasally inoculated nine fruit bats (*Rousettus aegyptiacus*), ferrets (*Mustela putorius*), pigs (*Sus scrofa domesticus*), and 17 chickens (*Gallus gallus*

domesticus) with 105 TCID₅₀ of a SARS-CoV-2 isolate per animal. Direct contact animals (n=3) were included 24 h after inoculation to test viral transmission. Animals were monitored for clinical signs and for virus shedding by nucleic acid extraction from nasal washes and rectal swabs (ferrets), oral swabs and pooled faeces samples (fruit bats), nasal and rectal swabs (pigs), or oropharyngeal and cloacal swabs (chickens) on days 2, 4, 8, 12, 16, and 21 after infection by quantitative RT-PCR (RT-qPCR). On days 4, 8, and 12, two inoculated animals (or three in the case of chickens) of each species were euthanised, and all remaining animals, including the contacts, were euthanised at day 21. All animals were subjected to autopsy and various tissues were collected for virus detection by RT-qPCR, histopathology immunohistochemistry, and in situ hybridisation. Presence of SARS-CoV-2 reactive antibodies was tested by indirect immunofluorescence assay and virus neutralisation test in samples collected before inoculation and at autopsy.

Findings: Pigs and chickens were not susceptible to SARS-CoV-2. All swabs, organ samples, and contact animals were negative for viral RNA, and none of the pigs or chickens seroconverted. Seven (78%) of nine fruit bats had a transient infection, with virus detectable by RT-qPCR, immunohistochemistry, and in situ hybridisation in the nasal cavity, associated with rhinitis. Viral RNA was also identified in the trachea, lung, and lung-associated lymphatic tissue in two animals euthanised at day 4. One of three contact bats became infected. More efficient virus replication but no clinical signs were observed in ferrets, with transmission to all three direct contact animals. Mild rhinitis was associated with viral antigen detection in the respiratory and olfactory epithelium. Prominent viral RNA loads of 0–10⁴ viral genome copies per mL were detected in the upper respiratory tract of fruit bats and ferrets, and both species developed SARS-CoV-2-reactive antibodies reaching neutralising titres of up to 1/1024 after 21 days.

Interpretation: Pigs and chickens could not be infected intranasally by SARS-CoV-2, whereas fruit bats showed characteristics of a reservoir host. Virus replication in ferrets resembled a subclinical human infection with efficient spread. Ferrets might serve as a useful model for further studies—e.g., testing vaccines or antivirals.

Reference

Schlottau, Kore, Melanie Rissmann, Annika Graaf, Jacob Schön, Julia Sehl, Claudia Wylezich, Dirk Höper et al. "Experimental transmission studies of SARS-CoV-2 in fruit bats, ferrets, pigs and chickens." *The Lancet Microbe* (2020).

Marked T cell activation, senescence, exhaustion and skewing towards TH17 in patients with COVID-19 pneumonia

Abstract

The immune system of patients infected by SARS-CoV-2 is severely impaired. Detailed investigation of T cells and cytokine production in patients affected by COVID-19 pneumonia are urgently required. Here we show that, compared with healthy controls, COVID-19 patients' T cell compartment displays several alterations involving naïve, central memory, effector memory and terminally differentiated cells, as well as regulatory T cells and PD1+CD57+ exhausted T cells. Significant alterations exist also in several lineage-specifying transcription factors and chemokine receptors. Terminally differentiated T cells from patients proliferate less than those from healthy controls, whereas their mitochondria functionality is similar in CD4+ T cells from both groups. Patients display significant increases of proinflammatory or anti-inflammatory cytokines, including T helper type-1 and type-2 cytokines, chemokines and galectins; their lymphocytes produce more tumor necrosis factor (TNF), interferon- γ , interleukin (IL)-2 and IL-17, with the last observation implying that blocking IL-17 could provide a novel therapeutic strategy for COVID-19.

