

**Plagues  
Pestilences  
Poxes and  
Pandemics  
Version 2.0**

March 19, 2024

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**OLLI Spring 2024**

**Session 3:**

**Other Infectious Pestilences**

# Course Overview

- 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: 20<sup>th</sup> Century Pandemics, Past & Current
- Session 6 April 2: HIV/AIDS
- Session 7 April 9: 20<sup>th</sup> and 21<sup>st</sup> Century Viruses
- Session 8 April 16: Looking into the crystal ball (?)

# Pestilence

A deadly and overwhelming infectious epidemic disease that is virulent, devastating and can kill many people in an area or community.

# Session Outline

- Viruses vs Bacteriae, contrasts and similarities:
  - DNA vs RNA viruses
- Historically important pestilences:
  - Polio (viral without vector)
  - Yellow Fever (viral with vector)
  - Cholera (bacterial)
  - Malaria (parasitic with vector)

A detailed microscopic image showing a variety of microorganisms. In the foreground, there are several large, spherical viruses with prominent, sharp spikes on their surfaces. Behind them and scattered throughout the field are various bacteria, including rod-shaped bacilli and smaller, more rounded cocci. The background is a dark, textured green, suggesting a biological or cellular environment.

Differences  
Similarities

# **VIRUSES and BACTERIAE**

# Virus vs Bacteria

## Viruses

- Require a living cell.
- Cannot self-replicate.
- Made up of DNA or RNA.
- From Latin: “poison”.
- 20-400 nm (billionth)
- No self-propulsion.
- Does not need oxygen.
- Antibiotics won’t work.

## Bacteriae

- Unicellular micro organisms.
- Can self-replicate.
- Reproduce by cell division.
- From Latin: “little stick”.
- 1000 nm (billionth).
- May self-propel.
- May/may not need oxygen.
- Antibiotics may work.

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# Diseases

## Viral

- Measles
- Smallpox
- Yellow fever
- HIV/AIDS
- Influenza
- Polio
- Herpes
- Hepatitis (A, B, C and D)

## Bacterial

- Syphilis, Gonorrhea
- Plague
- Whooping cough
- Rabies
- Tuberculosis & Leprosy
- Anthrax
- Typhus & Typhoid Fever
- Botulism

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Any organism or organ system can have bacterial and/or viral infections.

# Viruses

## Similarities

### DNA Virus

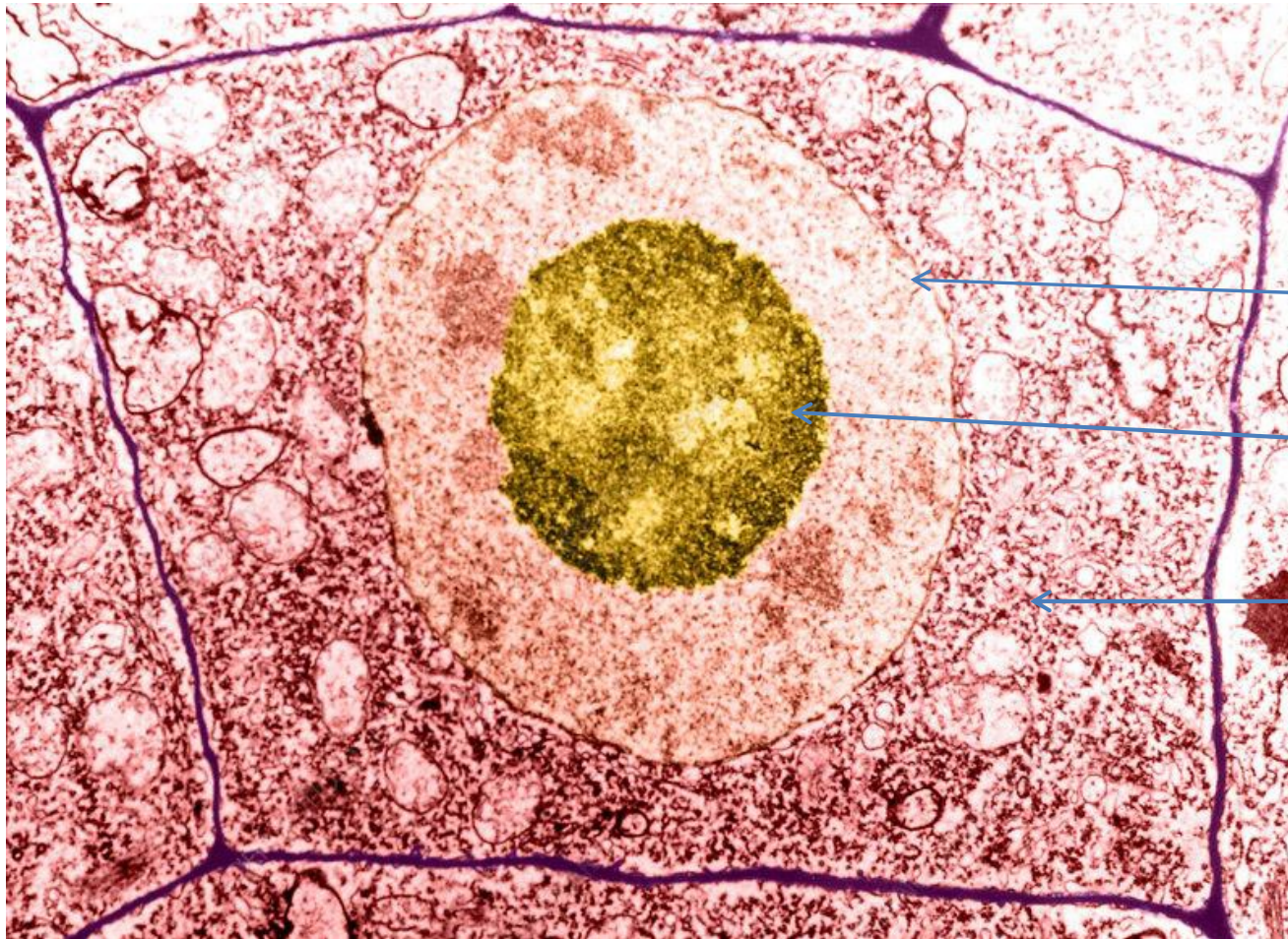
- obligate parasites
- contain protein capsids
- cause disease in many species
- naked or enveloped
- single or double strands

