

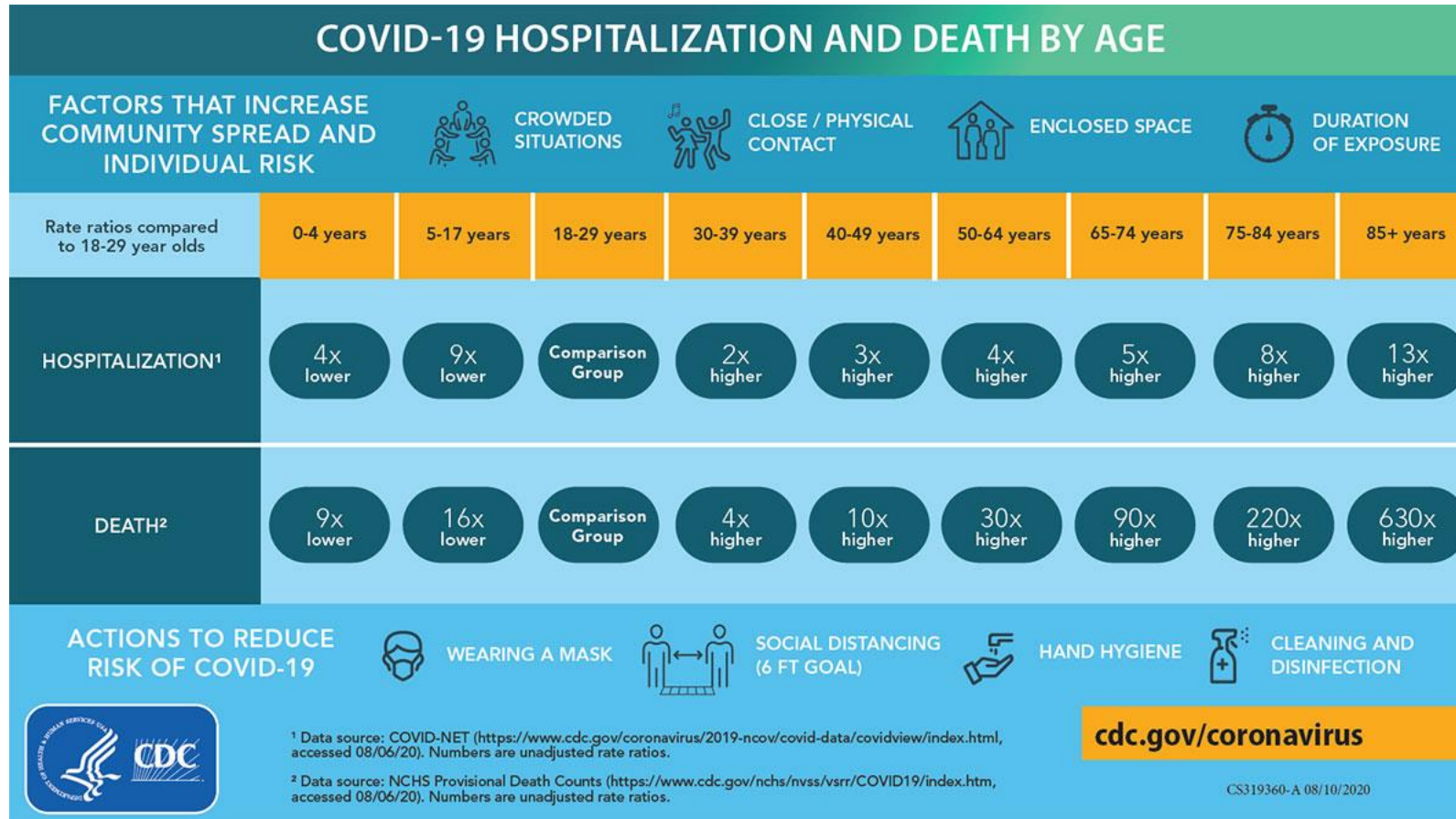
Clinical characteristics of Coronavirus Infections.

