



# Coronavirus, COVID-19, SARS

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SARS, COVID-19, 2019-nCoV, SARS-CoV-2

## Clinical Setting

SARS-CoV-2 / COVID-19

- **COVID-19 / SARS-CoV-2** (2019-nCoV)
  - SARS-CoV-2: a respiratory coronavirus that emerged in late 2019 in Wuhan, China. It has been determined to be a sister virus to the SARS coronavirus (2002-2003). The disease caused by this virus is called COVID-19. Situation is rapidly changing:
    - Updated U.S. CDC Guidance (3/8/20): HAN No. 429: <https://emergency.cdc.gov/han/2020/HAN00429.asp> and WHO guidance: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance>
    - Clinical criteria (evaluation/testing): <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>
    - Clinical guidance (disease presentation, patient management): <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
    - Estimation of prevalence and contagiousness (03/17/20): [Science 10.1126/science.abb3221](https://doi.org/10.1126/science.abb3221) (2020)
    - U.S. case reports: <https://www.cdc.gov/coronavirus/2019-ncov/cases-in-us.html>; WHO global situation dashboard.
- **Mean incubation time is estimated to be ~5 days after exposure** (range 4.1 - 7.0 days, but up to 14 days). Transmission can occur from an infected person who is asymptomatic (prior to onset of symptoms), although transmission is likely more efficient once symptoms develop.
- **Presentation:**
  - One week to 10 days prodrome of myalgias, malaise (bone-tired), cough, confusion (foggy mind), low grade fever, which may gradually progress to difficulty breathing in the second week. Average 8 days to development of dyspnea and average 9 days to onset of pneumonia/pneumonitis.
  - COVID-19 is not like influenza which is sudden onset and follows a different course of disease
  - Growing evidence for asymptomatic infection ([Euro Surveill. 2020 Mar;25\(10\). doi: 10.2807/1560-7917.ES.2020.25.10.2000180](https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180)) hence the absolute imperative of effective prevention measures (see Prevention below)

- **Patient management** ([https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected))
  - **Symptomatic/Mild-Moderate illness:** Stay at home and contact health care provider by phone or electronic means
  - **Severe symptoms**, e.g., difficulty breathing: seek immediate care
  - **If older (age  $\geq 65$  yrs) OR underlying conditions OR immunocompromised:** contact health care provider early in course of even mild illness
    - Monitor pulse ox (if possible): if drops below 93%, seek care
    - Risk factors for poor prognosis: older age, high SOFA score & d-dimer  $>1\text{mcg/mL}$  (retrospective cohort study, Lancet online ahead of print, 03/11/20)
- **Criteria for evaluation and laboratory testing (3/8/20)** (<https://emergency.cdc.gov/han/2020/HAN00429.asp>)
  - Work with local/state health departments to coordinate testing through public health labs
  - Determine whether patient has signs/symptoms compatible with COVID-19 (fever and acute respiratory illness, e.g., cough, difficulty breathing)
  - Testing priorities are rapidly evolving and may include:
    - Hospitalized patients with signs & symptoms of COVID-19 (in order to inform decisions about infection control)
    - Symptomatic individuals (age  $\geq 65$  yrs) and individuals with underlying chronic conditions (e.g., diabetes, heart diseases, lung disease, kidney disease) or immunocompromised individuals
    - Any person, including HCW, who within 14 days of onset had close contact with a suspect or lab-confirmed COVID-19 patient
    - Any person who has a history of travel to an affected area within 14 days of symptom onset
  - HCWs entering the room with a PUI should use standard precautions, contact precautions, airborne precautions, and eye protection (e.g., goggles or a face shield).
- **Diagnostic Tests**
  - CDC interim guidelines: <https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>
  - Specimen: upper respiratory NP swab preferred; CDC interim guidelines: <https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html> (see JAMA 2020 Mar 11. doi: 10.1001/jama.2020.3786 for yields of different specimen types).
  - Emergency Use Application (EUA) granted or pending for various diagnostic tests.
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Status	Test	Manufacturer
EUA granted	New York SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Panel	NYC public health labs

EUA granted (03/12/20)	cobas SARS-CoV-2 Test (runs on cobas 6800/8800 lab systems)	Roche Diagnostics
EUA granted (03/21/20)	Xpert Xpress SARS Cov-2 Test (runs on GeneXpert Systems)(45 min turnaround)	Cepheid
EUA pending, but available in U.S. and Europe	Logix Smart Coronavirus Disease 2019 (COVID-19) Test Kit	Co-Diagnostics
EUA pending, but available in U.S. and globally	ePlex RUO SARS-CoV-2 Test Kit	GenMark Diagnostics