### RNA Virus

- obligate parasites
- contain protein capsids
- cause disease in many species
- naked or enveloped
- single or double strands

**Both DNA and RNA can not be found in same virus.**

# Basic Human cell



Nucleus

Nucleolus

Cytoplasm

# Viruses

## Differences

### DNA Virus

- pass DNA into cell nucleus
- low mutation level
- DNA polymerase, stable
- 2-step viral protein process
- larger
- 2-strand most common
- accurate replication

### RNA Virus

- passes RNA into cytoplasm
- high mutation level
- RNA Polymerase, unstable
- 1-step 5 Viral proteins
- smaller
- single strand most common
- error-prone replication

VS

# Session 3 Working Plan

## For Each Disease:

- Name and meaning
- Nature of infection
- Transmission
- Morbidity and Mortality
- Distribution
- Prophylaxis/Prevention
- Treatment
- Looking to the future?
- Effect on USA



Viral Without Vector

# POLIO

# Name & Meaning

- Has had various names:
  - “debility of the lower extremities”
  - Heine-Medlin’s disease
  - infantile spinal paralysis
- Medical name: poliomyelitis
  - from the Greek “*polios*”= gray, “*myelos*”= marrow, and the Latin “*itis*”= inflammation
  - means: inflammation of nerve roots
- Reporters and headline writers trimmed it to “Polio”.

# Nature of Infection

- Poliovirus (PV) RNA *enterovirus* (intestinal)
- 3 Types: PV1, PV2, and PV3
- highly infectious, fecal-oral route
- mostly seasonal in warm, humid weather



# Transmission

- occurs naturally only in humans
- food or water contaminated with human feces
- less commonly from infected saliva
- infected persons may spread it for up to 6 weeks
- asymptomatic transmission may occur

# Morbidity & Mortality <sup>(1)</sup>

## Symptoms

- 70 % asymptomatic
- 25 %: minor symptoms (fever, sore throat)
- 5 %: headache, neck stiffness, leg & arm pains
- in ~0.5 % of cases, it moves from the gut to affect the Central Nervous System (CNS)

# Morbidity & Mortality (2)

- if muscle weakness → flaccid paralysis:
  - 2 to 5 % of children die
  - 15 to 30 % of adults die
- rest get back to normal within 1 - 2 weeks
- many people appear to recover fully
- years after, *post-polio syndrome* (PPS) may occur

# Distribution

- existed since antiquity
- worldwide
- currently endemic only in Afghanistan and Pakistan
- eradicated elsewhere

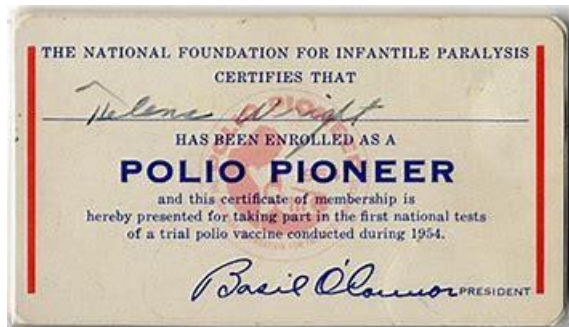


# Prophylaxis/Prevention

- oral Polio vaccine in 2 serotypes (1 and 3)
- reduced the number reported cases/year from 350,000 in 1988 to 33 in 2018
- safe in pregnancy and HIV/AIDS
- 3 cases of vaccine-associated paralytic polio (VAPP) per million doses, compared with 5K cases per million people paralyzed after a polio infection.

