



# **The Evolution of Plagues**

**“A recent problem for all parasites...is how to get from one host to another in a world in which such hosts are never contiguous entities.”**

**--William H. McNeill**

# The Evolution of Plagues

**Factors that influence plagues/outbreaks:**

- Virulence**
- Host immune status**
- Transmissibility**
- Duration of symptoms**
- Population density**

**$R_0$  = The basic reproductive ratio of the disease or the multiplier of the disease.**

# **The Evolution of Plagues**

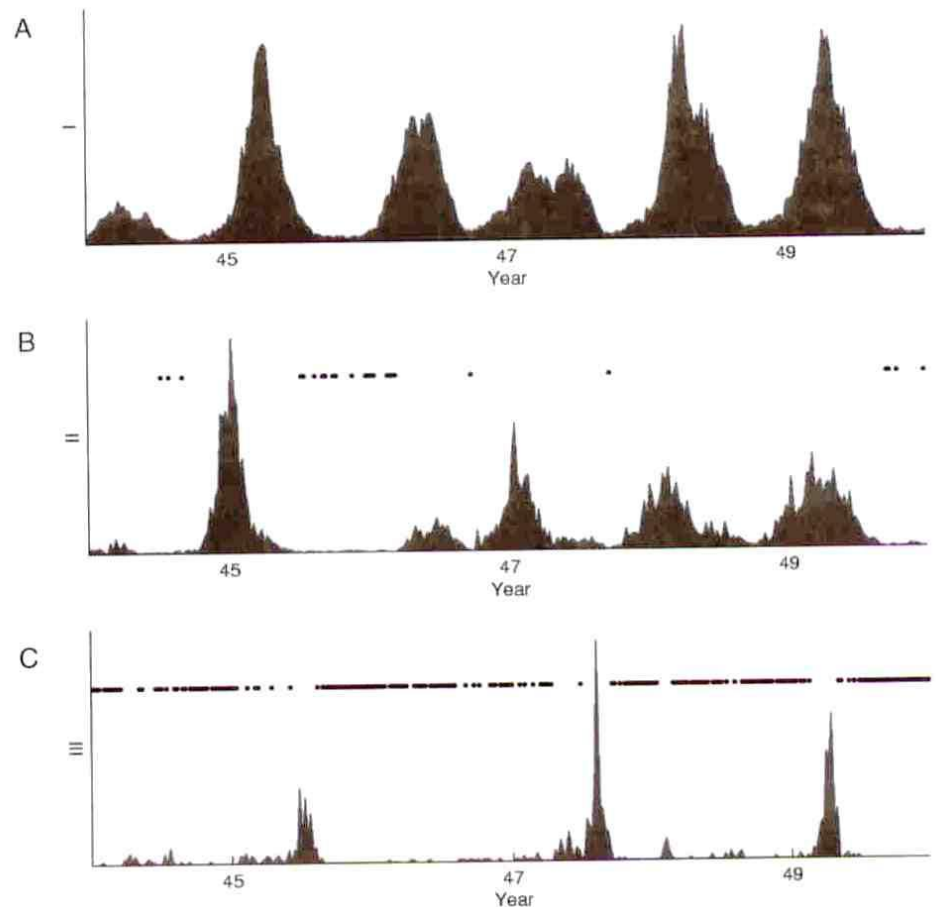
***e.g.* , measles**

- Although eradicated in the United States because of childhood immunization, it can be responsible for a death rate of about 30% in less developed countries.**
- It is one of the 10 most frequent causes of death in world today.**

# Types of Epidemics

*e.g.*, measles...population effects

- **I-3.4 million**  
–  $R_0 > 1$
- **II-300,000**
- **III-10,000**



# **Types of Epidemics**

***e.g., measles***

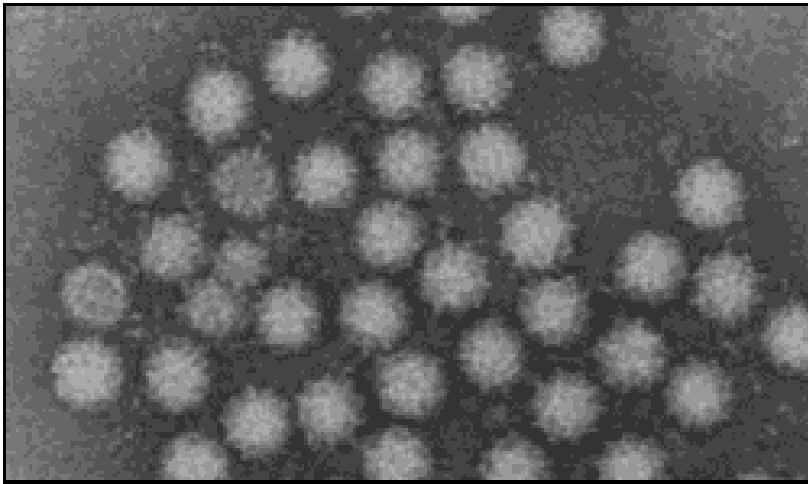
- **The  $R_0$  for measles is approximately 15.**
- **With this multiplier, measles will spread explosively without any effective control (*e.g.*, immunization), millions could become infected in months.**
- **To eliminate measles (and whooping cough), 95% of children under age of 2 must be immunized.**
- **However, to eliminate malaria in Africa, where  $R_0$  is 50-100, would require 99% coverage with a lifelong vaccine given at at 3 months of age.**

# **The Evolution of Plagues**

**“Prolonged interaction between the human host and an infectious organism, carried on across many generations and among suitably numerous populations on each side, creates a pattern of mutual adaptation to survive. Therefore...”**

