

# 2019 novel coronavirus: an emerging global threat

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## ABSTRACT

The coronavirus (CoV) epidemic that began in China in December 2019 follows earlier epidemics of severe acute respiratory syndrome CoV in China and Middle East respiratory syndrome CoV in Saudi Arabia. The full genome of the 2019 novel coronavirus (2019-nCoV) has now been shared, and data have been gathered from several case series. As of February 11, 2020, there have been 45,182 laboratory-confirmed cases, the vast majority in China, with 1115 deaths, for an overall case-fatality rate of 2.5%. Cases have been confirmed in 27 countries. On average, each patient infects 2.2 other people. Symptomatic infection appears to predominantly affect adults, with a 5-day estimated incubation period between infection and symptom onset. The most common presenting symptoms are fever, cough, dyspnea, and myalgias and/or fatigue. All cases reported to date have shown radiographic evidence of pneumonia. 2019-nCoV is diagnosed by real-time reverse transcriptase polymerase chain reaction. Treatment is largely supportive, with regimens including antiviral therapy. Corticosteroids are not routinely recommended. Hand hygiene, prompt identification and isolation of suspect patients, and appropriate use of personal protective equipment are the most reliable methods to contain the epidemic.

**KEYWORDS** 2019-nCoV; coronavirus; Covid-19; epidemic; infectious diseases

Coronaviruses (CoVs) are a family of single-stranded, enveloped RNA viruses that infect a variety of animal species, including humans. There are four genera of CoVs: alphacoronavirus ( $\alpha$ -CoV), betacoronavirus ( $\beta$ -CoV), gammacoronavirus ( $\gamma$ -CoV), and deltacoronavirus ( $\delta$ -CoV). Bats and rodents are the animal reservoirs of most  $\alpha$ -CoVs and  $\beta$ -CoVs, while avian species are the reservoirs for most  $\gamma$ -CoVs and  $\delta$ -CoVs. Previously, six CoVs were known to infect humans. Four of these  $\alpha$ -CoVs (HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1) typically cause mild upper respiratory illness in immunocompetent individuals (“the common cold”). In contrast, two more recently identified  $\beta$ -CoVs can cause severe illness in humans. Severe acute respiratory syndrome (SARS) CoV emerged in China in 2002 to 2003, resulting in 8098 infections and 774 deaths, for an estimated case-fatality rate of approximately 10%.<sup>1</sup> The animal reservoir of SARS-CoV has not been definitively determined, but it is thought that the virus originated in bats and crossed into another mammalian species, likely the Himalayan palm civet. For reasons that remain unclear, there have been no reported

cases of SARS-CoV since 2004.<sup>1</sup> Middle East respiratory syndrome (MERS)-CoV was first reported in Saudi Arabia in 2012 and has continued to cause sporadic cases. Again, this virus likely originated in bats and crossed the species barrier into dromedary camels before infecting humans. Since September 2012, 2494 cases have been reported to the World Health Organization (WHO) with 858 deaths, for a case-fatality rate of approximately 35%.<sup>2</sup>

## TIMELINE OF A NEW EPIDEMIC

Beginning on December 8, 2019, several cases of severe pneumonia of undetermined etiology were reported in Wuhan, a city of 11 million people in Hubei Province, China.<sup>3</sup> These cases were identified by local hospitals using a syndromic surveillance system for “pneumonia of unknown etiology” that was established after the SARS-CoV epidemic. “Pneumonia of unknown etiology” was defined as fever ( $>38^{\circ}\text{C}$ ), radiographic imaging consistent with pneumonia, leukopenia, lymphopenia, no identified pathogen, and no symptomatic improvement after antimicrobial therapy for 3

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to 5 days following accepted clinical guidelines. On December 29, 2019, it was recognized that four of the cases were epidemiologically linked to the Huanan Seafood Wholesale Market, a large open complex selling seafood, fresh meat, and wild animals for human consumption.<sup>4</sup> By December 31, 47 additional cases of pneumonia meeting the case definition had been reported. Twenty-six of these had been linked to the Huanan Seafood Wholesale Market, with patients either working at or visiting the market before symptom onset. The market was closed January 1, 2020.