- WPV2 has not been detected since 1999 and was declared eradicated in September 2015.
- Type 2 circulating vaccine-derived polioviruses (cVDPV2) were vaccine-derived strains that caused paralytic poliomyelitis cases.
- WPV3 has not been detected since November 2012.
- WPV1 remains the only WPV in circulation.

# Polio Vaccine in 1950's



# Polio Vaccines

## IPV

- killed poliovirus
- intramuscular
- \$1.00 to \$3.28 per dose
- trivalent: 1,2, & 3
- need training & supplies
- can't cause VDPV illness
- dose at 2, 4, 6 through 18 m
- booster 6 months after 3<sup>rd</sup>
- protects for life with 4 doses

## OPV

- live, attenuated poliovirus
- oral
- \$0.12 to \$0.18 per dose
- bivalent: 1 & 3
- anybody can administer
- can cause VDPV illness
- dose @ 6, 10 and 14 weeks
- last dose combined with IPV
- protects for life with 3doses



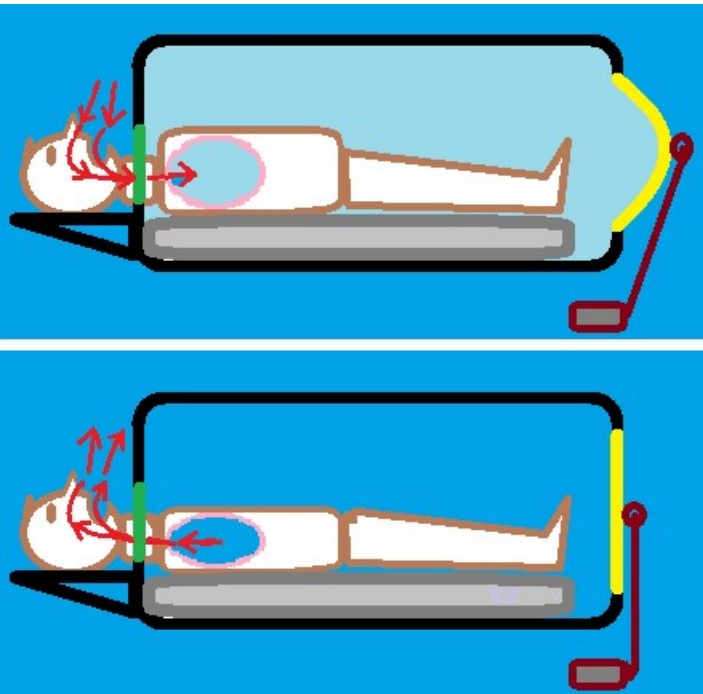
# Treatment

- No cure exists.
- Physical Therapy:
  - prevent deformity
  - loss of muscle function
- If post-polio syndrome (PPS), therapy as needed:
  - sleep apnea
  - problems with breathing or swallowing
  - muscle weakness and muscle mass loss
  - excessive sensitivity to low temperatures

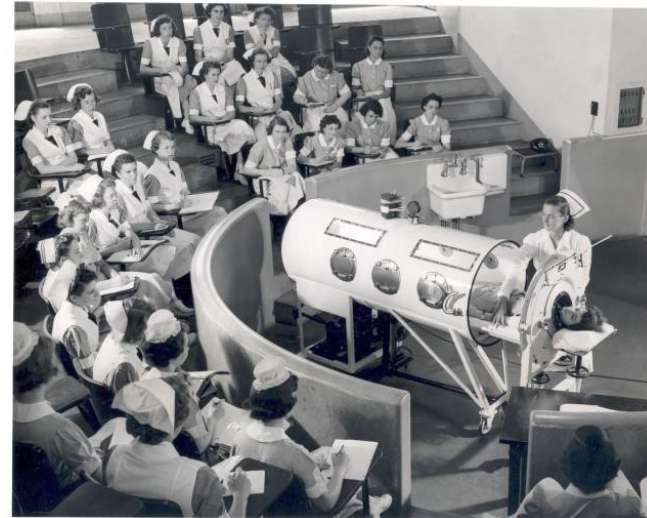
# Iron Lung

- Treatment for victims of polio who had lost control of their respiratory muscles.
- If no assisted ventilation, death would be imminent and inevitable.
- Humans breathe by *negative pressure breathing*: the rib cage expands and the diaphragm contracts, which brings air into the lungs.

