4-23-2020

Titan Talks: "The Epidemiology of SARS-CoV2" (slides only)

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TITAN TALKS

AN ILLINOIS WESLEYAN UNIVERSITY WEBINAR SERIES

The Epidemiology of SARS-CoV2

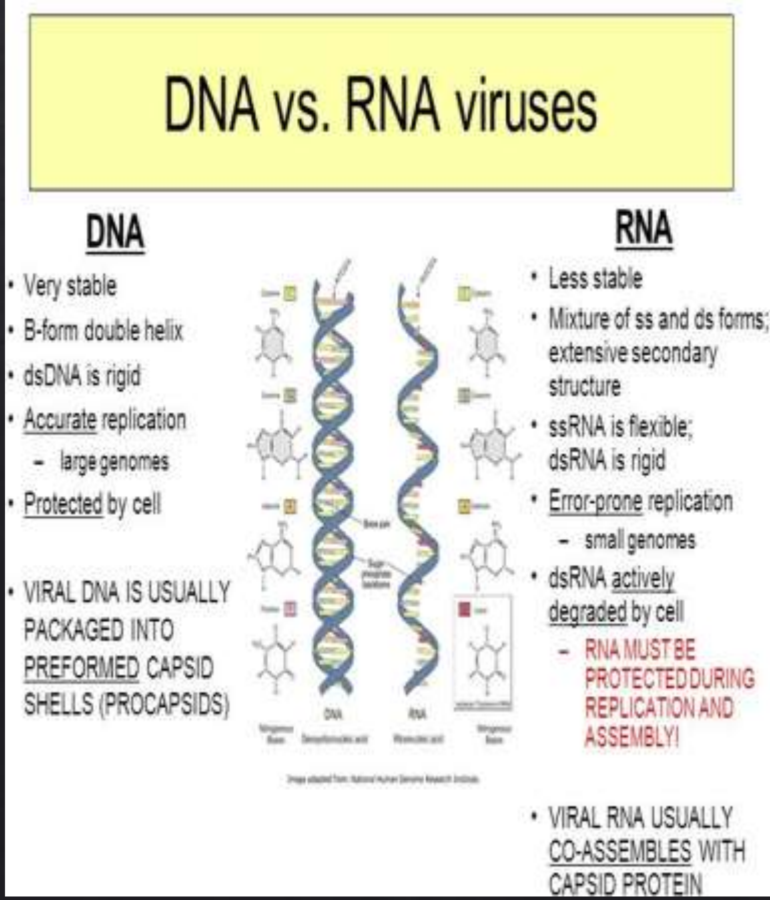
April 23 | 12 – 1 p.m. CDT

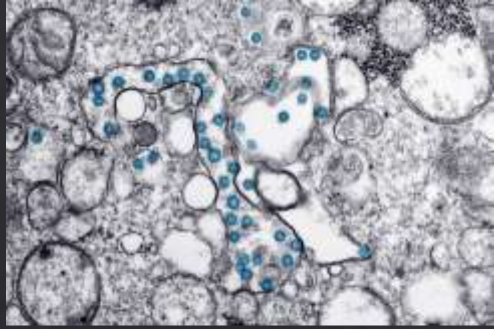
Dr. John Herrmann '74

ILLINOIS WESLEYAN UNIVERSITY

Viruses

- A virus is a small cellular "parasite" that cannot reproduce by itself.
  - Once it infects a susceptible cell, however, a virus can direct the cell machinery to produce more viruses.
- Most viruses have either RNA or DNA as their genetic material.
  - The nucleic acid may be single- or double-stranded.
- The entire infectious virus particle, called a virion, consists of the nucleic acid and an outer shell of protein/lipid.
- The simplest viruses contain only enough RNA or DNA to encode four proteins. The most complex can encode 100 – 200 proteins.
    - https://www.ncbi.nlm.nih.gov/books/NBK21523/