By January 3, the Chinese Center for Disease Control and Prevention had isolated a novel coronavirus from clinical specimens utilizing human airway epithelial cells and Vero E6 and Huh-7 cell lines. Complete sequencing of the viral genome revealed an 86.9% nucleotide sequence homology to a previously published bat SARS-like  $\beta$ -CoV genome.<sup>5</sup> Although the novel coronavirus was like some  $\beta$ -CoVs detected in bats, it proved distinct from SARS-CoV and MERS-CoV.<sup>5</sup> By January 10, Chinese health officials had shared the full genome of the 2019 novel coronavirus (2019-nCoV) in GenBank, the National Institutes of Health genetic sequence database, and in the Global Initiative on Sharing All Influenza Data (GISAID) portal.

Between January 1 and January 11, 248 additional cases were reported in Wuhan and epidemiologic investigation raised the question of human-to-human transmission. Twenty-three cases reported exposure to a wet market (where live and butchered animals are sold for consumption), of which 19 were directly linked to the Huanan Seafood Wholesale Market. Thirty-seven cases had exposure to another person with respiratory symptoms, of whom seven were health care workers, and 141 cases had no known exposure to either a market or to another person with respiratory symptoms, indicating solid evidence of human-to-human transmission.

By January 13, 2020, the first case of 2019-nCoV outside China was reported in Thailand in a woman from Wuhan. On January 20, 2020, the first case of 2019-nCoV was confirmed in the United States in a returning traveler from Wuhan. As of February 11, 2020, there have been 45,182 laboratory-confirmed cases, the vast majority in China, with 1115 deaths, for an overall case-fatality rate of 2.5%. Cases have been confirmed in 27 countries.<sup>6</sup> A variety of travel restrictions and isolation precautions, including quarantine measures, have been imposed by the governments of multiple countries around the world. The impact of these measures on the epidemic remains to be seen.

In a study of the first 245 cases reported in Wuhan, analysis of the epidemic curve between December 10, 2019, and January 4, 2020, revealed an epidemic growth rate of 0.10 per day (95% confidence interval [CI] 0.050–0.16) and a case doubling time of 7.4 days (95% CI 4.2–14). The estimated reproductive number, or  $R_0$ , was approximately 2.2 (95% CI 1.4–3.9), indicating that on average each patient infected 2.2 other people. In general, an epidemic will

increase as long as the reproductive number is  $>1$ ; control measures are deemed to be effective if the reproductive number is  $<1$ .<sup>7</sup>

## CLINICAL PRESENTATION

Clinical features of 2019-nCoV infection are evolving, with limited initial case descriptions from China. Symptomatic infection appears to predominantly affect adults. The average age of infected patients in the largest study to date ( $n = 425$ ) was 59 years of age, with a gender distribution of 56% male and 44% female.<sup>7</sup> One familial cluster of 6 patients involved an asymptomatic 10-year-old child with occult patchy pulmonary infiltrates on chest computed tomography and oropharyngeal and nasopharyngeal specimens positive for 2019-nCoV RNA by reverse transcriptase polymerase chain reaction (RT-PCR), raising the question of asymptomatic transmission.<sup>8</sup> The estimated incubation period between infection and onset of symptoms is approximately 5 days (95% CI 4–7 days).<sup>8</sup> Chronic medical comorbidities were noted in 33% to 50% of patients, most notably hypertension, cardiovascular disease, chronic lung disease, diabetes, and malignancy.<sup>4,8–10</sup> In one case series of nine pregnant women with 2019-nCoV pneumonia, there was no evidence of intrauterine vertical transmission to their infants. However, it should be noted that all patients underwent third-trimester cesarean section.<sup>11</sup>