**--William H. McNeill**

# Myxoma virus and Rabbits

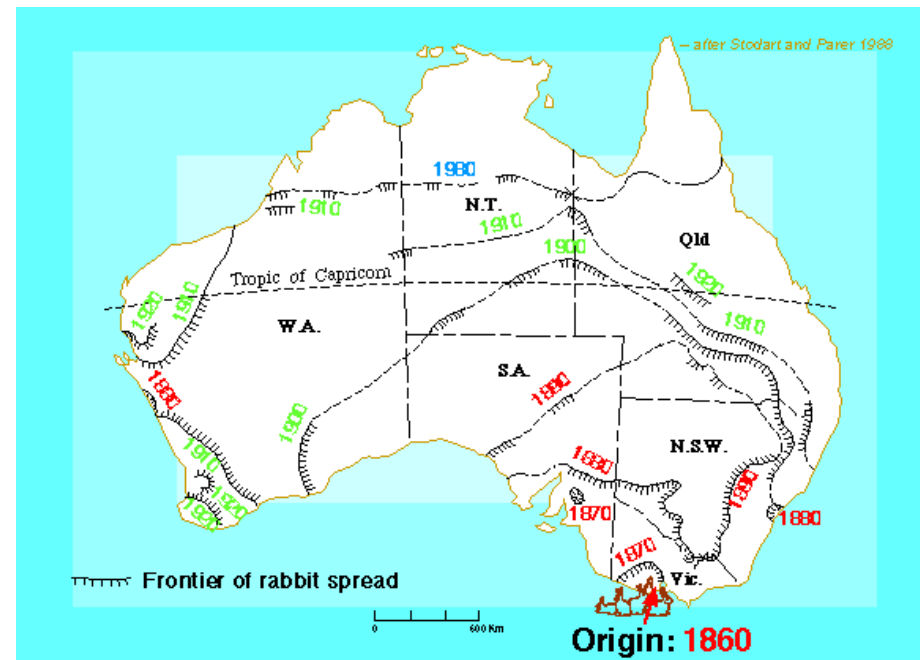


# **Myxoma virus and Rabbits**

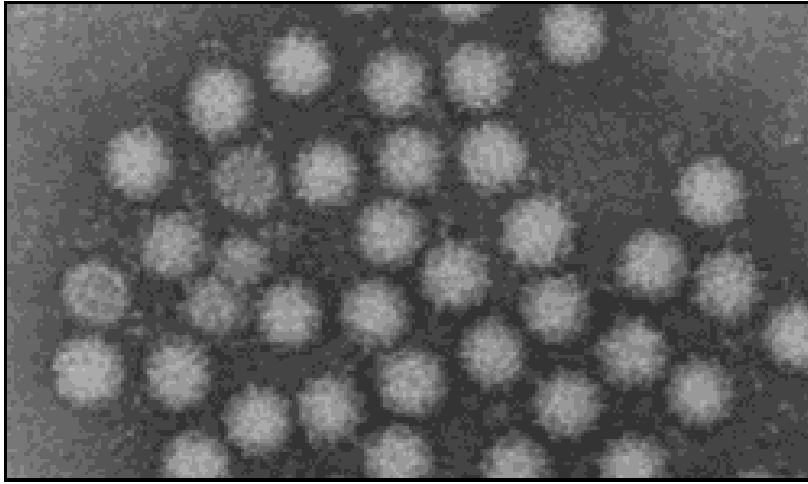
- **1839 Austin family migrated from England to Australia.**
- **To reestablish their English ‘environment,’ the Austin’s imported furniture, goods, and a variety of animals.**
- **In 1859, a ship arrived carrying rabbits.**
  - **No natural predators.**
- **By 1865, more than 20,000 rabbits were killed on the Austin estate.**

# Myxoma virus and Rabbits

- It has been estimated that rabbits cost Australian agriculture \$600 million each year (Wilson 1995).
- It also led to myxomatosis being introduced in 1950 as a biological control agent for wild rabbits.
  - Myxomatosis, a viral disease of wild rabbits from South America was introduced into Australia.



# Myxoma virus and Rabbits



**Selection favors an intermediate level of virulence.**

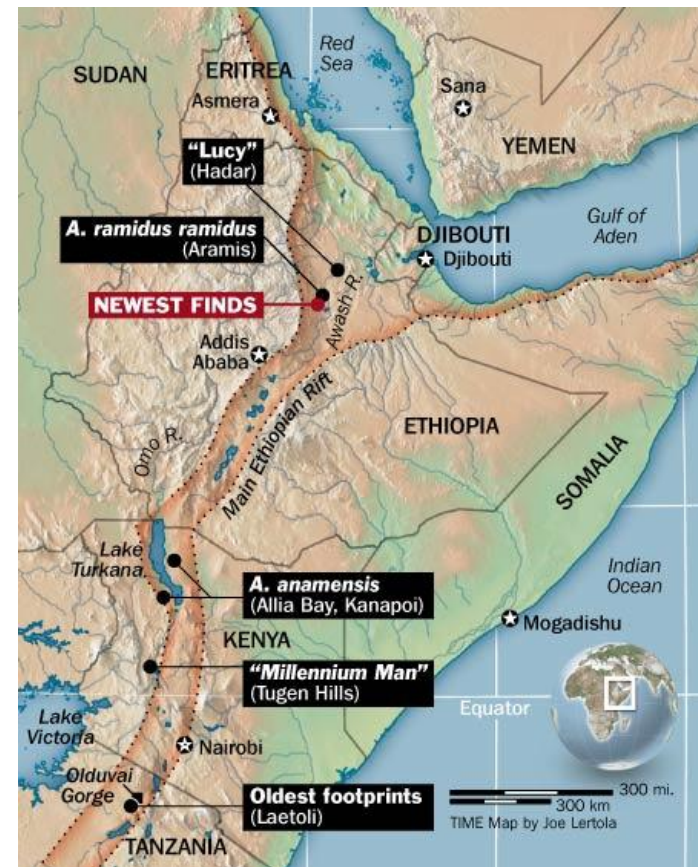


# **Plagues, the Price of Being Sedentary**

**Becoming human, Becoming  
parasitized**

# Becoming human, Becoming parasitized

- Earliest evidence of hominids.
- Moved from tree tops to ground—new environment, new niche.
- 3 million years ago African climate changed to a cooler and drier environment.



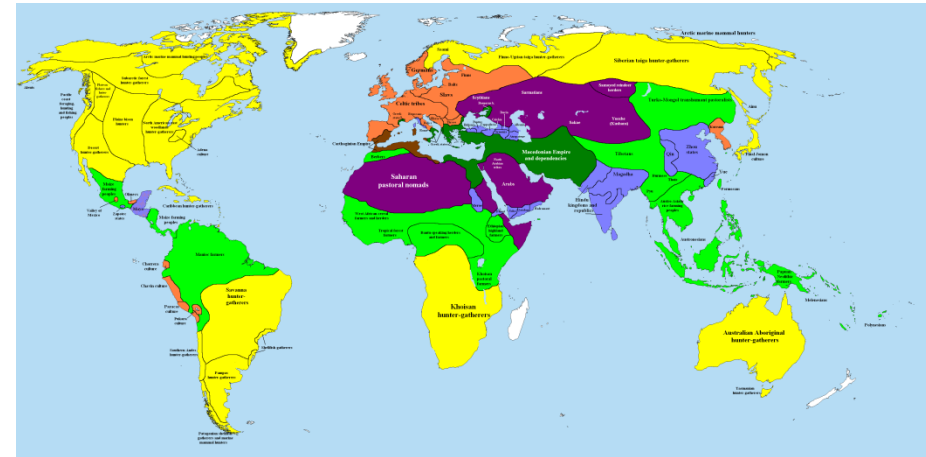
# Becoming human, Becoming parasitized

- **Climate change linked to changes in the fossil record.**
  - **Change in diet.**
  - **With meat consumption came exposure to certain parasites.**
  - **Likely, *H. habilis* exposed to various vector-borne diseases.**
  - **When migrations took place (*H. erectus*), only pathogens transmissible from human to human were carried along (vectors left behind).**



# Hunter-gatherers

- Roamed over large distances in search of wild edible plants, game animals, water sources.
- Nomadic bands were not surrounded by heaps of rotting meat or feces, and exposure to parasite-infested waters was limited.



# Hunter-gatherers

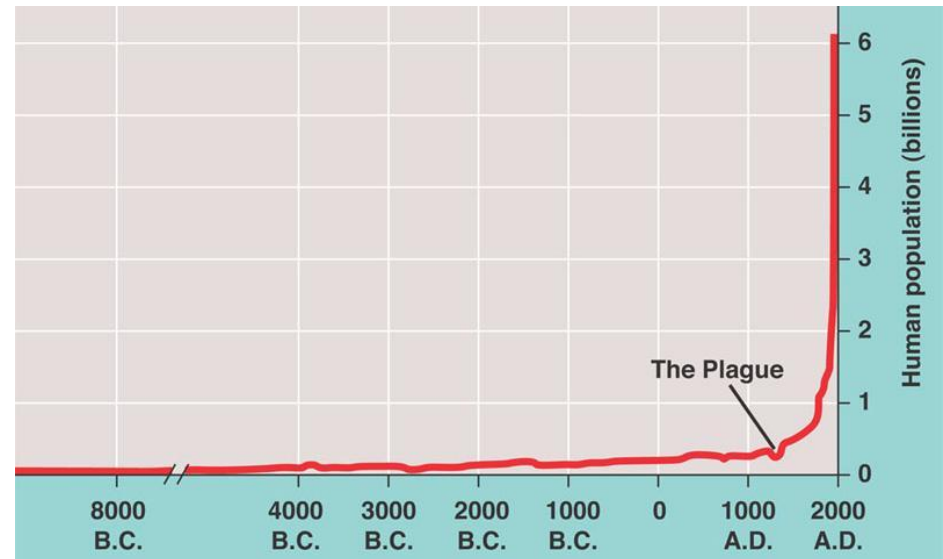
- **Based on what we know about modern hunter-gatherer societies, like those in present-day New Guinea, the Australian aborigines, and the Kalahari bushmen, we believe that our hunter-gatherer ancestors were a relatively healthy lot.**

# **Hunter-gatherers vs. Agriculture**

- **200 sq miles**
  - **Supported 50-60 hunters.**
  - **Supported 10, 000 farmers.**
- **Agriculture encouraged larger families.**
- **May not be accidental that the first known and highly organized religions arose coincident with the agricultural revolution.**

