



Who gave What to Whom?

- A disease is not just an infectious agent: it is a relationship between a pathogen and its human hosts; both sides can develop and change radically over time.
- Tuberculosis was **proven** in the late 2000s **not to have come to humans from cows, but to have been given to cows by humans.**
- *Mycobacterium bovis* is not the ancestor of human strains of *Mycobacterium tuberculosis*, but an early offshoot of lineages whose origins were in East Africa, perhaps no more than 4K years ago.

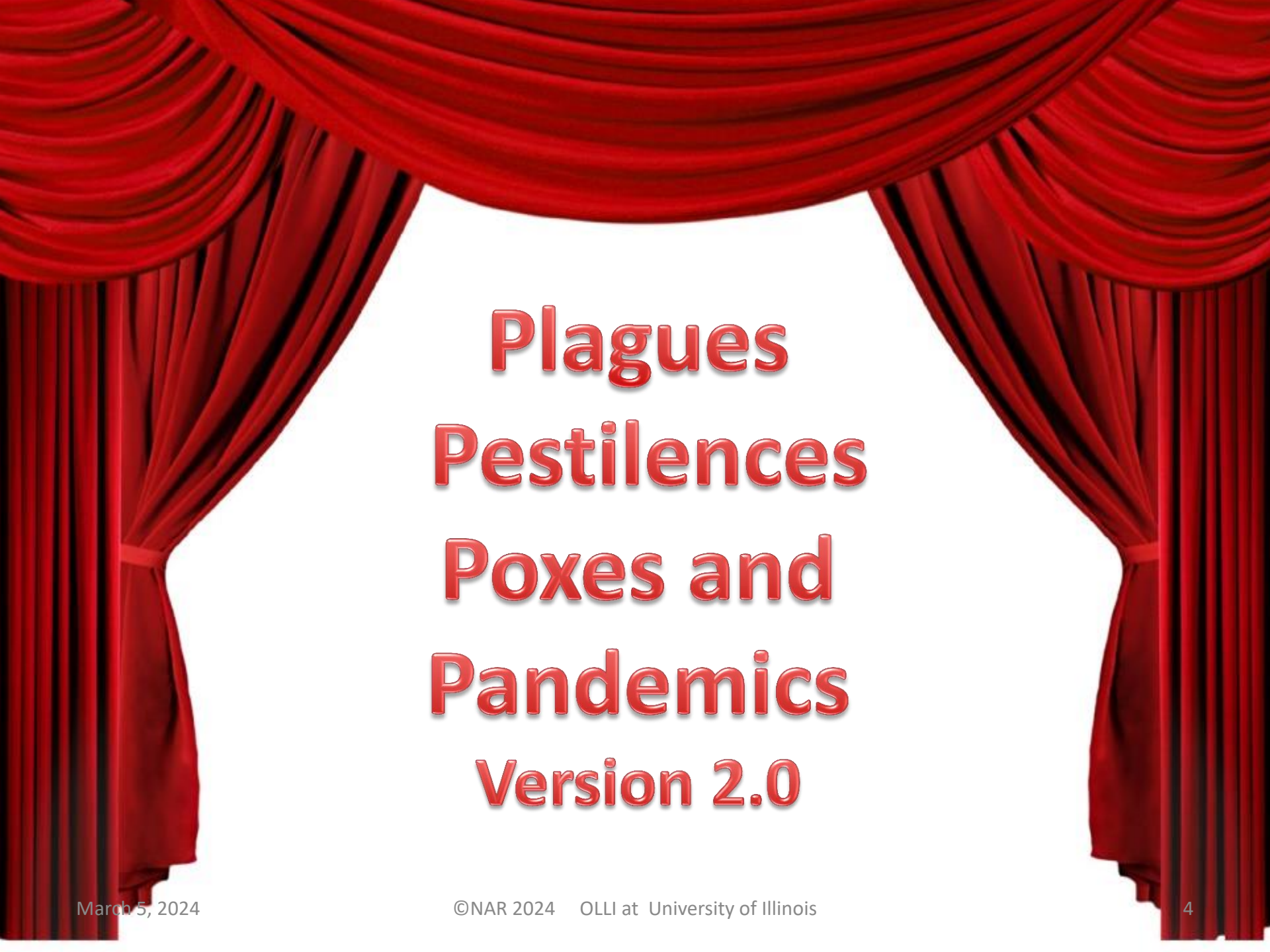
Monica Green

Citation

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Green MH. Emerging diseases, re-emerging histories. *Centaurus*. 2020;62:234–247.

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The background of the slide features a pair of rich red, draped curtains that are pulled back to reveal a white central area. The curtains have a soft, velvety texture and are lit from above, creating a dramatic, stage-like atmosphere.

Plagues Pestilences Poxes and Pandemics Version 2.0

Plan for the Course

- Session 1 Feb. 27: Definitions, Biblical Plagues.
- **Session 2 March 5: The PLAGUE through time, new theories**
- Session 3 March 12: Other Infectious Pestilences
- Session 4 March 19: The Columbian Exchange.
- Session 5 March 26: 20th Century Pandemics, Past & Current
- Session 6 April 2: HIV/AIDS
- Session 7 April 9: 20th and 21st Century Viruses.
- Session 8 April 16: Crystal Ball into the future?

Plan for the Session

- Ancient plagues: Athens, Antonine, Cyprian
- The 3 Plague Pandemics:
 - 1st: Justinian
 - 2nd: Medieval (Black Death)
 - 3rd: Modern
- Old stories, urban legends
- Controversies, contradictions, doubts
- New science and theories



OLLI Spring 2024
Session 2, March 5th

The Plague

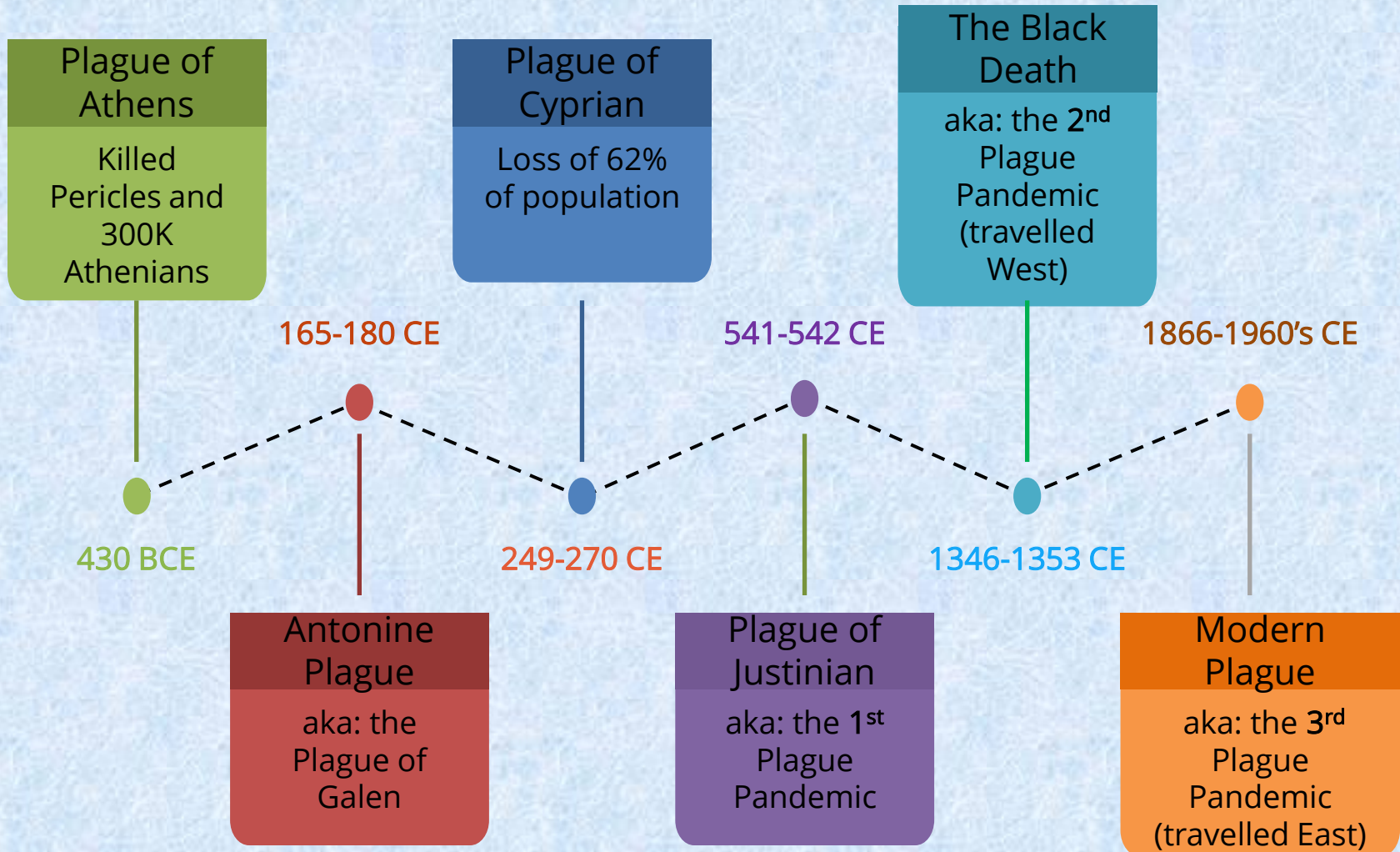
Néstor A. Ramírez, MD, MPH

The Plague

(Actually, the Many Plagues)

Review Through Times and Places
Ideas, Theories, Contradictions

TIMELINE of the Plagues



The image shows the Parthenon on the Acropolis in Athens, Greece. The temple is a large, ancient Greek temple dedicated to the goddess Athena. It features a series of tall, fluted columns supporting a heavy entablature. The sky is a clear, bright blue. The text "PLAGUE OF ATHENS" is overlaid in large, bold, black letters across the middle of the image.

PLAGUE OF ATHENS

430 BCE

Plague of Athens ⁽¹⁾

430 BCE

- Killed over 30,000 citizens, sailors, and soldiers of Athens (1/4 to 1/3 of the population).
- Returned in 429 BCE and in 427 BCE.
- Pericles, statesman, general, and ruler died.
- His 2 sons also died.

Plague of Athens

430 BCE

- Thucydides wrote about the epidemic that began in Ethiopia, passed through Egypt and Libya, then to the Greek world, and killed about 5K/day.
- Entered Athens through Piraeus, city's port.
- Athens' armies weakened, but Sparta didn't want to risk getting ill, so war slowed down.

Plague of Athens (2)

Symptoms

- headaches
- delusions and confusion
- chills
- lack of appetite
- stomach pain
- diarrhea/constipation
- slow-rising high fever
- low heart rate
- Weakness
- muscle pains
- rash of flat "rose spots"
- intestinal perforation or hemorrhage

Plague of Athens

430 BCE

- Was it an outbreak of the bubonic plague?
- Symptoms, epidemiology, and DNA studies of corpses, lead to alternative explanations:
 - measles
 - toxic shock syndrome (TSS)
 - anthrax
 - Ebola or a related viral hemorrhagic fever
 - typhus or typhoid fever
 - smallpox



ANTONINE PLAGUE

165-180 AD

Antonine Plague ⁽¹⁾

165-180 AD

- Named for Marcus Aurelius Antoninus.
- Also known as Plague of Galen, who described it.
- Death count about 5 million (1/3 of population).
- Devastated the Roman army.

Antonine Plague ⁽²⁾

165-180 AD

- Brought from the Parthian Wars (54 BC-217 AD) by Lucius Verus.
- Besides the great Parthian treasures, Roman troops brought home an Asian “souvenir”.
- Asia Minor to Greece, to Italy and then Rome.
- Infested Roman empire along trade routes.

OUTBREAK

The Roman Empire in 117 AD, at its greatest extent



Antonine Plague spread



Antonine Plague spread



Antonine Plague spread



Antonine Plague spread



Antonine Plague spread



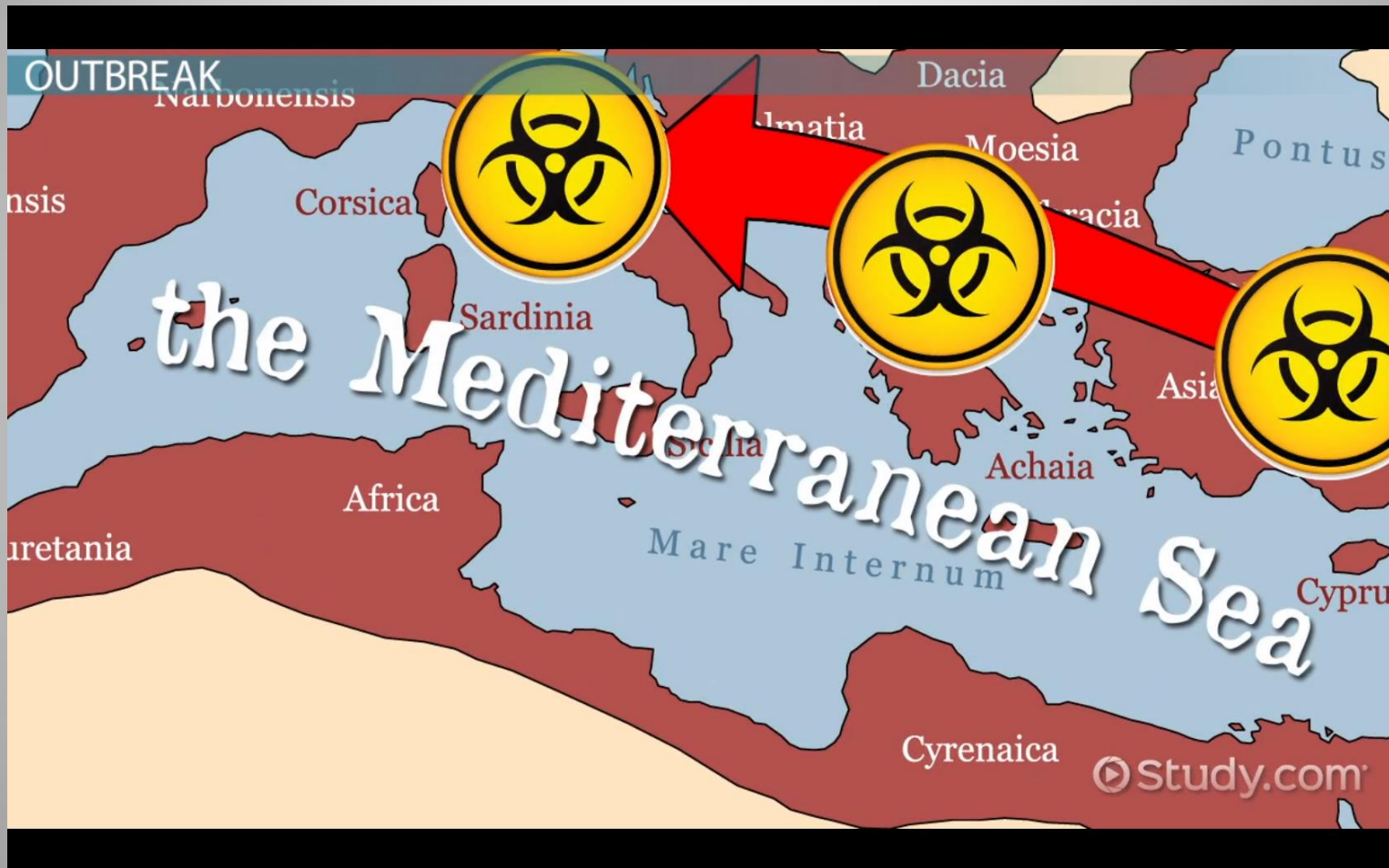
Antonine Plague spread



Antonine Plague spread



Antonine Plague spread



Antonine Plague spread



Antonine Plague (2)

165-180 AD

- Symptoms: fever, diarrhea, pharyngitis and a skin eruption on the 9th day of the illness.
- Scabbed over and left disfiguring scars.
- Reappeared in 189 AD with a mortality of 2K per day, about 25% of those affected.
- Possible etiologies: smallpox or measles ?

Antonine Plague (3)

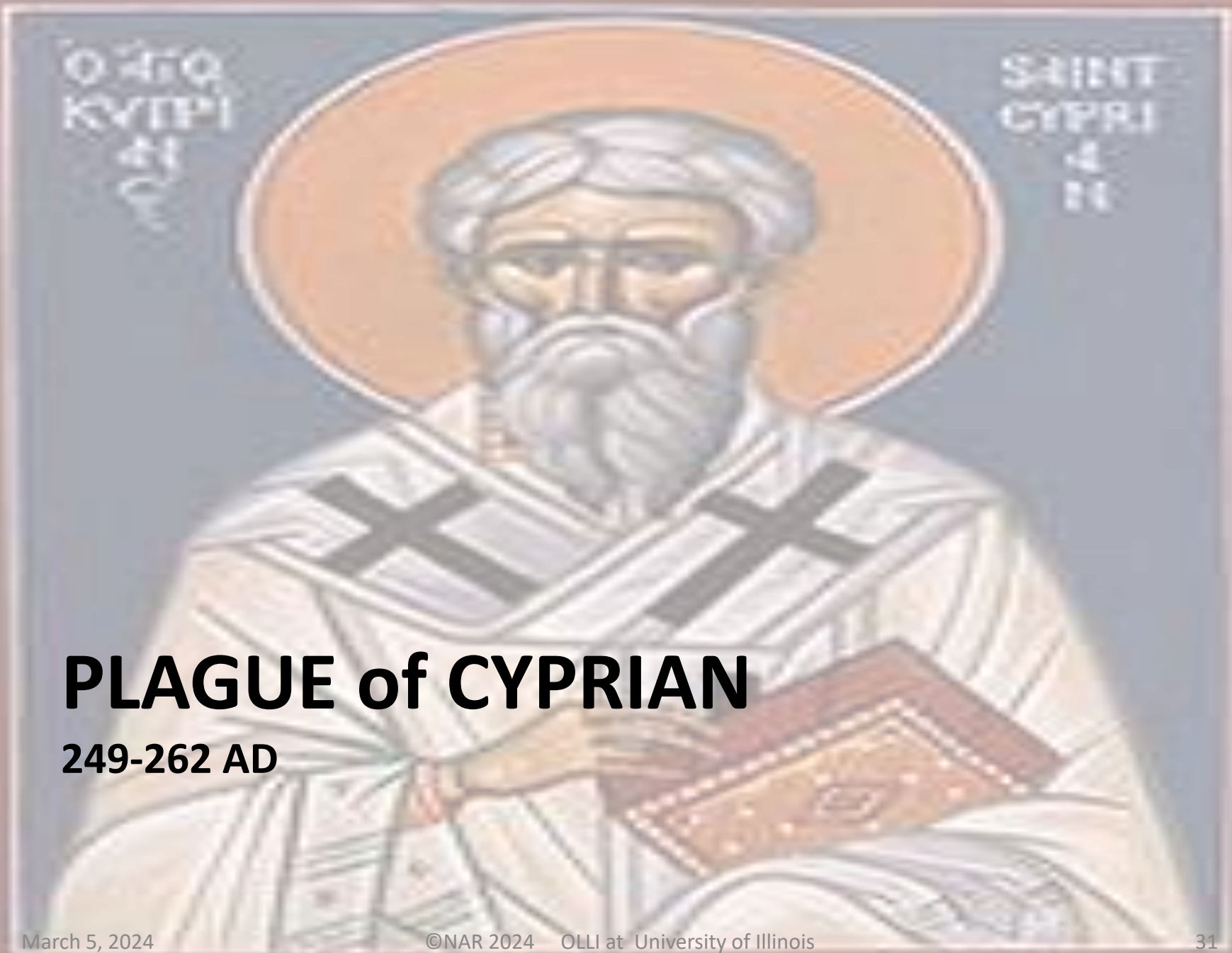
165-180 AD

- Partially blamed for demise of Roman Empire.
- Decreased Roman commerce in SE Asia.
- Damaged Roman sea trade with Egypt & India.
- Rise of healing by magic and faith in cults.

Antonine Plague (4)

165-180 AD

- The mortality was between 7% and 10%.
- The plague killed Marcus Aurelius Antoninus in 180 AD and his adoptive brother and co-emperor Lucius Verus in 169 AD.
- Under Commodus's reign, in 189 AD, it struck again killing about 2K/day.



PLAGUE of CYPRIAN

249-262 AD

Plague of Cyprian ⁽¹⁾

249-262 AD

- Named after Cyprian, Bishop of Carthage.
- Symptoms: fever, diarrhea, severe limb pain, conjunctivitis with loss of vision, deafness, bloody stool & vomit, weakness and distal gangrene.
- Suspect agents include: pandemic influenza, smallpox or a viral hemorrhagic fever virus.