Reference

De Biasi, Sara, Marianna Meschiari, Lara Gibellini, Caterina Bellinazzi, Rebecca Borella, Lucia Fianza, Domenico Lo Tartaro *et al.* "Marked T cell activation, senescence, exhaustion and skewing towards TH17 in patients with Covid-19 pneumonia." *Nature Communications* (2020) (I.F.: 11.880).

COVID-19 in patients with rheumatic disease in Hubei province, China: A multicentre retrospective observational study

Abstract

Background: In the ongoing COVID-19 pandemic, the susceptibility of patients with rheumatic diseases to COVID-19 remains unclear. We aimed to investigate susceptibility

to COVID-19 in patients with autoimmune rheumatic diseases during the ongoing COVID-19 pandemic.

Methods: We did a multicentre retrospective study of patients with autoimmune rheumatic diseases in Hubei province, the epicentre of the COVID-19 outbreak in China. Patients with rheumatic diseases were contacted through an automated telephone-based survey to investigate their susceptibility to COVID-19. Data about COVID-19 exposure or diagnosis were collected. Families with a documented history of COVID-19 exposure, as defined by having at least one family member diagnosed with COVID-19, were followed up by medical professionals to obtain detailed information, including sex, age, smoking history, past medical history, use of medications, and information related to COVID-19.

Findings: Between March 20 and March 30, 2020, 6228 patients with autoimmune rheumatic diseases were included in the study. The overall rate of COVID-19 in patients with an autoimmune rheumatic disease in our study population was 0.43% (27 of 6228 patients). We identified 42 families in which COVID-19 was diagnosed between Dec 20, 2019, and March 20, 2020, in either patients with a rheumatic disease or in a family member residing at the same physical address during the outbreak. Within these 42 families, COVID-19 was diagnosed in 27 (63%) of 43 patients with a rheumatic disease and in 28 (34%) of 83 of their family members with no rheumatic disease (adjusted odds ratio [OR] 2.68 [95% CI 1.14–6.27]; $p=0.023$). Patients with rheumatic disease who were taking hydroxychloroquine had a lower risk of COVID-19 infection than patients taking other disease-modifying anti-rheumatic drugs (OR 0.09 [95% CI 0.01–0.94]; $p=0.044$). Additionally, the risk of COVID-19 was increased with age (adjusted OR 1.04 [95%CI 1.01–1.06]; $p=0.0081$).

Interpretation: Patients with autoimmune rheumatic disease might be more susceptible to COVID-19 infection than the general population.

Reference

Zhong, Jixin, Guifen Shen, Huiqin Yang, Anbin Huang, Xiaoqi Chen, Li Dong, Bin Wu et al. "COVID-19 in patients with rheumatic disease in Hubei province, China: a multicentre retrospective observational study." *The Lancet Rheumatology* (2020) (I.F.: 18.545).

Effects of the COVID-19 pandemic on supply and use of blood for transfusion

Abstract

The COVID-19 pandemic has major implications for blood transfusion. There are uncertain patterns of demand, and transfusion institutions need to plan for reductions in donations and loss of crucial staff because of sickness and public health restrictions. We systematically searched for relevant studies addressing the transfusion chain—from donor, through collection and processing, to patients—to provide a synthesis of the published literature and guidance during times of potential or actual shortage. A reduction in donor numbers has largely been matched by reductions in demand for transfusion. Contingency planning includes prioritisation policies for patients in the event of predicted shortage. A range of strategies maintain ongoing equitable access to blood for transfusion during the pandemic, in addition to providing new therapies such as convalescent plasma. Sharing experience and developing expert consensus on the basis of evolving publications will help transfusion services and hospitals in countries at different stages in the pandemic.

Reference

Stanworth, Simon J., Helen V. New, Torunn O. Apelseth, Susan Brunskill, Rebecca Cardigan, Carolyn Doree, Marc Germain et al. "Effects of the COVID-19 pandemic on supply and use of blood for transfusion." *The Lancet Haematology* (2020) (I.F.: 10.406).