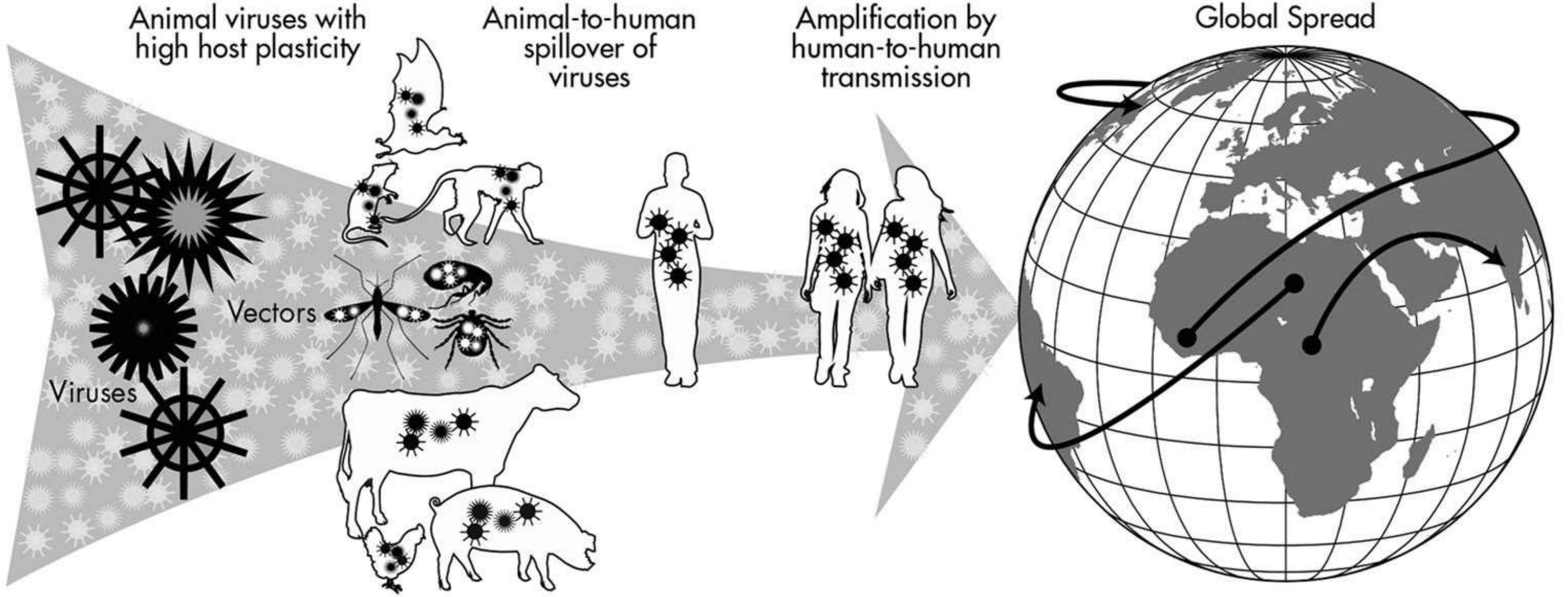
Coronaviruses

- Large family of viruses that usually cause mild to moderate upper-respiratory tract illnesses in humans, like the common cold.
- There are hundreds of coronaviruses, most of which circulate among domestic and wild animals (α, β, γ, δ)
  - Since 2003, three new (novel) coronaviruses have emerged from animal reservoirs to cause serious and widespread illness and death.
    - SARS (2002-3), MERS (2012+), SARS-CoV-2 (2019+)
      - https://www.niaid.nih.gov/diseases-conditions/coronaviruses
      - McIntosh K (1974), Kahn JS, McIntosh K (November 2005), Geller C, Varbanov M, Duval RE (November 2012)

Zoonoses and Spillover events

Zoonotic diseases: infectious diseases that are transmitted between animals and humans

Spillover events: occur when animal pathogens "spill over" into human populations


Animal viruses with high host plasticity
Animal-to-human spillover of viruses
Amplification by human-to-human transmission
Global Spread
Vectors
Viruses

Spillover events

Viral examples:

Filoviruses: Ebola virus disease, Marburg virus

Flaviviruses: Zika, West Nile, Dengue (all vector borne)

Coronaviruses: SARS, MERS, SARS-CoV-19, many in domestic animals

Henipaviruses: Nipah, Hendra

Lentiviruses: HIV

Estimated that 94% of zoonotic viruses are single strand RNA viruses; 91% from wild animals, 34% from domesticated animals (some = both)

Kreider Johnson C, Hitchens P, et al. Spillover and pandemic properties of zoonotic viruses with high host plasticity. *Nature*, 2015

Bacterial examples:

Borrelia burgdorferi – Lyme Disease

Francisella tularensis – Tularemia

Yersinia pestis – pneumonic and bubonic plague

***Brucella* spp**. – undulant fever, abortion,

Mycobacterium bovis – tuberculosis

Is SARS-CoV-2 a spillover event?

- Evidence of a spillover event

- Genomics suggest bats as the primary host species (88% genome homology)

- "The COVID-19 most likely developed from bat origin coronaviruses. Another piece of evidence that supports the COVID-19 is of bat origin is the existence of a high degree of homology of the ACE2 receptor from a diversity of animal species, thus implicating these animal species as possible intermediate hosts or animal models for COVID-19 infection."
  - Rothan HA, Byrareddy, SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020 May;109:102433. doi: 10.1016/j.jaut.2020.102433. Epub 2020 Feb 26.

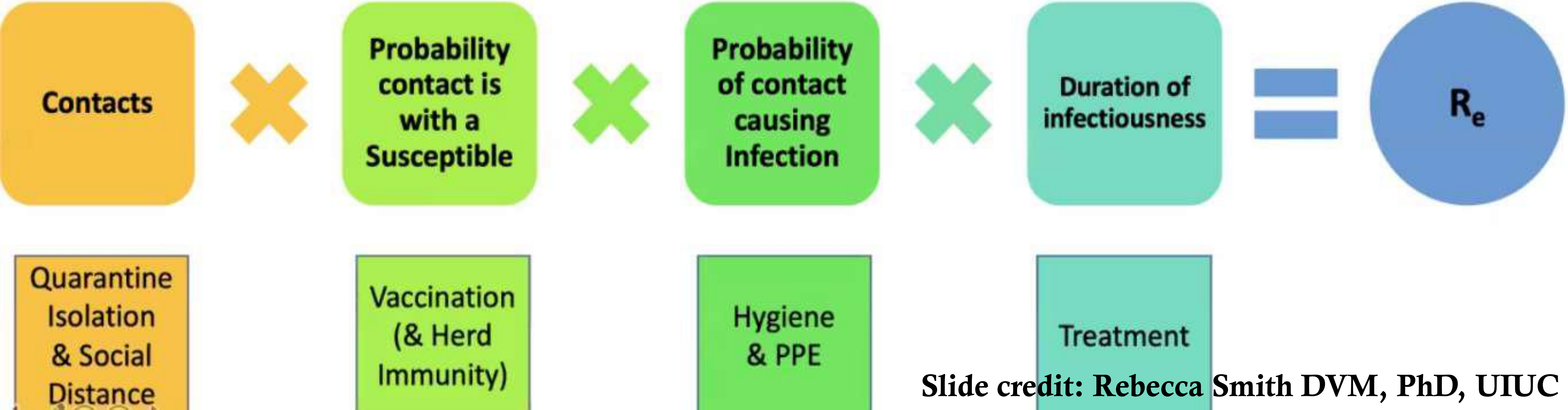
Is SARS-CoV-2 a spillover event?