# Iron Lung



# Iron Lung

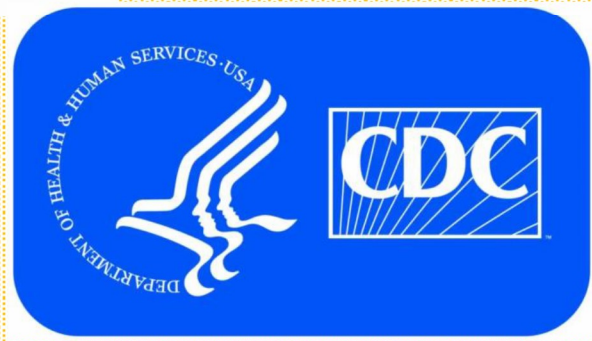
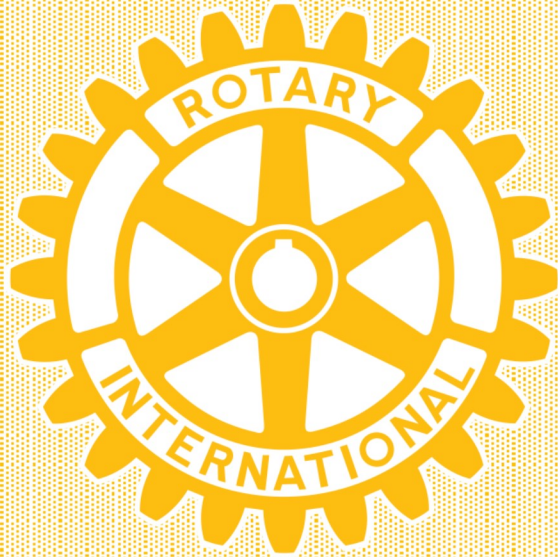


# Looking to the Future?

## Erradication

- Only a few cases in 2 countries in last 5 years.
- Prevention through:
  - massive vaccination
  - improvements in sanitation
  - community education
  - joint global action.

# Global Polio Eradication Initiative



**BILL & MELINDA  
GATES foundation**

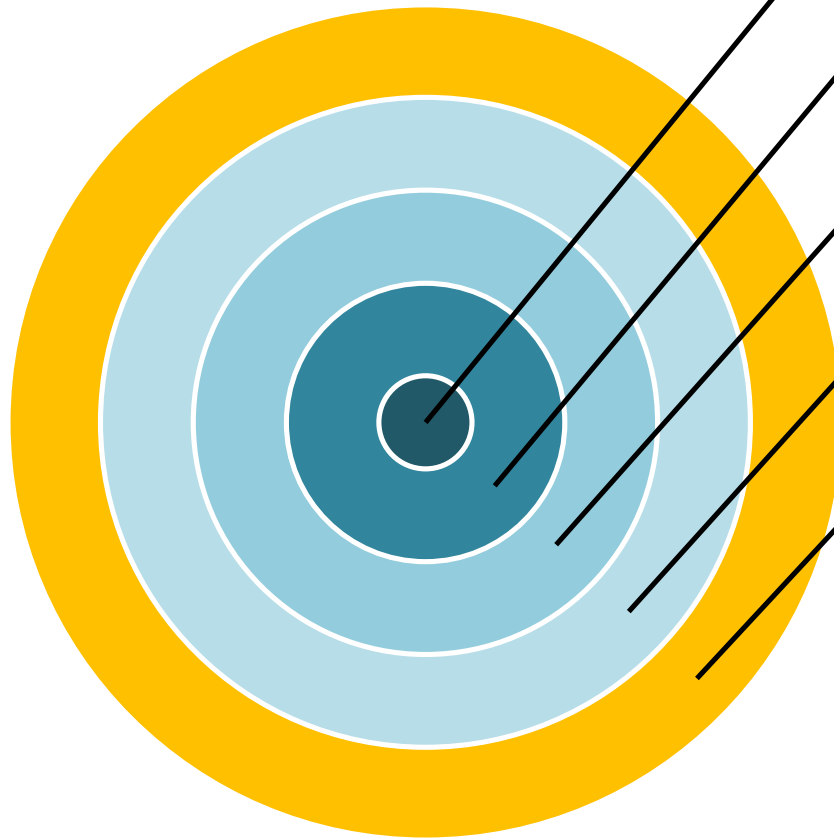
# Wild Polio Virus 1 Cases (WPV1) Cases

Year	Afghanistan	Pakistan	Total
2016	13	20	32
2017	14	8	22
2018	21	12	33
2019	29	147	176
2020	56	84	140
2021	4	1	5
2022	2	20	22
2023*	6	4	10

\* Through October 2023

GPEI 2023 data

# Polio in US



In 1916, a summer outbreak of polio started in NYC.

Epidemic lasted through October.