Coronavirus disease 2019 (COVID-19) outbreak: Some serious consequences with urban and rural water cycle

Abstract

The COVID-19 outbreak due to SARS-CoV-2 has raised several concerns for its high transmission rate and unavailability of any treatment to date. Although major routes of its transmission involve respiratory droplets and direct contact, the infection through faecal matter is also possible. Conventional sewage treatment methods with disinfection are expected to eradicate SARS-CoV-2. However, for densely populated countries like India with lower sewage treatment facilities, chances of contamination are extremely high; as SARS-CoVs can survive up to several days in untreated sewage; even for a much longer period in low-temperature regions. With around 1.8 billion people worldwide using faecal-

contaminated source as drinking water, the risk of transmission of COVID-19 is expected to increase by several folds, if proper precautions are not being taken. Therefore, preventing water pollution at the collection/distribution/consumption point along with proper implementation of WHO recommendations for plumbing/ventilation systems in household is crucial for resisting COVID-19 eruption.

Reference

Bhowmick, Gourav Dhar, Dhruva Dhar, Dibyojyoty Nath, Makarand Madhao Ghangrekar, Rintu Banerjee, Soumen Das, and Jyotirmoy Chatterjee. "Coronavirus disease 2019 (COVID-19) outbreak: some serious consequences with urban and rural water cycle." *npj Clean Water* 3, no. 1 (2020): 1-8 (I.F.: 4.870).

Making sense of mutation: What D614G means for the COVID-19 pandemic remains unclear

Abstract

Korber *et al.* (2020) found that a SARS-CoV-2 variant in the spike protein, D614G, rapidly became dominant around the world. While clinical and in vitro data suggest that D614G changes the virus phenotype, the impact of the mutation on transmission, disease, and vaccine and therapeutic development are largely unknown.

Reference

Grubaugh, Nathan D., William P. Hanage, and Angela L. Rasmussen. "Making sense of mutation: what D614G means for the COVID-19 pandemic remains unclear." *Cell* (2020) (I.F.: 36.216).

Publication Date: July 02, 2020

Tracking changes in SARS-CoV-2 Spike: Evidence that D614G increases infectivity of the COVID-19 virus

Abstract

A SARS-CoV-2 variant carrying the Spike protein amino acid change D614G has become the most prevalent form in the global pandemic. Dynamic tracking of variant frequencies revealed a recurrent pattern of G614 increase at multiple geographic levels: national,

regional and municipal. The shift occurred even in local epidemics where the original D614 form was well established prior to the introduction of the G614 variant. The consistency of this pattern was highly statistically significant, suggesting that the G614 variant may have a fitness advantage. We found that the G614 variant grows to higher titer as pseudotyped virions. In infected individuals G614 is associated with lower RT-PCR cycle thresholds, suggestive of higher upper respiratory tract viral loads, although not with increased disease severity. These findings illuminate changes important for a mechanistic understanding of the virus, and support continuing surveillance of Spike mutations to aid in the development of immunological interventions.

Reference

Korber, B., W. M. Fischer, S. Gnanakaran, H. Yoon, J. Theiler, W. Abfalterer, N. Hengartner et al. "Tracking changes in SARS-CoV-2 Spike: Evidence that D614G increases infectivity of the COVID-19 virus." *Cell* (2020) (I.F.: 36.216).

REPORT

Publication Date: July 02, 2020

Primary exposure to SARS-CoV-2 protects against reinfection in rhesus macaques

Coronavirus disease 2019 (COVID-19), which is caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic. It currently remains unclear whether convalescing patients have a risk of reinfection. We generated a rhesus macaque model of SARS-CoV-2 infection that was characterized by interstitial pneumonia and systemic viral dissemination mainly in the respiratory and gastrointestinal tracts. Rhesus macaques reinfected with the identical SARS-CoV-2 strain during the early recovery phase of the initial SARS-CoV-2 infection did not show detectable viral dissemination, clinical manifestations of viral disease, or histopathological changes. Comparing the humoral and cellular immunity between primary infection and rechallenge revealed notably enhanced neutralizing antibody and immune responses. Our results suggest that primary SARS-CoV-2 exposure protects against subsequent reinfection in rhesus macaques. For details, read the link given below.

