NATIONAL INSTITUTE FOR HEALTH AND WELFARE

A brief history of pandemics

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The Finnish Society for Natural Philosophy

6-Sep-2022

What is a pandemic

- A pandemic is an epidemic occurring on a scale that crosses international boundaries, usually affecting people on a worldwide scale
- Caused by a new disease/microbe (or variant) effectively transmitted between humans
- A disease or condition is not a pandemic merely because it is widespread or kills many people; **it must also be infectious**

- (WHO proclaims the presence of a pandemic?)

Historical ’snapshots’

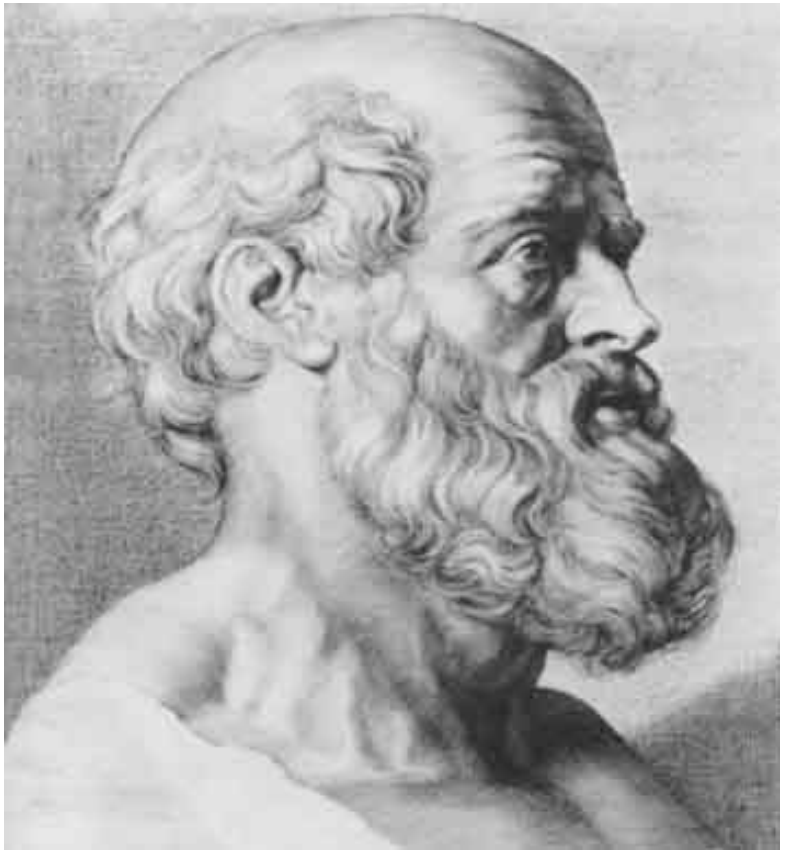
- Smallpox
- Plague
- Cholera
- Influenza
- SARS (2003, ’almost pandemic’)
- Covid-19

- (Others that would qualify: syphilis, tuberculosis, HIV)

Knowledge on disease concepts and control

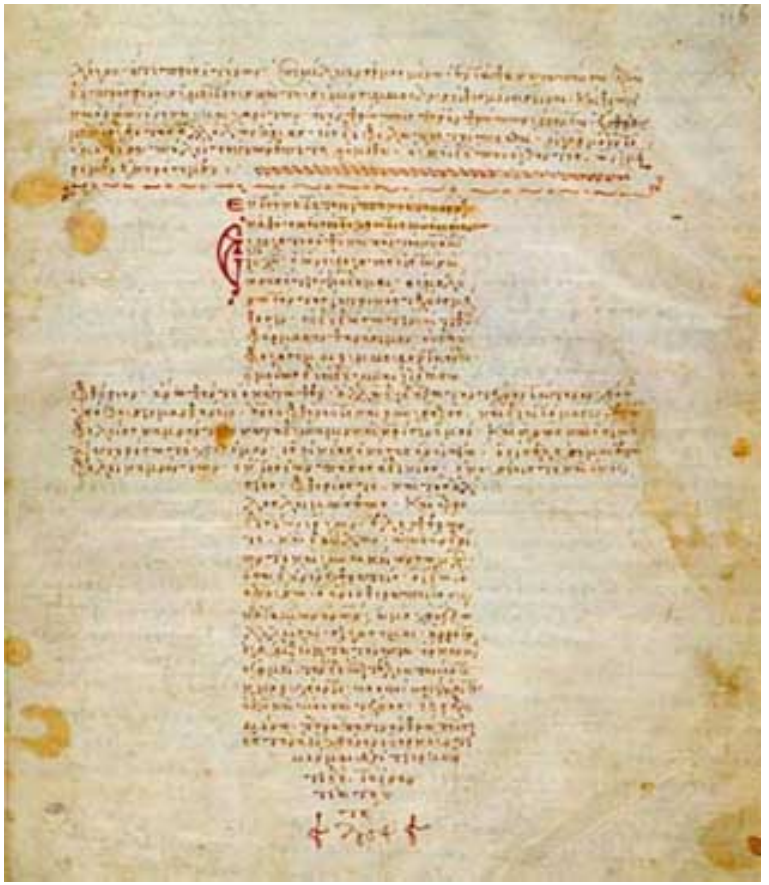
- The Old Testament
  - The Book of Leviticus (Third book of Moses) in Old Testament reaching its present form between 536 – 332 BC
    - three chapters on preventing the spread of ’leprosy’
    - **isolate** ’unclean’ sufferers, cleanse their clothes and belongings
    - **impose a period of separation followed by inspection** to determine their ’clean’ or ’unclean’ state
- Hippocrates (c460 – c370 BC)
- Galen (129 - c216 AD)
- ’Scientific’ and religious healing existed side by side
- Cure had to be ultimately credited to God

Hippocrates, c 450 – 370 BC



Hippocrates

http://www.praxisbenner.de/1/natverfahren.html



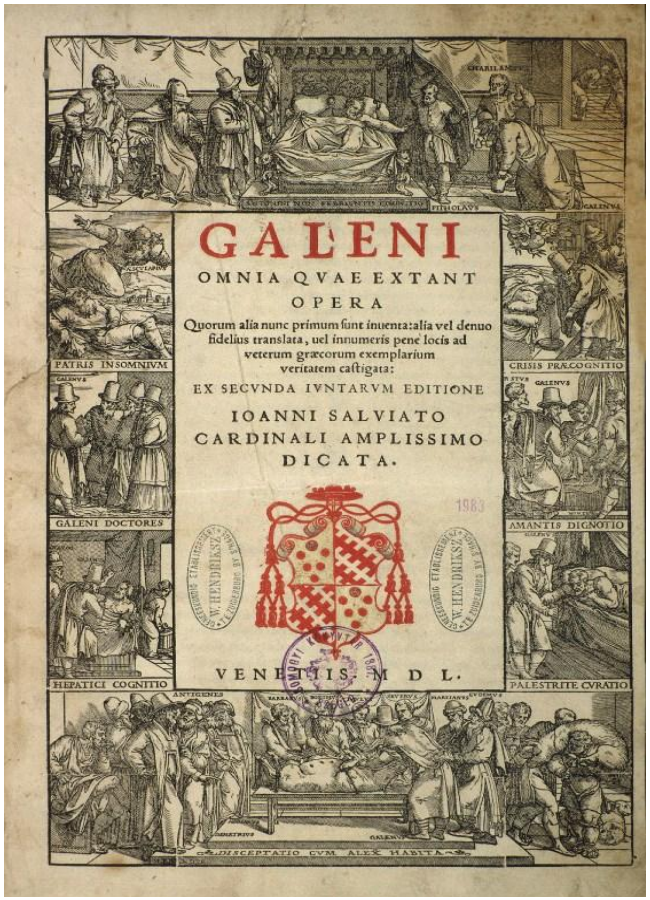
Oath of Hippocrates, 12. Century, Byzantine manuscript

http://homepage.univie.ac.at/michael.peintinger/main.html

Hippocrates' concepts of disease

- Epidemics (three books)
  - On the Nature of Man
  - On Airs, Waters, Places
- Influence of external and environmental factors
  - climate, prevailing winds, marshes, water supply and soil, geographic location, sick persons, habits and life-styles
  - humoral theory: 'bad air' **(miasma)** has a role in disease causation
  - 'exhalations that come from the ground through ruptures or clefts'
  - 'considering these, physician would know what epidemics to expect, and what particular disadvantages threatened an individual who changed his mode of life'
  - **epidemics 'not punishment for sins', naturalistic causes**
- **Theoretician looking for causes**

