

COVID-19

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INTRODUCTION

Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, in the Hubei Province of China. It is rapidly spreading, resulting in an epidemic throughout china, followed by an increasing number of cases in other countries throughout the world. In February 2020, the WHO designated the disease COVID-19, which stands for corona viruses 2019. The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-COV_2); previously, it was referred to as 2019-nCoV.

Understanding of COVID-19 is evolving. Interim guidance has been issued by the WHO and by the united states for disease control and prevention.

This topic will discuss the epidemiology clinical features, diagnosis, management, and prevention of COVID-19 community-acquired coronaviruses, severe acute respiratory syndrome (SARS) coronavirus and the middle east respiratory syndrome (MERS) coronavirus are discussed separately.

EPIDEMIOLOGY

Geographic distribution- Since the first reports of cases from Wuhan, a city in the hubei province of china at the end of 2019 more than 80,000 covid-19 cases have been reported in china; these include all laboratory-confirmed cases as well as clinically diagnosed cases in the hubei province. A joint world health organization (WHO) china fact-finding mission estimated that the epidemic in china peaked between late January and early February 2020. The majority of reports have been from hubei and surrounding provinces but numerous cases have been reported in other provinces and municipalities throughout china.

Increasing number of cases have also been reported in other countries across all continents except Antarctica and the rate of new cases outside of china has outpaced the rate in china. These cases initially occurred mainly among travellers from china and those who have had contact with

travellers from china. However ongoing local transmission has driven smaller outbreaks in some locations outside of china, including South Korea, Italy, Iran and japan and infections elsewhere have been identified in travellers from those countries.

In the united states several clusters of covid-19 with local transmission have been identified throughout the country.

Updated cases counts in English can be found on the WHO and european centre for disease prevention and control websites.

Transmission

Understanding of the transmission risk is incomplete. Epidemiologic investigation in wuhan at the beginning of the outbreak identified an initial association with a seafood market that sold live animals, where most patients had worked or visited and which was subsequently closed for disinfection. However, as the outbreak progressed person to person spread became the main mode of transmission.

Person to person spread of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) is thought to occur mainly via respiratory droplets, resembling the spread of influenza. With droplet transmission, virus released in the respiratory secretions, virus released in the respiratory secretion when a person with infection coughs, sneeze or talks can infect another person if it makes direct contact with the mucous membranes; infection can also occur if a person touches an infected surface and then touches his or her eyes, nose, or mouth. Droplets typically do not travel more than 6 feet and do not linger in the air. However, given the current uncertainty regarding transmission mechanisms, airborne precautions are recommended routinely in some countries and in the setting of certain high risk procedures in others.

Viral RNA levels appear to be higher soon after symptom onset compared with later in the illness; this raises the possibility that transmission might be more likely in the earlier stage of infection, but additional data are needed to confirm this hypothesis.

The reported rates of transmission from an individual with symptomatic infection vary by location and infection control interventions. According to a joint WHO-china report, the rate of secondary COVID-19 ranged from 1-5 percent among tens of thousands of close contact of confirmed patients in china. In the united states, the symptomatic secondary attack rate was 0.45 % among 445 close contacts of 10 confirmed patients.

Transmission of SARS-COV-2 from asymptomatic individuals has also been described. However, the extent to which this occurs remains unknown. Large-scale serologic screening may be able to provide a better sense of the scope of asymptomatic infections and inform epidemiologic analysis; several serologic tests for SARS-COV-2 are under development.

SARS-COV-2 RNA has been detected in blood and stool specimens. Live virus has been cultured from stool in some cases, but according to a joint WHO-China report, fecal-oral transmission did not appear to be a significant factor in the spread of infection.

