

and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of Reconciliation and collaboration.

Epidemiology and mathematical epidemiology

MATH 8xyz – Lecture 02

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Outline



History of epidemics & Historical epidemics

Epidemiology

Mathematical Epidemiology

Among the first events recorded

- ▶ Epidemic events are among the first events recorded in History
- ▶ Indeed their effect was devastating at a time when medicine virtually did not exist and thus easily observed

First known epidemics (from Wikipedia) I

| Event | Date | Location | Disease | Death toll |
|-------------------|-------------------------|--------------------------------|---------------------------------------|------------|
| Plague of Megiddo | 1350 BCE | Megiddo, land of Canaan | Unknown | Unknown |
| Plague of Athens | 429-426 BCE | Greece, Libya, Egypt, Ethiopia | Possibly typhus, typhoid fever or VHF | 75–100K |
| 412 BCE epidemic | 412 BCE | Greece, Roman Republic | Possibly influenza | Unknown |
| Antonine Plague | (possibly up to 190 CE) | Roman Empire | Possibly smallpox | 5–10M |
| Jian'an Plague | 217 CE | Han dynasty | Possibly typhoid fever or VHF | Unknown |
| Plague of Cyprian | 250-266 CE | Europe | Possibly smallpox | Unknown |

First known epidemics (from Wikipedia) II

| | | | | |
|---|------------|-------------------------------------|----------------|---------------------------------------|
| Plague of Justinian (1st plague pandemic) | 541-549 CE | Europe and West Asia | Bubonic plague | 15-100M (25% of population of Europe) |
| Roman Plague of 590 (1st plague pandemic) | 590 CE | Rome, Byzantine Empire | Bubonic plague | Unknown |
| Plague of Sheroe (1st plague pandemic) | 627-628 CE | Bilad al-Sham | Bubonic plague | 25K+ |
| Plague of Amwas (1st plague pandemic) | 638-639 CE | Byzantine Empire, West Asia, Africa | Bubonic plague | 25,000+ |
| Plague of 664 (1st plague pandemic) | 664-689 CE | British Isles | Bubonic plague | Unknown |

First known epidemics (from Wikipedia) III

| | | | | | |
|---|------------|-------------------------------------|---|----------------|--|
| Plague of 698-701 (1st plague pandemic) | 698-701 CE | Byzantine Empire, Asia, Mesopotamia | Em- pire, West Syria, Mesopotamia | Bubonic plague | Unknown |
| 735-737 Japanese smallpox epidemic | 735-737 CE | Japan | | Smallpox | 2M (approx. 1/ of Japanese population) |
| Plague of 746-747 (1st plague pandemic) | 746-747 CE | Byzantine Empire, Africa | Em- pire, West Asia, Africa | Bubonic plague | Unknown |

Epidemics with major human cost I

| Rank | Epidemic/Pandemic | Disease | Human cost | Global mortality | Regional mortality |
|------|---------------------|------------------|------------------|--|-------------------------------|
| 1 | Black Death | Bubonic plague | 75-200 M | 17-54% | 30-60% of European population |
| 2 | Spanish flu | Influenza A/H1N1 | 17-100 M | 1-5.4% | |
| 3 | Plague of Justinian | Bubonic plague | 15-100 M | 7-56% | 25-60% of European population |
| 4 | HIV/AIDS | HIV/AIDS | 36.3 M (in 2020) | Total population change too large to calculate | |

Epidemics with major human cost II

| | | | | | |
|----|-----------------------------------|---------------------|-------------------------------|-----------|-----------------------|
| 5 | COVID-19 | SARS-CoV-2 | 6.3-25 M (as of May 21, 2022) | 0.1-0.3% | |
| 6 | Third plague pandemic | Bubonic plague | 12-15 M | | |
| 7 | 1545-1548 Cocoliztli epidemic | Cocoliztli | 5-15 M | 1-3% | 27-80% of can populat |
| 8 | Antonine Plague | Smallpox or measles | 5-10 M | 3-6 | 25-33% of population |
| 9 | 1520 Mexican smallpox epidemic | Smallpox | 5-8 M | 1-2% | 23-37% of can populat |
| 10 | 1918-1922 Russian typhus epidemic | Typhus | 2-3 M | 0.1-0.16% | 1-1.6% of population |
| 11 | 1957-1958 influenza pandemic | Influenza A/H2N2 | 1-4 M | 0.03-0.1% | |