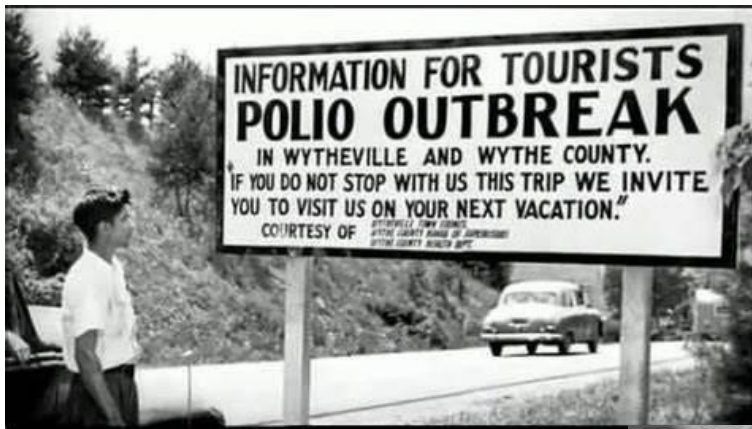
6,000 Americans lost their lives.

NYC had 8,900 cases, with 2,400 deaths.

80% of deaths were children under five.

**In 1921, at the age of 39, FDR got polio while on vacation in Canada.**





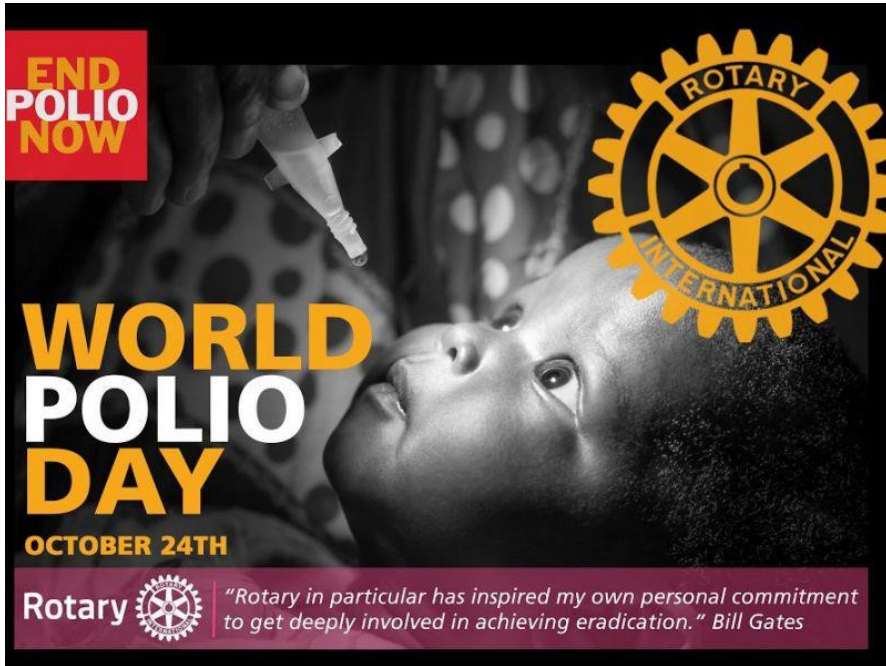
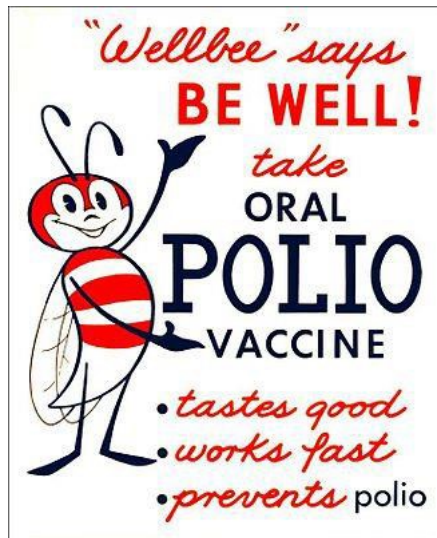
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# Polio Facts

- Between 1940's and 1950's:
  - 10X more children were killed in accidents than polio
  - 3X more were killed by cancer than polio
- National Foundation turned a relatively uncommon disease into the most feared affliction of its time.
- Disease of white middle-class children.
- False that **blacks are not as susceptible**, and that it is caused by filth, squalor or poverty.




