In support of improving medical care across the world, Project C.U.R.E. is pleased to share the second edition of our COVID-19 Education and Prevention Newsletter. Dr. Spaulding, senior medical advisor for Project C.U.R.E. and international medical doctor, will regularly provide up to date information on Coronavirus - what it is and how we can keep ourselves and our communities safe. This information is up-to-date as of May 2nd, 2020 from a variety of highly reliable sources. Our knowledge is rapidly increasing as doctors and researchers are working day-and-night globally. We still have much to learn and will keep you updated as new information comes in. Updated information and guidance are also regularly being provided by the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC).
WHO ARE THE MOST VULNERABLE FOR SEVERE / CRITICAL DISEASE WITH COVID-19?

DUANE R SPAULDING, MD

a) People >60 years old are at higher risk
b) People of any age with chronic diseases including Cardiovascular Disease, Diabetes, Chronic Obstructive Pulmonary Disease / Emphysema, Cancer, and now also adding immune-suppressed conditions and liver disease
c) However, the patients with the highest risk are those with preexisting Hypertension, Obesity (body mass index $\geq$30), or Diabetes
d) African-Americans are disproportionately being affected in the USA possibly related to underlying socioeconomic disparities and greater likelihood of other underlying diseases
e) Death rates of males have significantly exceeded females in China and Italy
f) Symptomatic infection in children appears to be relatively uncommon; when it occurs, it is usually mild, although severe cases have been reported

WHAT ARE THE SYMPTOMS AND SIGNS OF COVID-19?

a) Common symptoms may appear 2-14 days after exposure to the virus (Listed here in order of decreasing frequency):
   i) Fever with or without rigors (shaking) (1) On initial presentation, some patients’ fever may be remarkably low-grade, i.e. 99.5°F (37.5°C), although it typically rises subsequently
   ii) Cough
   iii) Shortness of breath of difficulty breathing
   iv) Myalgias (muscle pains)
   v) New loss of taste or smell
   vi) Fatigue
   vii) Less commonly: Headache / Sore Throat / Rhinorrhea / Gastrointestinal symptoms
b) **Emergency Warning Signs** include (this list is not all-inclusive):
   i) Trouble breathing
   ii) Persistent pain or pressure in the chest
   iii) New confusion of inability to arouse
   iv) Bluish lips or face
   v) These Emergency Warning Signs require urgent referral to a hospital

c) Remarkably, even patients with minimally symptomatic or asymptomatic infections may have objective clinical abnormalities:

   i) For example, one study of patients with only mild, nonspecific symptoms of COVID-19 were evaluated with a fingertip pulse oximeter and found to have significantly low oxygen saturation levels (<88-90%) on room air
   
   (1) This is despite the patients having no complaints of breathing difficulties
   
   (2) Perhaps this could serve as an “early warning sign” of COVID-19 when mildly febrile patients present to the clinic/healthcare facility – research is needed

d) In another study, chest computed tomography (CT) scans showed that 50% of these patients had significant changes in their lungs
RECOVERY TIME AFTER DEVELOPING AN ILLNESS DUE TO COVID-19

DUANE R SPAULDING, MD

a) If only mild illness: ~2 weeks
b) If the patient has severe illness: ~3-6 weeks or more
c) For patients who ultimately die from COVID-19, there are usually many days between first developing symptoms and dying

HOW DO COVID-19 SYMPTOMS COMPARE TO INFLUENZA?

a) There are NO specific clinical features that can reliably distinguish COVID-19 from other more common viral respiratory infections including Influenza
   i) Although, as noted, many COVID-19 patients have an abnormal chest x-ray consistent with pneumonia early in the course of their illness
b) Influenza is caused by a number of different strains of Influenza viruses vis-à-vis only 1 virus causes COVID-19
c) Both can cause fever, body aches, fatigue and sometimes diarrhea
d) Many more patients with COVID-19 have a dry cough as an early symptom
e) Of course, both illnesses can be mild or severe
f) Because of the overlapping symptoms, it is clinically not possible to reliably diagnose patient with COVID-19 without readily available and accurate SARS-CoV-2 test kits
HOW DOES COVID-19 SPREAD TO OTHER PEOPLE?

DUANE R SPAULDING, MD

a) Primarily by exposure to droplets from the mouth/nose/throat of an infected patient who coughs / sneezes / speaks
   i) Droplets typically travel <2 meters through the air
      (1) These respiratory droplets then make direct contact with another person’s mucous membranes
         (a) i.e., Eyes, Nose, or Mouth
       ii) Also, exposure occurs if a healthy person touches a surface contaminated by these infectious droplets (table top, door handle, etc.) and then touches their own eyes, nose, or mouth

b) To the best of our current knowledge, except during invasive procedures (for example, bronchoscopy, endotracheal intubation, etc.) SARS-CoV-2 virus cannot be transmitted to other people via the “airborne” route
   i) i.e., spreading by particles smaller than droplets that remain in the air for a much longer time and across a greater distance

c) Definition of “Close Contact”
   i) Being within 2 meters while caring for, living with, visiting, or sharing a hospital room with a patient with COVID-19 – without protective equipment
      (1) i.e., without gowns, gloves, masks, and eye protection

d) According to the WHO:
   i) Patients with COVID-19 are likely contagious and able to infect other people when they only have a mild cough and are not feeling sick
   ii) Currently, there are no studies on the survival of the SARS-CoV-2 virus in drinking water or sewage

CAN ANIMALS SPREAD THE VIRUS?

a) SARS-CoV-2 viral infection is thought to have originally been transmitted to humans from an animal host, but the ongoing risk of transmission through animal contact is uncertain
   i) There are no reports or evidence suggesting animals (including domesticated animals such as dogs, cats, livestock, etc.) can transmit SARS-CoV-2 to humans
   ii) However, given the uncertainty regarding the transmission risk, the CDC recommends that people with COVID-19 try to avoid close contact with household pets, as they should also do with human household members while self-isolating
How Long Does This Virus Remain Contagious on Dry Surfaces?