Epidemics with major human cost III

| | | | | | |
|----|------------------------------------|----------------------|---------|-----------|----------------------|
| 12 | Hong Kong flu | Influenza A/H3N2 | 1-4 M | 0.03-0.1% | |
| 13 | 1576 Cocoliztli epidemic | Cocoliztli | 2-2.5 M | 0.4-0.5% | 50% of M population |
| 14 | 735-737 Japanese smallpox epidemic | Smallpox | 2 M | 1% | 33% of Ja population |
| 15 | 1772-1773 Persian plague | Bubonic plague | 2 M | 0.2–0.3% | |
| 16 | Plague of Naples (1656) | Bubonic plague | 1.25 M | 0.2% | |
| 17 | 1846-1860 cholera pandemic | Cholera | 1+ M | 0.08% | |
| 18 | 1629-1631 Italian plague | Bubonic plague | 1 M | 0.2% | |
| 19 | 1889-1890 flu pandemic | Influenza (disputed) | 1 M | 0.07% | |

“Forgotten” killers

- ▶ Tuberculosis (TB). In 2020, estimated 10 M cases of active TB, leading to 1.5 M deaths
- ▶ Malaria: 229 M cases and 409 000 deaths in 2019

Neglected tropical diseases (NTD)

Often endemic diseases, sometimes major causes of death, but out of sight of rich countries. From Wikipedia, noting that the precise list varies according to authors:

| | | |
|----------------------|---------------------------|---------------------------------|
| Buruli ulcer | Chagas disease | Dengue & Chikungunya |
| Dracunculiasis | Echinococcosis | Yaws |
| Fascioliasis | African trypanosomiasis | Leishmaniasis |
| Leprosy | Lymphatic filariasis | Onchocerciasis |
| Rabies | Schistosomiasis | Soil-transmitted helminthiasis |
| Cysticercosis | Trachoma | Scabies and other ectoparasites |
| Snakebite envenoming | Mycetoma and deep mycoses | |

The Black Death

The British Plague of 1547

The Plague of Marseille of 1720

Definition

Wiki **Epidemiology** is the study and analysis of the distribution (who, when, and where), patterns and determinants of health and disease conditions in defined populations

BMJ **Epidemiology** is the study of how often diseases occur in different groups of people and why. Epidemiological information is used to plan and evaluate strategies to prevent illness and as a guide to the management of patients in whom disease has already developed

Etymology: *the study of what is upon the people*, derived from the Greek *epi* (upon, among), *demos* (people, district) and *logos* (study, word, discourse)

Who, when and where

Recall part of the definition on Wikipedia

Epidemiology is the study and analysis of the distribution (who, when, and where)