Plague of Cyprian (2)

249-262 AD

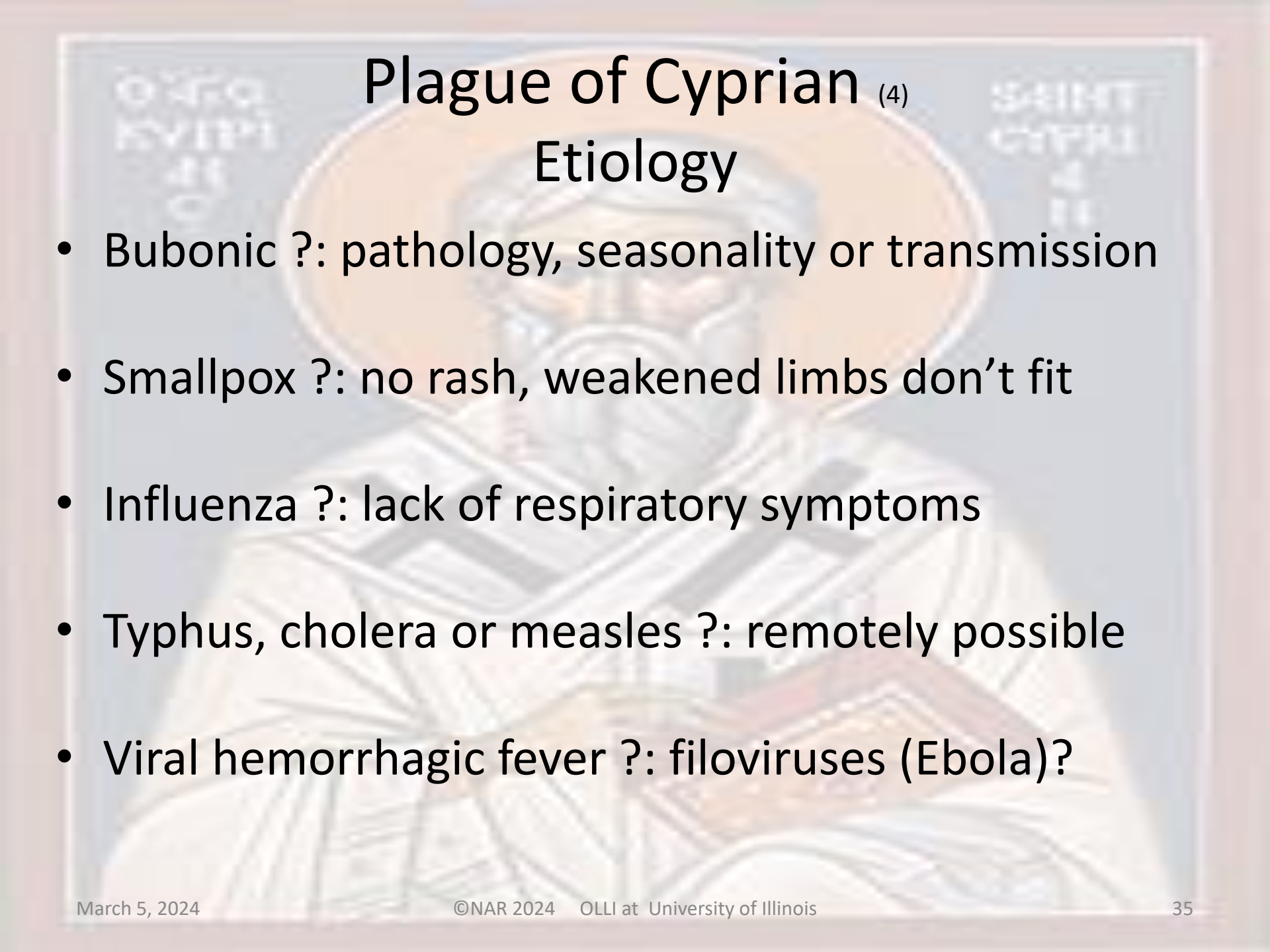
- First on the Balkan front, reached Alexandria 1 year before it reached Rome, and then spread all over the Empire.
- It decimated Rome's population, with loss of 62% of population (from 500K to about 190K).
- Dexippus, an Athenian historian writes of 5K deaths/day.
- Killed 2 Roman emperors: Hostilian and Claudius II.

Plague of Cyprian (3)

249-262 AD

Beliefs on origin:

- “poisonous airs and pestilent waters” that spread over the empire
- “disease was transmitted through the clothes or simply by sight” (instinctive sense of contagion!!!)
- punishment from the gods



Plague of Cyprian ⁽⁴⁾

Etiology

- Bubonic ? : pathology, seasonality or transmission
- Smallpox ? : no rash, weakened limbs don't fit
- Influenza ? : lack of respiratory symptoms
- Typhus, cholera or measles ? : remotely possible
- Viral hemorrhagic fever ? : filoviruses (Ebola)?

Ο Άγιος
ΚΥΠΡΙ
ΔΝ

SAINT
GYPRI
ΔΝ

Plague Controversies

- WH McNeill says:
 - Antonine and Cyprian Plagues were the 1st animal to human transfers
 - they were 2 different plagues, 1 of smallpox and 1 of measles, not necessarily in that order
- D Stathakopoulos asserts that both were smallpox
- Kyle Harper says:
 - the Antonine Plague was smallpox
 - symptoms of Plague of Cyprian don't match smallpox
 - symptoms of Plague of Cyprian match a hemorrhagic viral fever

Smallpox

- found in 400 BCE Egyptian mummies
- occurred in outbreaks
- 18th-century Europe, killed 400K people/year
- produced 1/3 of all cases of blindness
- killed up to 300 M (?) people in 20th century
- killed 500M people in last century of its existence
- by 1967, 15M cases/year
- eradicated in 1977

Viral Hemorrhagic Fevers (VHF)

- Diseases that can cause severe, life-threatening illness, damage the cardiovascular system, make vessels leak, and hamper the blood clotting.
- Some viral hemorrhagic fevers include:
 - *Dengue
 - *Ebola
 - *Hanta
 - *Lassa
 - *Marburg
 - *Omsk
 - *Yellow fever
 - *Rift Valley

Viral Hemorrhagic Fevers (VHF)

Early signs/symptoms

- fever
- fatigue and/or weakness
- general malaise
- dizziness
- muscle, bone or joint aches
- nausea and vomiting
- diarrhea

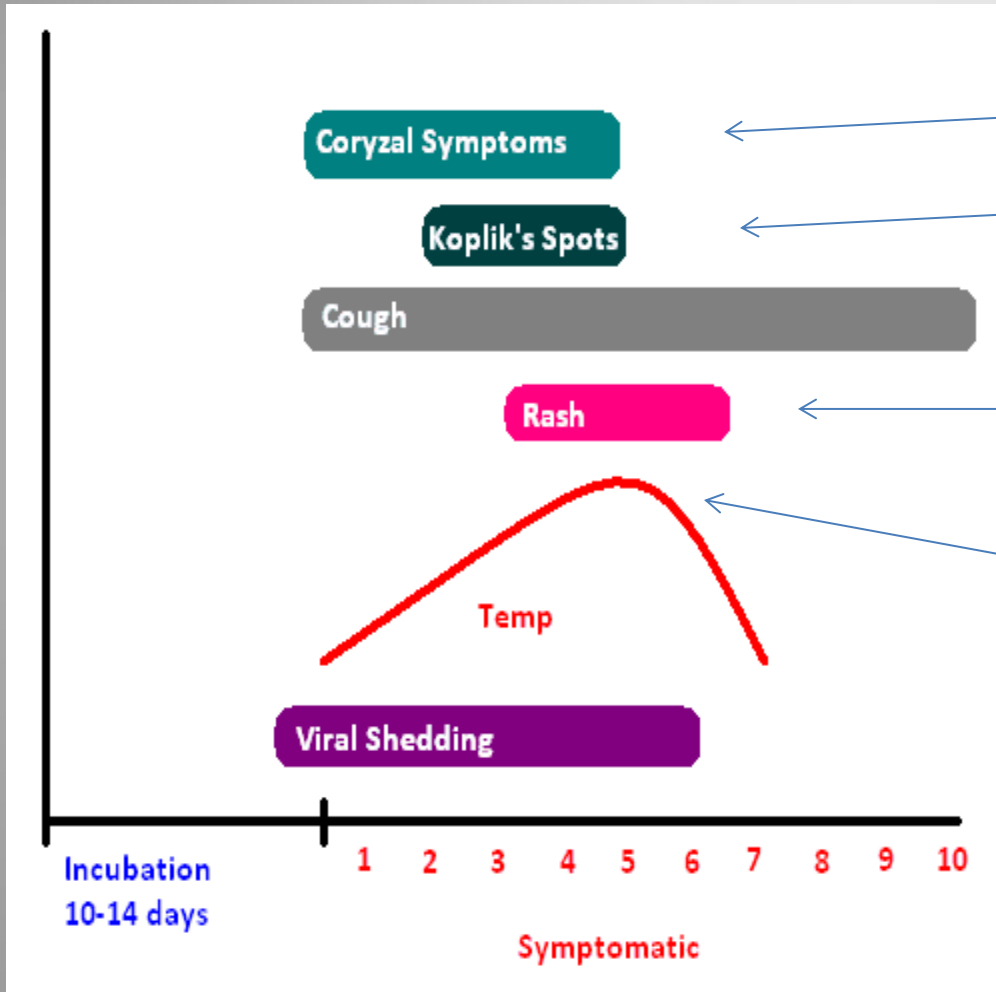
Late/severe symptoms

- bleeding under the skin, in internal organs, or from the mouth, eyes or ears
- CNS malfunctions
- coma
- delirium
- kidney failure
- respiratory failure
- liver failure

Measles

- Highly contagious infectious viral disease:
R zero (R_0) = 12 to >200 [NIH 2017]
- Of 1,000 unvaccinated people exposed:
 - 900 may get measles (90%)
 - 200 may need hospitalization (20%)
 - 1 (0.1%) may develop encephalitis or deafness
 - 2 may die (0.2%)
 - 70% of deaths may be due to pneumonia

Measles



Conjunctivitis, runny nose

Enanthem

Exanthem

May spike to $>104^{\circ}$ F

Typhus Fever


- A group of infectious diseases that include:
 - epidemic typhus: *Rickettsia prowasekii* (body lice)
 - scrub typhus: *Orientia tsutsugamushi* (chiggers)
 - murine: *Rickettsia typhi* (fleas on rats)
 - spotted fevers: *Rickettsia rickettsii* (dog & wood ticks)
- Symptoms include a rash, fever, headache, that begin 1 to 2 weeks after exposure.

Questions? 1



The Plague In Europe

- Three major pandemic outbreaks of plague in the 6th, 14th, and 19th centuries.
- It did not completely disappear in between.
- It kept reappearing in milder forms, with some regularity in Europe until the 17th century.



PLAGUE of JUSTINIAN

aka The First Plague Pandemic

Plague of Justinian ⁽¹⁾

541-542 AD

- Justinian I, emperor at the initial outbreak.
- He contracted the disease, but survived.
- Originated in Central Asia, in Qinghai, China.
- First reported from the port of Pelusium in Egypt.
- Spread east to Palestina and north to Alexandria.

Plague of Justinian ⁽²⁾

541-542 AD

- Several recurrences until 750 AD (2 centuries).
- About 25–50M dead (13–26% of the world's population in 541 AD).
- Procopius described 5,000 deaths/day in the capital Constantinople (killed 40% of city).

Plague of Justinian ⁽³⁾

541-542 AD

- Description of typical buboes and symptoms.
- Plague started in seaports and went inland.
- Typical of rat/flea transmission.
- Self-limited because it killed off susceptibles.

Plague of Justinian ⁽⁴⁾

541-542 AD

Symptoms:

- delusion
- high fever*
- swellings in armpits, groin, behind ears*
- some lapsed into comas
- others died almost immediately*
- rest of victims suffered for days before death

Plague of Justinian ⁽⁵⁾

541-542 AD

- Hit the Byzantine Empire, Constantinople, the Sasanian Empire and Mediterranean ports.
- Weakened Justinian's efforts to reunite the Western and the Eastern Roman Empires.
- Economic collapse of Byzantium:
 - agriculture and trade decreased
 - lost manpower
 - taxes lost
 - money spent on multiple wars

Plague of Justinian ⁽⁶⁾

Effects on the Empire

- In 568, the Lombards invaded Northern Italy and split the Italian peninsula.
- In North Africa & the Near East, the empire was unable to block Arabic invasions.
- Ongoing wars with the Goths in Italy and the Vandals in Carthage drained the empire's money.
- Armed forces decreased due to plague, loss of crops, lack of new recruits.

Plague of Justinian ⁽⁷⁾

Effects on the Empire

- Justinian liked luxuries and exporting goods, so his capital city became the leading market of the bubonic plague.
- Procopius, in his work *Secret History*, declared that Justinian was a demon of an emperor who either created the plague himself or was being punished for his sinfulness.
- Society subsequently became more violent as the mass mortality rate cheapened life, increased warfare, crime, popular revolt, waves of flagellants, and persecution.

Plague of Justinian

- The Justinian Plague has been conceived by historians as a Mediterranean phenomenon.
- Bacterial genetics reveals that the Justinian Plague was a biological disease event originating thousands of miles away, in Central China.
- When and by what route plague made its trek from Central Asia to the Mediterranean, we still don't fully know.



**SECOND PLAGUE PANDEMIC
1347-1351**

In the 14th Century: 1346-1353

The Great Plague

Issues of Dissent

1. Agent

- Were some of the plagues viral epidemics ?
- Were all Plagues caused by *Yersinia pestis*?
- Were some a combination of agents?
- Do we even have a clue?

Issues of Dissent

2. Origin

- The Tibetan plateau?
- Central China?
- Khanate of the Golden Horde?
- Land Silk Route?

Issues of Dissent

3. Number

- Were the 3 plague pandemics the same plague?
- Was the 2nd plague pandemic one single disease?
- Is the 3rd plague pandemic over?

Issues of Dissent

4. Speed and Distance

- Speeds of medieval vs. modern plagues differ
- Rat-flea theory can't explain rapid land spread
- How did it go so far so fast?
- Human to human transfer a real possibility

Issues of Dissent

5. Vector

- Black ship rats and their fleas?
- Other rodents (marmots, voles, gerbils)?
- Humans and their fleas and ticks?
- Foods, grains, spices, merchandise?

The Plague

- **First:** forget almost everything you have ever learned about the Plague.
- **Second:** Separate the tales and stories from the historical writings and the epidemiologic facts.
- **Third:** Partially absolve the rats and their fleas.
- **Fourth:** Blame humans, their lice and fleas.

Stories

- Every story we tell has a history.
- Every argument we propose in reconstructing the histories of plague is made up of layers of prior “truths” originated in stories.
- That includes the stories from which science investigations begin.

Previously Believed

- The Genoese traders fled, taking the plague by ship into Sicily, then the Italian mainland, then it spread north.
- By the end of 1346, reports of plague had reached the seaports of Europe.
- Several pre-existing conditions, such as war, famine, malnutrition and weather, contributed to the severe mortality of the Black Death.

Previously believed

- Mongols may have brought plague along the Silk Road with armies and traders, from the Ulus of Jochi and the Khanate of the Golden Horde.
- Genoese traders from the port city of Caffa in the Crimea first brought Plague to Europe in 1347.
- During a long siege of the city by the Mongol Jani Beg, his army, (which was suffering from the disease) catapulted infected corpses over the city walls of Caffa to infect the inhabitants (1st instance of biologic warfare).

New Theories

- Long-standing marmot foci in the Tian Shan mountains, not the Tibetan Plateau, were the likely site of plague's proliferation in the Big Bang.
- The Second Plague Pandemic was the sustained transmission of multiple clones of a single strain of *Yersinia pestis*.
- Once they moved into new ecologies and proliferated, each niche originated new lineages with their own genetic signatures.
- Those proliferating strains even when carried into new marmot populations, were not contiguous with the foci in the Tian Shan.

Mongols and the Plague

- The lineages created by the late medieval polytomy come from the Tian Shan Mountains, between modern China and Kyrgyzstan.
- Mongols got the disease through plague-ridden marmots, which they used not only for food and fur, but also as a source of leather.
- Foreign observers of the Mongols (Islamic, Christian, & Buddhist) noted the predilection the Mongols had for eating rodents.
- To successfully move long distances, plague doesn't need to have caused massive deaths.

Newer Beliefs

- Most (or all) late medieval and early modern plague epidemics were caused by *Yersinia pestis*, as were the Justinian plagues (AD 542–767), and possibly the Plague of the Philistines, described in 1 Samuel, about 1100 BC.
- Most (or all) of the historical European plague epidemics did not involve rats as intermediate hosts.
- The main mode of transmission was from human to human via an insect vector.
- *Pulex irritans* may have been the most important arthropod vector in Europe prior to the late 19th century, but other ectoparasites (other fleas, lice, etc.) could also have been involved.

Where did it Start?

- Black Death historiography connects the outbreak that started in 1346 in the Ulus of Jochi to events farther East, around Lake Issyk Kul in Kyrgyzstan, or as far as Eastern China.
- The plague events of either central or eastern Asia are dated a decade or so before the events several thousand kilometers away, in the Caucasus and Crimea (the previously accepted history).
- Plague, incapable of sustained human transmission and with implausible rapid long-distance movement causes skepticism about a single, west-moving, late medieval, Eurasian pandemic.

Monica Green 2020

Plague Historiography

(**False** Assumptions)

- The Black Death was a single continent-wide, limited plague with East-to-West sweep across Eurasia in the 14th century.
- The Black Death was a story of “rodents on the march” across vast landscapes.
- Plague’s story is about the creeping spread of disease by waves of traveling merchants along the “Silk Road” during a *Pax Mongolica*.

Monica Green

Questions for Biology

- “What was the disease?” has been set aside, and replaced by:
 - What strains were involved in particular outbreaks?
 - To which other strains are they most closely related?
 - Where and when can these be documented?
- The biological archive provides support for both the traditional narratives about the western Eurasian experience of the Black Death and the new evolutionary history of *Y. pestis*.
- Plague was, indeed, suddenly and terrifyingly visible in the Ilkhanate, the Golden Horde, the Black Sea, and the Mediterranean in the 1330s and 1340s

Differences between 2nd and 3rd Pandemics

no accounts of rat deaths before outbreaks between 14th and 17th centuries

temperatures too cold in northern Europe for the survival of fleas

despite primitive transportation, spread of the Black Death was much faster than modern bubonic plague

the Black Death indiscriminately struck urban and rural areas with very high mortality, while modern bubonic plague is a largely endemic rural disease

major outbreaks of the Black Death occur every 5 to 15 years in the same areas while modern bubonic plague often becomes endemic with annual flare-ups

Transmission Theories

- Most authors believed that Simond's infection model, **black rat** → **rat flea** → **human**, is the only way an epidemic of *Yersinia pestis* infection could spread.
- Green has argued that greater attention is needed to the range of animals (especially non-commensal) that might be involved in the transmission of plague.

Transmission Theories

- Barney Sloane argues that there is insufficient evidence of numerous rat deaths in the medieval waterfront in London or that plague was spread from fleas on rats.
- His theory is that transmission must have been person-to-person.
- This is supported by research in 2018 which suggested transmission during the 2nd plague pandemic was more likely by human body lice and human fleas.

What a Lousy Story!



Body Lice

Pediculus humanus corporis



Pubic Lice

Pthirus pubis



Head Lice

Pediculus humanus capitis



Can carry Plague!

Lice

- Many species of insects, lice, ticks and fleas, have been shown to be capable of transmitting plague between different animal species and from different animals to humans.
- Only the human flea *Pulex irritans* and the human body louse *Pediculus humanus humanus* could possibly have been present in all European countries and in sufficient numbers to be real candidates.
- The body louse transmits typhus between human subjects, and there is now evidence that it can also spread plague.
- The report from the plague in Glasgow in 1900 says: “The homes (of the plague victims) consisted of a single room kept in a dirty, unventilated and overcrowded state, and swarming with vermin.”

Lice and the Plague

- Fleas are undisputed vectors of *Y. pestis* from rodents to humans, but body lice had a strong role as a **human-to-human** vector of plague during the Black Death.
- 10 infected lice are sufficient to transmit plague, and a dead plague patient with as few as 30 body lice can be a source of plague for 3 days after death.

Lice and Diseases

Human lice can be very efficient plague vectors through infected feces, suggesting that *Y pestis* could be a louse-borne disease, similar to:

- *Borrelia recurrentis* (relapsing fever)
- *Rickettsia prowazekii* (epidemic typhus)
- *Bartonella quintana* (trench fever)

Lice and Diseases

- Louse-borne outbreaks often involve multiple pathogens: several cases of co-transmission of *Y pestis* and *B quintana* have been reported and *B recurrentis*, was found to be circulating in northern Europe during the 2nd plague pandemic (14th–18th centuries).
- Large historical pandemics can be blamed on multiple bacteria, suggesting that human lice played a preponderant role in the interhuman transmission of plague and co-transmission of pathogens.

Rat fleas or Human fleas?

- In 1914, AW Bacot and CJ Martin showed that *Xenopsylla cheopis* fleas are particularly able to transmit plague between rats.
- In most modern plague epidemics where no *Xenopsylla cheopis* have been identified, large numbers of the human flea *Pulex irritans* have been found instead.
- In an official WHO publication on plague in 1960, Robert Pollitzer concluded, “*Pulex irritans* plays the main role in the spread of human plague.”