- Other tests under development (Abbott Laboratories, bioMérieux, LabCorps, and Qiagen) and WHO has procured/shipped a commercial assay to 150+ labs worldwide (Ref: <https://coronavirus.travax.com/library/coronaviruses/events/coronavirus-disease-2019>). See also, WHO emergency use listing (EUL) procedure: [https://www.who.int/diagnostics\\_laboratory/EUL/en/](https://www.who.int/diagnostics_laboratory/EUL/en/)
- HKU1, NL63, 229E, OC43 are human coronaviruses that are detected by some multiplex panels. They are associated with URI and viral pneumonia, but unlike SARS CoV, MERS CoV and SARS-CoV-2 (Wuhan), they are not associated with major outbreaks or severe respiratory distress syndrome.
- SARS-CoV-2 does not appear to cross-react with the URI-associated strains HKU-1, NL63, OC43, and 229E that are detected by multiplex panels such as BioFire FilmArray or Luminex

- **Prevention measures**

- **Break transmission pathways!! Do not be complacent!!**
- Basic precautions (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>)
  - Frequent handwashing (alcohol-based sanitizer and/or soap and water)
  - **Social distancing** (at least 6 feet / 1.8 meter)
    - **STAY AT HOME** except for essential activities, e.g., food, medicines, healthcare and essential work such as police, fire, sanitation and healthcare.
    - **AVOID CROWDS AND/OR CONGESTED PLACES**
    - **TAKE THIS SERIOUSLY**
      - Self-isolation for 14 days of return from Europe, other CDC level 3 country
  - Avoid touching eyes, nose, mouth
  - Respiratory hygiene, i.e., cover nose and mouth when sneezing or coughing
- Avoid cruise ships, including river cruises: CDC HAN No. 430 (03/15/20): <https://emergency.cdc.gov/han/2020/han00430.asp>

## Etiologies

- Coronavirus CoV (SARS-CoV)(2003)
- Coronavirus SARS CoV-2 (COVID-19)

## Primary Regimens

- Therapy is predominantly supportive care.
- No specific antiviral therapy is known to be effective

## Alternative Regimens

- None

## Comments

- **SARS-CoV-2 / COVID-19:**
  - Drugs under evaluation:
    - **Chloroquine or Hydroxychloroquine** (Int J Antimicrob Agents. 2020 Mar 4:105932. doi: 10.1016/j.ijantimicag.2020.105932): rationale, pre-clinical evidence of effectiveness and safety for use in COVID-9 patients (J Crit Care, online ahead of print, 03/10/20)(systematic review)
    - **Remdesivir** (GS 5734) has activity in rodents against beta coronaviruses (Antimicrob Agents Chemother. 2020 Mar 9. pii: AAC.00399-20. doi: 10.1128/AAC.00399-20) available for compassionate use or through clinical trials (ClinicalTrials.gov NCT04280705, NCT04257656, NCT04252664, NCT04292899).
    - **Lopinavir/ritonavir:** RCT showed no benefit and nor antiviral effect vs. standard care (N Engl J Med DOI: 10.1056/NEJMoa2001282)(03/18/20). High risk of adverse drug-drug interactions in critically ill patients so should await further trial data. See University of Liverpool compilation of drug-drug interactions: <https://www.covid19-druginteractions.org/>
  - Insights and concise summary of the situation as of late February published on 28 Feb 2020 in JAMA. Detailed clinical and epidemiologic description of the first 425 cases reported in Wuhan (N Engl J Med 2020 Jan 29 [Epub ahead of print]) with an associated editorial from Fauci et al (N Engl J Med 2020 Feb 28 [Epub ahead of print]).
- Severe Acute Respiratory Syndrome (SARS)(2002-2003).
  - A coronavirus (SARS-CoV), isolated in Spring 2003 (N Engl J Med 348:1953, 2003 & N Engl J Med 348:1967, 2003), emerged from southern China and spread to Beijing, Hong Kong and 32 countries. Bats were a primary reservoir for SARS virus (Proc Natl Acad Sci 102:14040, 2005). Thin section micrograph of SARS virus.
  - Transmission by close contact: effective infection control practices (mask [changed frequently], eye protection, gown, gloves) proved key to stopping transmission in 2003 epidemic. Health care workers accounted for most secondary cases.
  - Therapy tried or evaluated during 2002-2003 outbreak:

- Ribavirin, baloxavir, neuraminidase inhibitors, lopinavir/ritonavir, and acyclovir are ineffective.
  - Interferon alfa ± steroids used in a small case series. Interferon-beta and mycophenolate mofetil. Pegylated IFN- $\alpha$  effective in monkeys.
  - Low dose steroids alone successful in one Beijing hospital during 2002-2003 outbreak. High dose steroids increased viral load & serious fungal infections.
  - Inhaled nitric oxide improved oxygenation and improved chest x-ray (Clin Infect Dis 39:1531, 2004).
- Other respiratory human coronaviruses (HCOV-229E, OC43, NL63, etc.) implicated as cause of croup, pneumonia, asthma exacerbations, and other respiratory tract infections (RTI) in children (Clin Infect Dis 40:1721, 2005; J Infect Dis 191:492, 2005). Other respiratory human coronaviruses may cause severe disease in HSCT recipients (Blood 115:2088; 2010).
  - See also Middle East Respiratory Syndrome (MERS).