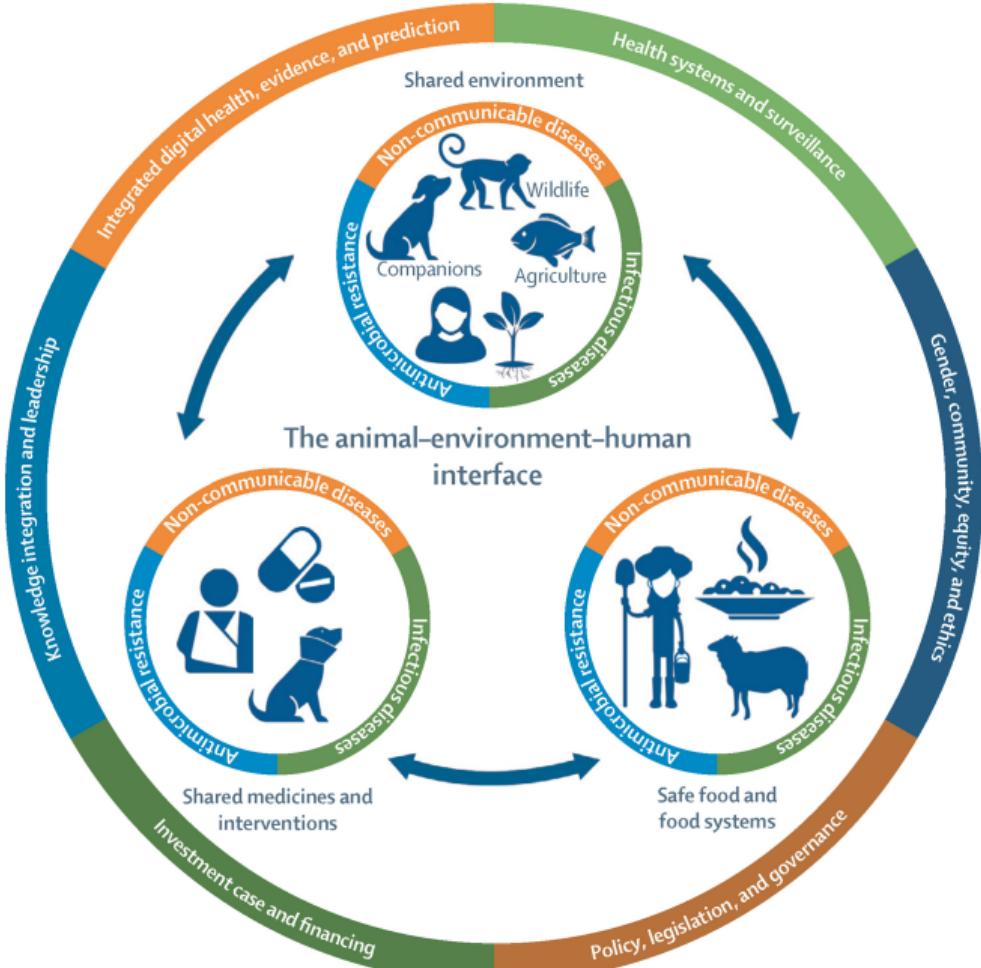
A terminologically heavy domain

A few pointers:

- Moghadas and Laskowski. Review of terms used in modelling influenza infection.
NCCID 2014
- Milwid et al. Toward standardizing a lexicon of infectious disease modeling terms.
Frontiers in Public Health 2016

Who

- **Epidemiology** typically used when dealing with humans, but sometimes also generically when an easy description is sought; e.g., plant disease epidemiology
- **Epizootic**: denoting or relating to a disease that is temporarily prevalent and widespread in an animal population
- **Panzootic** is like a pandemic for animals
- **One Health**: considers health of humans, animals and their environment (including plants)



Incidence & Prevalence (when?)

Incidence: number of new cases in a population generated within a certain time period

Prevalence: number of cases of a disease at a single time point in a population

⇒ $I(t)$ in an epidemiological model is **prevalence**, not **incidence**

Exposition versus Exposed

- Some bright bulb (not sure who) in days of yore: let's call **exposed** someone who has contracted the disease but is not yet showing symptoms (\Rightarrow SEIR model)
- "Real" epidemiologist: let's trace people who were exposed to the virus, i.e., people having come into contact with the virus (whether they have contracted the disease or not)
- Interestingly, I have embarked on a quixotic quest to make people use *L* instead of *E*, only to be told by real epidemiologists that they don't care :)