Spread of the Plague

Mediterranean
and Italian
Seaports

Sea of
Azof,
Caffa,
and the
Black Sea

Khanate
of the
Golden
Horde

Caravans,
trade
routes,
and the
Silk Road

CHINA

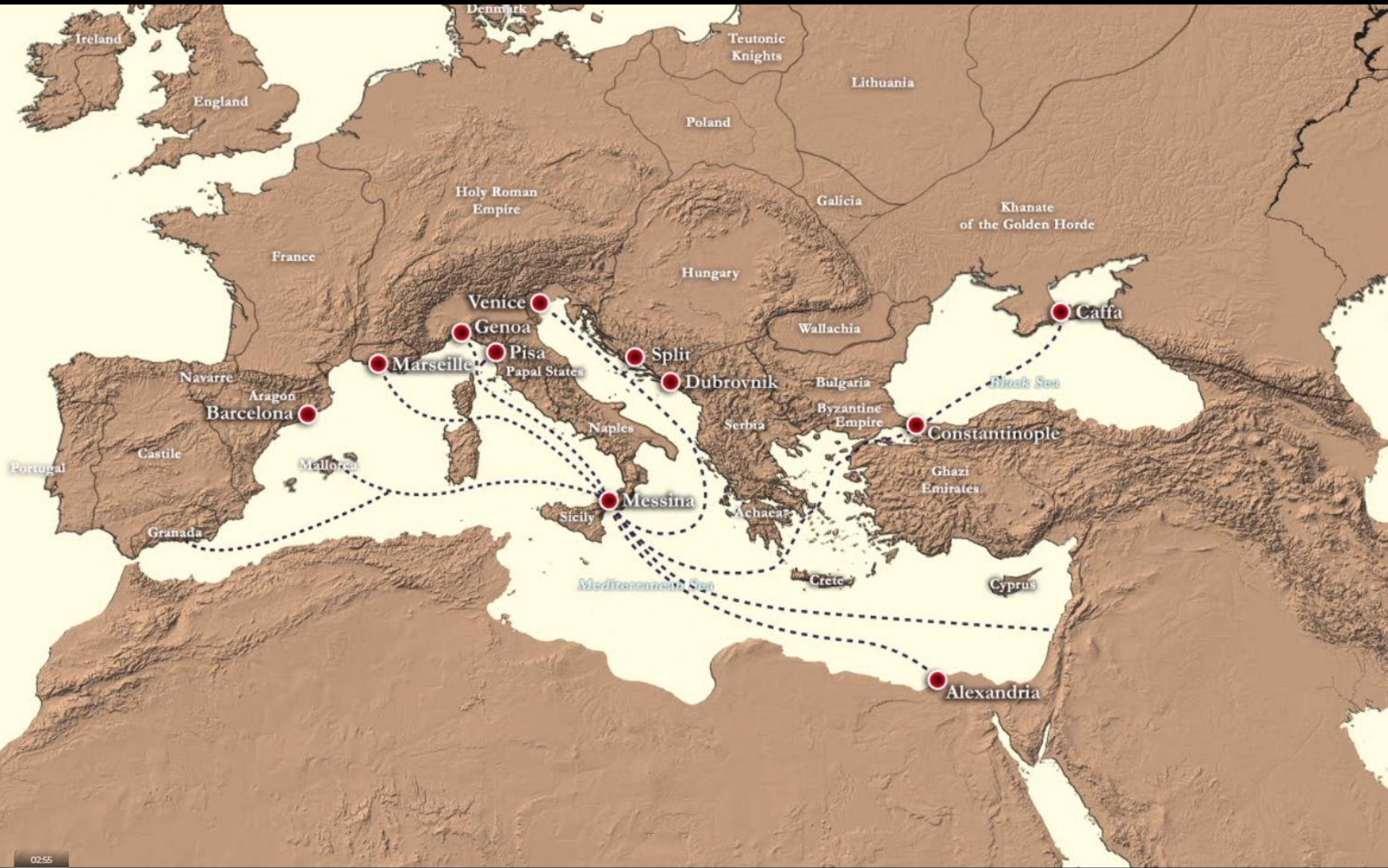
WEST

EAST

Khanate of the Golden Horde (Ulus of Jochi)



Plague Spread Over Water Routes



1 - 7 - 23 Rule

Distance and rate of movement

- 1 day by sea



- 7 days by horse

The Plague
traveled about
2.5 miles/day

- 23 days by foot



World Spread of the Plague

Spread graphic starts from the East (right) and progresses to the West (left).