# Questions? (1)



Bacterial No vector

# CHOLERA





The Basics  
The Seven Pandemics  
**CHOLERA**

# Cholera

*“Cholera is something else, it is the invisible, it is the curse of the olden days, of times passed, a sort of evil spirit that comes back and that surprises us so much that it haunts us, because it belongs to what appears to be a forgotten age.”*

Guy de Maupassant

# Name and Meaning

- the name may come from the Greek words:
  - *chole* (bile) and *rein* (flow)
  - *cholera* which means gutter of a roof
  - *choler*, irascibility, anger, irritability
- old physiology: yellow bile, related to 1 of the 4 basic humors
- known as “*cholera morbus*”, and also called “the blue death”



# Nature of Infection.

- extremely transmissible contagious disease:
  - contamination of water supplies
  - contact with infected feces
- deadly if not treated quickly and efficiently:
  - kills ~ 135,000 per year worldwide
  - can kill in about 24 hours

# Transmission

- Fecal-Oral transmission route due to poor sanitation.
- *Vibrio cholerae* accumulates in zooplankton copepods (mini-crustaceans), which oysters eat.
- People drink water or foods contaminated with the mini-crustaceans and the germ, *Vibrio cholerae*.
- People can acquire infection eating undercooked or raw oysters and shellfish from warm and salty waters.

# Morbidity and Mortality <sup>(1)</sup>

- Infects 3M to 5M people yearly worldwide and kills 28K to 120K according to WHO.
- 80% to 90% of infected people don't get symptoms and the infection resolves on its own.
- 10% to 20% develop cholera, get massive diarrhea, vomiting, and leg cramps; untreated mortality is ~60%.
- A person may make **3 to 5 gallons** of painless rice-water diarrhea a day, lose electrolytes, and become dehydrated.

# Morbidity and Mortality (2)

- ~100M bacteria must be ingested to cause cholera in a normal healthy adult
- less with lowered gastric acidity (PPI users)
- increased susceptibility:
  - children
  - 2-4 year-olds have highest rates of infection
  - persons with type O blood
  - people with lowered immunity
  - people with AIDS
  - malnourished people of all ages

# Mechanism of Disease

- The vibrio multiplies massively, and attaches to the intestinal mucosa with a pilus.
- Joins with other vibrios to blanket the wall.
- Secretes enterotoxin that extracts water and electrolytes from the upper GI tract.
- Pumps it into the lumen where the fluid and electrolytes are excreted as diarrheal fluid.

# Thoughts on the Causes

- French doctors believed it was a disease of communities with poverty or poor environment.
- Russian doctors believed it was contagious, although they did not understand how it spread.
- US doctors initially believed that cholera was brought by recent Irish immigrants from British ports.
- British doctors thought the disease might arise from divine intervention.

# Distribution

- Worldwide but mostly in countries with bad sanitation.
- Currently limited to the Indian subcontinent and some countries in Africa.
- War and natural disasters increase risks:
  - wars impede sanitation, hinder water supply
  - earthquakes, volcanoes, hurricanes, floods
  - UN story in Haiti\*

Notification rate per 100 000 persons



Note: Data refer to cases reported in the last 12 months. Administrative boundaries: © Eurographics  
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 17 January 2023

March 19, 2024

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# Prophylaxis/Prevention

- Oral Vaccines available, about 90% effective.
- Protection starts at 10 days, lasts 3-6 months.
- For adults traveling to an active cholera area.
- Sanitation and safe water are chief measures.



# Cholera Vaccines

- 2 oral vaccines are available:
  - **Dukoral** protects against traveler's diarrhea for up to 3 months
  - **Mutachol** is partially effective against one strain of cholera
- Neither WHO nor CDC recommend oral cholera vaccines:
  - the risk of contracting the disease for travelers is low
  - the vaccines are expensive
  - the vaccines offer limited protection
- The WHO does recommend pre-emptive use of oral cholera vaccines in emergency situations.

# Treatment

- Aggressive rehydration:
  - intravenous dextrose-saline solutions
  - **Oral Rehydration Solution (ORS):**
    - US Commercial \$1.50 -\$5/liter
    - WHO powder: 10-25¢/liter
    - **Homemade: 5-10¢/liter**
- Supportive measures: B.R.A.T. diet.
- Antibiotics.