Les différentes phases de la propagation

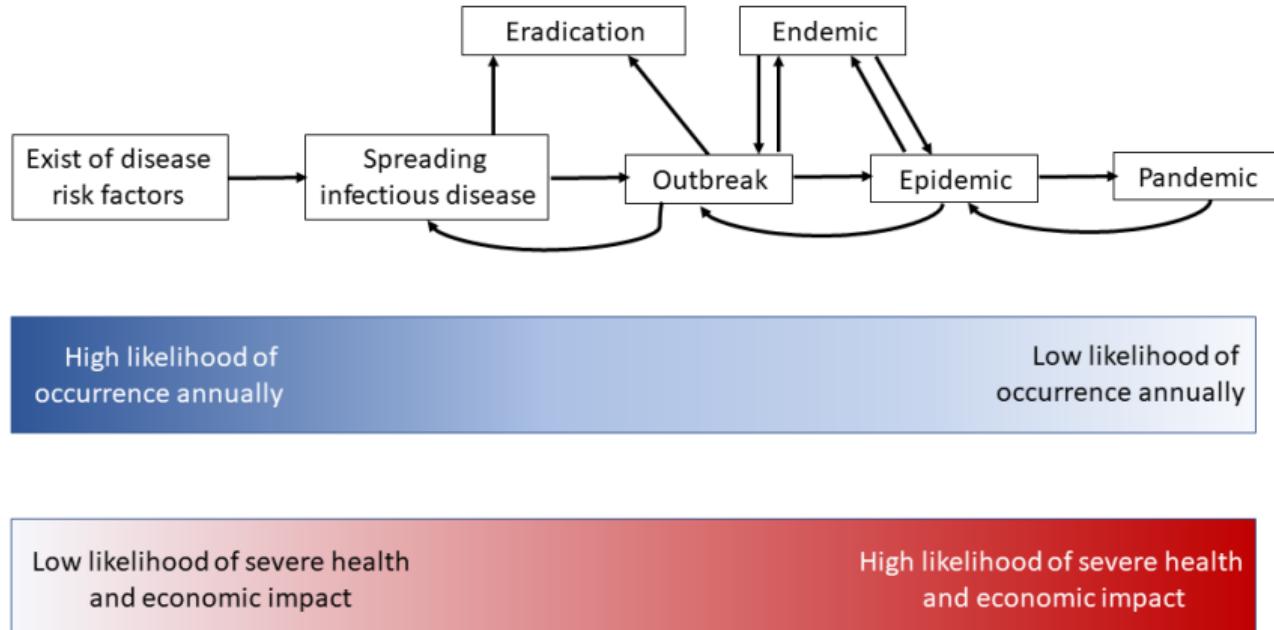
- Spreading infectious disease: sporadic isolated cases
- **Outbreak**: the number of cases rises rapidly locally
- **Epidemic**: rapid rise and spread of an infectious disease in a given region
- **Endemic**: persistence habituelle d'une maladie infectieuse et contagieuse dans une région donnée
- **Pandemic**: épidémie qui s'étend au-delà des frontières des pays et qui peut se répandre sur un continent, un hémisphère ou dans le monde entier

Outbreak
sudden increase in occurrences of a disease in a particular time and place.

Endemic
constant maintained increase in occurrences of a disease in a geographic area.

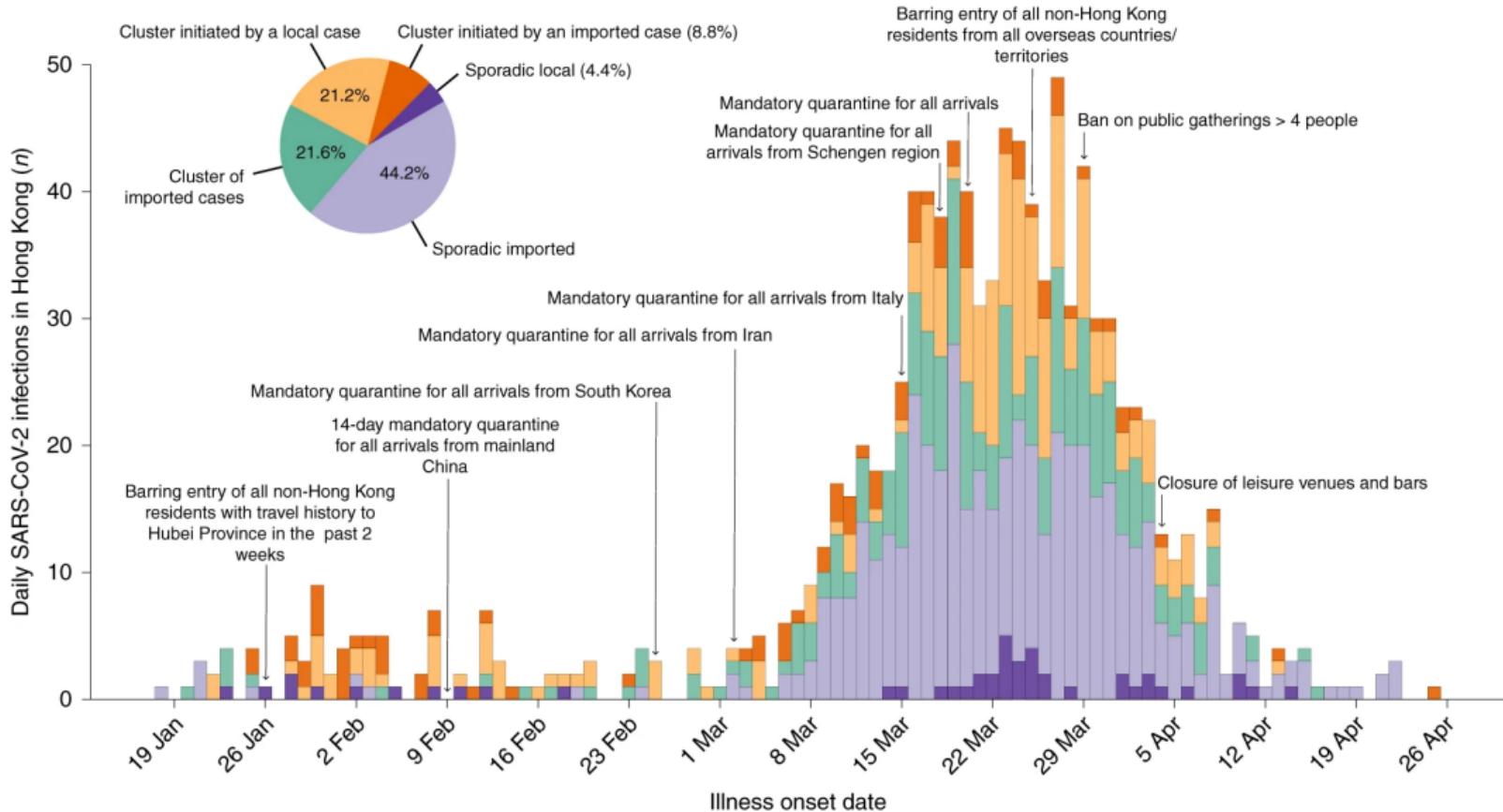
Epidemic
rapid spread of disease to a large number of people in a given population within a short period of time.