Reference

<https://science.sciencemag.org/content/early/2020/07/01/science.abc5343>

PERSPECTIVE

Publication Date: July 08, 2020

Is hydroxychloroquine beneficial for COVID-19 patients?

The outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in December 2019. As similar cases rapidly emerged around the world^{1,2,3}, the World Health Organization (WHO) declared a public health emergency of international concern on January 30, 2020 and pronounced the rapidly spreading coronavirus outbreak as a pandemic on March 11, 2020⁴. The virus has reached almost all countries of the globe. As of June 3, 2020, the accumulated confirmed cases reached 6,479,405 with more than 383,013 deaths worldwide. The urgent and emergency care of COVID-19 patients calls for effective drugs, in addition to the beneficial effects of remdesivir⁵, to control the disease and halt the pandemic.

Reference

<https://www.nature.com/articles/s41419-020-2721-8>

CORRESPONDANCE

Publication Date: July 03, 2020

Pulse oximetry in low-resource settings during the COVID-19 pandemic

Pulse oximetry is essential for assessing oxygen saturation during respiratory compromise and for monitoring patients undergoing anaesthesia, who are critically ill, or whose condition is rapidly evolving. More immediately, during the ongoing COVID-19 pandemic, silent hypoxia (*i.e.*, abnormally low oxygen saturation without symptoms of dyspnoea), is common in patients with COVID-19.^b In low-resource settings where oxygen supplies and monitored beds are scarce, pulse oximetry is a crucial device for triaging patients and establishing the need for supplemental oxygen.² Early recognition of hypoxia and oxygen administration has been shown to reduce mortality,³ and a triage tool developed in collaboration with WHO uses pulse oximetry to guide management of oxygen therapy.

In Ethiopia, pulse oximetry is not widely available.⁴ The Federal Ministry of Health has developed a National Newborn and Child Survival Strategy to address these gaps, and efforts have been made between the Ministry and aid organisations to combat pneumonia and neonatal hypoxaemia and tackle shortfalls in perioperative care.

Reference

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30287-4/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30287-4/fulltext)

EDITORIAL

Publication Date: July 03, 2020

Surviving the trauma of COVID-19

Psychological scientists investigated how individuals and communities respond to collective traumas, and study human resilience in a range of situations—from earthquakes and hurricanes to mass violence and war. In this editorial, effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on human and communities is discussed, which is the virus that causes coronavirus disease-2019 (COVID-19), and has infected over 10 million people, killed over 125,000 Americans, and led to more than 500,000 deaths worldwide. A vaccine for COVID-19 is perhaps a year away. What does psychological science tell us about how individuals are responding—and will respond—as the pandemic waxes and wanes? What will the postpandemic “normal” look like? Will our society prove to be resilient?

Scientists are trying to understand COVID-19 from many angles. But the pandemic and its associated stressors also are likely to have serious mental health consequences. Such as, grief due to losses that are real (of loved ones, without the opportunity for a ritual funeral) or symbolic (graduation celebrations) abound. Isolation may lead to depression for many and suicidal ideation for some. But there will be no “one size fits all” response to this crisis. Decades of psychological science on collective traumas indicated that individuals' responses are likely to be based on several factors, including their prepandemic circumstances and resources—prior exposures to adversity, physical and mental health vulnerabilities, and economic and social supports.

As the death toll due to COVID-19 crossed 125,000 in the US, behavioral restrictions have been relaxed nationwide. Current public health guidance recommended self-protective behaviors, including frequent hand washing, social distancing, and wearing face coverings. Yet media reports showed people are not following these. Research suggested that exposure to conflicting information from government authorities, media sources, and social networks played a role in understanding whether or not individuals follow science-based recommendations to minimize risk and maximize public health. Therefore, behavioral scientists should provide a roadmap for public officials to ensure

the public's cooperation, trust in, and implementation of what is learned from biomedical science. Responsible health-protective behaviors must be encouraged to ensure the physical and mental health of community. For more details, see the link given below.