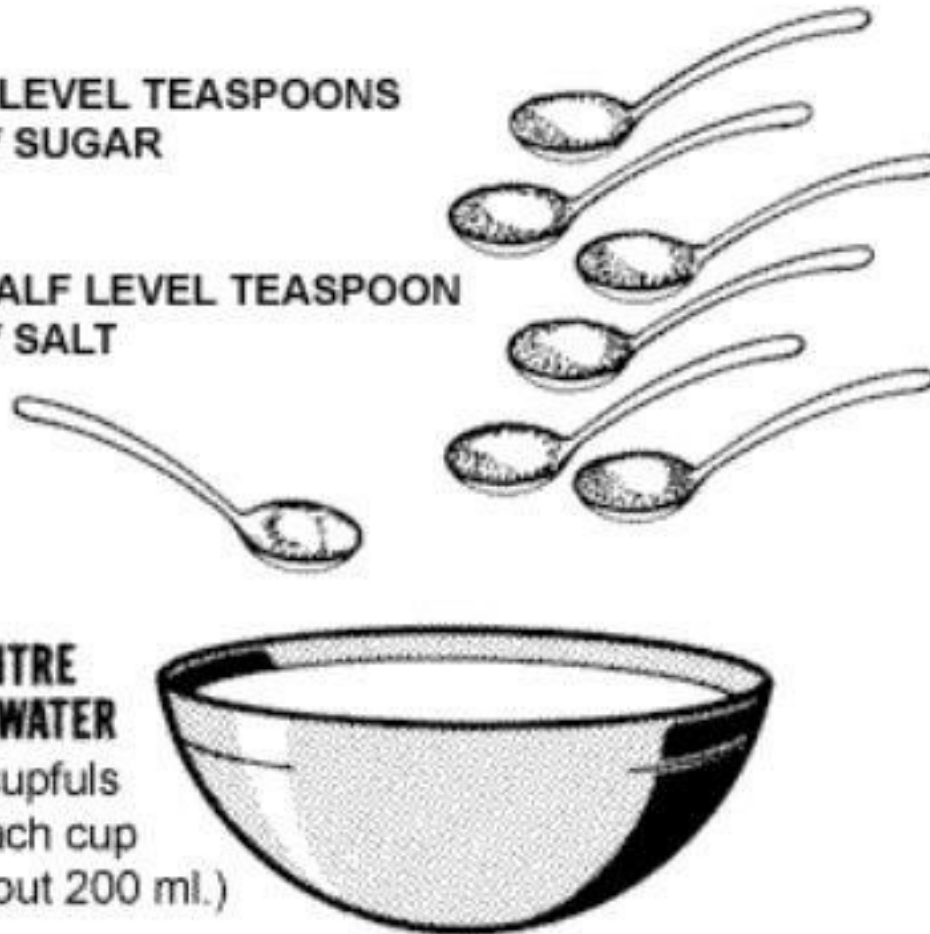
20 packs for \$36 @WalMart

# Home – made ORS

6 LEVEL TEASPOONS  
of SUGAR

HALF LEVEL TEASPOON  
of SALT

1 LITRE  
OF WATER  
5 cupfuls  
(each cup  
about 200 ml.)



[www.rehydrate.org](http://www.rehydrate.org)

# NY Newspaper Ad

## **NOTICE.**

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# **PREVENTIVES OF CHOLERA!**

Published by order of the Sanatory Committee, under the sanction of the  
Medical Counsel.

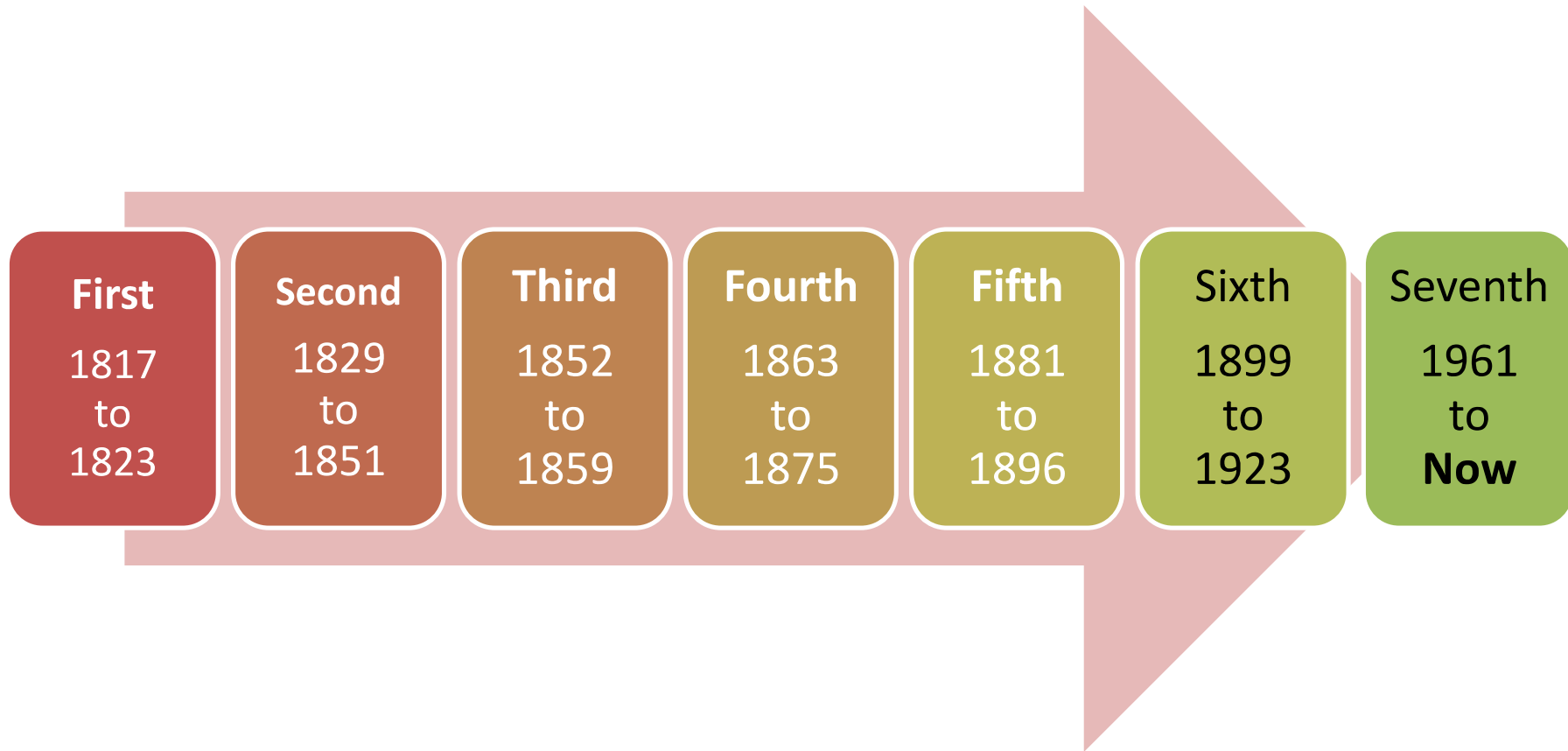
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**BE TEMPERATE IN EATING & DRINKING!**