Pandemic
spread across a large region, for instance multiple continents, or worldwide.



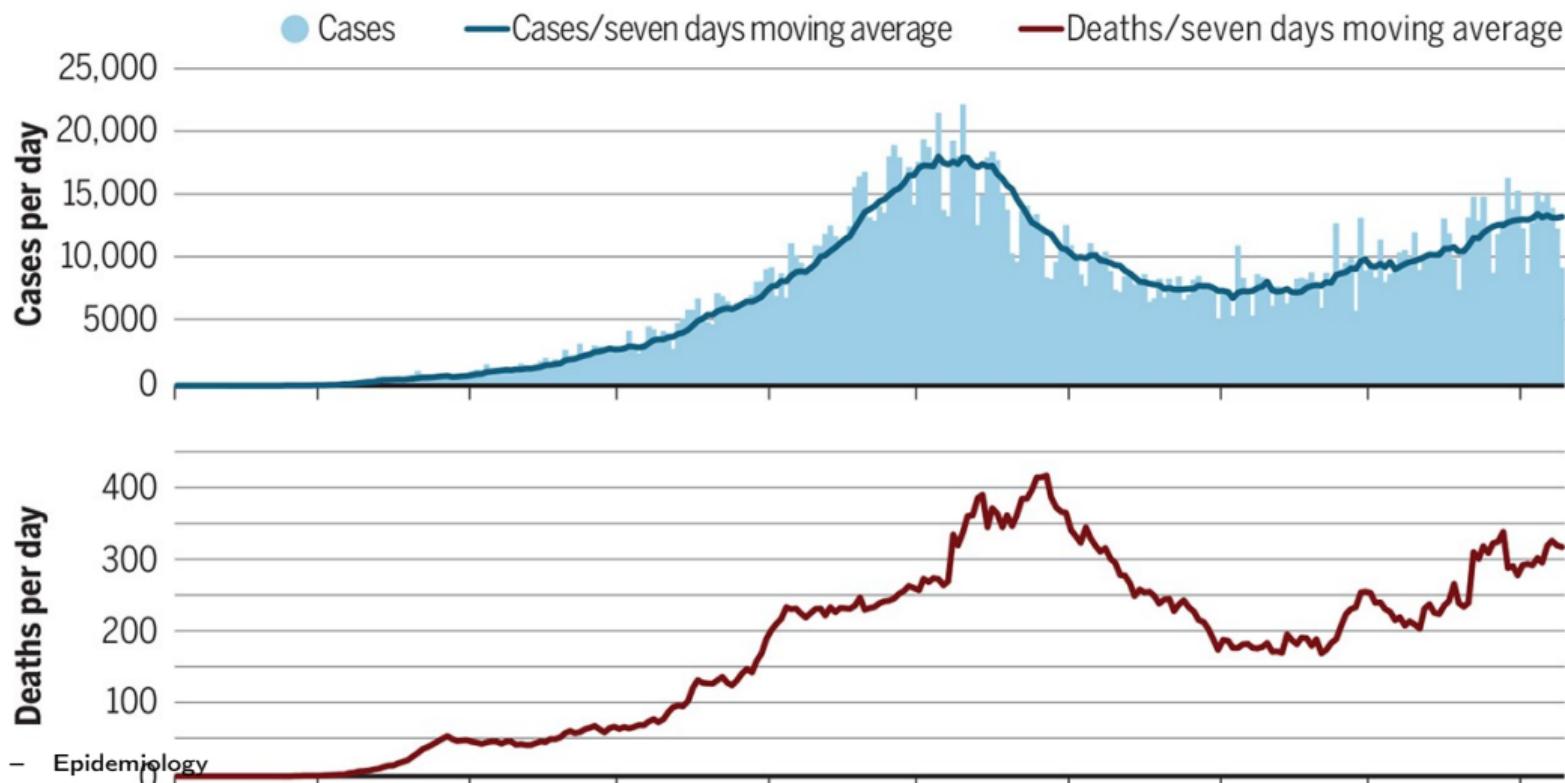
Epidemic curves

- Used to record the occurrence of new cases as a function of time
- When not too many cases, usually "individualised" (bar plots)
- When number of cases is large, continuous curve



COVID-19 cases and deaths in Africa

The trend of daily reported cases of COVID-19 for the African continent, February to November 2020, shows the first peak of cases occurred July to August (mostly attributed to the Southern African Region) followed by a second peak, which started in October (mostly attributed to the Northern Region).



Some terminology for “where”

- **Epidemic**: diseases that are *visited upon* a population