# The Lethal Gifts of Agriculture

- **Agriculture did not itself create new infections; it simply accentuated those that were already present.**
- **Created a perfect combination.**
- **Zoonotic diseases: dogs (65), cattle (45), sheep and goats (46), pigs (42), horses (35), rats (32), and poultry (26).**

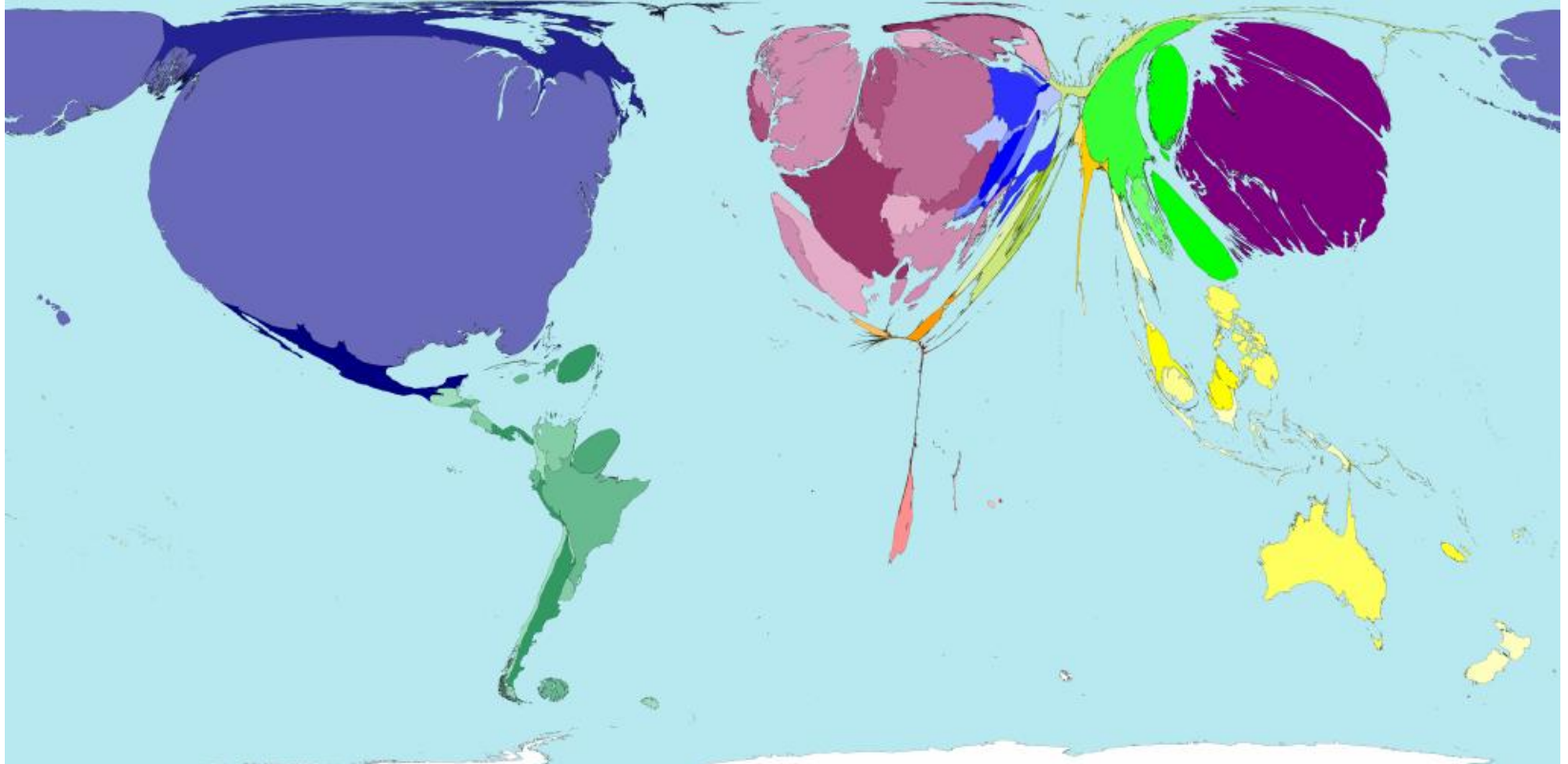


↑  
**Agricultural revolution begins**

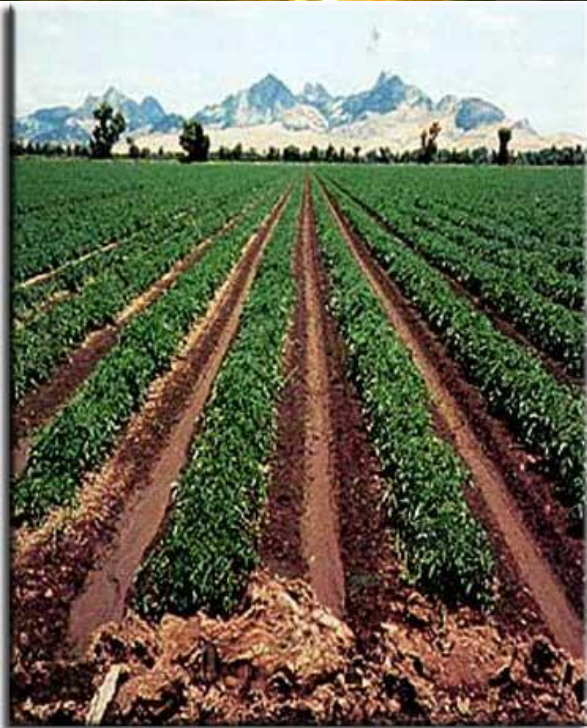
**What makes a developed  
nation?**



**Territory size shows the proportion of all McDonalds restaurants that were open in 2004, that were found there.**



**By 2004 there were 30,496 of these outlets worldwide. Of these, 45% were located within the United States so it appears large on this map.**



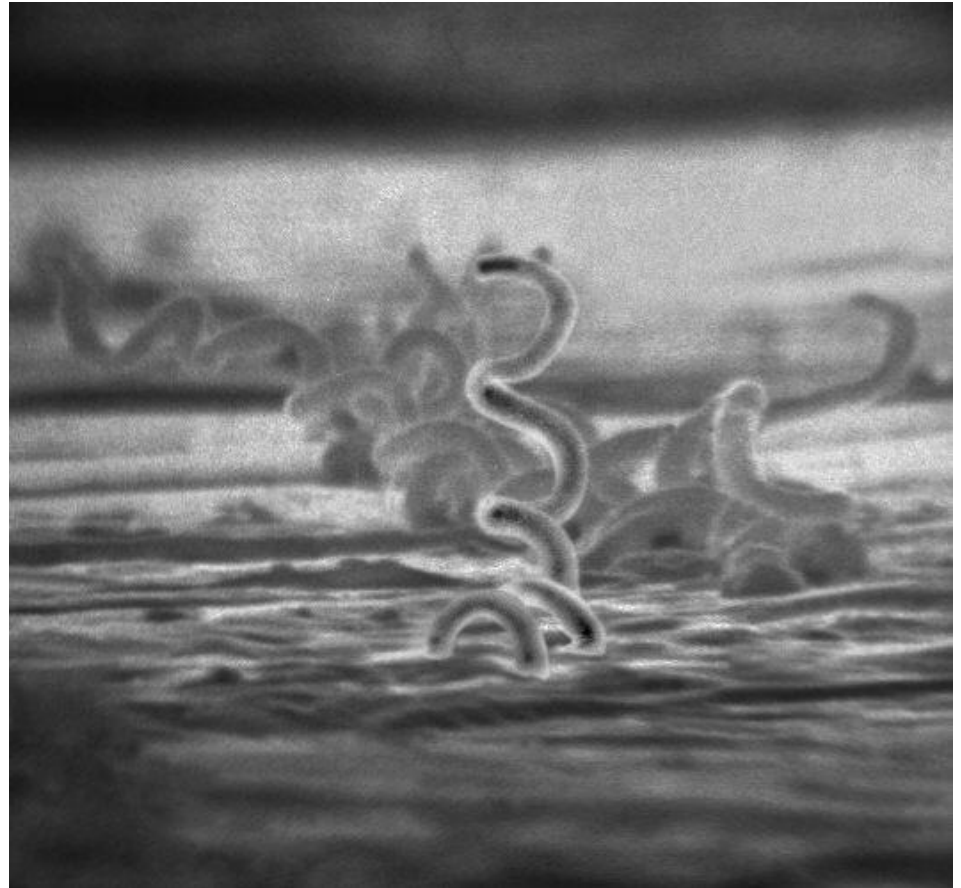
# Syphilis

*'He first wore buboes dreadful to the sight  
Felt strange pains, and sleepless passed the night.  
From him the malady received its name  
The neighboring shepherds catch'd the spreading  
flame.'*

