# Emerging infectious diseases in history

*(Morens & Fauci, Cell, 2020)*

<table>
<thead>
<tr>
<th>Year</th>
<th>Name</th>
<th>Deaths</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>430 BCE</td>
<td>“Plague of Athens”</td>
<td>~100,000</td>
<td>First identified trans-regional pandemic</td>
</tr>
<tr>
<td>541</td>
<td>Justinian plague (<em>Yersinia pestis</em>)</td>
<td>30-50 million</td>
<td>Pandemic; killed half of world population</td>
</tr>
<tr>
<td>1340s</td>
<td>“Black Death” (<em>Yersinia pestis</em>)</td>
<td>~50 million</td>
<td>Pandemic; killed at least a quarter of world population</td>
</tr>
<tr>
<td>1494</td>
<td>Syphilis (<em>Treponema pallidum</em>)</td>
<td>&gt;50,000</td>
<td>Pandemic brought to Europe from the Americas</td>
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<tr>
<td>c. 1500</td>
<td>Tuberculosis</td>
<td>High millions</td>
<td>Ancient disease; became pandemic in Middle Ages</td>
</tr>
<tr>
<td>1520</td>
<td><em>Hueyzahuati</em> (<em>Variola major</em>)</td>
<td>3.5 million</td>
<td>Pandemic brought to New World by Europeans</td>
</tr>
<tr>
<td>1793–1798</td>
<td>“The American plague”</td>
<td>~25,000</td>
<td>Yellow fever terrorized colonial America</td>
</tr>
<tr>
<td>1832</td>
<td>2nd cholera pandemic (Paris)</td>
<td>18,402</td>
<td>Spread from India to Europe/Western Hemisphere</td>
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<tr>
<td>1918</td>
<td>“Spanish” influenza</td>
<td>~50 million</td>
<td>Led to additional pandemics in 1957, 1968, 2009</td>
</tr>
<tr>
<td>1981</td>
<td>Acute hemorrhagic conjunctivitis</td>
<td>rare deaths</td>
<td>First recognized in 1969; pandemic in 1981</td>
</tr>
<tr>
<td>1981</td>
<td>HIV/AIDS</td>
<td>~37 million</td>
<td>First recognized 1981; ongoing pandemic</td>
</tr>
<tr>
<td>2002</td>
<td>SARS</td>
<td>813</td>
<td>Near-pandemic</td>
</tr>
<tr>
<td>2009</td>
<td>H1N1 “swine flu”</td>
<td>284,000</td>
<td>5th influenza pandemic of century</td>
</tr>
<tr>
<td>2014</td>
<td>Chikungunya</td>
<td>uncommon</td>
<td>Pandemic, mosquito-borne</td>
</tr>
<tr>
<td>2015</td>
<td>Zika</td>
<td>~1,000*</td>
<td>Pandemic, mosquito-borne</td>
</tr>
</tbody>
</table>

Selected important emerging and re-emerging infectious diseases of the past and present, 430 BCE–2020 CE. Mortality estimates are in most cases imprecise; see text.

*Zika mortality has not been fully established. Most deaths are fetal or related to outcomes of severe congenital infections.*
Ebola & Marburg Virus Outbreaks in Africa

Poverty
• Hu et al (2017) identified 11 new strains of SARS virus in multiple species of horseshoe bats in a single cave in Yunnan Province, China.

• Newly identified bat strains, as well as several strains identified in a previous study of the same bat cave, contained all the essential genetic building blocks of the human SARS coronavirus.

• They hypothesized that genetic recombination between precursor strains that later evolved into the newly identified strains may also have given rise to a strain that directly evolved into SARS coronavirus.

• Continued monitoring of the cave they studied, as well as other sites.

Chinese horseshoe bat (Zhang, PLOS, EurekAlert, 2017)
Transmission of infection and amplification in people (bright red) occurs after a pathogen from wild animals (pink) moves into livestock to cause an outbreak (light green) that amplifies the capacity for pathogen transmission to people. 

(World Bank, One Health Operational Framework, 2018)
As of 20 October:
- **40,652,097** confirmed cases
- **1,222,036** confirmed deaths

*Johns Hopkins, 2020*
COVID-19 resurgence in Europe

As of 20 October (ECDC):
• **5,039,783** confirmed cases in the EU/EEA and the UK
• **202,062** deaths in the EU/EEA and the UK
Long COVID-19
(Couzin-Frankel, Science, 2020)

**Pain that lingers**
A subset of COVID-19 patients experiences ongoing symptoms and complications such as organ damage, and researchers are proposing reasons for some of them (bottom). Scientists are trying to identify such symptoms, how common they are, how long they last, who’s at risk, and how to treat and prevent them.

**1 Brain fog**
Difficulty thinking can occur after acute COVID-19 infection. The virus may damage brain cells, and inflammation in the brain or body may also cause neurologic complications. Other viral infections can also lead to brain fog.

**2 Shortness of breath**
Doctors are seeing lung and heart complications including scarring. Patients who become critically ill with COVID-19 seem more likely to have lingering shortness of breath, but those with mild cases are also at risk.

**3 Heart arrhythmia**
The virus can harm the heart, and doctors are concerned about long-term damage. How the heart heals after COVID-19 could help determine whether a patient develops an irregular heartbeat.