- **Pandemic**: (will revisit this later in the course) epidemic that has spread across a large region, e.g., multiple continents or worldwide
- **Endemic**: diseases that *reside within* a population
- We don't say "panendemic"

Where? 1854 cholera outbreak



Cholera outbreak near Broad Street,
London (UK)
Studied by John Snow

*I found that nearly all the
deaths had taken place within
a short distance of the [Broad
Street] pump*

WHO pandemic (influenza) phases

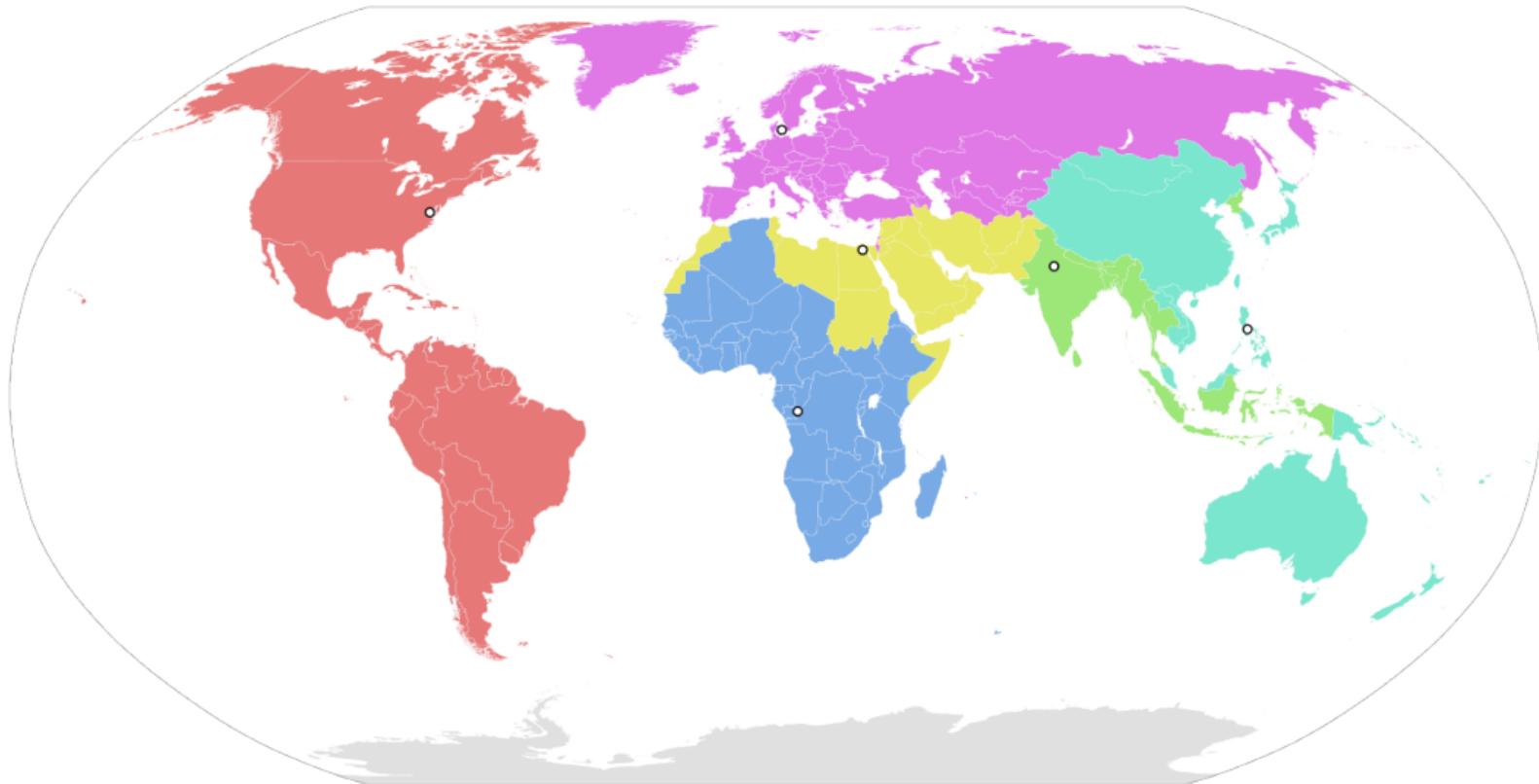
| Period | Phase | Description |
|---------------|-------|---|
| Interpandemic | 1 | No animal influenza virus circulating among animals has been reported to cause infection in humans |
| | 2 | Animal influenza virus circulating in domesticated or wild animals known to have caused infection in humans and therefore considered a specific potential pandemic threat |