1345



1345



1345



1346



1346



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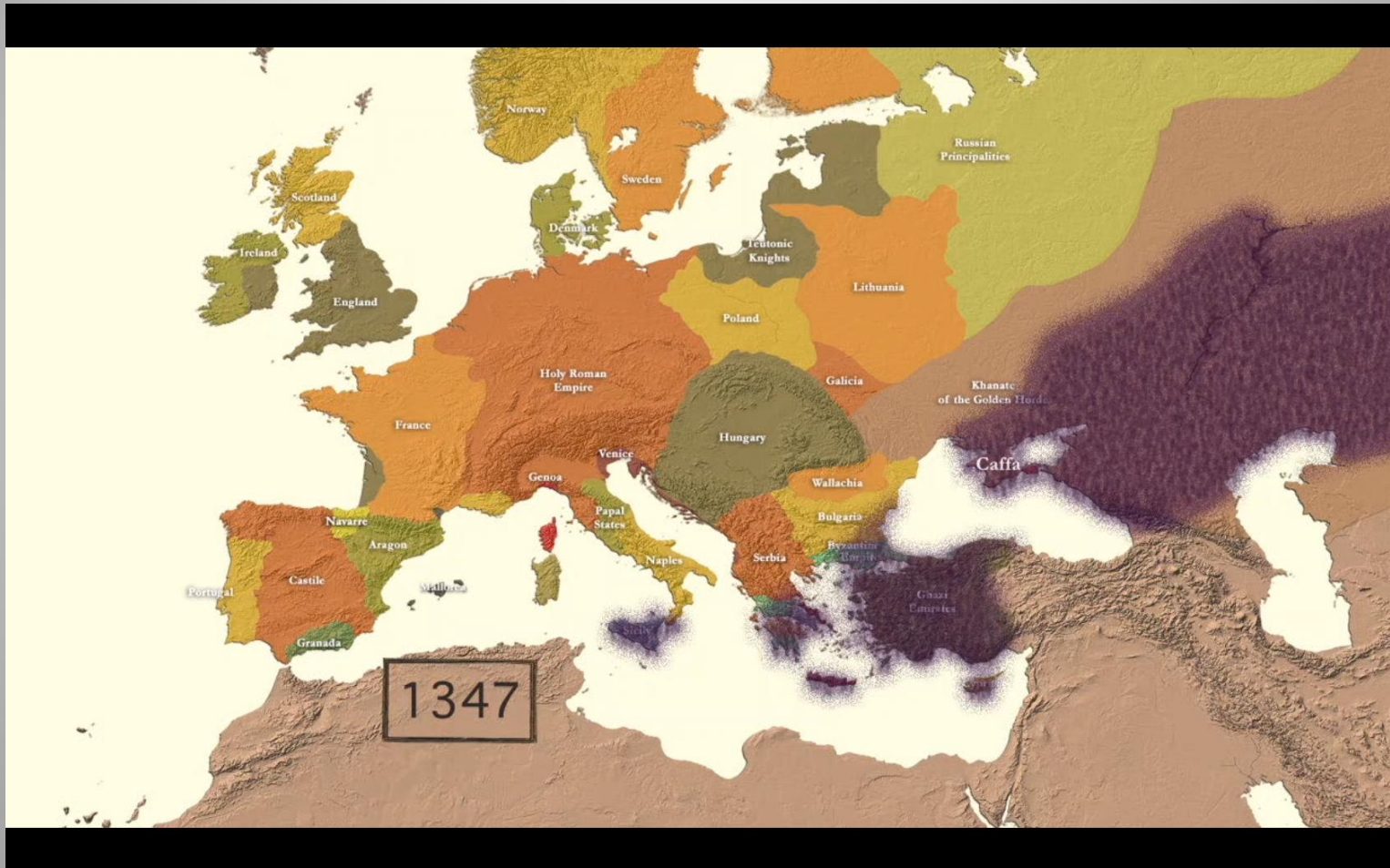
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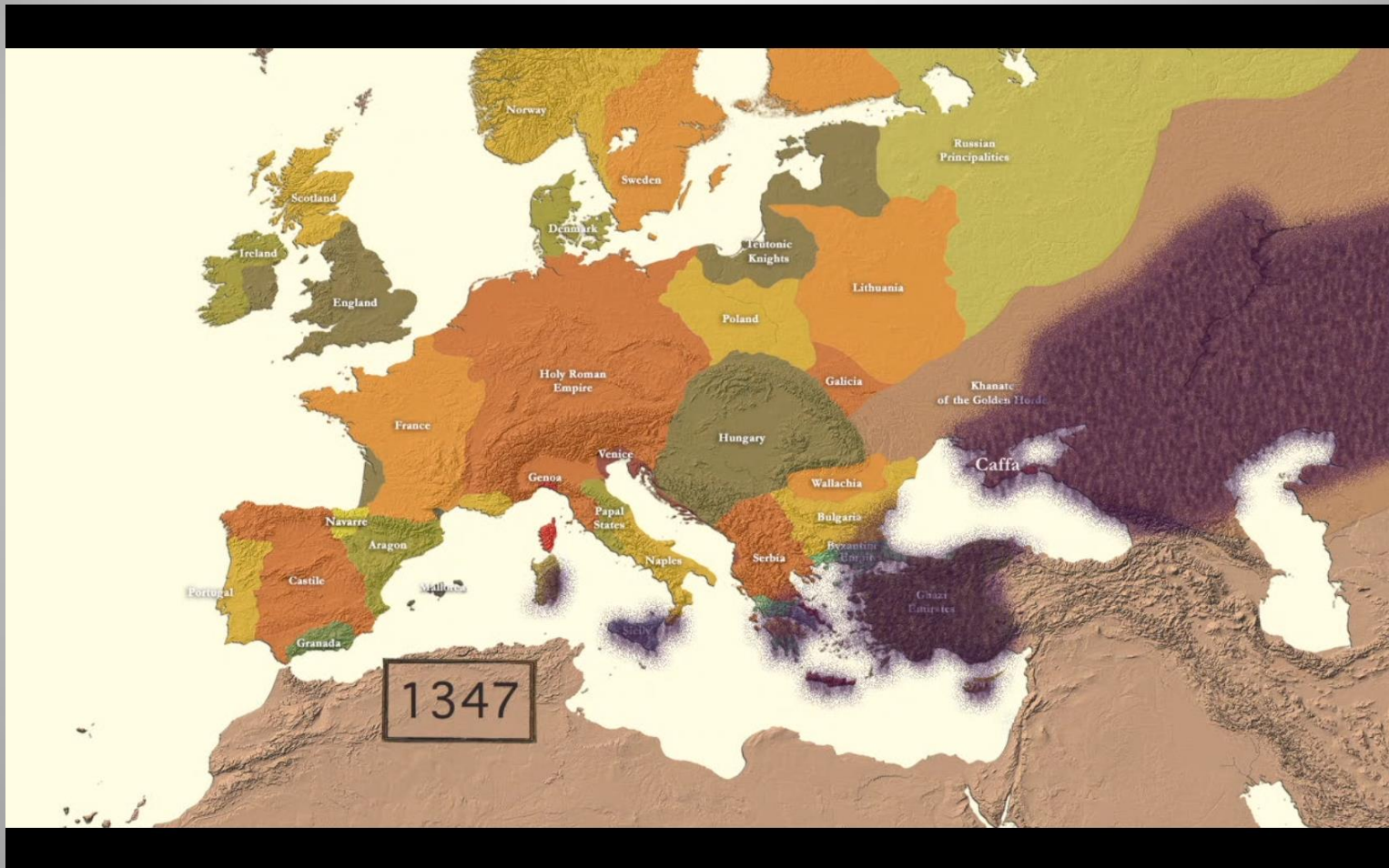
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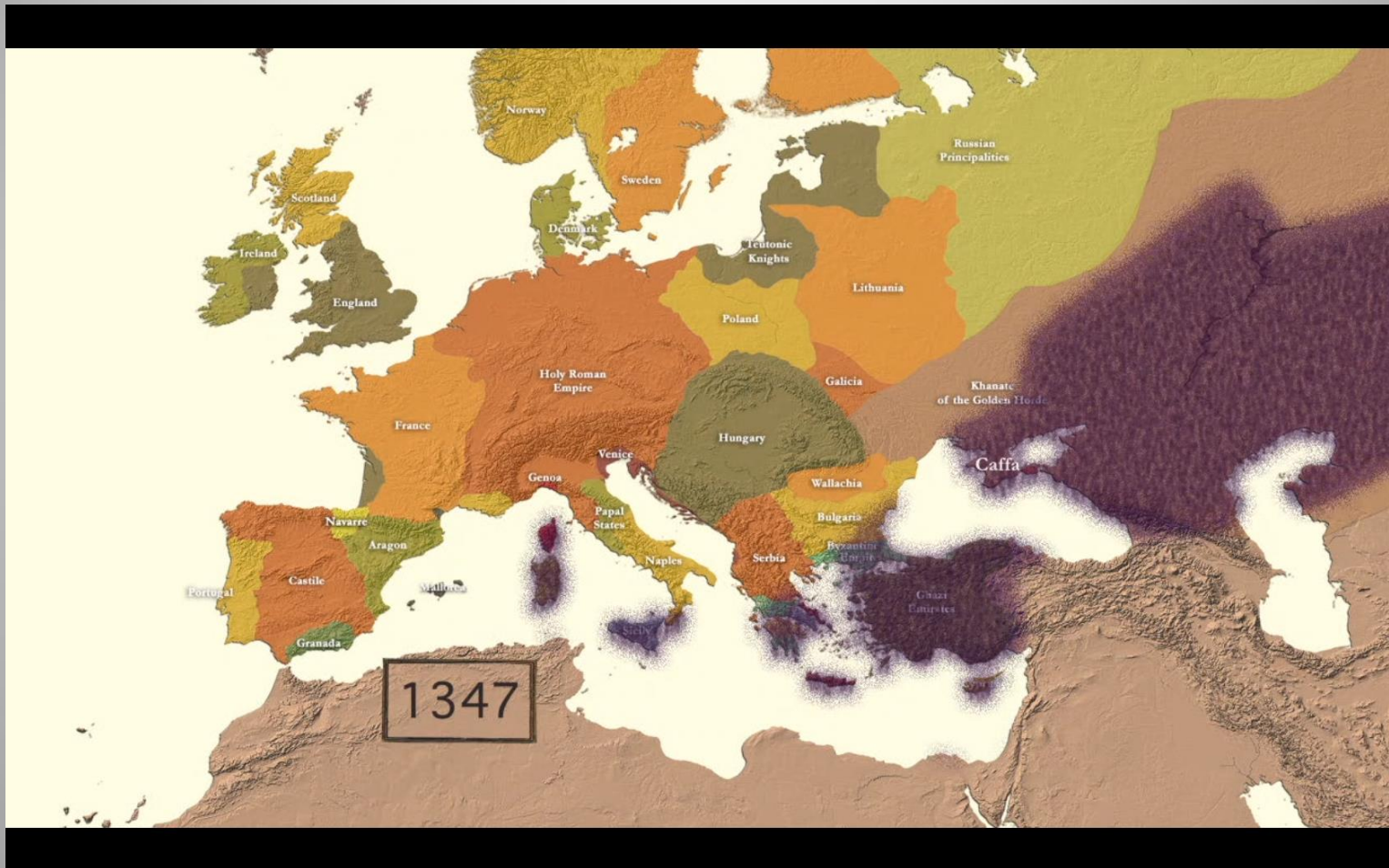
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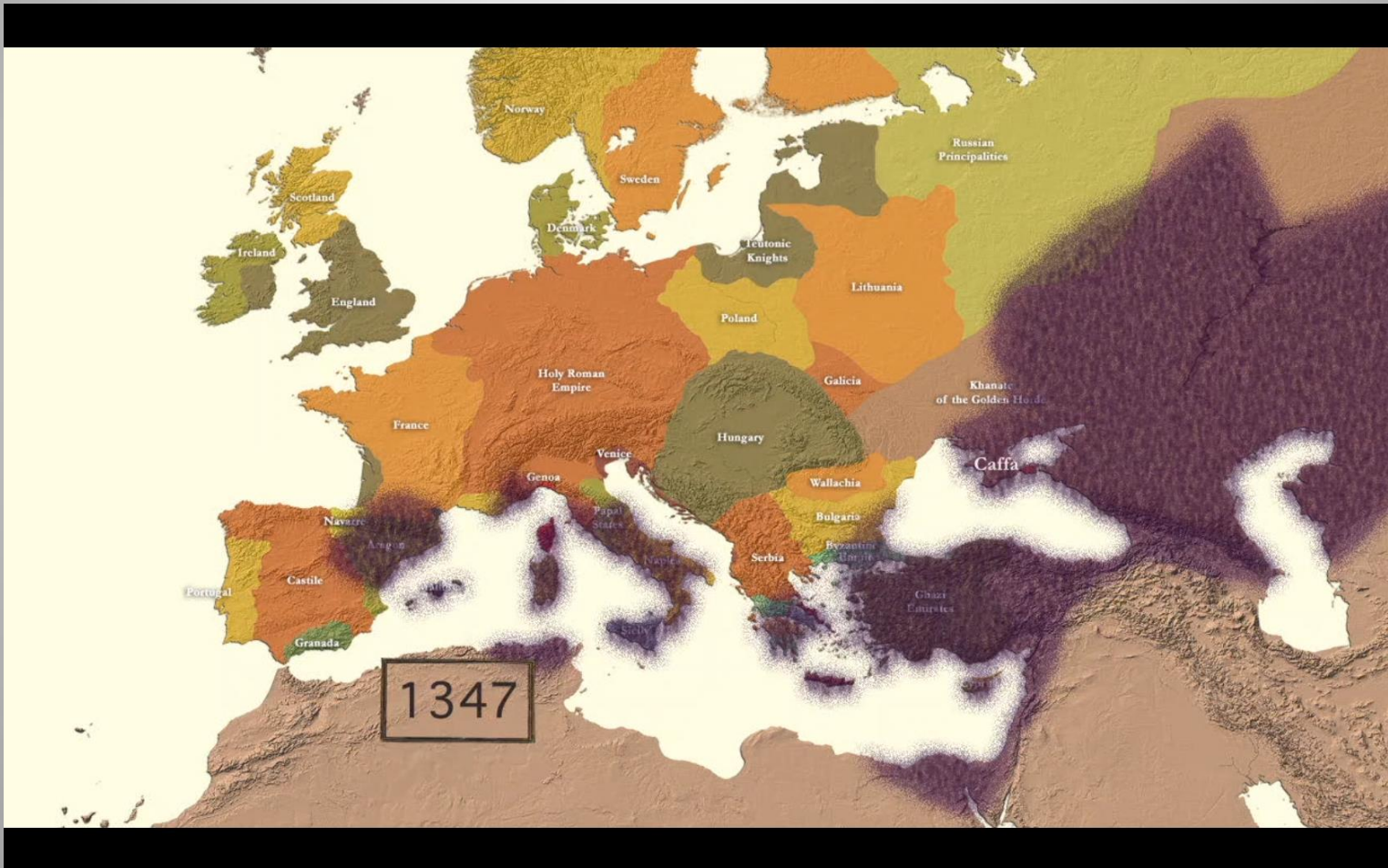
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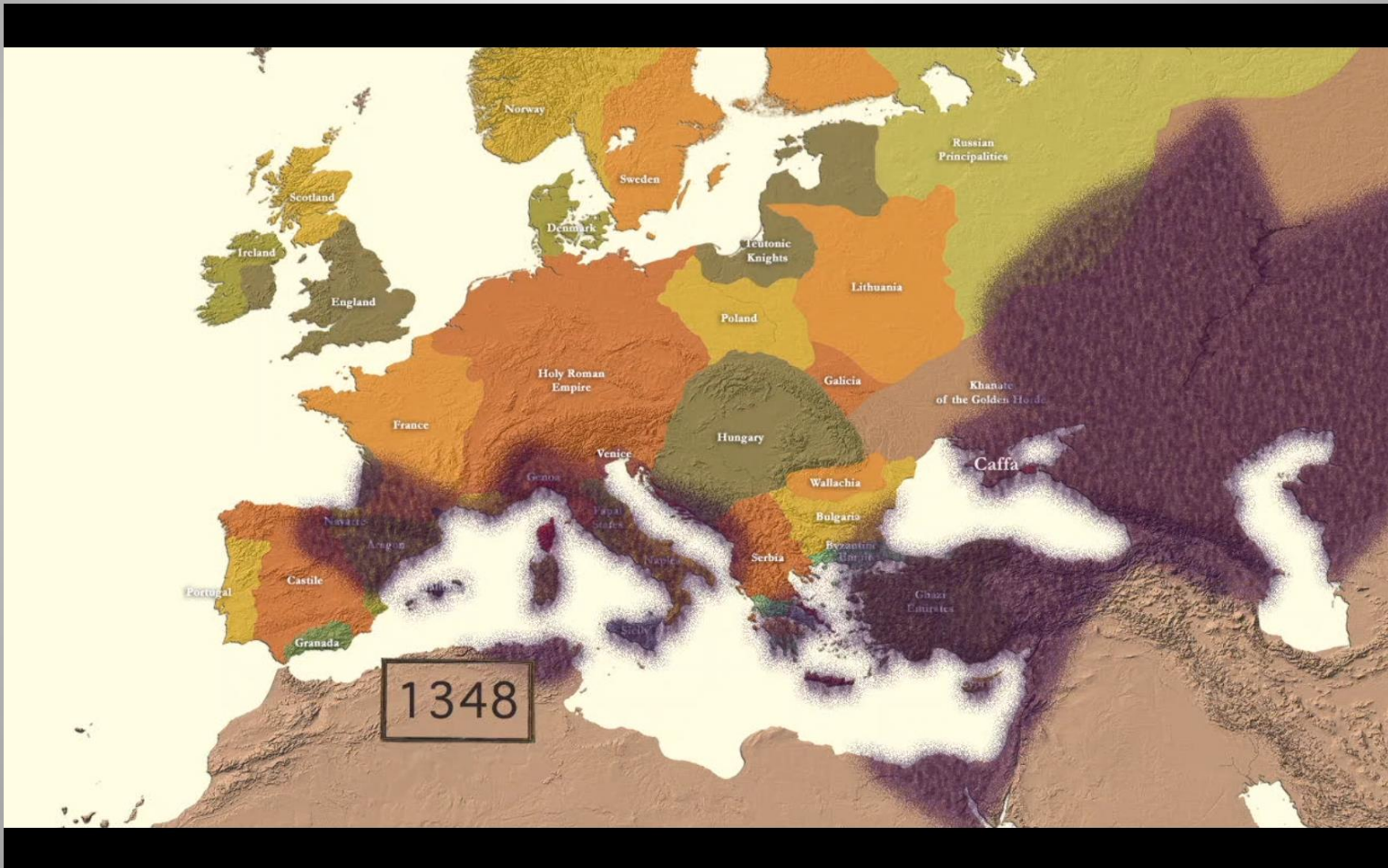
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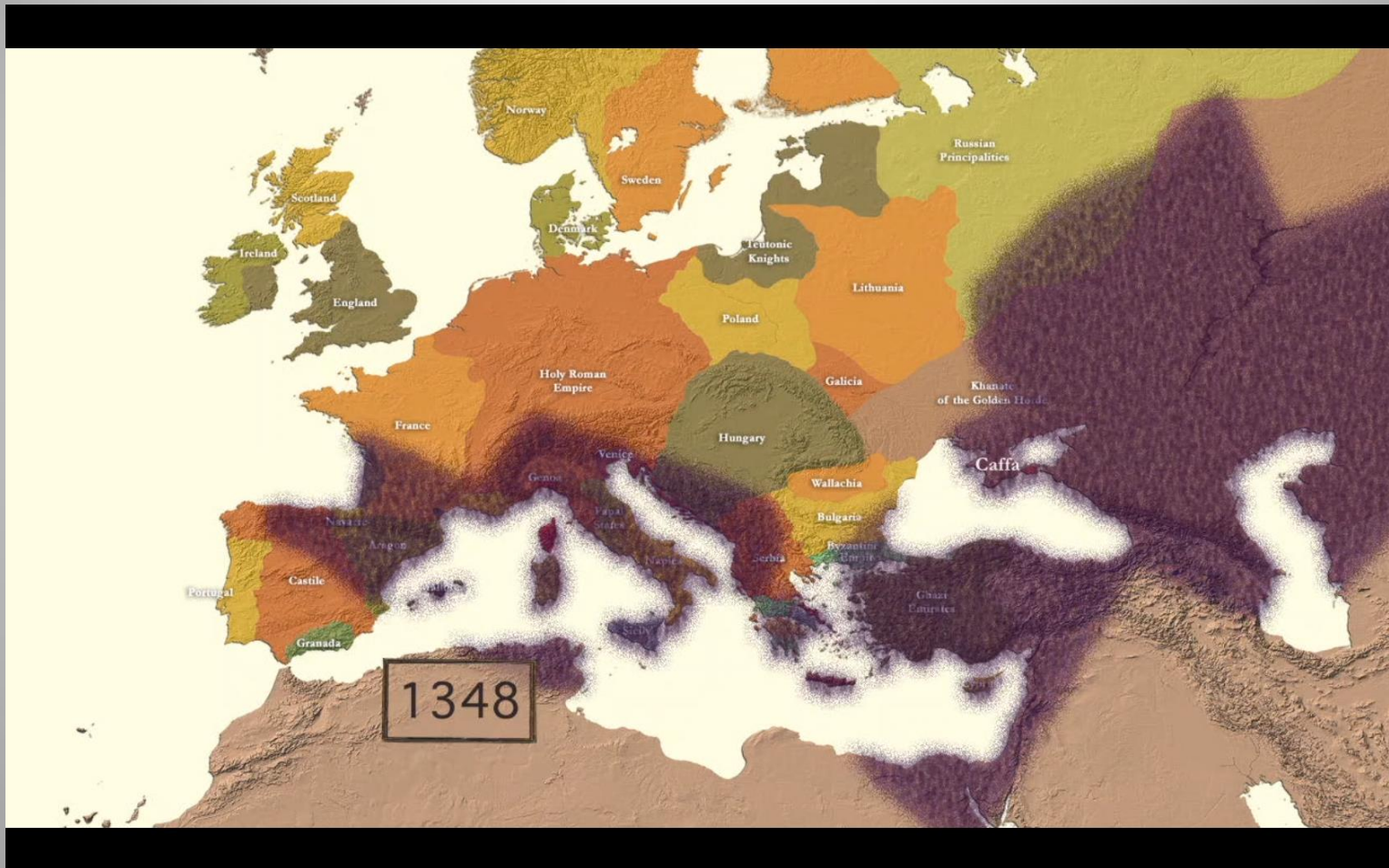
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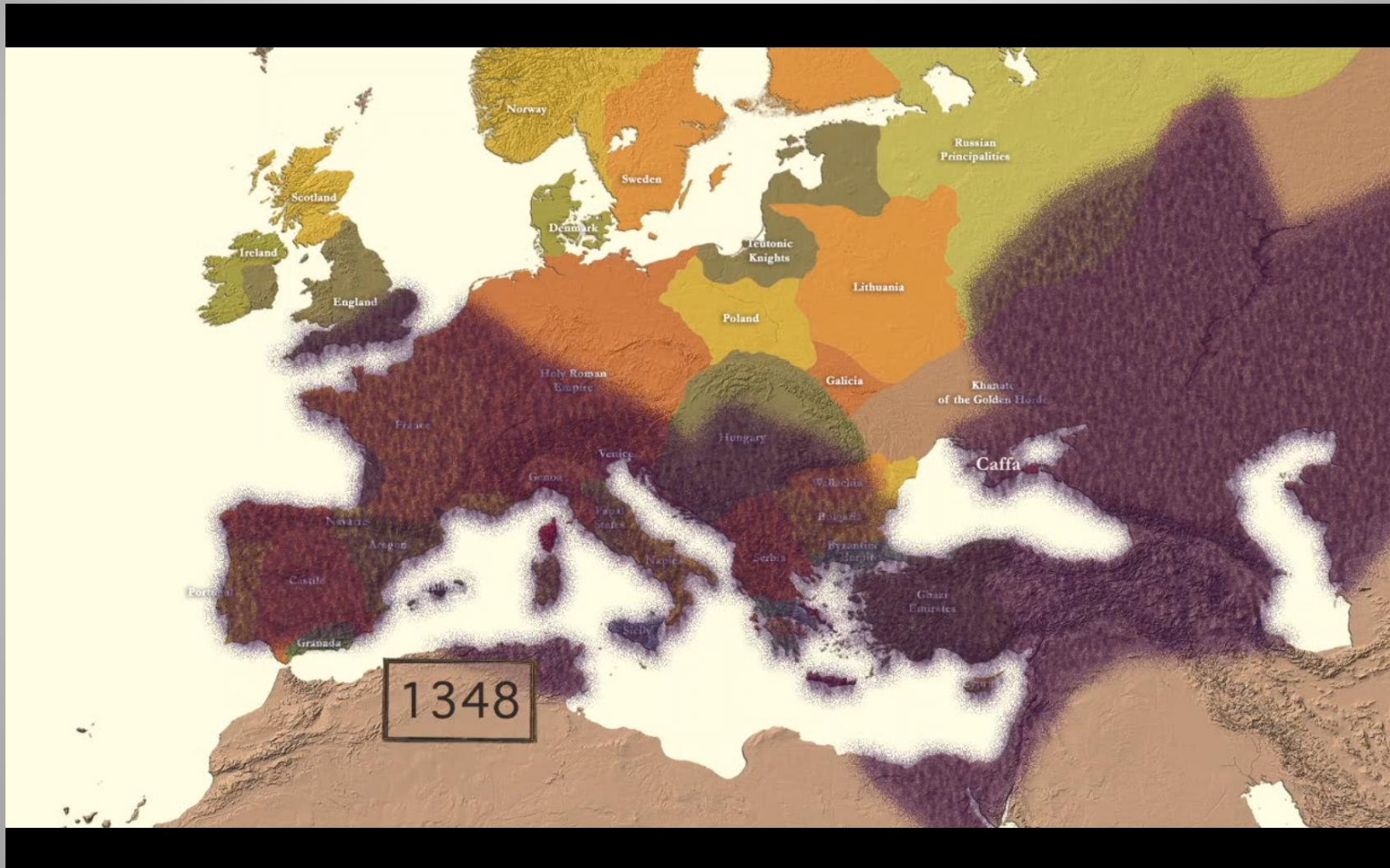
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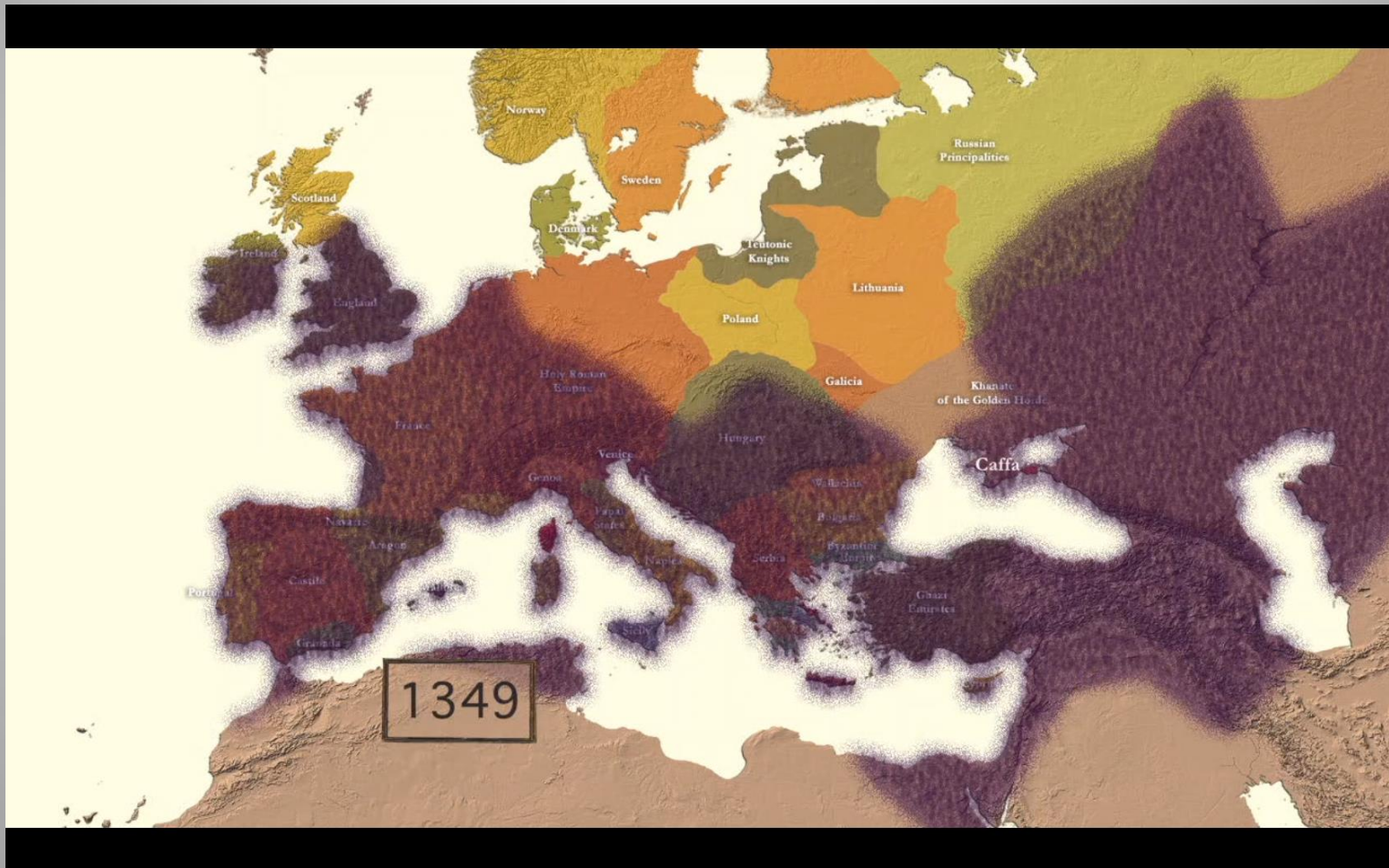
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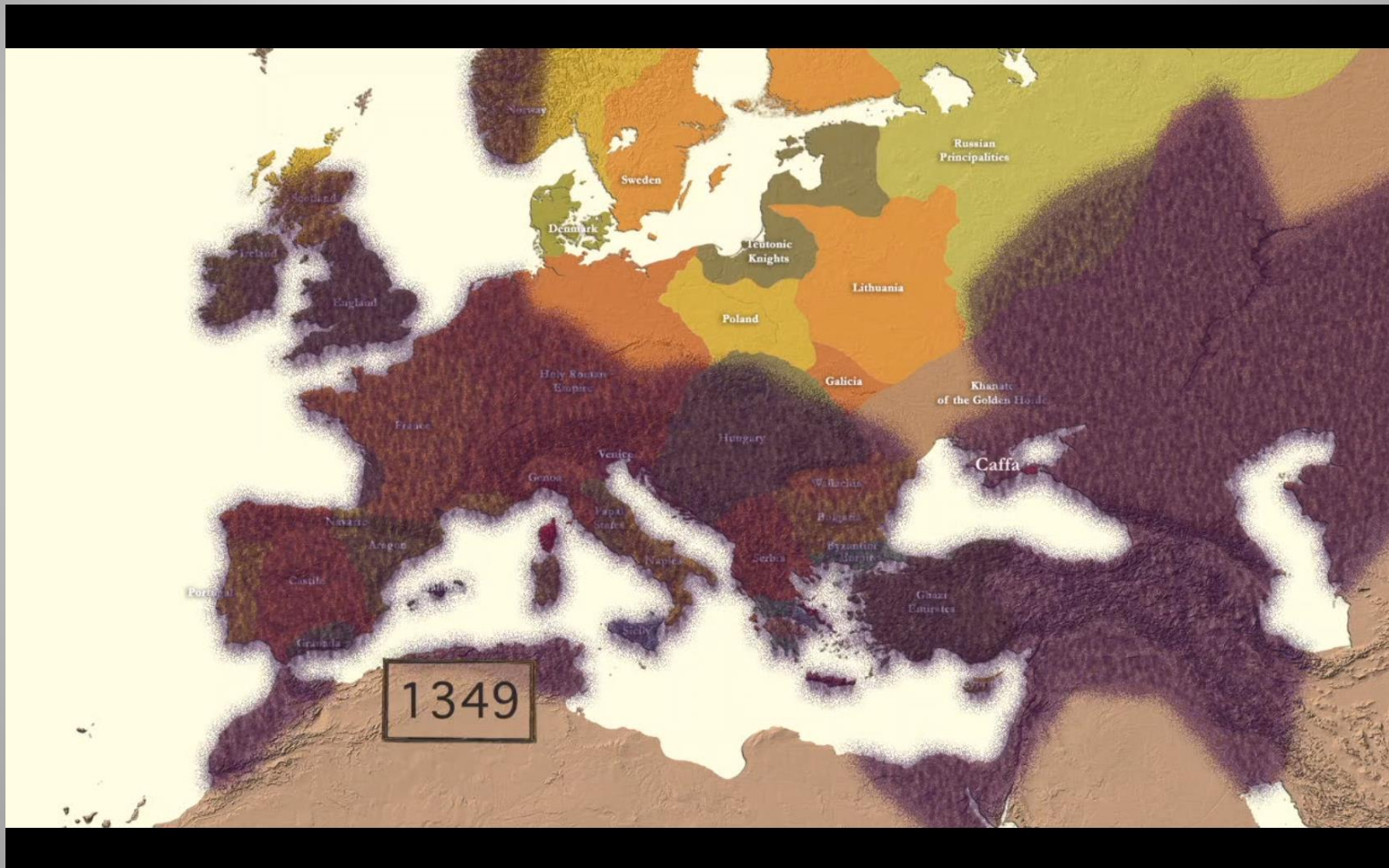