VIROLOGY

Full-genome sequencing and phylogenetic analysis that the coronavirus that causes COVID-19 is a betacoronavirus in the same subgenus as the severe acute respiratory syndrome (SARS) virus (as well as several bat coronavirus), but in a different clade. The structure of the receptor-binding gene region is very similar to that of the SARS coronavirus and the virus has been shown to use the same receptor, the angiotensin-converting enzyme 2 (ACE2), for cell entry. The corona virus study group of the international committee on taxonomy of viruses has proposed that this virus be designated severe acute respiratory syndrome coronavirus 2 (SARS-COV-2).

The middle east respiratory syndrome (MERS) virus, another betacoronavirus, appears more distantly related. The closest RNA sequence similarity is to two bat coronavirus and it appears likely that bats are the primary source; whether COVID-19 virus is transmitted directly from bats or through some other mechanism is unknown.

In a phylogenetic analysis of 103 strains of SARS-COV-2 from china, two different types of SARS-COV-2 were identified, designated type L and type S. the L type predominated during the early days of the epidemic in china but accounted for a lower proportion of strains outside of wuhan than in wuhan. The clinical implications of these findings are uncertain.

CLINICAL FEATURES

Incubation period- the incubation period for covid-19 is thought to be within 14 days following exposure, with most cases occurring approximately 4-5 days after exposure.

In a study of 1099 patients with confirmed symptomatic covid-19, the median incubation period was 4 days.

Using data from 181 publicly reported, confirmed cases in china with identifiable exposure, one modeling study estimated the symptoms would develop in 2.5% of infected individuals within 2.2 days and in 97.5% of infected individuals within 11.5 days. The median incubation period in this study was 5.1 days.

Spectrum of illness severity- Most infections are not severe, although my patients with covid-19 have critical illness. Specifically, in a report from the chinese centre for disease control and prevention that included approximately 44,500 confirmed infections with an estimations of disease severity:

- Mild was reported in 81 percent.
- Severe disease was reported in 14 %.
- Critical disease was reported in 5%.
- The overall case fatality rate was 2.3%; no deaths were reported among noncritical cases.

According to a joint WHO china fact-finding mission, the case fatality rate ranged from 5.8% in wuhan to 0.7% in the rest of china. Most of the fatal cases have occurred in patients with advanced age or underlying medical comorbidities.

Age range- Individuals of any age can acquire severe acute respiratory syndrome coronavirus 2 (SARS-cov-2) infection, although adults of middle age and older are most commonly affected.

In several cohorts of hospitalized patients with confirmed COVID-19, the median age ranged from 49-56 years. In a report from the chinese centre for disease control and prevention that included approximately 44,500 confirmed infections, 87% of patients were between 30-79 years old. Older age was also associated with increased mortality, with a case fatality rate of 8 and 15% among those aged 70-79 years and 80 years or older respectively.

Symptomatic infection in children appears to be unknown; when it occurs, it is usually mild, although severe cases have been reported. In the large chinese report described above only 2% of infections were in individuals younger than 20 years old. In a small study of 10 children, clinical illness was mild; 8 had fever, which resolve within 24 hours, 6 had cough, 4 had sore throat, 4 had evidence of focal pneumonia on CT and none required supplemental oxygen. In another study of

6 children aged 1-7 years who were hospitalized in Wuhan with COVID-19, all had fever $>102.2^{\circ}\text{F}/39^{\circ}\text{C}$ and cough, 4 had imaging evidence of viral pneumonia, and one was admitted to the intensive care unit; all children recovered.

Asymptomatic infections- Asymptomatic infections have also been described but their frequency is unknown.

In a COVID-19 outbreak on a cruise ship where nearly all passengers and staffs were screened for SARS-CoV-2, approximately 17% of the population on board tested positive as of February 20; about half of the 619 confirmed COVID-19 cases were asymptomatic at the time of diagnosis.

Even patients with asymptomatic infection may have objective clinical abnormalities. In another study of 24 patients with asymptomatic infection who all underwent chest computed tomography (CT), for 50% had typical ground glass opacities or patchy shadowing and another 20% had atypical imaging abnormalities. 5 patients develop low grade fever with or without typical symptoms, a few days after diagnosis.