Francastoro, 1530

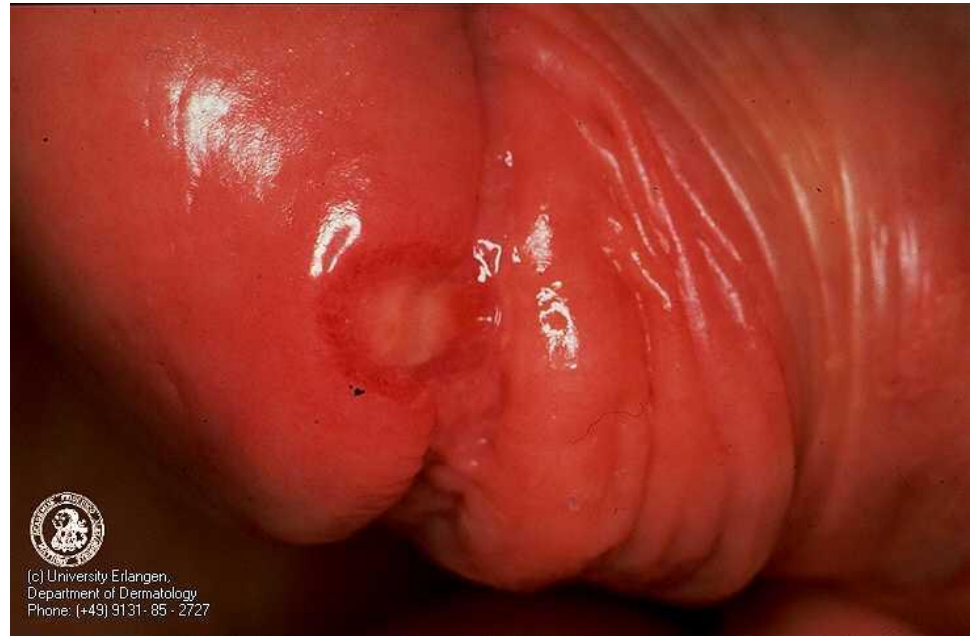
# Syphilis

- **Caused by the spirochete *Treponema pallidum*.**
- **Gram negative.**
- **To date, can not be grown in culture.**
  - ‘Trep’-corckscrew
  - ‘nema’-thread
  - ‘pallidum’-pale



# Pre-20th Century

- **If you were a sexually active man or woman in the pre-20th century U. S. or European city, syphilis was a very real threat.**
- **Untreated syphilis progresses through 3 stages:**
  - **stage 1-bacterial growth at the site of infection.**
  - **chancre**
  - **as awful as it looks, it is not painful...**
  - **heals in 1-2 weeks...false sense of security.**



**Primary lesion**

# Stage 2 Syphilis

- **Bacteria enter blood stream.**
- **Rash appears on the palms or feet.**
- **Clears up like the chancre even though bacteria still present.**
- ***T. pallidum* move out of the blood stream into tissues (as a result of immunity).**
- **Lay dormant for months or years.**
- **A painful death will ensue.**



# Origin of the Word

- The word itself (Syphilis) was coined by Girolamo Fracastoro, an Italian poet and physician.
- He published a poem called '*Syphilis, sive Morbus Gallicus*,' which translates as 'Syphilis, or the French Disease.'
- First proponent of the 'Germ Theory.'



1478-1553



# *Syphilis, sive Morbus Gallicus*

- **In the poem, a shepherd named Syphilis is supposed to have been the first victim of the disease.**
- **The original source of the name Syphilis is uncertain but may have come from the poetry of Ovid.**
  - **Bottom line was that the Italians blamed the French for syphilis.**
  - **The French blamed the Italians.**
  - **In Spain, the disease was blamed on the Jews, who had been forced out of Spain, also in that memorable year of **1492**.**
  - **Russians called it ‘the Polish disease.’**
  - **The Japanese called it ‘the Chinese disease.’**
  - **The English called it ‘the Spanish disease.’**

# Did Columbus's men bring syphilis back to Europe?

- “Contemporaries thought it was a new disease against which Eurasian populations had no established immunities. **The timing** of the first outbreak of syphilis in Europe and the place where it occurred certainly seems to fit what one would expect of the disease had it been imported from America by Columbus' returning sailors. This theory...became almost universally accepted...until recently.”
  - W. H. McNeill. *Plagues and People*. 1977
  - This urban legend acquired a sort of mystique as an unintended form of ‘**revenge**’ unwittingly exacted by the Indians for what Columbus and the the arrival of the Europeans had done to them.

# Evidence against Columbus

- **Pre-Columbian syphilis in the Old World.**
  - **245 skeletons recently unearthed from a medieval monastery known as Blackfriars (Hull, England) showed distinctive signs of syphilis (1300-1420).**
  - **Notched teeth from the remains of individuals from the port city of Metaponto, Italy (600 B.C.).**
  - **Also in remains from those who died in Pompeii following the eruption of Mount Vesuvius (79 A.D.).**
    - **Some believe syphilis has been in Europe for thousands of years.**

# Notched teeth & caries sicca



# The Beginning of the Outbreak

- The return of Columbus and his men coincided with a massive outbreak of syphilis in Europe.
- Syphilis in epidemic proportions 1st appeared during a war being fought in Naples in 1494.
- The army of the French king, Charles the VIII, withdrew from Naples, and the disease was soon spreading throughout Europe.



# The spread of syphilis--‘The Great Pox’

- **The mercenaries of Charles VIII spread the disease over Europe.**
  - **Some of these mercenaries joined Perkin Warbeck in Scotland and, with the support of James IV, invaded England. **The pox was evident in the invading troops.****
  - **Hungary and Russia by 1497**
  - **Africa and the Middle East by 1498**
  - **The Portuguese carried it around the Cape of Good Hope (Vasco de Gama) to India in 1498.**
  - **China by 1505.**
  - **Australia by 1515.**
  - **Japan by 1569.**

# **The spread of syphilis--‘The Great Pox’**

- **European sailors carried the Great Pox to every continent save for Antarctica.**
- **Syphilis was so ubiquitous by the 19th century that it could be considered to be the AIDS epidemic of that era.**
- **The parallel between AIDS and syphilis does not end there.**

# Progression of symptoms and Severity

- Favoring the theory that syphilis was a **new disease** was its severity during the beginning years of the outbreak.
  - From **1494-1516** the symptoms were described as genital ulcers, followed by a rash, and then the disease spread throughout the body, affecting the gums, palate, uvula, jaw, and tonsils eventually destroying these organs.
    - the victims suffered pains in the muscles and there was early death--an **acute disease**.

# Progression of Symptoms & Severity

- From **1516-1526**, two new symptoms were added to the list: bone inflammation and hard pustules.
- From **1526-1560**, the severity of symptoms diminished, and thereafter its lethal effects continued to decline but...
- From **1560-1610** there was another symptom: ringing in the ears.
- In the **1700s**, syphilis was a dangerous but not an explosive infection.
- By the **1800s**, both the virulence of the pathogen and the number of cases declined.
- Even so, by the end of the **19th century**, 10% of the European population was infected.
- Early **20th century**, 1/3 of the patients in mental institutions could trace their neurological symptoms to syphilis.