Reference

<https://science.sciencemag.org/content/369/6499/11>

COMMENT

Publication Date: July 08, 2020

Correction: Women are most affected by pandemics — lessons from past outbreaks

Women are affected more than men by the social and economic effects of infectious-disease outbreaks. They bear the brunt of care responsibilities as schools close and family members fall ill. They are at greater risk of domestic violence and are disproportionately disadvantaged by reduced access to sexual- and reproductive-health services. Because women are more likely than men to have fewer hours of employed work and be on insecure or zero-hour contracts, they are more affected by job losses in times of economic instability. In short, the social and economic impacts of COVID-19 fall harder on women than on men. Governments need to gather data and target policy to keep all citizens equally safe, sheltered and secure. For more details, read the link given below.

Reference

<https://www.nature.com/articles/d41586-020-02006-z>

NEWSLETTER

Publication Date: July 08, 2020

Can boosting interferons, the body's frontline virus fighters, beat COVID-19?

Interferons are molecular messengers that launch an immediate, intense local response when a virus invades a cell. They trigger production of myriad proteins that attack the virus at every stage of invasion and replication, and they alert uninfected neighboring cells to prepare their own defenses. Interferons also help recruit immune cells to the site of infection and activate them when they arrive. But according to Benjamin tenOever, a virologist at Mount Sinai, SARS-CoV-2 disables this defense by blocking the powerful interferons that lead it. In addition, the virus also ramps up the production of chemokines, a different set of messenger molecules that summon distant immune cells and trigger inflammation. At least five studies since April have found that interferon treatment or pretreatment has a protective effect in cells and in mice infected with SARS-CoV-2. These studies parallel earlier ones that found beneficial effects of early interferon administration in mice infected with the new coronavirus' cousins, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome. The data support giving interferons as a treatment for COVID-19, especially early in infection, advocates say.

However, a small flurry of recent papers suggested the novel coronavirus does some of its deadly work by disabling interferons, powerful proteins that are the body's own frontline defenders against viral invasion. If so, synthetic interferons given before or soon after infection may tame the virus before it causes serious disease—a welcome possibility that additional recent studies support. Even as scientists debate the underlying biology, they are keenly aware that only controlled clinical trials will answer their questions. For more details, see the link given below.

Reference

<https://www.sciencemag.org/news/2020/07/can-boosting-interferons-bodys-frontline-virus-fighters-beat-covid-19>

Mounting evidence suggests coronavirus is airborne — but health advice has not caught up

Converging lines of evidence indicated that SARS-CoV-2, the coronavirus responsible for the COVID-19 pandemic, can pass from person to person in tiny droplets called aerosols that waft through the air and accumulate over time. After months of debate about whether people can transmit the virus through exhaled air, there is growing concern among scientists about this transmission route. Morawska and aerosol scientist Donald Milton at the University of Maryland, College Park (supported by an international group of 237 other clinicians, infectious-disease physicians, epidemiologists, engineers and aerosol scientists) urged the medical community and public-health authorities to acknowledge the potential for airborne transmission, and called for the preventive measures to reduce this type of risk. The researchers are frustrated that key agencies, such as the World Health Organization (WHO), haven't been heeding their advice in their public messages.

Previously for months, the WHO has steadfastly pushed back against the idea that there is a significant threat of the coronavirus being transmitted by aerosols that can accumulate in poorly ventilated venues and be carried on air currents. The agency has maintained that the virus is spread mainly by contaminated surfaces and by droplets bigger than aerosols that are generated by coughing, sneezing and talking. These are thought to travel relatively short distances and drop quickly from the air. And after months of denying the importance of this, the WHO is reconsidering its stance. On July 7, the WHO has softened its position, by saying in a press conference that it will issue new guidelines about transmission in settings with close contact and poor ventilation. In addition, governments are starting to change policies amid concerns that tiny droplets can carry SARS-CoV-2. For more details, see the link given below.