Clinical presentation- Pneumonia appears to be the most frequent serious manifestation of infection, characterized primarily by fever, cough, dyspnea and bilateral infiltrates on chest imaging. There are no specific clinical features that can yet reliably distinguish COVID-19 from other viral respiratory infections.

In a study describing 138 patients with COVID-19 pneumonia in Wuhan, the most common clinical features at the onset of illness were:

- Fever in 99%
- Fatigue in 70%
- Dry cough in 59%
- Anorexia in 40%
- Myalgias in 35%
- Dyspnea in 31%
- Sputum production in 27%

The dyspnea developed after a median of 5 days of illness. Acute respiratory distress syndrome developed in 20% and mechanical ventilation was implemented in 12.3%.

Other cohort studies of patients from Wuhan with confirmed COVID-19 have reported a similar range of clinical findings. However fever might not be a universal finding. In one study fever was reported in almost all patients but approximately 20% had a very low grade fever $<100.4^{\circ}\text{F}/38^{\circ}\text{C}$. In another study of 1099 patients from Wuhan and other areas in China, fever was

present in only 44% on admission but was ultimately noted in 89% during the hospitalization.

Other, less common symptoms have included headache, sore throat and rhinorrhea. In addition to respiratory symptoms, gastrointestinal symptoms have also been reported in some patients but these are relatively uncommon. Reports of cohorts in locations outside of Wuhan have described similar clinical findings, although some have suggested that milder illness may be more common. As an example, in a study of 62 patients with COVID-19 in the Zhejiang province of China, all but one had pneumonia, but only two developed dyspnea, and only one warranted mechanical ventilation.

According to the WHO, recovery time appears to be around two weeks for mild infections and 3-6 weeks for severe diseases.

Laboratory findings:- In patients with COVID-19, the WBC count can vary. Leukopenia, leukocytosis, and lymphopenia have been reported, although lymphopenia appears most common.

EVALUATION AND DIAGNOSIS

Clinical suspicion and criteria for testing:- The approach to initial management should focus on early recognition of suspected cases, immediate isolation, and institution of infection control measures. At present, the possibility of COVID-19 should be considered primarily in patients with fever and/or lower respiratory tract symptoms who have had any of the following in the prior 14 days:

- Close contact with a confirmed or suspected case of COVID-19, including through work in health care settings. Close contact includes being within approximately six feet (about two meters) of a patient for a prolonged period of time while not wearing personal protective equipment or having direct contact with infectious secretion while not wearing personal protective equipment.
- Residence in or travel to areas where widespread community transmission has been reported (eg, China, South Korea, most of Europe including Italy, Iran, Japan).
- Potential exposure through attendance at events or spending time in specific settings where COVID-19 cases have been reported.
- Case definition from the WHO are found in its technical guidance online.
- Case definitions from the European centres for disease prevention and control are found on its website..

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Laboratory testings- Patients who meet the criteria for suspect cases as discussed above should undergo testing for SARS-COV-2(the virus that causes covid-19), in addition to testing for other respiratory pathogens.

SARS-COV-2 RNA is detected by polymerase chain reaction; in the United states, testing is performed by the CDC or a CDC-qualified lab. A positive test for SARS-COV-2 confirms the diagnosis of covid-19. If initial testing is negative but the suspicion for covid-19 remains the WHO recommends resampling and testing from multiple respiratory tract sites. Negative reverse-transcription polymerase chain reaction (RT-PCR) tests on oropharyngeals swabs despite CT findings suggestive of viral pneumonia have been reported in some patient who ultimately tested positive for SARS-COV-2.

For safety reasons specimens from a patient with suspected or documented COVID-19 should not be submitted for viral culture.

The importance of testing for other pathogens was highlighted in a report of 210 symptomatic patients with suspected COVID-19 30 tested positive for another respiratory viral pathogen and 11 tested positive for SARS-COV-2.