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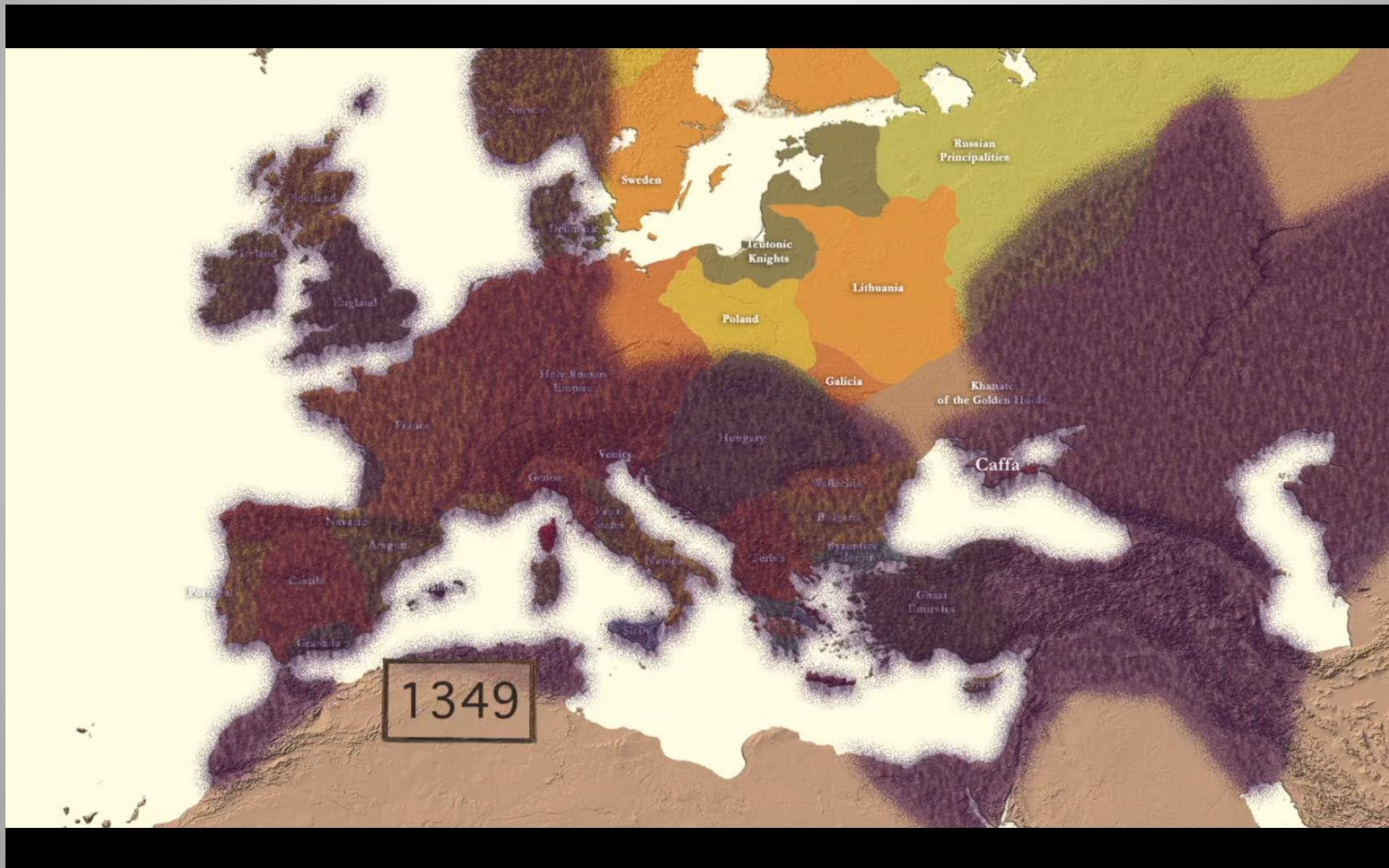
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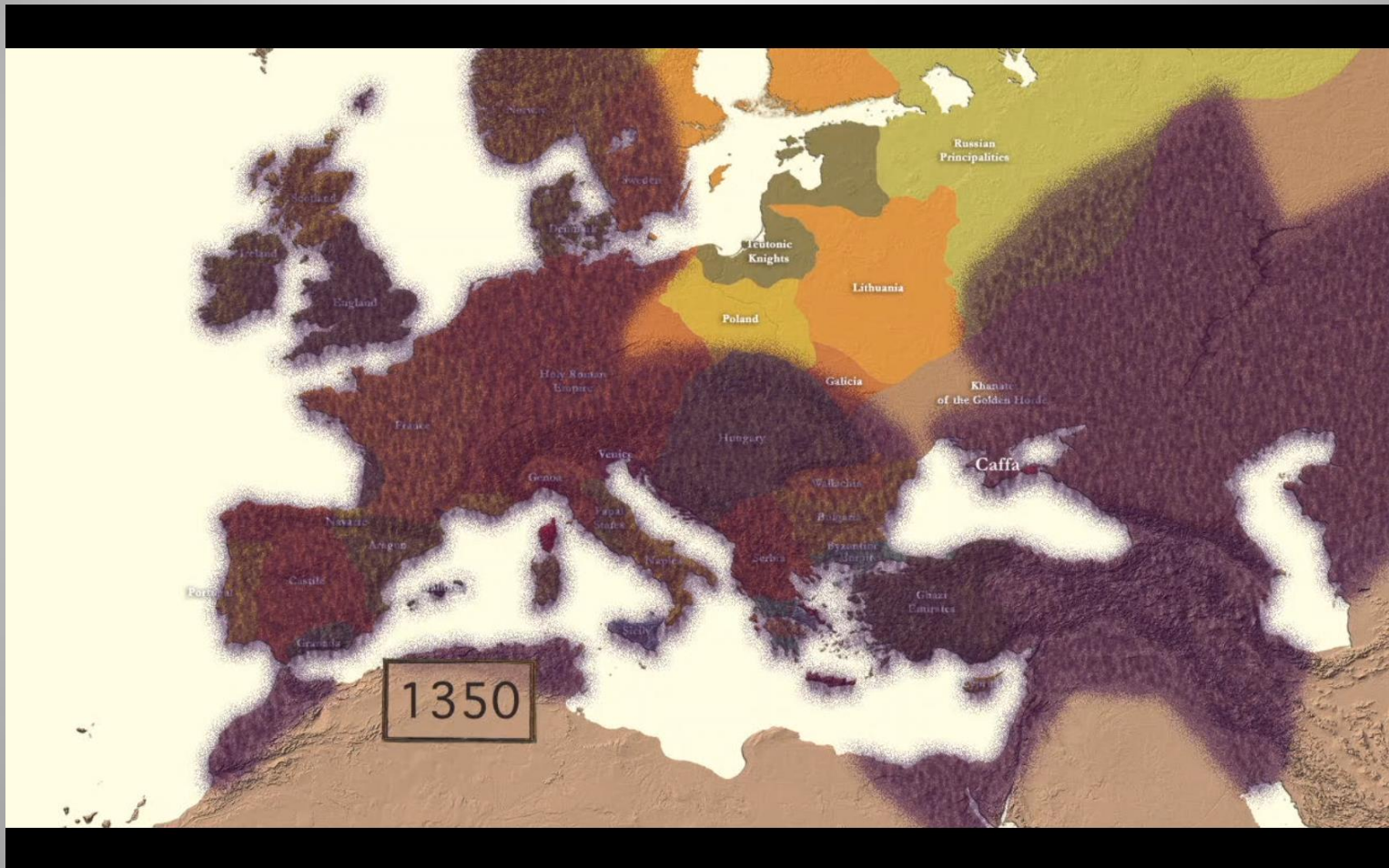
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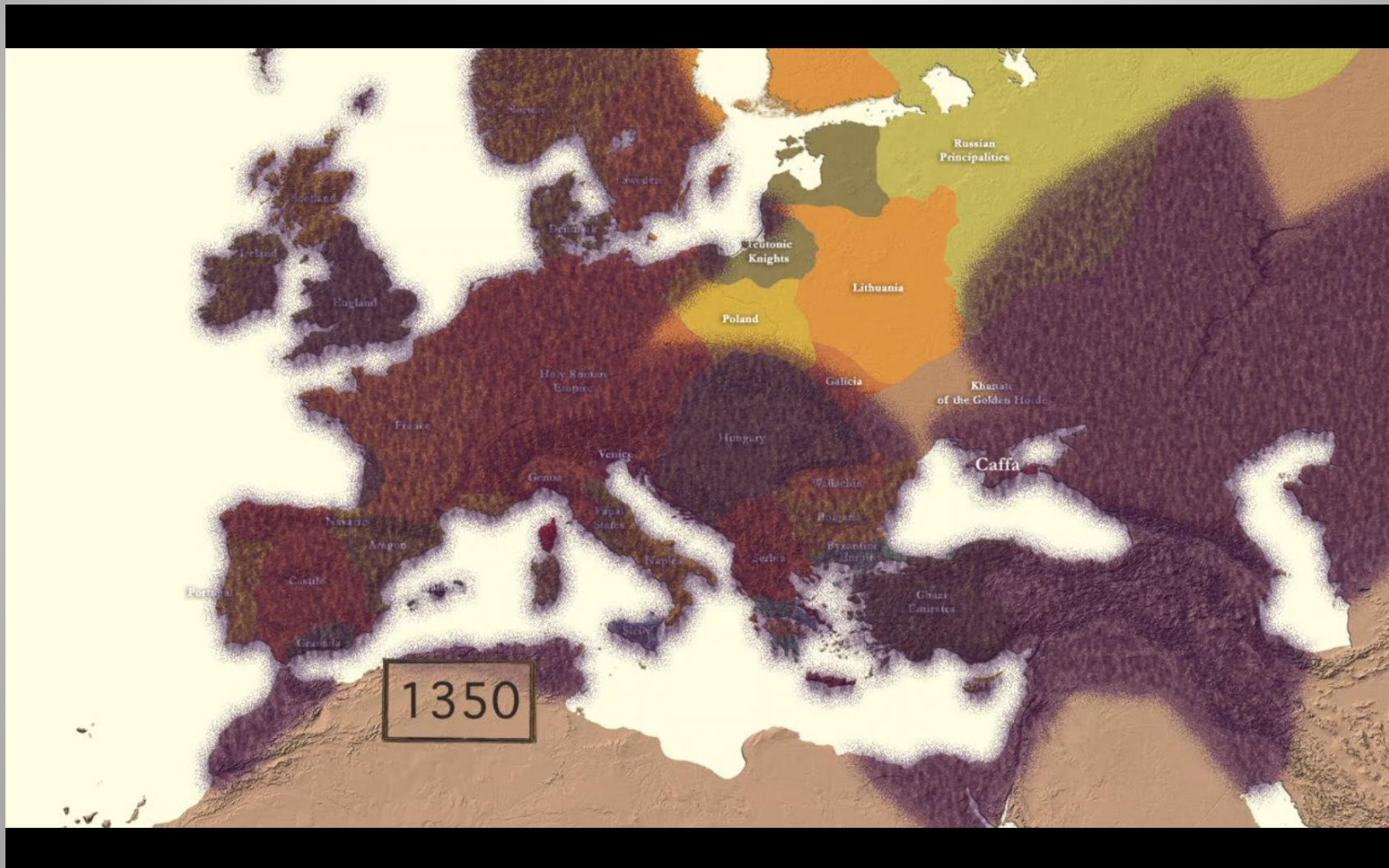
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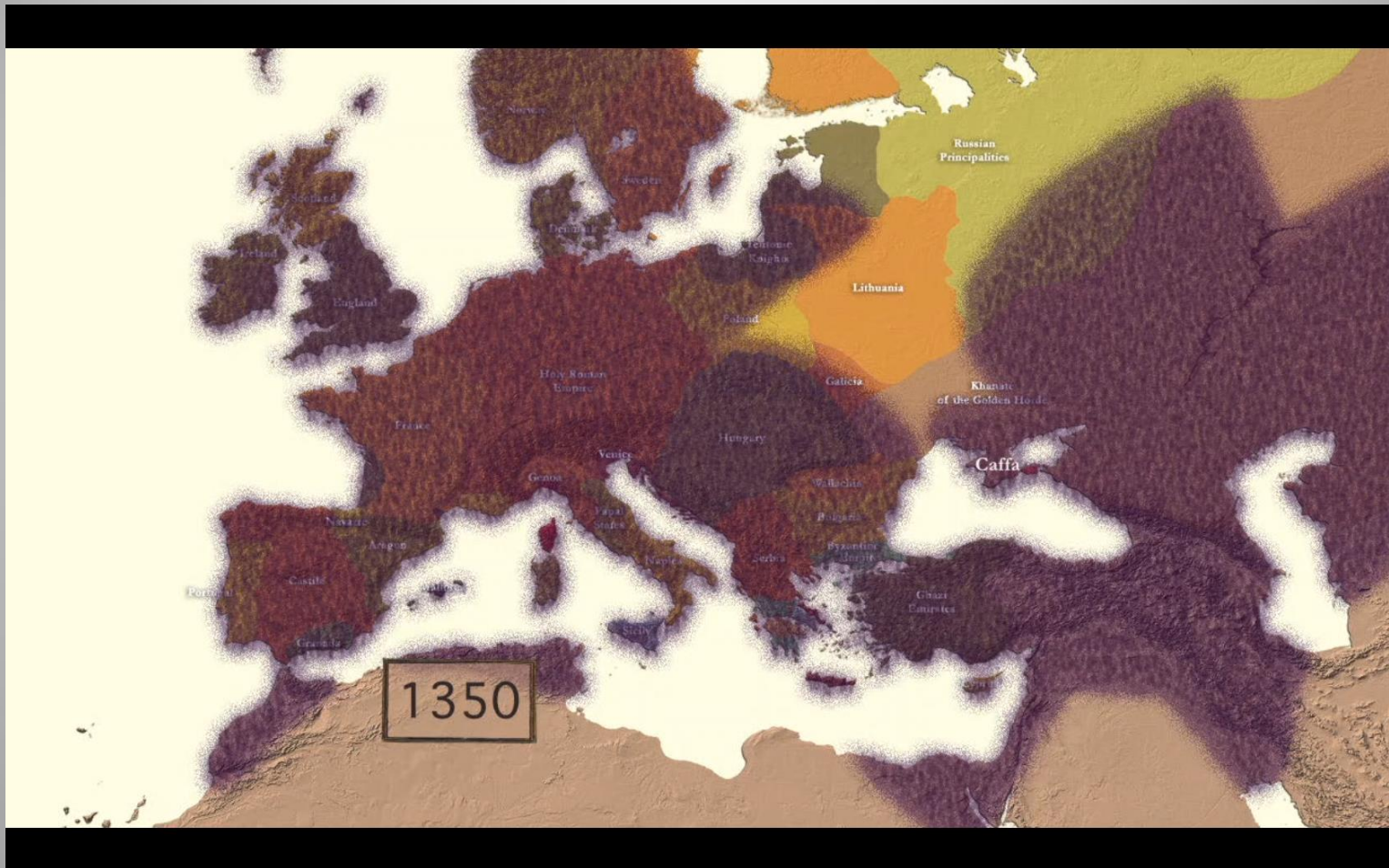
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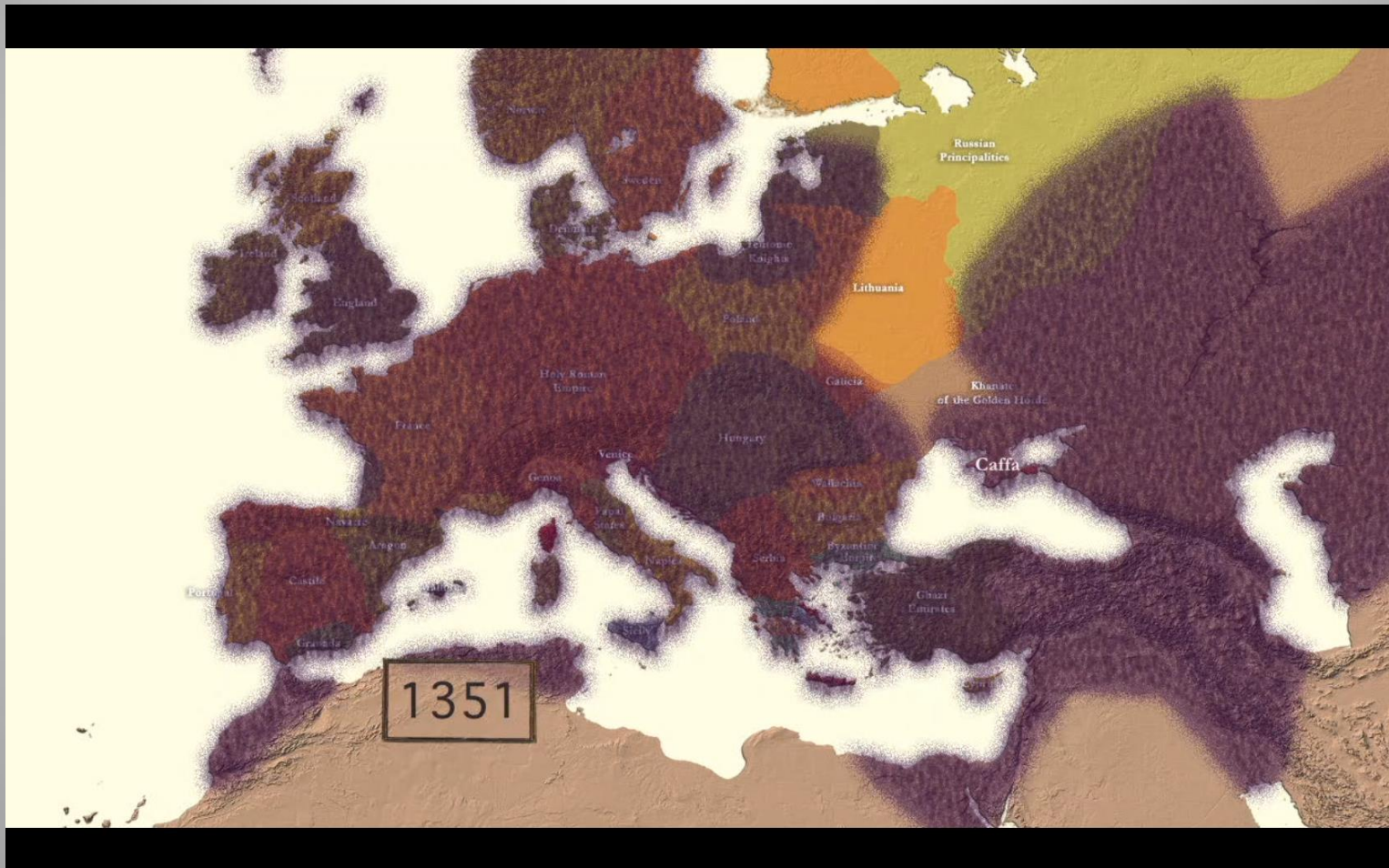
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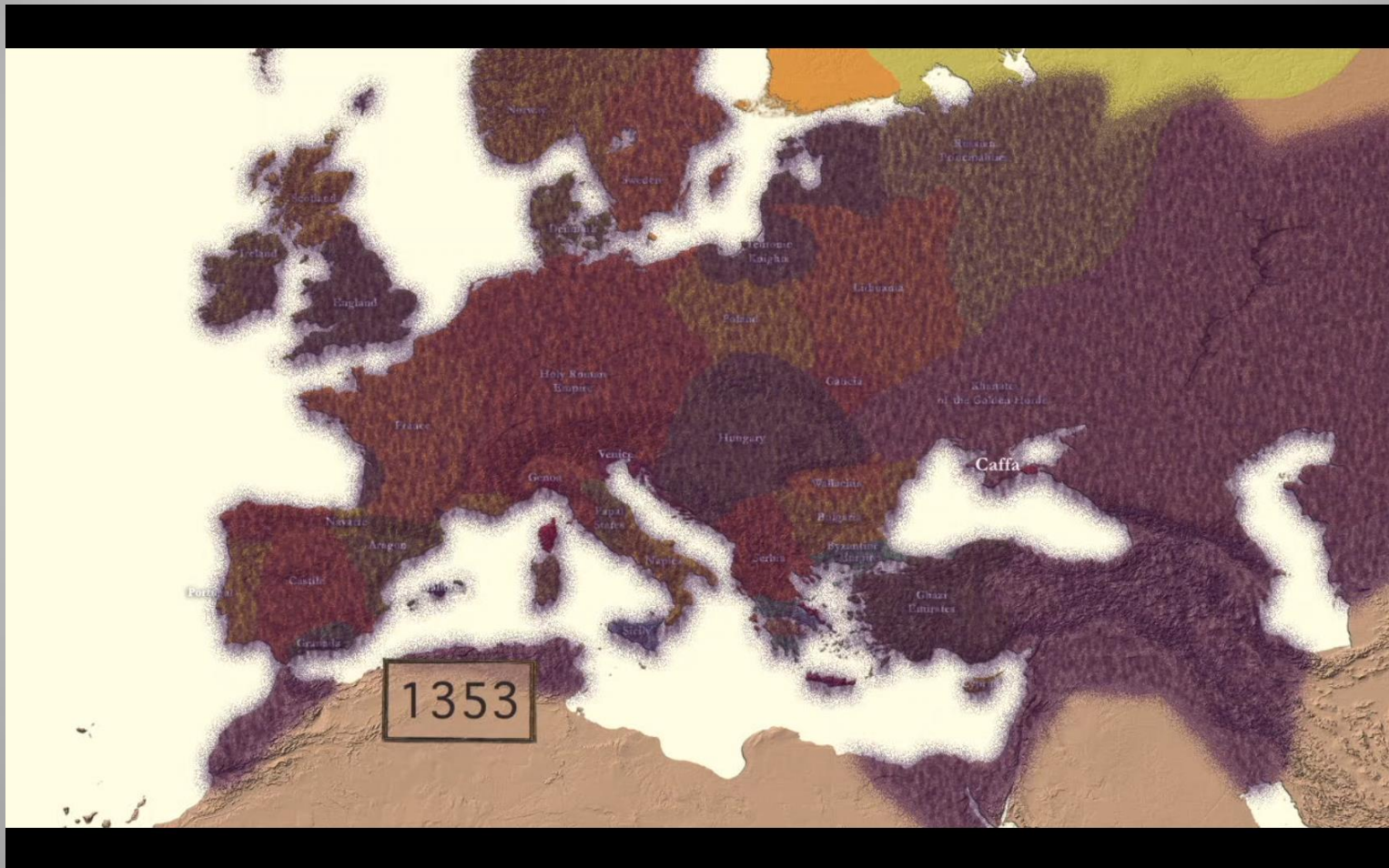
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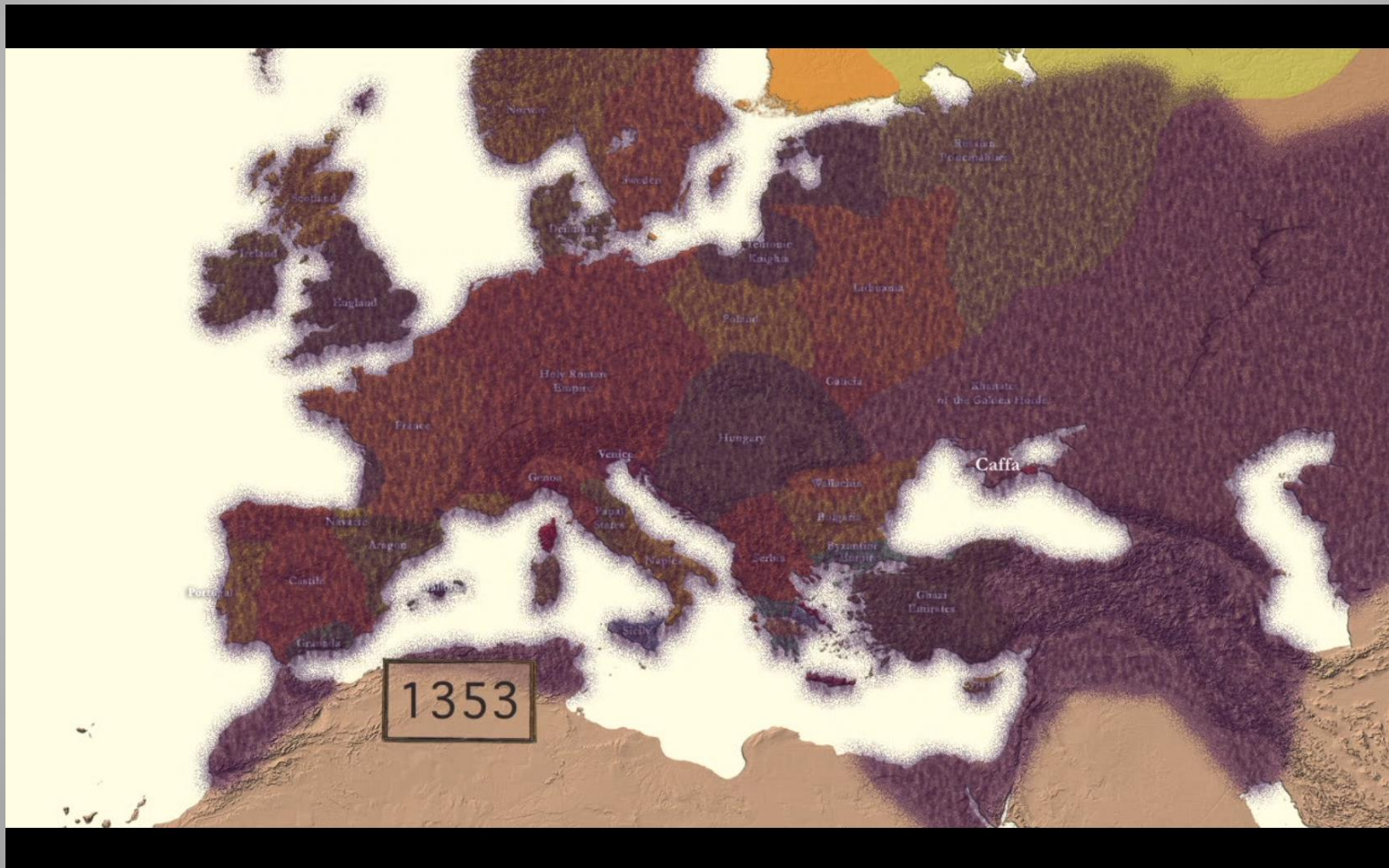
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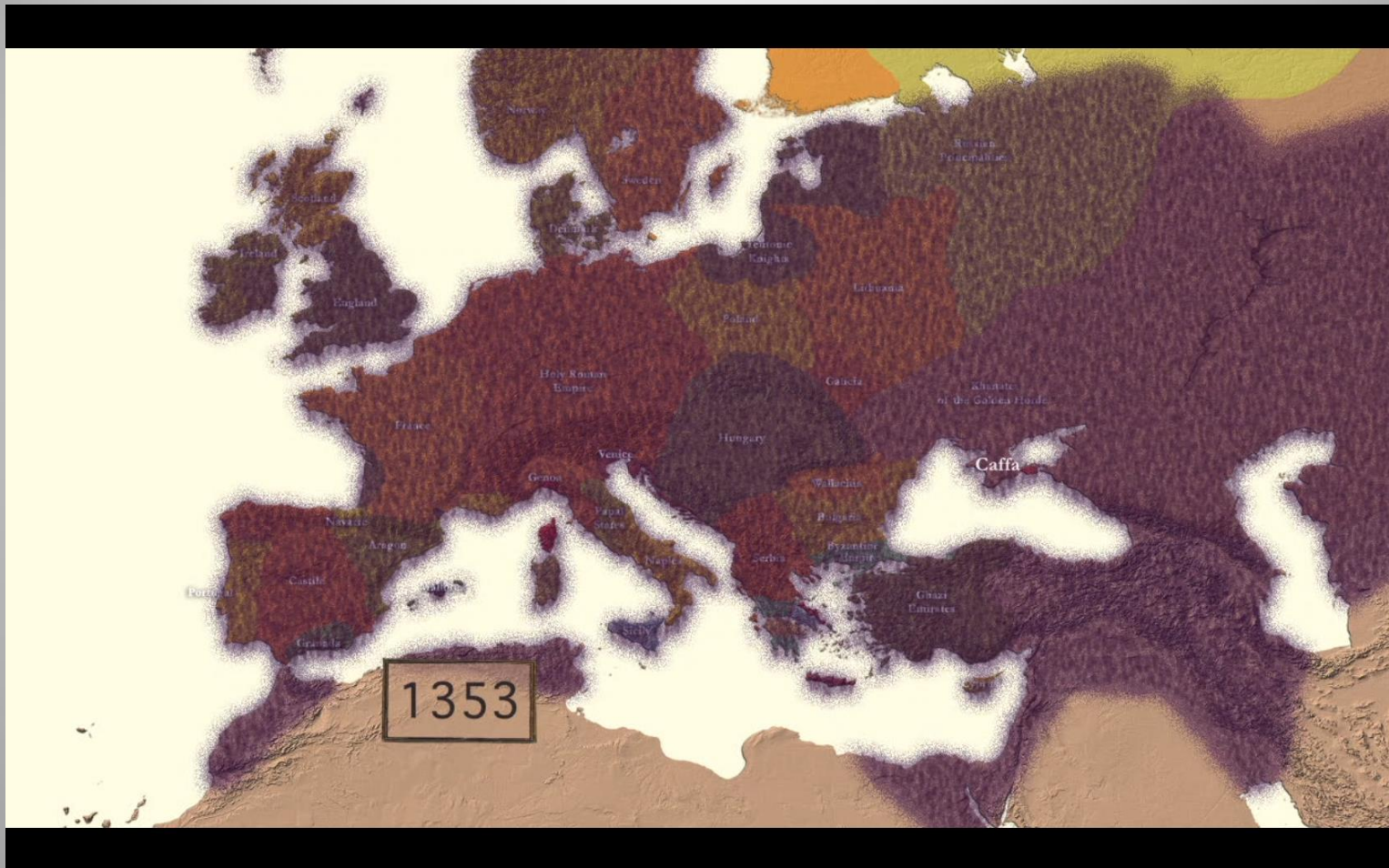
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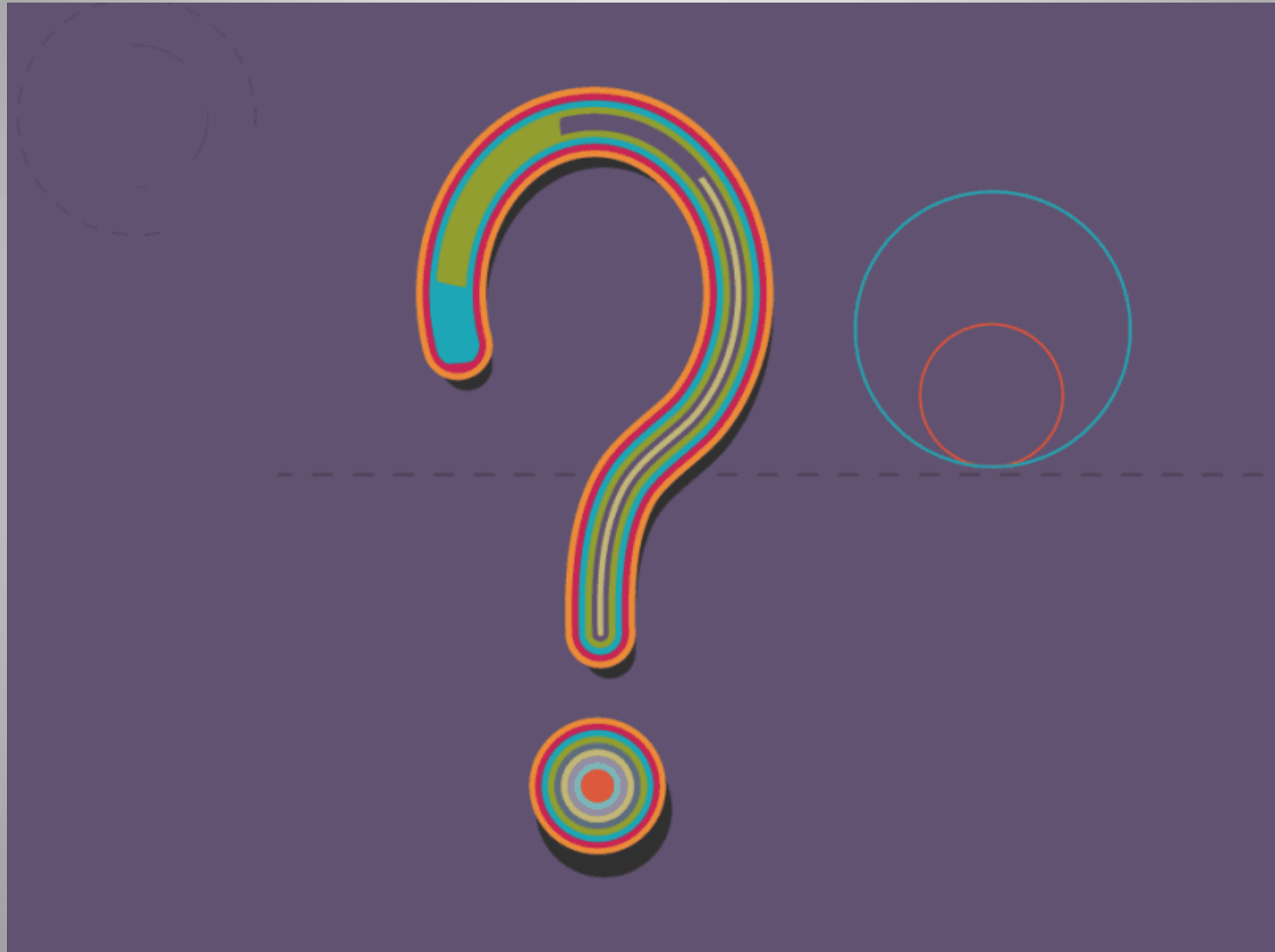
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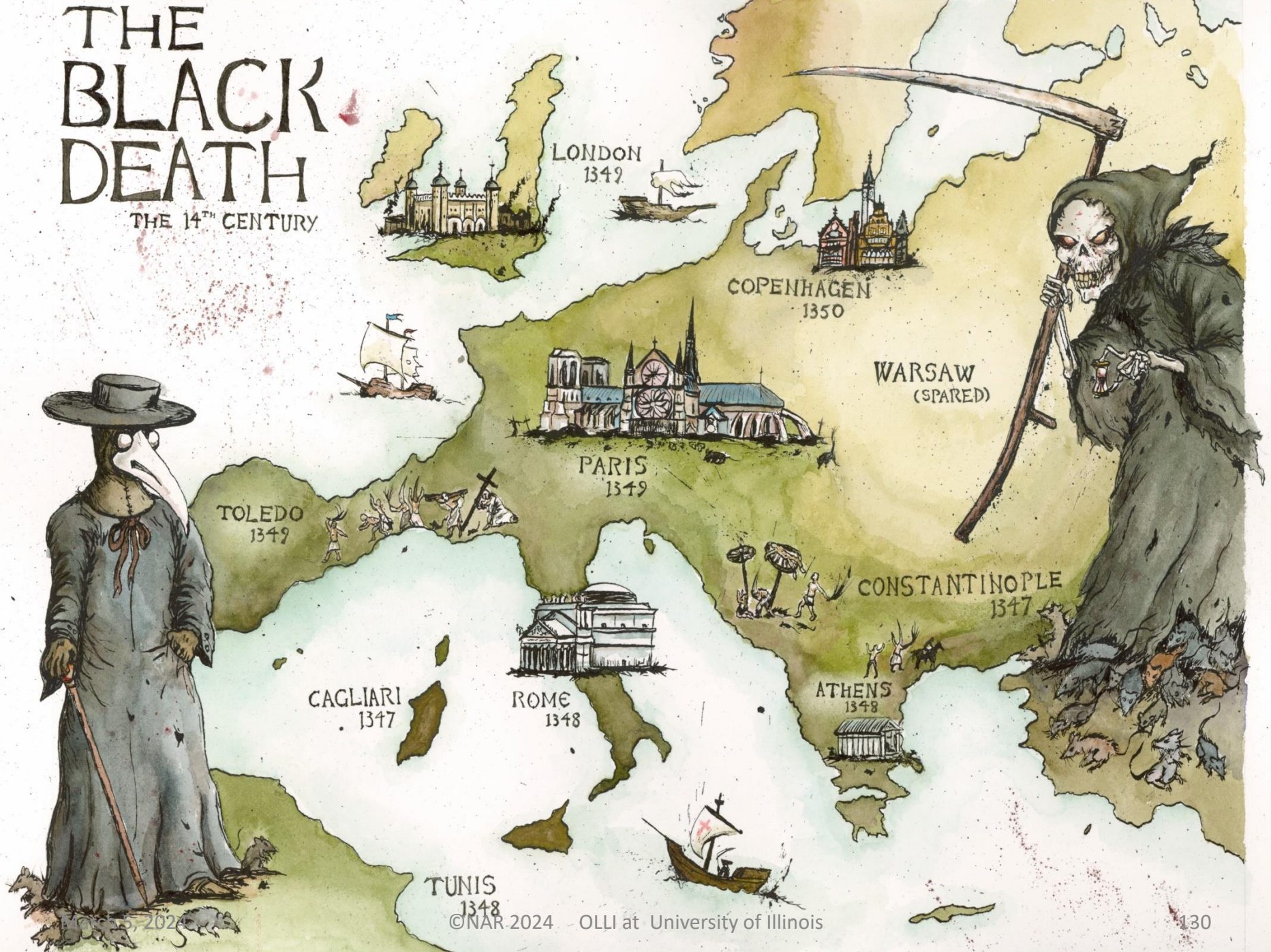