# Pre-Columbian Origin

- **All of the treponemes that cause the human diseases yaws, pinta, and syphilis are identical in their morphology.**
- **Genomes contain only 1000 genes.**
- **No gene(s) has been found to be specifically associated with virulence.**
- **Only symptoms differ.**

# Pre-Columbian Origin

- This theory suggests that human treponemes may have come from animals and that an infection similar to **pinta** (*T. carateum*) resulted.
- Localized in the skin.
- Arose about 15,000 B.C. in Africa.
- With human migration passed across the Bering Straits it became isolated in the tropics of the Americas.
- **Pinta** only found in skin-- disseminated by introduction into skin.



# Pre-Columbian Origin

- Around 10,000 B.C., the pinta-causing spirochete mutated into a pathogen causing a disease similar to **yaws**.
  - *T. pallidum pertenue*
- Restricted to tropical areas of Africa.
- Brought to the Americas by the slave trade.
- Yaws exists today in tropical climates.
- Not benign.
- Causes disfigurement.



# Pre-Columbian Origin

- As populations of *Homo sapiens* began to penetrate into **temperate and drier regions**, the presence of cooler climate provoked another mutation, allowing the bacteria to colonize the throat and to produce skin lesions similar to those of endemic syphilis.
  - *T. pallidum endemicum*
- Transmission occurs via contaminated objects (drinking vessels, utensils, saliva, mouth-to-mouth).
- It has been known to exist in Africa for centuries.
- Today found in pre-pubescent children living under semi-nomadic conditions in the northern Sahara, southwest Asia and Australia.

# Pre-Columbian Origin

- A third mutation resulted in the true venereal transmission form of spirochetes.
- Coincided with the emergence of cities about 3000 B.C. in the Middle East.
- Spread to the Mediterranean in mild form.
- Remained endemic for centuries.
- **Fourth mutation occurred in Europe in the 15th century**
  - environmental conditions, behavioral patterns allowed the venereal form of the disease to emerge.

# Syphilis and Its Social Context

- **Charles VIII**
- **Francis I**
- **Pope Alexander Borgia**
- **Benvenuto Cellini**
- **Henri Toulouse-Lautrec**
- **Heinrich Hinze**
- **Franz Schubert**
- **Peter the Great**
- **Catherine the Great**
- **Florence Nightingale**
- **John Keats**
- **Guy de Maupassant**
- **Al Capone**
- **Randolph Churchill**
- **Beethoven's deafness?**

# Syphilis and Its Social Context

- **Ivan, Grand Duke of Muscovy, born 1530.**
- **In 1552 wife Anastasia gave birth to a son, Dimitri, who died at age 6 months of congenital syphilis.**
- **9 months later Ivan was born and in 1558 a third son, Fedor, was born.**



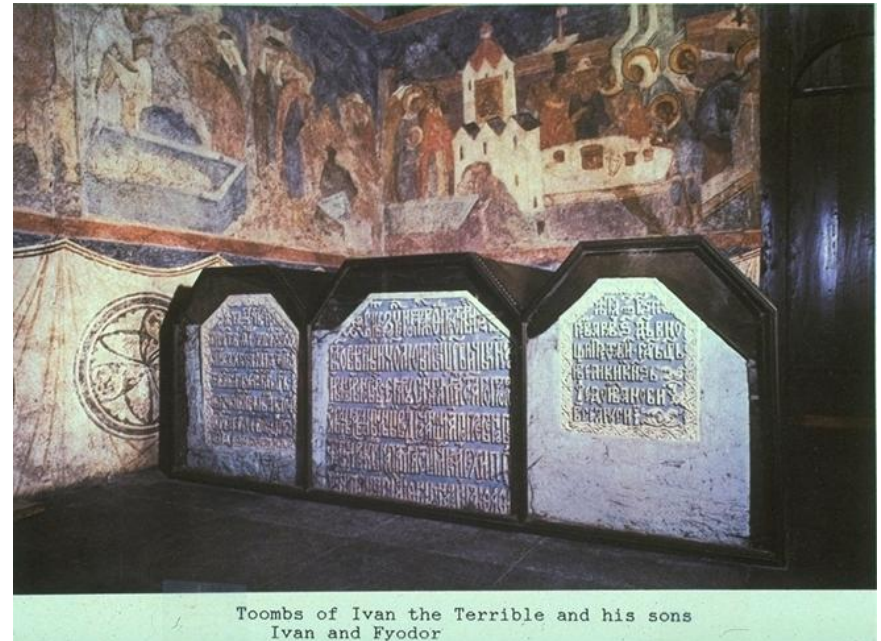
# Syphilis and Its Social Context

- **It was suspected that Ivan was infected with syphilis prior to his marriage.**
- **Anastasia died in 1560 and Ivan remarried in 1561.**
- **She gave birth to Vassili, who lived 5 weeks.**
- **By 1563, there was evidence that Ivan was suffering from neurosyphilis.**
- **From 1565-1584, Ivan engaged in a reign of terror.**



# Syphilis and Its Social Context

- **Ivan tortured, flogged, burned, and boiled those he considered to be his enemies.**
- **Claiming conspiracy, he had thousands of citizens of Novgorod flogged to death, roasted alive, or drowned under the ice.**
- **Ivan and his son raped the widow and daughter of Prince Viskavati (whom they hanged).**
- **In 1581, during a fit of rage, he stabbed his son to death.**
- **Ivan died a gibbering idiot at 54.**
- **This left the throne to the congenital idiot Fedor.**



Toombs of Ivan the Terrible and his sons  
Ivan and Fyodor

# Henry the VIII and the Decline of the Tudor Line

- Catherine of Aragon → -Birth to a child who died within days.  
-She had 3 more stillborns.
- Anne Boleyn → Miscarried on child at 6 months and another at 3.5 months.
- Jane Seymour → One son Edward who died of 15(?).
- Elizabeth I (born of Boleyn)
- Marry Tudor → Also nearsighted, deaf, large flat nose that discharged a foul smelling pus

# The man himself...Henry the VIII

- **Became sterile or impotent in his late forties.**
- **His character (like Ivan) began to change.**
- **Suffered from ulcers, headaches, sore throats.**
- **Had a gumma on his nose.**
- **Bent on terror--slaughtered the Lollards, Lutherans, Anabaptists, and Catholics.**



**“The inability of royal and aristocratic leaders to give birth to healthy children accelerated social mobility making more room at the top than there would have been otherwise--thanks to syphilis!”**

**William H. McNeill**

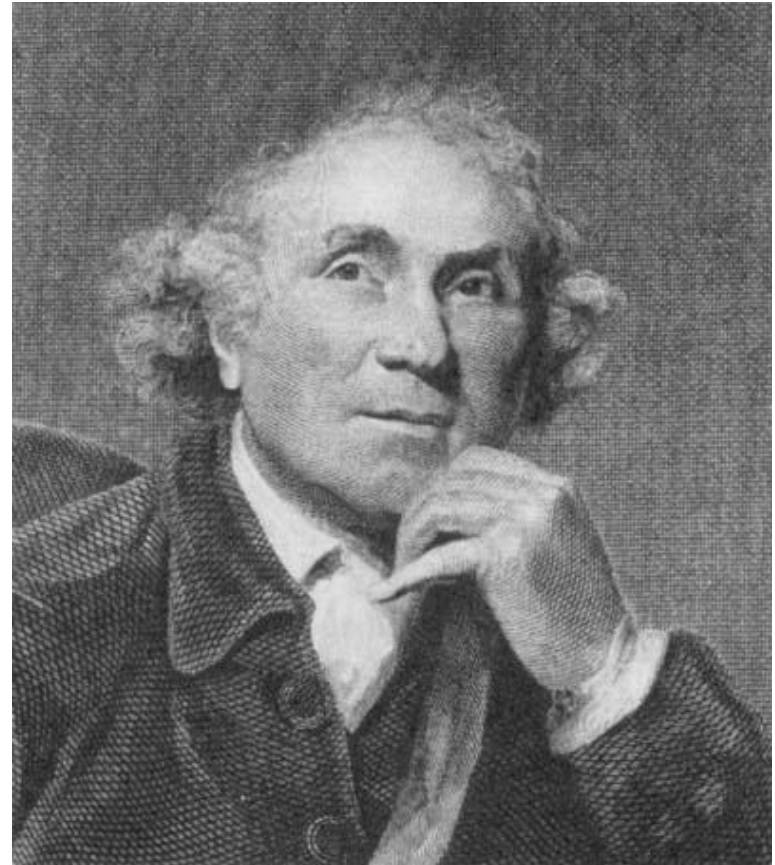
# Spirochete Discovered

- **One of the reasons it took so long for microbe hunters to identify the cause of syphilis was that it was confused and associated with another STI, gonorrhoea.**
- **Even the great anatomist and physician John Hunter (1748), of St. George's hospital in London, could not solve the puzzle...**



# John Hunter (1728-1793)

- Considered one of the greatest anatomists of all time and the founder of experimental pathology in England. Hunter put the practice of surgery on a scientific foundation and laid the framework for the twentieth century developments. His saying "**Don't think, try the experiment**" has inspired generations of modern surgeons.