Galen, 129 – c200/210



Galen: http://home.tiscalinet.ch/biografien/biografien/galen.htm
Omnia Qvae Extant Opera: http://www.sk-szeged.hu/tortenet/galen.htm

Galen's concepts of disease

- An **'epidemic constitution of the surrounding air'** the most important initiating factor for epidemics
- The presence of **'miasmas' ('polluting agent')** due to
  - filth
  - putrefaction
  - swampy conditions
  - seasons
- Astronomical phenomena; solstices, equinoxes, positions of stars
- 'Seeds of disease' carried by the air
- **Practical clinician, practical advice**
- Concepts not seriously challenged scientifically prior to the 15th-17th centuries

History of smallpox – the only eradicated disease

- Caused by variola virus
- Evidence of disease from Egyptian mummies of 3rd century BC
- Caused large outbreaks
  - Killed around 500 million people in the last 100 years of its existence
  - Risk of death 30%
- Inoculation to prevent disease appears to have started in China around 1500s, spreading to Europe early 18th century
- Edward Jenner introduced the modern smallpox vaccine in 1796
- The last case diagnosed in 1977, global eradication certified in 1980
- Only humans are affected, no other reservoir (not a zoonosis)

A child with smallpox in Bangladesh, 1973

Plague as disease

- Caused by bacterium Yersinia pestis
- Two main clinical forms
  - Bubonic form (multiple abscesses), mortality 50%
  - Pulmonary form (pneumonia), mortality close to 100%

- Transmission
  - by droplets from person to person in pulmonary form
  - by fleas from rats (which are the major reservoire)

Black death (Plague)

Illustration of the Black Death from the Toggenburg Bible (1411)
http://en.wikipedia.org/wiki/Black_Death

Major Plague Pandemics

- Plague of Justinianus, 6th century
- Black death, 14th century
- The third plague pandemic, 19th century

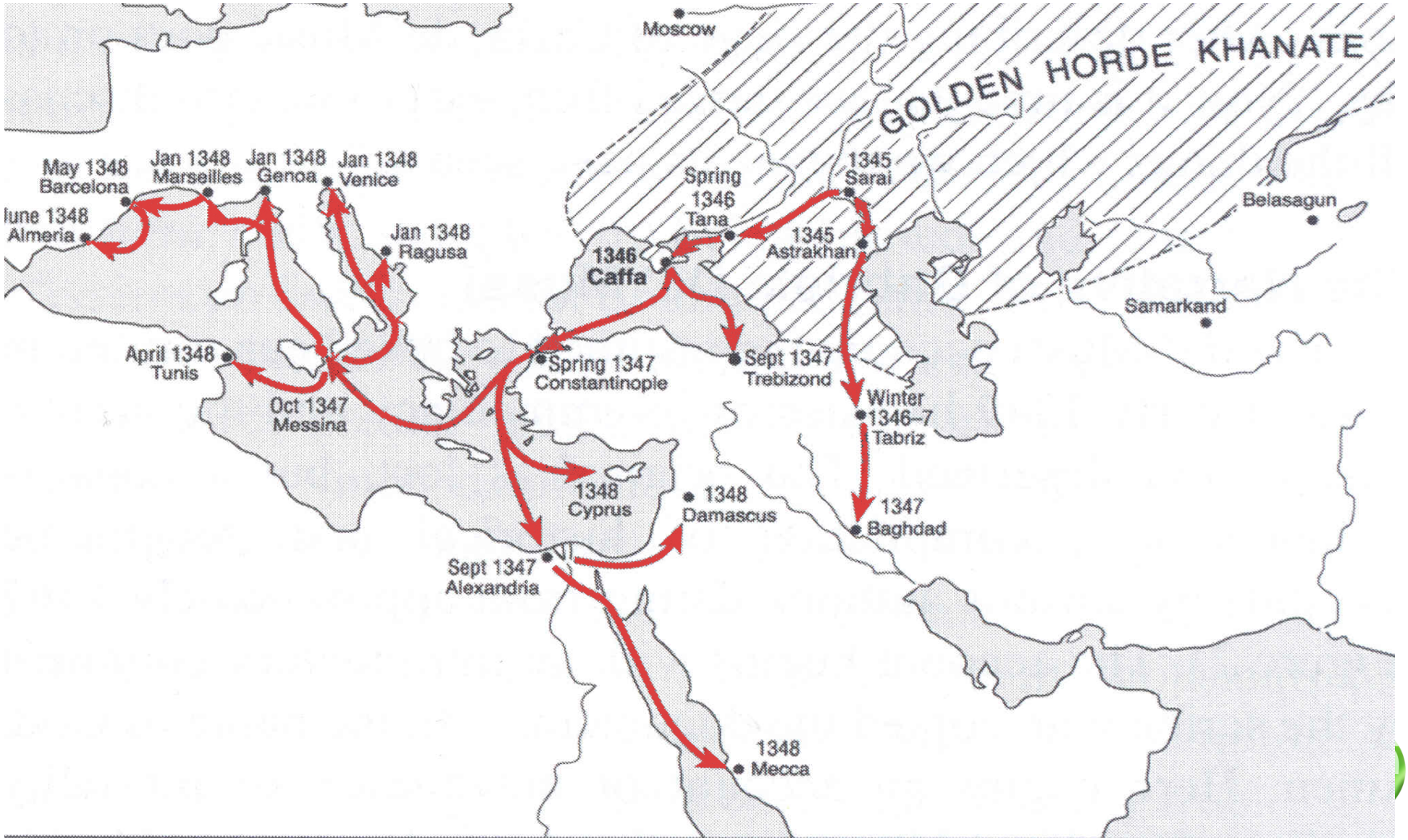
Justinian Plague

- Started in 541 AD
- Constantinople in 542
  - at the peak of the epidemic killed 10 000 per day
  - ’not enough of the living to bury the dead’
- Reached Western Europe by 547 AD
  - recurring epidemics in Mediterranean over 200 years
- No reference to any systematic control measures

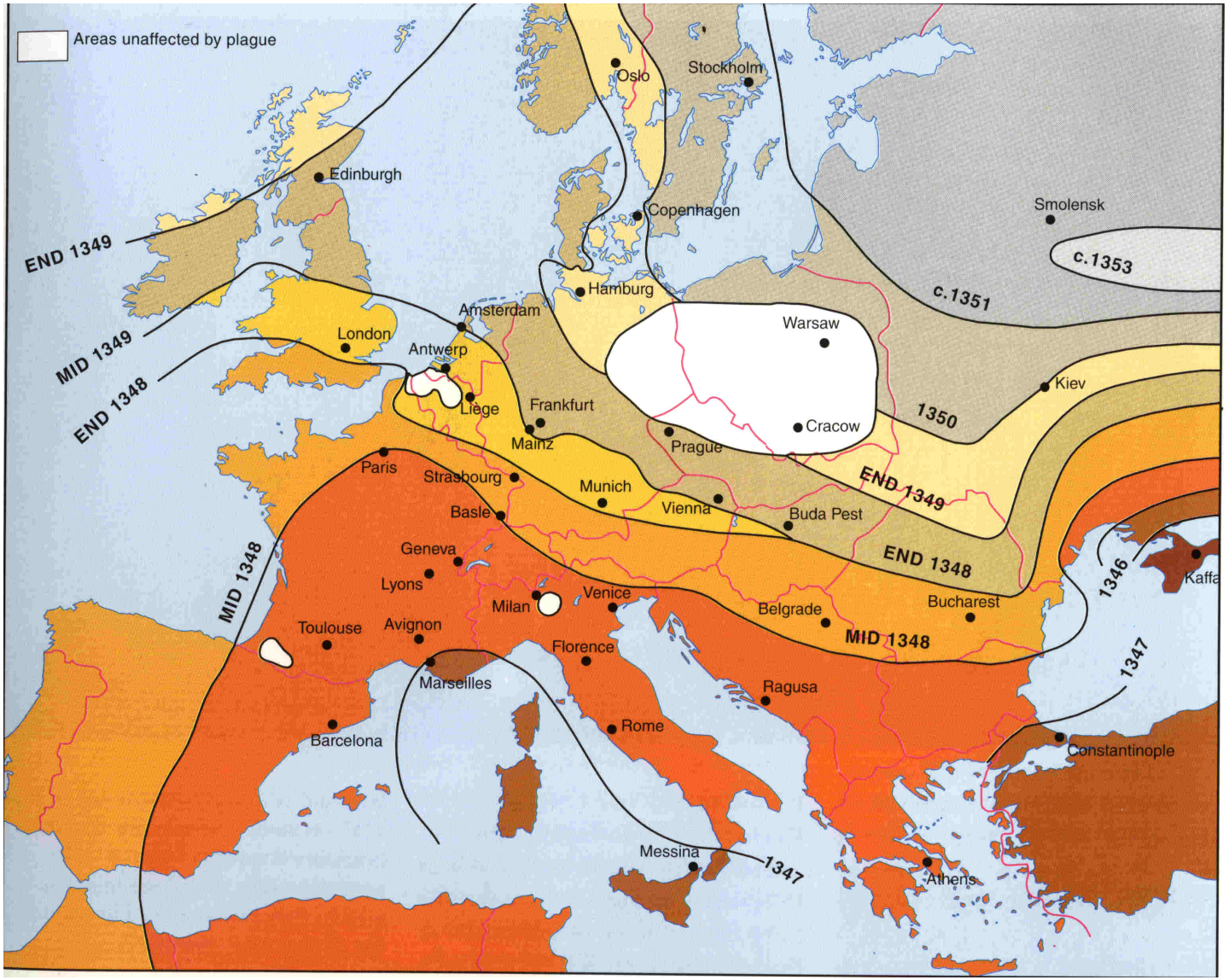
Reasons for the emergence of Black Death