Reference

<https://www.nature.com/articles/d41586-020-02058-1>

Coronavirus research updates: One nation shows wildly disparate local infection rates

According to a report on July 8, 2020, Europe's largest effort to identify people, who have been infected by the new coronavirus has found that roughly one-third of them did not

show symptoms. Between 27 April and 11 May, Marina Pollán at the Institute of Health Carlos III in Madrid and her colleagues tested more than 61,000 people from randomly selected households across Spain for SARS-CoV-2 antibodies, which are produced by the body's immune system in response to coronavirus infection. The study reported large geographical variations in the prevalence of antibodies: more than 10% of people in central areas such as Madrid tested positive, compared with less than 3% in most coastal provinces. Nationwide, some 5% of people tested positive, of which around one in three were asymptomatic. On the basis of their results, the researchers estimate that roughly one million people previously infected with the coronavirus could have gone undetected in Spain because they did not show symptoms.

According to an autopsy-based study (*July 7, 2020*) of 11 people, who died from COVID-19 showed a mismatch between viral hotspots in the body and sites of inflammation and organ damage, suggesting that immune responses, rather than the virus itself, are responsible for death. Numerous studies have suggested that the immune system contributes to the organ damage seen in some severe cases of COVID-19.

Reference

<https://www.nature.com/articles/d41586-020-00502-w>

Publication Date: July 07, 2020

WHO experts to travel to China

WHO experts will travel to China to work together with their Chinese counterparts to prepare scientific plans for identifying the zoonotic source of the SARS-COV-2 virus. The experts will develop the scope and TOR for a WHO-led international mission.

Reference

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>

VIEWPOINT

Publication Date: July 06, 2020

COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted?

The COVID-19 pandemic has seen a surge of patients with acute respiratory distress syndrome (ARDS) in intensive care units across the globe. As experience of managing patients with COVID-19-associated ARDS has grown, so too have efforts to classify patients according to respiratory system mechanics, with a view to optimising ventilatory management. Personalised lung-protective mechanical ventilation reduces mortality and has become the mainstay of treatment in ARDS. In this Viewpoint, we address ventilatory strategies in the context of recent discussions on phenotypic heterogeneity in patients with COVID-19-associated ARDS. Although early reports suggested that COVID-19-associated ARDS has distinctive features that set it apart from historical ARDS, emerging evidence indicates that the respiratory system mechanics of patients with ARDS, with or without COVID-19, are broadly similar. In the absence of evidence to support a shift away from the current paradigm of ventilatory management, we strongly recommend adherence to evidence-based management, informed by bedside physiology, as resources permit.

Reference

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30304-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30304-0/fulltext)

Publication Date: July 03, 2020

Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics

The objective of this Personal View is to compare transmissibility, hospitalisation, and mortality rates for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with those of other epidemic coronaviruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), and pandemic influenza viruses. The basic reproductive rate (R_0) for SARS-CoV-2 is estimated to be 2.5 (range 1.8–3.6) compared with 2.0–3.0 for SARS-CoV and the 1918 influenza pandemic, 0.9 for MERS-CoV, and 1.5 for the 2009 influenza pandemic. SARS-CoV-2 causes mild or asymptomatic disease in most cases; however, severe to critical illness occurs in a small proportion of infected individuals, with the highest rate seen in people older than 70 years. The measured case fatality rate varies

between countries, probably because of differences in testing strategies. Population-based mortality estimates vary widely across Europe, ranging from zero to high. Numbers from the first affected region in Italy, Lombardy, show an all age mortality rate of 154 per 100 000 population. Differences are most likely due to varying demographic structures, among other factors. However, this new virus has a focal dissemination; therefore, some areas have a higher disease burden and are affected more than others for reasons that are still not understood. Nevertheless, early introduction of strict physical distancing and hygiene measures have proven effective in sharply reducing R0 and associated mortality and could in part explain the geographical differences.

Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30484-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30484-9/fulltext)