Questions? 2



THE BLACK DEATH

THE 14TH CENTURY



TUNIS
1348

The PLAGUE

- The Second Plague Pandemic.
- Called the Bubonic Plague because of the large dark buboes around the lymph nodes, and also called The Great Mortality, or the Great Pestilence.
- Plague was not called the Black Death until centuries after its initial spread through Europe, and it suggests the horror of the epidemic as a dark, black, terrifying time, not the color of some lesions.

The Plague

- The Black Death is known to have killed 30% to 60% of Europe's total population, but recent evidence shows that this estimate is too low.
- Actually, the plague inflicted death “on an eye-watering scale”.

Y. pestis Migrations

- Ruminant animals and predators do not act as primary plague hosts.
- They catch the bacterium from rodents (through their fleas or by eating them) which explains why the plague is still present today across the globe.
- Plague reservoirs and the capacity of *Y. pestis* to be carried by >350 species of mammals explain its wide spread and range in the medieval world.

Types of Plague

- Bubonic
- Pneumonic (pulmonary)
- Septicemic

Bubonic Plague

- most common form
- 2-7 days incubation
- most survivable
- 60% mortality
- vomiting, diarrhea
- lymphatic system
- egg-shaped painful buboes
- petechiae
- malodorousness
- chills, fever

Pneumonic Plague



- second most common
- ***spreads person-person***
- rapid contagion
- 2-3 days of symptoms
- 90-95% mortality
- transmitted by blood, sputum or saliva
- fever, coughing and spitting blood
- invasion of lungs and airways by bacillus

Septicemic Plague



- Least frequent type.
- Almost 100% mortality.
- Very fast progression.
- No time to get buboes.
- Death in 1-3 days
- high fevers
- widespread blood infection
- purple skin patches
- purpura due to DIC*

* Disseminated Intravascular Coagulation

Septicemic Plague

- DIC produces red/black patchy rashes and bumps all over the body.
- Medieval people said that a dead person bore “the sign” of the plague.
- A final common sign of advanced septicemic plague is the vomiting of blood.

Pestis Secunda

- First of a series of plague outbreaks in Europe that followed the Black Death (1346–1353 CE), occurred between 1356 and 1366 CE.
- Unlike the Black Death, which seems to have originated in Central Asia, the *pestis secunda* emerged in Central Germany.
- The *pestis secunda* outbreak is also known as the second wave of the Second Plague Pandemic.

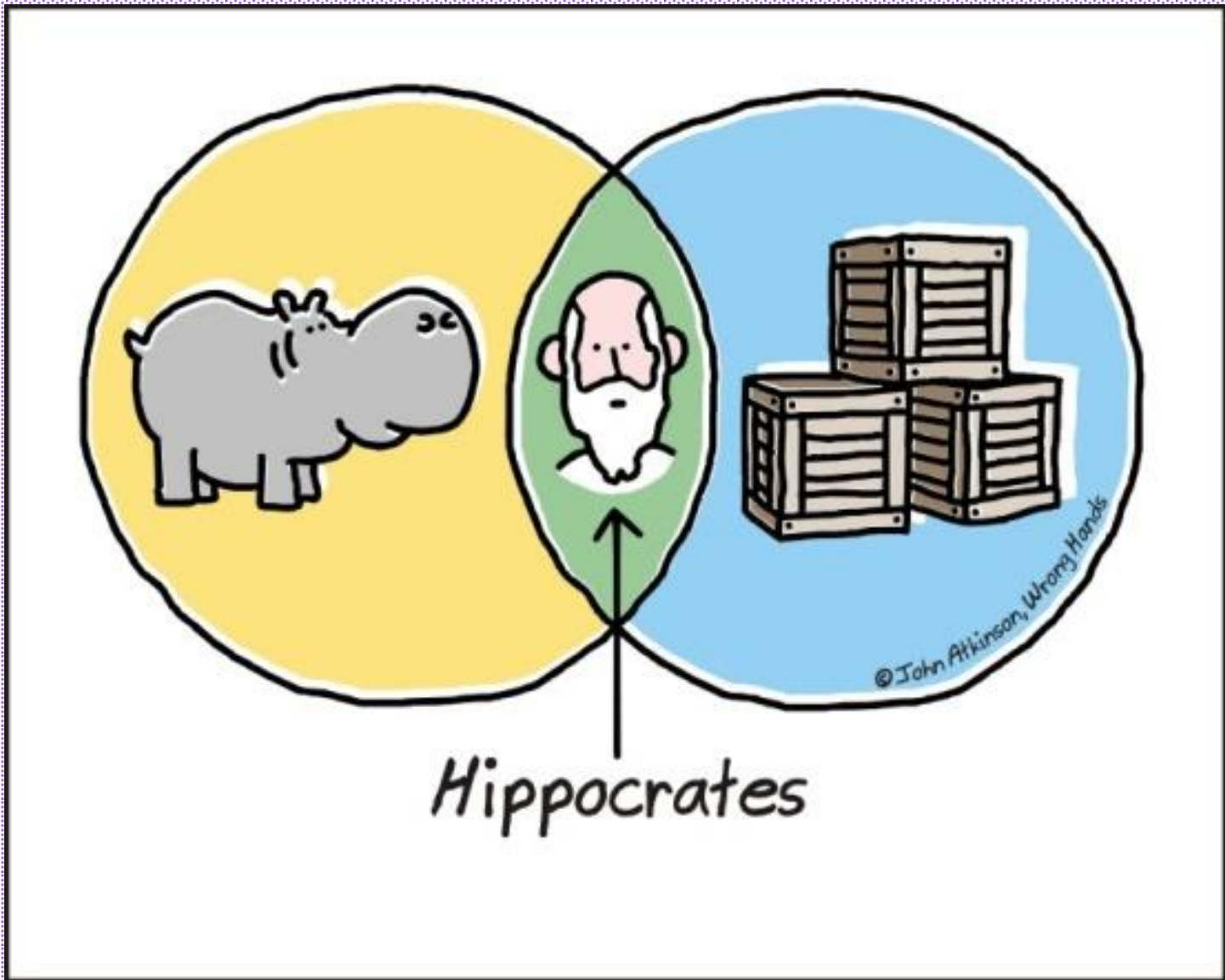
Traditional Medical Knowledge

Plague Doctors

Plague Precautions

Plague Treatments

DOCTORS and the PLAGUE



Hippocrates

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Medical Knowledge

Hippocrates of Cos ~ 460-370 BCE

- Disease has natural (not supernatural or divine) causes.
- Health = balance of the 4 humors.
- Illness = imbalance: dyscrasia (bad mixture of humors).
- Cure is accomplished by evacuating undesired humors:
 - emetics
 - purgation
 - bloodletting
 - dietary and behavioral measures

Roots of Hippocratic Medicine



Four Basic Body Humors:

Blood

Yellow bile

Black bile

Phlegm

Medical Knowledge

Aristotle of Stageira ~ 384-322 BCE

- The heart, not the brain controls the body.
- Physical pain is the body's inability to assimilate certain foods.
- Maintained the Doctrine of the **Four Basic Qualities**:
 - Hot.
 - Cold.
 - Wet.
 - Dry.
- Laid the foundation for notions of balance and homeostasis.

Humors and their Correlations

HUMOR	ELEMENT	QUALITIES	AGE	ORGAN	TEMPERAMENT	SEASON
Blood	Air	Moist and Warm	Infancy	Liver	Sanguine	Spring
Yellow Bile	Fire	Warm and Dry	Youth	Gallbladder	Choleric	Summer
Black Bile	Earth	Dry and Cold	Adulthood	Spleen	Melancholic	Autumn
Phlegm	Water	Cold and moist	Old Age	Brain/lung	Phlegmatic	Winter

Ramírez 2019

Medical Knowledge

Galen of Pergamon ~ 130-210 CE (1)

- The circulatory system consisted of two separate one-way systems of distribution.
- Venous blood was generated in the liver, and arterial blood originated in the heart.
- After use by the body, the blood was then regenerated in either the liver or the heart, completing the cycle.

Medical Knowledge

Galen of Pergamon ~ 130-210 CE (2)

- Described the Antonine Plague.
- Believed in predeterminism (God's master plan).
- Tuberculosis (*phthisis*) is not caused by “evil airs.”
- Cure for the plague according to the early Romans:
 - bathe in human urine
 - drink elephant's blood
 - eat wolves' livers

Medical Knowledge

Galen of Pergamon ~ 130-210 CE (3)

- Believed in the humors.
- Used blood-letting by cupping.
- Described the plague but did not involve himself with treating victims of it.

PLAGUE PHYSICIANS



Plague Physicians

- Hired and paid by towns to treat everyone in the hope of completely eradicating the disease, but doctors could also charge patients.
- Towns often provided other benefits, such as a free home, payment of expenses, and a pension, so plague doctors actually had lucrative careers.
- The position paid well, but it was generally taken by three types of people:
 - new doctors
 - those who struggled in private practice
 - volunteers who weren't trained but were willing to try
- As they were often with patients in their final moments, plague doctors were also required to record wills and testify in court if needed.

Plague Physicians

- Data collection was a major part of being a plague doctor:
 - suspected cases
 - confirmed cases
 - fatalities
 - cured patients
 - treatment (s) used
- These data helped the plague doctors to start ruling out ineffective treatments.
- They also performed autopsies to learn more about the effects of this condition on the human body.

Plague Physicians

- Some were kidnapped for ransom and were often quickly returned, while others simply vanished .
- They may have fled, died of the plague, or were nabbed to treat people in another city.
- It was maybe a combination of all three.