- Disruption of geographic and epidemiologic borders
  - Expansion of the Mongol nation
  - Climatic fluctuations affected populations of rodents infested with plague-carrying flreas
- Increase in movement due to trade
  - Caravan and ship traffic
- Population growth and increase in living density
  - Humans meet infected fleas more frequently
  - Close contact between infected humans

The spread of Black Death in the 14th century



Spread of Black Death further north



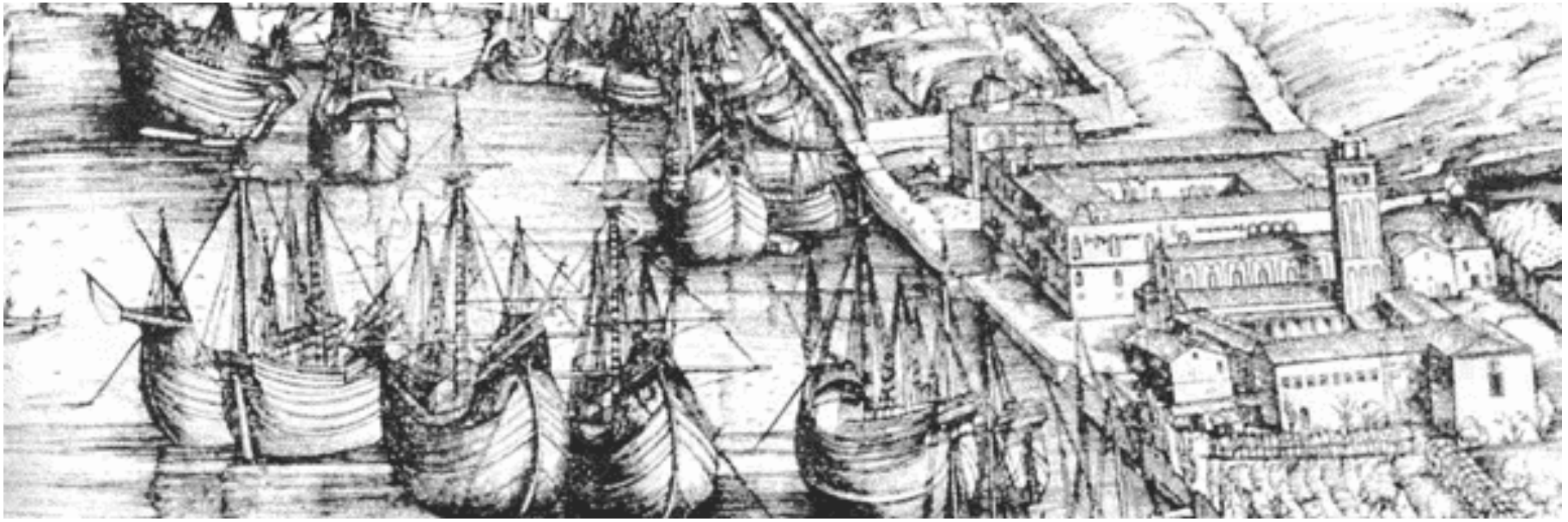
Disease concepts during Black Death

- University of Paris (established in the 12th century), Faculty of Medicine, **during Black Death**:
  - 'It is known that in India in the region of the big ocean ***the stars which fought the sunbeams and warmth of the celestial fire had exerted their power above all against that ocean***, and had vehemently sruggled with its waters. Thus often vapors develop which hide the sun, transforming its light to darkness. These vapors continuously repeated their descending and ascending for 28 days…….'
  - '… these vapors spread by air to many parts of the world and veiled them with mist…'
  - '.. If it comes to Sardinia, nobody will remain alive and the same will happen on all islands and in the neigbouring countries whereto this corrupted sea water from India shall reach ….'
- ***Strong beliefs in cosmic or astral forces***

Public health measures

- **Starting from Italy, secular public health authorities were granted authority for implementing control measures**
- Observations: plague was **a contagious disease of the poor**
- Massacre of dogs and cats (no effect)
- The rich fled the city (could afford)
- **Keeping ships arriving from suspect areas separated for 30 days (Ragusa 1377; *trentina*) or 40 days (Marseille 1383; *quarantina*)**
- Closing public bath houses and schools
- Measures much directed to protect the rich elite
- 'Moving about slowly while inhaling through aromatic sponge'
- Elaborate protective costumes: bird-beaked masks contained aromatic substances

Ships docking, Venice Lazzaretto



Ships docking at the *Lazzaretto Vecchio*, Venice, 14th century

http://www.cdc.gov/ncidod/EID/vol11no05/04-0616.htm

Plague mask

http://www.brlsi.org/proceed03/science200203.htm

Black Death: impact on the population

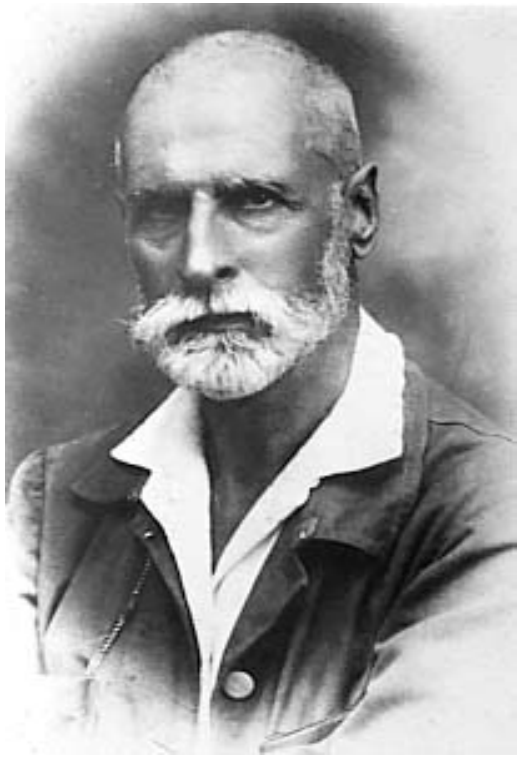
- Deaths
  - Estimated at 20-25 million in Europe (40% of the population)
  - Throughout the world possibly >40 million

- ’Ended the Middle Ages and destroyed medieval social, economic and political arrangements’

Plague pandemic in the late 19th century

- Origin and impact
  - China (1855), Hongkong (1894) → globally
- Changing concept of disease
  - Advent of bacteriology (Anthrax, Tuberculosis etc) in the late 19th century to define the etiology of infectious diseases
  - Competition to identify the cause of plague between Kitasato and Yersin in June – September, 1894
- Followed by
  - The chain of plague transmission discovered in a few years (humans, rats, fleas, bacteria; **zoonosis**)
  - Antiserum used for treatment
  - Vaccine later developed

Kitasato and Yersin



Yersin: http://www.pasteur-international.org/images/personnalites/yersin.jpg
Kitasato: http://www.discoveriesinmedicine.com/images/mdis_0000_0002_0_img0094.jpg

THE BACILLUS OF BUBONIC PLAGUE.[1]

BY PROFESSOR S. KITASATO.

