SARS-CoV-2: Virological & clinical features and questions

SARS-CoV-2 = virus
COVID-19 = disease

Dennis Kolson, MD, PhD
Neurology Dept.
University of Pennsylvania
March 12, 2020

Disclosure: Dr. Kolson serves as a consultant to the National NeuroAIDS Tissue Consortium
Coronavirus virion

- Spike protein (S)
- Small membrane protein (E)
- Genome RNA
- Membrane protein (M)
- Nucleocapsid protein (N)
- Hemagglutinin-Esterase (HE)

SARS-CoV-2: Uses human ACE 2 receptor for entry
SARS-CoV-2: sources of information:

https://special.croi.capitalreach.com/

Susan R. Weiss
Director, Upenn NIH T32 'Training in Neurovirology'

Description of Research Expertise

- Murine coronavirus pathogenesis, central nervous system, liver and lung
- Murine coronavirus antagonism of the OAS-RNase L pathway
- Organ specific virus-host interactions
- Viral and cellular phosphodiesterases
- Middle East Respiratory Syndrome Coronavirus pathogenesis
- Role of inflammasome-related cytokines in murine coronavirus acute disease and chronic demyelination

Key words: murine coronavirus, human respiratory coronavirus, viral pathogenesis, interferon antagonist.

Description of Research

Susan Weiss, Ph.D.
Human coronaviruses: time line

Common cold
OC43 can infect lower respiratory track

229E
OC43

HKU1; Pneumonia
NL63; Bronchiolitis, croup

SARS-CoV HKU1 NL63

2002 2004/2005

MERS-CoV

2012

SARS-CoV-2 (CSG/ICTV))
COVID-19 (WHO)
(2019-nCoV)

1967/1970

OC43 genome similar to Bovine coronavirus

SARS-CoV, MERS-CoV, SARS-CoV-2
Severe respiratory disease

coronavirus disease-2019 or COVID-19

Courtesy of Susan Weiss, PhD, Upenn Dept. Microbiology
Epidemiology: spread from China
(apparent control now in China)

Distribution of COVID-19 cases in accordance with the applied case definitions in the affected countries, as of 05 March 2020

Number of cases

Outside China
China

March 4
Deaths outside China exceed death reports in China

February 25
Cases outside China exceed cases reports in China

Day, month and year of reporting
Most common symptoms: fever, dry cough, fatigue

Median incubation period estimated to be 4-6 days (range 2-14 days)

Fever: ~ 80%
Cough: ~ 50%
SARS-CoV-2 can be shed 24-48 hours before symptoms

Key epi/technical insights from China (3 of 3)

3-Virology:

- Virus **shedding** is highest early in the course of disease (vs. SARS shedding, which peaks at least 5 days after onset)
  - **Virus shedding** can occur in the 24-48 hours prior to symptom onset
- Virus can be **isolated** from stool but there is no epidemiologic evidence of fecal-oral transmission
- Virus **shedding** usually continues for 7-12 days in mild/moderate cases, and for >2 weeks in severe cases
- Patients who recover can be PCR positive after symptoms resolve

Aylward B et al, WHO-China Mission, 2020

Presented at: 27th annual Conference on Retroviruses and Opportunistic Infections (CROI) International Meeting (virtual meeting)
March 8-11, 2020
SARS-CoV-2 can be shed 24-48 hours before symptoms

**Viral Shedding Greatest At Time Symptoms Start**

- SARS-CoV-2 viral loads in 17 symptomatic patients
- No data regarding duration of replication-competent virus shedding (e.g., culture)

![Graph showing Aggregated Ct Values over Days since Onset of Symptoms](image_url)

SARS-CoV-2 Therapeutics

Therapeutic Interventions

- No approved drugs, immune therapeutics and vaccines against any group 2b coronavirus
- Experimental Drugs (nsp12-RdRp target)
  - Remdesivir
    - Inhibits RNA-dependent RNA polymerase

At least 6 Remdesivir controlled trials planned/currently underway

- Combination lopinavir, ritonavir, and interferon beta tested in China?
- Therapeutic antibodies (MERS, likely soon for SARS-CoV 2)


Presented at: 27th annual Conference on Retroviruses and Opportunistic Infections (CROI) International Meeting (virtual meeting)  March 8-11, 2020
Many remaining questions

✦ How extensively will the virus spread?
✦ Will it be seasonal?
✦ How soon will therapeutics (Remdesivir, others) be ready?

Thank you!