- Evidence of a early human to human transmission?
  - SARS-CoV-2 from betacoronavirus genus
- Evidence of novel coronaviruses in North American bats?
  - Alphacoronavirus genus only?

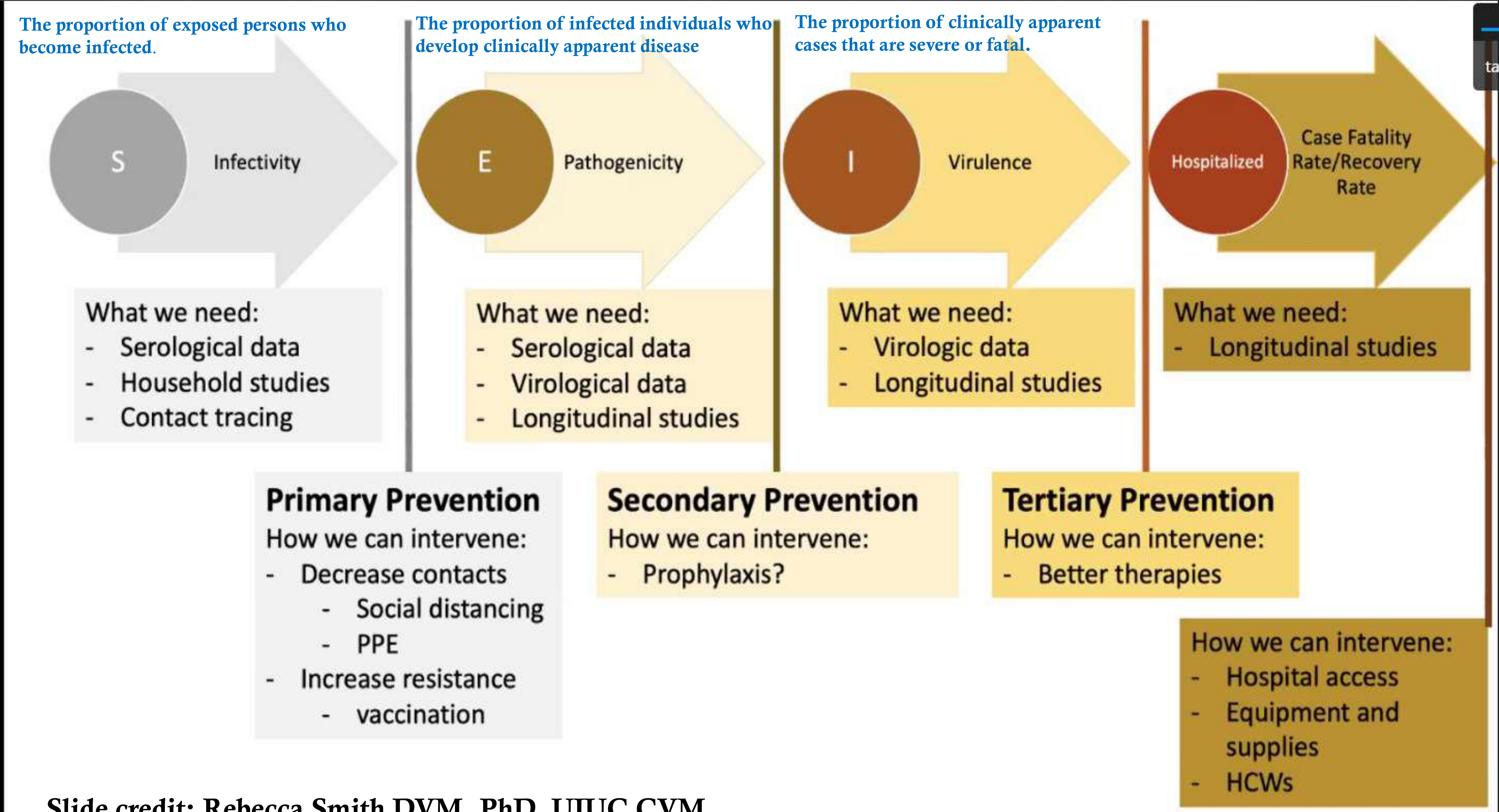
A Primer on R_0

- Expected number of secondary cases caused by a single infected individual in a fully susceptible population
- R_e: Population is not fully susceptible (R_0 * %S)
- Herd Immunity = $1 - 1/R_0$

Estimates of R0	MINIMUM % Immune Needed
2.3 (cruise)	56.5%
2.35 (Wuhan)	57.4%
5.7 (China)	82.5%
15.4 (asymp)	93.5%



Slide credit: Rebecca Smith DVM, PhD, UIUC CVM



Slide credit: Rebecca Smith DVM, PhD, UIUC CVM

Epidemiology basics and the current pandemic

- **Brief history of the pandemic**
  - From December 18, 2019 through December 29, 2019, five patients were hospitalized in Wuhan, China with acute respiratory distress syndrome and one of these patients died
  - December 31, 2019 - China reports to WHO suspected SARS-like illnesses in Wuhan
  - January 7 – genome sequence identified and shared with WHO
  - January 17 – German diagnostic test validated and adopted by WHO
  - January 20 – first identified US case in Snohomish County, WA
  - January 28 – US develops own test; has trouble with consistent results
  - January 30 – WHO declares PHEIC
  - February 6 – first US death (CA)
  - February – due to test validation and lack of surge capacity, US testing < 100 samples per day for entire month at CDC Atlanta
  - March 5 – US allows private labs to use own tests and labs to process samples
  - March 11 – WHO declares a pandemic