[PRELIMINARY NOTICE.]

EARLY this year an epidemic of bubonic plague broke out in the south of China and Canton, from which city the disease was imported into the neighbouring island of Hong-Kong, where it has prevailed from the beginning of May until now. The Imperial Japanese Government sent a commission to Hong-Kong in order to study the plague, especially as regarded its bacteriological character and its pathological and clinical features. The pathology and medicine were the special study of Professor Aoyama, and the bacteriological part received the care of the writer. Having left Japan on June 5th, 1894, we arrived at Hong-Kong on the 12th of the same month. Here Dr. Lowson, Acting Superintendent of the Government Civil Hospital, put everything needful at our disposal in the most friendly spirit. A room in the Kennedy Town Hospital (one of the plague establishments) was given to us, and there we began our work on June 14th. On that day we were able

Lancet 1894;2:428-430 (25th August)

8me ANNÉE SEPTEMBRE 1894 No 9.

ANNALES
DE
L'INSTITUT PASTEUR

LA PESTE BUBONIQUE A HONG-KONG

PAR LE Dr YERSIN

Ancien préparateur à l'Institut Pasteur, médecin de 2 classe des Colonies.

AVEC LA PLANCHE XII

Au commencement du mois de mai dernier, éclatait, à Hong-Kong, une épidémie de peste bubonique très meurtrière pour la population chinoise de cette ville. La maladie sévissait depuis très longtemps, à l'état endémique, sur les hauts plateaux du Yunnam et avait fait, de temps à autre, quelques apparitions tout près de la frontière de nos possessions indo-chinoises, à Mong-tzé, à Lang-Tchéou et à Pakhoï. En mars, cette année, elle fit son apparition à Canton et, en quelques semaines, occasionna plus de 60,000 décès dans cette ville. Le grand mouvement commercial existant entre Canton et Hong-Kong d'une part, entre Hong-Kong et le Tonkin d'autre part, et la difficulté d'établir, sur le littoral de ces contrées, une quarantaine réellement efficace, fit craindre au gouvernement français que l'Indo-Chine ne fût envahie par l'épidémie.

Yersin ’proclaimed the winner’

- Yersin described unequivocally the causative bacterium accurately (current name Yersinia pestis)
- Yersin’s article delivered at the French Academy of Sciences on July 30, 1894
- Some of Kitasato’s findings were not internally consistent (preparates contaminated with other bacteria?)

- Controversy on who has the priority on finding the bacterium, resolved gradually in Yersin’s favour

Priority diseases are mainly zoonoses

- Zoonoses
  - Zoonoses are infectious diseases that can be naturally transmitted between animals (usually vertebrates) and humans
  - Transmission can be directly from animals to humans, or take place through food/water or other vectors (eg mosquitoes)
  - Approximately 60% of microbes important for human disease are zoonoses
  - A large proportion of recently emerging infectious diseases are zoonoses

- Prevention and control require multi-sectoral collaboration

THL

Cholera

- Bacterium Vibrio cholerae
  - transmission through contaminated liquids or food
  - classical cholera causes massive watery diarrhoea, leading to death in appr 20% of cases due to water/electrolyte loss
- First descriptions of compatible disease from around 5th cent. BC
- One of the first major cholera epidemics described in India 1543
- Seven ’official’ pandemics between 1817 – present
  - Varying geographic spread
  - The latest pandemic started 1961 and continues, particularly in areas of war, civil unrest, famine, poverty, natural disasters etc
  - In the first six pandemics appr 40 million died in India alone
- Prevention: safe water and food, hygiene (vaccine exists)

What is an influenza pandemic?

- An epidemic caused by a new **influenza A virus subtype**, which is transmitted from person to person similarly to regular seasonal influenza.
- Morbidity is expected to be greater than in seasonal influenza

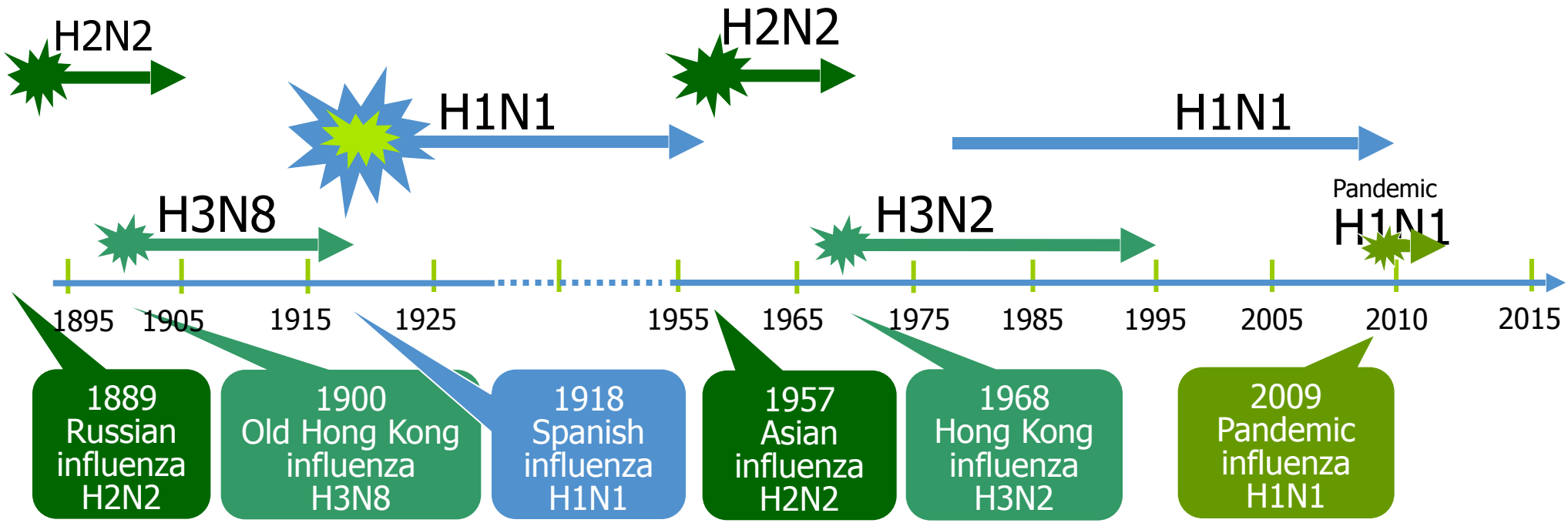
Influenza A typing system (’subtypes’)

- Surface structures
  - H = hemagglutinin (types numbered 1-16)
  - N = neuraminidase (types numbered 1-9)

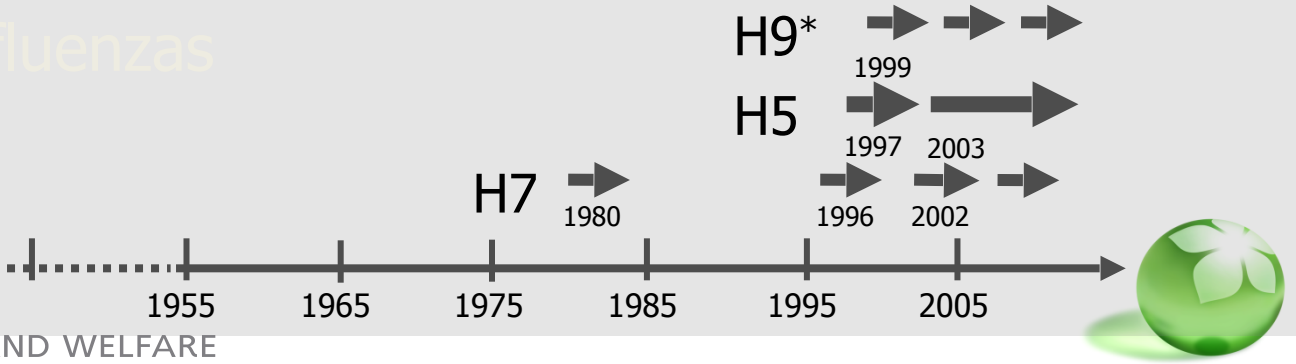
- Around 150 possible combinations
  - only a proportion of these has been identified in humans
  - **Influenza is a zoonosis:** a great diversity of animals can be infected in addition to humans

Pandemics of influenza

Recorded human pandemic influenza
(early sub-types inferred)



Recorded new avian influenzas



Animated slide: Press space bar

’Spanish influenza’ in 1918-1920

- **Influenza A H1N1**
- **Convergence of armies in Northern France**
- **Spread explosively through the world**
- **30-50 million people died in three waves**
- **High mortality among young adults**