Presenting symptoms include fever (83%–99%), predominantly nonproductive cough (67%–82%), dyspnea (38%), and myalgias and/or fatigue (11%–70%). Less common symptoms include headache, sore throat, nasal congestion, rhinorrhea, nausea, vomiting, and diarrhea.<sup>3,8–10,12</sup> In a case series of 138 hospitalized patients, 14 patients presented with atypical nausea and diarrhea preceding fever and dyspnea by 1 to 2 days. A “superspreader” in this hospitalized cohort presented with gastrointestinal symptomatology and is thought to be the source of 2019-nCoV nosocomial transmission to more than 10 health care workers and at least three other patients on the same ward.<sup>10</sup>

A variety of laboratory abnormalities have been described upon admission to the hospital, but lymphopenia, elevated aspartate aminotransferase, elevated lactate dehydrogenase, elevated D-dimer, and prolonged prothrombin time are most commonly described.<sup>3,9,10,12</sup> Radiographic evidence of pneumonia by either chest x-ray or computed tomography of the chest has been described in all patients in case series to date. Bilateral involvement is most commonly described, with findings typical of viral pneumonia, including ground-glass opacities and subsegmental and multilobar consolidation.<sup>3,9,10,12</sup>

Approximately 25% of patients in case reports to date required intensive care,<sup>3,9,10</sup> with the suggestion of clinical deterioration at approximately day 8 of illness.<sup>3,10,12</sup> Of patients requiring admission to the intensive care unit, most had chronic comorbidities. Complications included acute respiratory distress syndrome (20%), acute kidney injury (4%), shock (7%),<sup>3,9,10</sup> and acute cardiac injury (10%).<sup>9,10</sup>

Approximately 10% required intubation and mechanical ventilation; approximately 3% required extracorporeal membrane oxygenation. Specific treatment regimens included antiviral therapy, usually with oseltamivir, in 85% of patients. Antibiotic therapy was given in 72% of patients, and corticosteroid therapy in 32% of patients. Overall mortality in hospitalized patients was approximately 8%, but data are incomplete as most patients were still hospitalized at the time the case series were published.<sup>3,9,10</sup>

## DIAGNOSIS

Diagnosis of suspect cases is made by RT-PCR analysis of upper respiratory (nasopharyngeal and/or oropharyngeal swabs or nasopharyngeal wash/aspirate), lower respiratory (sputum, tracheal aspirate, bronchoalveolar lavage), and serum specimens. Stool and urine specimens may also be utilized for RT-PCR analysis. At present in the United States, molecular analysis is limited to the US Centers for Disease Control and Prevention (CDC). It will eventually be available at partner state and local public health laboratories. Exclusion of other respiratory pathogens, particularly influenza, is also recommended.

## MANAGEMENT

Treatment is largely supportive. Although widely used in initial case reports, oseltamivir has unclear benefits on the course of 2019-nCoV infection. Clinical trials are planned in China to assess the efficacy of combination ritonavir-boosted lopinavir, drugs typically used to treat HIV. Remdesivir, a novel nucleotide analog that has activity against SARS-CoV and MERS-CoV in vitro and in animal studies, is planned to be utilized in randomized clinical trials in China to assess efficacy and safety against 2019-nCoV. Remdesivir was used on a compassionate basis to treat the first reported case of 2019-nCoV in the United States.<sup>12</sup> Additionally, the WHO and CDC generally recommend that corticosteroids not be routinely utilized in the treatment of 2019-nCoV pneumonia unless there are other indications for their use (e.g., exacerbation of chronic obstructive pulmonary disease or treatment of septic shock per the Surviving Sepsis guidelines). Though theoretically of benefit in instances of cytokine release syndrome, corticosteroids have been associated with delayed viral clearance in patients with MERS-CoV infection and thus at this point are not routinely recommended as standard therapy for 2019-nCoV infection.<sup>13</sup> Investigations regarding vaccine development are also underway.