*Avoid Raw Vegetables and Unripe Fruit !.*

**Abstain from COLD WATER, when heated, and above all from Ardent Spirits, and if habit have rendered them indispensable, take much less than usual.**

# Cholera Pandemics



# 1<sup>st</sup> Cholera Pandemic

(1817-1823)

- Ganges Delta in Jessore, India, in **1817**, originating in contaminated rice.
- Spread throughout most of India, Myanmar, and Sri Lanka along trade routes.
- By 1820, it spread to Thailand, Indonesia (killed 100K people on Java) and the Philippines.
- Spread to China in 1820 and Japan in 1822 by way of infected people on ships.

# 1<sup>st</sup> Cholera Pandemic

(1817-1823)

- In 1821, British troops traveling from India to Oman brought cholera to the Persian Gulf.
- Got to Europe, reaching modern-day Turkey, Syria and Southern Russia.
- Pandemic died out in 1823 due to a severe winter which may have killed the bacteria in water supplies.

# 2<sup>nd</sup> Cholera Pandemic

(1826-1837)

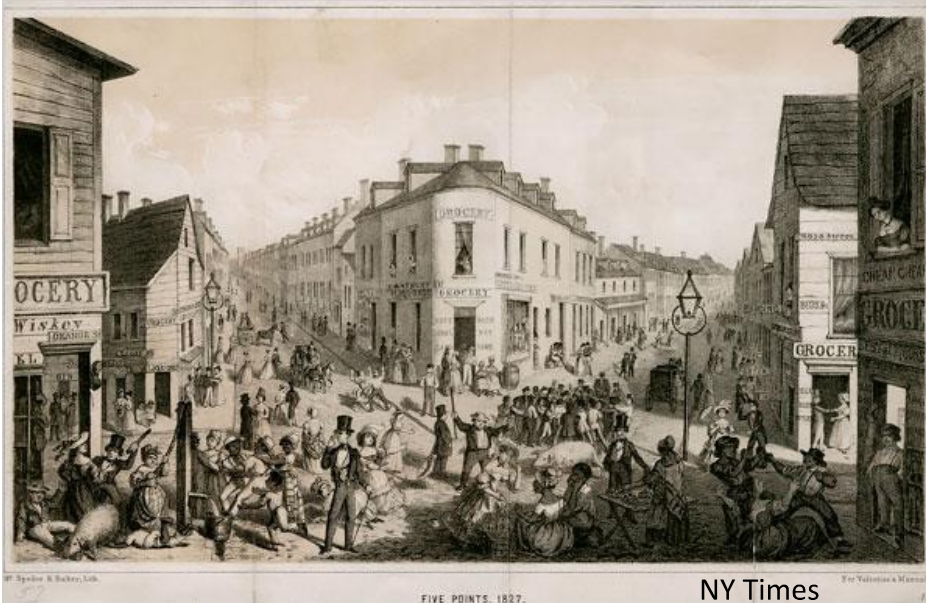
- Restarted in India, followed trade routes, and in autumn of 1830, made it to Moscow.
- In spring of 1831, reached Finland, Poland, