

Back to the spring of 2020: facts and hope of COVID-19 outbreak

Guangbiao Zhou (✉)¹, Saijuan Chen (✉)², Zhu Chen²

¹State Key Laboratory of Molecular Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China; ²State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, National Research Center for Translational Medicine (Shanghai), Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

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Since December 2019, an atypical pneumonia has occurred in Wuhan, a beautiful city located at the center of China (Fig. 1), and the whole country. The origin of the disease remains unclear and the suspected Huanan Seafood Wholesale Market was closed on January 1, 2020. Very rapidly, a novel coronavirus was isolated and named first the 2019 novel coronavirus (2019-nCoV) [1] and subsequently severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2], and is suggested to be named as human coronavirus 2019 (HCoV-19) [3]. Meanwhile, the disease is chronologically called pneumonia of unknown origin, novel coronavirus pneumonia (NCP), and coronavirus disease-2019 (COVID-19) (Fig. 2). Superspreading events of this virus have also taken place on the Diamond Princess cruise off the coast of Yokohama, Japan [4]. The Chinese central [5] and local governments [6] have been endeavoring unprecedented efforts to constrain the outbreak, and more than 30 000 medical professionals especially doctors and nurses outside Wuhan have been joining the local ones to handle this emergency.

Epidemiology and clinical characteristics

In early December 2019, the first case was reported; by December 31, 104 cases were diagnosed [7]. The disease took 30 days to spread to all the 34 provinces/regions (including Hong Kong, Macao, and Taiwan) of China. The number of confirmed cases of COVID-19 rose to 11 791 in Chinese mainland as of January 31, including 259 deaths.

The confirmed cases increased rapidly, and by February 21, 75 567 confirmed cases, 5206 suspected cases, and 2239 deaths, have been reported in China. The disease also occurred in 26 countries, with 1151 confirmed cases and 8 deaths reported by February 21 [8]. By February 21, severe cases in Wuhan, other regions of China, and the whole country were 9628 (21.2%), 2005 (6.6%), and 11633 (15.4%), respectively (Table 1). The reproduction number (R_0) is between 2.2 and 4.8 [9,10].

The commonest symptoms of the COVID-19 include



Fig. 1 Back to the spring of 2020. Sakura garden of East Lake, Wuhan, 2019. Courtesy of Mr. Zhenyin Chen, a postgraduate student of Guizhou University.

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Correspondence: Guangbiao Zhou, gzbzhou@cicams.ac.cn;
Saijuan Chen, sjchen@stn.sh.cn

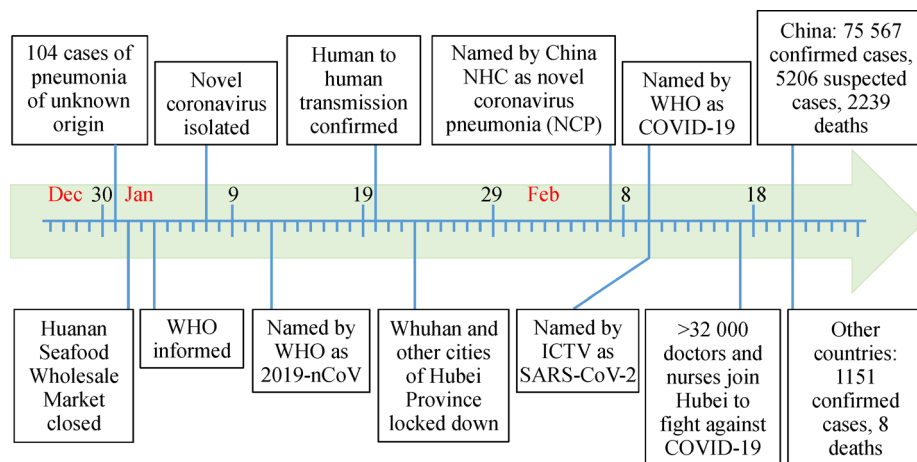


Fig. 2 A brief timeline of the COVID-19 outbreak. ICTV, International Committee on Taxonomy of Viruses; NHC, National Health Commission; WHO, World Health Organization.