# The opposite of Jenner...

- **No vaccine available.**
- **An early disastrous attempt by Joseph Auzias-Turenne (1812-1870) drew inspiration from Jenner's small pox vaccine.**
- **He took a part of a **soft chancre** and prepared it for use as vaccine.**
- **The chancre was caused by *H. ducreyi*.**
- **Had the scheme prevailed in 19th century France, thousands would have been mistakenly believed to have been vaccinated against syphilis; instead, they would have gotten chancroid!**

# Syphilis Cure

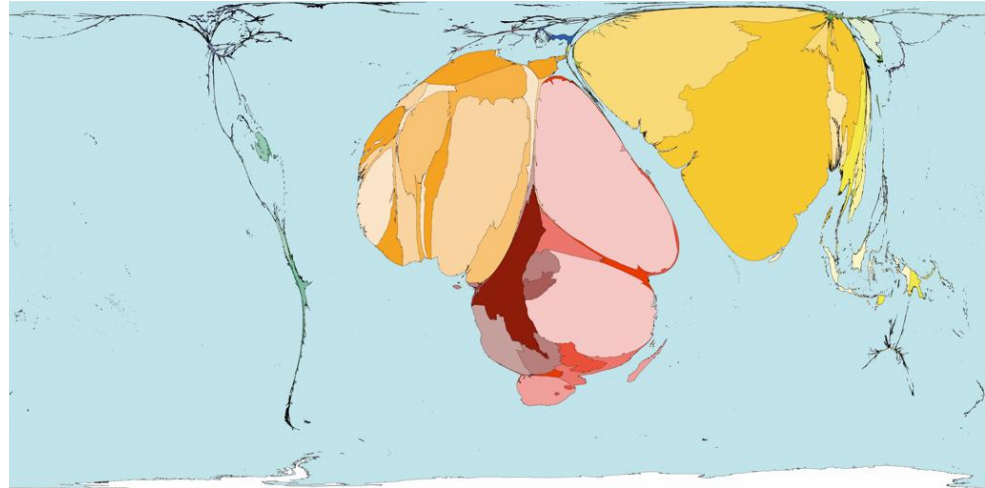
- **Moralists living at the time when syphilis ran its course unimpeded would have disapproved of a cure for syphilis.**
  - **‘Wages of sin.’**
- **What about unsuspecting spouses or fetuses?**
- **What about present time? Who worries about syphilis? How would antibiotics have changed history?**

# *The Wages of Sin: Sex and Disease, Past and Present--Peter Allen*

- **15th and 16th century treatments for syphilis.**
  - Patients were smeared with a cream containing a high concentration of mercury.
    - shut into a small hut called a ‘stew.’
    - many died from the treatment
    - few were cured.
  - Ingestion of arsenic derivatives introduced in the 1800s.
    - many deleterious side effects that did not cure disease
    - in 1909 Paul Ehrlich developed an arsenical derivative (**salvarsan**), that was effective in reducing severity.
      - years of treatment
      - toxic
      - remained the treatment until 1943

# Syphilis Today

- Syphilis caused **0.3%** of deaths worldwide in 2002 or **25 deaths/million**.
- Territories are sized in proportion to the absolute number of people who **died from syphilis** in one year.

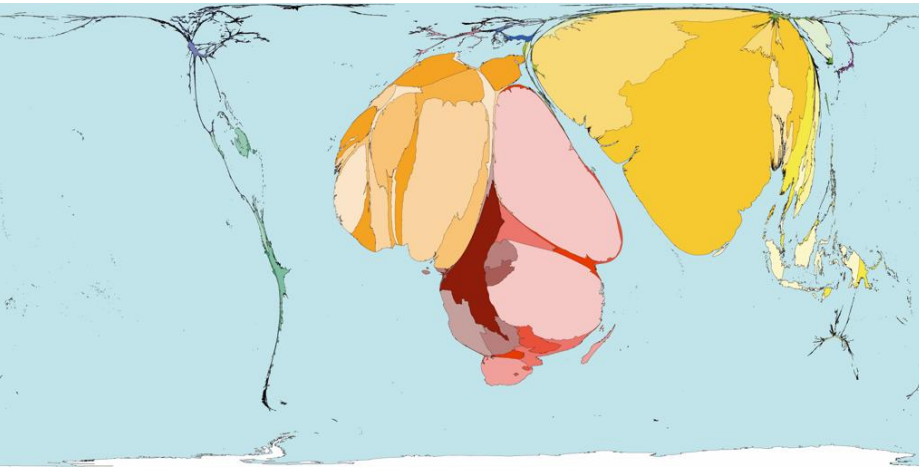


# Syphilis Today

## STDs Excluding HIV Deaths

The diseases, described below, are the sum of (with their contribution to the total STDs excluding HIV deaths in 2002):

- **A- Syphilis, Map 375, (87% of deaths).**
- **B- Chlamydia, Map 376, (5% of deaths).**
- **C- Gonorrhoea, Map 377, (1% of deaths).**
- **D- Other STDs, no map, (7% of deaths).**



**Territories are sized in proportion to the absolute number of people who died from sexually transmitted disease in one year.**