Iowa State University Gym 1918

Global air traffic

The beginning of H1N1 Pandemic/2009

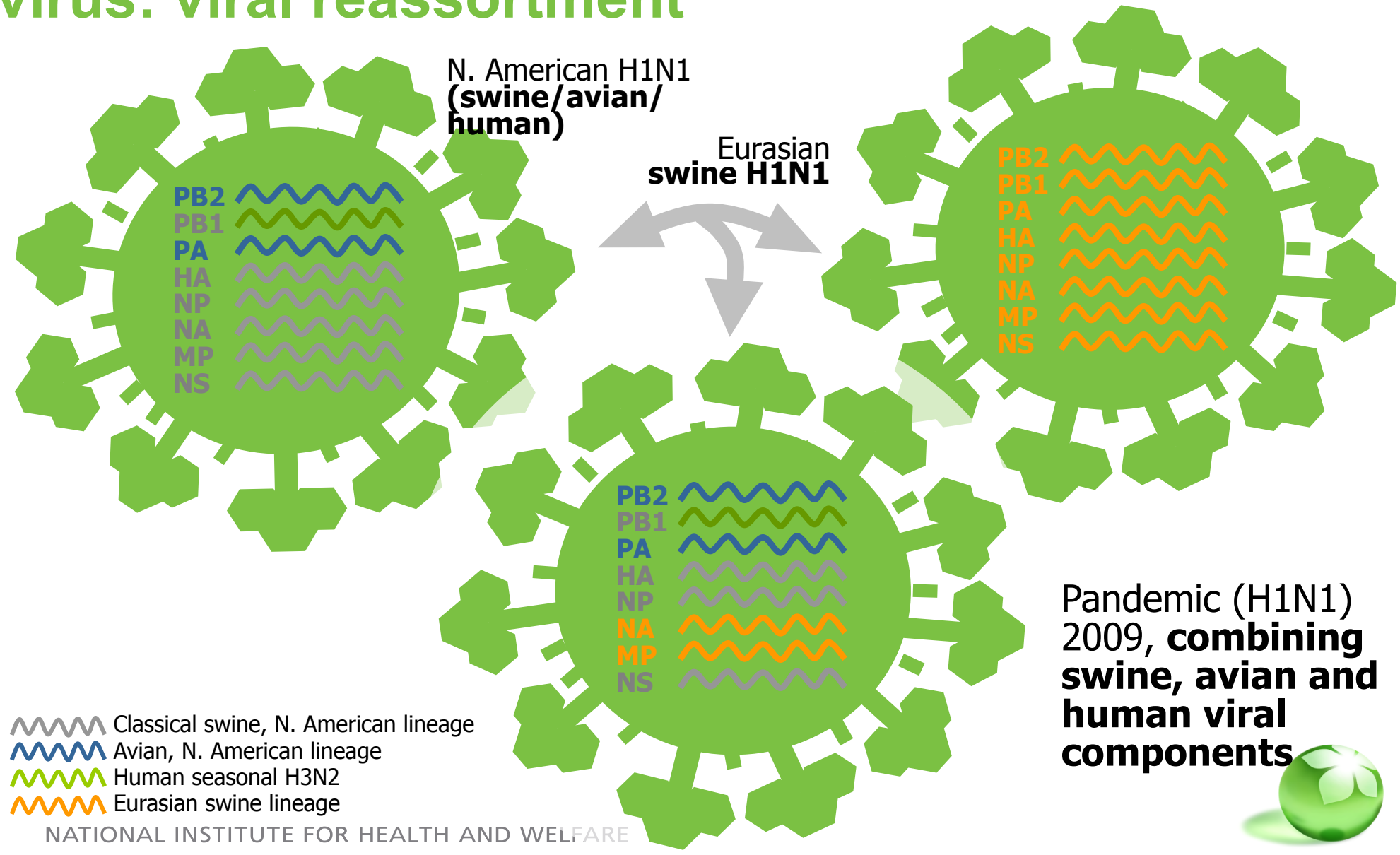
28 & 29 March, 2 sporadic ARI cases in California

4 April: outbreak of ILI in Veracruz

March | April | May | ember | October

15-17 April: clusters of severe pneumonia in Mexico

Genetic origins of the pandemic (H1N1) 2009 virus: viral reassortment



Influenza A/H1N1/pdm2009 pandemic ('swine flu')

- Turned out to be 'mild'
  - The majority of the aged had protection from exposure to a closely related virus decades earlier in early-mid 1900s
  - Vaccine developed and distributed quickly
- However, a limited number of young persons without serious underlying diseases died
- In some countries, second or third waves were more serious than the first

- (Preceded for several years by intense preparations for an anticipated severe pandemic to be caused by influenza A/H5N1 'bird flu')

For any future pandemic influenza virus – what can and cannot be assumed?

- ***What probably can be assumed:***
- Modes of transmission (droplet, direct and indirect contact)
- Broad incubation period and serial interval
- At what stage a person is infectious
- Broad clinical presentation and case definition (what influenza looks like)
- The general effectiveness of personal hygiene measures (frequent hand washing, using tissues properly, staying at home when you get ill)
- That in temperate zones transmission will be lower in the spring and summer than in the autumn and winter

What cannot be assumed:

- Antigenic type and phenotype
- Susceptibility/resistance to antivirals
- Age-groups and clinical groups most affected
- Age-groups with most transmission
- Clinical attack rates
- Pathogenicity (case-fatality rates)
- 'Severity' of the pandemic
- Precise parameters needed for modelling and forecasting (serial interval, R_o)
- Precise clinical case definition
- The duration, shape, number and tempo of the waves of infection
- Will new virus dominate over seasonal type A influenza?
- Complicating conditions (super-infections)
- The effectiveness of interventions and counter-measures including pharmaceuticals
- The safety of pharmaceutical interventions

Corona viruses

Out of seven corona viruses infecting man

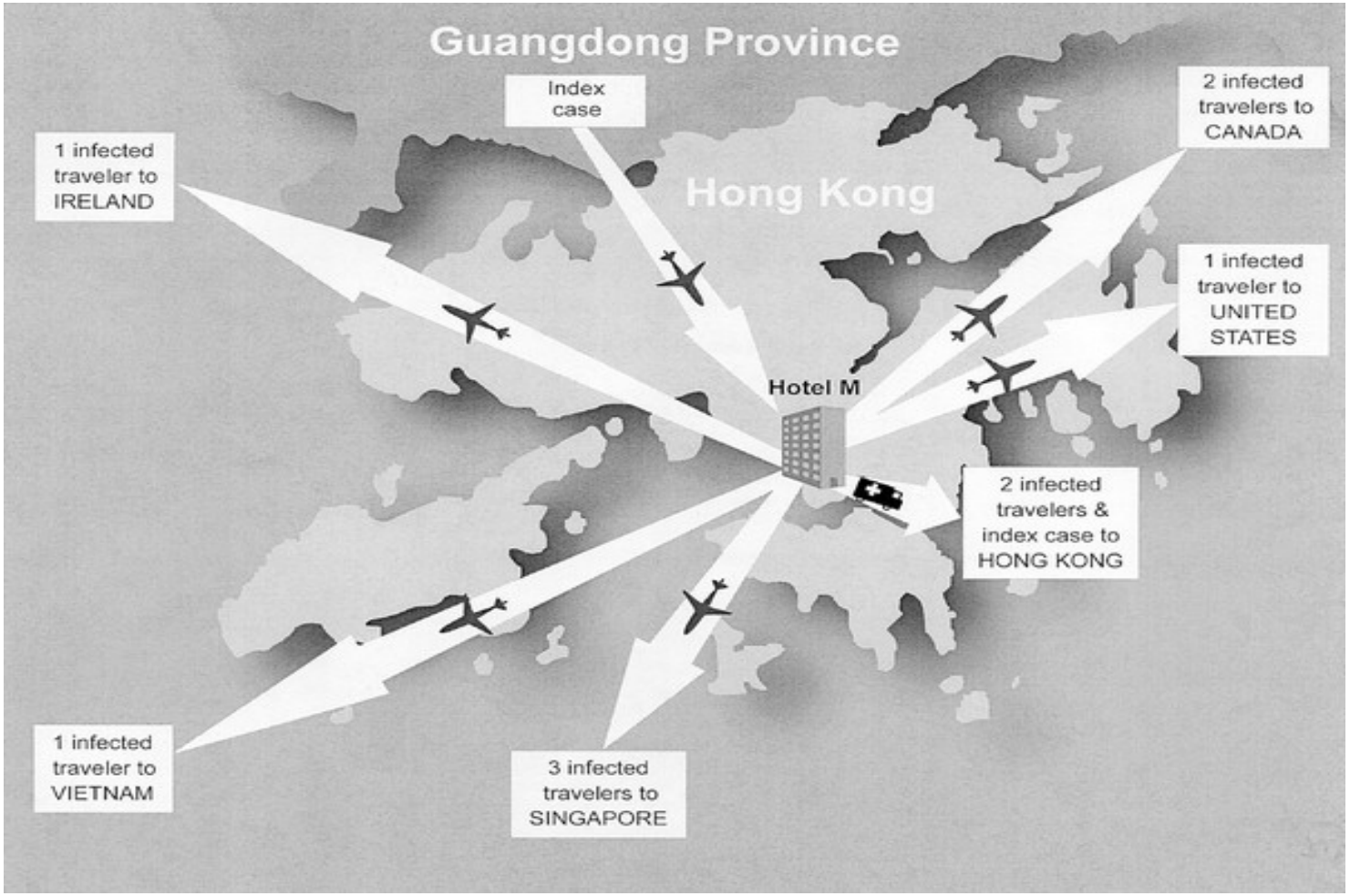
- Four cause mild respiratory infections
  - OC43, HKU1, 229E ja NL63
- Three new identified since 2000 can cause severe disease
  - SARS-CoV-1 (SARS-epidemic 2003; from bats?)('almost pandemic')
  - MERS-CoV (Near East 2013 -->; from camels)
  - SARS-CoV-2 (Covid – 19 pandemic; source unknown)