Signs and symptoms

- Fever (83–99%)
- Cough (59–82%)
- Fatigue (44–70%)
- Anorexia (40–84%)
- Shortness of breath (31–40%)
- Loss of smell and taste (~50%?)
- Sputum production (28–33%)
- Myalgias (11–35%)

- The largest cohort of >44,000 persons with COVID-19 from China showed that illness severity can range from mild to critical:
  - Mild to moderate (mild symptoms up to mild pneumonia): 81%
  - Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
  - Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%
    - https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

Signs and symptoms

- Additional possible complications:
  - Acute respiratory distress syndrome
  - Acute liver, kidney, or cardiac injury
  - Secondary infection
  - Septic shock
  - Disseminated intravascular coagulopathy
  - Rhabdomyolysis

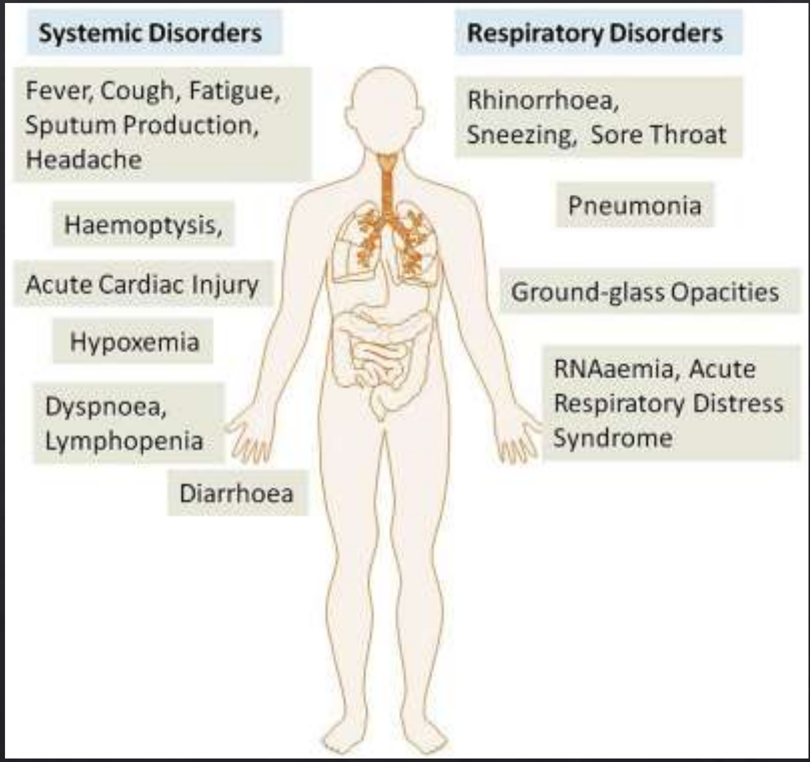


TABLE. Underlying conditions and symptoms among adults aged ≥18 years with coronavirus disease 2019 (COVID-19)–associated hospitalizations — COVID-NET, 14 states,* March 1–30, 2020†