WHO pandemic (influenza) phases

| Period | Phase | Description |
|----------------|-------|---|
| Pandemic alert | 3 | Animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in H2H transmission sufficient to sustain community-level outbreaks |
| | 4 | Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified |

WHO pandemic (influenza) phases

| Period | Phase | Description |
|----------------|-------|---|
| Pandemic alert | 5 | Same identified virus has caused sustained community-level outbreaks in at least 2 countries in 1 WHO region |
| Pandemic | 6 | In addition to criteria in Phase 5, same virus has caused sustained community-level outbreaks in at least 1 other country in another WHO region |



Fighting against infections

*Epidemiological information is used to plan and evaluate **strategies to prevent illness** and as a guide to the **management of patients** in whom disease has already developed*

- Preventing illness
 - ▶ Prophylactic measures
 - ▶ Vaccination
- Managing illness
 - ▶ Prevention of further spread (e.g., in hospital)
 - ▶ Treatment

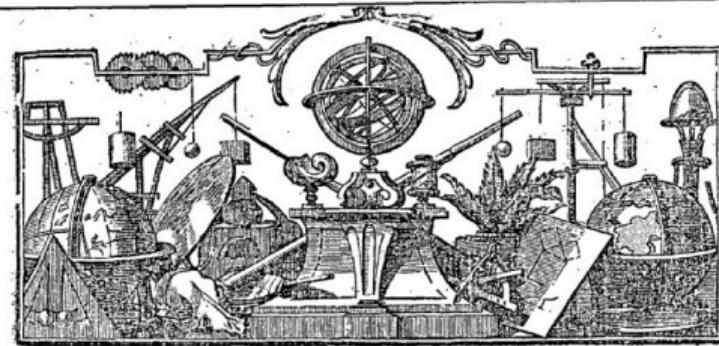
Immunisation

- Smallpox first disease for which it was known
- Mentioned in a 1549 Chinese book
- China: powdered smallpox scabs blown up noses of the healthy; variolation-induced mortality not negligible (0.5-2%) but lower than normal (20%)
- 1798: Edward Jenner introduces safer inoculation with cowpox (vaccination)
- 1880s: Pasteur extends vaccination to chicken cholera and anthrax in animals and human rabies

At the time, *herd immunity* was not understood so this was for personal protection

Domain is quite old ..

.. but has only become a thing in recent years!



