

Notable Advances in understanding COVID-19 2020

2020 saw the declaration of a global pandemic in March, by the World Health Organization, of a coronavirus, SARS-CoV-2, that causes the disease COVID-19. Studies undertaken this year have advanced the understanding of the clinical characteristics, viral entry and immune response, and have made inroads into vaccine development, among other advances.

CLINICAL CHARACTERISTICS

New year, new outbreak

N. Engl. J. Med. **382**, 727–733 (2020)
Lancet **395**, 497–506 (2020)

On 31 December 2019, Chinese authorities notified the World Health Organization of a series of cases of pneumonia of unknown etiology in Wuhan, the capital of Hubei province. Less than two weeks later, the putative cause of the outbreak, a novel coronavirus, was identified, and its draft genome was made public.

At this early stage in the outbreak, Zhu et al. reported that they were able to isolate the novel coronavirus from the bronchoalveolar-lavage fluid of three patients with pneumonia. They were able to propagate it in cultures of human airway epithelial cells and sequence it. Huang et al. described the clinical characteristics of 41 patients infected with the novel coronavirus. They reported fever and coughing as the most common symptoms at onset, and described pneumonia sometimes followed by acute respiratory distress in infected people. They also noted a prominent sex bias, in that 73% of patients were male, and that diabetes and hypertension were the most frequent comorbidities. TC

<https://doi.org/10.1038/s41591-020-01160-1>

RISK FACTORS

Interferon linked to COVID-19 severity

Science **370**, eabd4570 (2020)
Science **370**, eabd4585 (2020)

Infection with SARS-CoV-2 has a wide range of outcomes, from asymptomatic to lethal. An international consortium launched the COVID Human Genetic Effort in the spring to identify patients with monogenic immunodeficiencies that conferred susceptibility to severe COVID-19.

They found that among 659 patients with severe COVID-19, 23 (3.5%) had functionally relevant mutations in 1 of 13 loci encoding components of the type I interferon pathway. In 534 people with asymptomatic or mild SARS-CoV-2 infection, only one variant with predicted loss of function at any of the 13 loci was found. A companion study showed that 10% of 987 patients with life-threatening COVID-19 had neutralizing antibodies to type I interferons. Together, the two studies suggest that functional deficits in the type I interferon response may account for as much as 14% of severe COVID-19 cases. TC

<https://doi.org/10.1038/s41591-020-01164-x>

CONTAGION

COVID-19 clusters

Nat. Med. <https://doi.org/10.1038/s41591-020-1092-0> (2020)

Analysis of contact-tracing data of 1,038 laboratory-confirmed cases of SARS-CoV-2 infection in Hong Kong between January and April revealed a striking pattern. The authors estimate that 80% of the cases were seeded by just 19% of the infected people; conversely, the majority of patients failed to infect even one other person.

The majority of infector-infected transmission pairs identified (92 of 169) involved household contacts, but transmission in external social settings was not far behind (56 of 169). Notably, although the median size was two, the largest cluster (defined as “two or more confirmed infections with close contact”) involved 106 cases linked to four Hong Kong bars with live music — although the authors could not conclusively demonstrate this, this points toward one (or more) infectious band member(s). Two other large clusters were tied to a wedding and a temple. Overall, social settings were associated with younger patients and more secondary infections. TC

<https://doi.org/10.1038/s41591-020-01159-8>

PATHOLOGY

Extrapulmonary

SARS-CoV-2 manifestations

Ann. Intern. Med. <https://doi.org/10.7326/M20-2003> (2020)

The infection of the upper and lower respiratory tract that becomes life-threatening pneumonia in severe cases is the hallmark of COVID-19. But SARS-CoV-2 infection is not always limited to the respiratory system.

A series of autopsies performed at the University Medical Center Hamburg-Eppendorf on twelve PCR-confirmed cases of COVID-19 found detectable SARS-CoV-2 in the blood of six patients. Of those six, five showed viral RNA titers in the liver, kidneys or heart. The study also supported the possibility of a role for coagulopathy in COVID-19, as seven of the twelve patients had signs of deep venous thrombosis and, for four patients, pulmonary embolism was the direct cause of death. TC

<https://doi.org/10.1038/s41591-020-01162-z>

CLINICAL TRIALS

Dexamethasone reduces mortality

N. Engl. J. Med. <https://doi.org/10.1056/NEJMoa2021436> (2020)

Due to the urgency of the COVID-19 crisis, the testing of pharmaceuticals that had already cleared safety and production hurdles began within the first month of the outbreak.

Observational and compassionate-use studies of repurposed drugs proliferated rapidly, as did clinical trials. The corticosteroid dexamethasone was shown, in the large-scale UK RECOVERY trial, to reduce 28-day mortality by as much as a third in patients hospitalized with COVID-19 and receiving either mechanical ventilation or oxygen alone, compared with the mortality of those receiving the usual care. TC

<https://doi.org/10.1038/s41591-020-01158-9>