MMWR / April 8, 2020 / Vol. 69

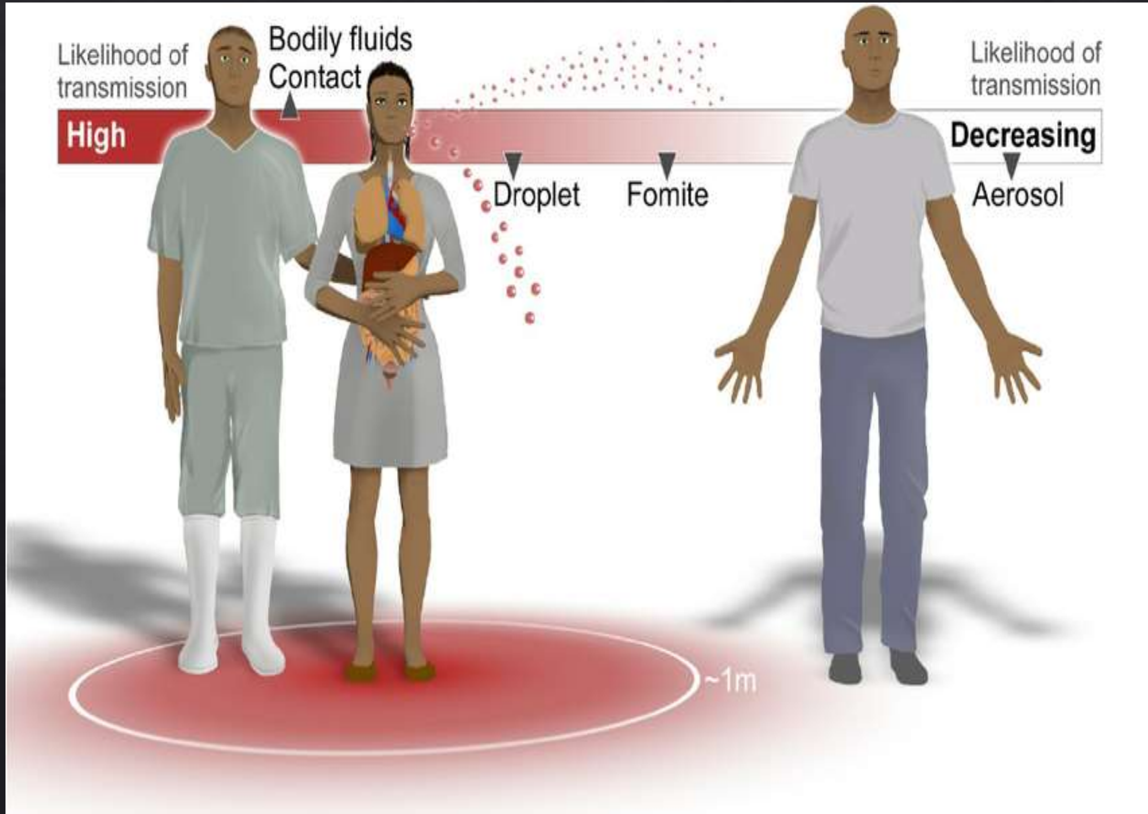
	Age group (yrs), no./total no. (%)			
Underlying condition	**Overall**	**18–49**	**50–64**	**≥65 years**
Any underlying condition	159/178 (89.3)	41/48 (85.4)	51/59 (86.4)	67/71 (94.4)
Hypertension	79/159 (49.7)	7/40 (17.5)	27/57 (47.4)	45/62 (72.6)
Obesity§	73/151 (48.3)	23/39 (59.0)	25/51 (49.0)	25/61 (41.0)
Chronic metabolic disease¶	60/166 (36.1)	10/46 (21.7)	21/56 (37.5)	29/64 (45.3)
Diabetes mellitus	47/166 (28.3)	9/46 (19.6)	18/56 (32.1)	20/64 (31.3)
Chronic lung disease	55/159 (34.6)	16/44 (36.4)	15/53 (28.3)	24/62 (38.7)
Asthma	27/159 (17.0)	12/44 (27.3)	7/53 (13.2)	8/62 (12.9)
Chronic obstructive pulmonary disease	17/159 (10.7)	0/44 (0.0)	3/53 (5.7)	14/62 (22.6)
Cardiovascular disease**	45/162 (27.8)	2/43 (4.7)	11/56 (19.6)	32/63 (50.8)
Coronary artery disease	23/162 (14.2)	0/43 (0.0)	7/56 (12.5)	16/63 (25.4)
Congestive heart failure	11/162 (6.8)	2/43 (4.7)	3/56 (5.4)	6/63 (9.5)
Neurologic disease	22/157 (14.0)	4/42 (9.5)	4/55 (7.3)	14/60 (23.3)
Renal disease	20/153 (13.1)	3/41 (7.3)	2/53 (3.8)	15/59 (25.4)
Immunosuppressive condition	15/156 (9.6)	5/43 (11.6)	4/54 (7.4)	6/59 (10.2)
Gastrointestinal/Liver disease	10/152 (6.6)	4/42 (9.5)	0/54 (0.0)	6/56 (10.7)
Blood disorder	9/156 (5.8)	1/43 (2.3)	1/55 (1.8)	7/58 (12.1)
Rheumatologic/Autoimmune disease	3/154 (1.9)	1/42 (2.4)	0/54 (0.0)	2/58 (3.4)
Pregnancy††	3/33 (9.1)	3/33 (9.1)	N/A	N/A
Symptom§§				
Cough	155/180 (86.1)	43/47 (91.5)	54/60 (90.0)	58/73 (79.5)
Fever/Chills	153/180 (85.0)	38/47 (80.9)	53/60 (88.3)	62/73 (84.9)
Shortness of breath	144/180 (80.0)	40/47 (85.1)	50/60 (83.3)	54/73 (74.0)
Myalgia	62/180 (34.4)	20/47 (42.6)	23/60 (38.3)	19/73 (26.0)
Diarrhea	48/180 (26.7)	10/47 (21.3)	17/60 (28.3)	21/73 (28.8)
Nausea/Vomiting	44/180 (24.4)	12/47 (25.5)	17/60 (28.3)	15/73 (20.5)
Sore throat	32/180 (17.8)	8/47 (17.0)	13/60 (21.7)	11/73 (15.1)
Headache	29/180 (16.1)	10/47 (21.3)	12/60 (20.0)	7/73 (9.6)
Nasal congestion/Rhinorrhea	29/180 (16.1)	8/47 (17.0)	13/60 (21.7)	8/73 (11.0)
Chest pain	27/180 (15.0)	9/47 (19.1)	13/60 (21.7)	5/73 (6.8)
Abdominal pain	15/180 (8.3)	6/47 (12.8)	6/60 (10.0)	3/73 (4.1)
Wheezing	12/180 (6.7)	3/47 (6.4)	2/60 (3.3)	7/73 (9.6)
Altered mental status/Confusion	11/180 (6.1)	3/47 (6.4)	2/60 (3.3)	6/73 (8.2)

Abbreviations: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network; N/A = not applicable.

* Counties included in COVID-NET surveillance: California (Alameda, Contra Costa, and San Francisco counties); Colorado (Adams, Arapahoe, Denver, Douglas, and Jefferson counties); Connecticut (New Haven and Middlesex counties); Georgia (Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, and Rockdale counties);

Transmission

- Contact (fomites) up to 72 hrs?
  - Touching face, especially nose and eyes
- Aerosol – up to 6 feet? For how long?
  - Coughing
  - Sneezing
  - Talking/breathing?



Transmission

Contact tracing in the early stages at various locations suggested that most secondary infections were among household contacts, with a secondary attack rate of up to 10 percent

Burke RM, Midgley CM, Dratch A, et al. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep 2020; 69:245.

COVID-19 National Emergency Response Center, Epidemiology and Case Management Team, Korea Centers for Disease Control and Prevention. Coronavirus Disease-19: Summary of 2,370 Contact Investigations of the First 30 Cases in the Republic of Korea. Osong Public Health Res Perspect 2020; 11:81.