# Plague

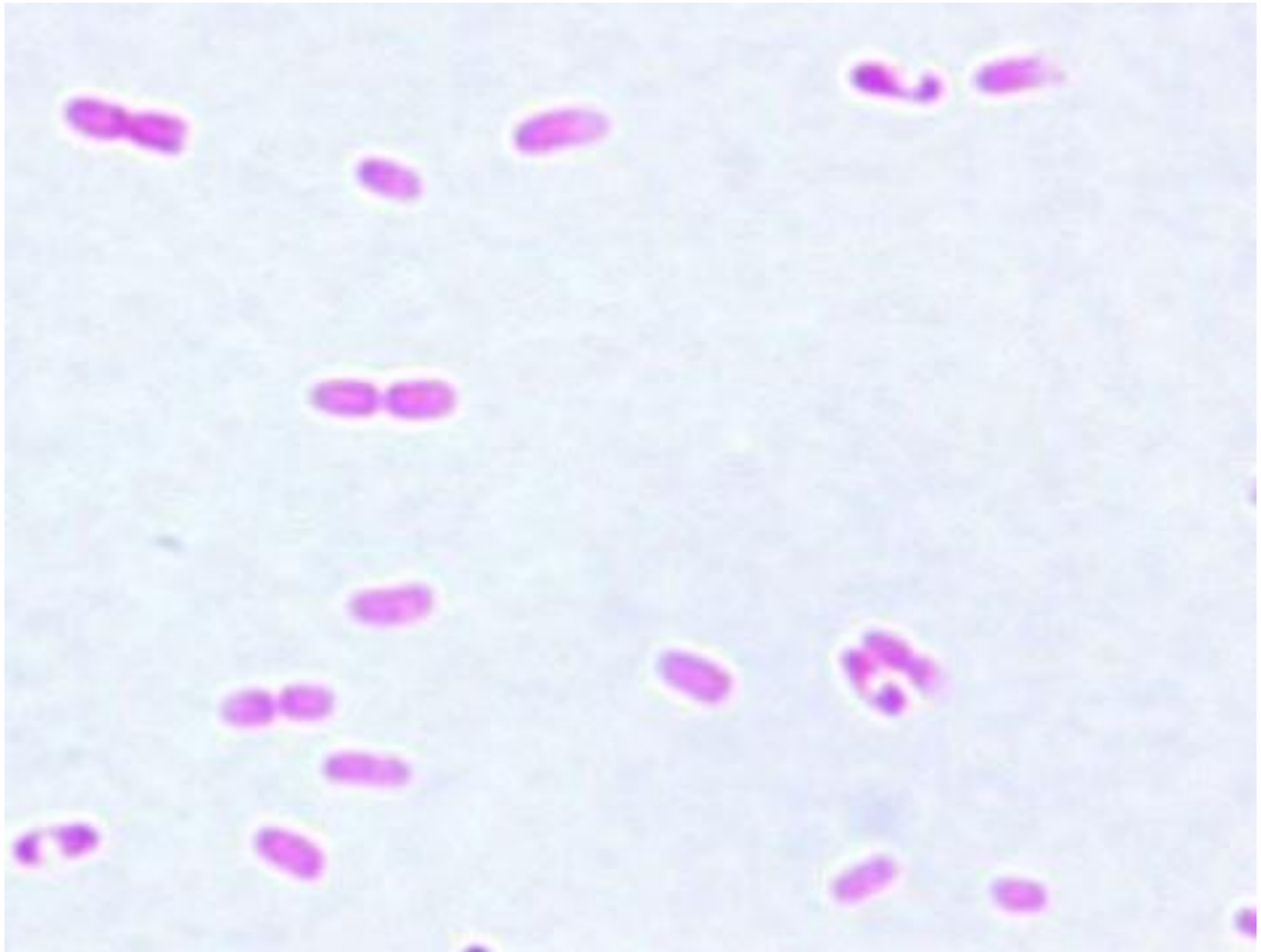
*‘Lord! how sad it is to see the streets empty of people, and very few upon the ’Change. Jealous of every door that one sees shut up, lest it should be the plague; and about us two shops in three, if not more, generally shut up.*

**Samuel Pepys Diary, August 16, 1665**

# Plague--Definition

- **Acute, febrile, contagious disease caused by *Yersinia pestis* (formerly *Pasteurella pestis*).**
- **Bipolar gram-negative bacillus of the family Enterobacteriaceae.**
- **Aerobic, facultatively anaerobic.**





# Plague--Synonyms

- **Black plague**
- **Black death**
- **the pest**
- **pestis**
- **Bubonic plague**
- **septicemic plague**
- **pneumonic plague**



# Plague--**Clinical Features**

- **Three clinical forms:**
  - **bubonic**
  - **primary septicemic**
  - **primary pneumonic**

# Plague--**Clinical Features**

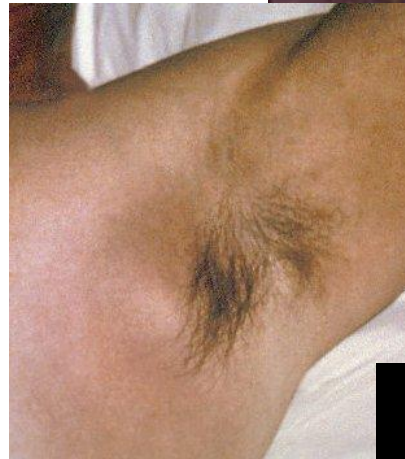
- **Bubonic**

- **most common; contracted by flea bite**
- **minute lesion at bite sight in 25% of patients**
  - **phenotype of lesion variable**
- **following a 2-4 day incubation there is an onset of chills, high fever, tachycardia, tachypnea, anxiety accompanied by the appearance of the bubo with its sharp stabbing pain and swollen, nonfluctuant lymphadenitis**

# Plague--Clinical Features

- **Bubonic**

- neutrophilic leucocytosis with the WBC count reaching 40,000/ $\mu$ l.
- in children it can reach 100,000/ $\mu$ l
- blood cultures are positive in 50% of patients
- buboes very painful.
  - mainly inguinal but in children can be axillary or cervical



# Plague--Clinical Features

- **Bubonic**

- **Lymph node involvement progresses proximally.**
- **Septecemia and secondary pneumonic plague follow.**
- **Terminal petechiae and hemorrhagic cutaneous infarcts caused by DIC result in ‘black’ lesions.**
- **Untreated mortality is 60-90%.**
- **Death is rapid, sometimes within 1 day (usually 5).**
  - **If treatment is delayed, the endotoxemia may kill the patient even though all bacilli are dead.**

# Plague--Clinical Features

- **Primary septicemic**
  - 1% of infections
  - sudden clinical onset with chills, fever, anxiety and prostration
  - meningitis is common
  - course of disease is rapid--90% fatal with 1-2 days
  - Pneumonia and hemorrhage are common
  - Pathogenesis is not clear but it has been postulated that the flea may introduce bacilli directly into the blood stream.

# Plague--Clinical Features

- **Primary pneumonic**
  - **develops when airborne bacilli are inhaled, usually from cadavers or animal carcasses or more commonly from the cough of a patient with pneumonic plague.**
  - **24-60 hour incubation results in sudden chills, high fever, severe cough, and dyspnea.**
  - **sputum is watery and frothy, occasionally bloody, and teeming with bacteria**
  - **mortality is 90%** in 8-24 hours if untreated
  - **death results from respiratory insufficiency or endotoxic shock**

# Plague--**Synonyms**

- **Some contend that the black splotches on the skin resulting from hemorrhages is why it was called the ‘Black Plague.’**
- **Others speculate that ‘*black*’ is a mistranslation of ‘*pestis atra*,’ meaning , not black, but a ‘*terrible*’ or ‘*deadly*’ disease.**

# The Plague--History

- **During the last 2000 years, three great bubonic plague pandemics have resulted in social and economic upheavals that are unmatched by those caused by any armed conflict or any other infectious disease (to date).**



***The Plague*, by Felix Jenewein (1900), shows a mother carrying a coffin with her child.**

# The Plague-**Three Pandemics**

- **542-543**-Constantinople, Roman capital in the East. Plague contributed to Justinian's failure to restore imperial unity.
- **1346-1352**-By the time it dissipated, the population of Europe and the Middle East had been reduced from 100 million to 80 million.
  - put an end to the rise in human population that had begun in 5000 B.C.
  - 150 years to recover
- **1860s**-Yunnan region of China
  - killed more than 200 million people

# **The Plague-Three Pandemics**

- **In the early part of the nineteenth century, India bore the heaviest plague burden, but this was exhausted by 1950.**
- **In the 1960s, Vietnam had 10,000 deaths/yr.**
- **In recent times, plague has existed principally as sylvatic foci in the southwestern U.S., Africa, South America, and the Far East.**
  - **sporadic accidental human infections occur with these sylvatic foci**