MÉMOIRES
DE
MATHÉMATIQUE
ET
DE PHYSIQUE,
TIRÉS DES REGISTRES
de l'Académie Royale des Sciences;
De l'Année M. DCCLX.

ESSAI D'UNE NOUVELLE ANALYSE
*De la mortalité causée par la petite Vérole, & des
avantages de l'Inoculation pour la prévenir.*

Par M. DANIEL BERNOULLI.

INTRODUCTION PHILOGÉTIQUE*

- ▶ BNF scan or pdf
- ▶ Probably the first epidemic model
- ▶ About petite vérole (smallpox) inoculation

Ross (early 1900)



- ▶ On 20 August 1897, observed malaria parasites in the gut of a mosquito fed several days earlier on a malaria positive human
- ▶ Nobel Prize for Medicine 1902
- ▶ Started considering malaria eradication using mathematical models; for some history, read this 2012 paper

Kermack and McKendrick (1927+)

- ▶ We spend a lot more time on this in Lecture 05
- ▶ Groundbreaking set of papers starting in 1927
- ▶ We will see one particular case, the most well known, but I point out here and point out in Lecture 05 that this is just the tip of the iceberg of their work

Macdonald, Dietz and malaria

- ▶ Read for instance this paper, which presents a history of the development of the so-called Ross-Macdonald model
- ▶ Klaus Dietz also worked a lot on malaria

Some activity later, but not much until 1990s

- ▶ In recent years, explosion
- ▶ Since the beginning of COVID-19: just nuts..

Reading recommendations

- ▶ Waltman. Deterministic threshold models in the theory of epidemics (1974)
- ▶ Capasso. Mathematical structures of epidemic systems (1993)
- ▶ Daley & Gani. Epidemic modelling: An introduction (1999)
- ▶ Hethcote. The mathematics of infectious diseases. SIAM Review (2000)
- ▶ Brauer, PvdD & Wu. Mathematical Epidemiology (2008)
- ▶ Brauer & C³. Mathematical Models in Population Biology and Epidemiology (2012)
- ▶ Brauer, C³ & Feng. Mathematical Models in Epidemiology (2019)

Some landmarks in mathematical epidemiology (IMBO)

- ▶ Macdonald. The epidemiology and control of malaria. 1957
- ▶ Baroyan, Rvachev et al. Deterministic epidemic models for a territory with a transport network. Kibernetika, 1967
- ▶ Hethcote & Yorke. Gonorrhea Transmission Dynamics and Control. LNB M 56, 1984
- ▶ Anderson & May. Infectious diseases of humans: dynamics and control. 1991
- ▶ Capasso. Mathematical Structures of Epidemic Systems. LNB M 97, 1993
- ▶ Hethcote. The mathematics of infectious diseases. SIAM Review, 2000
- ▶ van den Driessche & Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. MBS, 2002

A more recent trend

- Some rare numerical work \leq 1980s, mostly simulation of math models
 - ▶ Baroyan, Rvachev et al. Computer modelling of influenza epidemics for the whole country (USSR). *Advances in Applied Probability* (1971)
 - ▶ Rvachev & Longini. A mathematical model for the global spread of influenza. *Mathematical Biosciences* (1986)
 - ▶ Flahault, Letrait et al. Modelling the 1985 influenza epidemic in France. *Statistics in Medicine* (1988)
- More and more frequent now, to the point that some modelling studies are purely simulation-based

Agent-based models (ABM)

- ▶ Early in the life of these models, they were called IBM (individual-based models)
- ▶ Over the years, a "philosophical" distinction has emerged:
 - ▶ IBM are mathematical models that consider individuals as the units; e.g., DTMC, CTMC, branching processes, etc.
 - ▶ ABM are computational models whose study is, for the most part, only possible numerically

Network models

- ▶ Network models endow vertices with simple systems and couple them through graphs
- ▶ Can be ABM, but some networks can also be studied analytically

Has happened all along, undergoing a transformation

- ▶ Epidemiology has long relied on data
- ▶ Many developments in statistics originate there
- ▶ Data has traditionally been better for chronic diseases than for infectious ones
- ▶ Near-real-time surveillance of infectious diseases ongoing since the 1980s (e.g., Réseau Sentinelles)
- ▶ SARS-CoV-1 saw the beginning of a move towards real-time emerging infectious disease data
- ▶ With SARS-CoV-2, the system has really progressed a lot, both in terms of "citizen science" and governmental initiatives