SYMPTOMATIC SECONDARY ATTACK RATE	Close contacts	Household members
U.S. Study (n = 445)	0.45%	10.5%
South Korea (n = 2370)	0.55%	7.6%

Transmission

- Asymptomatic carriers?
  - Estimates = 25% ??? (WHO 4/1/20)
    - ”However, it is notable that the infection appears to have been transmitted during the incubation period of the index patient, in whom the illness was brief and nonspecific.”
    - Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. March 5, 2020, *N Engl J Med* 2020; 382:970-971
  - Incubation period ~2-14 days
  - Duration of viral shedding –
    - Study 1 - 90% no virus after 10 days (n =21)
    - Study 2 - range of shedding range = 8 to 37 days (dependent on severity of illness; n = 137)
    - ***detection of virus doesn’t mean recovery of infectious virus

Transmission

- Environmental contamination
  - **The frequency and the relative importance of this type of transmission remain unclear.**
  - It is unknown how long SARS-CoV-2 can persist on surfaces.
  - Other coronaviruses have been tested and may survive on inanimate surfaces for up to six to nine days without disinfection. However, in a systematic review of similar studies, various disinfectants inactivated a number of coronaviruses related to SARS-CoV-2 within one minute.
  - Based on data concerning other coronaviruses, duration of viral persistence on surfaces also likely depends on the ambient temperature, relative humidity, and the size of the initial inoculum.
  - It may be more likely to be a potential source of infection in settings where there is heavy viral contamination (eg, in an infected individual's household or in health care settings).
    - McIntosh, K. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention

Transmission

- Animals and SARS-CoV-2

  - Cats and ferrets – showed viral replication and recovery after intranasal inoculation
  - Dogs, pigs, chickens – seroconverted but no viral replication or recovery
    - Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. Science 2020.
  - Bronx Zoo – Tiger tested (+) April 5, 2020

Immunity

- Preliminary evidence suggests that some of these antibodies are protective, but this remains to be definitively established.
    - Moreover, it is unknown whether all infected patients mount a protective immune response and how long any protective effect will last.
- Antibodies to the receptor-binding domain of the spike protein and the nucleocapsid protein were detected by enzyme-linked immunosorbent assay (ELISA) in most patients by 14 days following the onset of symptoms (n = 23); ELISA antibody titers correlated with neutralizing activity
    - To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020.

Epidemiology basics and the current pandemic

- Diagnostic Testing
  - Reverse Transcriptase- Polymerase Chain Reaction (RT-PCR)
  - Sensitivity
    - "In a series of 51 patients with chest CT and RT-PCR assay performed within 3 days, the sensitivity of CT for COVID-19 infection was 98% compared to RT-PCR sensitivity of 71% (p<.001)."

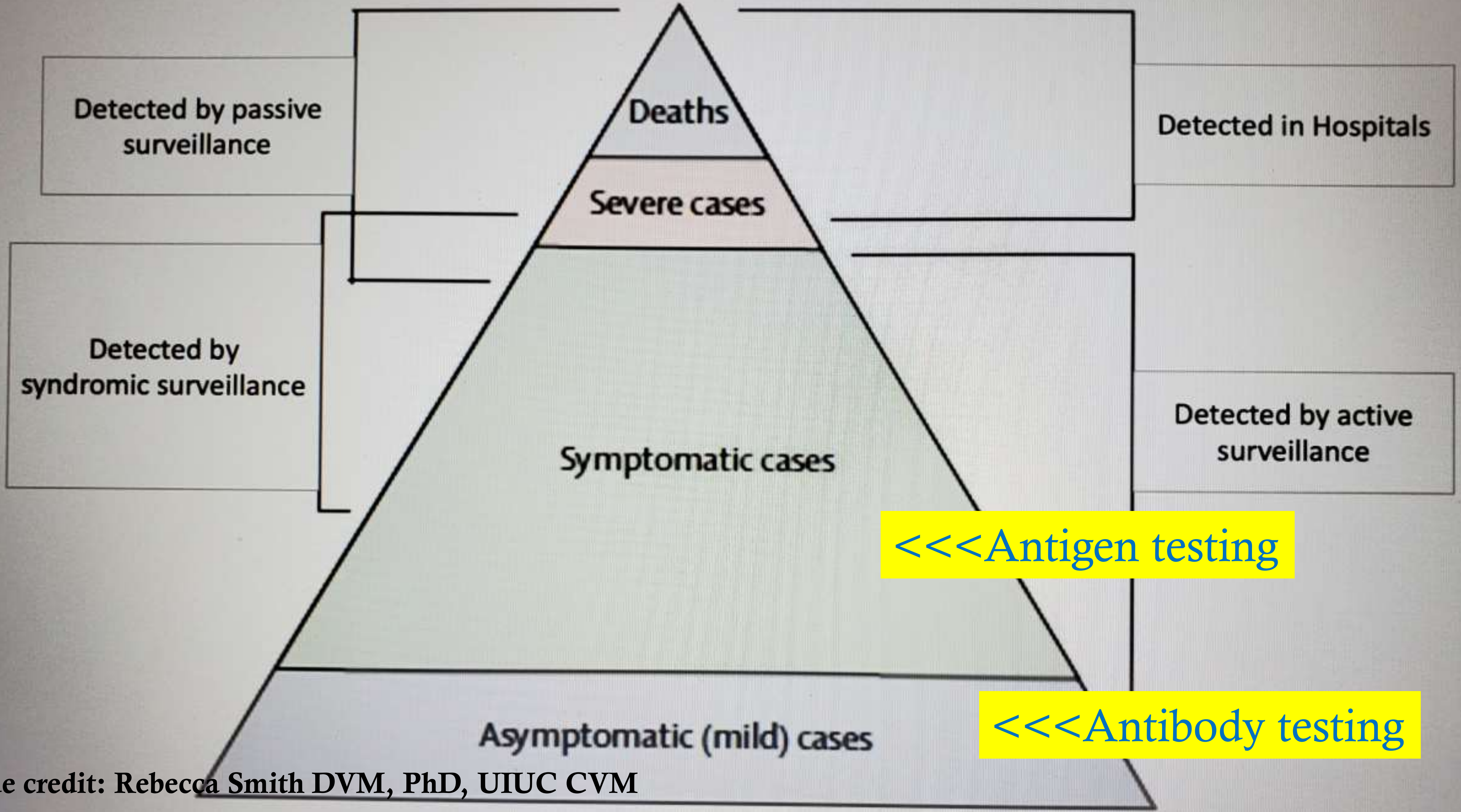
      - Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. Published online Feb 19 2020; https://doi.org/10.1148/radiol.2020200432. Accessed April 2, 2020.
      - West CP, Montori VM, Sampathkumar P. COVID-19 testing: the threat of false-negative results [published online ahead of print April 9, 2020]. Mayo Clin Proc. [https//doi.org/10.1016/j.mayocp.2020.04.004].