**4 Hypertension**
Some patients have high blood pressure after an acute infection, even when cases were relatively mild and people were previously healthy, possibly because the virus targets blood vessels and heart cells.
• Huge impacts on health outcomes beyond COVID
• Nearly 100 million more people at risk of extreme poverty in 2020
• Growing food insecurity worldwide
• More than a billion children are or have been out of school
• Mental health crisis
• Increased risk of violence and threatened social cohesion
• Deepens social inequalities
Herd immunity?

- Only a proportion of a population needs to be immune to stop an epidemic
- \( R = (1-pC)(1-pI)R_0 \) with herd immunity: \( R < 1 \)
  - SARS-Cov-2 \( R_0 \) is 2.5 – 4
- Herd immunity threshold around 67\%, and probably at least 50\% of population must be immune (for how long? Several rounds of re-infection? Duration of immunity? ...)
- In influenza herd immunity after 2 or 3 waves
- Mortality can be enormous at 0.3-1.3\% infection fatality rate = >15 million deaths for 7.8 billion population
The future?

René Magritte, *La Clairvoyance*
Future course of the pandemic?

(Scudellari, Nature, 2020)
Factors influencing postpandemic transmission of SARS-CoV-2

Rates of repeat infection, factors modulating seasonality, competition with other circulating respiratory viruses, and control measures will influence the endemic pattern of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission.

**Immunity**
- Adaptive immune response following infection
- Severity of infection
- Waning of immunity
- Immune escape

**Interventions**
- Vaccination (timing, efficacy, coverage)
- Drug treatments
- Nonpharmaceutical interventions (personal protective equipment, social distancing, travel restrictions, hygiene measures)

**Seasonality**
- Impact of environmental conditions on transmissibility
- Seasonal changes in host behavior, school calendar, and indoor/outdoor gatherings
- Seasonal changes in immune function

**Virus interactions**
- Transmissibility of each virus
- Order of exposure
- Degree of cross protection

**Endemic pattern**

(Shaman & Galanti, Science, 2020)
COVID-19 vaccine candidates in Phase III
(LSHTM Vaccine Centre, 18 October, 2020)

1. BioNTech/Fosun Pharma/Pfizer
2. Moderna/NIAID
3. CanSino Biological Inc/Beijing Institute of Biotechnology
4. Gamaleya Research Institute
5. Janssen Pharmaceutical Companies
6. University of Oxford/AstraZeneca
7. Beijing Institute of Biological Products/Sinopharm
8. Sinovac/Instituto Butantan
9. Novavax
10. Wuhan Institute of Biological Products/Sinopharm

Phase III:
Testing of vaccine in a large number of healthy volunteers (1,000-10,000+)

Primary questions: Is the vaccine effective at preventing disease? Is the vaccine safe in a larger, more varied population?
How long does it take to make a vaccine?
Solid progress against Ebola in recent years

- **Merck’s Ebola vaccine** - rVSV-ZEBOV (ERVEBO)- **licensed** by EC (11.2019) and FDA (12.2019)
  - **2002**: Vaccine developed at the Public Health Agency of Canada’s National Microbiology Laboratory; research began years earlier
- **Janssen’s Ebola vaccine regimen** - Zabdeno (Ad26.ZEBOV) and Mvabea (MVA-BN-Filo) - **approved** by EC (7.2020)
  - **2002**: Crucell (Janssen) begins Ebola vaccine research program with NIH support
- **Two treatments that significantly increase the chance of survival** - REGN-EB3 & mAb114
COVID-19 vaccine initiatives

Coalition for Epidemic Preparedness Innovation

COVAX: Ensuring global equitable access to COVID-19 vaccines

Operation Warp Speed

African Union Commission launches Consortium for COVID-19 Vaccine Clinical Trial
Challenges ahead for a safe and effective COVID-19 vaccine:

1. Will it work? For how long?
2. Will it be safe?
3. Will there be enough?
4. Who gets it first?
5. Will people accept it?
6. Close cost-marketing monitoring

Source: Figueiredo et al, 2020
Standard measures not predictive
(Crosby et al, Think Global Health, 2020)
• Build a stronger European Health Union:
  • Strengthen crisis preparedness and management of cross-border health threats (reinforce ECDC and EMA)
  • Build a European BARDA
  • Discuss question of health competences
  • Learn global lessons – President von der Leyen, Prime Minister Conte and the G20 to convene a Global Health Summit in 2021 in Italy
• Vaccine development and access (ACT-A & Covax)
Lessons from past epidemics

1. **The sooner you act**, the higher your chance of impact.
2. **Political leadership at the highest levels.**
3. Use **all of tools that science offers** to inform decisions, **promptly adopt innovation**, and massively invest in R&D.
4. **No magic bullets**: use a **combination** of prevention measures, even if when we have a vaccine
5. Invest in public health **systems** and societal preparedness
6. **Build coalitions and involve communities for a whole of society approach!**
Societies living with COVID-19

• Series of outbreaks & new pandemics
• Change in cultural and behavioural norms
• Strong public health institutions
• Safe spaces for vulnerable communities
• Long-term care for survivors
• Research and innovation
• Mitigate acute and long-term health, social and economic costs
• Change how we live, work, travel, interact with nature

No country is safe, unless every country is safe

(National University of Singapore, 2020)
Congratulations Quarraisha and Slim!!!!