Duane R Spaulding, MD

a) This question is important because: Studies have suggested extensive viral contamination of many surfaces in the rooms of COVID-19 patients.

b) The answer varies under different conditions:
   i) For example, the type of surface, the ambient temperature, and the humidity of the environment all affect how long this virus remains viable and contagious.

c) Studies suggest that the family of coronaviruses (including preliminary information on the COVID-19 virus).

   i) May survive and be infectious on various surfaces for a few hours or as long as several days.
      (1) Specifically, if on cardboard \(\leq 1\) day; if on plastic and metal \(\leq 3\) days.
   ii) Latest report in last week’s NEJM (New England Journal of Medicine):
      (1) Shows similarity between SARS-CoV-2 and prior SARS-CoV virus viability studies.
   iii) Overall, current studies are inconclusive although most report viability of \(\leq 3\) days.
      (1) However, according to the WHO: In special environmental conditions, 6-9 days seems to be the maximum amount of time.

d) This reemphasizes the importance of effective environmental disinfection practices for all potentially affected surfaces in the home and healthcare setting.
   i) Which can kill this virus in just 1 minute!
INCUBATION PERIOD

DUANE R SPAULDING, MD

a) i.e., the time interval between being exposed to the virus and actually developing symptoms of COVID-19 illness
b) <14 days, with most cases occurring ~5 days after exposure

DIAGNOSIS

a) Unfortunately, the accuracy and predictive values of most of the SARS-CoV-2 testing kits have not been systematically evaluated
   i) The sensitivity of testing likely depends on the precise RT-PCR assay selected, the type of specimen obtained, the quality of the specimen, and duration of illness at the time of testing
   ii) Some reports indicate certain assays may give a ~30% FALSE NEGATIVE result
(1) i.e., the test is negative but the patient actually does have COVID-19
b) In many cases, because of the limited availability of testing and concern for false-negative results:
   i) The diagnosis of COVID-19 is made presumptively based on a compatible clinical presentation in the setting of an exposure risk

IMMUNITY

a) Preliminary evidence suggests that some antibodies are “protective”, but this remains to be definitively established
   i) It is unknown whether all infected patients mount a protective immune response, and generally how long any protective effect will persist
   ii) If, and ONLY if, research evidence ultimately confirms that these antibodies reflect a protective immune response, serologic antibody screening will be an important tool to understand population immunity and distinguish individuals who have these protective antibodies and are therefore at lower risk for reinfection
TREATMENTS

DUANE R SPAULDING, MD

a) Patients with fever, cough, and shortness of breath should promptly seek medical attention
b) Initial management when COVID-19 is suspected should focus on early recognition of suspected cases, immediate isolation, and initiating infection control measures
c) Determining if caring for patients with COVID-19 at home is appropriate
   i) Acceptable for patients with mild infection who can be adequately isolated in the outpatient setting
   ii) Must emphasize the best efforts for preventing transmission of the virus to others by ensuring that these patients should:
       (1) Stay at home
       (2) Separate themselves from other people and animals in the household
       (3) Wear a well-fitting facemask when in the same room (or vehicle) as other people and when going to a medical clinic or hospital
   iii) In addition, these patients need to be monitored by someone else for worsening severity of their illness
d) Medications for symptoms
   i) Acetaminophen/Paracetamol may be used for musculoskeletal discomfort and, if necessary, to reduce very high fevers
   ii) Preliminary data warns against the routine use of “NSAIDs” in these patients until more information is available
       (1) i.e., Ibuprofen, Naproxen, Diclofenac, etc., as well as Aspirin
e) Antiviral treatments are being researched worldwide
   i) Use of these agents is generally limited to hospitalized patients who have or are at risk for severe disease
       (1) When possible, treatment should be given as part of a clinical research trial
   ii) Preliminary Reports from RCTs (Randomized Controlled Trials) being performed on COVID-19 patients are showing the following:
Remdesivir (an antiviral agent with unimpressive effectiveness against Ebola) is showing some encouraging results in the laboratory and is now undergoing testing in very ill ICU patients in multiple hospitals.

Hydroxychloroquine (an antimalarial drug previously showing some activity against other coronaviruses) has had very disappointing results.

Because of its cardiac toxicity, this medication should NOT be used outside of a hospital setting as part of a clinical trial.

Hundreds of other potential treatment candidates (both prescription medications and “alternative, non-traditional” therapies) with antiviral activity are also being tested in laboratories and hospitals around the world.

“Convalescent Plasma” Therapy

i.e., Taking plasma from the bloodstream of patients who have recovered from COVID-19 and transfusing this plasma (hopefully containing high level of antibodies) into very sick COVID-19 patients.

Studies are currently underway regarding the effectiveness of this procedure with preliminary reports suggesting some benefits.

If hospitalized, the overall medical management of documented cases is primarily “supportive” - including oxygen, IV fluids, etc. and careful monitoring for worsening trends that might require transferring to the ICU and perhaps Mechanical Ventilation.

Steroids should not be used to treat COVID-19 patients.

Exception: permissible in the very specific situation of a severe COPD/Asthma exacerbation in a hospitalized patient.

UpToDate®: www.uptodate.com - personal online subscription with all sections reported as having been updated on 17 April 2020 - licensed to Dr. Spaulding
Johns Hopkins University: www.coronavirus.jhu.edu/map.html - a dashboard available to the public of various maps and charts of data about COVID-19 - “updated virtually continuously”