- **If current test have a Sn of 90%, we are missing 10% of cases.**
- **The results from viral genome testing is only good <u>for that point in time.</u>**

All | Europe | North America | Asia | South America | Africa | Oceania

www.worldometer.com 4/22/20

Country, Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/ 1M pop	Deaths/ 1M pop	Total Tests	Tests/ 1M pop
World	2,629,951	+74,191	183,723	+6,264	716,731	1,729,497	56,678	337	23.6		
USA	844,992	+26,248	47,430	+2,112	83,910	713,652	14,014	2,553	143	4,307,429	13,013
Spain	208,389	+4,211	21,717	+435	85,915	100,757	7,705	4,457	464	930,230	19,896
Italy	187,327	+3,370	25,085	+437	54,543	107,699	2,384	3,098	415	1,513,251	25,028
France	159,877	+1,827	21,340	+544	40,657	97,880	5,218	2,449	327	463,662	7,103
Germany	150,062	+1,609	5,250	+164	99,400	45,412	2,908	1,791	63	2,072,669	24,738
UK	133,495	+4,451	18,100	+763	N/A	115,051	1,559	1,966	267	559,935	8,248
Turkey	98,674	+3,083	2,376	+117	16,477	79,821	1,814	1,170	28	750,944	8,904
Iran	85,996	+1,194	5,391	+94	63,113	17,492	3,311	1,024	64	377,396	4,493
China	82,788	+30	4,632		77,151	1,005	78	58	3		
Russia	57,999	+5,236	513	+57	4,420	53,066	700	397	4	2,250,000	15,418
Brazil	45,757	+2,678	2,906	+165	25,318	17,533	8,318	215	14	291,922	1,373
Belgium	41,889	+933	6,262	+264	9,433	26,194	1,020	3,614	540	171,400	14,789