Tall, Wide-Brim hat

Long beak mask

Long Pole

Lamp for Illumination

Medical Kit

Quill jar

Document Case

Long, waxed robe

Pointed shoes

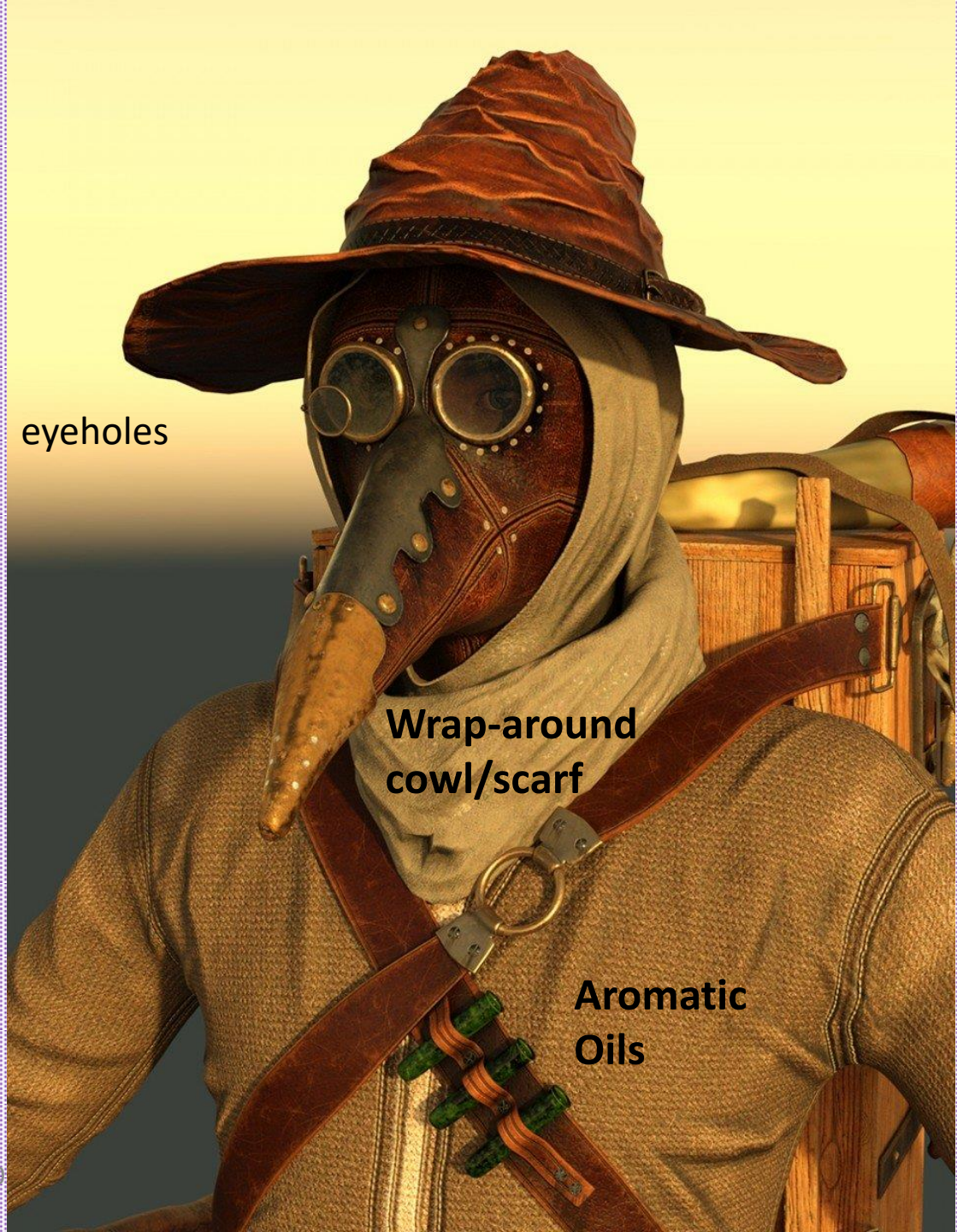


Glass-covered eyeholes

Meet the Plague Doctor

Wrap-around
cowl/scarf

Aromatic
Oils



Gear for Plague Doctor



Medical Plague Kit



The English plague nursery rhyme

*Ring around the rosy
A pocketful of posies
“Ashes, Ashes”
We all fall down.*

Meaning:

*Red rash around the mouth
Flowers to mask plague odors
Violent sneezing associated with plague
Death of all the infected*

PLAGUE PRECAUTIONS and TREATMENTS

Treat According to Cause

- Supernatural causes:
 - wrath of God
 - work of the devil
 - alignment of the planets
- Natural causes:
 - “bad air” (miasma)
 - unbalance of the body’s humors
- Real cause unknown, so real cure not possible.

Plague Precautions (1)

Avoid the Sick

- In a panic, doctors refused to see patients, priests refused to administer last rites, and shopkeepers closed stores.
- Many people fled to the country, but they could not escape the plague: it affected cows, chickens, pigs, goats & sheep.
- So many sheep died that one of the effects of the Black Death was a European wool shortage.

Plague Precautions (2)

Avoid the summer, seal the house

- There was never a winter epidemic of plague.
- Seal the house (and the people in it): quarantine any house that had been host to a plague victim by sealing it shut under guard for 40 days.
- Even with a sealed and guarded house, people tunneled to freedom, or made daring rooftop escapes at night with the help of friends who poisoned or drugged the guards.

Plague Precautions (3)

Avoid Gerbils

- The Black Death was plague borne by fleas living on rodents, which may have been gerbils.
- Some researchers suggest that the disease could have been anything from influenza to anthrax.
- Many uncertainties remain around the nature and spread of the Black Death pandemic.

Plague Precautions (4)

Kill the troublemakers

- Many believed that the Black Death was divine punishment for sins against God like greed, blasphemy, heresy, fornication and worldliness.
- The only way to overcome the plague and win God's forgiveness was by purging communities of heretics and other troublemakers, like Jews, so many thousands were massacred in 1348-1349.

Plague Precautions (5)

Flowers and herbs

- Some people did not shut themselves up, but went about, carrying flowers or scented herbs or perfumes.
- They believed that they could comfort the brain with such aromas, since the whole air was poisoned with the smell of dead bodies, sick persons and medicines.
- Plague doctors carried aromatic flowers & herbs in the beaks of their costume, to filter out the evil miasmas.

Plague Precautions (6)

Overstink the Miasma

- John Colle, an English physician said that the best way to counteract bad air that carried infection was with more bad air: *“One foul smell drives out another”*.
- He prescribed sniffing a latrine every morning.
- People gathered around public latrines inhaling deeply.
- They thought that smelling a bigger stink would ward off contagion from the bad smell that “carried” plague.

Plague Precautions (7)

Prayer

- Prayer, prayer, and more prayer: there were set prayers and Bible excerpts designated for use in time of plague.
- A special Mass of St. Sebastian (a patron saint of the plague) was used.
- Spiritual health remained paramount and people still regarded prayer and penance as their first line of defense.

Plague Precautions (8)

Whipping

- Some worried about their own souls but protested against the Church, which they blamed for the Plague.
- Many men joined processions of flagellants in public displays of penance and punishment, beating themselves and one another with leather straps studded with sharp metal.
- The flagellants did this ritual 3 times/day, and then moved on to the next town and began the process again, for 33 ½ days.



The Pope, worried about loss of respect and authority, reviled the movement and it disintegrated

Plague Precautions (9)

Lucky charms and cures

- Wearing lucky charms was recommended by doctors, like Ambroise Paré, who believed that they would keep away the plague, and Dr. George Thomson who wore a dead toad around his neck.
- Charlatans often sold high-priced plague ‘cures’ like:
 - plague water (many recipes)
 - powdered frog legs and rhinoceros horns
 - potions laced with mercury or arsenic
 - ground horn from the mythical unicorn
 - tying live chickens around buboes
- A popular “cure” was making a plague victim sweat, and then applying to their buboes a recently killed pigeon.

Plague Precautions (10)

Smoking and vinegar

- In 1665, the College of Physicians recommended brimstone ‘burnt plentiful’ as a cure for the bad air that caused the plague.
- The authorities ordered bonfires to be kept burning at all times, and homes had fires going day and night, at any temperature.
- Many started smoking tobacco, and people of all ages, including children, were forced to smoke (it became urban legend that no tobacconists in London ever had the plague).
- If coins were used in transactions in shops, they were placed in a bowl of vinegar before being handed over to the recipient.

Questions? 3





*Yersinia
pestis*

WHAT CAUSED THE PLAGUE?

What Caused the Plague?

- University of Paris issued the *Compendium de Epidemia per Collegium Facultatis Medicorum Parisius* (1497).
- Written by 46 medical eminences of the Paris School of Medicine.
- Emphasized how earthquakes, floods, rare weather, planetary conjunctions and “bad air” contributed to the outbreak of plague.

What Caused the Plague?

According to those French scholars,
the Great Plague was created from :

“a triple conjunction of Saturn,
Jupiter and Mars in the 40th
degree of Aquarius, occurring
on the 20th of March 1345”

What Caused the Plague?

Chroniclers such as the friar Bartolomeo of Ferrara, claimed to have received their evidence from eyewitness merchant accounts who reported tales of the plague's origins:

- floods of snakes and toads
- snows that melted mountains
- black smoke
- venomous fumes
- deafening thunder
- lightning bolts
- hailstones
- eight-legged worms that killed with their stench

Origin of the Plague

- The Black Death originated in Central Asia near Lake Issyk-Kul in Kyrgyzstan and spread to Italy and then throughout other European countries.
- Arab historians Ibn Al-Wardni and AlMaqrizi believed the Black Death originated in Mongolia, and Chinese records also show a huge outbreak in Mongolia in the early 1330s.
- The Mongols had cut the Silk Road between China and Europe, which slowed the spread of the Black Death from eastern Russia to Western Europe.

Yersinia pestis

- Since 1998, studies have ***conclusively*** shown that the epidemics called *plague* between the mid-13th and the mid-17th centuries in Europe, were caused by *Yersinia pestis*.
- *Y. pestis* DNA sequences have also been found in skeletons buried in the 2nd half of the 6th century indicating that the ***Plague of Justinian*** (1st plague pandemic) was also caused by *Yersinia pestis*.

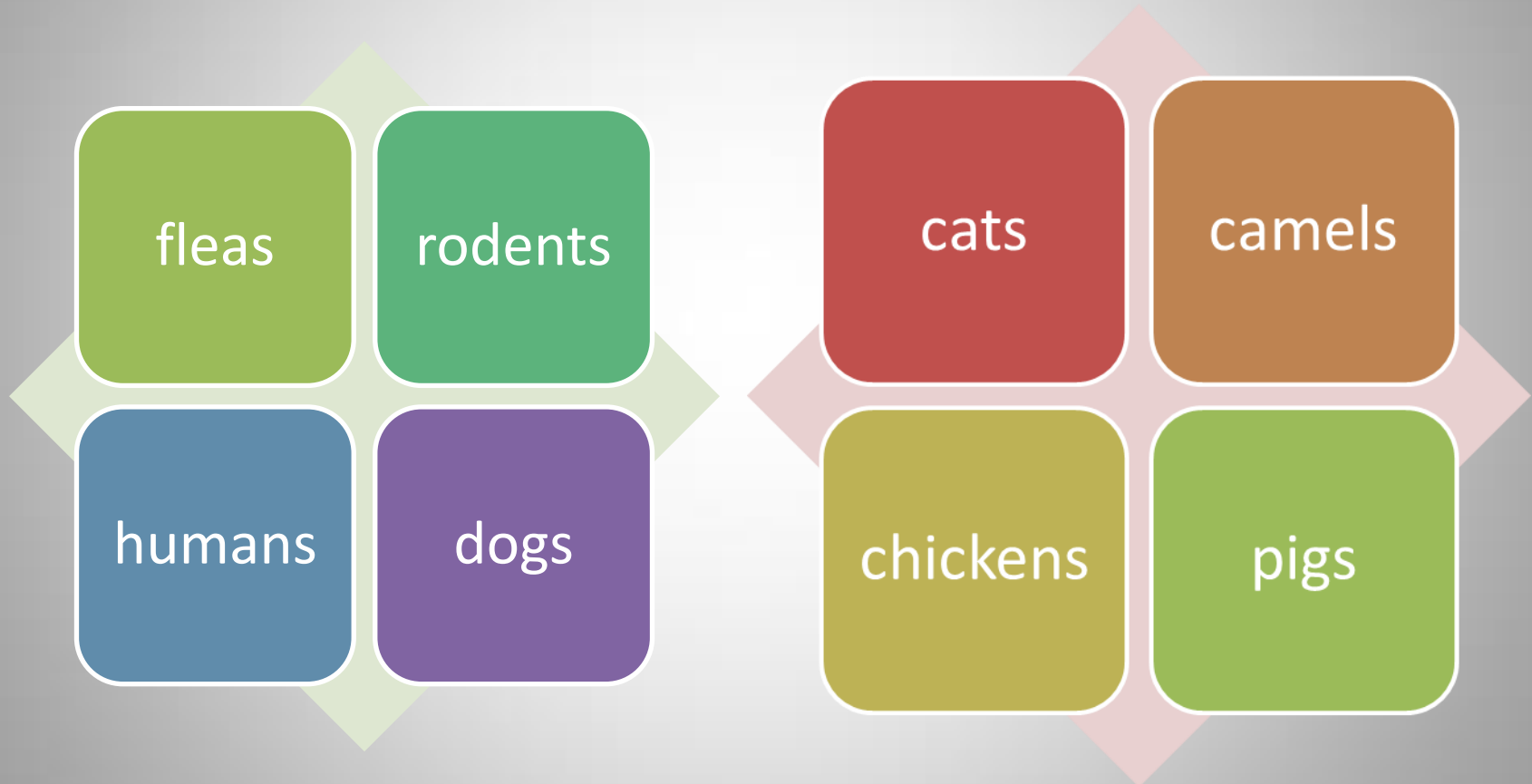
Yersinia Pestis

- cocobacillus
- stick-shaped
- Gram-negative
- non-Spore forming
- non-motile
- facultative anaerobe
- inhibits antibodies
- avoids destruction by the immune system
- suppresses phagocytosis
- grows in lymph nodes
- causes lymphadenopathy

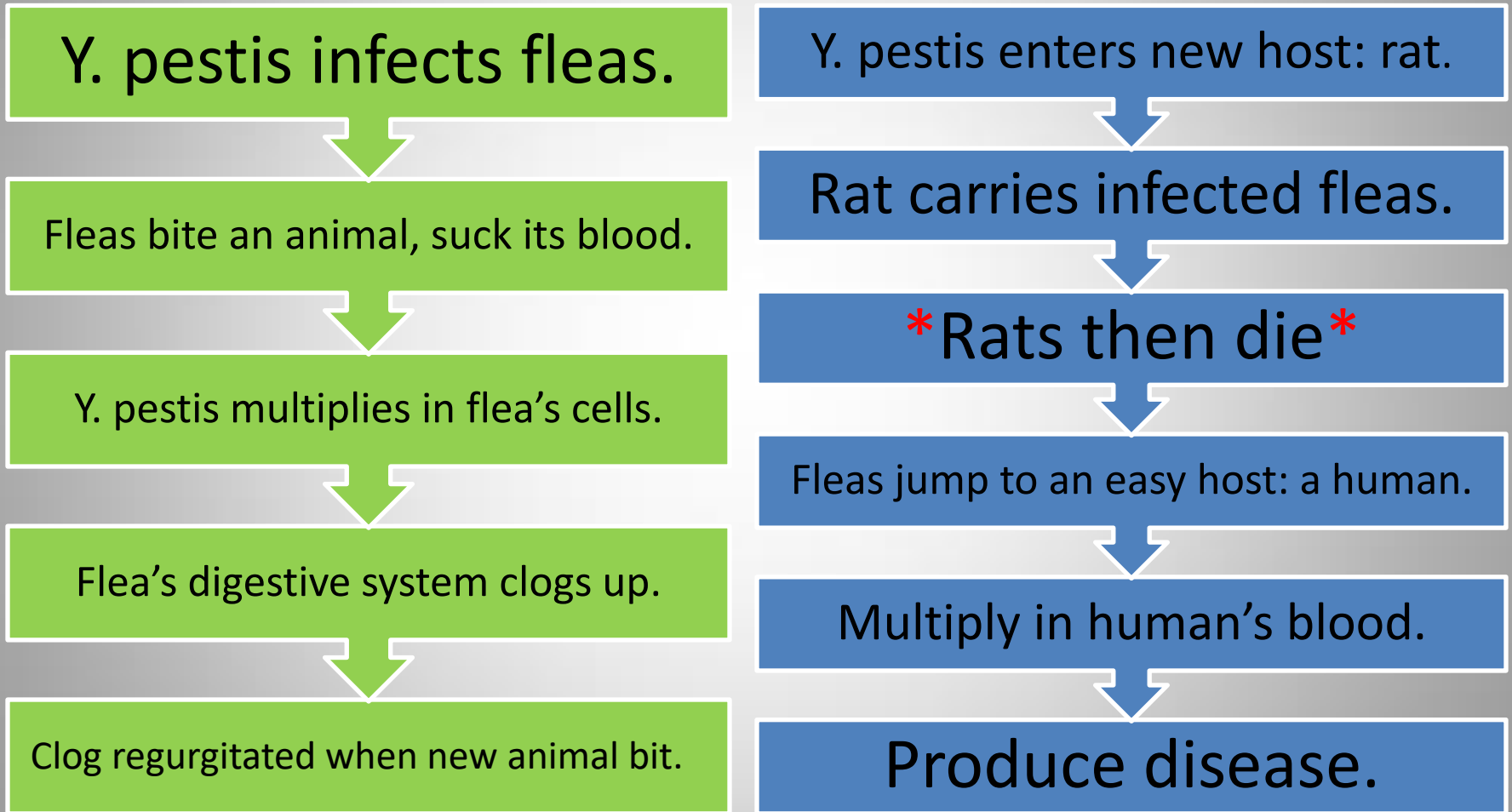
Multiplies very rapidly: Numbers double every 2 hours and may reach 100 Billion per gram of host's tissue.

Yersinia Pestis

An equal opportunity killer



Yersinia Pestis



Rats and *Y. pestis* during medieval plague

- It is commonly accepted that plague is a disease of rodents that is transmitted to humans from black rats, with rat fleas as vectors.
- Historians have assumed that this transmission model is also valid for the Black Death and later medieval plague epidemics in Northern Europe.
- A study examined the population density and distribution of the black rat (*Rattus rattus*) in Norway and other Nordic countries in medieval times.

Anne Karin Hufthammer & Lars Walløe

Oslo, 2013

- There are **NO** findings of black rats from excavations in rural areas, inland towns or medieval harbor towns in Norway.
- Archaeological evidence from other Nordic countries shows that rats were also uncommon there, so it's unlikely they were responsible for the wide spread of human plague.
- The hypothesis is now that the mode of transmission during the historical plague epidemics was from *human-to-human* via an insect ectoparasitic vector.

Plague = *Y. pestis*

These results definitively refute the hypotheses put forward by:

- Shrewsbury, a microbiologist, in 1970
- Twigg, a zoologist, in 1984
- Scott, a demographer, in 2001
- Duncan, a physiologist, in 2001
- Cohn, a historian, in 2001

that some or all of the medieval plagues in Europe had been diseases different in bacteriological and medical terms from modern plague!!!

Paleopathology

Bioarcheology, Paleogenetics

- Could potentially find common biological effects of plague, in terms of its effects on populations defined by common nutritional or syndemic stresses.
- The newer epidemiology of plague needs to determine:
 - location of initial spillover events that made the “Big Bang”
 - forces that caused long-distance spread of new strains
 - factors that helped plague focalize in new environments
 - socio-cultural responses to the chaos and destruction caused by the bacteria

Yersinia pestis

In the 1950's, Belgian researcher René Devignat developed a biochemical technique for differentiating strains of plague (biovars):



Name	20 th Century Location	Ferments Glycerine	Reduces Nitrates
<i>Antiqua</i>	Central Asia, Central Africa	Yes	Yes
<i>Medievalis</i>	SE Russia, Kurdistan	Yes	No
<i>Orientalis</i>	India, Burma, South China, N and S America	No	Yes

Yersinia pestis

- 3 main biovars (strains) were presumed to have arisen with each of the three different historical plague pandemics:
 - *Y. pestis Antiqua*: 6th century plague pandemic (Justinian)
 - *Y. pestis Medievalis*: Black Death and 14th pandemic waves
 - *Y. pestis Orientalis*: 3rd pandemic and current outbreaks
- In 2011, Devignat's biovars were shown to be chimeras:
 - *Antiqua* was found in both East Africa and Central Asia
 - *Orientalis* caused the Black Death and early modern outbreaks in west Europe
 - *Medievalis* emerged in the early modern period and is not of medieval origin

Y. Pestis is a versatile killer

- besides rodents and humans, it kills camels, chickens, and pigs, but symptoms similar to those of humans can be deadly to animals
- domestic dogs and cats are also susceptible but cats are more likely to develop illness when infected
- people can be exposed by:
 - coming into contact with an infected animal (dead or alive)
 - inhaling infectious droplets coughed into the air by a sick dog or cat

Clearing the Doubts

- Late 20th century was full of doubt and contention about the cause of the Black Death and other major epidemics.
- A 2011 study sequenced *Y. pestis* from 14th-century London and confirmed that *it*, **and no other** germ, retrieved from Black Death victims was the agent for the largest mortality event in history.
- This study created the possibility of researching the history of plague, **and** also the history of strains of the plague bacterium as causes of different plague outbreaks.

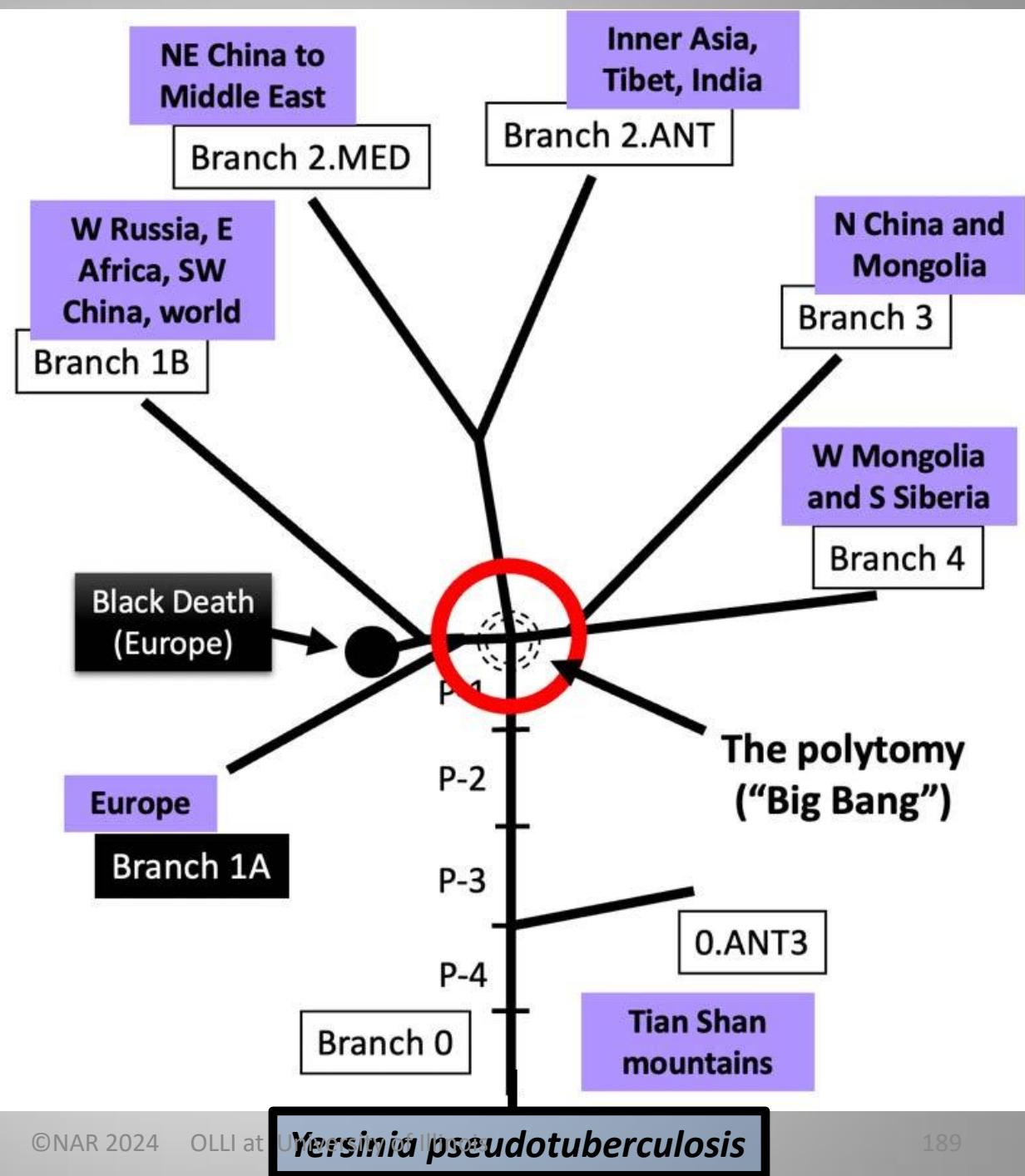
Phylogenetics

- Tracking the evolution of an organism implies acceptance of the double premise that:
 - the organism's biological character and molecular genetic structure changes over time and place
 - those changes are inherited by future lineages
- Phylogenetic connections between different strains of plague document the points at which the history of the bacterium has intersected with that of humans.