## INFECTION CONTROL

Scrupulous attention to infection control practices is tantamount to containment of this epidemic. A high level of vigilance toward potential cases, early involvement of the infection prevention and control team, and timely consultation of public health authorities remain the backbone to limit transmission. Any patient with a contagious illness

should don a surgical mask and be placed in a private room with the door closed; if 2019-nCoV is suspected, the patient should be placed in an airborne infection isolation room if available. The patient should also be in enhanced precautions, which consist of standard, contact, and airborne precautions with the addition of eye protection. This consists of the use of a disposable gown, gloves, N-95 or higher particulate respirator or powered air purified respirator, and goggles or face shield to protect the mucous membranes of the eyes. Meticulous attention to removal of personal protective equipment (PPE) to avoid contamination of the health care worker and the environment and strict hand hygiene should be observed as well. Guidance regarding evaluation of potential cases of 2019-nCoV<sup>14</sup> as well as use of PPE<sup>15</sup> can be found on CDC's website.

## UNRESOLVED ISSUES

Several unanswered questions remain regarding 2019-nCoV. Although the animal reservoir is likely a species of bat, this is not definite, nor is the intermediate host. Routes of infection are not definitively characterized. Ultimate morbidity and mortality are undetermined. Likewise, the role of asymptomatic or mildly symptomatic infections, particularly in children, in disease transmission is unknown, as is the potential of "superspreaders," as was seen in the SARS-CoV epidemic. Even the name of the 2019-nCoV is yet to be determined; while the WHO officially designated the disease caused by 2019-nCoV as Covid-19 on February 11, 2020, the International Committee on Taxonomy of Viruses, which is responsible for naming new viruses, has proposed designating 2019-nCoV as SARS-CoV-2. Regardless of the unknown elements surrounding this pathogen and disease, established infection control strategies will help abate the outbreak. Meticulous hand hygiene, prompt identification and isolation of suspect patients, and appropriate use of PPE remain the most reliable mechanisms to contain epidemics of all infectious diseases. Additionally, information regarding the virology, epidemiology, and transmission of 2019-nCoV continues to evolve.

1. Centers for Disease Control and Prevention. *SARS Basics Fact Sheet*. <https://www.cdc.gov/sars/about/fs-sars.html>. Last updated December 6, 2017.
2. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV): MERS monthly summary, November 2019. <https://www.who.int/emergencies/mers-cov/en/>. Accessed February 10, 2020.
3. Chen N, Zhou M, Dong X, Jr, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223): 507–513. doi:10.1016/S0140-6736(20)30211-7.
4. Wu P, Hao X, Lau EHY, et al. Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020. *Euro Surveill*. 2020;25(3): 2000044. doi:10.2807/1560-7917.ES.2020.25.3.2000044.

5. Zhu N, Zhang D, Wang W, et al; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727–733. doi:10.1056/NEJMoa2001017.
6. Johns Hopkins University CSSE. Coronavirus COVID-19 global cases. <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>. Accessed February 10, 2020.
7. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.* 2020 Jan 29 [Epub ahead of print]. doi:10.1056/NEJMoa2001316.
8. Chan J-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020; 395(10223):514–523. doi:10.1016/S0140-6736(20)30154-9.
9. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020; 395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5.
10. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020. [Epub ahead of print]. doi:10.1001/jama.2020.1585.
11. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020 Feb 12 [Epub ahead of print]. doi:10.1016/S0140-6736(20)30360-3.
12. Holshue ML, DeBolt C, Lindquist S, et al; Washington State 2019-nCoV Case Investigation Team. First case of 2019 novel coronavirus in the United States. *N Engl J Med.* 2020 Jan 31 [Epub ahead of print]. doi:10.1056/NEJMoa2001191.1.
13. Centers for Disease Control and Prevention. *Interim Clinical Guidance for Management of Patients with Confirmed 2019 Novel Coronavirus (2019-nCoV) Infection.* <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>. Updated February 12, 2020. Accessed February 13, 2020.
14. Centers for Disease Control and Prevention. *Evaluating and Reporting Persons Under Investigation (PUI).* <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>. Updated February 12, 2020. Accessed February 13, 2020.
15. Centers for Disease Control and Prevention. *Interim Infection Prevention and Control Recommendations for Patients with Confirmed 2019 Novel Coronavirus (2019-nCoV) or Persons Under Investigation for 2019-nCoV in Healthcare Settings.* <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html>. Updated February 12, 2020. Accessed February 13, 2020.