Slide credit: Rebecca Smith DVM, PhD, UIUC CVM

Case fatality rate vs. Mortality rate

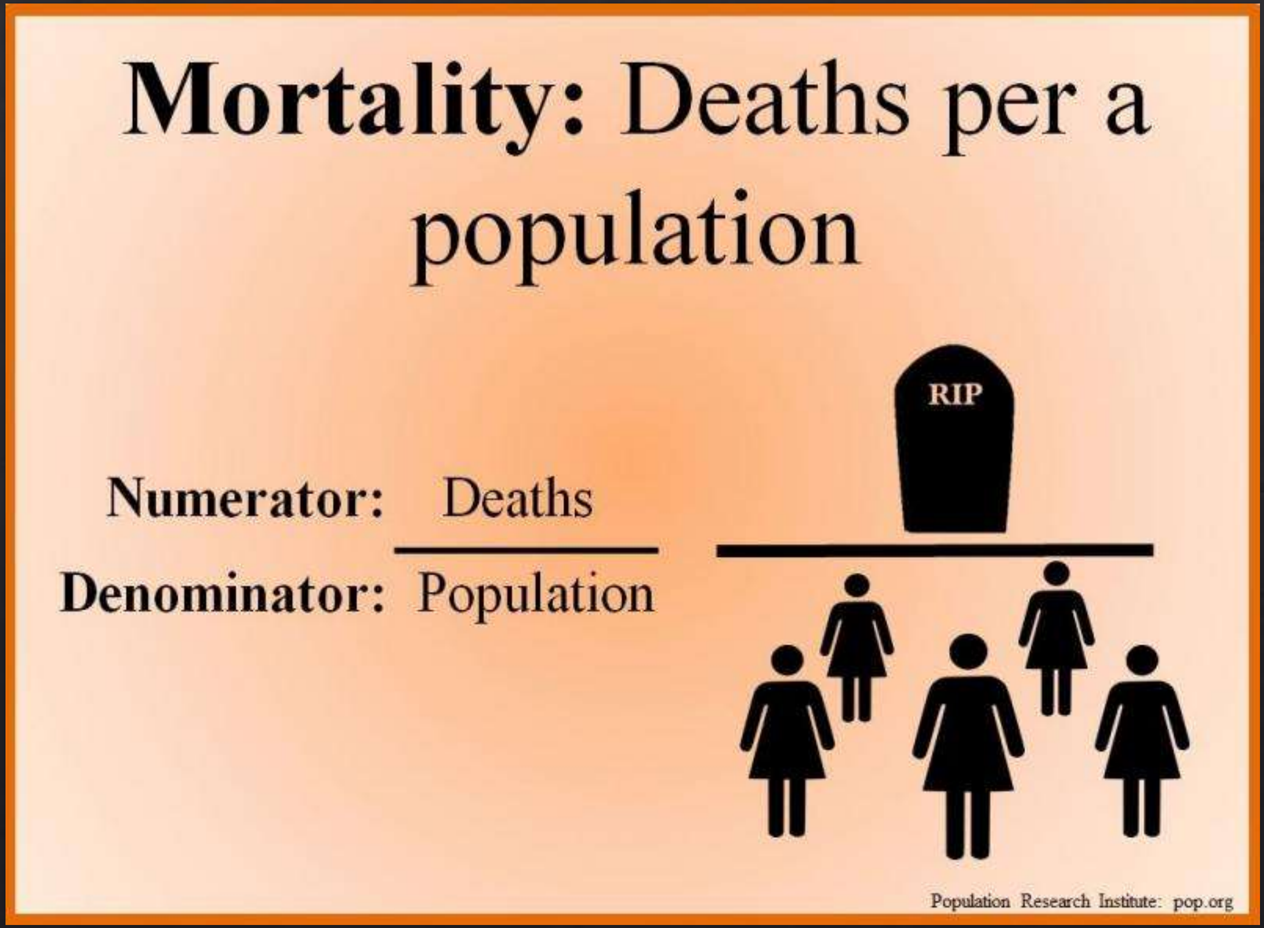
Case Fatality Rate

- This is not a rate, this is a proportion
- Proportion of deaths from a specific illness

$$\text{Case Fatality Rate} = \frac{a}{N}$$

Where:
a = Number of deaths from an illness
N = Number of people with that illness

What percentage of people diagnosed as having a disease die within a certain time after diagnosis?



Also cause specific mortality, age specific, etc. and proportionate mortality

Illinois Data 4/22/2020

- Population 12,659,682
  - Assume 4% prevalence = 506, 387 cases
- Tested 164,346 (55.5% F)
- Cases 35,108 (50.3% F)
- Deaths 1565 (41.3% F)
- Case Fatality Rate 4.46%

AGE	CASES %	DEATHS (n)
< 20	2.7	2
20-29	12.6	5
30-39	15.4	27
40-49	18.3	59
50-59	19.8	141
60-69	14.6	281
70-79	8.9	85% 406
>80	7.7	67% 644

Illinois Data 4/22/2020

*Numbers do not equal 100% due to missing data – 50% tested did not specify RE group

	White	Black	LatinX
TESTED	38415	21670	9958
CASES	8573 (22.3% tested) (24.4% of total)	8504 (39.2% tested) (24.2% of total)	6195 (62.2% tested) (17.6% of total)
DEATHS (CFR)	621 (7.2%)	596 (7%)	181 (2.9%)
% ILLINOIS POPULATION	60.9%	13.8%	17.3%
% OF DEATHS	39.7%	38.1%	11.6%

Wearing masks in a community setting

- WHO (4/4/20)
  - “Wide use of masks by healthy people in the community setting is not supported by current evidence…”
    - https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak

- Annals of Internal Medicine (4/6/20)
  - “In conclusion, both surgical and cotton masks seem to be ineffective in preventing the dissemination of SARS–CoV-2 from the coughs of patients with COVID-19 to the environment and external mask surface.”
    - https://annals.org/aim/fullarticle/2764367/effectiveness-surgical-cotton-masks-blocking-sars-cov-2-controlled-comparison

Social distancing

- Slipstream effect - NYT article 4/17/20
  - "A droplet that is small enough to float in air for a while also is unlikely to deposit on clothing because of aerodynamics. The best way to describe it is that they follow the streamlines, or air flow, around a person, because we move relatively slowly. It's kind of like small insects and dust particles flowing in the streamlines around a car at slow speed but potentially slamming into the windshield if the car is going fast enough,"
  - "As we move, we push air out of the way, and most of the droplets and particles get pushed out of the way, too. Someone would have to spray large droplets through talking — a spit talker — coughing or sneezing for them to land on our clothes. The droplets have to be large enough that they don't follow the streamlines."
    - Dr. Linsey Marr, Aerosol Scientist at Va. Tech

- Virus on packages, hair, clothes, etc.
  - "When you go through the string of events that must occur, such an extended number of things have to happen just right. That makes it a very low risk."
    - Dr. Andrew Janowski, Pediatrician at Washington University Hospitals St. Louis Children's Hospital
    - https://www.nytimes.com/2020/04/17/well/live/coronavirus-contagion-spead-clothes-shoes-hair-newspaper-packages-mail-infectious.html?algo=top_conversion&fellback=false&imp_id=558018451&imp_id=857904272&action=click&module=Most%20Popular&pgtype=Homepage

The current SARS-CoV-2 pandemic

- The way forward…
- Sero-surveillance
  - Testing for antibody acute (IgM) and convalescent (IgG)
- Trace backs (active case finding and contact tracing)
- Vaccine – 2021?
- Therapeutics – so we can say that if you take xyz, you'll recover; take load off of ICUs, ventilators, etc.
- Potentiate your immune system!
  - Eat, sleep, exercise well!
  - Extracellular superoxide dismutase (EcSOD)
    - https://eurekalert.org/pub_releases/2020-04/uovh-cem041520.php

TITANTALKS

AN ILLINOIS WESLEYAN UNIVERSITY WEBINAR SERIES

Thank you for joining today's webinar!

Save the date for our next webinar:

May 6 | 12 – 1 p.m. CDT

Speaker: President Georgia Nugent

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