

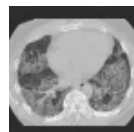


SUBSCRIBE
OR RENEW



ORIGINAL ARTICLE

Covid-19 in Critically Ill Patients
in the Seattle Region — Case
Series



Notable Articles of 2019
12 practice-changing articles



PERSPECTIVE

Critical Supply Shortages — The
Need for Ventilators and
Personal Protective Equ...

PERSPECTIVE

Novel Coronavirus
Lessons — Prepari
System for the Pan



EDITORIAL

Covid-19 — Navigating the Uncharted

Anthony S. Fauci, M.D., H. Clifford Lane, M.D., and Robert R. Redfield, M.D.

March 26, 2020

N Engl J Med 2020; 382:1268-1269

DOI: 10.1056/NEJMe2002387

Chinese Translation [中文翻译](#)

Article



12 References 11 Citing Articles

THE LATEST THREAT TO GLOBAL HEALTH IS THE ONGOING OUTBREAK OF THE RESPIRATORY DISEASE THAT was recently given the name Coronavirus Disease 2019 (Covid-19). Covid-19 was recognized in December 2019.¹ It was rapidly shown to be caused by a novel coronavirus that is structurally related to the virus that causes severe acute respiratory syndrome (SARS). As in two preceding instances of emergence of coronavirus disease in the past 18 years² — SARS (2002 and 2003) and Middle East respiratory syndrome (MERS) (2012 to the present) — the Covid-19 outbreak has posed critical challenges for the public health, research, and medical communities.

In their *Journal* article, Li and colleagues³ provide a detailed clinical and epidemiologic description of the first 425 cases reported in the epicenter of the outbreak: the city of Wuhan in Hubei province, China. Although this information is critical in informing the appropriate response to this outbreak, as the authors point out, the study faces the limitation associated with reporting in real time the evolution of an emerging pathogen in its earliest stages. Nonetheless, a degree of clarity is emerging from this report. The median age of the patients was 59 years, with higher morbidity and mortality among the elderly and among those with coexisting conditions (similar to the situation with influenza); 56% of the patients were male. Of note, there were no cases in children younger than 15 years of age. Either children are less likely to become infected, which would have important epidemiologic implications, or their symptoms were so mild that their infection escaped detection, which has implications for the size of the denominator of total community infections.

On the basis of a case definition requiring a diagnosis of pneumonia, the currently reported case fatality rate is approximately 2%.⁴ In another article in the *Journal*, Guan et al.⁵ report mortality of 1.4% among 1099 patients with laboratory-confirmed Covid-19; these patients had a wide spectrum of disease severity. If one assumes that the number of asymptomatic or minimally

influenza (which has a case fatality rate of approximately 0.1%) or a pandemic influenza (similar to those in 1957 and 1968) rather than a disease similar to SARS or MERS, which have had case fatality rates of 9 to 10% and 36%, respectively.²

The efficiency of transmission for any respiratory virus has important implications for containment and mitigation strategies. The current study indicates an estimated basic reproduction number (R_0) of 2.2, which means that, on average, each infected person spreads the infection to an additional two persons. As the authors note, until this number falls below 1.0, it is likely that the outbreak will continue to spread. Recent reports of high titers of virus in the oropharynx early in the course of disease arouse concern about increased infectivity during the period of minimal symptoms.^{6,7}

China, the United States, and several other countries have instituted temporary restrictions on travel with an eye toward slowing the spread of this new disease within China and throughout the rest of the world. The United States has seen a dramatic reduction in the number of travelers from China, especially from Hubei province. At least on a temporary basis, such restrictions may have helped slow the spread of the virus: whereas 78,191 laboratory-confirmed cases had been identified in China as of February 26, 2020, a total of 2918 cases had been confirmed in 37 other countries or territories.⁴ As of February 26, 2020, there had been 14 cases detected in the United States involving travel to China or close contacts with travelers, 3 cases among U.S. citizens repatriated from China, and 42 cases among U.S. passengers repatriated from a cruise ship where the infection had spread.⁸ However, given the efficiency of transmission as indicated in the current report, we should be prepared for Covid-19 to gain a foothold throughout the world, including in the United States. Community spread in the United States could require a shift from containment to mitigation strategies such as social distancing in order to reduce transmission. Such strategies could include isolating ill persons (including voluntary isolation at home), school closures, and telecommuting where possible.⁹

approaches are being explored.¹¹ Among these are the antiviral medication lopinavir–ritonavir, interferon-1 β , the RNA polymerase inhibitor remdesivir, chloroquine, and a variety of traditional Chinese medicine products.¹¹ Once available, intravenous hyperimmune globulin from recovered persons and monoclonal antibodies may be attractive candidates to study in early intervention. Critical to moving the field forward, even in the context of an outbreak, is ensuring that investigational products are evaluated in scientifically and ethically sound studies.¹²

Every outbreak provides an opportunity to gain important information, some of which is associated with a limited window of opportunity. For example, Li et al. report a mean interval of 9.1 to 12.5 days between the onset of illness and hospitalization. This finding of a delay in the progression to serious disease may be telling us something important about the pathogenesis of this new virus and may provide a unique window of opportunity for intervention. Achieving a better understanding of the pathogenesis of this disease will be invaluable in navigating our responses in this uncharted arena. Furthermore, genomic studies could delineate host factors that predispose persons to acquisition of infection and disease progression.