MANAGEMENT

Home care:-Home management is appropriate for patient with mild infection who can be adequately isolated in the outpatient setting. Management of such patients should focus on prevention of transmission to others and monitoring for clinical deterioration, which should prompt hospitalization.

Hospital care:-Some patients with suspected or documented covid-19 have severe disease that warrants hospital care. Management of such patient consists of ensuring appropriate infection control, as below and supportive care.

Patients with severe disease often need oxygenation support. High flow oxygen and noninvasive positive pressure ventilation have been used, but the safety of these measures is uncertain and they should be considered aerosol-generating

procedures that warrant specific isolation precautions.

Some patients may develop acute respiratory distress syndrome and warrant intubation with mechanical ventilation; extracorporeal membrane oxygenation may be indicated in patients with refractory hypoxia. Management of acute respiratory distress syndrome is discussed in detail elsewhere.

PREVENTION

In the health care setting

Screening and precautions for fever or respiratory symptoms:-Screening patients for clinical manifestations consistent with COVID-19 (eg fever, cough, dyspnea) prior to entry into a health care facility can help identify those who may warrant additional infection control precautions. This can be done over the phone before the patient actually presents to a facility. Any individual with these manifestations should be advised to wear a facemask. Separate waiting areas for patients with respiratory symptoms should be designated if possible at least six feet away from the regular waiting areas.

Symptomatic patients should also be asked about recent travel or potential COVID-19 exposure in the prior 14 days to determine the need for evaluation for COVID-19.

In some settings such as long-term care facilities, the United States Centres for disease control and prevention recommends that standard, contact and droplet precautions in addition to eye protection be used for any patient with an undiagnosed respiratory infection who is not under consideration for COVID-19. This may help to reduce the risk of spread from unsuspected COVID-19 cases. Infection control precautions for suspect COVID-19 cases are discussed below.

In locations where community transmission is ongoing, postponing elective procedures or non-urgent visits and using virtual(eg, through video communication) visits may be useful strategies to reduce the risk of exposure.

Infection control for suspected or confirmed cases:- Infection control to limit transmission is an essential component of care in patients with suspected or documented COVID-19. In one report of 138 patients with COVID-19 in China, it was estimated that 43% acquired infection in the hospital setting.

Individuals with suspected infection in the community should be advised to wear a medical

mask to contain their respiratory secretions prior to seeking medical attention.

SPECIAL SITUATIONS

Pregnant women:-Minimal information is available regarding COVID-19 during pregnancy. Intrauterine or perinatal transmission has not been identified. In two reports including a total of 18 pregnant women with suspected or confirmed COVID-19 pneumonia, there was no laboratory evidence of transmission of the virus to the neonate. However two neonatal cases of infection have been documented.

SUMMARY AND RECOMMENDATIONS

- In late 2019 a novel coronavirus now designated SARS-COV-2 was identified as the cause of an outbreak of acute respiratory illness in Wuhan, a city in China. In February 2020, the WHO designated the disease COVID-19 which stands for coronavirus disease 2019.
- Since the first reports of COVID-19, infection has spread to include more than 80000 cases in China and increasing cases worldwide, prompting the WHO to declare a public health emergency in late January 2020 and characterize it as a pandemic in march 2020. The rate of new infection outside of China has surpassed that within China as epidemic has grown in other countries.
- In addition to testing for other respiratory pathogens upper respiratory tract specimens and if possible, lower respiratory tract specimens should be tested for SARS-COV-2.
- Management consists of supportive care. Home management may be possible for patients with mild illness who can be adequately isolated in the outpatient setting.
- To reduce the risk of transmission in the community, individuals should be advised to wash hands diligently, practice respiratory hygiene(eg cover their cough), and avoid crowds and close contact with ill individuals if possible. Facemasks are not routinely recommended for asymptomatic individuals to prevent exposure in the community. Social distancing is advised in locations that have community transmission.
- Interim guidance has been issued by the WHO and by the CDC. These are updated on an ongoing basis.