Table 1 Comparison of disease severity and mortality in patients from different regions or countries

	China			Other countries
	Wuhan	Other regions	Total	
Total cases*	45 346	30 221	75 567	1151
Disease severity				
Non-severe, <i>n</i> (%)	34 034 (75.1%)	27 661 (91.5%)	61 695 (81.6%)	–
Severe, <i>n</i> (%)	9628 (21.2%)	2005 (6.6%)	11 633 (15.4%)	–
Mortality, <i>n</i> (%)	1684 (3.7%)	555 (1.8%)	2239 (3.0%)	8 (0.6%)

*The data were collected from the National Health Commission, P.R. China and World Health Organization. Date of assess: February 21, 2020.

fever, dry cough, fatigue, sputum, and shortness of breath, with a small proportion of patients (889/72 314, 1.2%) as asymptomatic and probably spreaders [7]. Cytokine storm that is induced by virus particles, is associated with disease severity [11,12]. A first histological examination of COVID-19 patient showed diffuse alveolar damage with cellular fibromyxoid exudates, desquamation of pneumocytes and hyaline membrane formation, pulmonary edema with hyaline membrane formation, interstitial mononuclear inflammatory infiltrates, and multinucleated syncytial cells with atypical enlarged pneumocytes in the lungs [13]. These results shed insights into the pathogenesis of COVID-19 and may help design therapeutic strategies against the disease.

The virus

A previously unknown betacoronavirus was discovered from bronchoalveolar-lavage fluid samples of the patients, which is the seventh member of the family of coronaviruses that infect humans [1,14]. The virus was most closely related to a group of SARS-like coronaviruses (genus Betacoronavirus, subgenus Sarbecovirus) previously sampled from bats in China [14,15], and a virus with 99% sequence homology to the receptor-binding

domain (RBD) and 90% to the SARS-CoV-2 genome was also found in Malayan pangolins in southern China [16]. However, higher viral loads were detected in the nose than in the throat of symptomatic and asymptomatic COVID-19, a pattern resembling that of influenza but not SARS-CoV [17]. Human angiotensin-converting enzyme 2 (ACE2) has been shown to be the putative receptor for the virus to enter into host cells [15,18], and biophysical and structural evidence shows that the SARS-CoV-2 spike glycoprotein binds ACE2 with high affinity [19]. ACE2 can also bind spike protein through association with B0AT1 [20]. ACE2 locates on the organs such as lung, heart, esophagus, kidney, bladder and ileum, and in particular on the cell types such as type II alveolar cells, myocardial cells, proximal tubule cells of kidney, ileum and esophagus epithelial cells, and bladder urothelial cells, providing clues for further investigating the pathogenesis COVID-19 [21].

Therapeutic strategies

So far, neither drug nor vaccine has been approved to treat the novel COVID-19. While supportive treatment regimens including oxygen therapy are widely used, antiviral (oseltamivir) and anti-HIV (lopinavir/ritonavir) drugs are

also applied in treating COVID-19. Some emerging therapeutics are being tested in clinical trials. For example, virally targeted agents, approved nucleoside analogs (favipiravir and ribavirin) and experimental nucleoside analogs (remdesivir and galidesivir), may have potentials against SARS-CoV-2 [22]. Remdesivir has been shown to be able to block virus infection [23] and exert therapeutic efficacy in the first COVID-19 case in the United States [24]. Two phase III trials have been initiated to evaluate remdesivir in COVID-19. Anti-malaria drug chloroquine shows activity in blocking SARS-CoV-2 infection [23] and is being evaluated in an open-label trial [22]. Convalescent patient plasma that contain anti-SARS-CoV-2 antibody holds promise to beat this disease [25]. ACE2 and Spike protein represent two novel therapeutic targets for the disease. An ongoing study using Tocilizumab, a specific monoclonal antibody antagonist of interleukin-6 receptor (IL-6R) which proved to be effective in alleviating cytokine release syndrome, showed preliminary positive effects [26].

Traditional Chinese medicine (TCM) plays an active role in fighting infectious disease, exemplified by ancient formula Maxingshigan-Yinqiaosan in the treatment of H1N1 influenza [27]. In combination with Western medicine [28] or used alone, TCM is widely applied or being evaluated in clinical trials to treat COVID-19.

Hope and perspectives

Two and a half months have witnessed the great efforts that China has been endeavoring to control the outbreak of the COVID-19. These include lockdown of Wuhan and related cities, control of population mobility, and input of huge resource to the regions. China races against the clock to build virus hospitals, including Huoshenshan Hospital with 1000 beds built in 9 days and Leishenshan Hospital with 1500 beds completed in 15 days. More than 15 Fangcang hospitals (with large open space and necessary anti-infection conditions) have been built with a capacity of more than 20 000 beds for the isolation and treatment of the patients. The updated genome sequence of SARS-CoV-2 has been shared to the public, clinical trials are undergoing, and scientists from China and overseas are working together to combat this public health emergency. With great contributions of our domestic selfless medical professionals and supports from public health scientists around the world [29], by using smart but firm public health measures preventing spreadout of the virus and more specific combinatorial therapeutic strategies, such as the anti-viral convalescent plasma and drugs against cytokine storm for severe cases, as well as effective TCM drugs and technologies, we believe that the mankind will win this battle, and Wuhan will be back to the spring.

Compliance with ethics guidelines

Guangbiao Zhou, Saijuan Chen, and Zhu Chen declare no conflict of interests. This manuscript does not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

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