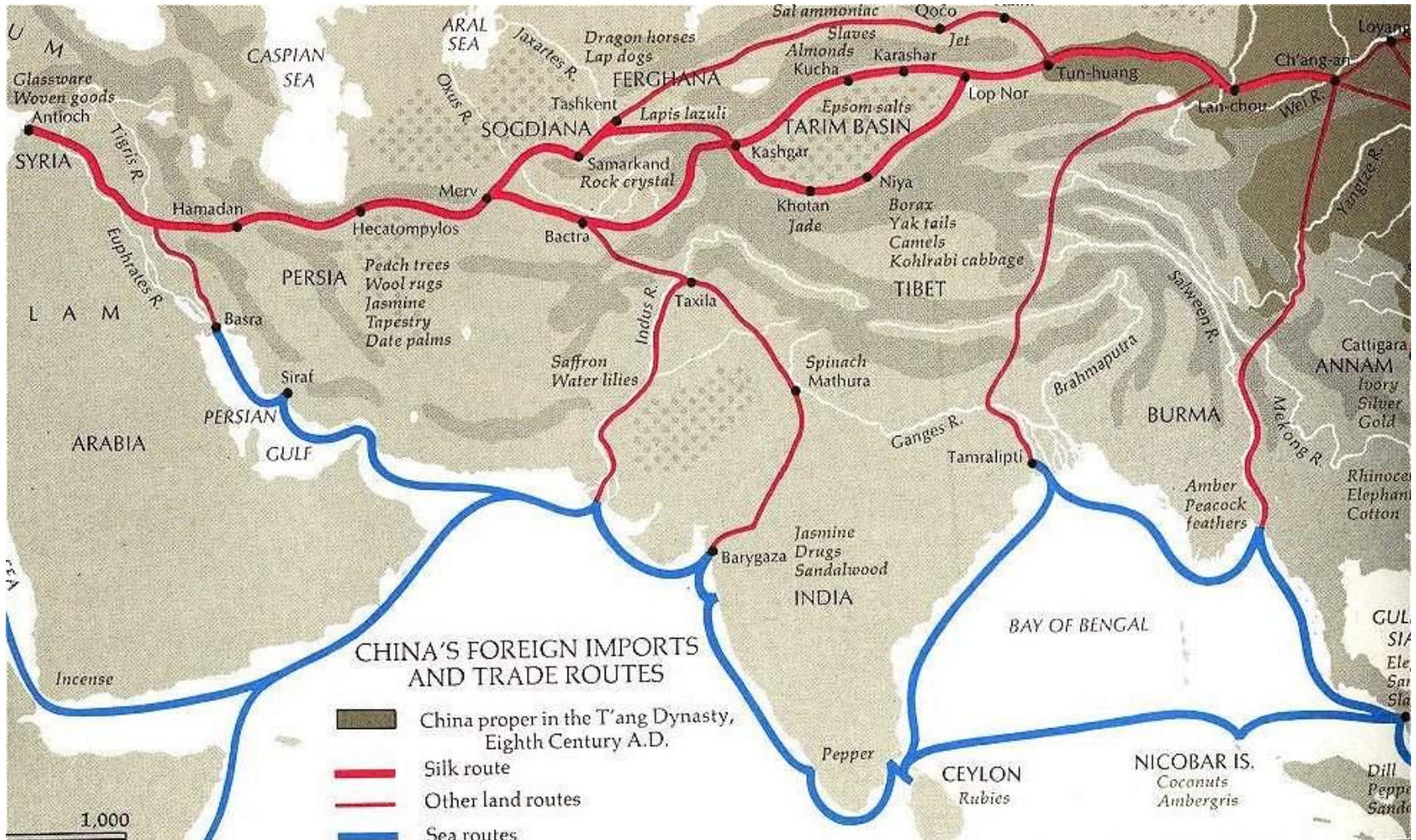
# The Plague--History

- Although those living in the medieval period recognized that plague was a contagious disease spread from person-to-person, **its cause was not identified.**
- We now know that the source of the second pandemic was microbes left over from the first pandemic (Justinian plague).
- Disease had moved eastward and remained endemic for 7 centuries in voles, marmots, and the highly susceptible black rats (*Rattus rattus*).

# The Plague--History

- **Plague-infected rats moved along the the caravan routes between Asia and the Mediterranean known collectively as the **Silk Road**.**
- **Asia--around the Caspian Sea--Crimea.**
- **There the rats boarded ships and moved from port to port and country to country, spreading plague to the human populations living in filthy, rat-infested cities.**

# The Silk Road



# The Plague--History



# **The Plague--History**

- **The story of the Pied Piper of Hamelin (or Hameln) may have had its roots in the plague-ridden cities of Germany.**
- **Legend has it that on June 26, 1284, the city became infested with rats.**
- **A pied piper was hired to lure the rats to their death by drowning them in a river.**
- **Grimm Brothers (1812).**

# The Plague--History

- **The contagious nature of the plague led to the belief that the only way security could be achieved was total isolation of the sick.**
- **In 1374, the Venetian Republic required that all ships, their crew, passengers and cargo had to remain on board for 40 days while tied up at the dock; this gave rise to the term “quarantine” (from the Italian word *quaranta* meaning 40).**
- **However....**

# The Plague--History

- The contagious nature of the plague led to the belief that only way security could be achieved was total isolation of the sick.
- In 1374, the Venetian Republic required that all ships, their crew, passengers and cargo had to remain on board for 40 days while tied up at the dock; this gave rise to the term “quarantine” (from the Italian word *quaranta* meaning 40).
- However....



# The Plague--History

- **Cordon sanitariums or people shut up in their homes.**
- **Burning of clothes from the sick or dead.**
- **Led to societal and religious changes:**
  - **feudal structure began to break down**
  - **laboring classes became more mobile**
  - **merchants and craftsmen became more powerful**
  - **decline in papal authority**
  
  - **From 1347-1722, plague epidemics occurred in Europe at infrequent intervals**
  - **In England, every 2-5 years (1361-1480)**
  - **Half the population of Milan died in 1630**
  - **60% of the population in Genoa died in 1656-1657**



***Triumph of the Dead, Pieter Brughel, 1562.***

# **The Plague--History-Religion**

- **500 people died/day in cities of 50,000.**
  - **Priests who gave last rites had a very high mortality**
  - **Loss of faith in the clergy.**
- **The Roman Catholic Church passed the responsibility for the plague on to God.**
  - **However, even God's servants were not spared.**
  - **All of the friars of a monastery near Avignon, and another near Marseilles, succumbed to the plague.**
- **Healer saints and pilgrim movements (the Brethren of the Flagellants) further threatened the Church.**

# ‘A Procession of Flagellants,’ Goya



# St. Roch



# **The Plague--History-Medicine**

- **Medieval society had four kinds of medical practitioners:**
  - **Academic physicians-followed the teachings of Galen.**
    - **believed disease was an imbalance in the humors**
    - **usually older men**
    - **people lost confidence**
  - **surgeons**
  - **barbers**
  - **folk medicine**

# The Plague--**History-Medicine**

- **Surgeons**
  - died at higher rates than did other medical practitioners.
  - Role in curing disease was little valued.
  - Beak contained perfumes or spices.



# The Plague--History-Medicine

- The stench of death was so great during the plague years that to ‘purify’ the air, the perfume eau de cologne was invented in Germany and named after the city of Cologne.
- Today the perfume is known as ‘4711,’ the street address of the household where it was first made.



# The Plague--**History-Medicine**

- **New prestige fell to barbers, bloodletting and surgery.**
- **A new emphasis on studies of human anatomy in health and disease.**
- **Galenic system (which had no clear theory of contagion, declined in importance).**



# Plague--**Finding the Killer**

- **Even in medieval Europe, it was obvious the disease was contagious.**
- **However, even if Francastoro's idea of "seeds of contagion" was accepted, there were no means of identifying the agent of disease.**
- **Two schools of thought (one in France-*Pasteur* and the other in Germany-*Koch*) were responsible for firmly grounding the germ theory.**
  - **Throughout their lives, these microbe hunters remained fierce competitors.**

# Plague--Finding the Killer

- As the plague ravaged China during the 3rd pandemic, Pasteur dispatched Alexandre Yersin (1863-1943).
- On June 24, 1894, he wrote to Pasteur that the fluid taken from the bubo contained Gram negative bacilli.
- Now referred to as *Y. pestis* NOT *P. pestis*.
- He did not, however, find the means by which it was transmitted.
  - Paul-Louis Simond identified the flea vector in 1898.



# Plague--the Vector

- The rat flea (*Xenopsylla cheopis*) is the most important vector species.
- On ingesting blood from an infected mammal, *Y. pestis* replicates unchecked.
- Bacteria produce a coagulase active at 20-28°C (but inactive at 35-37°C).
  - this prevents the flea from digesting the blood meal
  - no plague when it is too hot



# Primary Pneumonic Plague-- Sputum