The “Big Bang”

- What circumstances allowed the long-distance transmission of the plague bacterium?
- All the plague foci that late 19th century scientists observed in Africa and Asia arose from one single event: the “Big Bang”.
- The “Big Bang” was a quiet microbiologic event, when compared to the visible chaos caused by the early Mongol conquests and displacements of peoples across central Eurasia.

The Polytomy of *Yersinia pestis* (The “Big Bang”)



Monica Green 2020

Yersinia Strains

- Plague can now be analyzed as a branching network of genetic strains, each tied to specific times and places.
- The evolutionary changes of *Y. pestis* show that Plague is not a generic and non-distinguishable disease, equal from one instance to another.

Finding *Yersinia*

- Just before a mammalian host dies of plague, the germ passes into the bloodstream, and replicates endlessly.
- Teeth are vasculated, so the bacterium ends up there, too.
- After the host succumbs, the hard enamel of the tooth can help to preserve bits of blood.
- All *Y. pestis* aDNA that has been retrieved has come from human teeth, and has allowed scientists to track the germ's **SNPs** (single nucleotide polymorphisms).

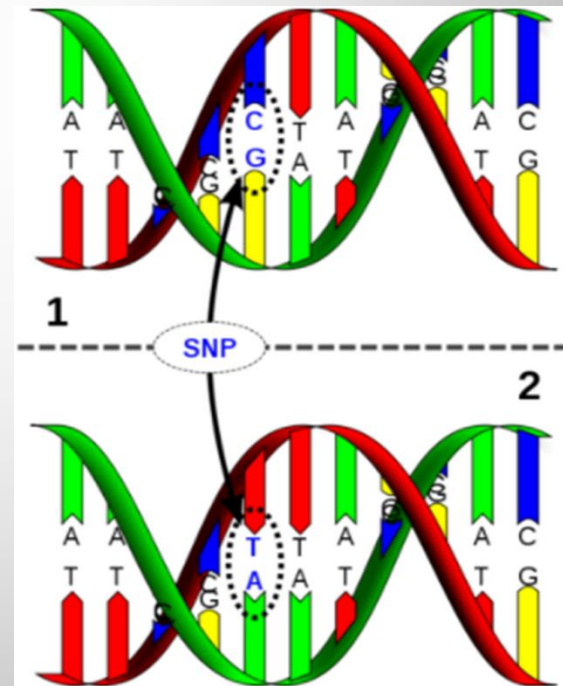
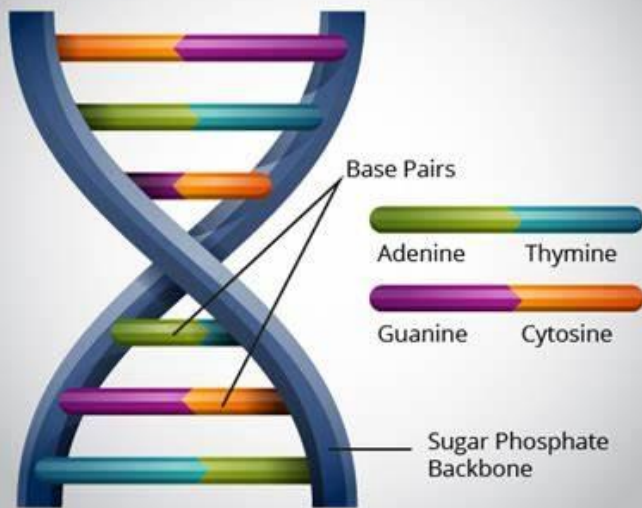
Single Nucleotide Polymorphisms (SNPs)

- Alterations in the DNA sequence, which are the most common type of genetic variation among organisms.
- SNPs occur naturally throughout a person's DNA and can be used as biological markers to locate genes associated with diseases .
- SNPs can also help predict an individual's response to certain drugs, susceptibility to environmental factors such as toxins, and risk of developing diseases .

DNA and SNP's

In **S**ingle **N**ucleotide **P**olymorphisms (SNP's) one nucleobase on the genome (A, C, G, or T) is replaced by another one.

DNA Structure



Single Nucleotide Polymorphisms (SNPs)

- If a SNP occurs in a host early in the infectious process, the newly altered bacterium will dominate its current host's body after successfully replicating many millions of times.
- Such a mutation would have the best chance to replicate freely and precipitously when just a few identical bacteria come into a new environment, with fresh hosts.
- The SNP strain would not have to compete against other strains, so its genetic sequence comes to define the organism through a *founder effect*, and if it proves successful replicating in many surviving progeny, it becomes a defining feature of the lineage.

THIRD PLAGUE PANDEMIC

1866-1960'S

Tarbagan Marmots

- Rodent plague found in China (Inner Mongolia & Heilongjiang), N and W Mongolia, and Russia (SW Siberia, Tuva, Transbaikalia).
- Epizootics of the plague occur in tarbagan marmots in northeastern China and Mongolia (Manchurian plague of 1910–1911).
- The pneumonic plague in marmots is spread by marmots coughing, and can jump from marmots to humans through the bite of the tarbagan flea (*Ceratophyllus silantievi*), or by consumption of meat.
- Marmot epizootics are known to co-occur with human epidemics in the same area.

Third Pandemic

- Originated in Yunnan, China in 1792, with outbreaks in 1855 and 1866-1867.
- An outbreak in neighboring Guangzhou from January 1894 onwards killed 80K.
- The consular surgeon for Canton, identified it as the bubonic plague, but said it would not be not particularly contagious except to those living in filth, poor ventilation, with a poor water supply.

Third Pandemic

- The plague in the late 19th century was rather weak compared to the Great Mortality of the 14th century.
- Scientists propose that the modern plague was caused by a weaker form of *Yersinia pestis*.
- The medieval plague was so virulent it almost wiped itself out by killing all its potential hosts.

Science to the Rescue

- Gram (-) bacillus discovered in Hong Kong in 1894.
- Independently by Alexandre Yersin and Kitasato Shibazaburō.
- Initially named Pasteurella, later Yersinia.
- Paul-Louis Simond discovered the rat-flea vector for transmission of the disease.

Third Pandemic Transmission

Simond's mechanism

In China before 1894, in Hong Kong, in many areas of India, and in cities like Bombay, Colombo, Alexandria and Sydney, the most important arthropod vector was *Xenopsylla cheopis*, and the mode of transmission was from *Rattus rattus* (or *Rattus norvegicus*) to man.

Rat + Flea = Guilty!



The black roof rat, *Rattus rattus* and the Oriental rat flea, *Xenopsilla cheopis* are blamed for transmission of *Yersinia pestis*.

Rattus rattus

(Ship rat, Roof rat or House rat)

- Typical adult is 5.0 to 7.2 in long, tail is 5.9 to 8.7 in, and weighs 2.6 to 8.1 oz.
- Other rodents may be implicated in the plague:
 - voles
 - marmots
 - gerbils
 - ground squirrels
 - prairie dogs
 - chipmunks
 - rabbits

Xenopsylla Cheopis

Rat Flea

- Body is about 2.5 mm ($\frac{1}{10}$ of an inch) long.
- Flea's mouth has two functions:
 - squirting saliva or partly digested blood into the bite
 - sucking up blood from the host (to transmit pathogens)
- Fleas smell exhaled CO₂ from humans & animals and jump rapidly to feed on a new host when their primary host dies.
- Wingless, but can use its legs to jump up to 200 times its own body length (about 20 in).

Xenopsylla Jumping



Mortality of Third Pandemic

- India hardest hit (North and West regions).
 - killed about 12 million people by 1930
 - this was 95% of total world's mortality (>15M)
- In Manchuria (Northeastern China):
 - mostly pneumonic plague
 - killed 60K in 1910-1911 and 8.5K in 1920-1921

Third Pandemic

Waves of the late-19th century/early-20th -century pandemic may have come from 2 different sources:

- the 1st wave was primarily **bubonic** and was carried around the world through ocean-going trade, transporting infected persons, rats, and cargoes harboring fleas
- the 2nd, more virulent strain, was primarily **pneumonic** in character with a strong person-to-person contagion, and largely confined to Asia.

Third Pandemic

- In Canton, beginning in March 1894, the disease killed 80K people in a few weeks.
- Daily water-traffic with Hong Kong rapidly spread the plague.
- After 100K deaths in 2 months, the death rates dropped below epidemic rates (200/year), but plague became endemic in Hong Kong until 1929.

Third Pandemic

- From May to October 1894, the Hong Kong plague killed more than 6K people, leading to the exodus of 1/3 of the population, and during 1926 to 1956, it re-occurred almost every year and killed more than 20K people.
- Through maritime traffic, the epidemic spread to the rest of the country after 1894, and eventually spread to India where about 10M were killed.
- Great Britain, France, and other areas of Europe, had plague outbreaks until the 1960s, but very few after 1950; the last significant outbreak of the pandemic plague occurred in Perú and Argentina in 1945.

“Rat Falls”

- Rats are not blameless: they are believed to be carriers of the disease in the 3rd Pandemic, starting in 1855.
- That plague was accompanied by "rat falls," or mass deaths of *rattus rattus* in the streets, not described for the 2nd Pandemic.

Public Health

- Extreme conflict between Western control measures and Chinese medical beliefs.
- Traditional Chinese medicine not allowed to be used in British hospitals.
- Chinese thought that Western style medicine was useless, dangerous and harmful.

Public Health

- The *Office International d'Hygiene Publique* (OIHP) in Paris created the standard Protocols to deal with the bubonic plague throughout the early 1900s.
- These often old-fashioned Protocols were summarized as the *Three "I's"*:
 - isolation
 - incineration (unique in bubonic plague)
 - inoculation (new vaccines >50% effective?)

Public Health

Bias and Social Harm

- In 1900, much of Chinatown in Honolulu was burned by the Board of Health to control the plague, making >7,000 Chinese and Japanese residents homeless.
- When the plague reached San Francisco, the Medical Board implemented a strict quarantine of the entire Chinatown district after discovering only 1 case of the plague.

Public Health

Bias and Social Harm

- In India, harsh quarantines were implemented by the British government, leading to Indian resentment of quarantine measures.
- When the plague broke out in Cape Colony, white colonial government forced a large group of black South Africans to be segregated into areas on the outskirts of the city.
- In Hong Kong, the British floated plague victims out on boats and cooled plague victims with ice; this angered many Chinese, who migrated back to mainland China, which was even more badly affected by the plague.

Plague Immunity?

- Recessive gene mutations for *Familial Mediterranean Fever* (FMF) in people of Arab, Armenian, Jewish, or Turkish ancestry may be linked to plague immunity.
- *Pyrin*, the FMF gene protein product, participates in *IL-1 β* and *IL-18* processes to produce fever and mounting and maintaining human defense systems against pathogens.
- *Y. pestis* shuts off *Pyrin* in subjects who lack the mutation, reduces production of *IL-1 β* and *IL-18*, and blocks the immune system response, which increases susceptibility to plague infections.
- Patients who carry the FMF mutation have a *Pyrin* gene whose activity is always “ON”.

Plague Immunity?

- Like sickle cell trait and resistance to malaria, people with the FMF mutation may have plague immunity.
- Up to 20%-40% of Israeli Jews may carry a recessive mutation in the FMF gene.
- During the Black Death, Jews were the only large European community with Middle Eastern origins.
- Presence of the FMF mutation may have allowed 14th Century Jews to survive plague at higher rates than their non-Jewish neighbors. **

Plague Vaccine (1)

- On January 10, 1897 Waldemar Haffkine tested a killed germ vaccine on himself and then on volunteers at the Byculla jail.
- All inoculated prisoners survived the epidemics, while seven inmates of the control group died.
- By 1925, >20M doses had been given, with 4M inoculees in India alone.

Plague Vaccine (2)

- The Haffkine formulation had nasty side effects, and did not provide complete protection, but reduced risk of death by up to 50%.
- Other types have failed to satisfy the WHO safety and efficacy requirements for a useful vaccine.
- Combinations of *Y. Pestis* vaccines might be able to prevent a plague outbreak or a war attack.

Plague Vaccine (3)

- A *prophylactic* plague vaccine needs to elicit long lasting immunity, and be feasibly administered in endemic populations or in health workers during plague outbreak investigation or surveillance.
- A *therapeutic* plague vaccine must elicit a rapid protective immunity after the 1st dose within a few days, and protect individuals in outbreak areas by blocking transmission chains.

Commonalities of the Pandemics

- What unites historical pandemic events is not the type of pathogen, it is human agency.
- Factors that have turned small outbreaks and spillover events into global scourges:
 - our choices in food acquisition
 - our networks of commodity distribution
 - our drive for cheap labor
 - our drive for sex
- There are no villains, only patterns of humans doing what humans do.

Monica Green

Discrepancies

Between the 1st, 2nd and 3rd plague pandemics

- Speed, distance and extent
- Rats?
- Lethality
- Contagion
- Famine
- Climate
- Temperature

Speed and Distance (1)

- The First pandemic extended rapidly, not only with its first appearance in 541 but also with subsequent waves.
- In 664, the plague took only 91 days to travel 240 miles (2.7 miles/day), the fastest overland speed of *Y. pestis* spread in any plague.

Speed and Distance (2)

- The black plague traveled 5 miles/day
- In New Orleans and South Africa, during the early 20th century, *Y. pestis* was shown to be a slow mover, travelling at only 7 to 12 miles/year.
- Modern plague, even with railways, automobiles, and higher population densities, would have needed 25 years to cover the distance the early medieval plague travelled in just 3 months!

Rats?

- No scholar has found any evidence, narrative or archaeological, of a mass death of rodents that preceded or accompanied any wave of plague for the 1st or 2nd pandemics.
- But the bubonic plague of the “3rd pandemic” was definitely a rodent disease, complete with documented mass rat deaths (“rat falls”).

Lethality

- Descriptions of the 2nd pandemic say it wiped out entire communities and regions, leading to mass burials or even no burials because of the paucity of survivors.
- The 3rd pandemic never killed more than 3% of the populations of major cities.

Contagion

- Contemporary accounts of the 1st pandemic suggest a highly contagious person-to-person disease.
- Plague doctors of the 3rd pandemic discovered, to their surprise, that the bubonic plague of the late 19th and 20th centuries was rarely contagious.
- The worst epidemic of pneumonic plague, in Manchuria in 1911, infected and killed <0.3% of the population affected.

Famine

- In the 1st pandemic, plague and famine correlated closely, with famine often preceding and sparking a wave of plague, as in Constantinople and Alexandria in 618 and 619.
- In the 3rd pandemic, by contrast, famine has tended to dampen epidemics of *Yersinia pestis*, while bumper crops have intensified them.
- Increased grain yields feed higher populations of infected rats and their fleas, giving rise to higher numbers of human cases and more fatalities.

Season and Climate

- The 1st and 2nd pandemics could strike at any time of year before usually settling into a summer pattern for the southern Mediterranean and the Near East.
- But *Yersinia* plague would not strike during the hottest and driest times of the year, the least hospitable season for the flea vector.
- Scholars of the Justinian plague have been absolutely certain that the causative agent of the first pandemic must have been *Yersinia pestis*.

Temperature

- Due to the flea vector, the bubonic form of *Yersinia pestis* is sustained at epidemic levels only within 50° to 77° F (10°C to 25°C) and with high levels of relative humidity.
- Plague in cities, like Genoa, Florence, and Naples, continued to peak often through the 17th century during the hottest and driest months of the year, the least likely months of plague if a rat flea was the vector.
- Bouts of late medieval plague occurred at any time of year, including January, in places as inhospitable to the subtropical rat flea as Norway, Sweden, and Scotland.

Speed and Extent

- Like the early medieval plague, the 2nd pandemic was a fast mover, travelling sometimes almost as quickly per day as modern plague did per year.
- George Christakos et al. recently used sophisticated mapping tools to calculate:
 - the varying speeds of dissemination
 - the areas afflicted by the Black Death in 1347-1351
 - effects in all parts of Europe at different seasons

Yersinia pestis

2010

German researchers definitively established, that *Y. pestis* was the cause of the medieval Black Death.

2011

The 1st genome of *Y. pestis* showed that this medieval strain was ancestral to most modern forms of *Y. pestis*.

2015

Plasmids of *Y. pestis* were detected in teeth of 7 Bronze Age individuals, in Siberia, Estonia, Russia, and Poland.

2018

Emergence and spread of the pathogen as far back as 6K years ago proposed trade networks as the likely avenue of spread rather than migrations of populations.

2019

Evidence that suggests *Y. pestis* may have originated in Europe, not in Asia as is more commonly believed.

Y. pestis from Eurasia?

- DNA evidence published in 2015 indicates *Y. pestis* infected humans 5K years ago in Bronze Age Eurasia, but genetic changes that made it highly virulent did not occur until about 4K years ago.
- This indicates that at least two lineages of *Y. pestis* were circulating during the Bronze Age in Eurasia.

Y. pestis from Eurasia?

- A strain identified from about 4,000 YBP (the Late Neolithic and Bronze Age, LNBA) in western Britain, indicates that this highly transmissible form spread from Eurasia to the far NW edges of Europe.
- In 2016, the *Y. pestis* bacterium was identified from DNA in teeth found at a burial site in London with human remains of victims of the Great Plague of London (1665-1666).
- In 2021, researchers found a 5K year-old victim of *Y. pestis*, the world's oldest-known victim, in hunter-gatherer remains in the modern Latvian and Estonian border area.

Humans and Disease

- Global history of health looks primarily, at humans' responses to disease, at the impact of disease on individuals or populations and at the question of why humans get sick in the first place.
- The commonalities of our global diseases lie in the particular “fit” between the pathogen and the circumstances of its emergence and proliferation.
- As human social structures and connectivities change, certain pathogens have shown themselves adept at exploiting the changing characteristics of the global human species.

Humans and Disease

- The novel CoVid19 coronavirus, like tuberculosis, plague, cholera, and HIV/AIDS before it, is a disease of its time.
- All of them were once “emerging diseases,” too, but we are still living with all of them.
- We should be looking beyond the circumstances of disease emergence, and even beyond the “crisis control” model of epidemiological interventions.
- We need to look at what allows persistence.

Final Questions?



Next Week

- Session 1 Feb. 27: Definitions, Biblical Plagues.
- Session 2 March 5: The PLAGUE through time, new theories
- **Session 3 March 12: Other Infectious Pestilences**
- Session 4 March 19: The Columbian Exchange.
- Session 5 March 26: 20th Century Pandemics, Past & Current
- Session 6 April 2: HIV/AIDS
- Session 7 April 9: 20th and 21st Century Viruses.
- Session 8 April 16: Crystal Ball into the future?



THE ARTS AND THE PLAGUE

PAINTINGS



The Triumph of Death

(Trionfo della Morte)

Unknown, Circa 1488

**Fresco in the
Pallazzo Abatelli
Palermo, Italy**

Size: 19 by 21 feet



The Triumph of Death

Enhanced photograph.

Not attributed in Internet

Death on its Pale Horse



Dead and Dying Prelates & Clerics



Surviving Religious People and Surviving Nobles



LITERATURE

Literature

- *La Peste* (Albert Camus).
 - *The Masque of the Red Death* (Edgar Allan Poe).
 - *The Canterbury Tales* (Geoffrey Chaucer).
 - *A Journal of the Plague Year*
(The Marseilles Plague)
 - *Due Preparations for the Plague*
(The London Plague)
- Daniel Defoe

The Decameron of Boccaccio



- 100 stories told by 7 women and 3 men over 10 days, fleeing Florence during the Plague.
- Humor, love, pain, passion, lust, resignation.
- Graphic description of the Plague and its effects on people and society.

Poetry

- *A Litany in Time of Plague*: Thomas Nashe
- *The Triumph of Death*: John Davies
- *Soliloquy XVI*: Mary Latter
- *Pestilence*: Philip Freneau
- *The Plague*: Christina Rossetti
- *There It Is*: Jayne Cortez