’Almost pandemic SARS, 2003’

SARS epidemic, 2003

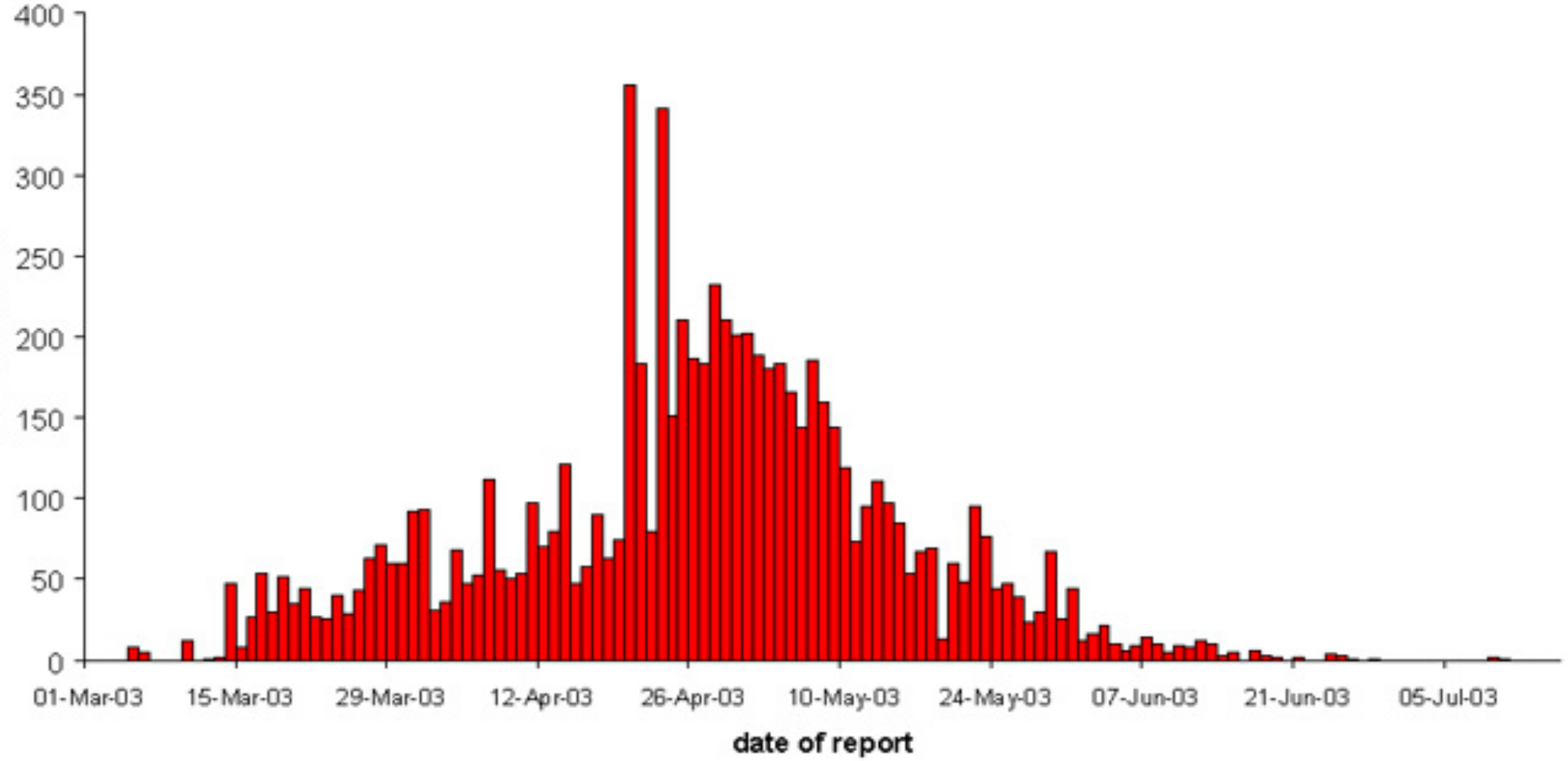
- Sudden acute respiratory syndrome
- A definitely new human disease caused by SARS-CoV-1
- Zoonosis, proposed origin from bats via civet cats (?)

SARS transmission by an individual from Guangdong to Hotel M in Hong Kong, and globally by infected hotel guests



CID 2004;38:1422

Probable cases of SARS by date of report
Worldwide* (n=7,588), 1 March - 10 July 2003

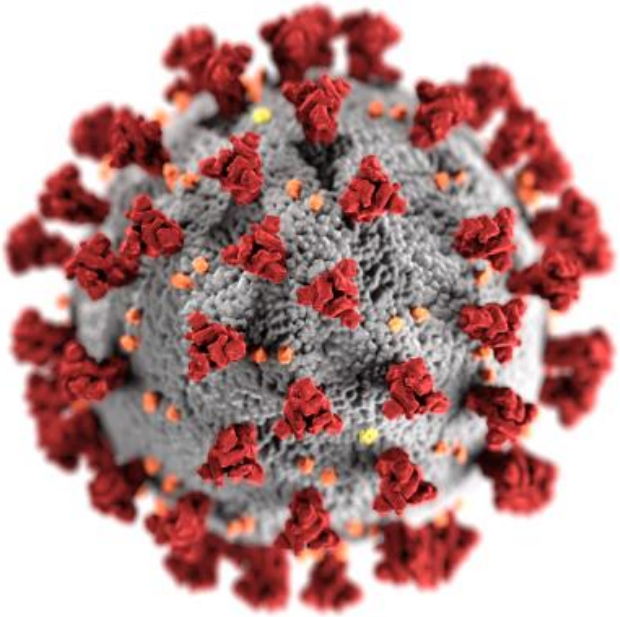


*As of 10 July 2003, 8,437 probable cases of SARS have been reported to WHO.
This graph includes all cases from Hong Kong SAR, Macao SAR and Taiwan, China, but only those cases elsewhere in China reported after 3 April 2003 (1,190 cases between 16 November 2002 and 3 April 2003 not shown). Also includes 341 probable cases of SARS who have been discarded and for whom dates of report could not be identified. The United States of America began reporting probable cases of SARS to WHO on 20 April 2003

What stopped SARS in 2003?