The Covid-19 outbreak is a stark reminder of the ongoing challenge of emerging and reemerging infectious pathogens and the need for constant surveillance, prompt diagnosis, and robust research to understand the basic biology of new organisms and our susceptibilities to them, as well as to develop effective countermeasures.

[Disclosure forms](#) provided by the authors are available with the full text of this editorial at [NEJM.org](https://www.nejm.org).

This editorial was published on February 28, 2020, at [NEJM.org](https://www.nejm.org).

From the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD (A.S.F., H.C.L.); and the Centers for Disease Control and Prevention, Atlanta (R.R.R.).

Supplementary Material

[Disclosure Forms](#)

PDF

146KB

References (12)



Citing Articles (11)



More about

INFECTIOUS DISEASE

VACCINES

VIRAL INFECTIONS

GLOBAL HEALTH

DIAGNOSTICS

INFLUENZA

Related Articles

ORIGINAL ARTICLE MAR 26, 2020

Chiefs / Directors / Dept. Heads

New York

Chief, Otolaryngology - Northwell Health - Long Island Jewish Forest Hills Hospital

Hospitalist

Lake Forest, Illinois

Hospitalist - Northwestern Medicine Lake Forest Hospital

Family Medicine

Teaneck, New Jersey

FAMILY MEDICINE PHYSICIAN

Psychiatry

Norwich, Connecticut

Psychiatrist - Outpatient

Hematology / Oncology

Maine

Medical Director for Cancer Network on Maine's Mid Coast

Primary Care

Cleveland, Ohio


Primary Care Opportunity- Madison, OH

Free Exclusive Collection

Notable Articles of 2019

ACCESS NOW →

The NEW ENGLAND JOURNAL of MEDICINE



Sign up for the free NEJM
Weekly Table of Contents email

→

More from the week of March 26, 2020



IMAGES IN CLINICAL MEDICINE

“Coat Hanger” Appearance of the Ribs

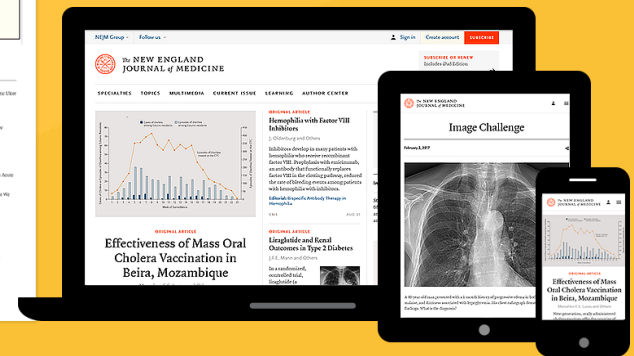
CLINICAL IMPLICATIONS OF BASIC RESEARCH

Activating Immunity to Fight a Foe — A New Path

Tap into groundbreaking research and clinically relevant insights

SUBSCRIBE →

Already a subscriber? [Sign In](#) or [Renew](#)



▲ BACK TO TOP

[Reviews](#)

[Clinical Cases](#)

[Perspective](#)

[Commentary](#)

[Other](#)

[Browse all Articles](#)

[Current Issue](#)

[Issue Index](#)

[Submit a Manuscript](#)

[Subscribers](#)

[Institutions](#)

[Media](#)

[Advertisers](#)

[Agents](#)

[Permissions](#)

[Reprints](#)

[NEJM CareerCenter](#)

[Products & Services](#)

[Editors & Publishers](#)

[Advertising Policies](#)

[Contact Us](#)

[Accessibility](#)

[FAQs](#)

[Help](#)

[Site Feedback](#)

[Renew](#)

[Activate Subscription](#)

[Create Account](#)

[Manage Account](#)

[Pay Bill](#)

[Special Offers](#)

STAY CONNECTED

[Email Alerts](#)

[Create Account](#)

[Apps](#)

[NEJM CareerCenter](#)

[Podcasts](#)

[RSS Feed](#)

FOLLOW US

[f Facebook](#)

[t Twitter](#)

[@ Instagram](#)

[v YouTube](#)

[in LinkedIn](#)

Copyright © 2020 Massachusetts Medical Society. All rights reserved. Electronic ISSN 1533-4406. Print ISSN 0028-4793.
The content of this site is intended for health care professionals.

NEJM
GROUP