Stanley Perlman, MD, PhD
University of Iowa Distinguished Chair
Department of Microbiology and Immunology
Department of Pediatrics

Common clinical features of SARS, MERS, COVID-19

- Severe pulmonary disease occurs in a fraction of infected people.
- Incubation period is 5-7 days with shorter time to ICU admission in MERS.
 - Incubation time decreased with many SARS-CoV-2 VOCs
 - Human challenge studies suggest that virus can be detected in nasopharynx in 2 days in COVID-19; comparable information not available for SARS, MERS
- Respiratory and nonspecific symptoms include cough, fever, myalgias, shortness of breath, etc.
- Many people infected with all three entities have mild disease.
- A fraction are asymptomatic, although this fraction was low for SARS and is much higher for COVID-19.
- **Those at greatest risk are those over 75 years, and those with co-morbidities (diabetes, obesity, lung disease, heart disease).**
- Diarrhea and detection of viral RNA in feces is common in all three diseases.
- Renal dysfunction present in all three, although may be greatest in MERS.

COVID-19, like MERS and SARS is a disease of the elderly



Common laboratory/radiological features of SARS, MERS, COVID-19

- Lymphopenia is found in all three diseases, but is more common in SARS and COVID-19. Steroid treatment in SARS and MERS contributed to lymphopenia
- Neutrophilia occurs most commonly in COVID-19 (not noted in SARS or MERS).
- Chest x-ray and CT findings are consistent with viral pneumonia but otherwise not diagnostic.
 - May be diagnostic in setting where most cases of viral pneumonia are caused by a single pathogen, such as occurred early in the pandemic.
- Myeloid cells are infected, IFN is not induced but pro-inflammatory mediators are induced, infection is abortive in all studies (except one MERS study).

Features of clinical SARS, MERS and COVID-19 that differ

- Mortality is substantially different.
 - SARS-10%
 - MERS-35%
 - COVID-19-1.3%
- Significant disease occurs in 10-20% of COVID-19 patients. An 1-2% overall mortality is equivalent to a 10% mortality in those with severe pneumonia, the same as SARS.
- Other differences are hard to assess because all SARS patients were treated with corticosteroids and ribavirin and there have been only two MERS autopsies.

Features that are shared by SARS and COVID-19

- In both diseases, multiple organs are affected.
- Less information from SARS, but SARS-CoV was found in many organs in one study. These results were not confirmed in other studies.
- In COVID-19, little evidence of virus outside of respiratory tract.
- However, postmortem findings in association with COVID-19 apart from pneumonia include cytopathic effects within pneumocytes, thromboembolism, brain infarction, endotheliitis, acute renal tubular damage, white pulp depletion of the spleen, cardiac myocyte necrosis, megakaryocyte recruitment, and hemophagocytosis.
- We still do not fully understand pathogenesis, since virus is found only in the lungs for the most part. However, even in the absence of infectious virus, viral RNA or protein could contribute to pathogenesis.

Features that are unique to COVID-19

- Clinical findings that appear to be unique to COVID-19 include
 - Neurological (brain fog, memory loss, confusion, anosmia, ageusia, stroke)
 - Cardiovascular (myocarditis, clotting abnormalities, myocardial infarction).
 - Rashes that often take prolonged times to resolve).
- Postmortem findings in association with COVID-19 apart from pneumonia include cytopathic effects within pneumocytes, thromboembolism, brain infarction, endotheliitis, acute renal tubular damage, white pulp depletion of the spleen, cardiac myocyte necrosis, megakaryocyte recruitment, and hemophagocytosis. Some of these findings explain clinical findings.
- We still do not fully understand pathogenesis, since virus is found only in the lungs for the most part. However, even in the absence of infectious virus, viral RNA or protein could contribute to pathogenesis.

Long COVID

- Long COVID occurs after severe or mild disease, even after apparent disease resolution.
- Has some similarities with encephalitis lethargica, which followed the 1918 influenza epidemic, but may not have been virus-induced.
- Long COVID symptoms include:
 - Neurological-cognitive losses, mood changes, prolonged anosmia, tinnitus, headaches
 - Pulmonary-shortness of breath, cough
 - Cardiac-chest pain, palpitations, myocarditis, POTS (Postural Orthostatic Tachycardia Syndrome).
 - Endocrine-increased risk of developing diabetes mellitus
 - Many similarities with Chronic Fatigue Syndrome.
- Pathogenesis not understood because infectious virus not found in these organs.
- Vaccination likely protects against Long COVID. However, if virus antigen is contributory factor to Long COVID, effects of vaccination may be nuanced.

Long COVID #2

- Concern is that Long COVID may not resolve in some patients, resulting in long term disabilities.
- For example, could unresolved anosmia/ageusia lead to neurodegenerative disease (e.g., Parkinson's, Alzheimer's)?
- Vaccination likely protects against Long COVID. However, if virus antigen is contributory factor to Long COVID, effects of vaccination may be nuanced.