- Intensive surveillance for respiratory infections
- **Aggressive case finding where cases were occurring;**
  - **No non-symptomatic cases**
  - **No transmission before symptoms started**
- **Early isolation of possible cases**
- **Contact tracing around confirmed cases --> quarantine**
- Strict infection control in health care settings;
- Reducing aerosol generating procedures
- Reduce movement and transfer of patients;
- Stopping / discouraging febrile people travelling

SARS - CoV – 2 virus (cause of Covid-19)



SARS-CoV-2 is difficult to control

Transmission mechanisms

- Droplet transmission within short distance is the main mechanism
- Transmission via surfaces (fomites) is of little significance
- There is possibly also some aerosol – transmission

Transmissibility/infectiousness starts well before symptoms

- The transmitter is not identified prior to the start of transmission

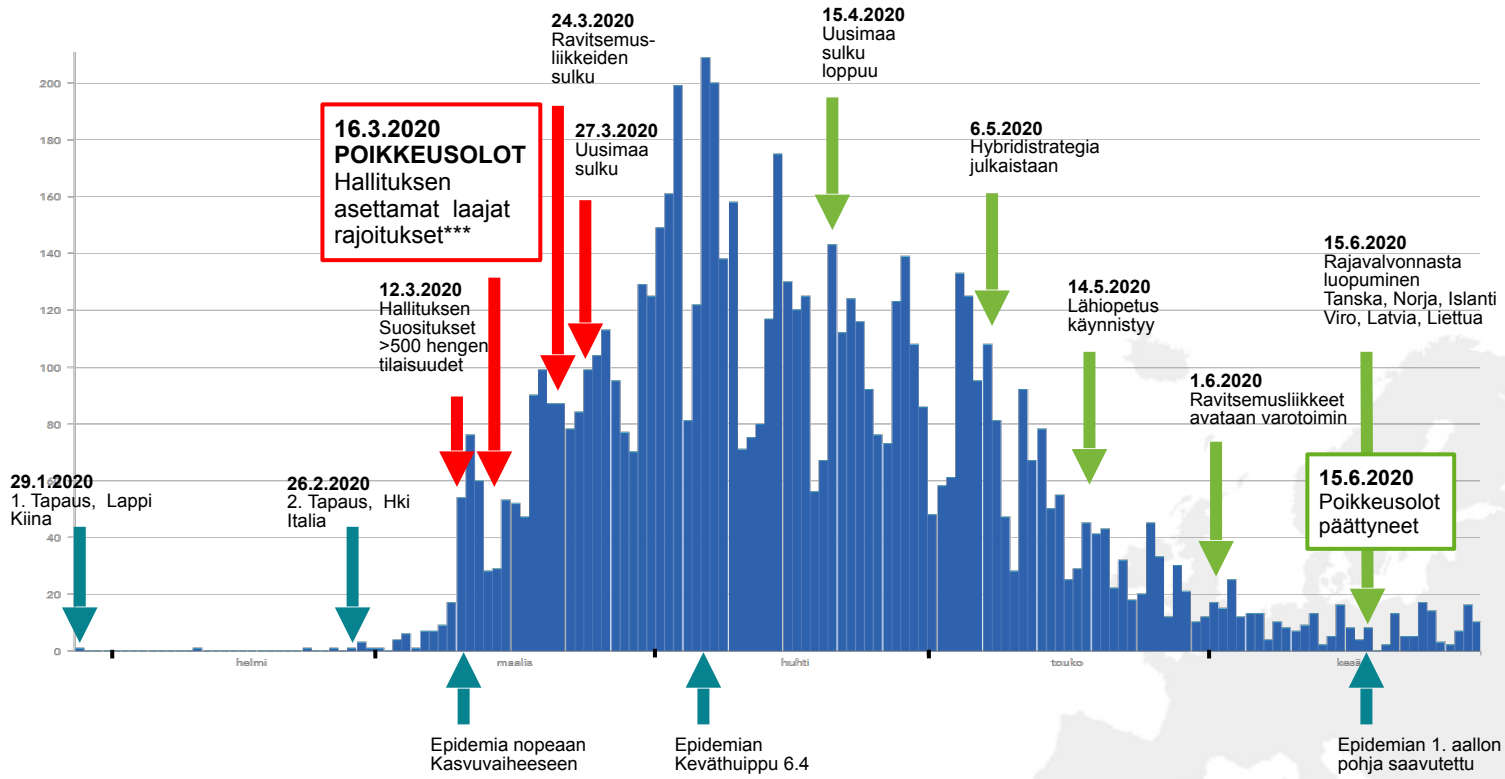
A large proportion of infected persons are symptomless

Symptoms cannot be distuingished from other respiratory viruse infections

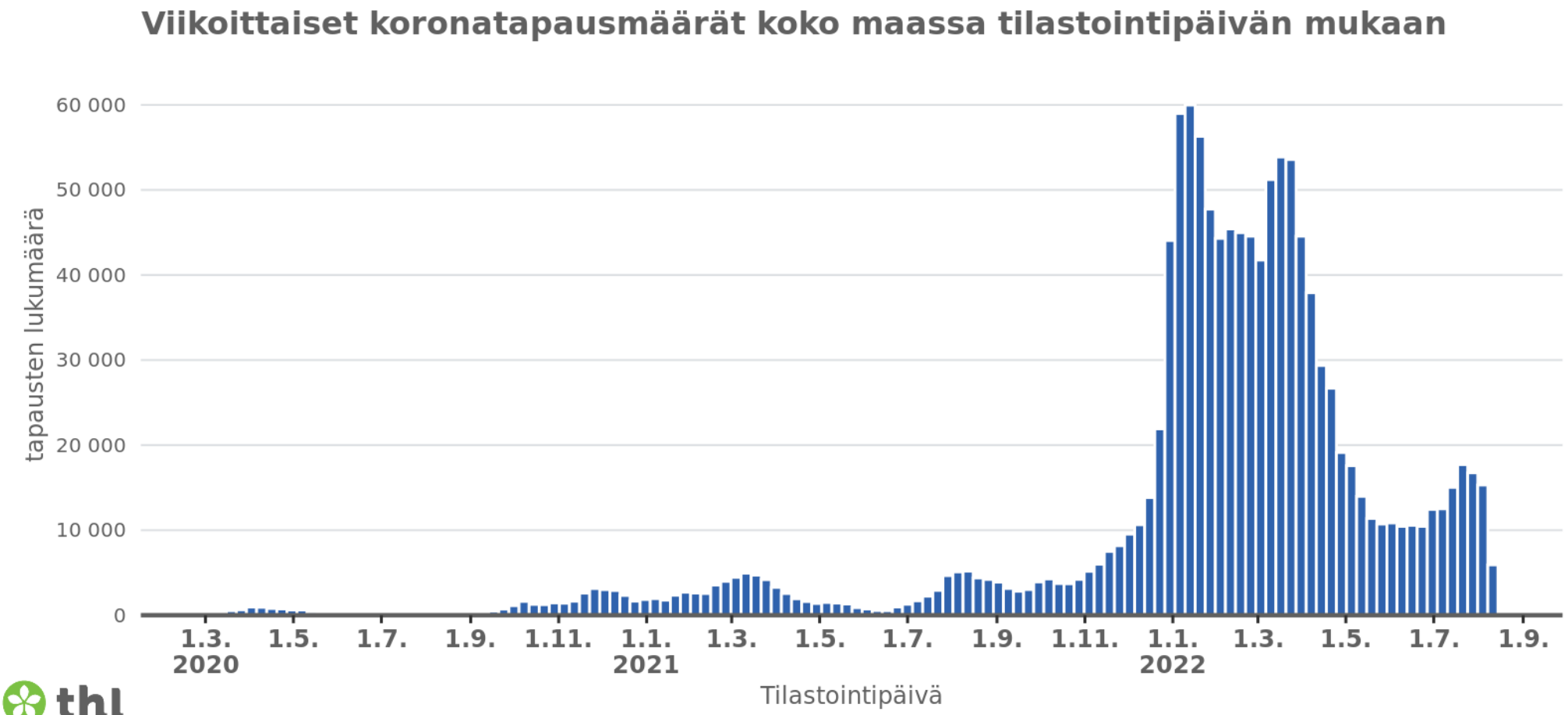
Leads to considerable burden in hospitals

- The proportion hospitalized has varied greatly in epidemic phases
- No treatment available for treating early disease to reduce hospital admissions

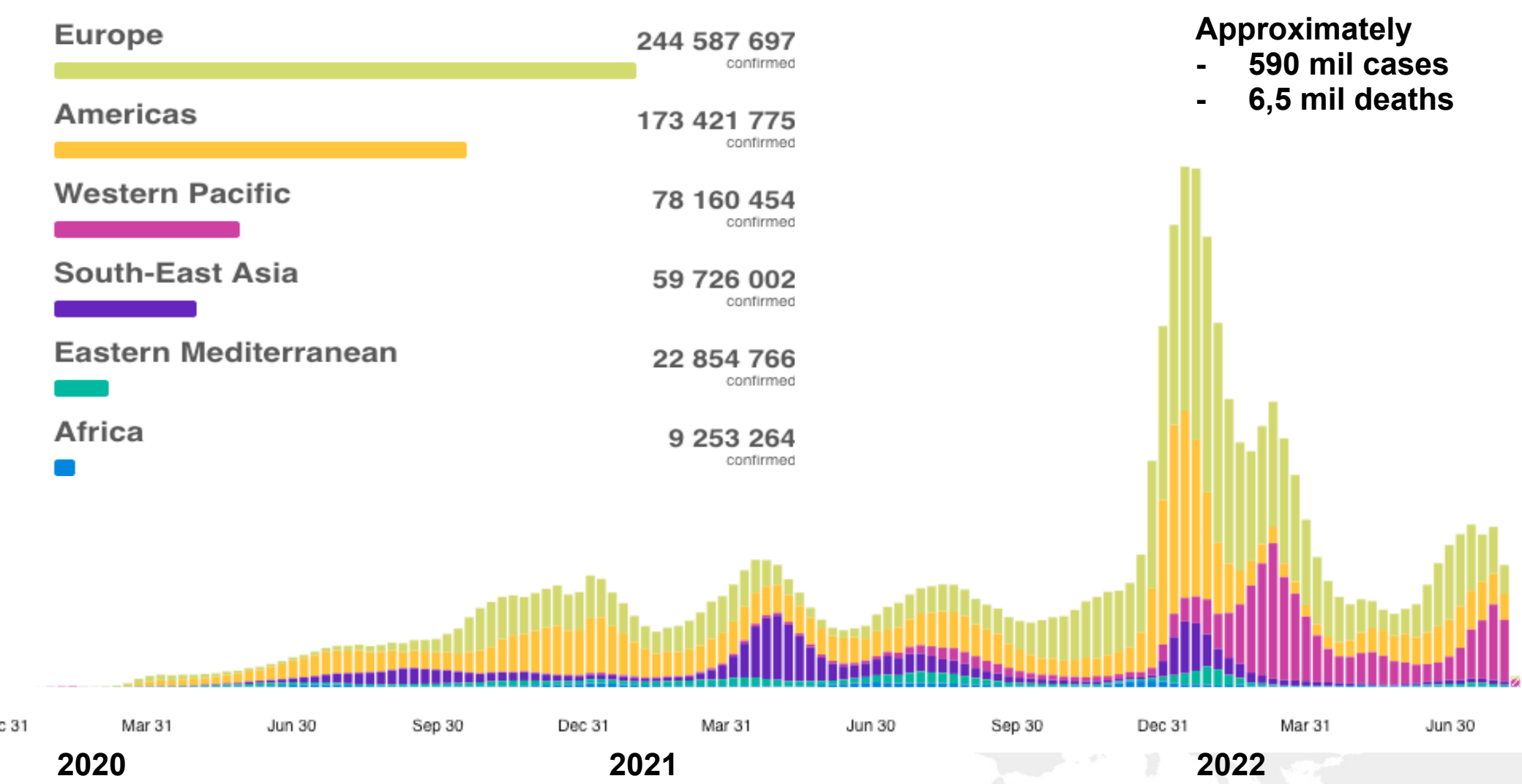
The first wave of pandemic in Finland from 29.1. – 30.6.2020 with societal control measures



Weekly numbers of confirmed Covid cases in Finland

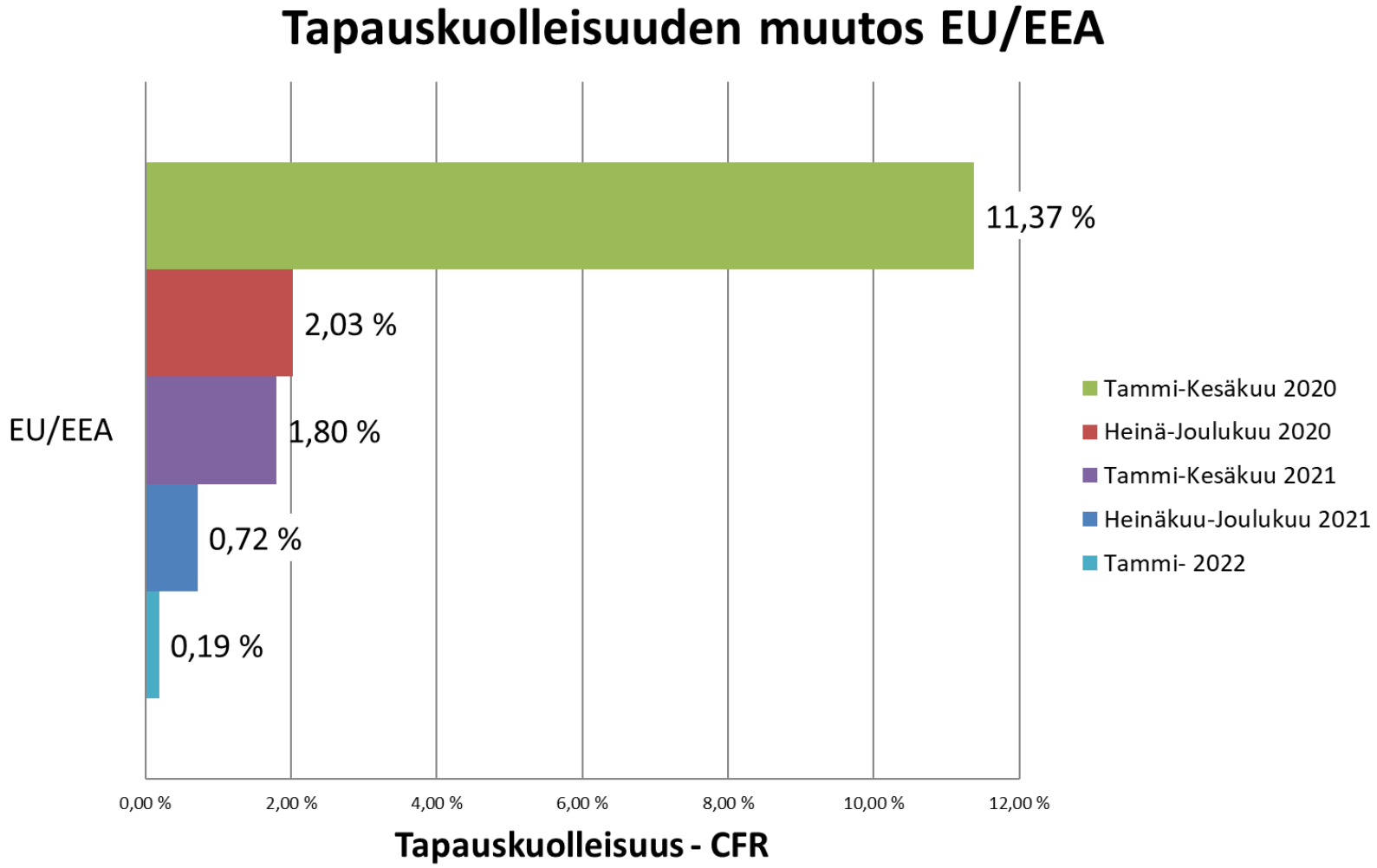


Global course of Covid-19 pandemic by WHO region (confirmed cases and deaths, Aug. 2022)



Approximately
- **590 mil cases**
- **6,5 mil deaths**

The development of case fatality rate by half-year periods in EU/ETA 2020 – 2022 spring



Unexpected developments in Covid-19

Total border closure in numerous countries

The mass return home of Finns residing abroad

Massive global shortage of personal safety materials

Other 'demand shocks': testing materials and devices

Fast vaccine development

The difficult adaptation of western health care to meet a massive communicable disease epidemic

The great impact of the epidemic on economy

What about next pandemic ?

- WHO International Health Regulations 2005 (2007)
  - WHO and Member State (MS) obligations (capacities) and rights described
  - Strengthens the WHO position as a coordinator
  - Transparency in information flow
  - Strengthened WHO role in giving guidelines for control measures
  - **Assessment of the surveillance and control capacities of Member States (MS)(Finland has been very active!)**
- Support to poor MS by a diversity international actors
- Epidemic Intelligence and dissemination of knowledge
  - WHO
  - European CDC
  - US CDC etc

Some slides have been provided by

Mika Salminen, THL
Hanna Nohynek, THL
Asko Järvinen, HUS
Angus Nicoll, ECDC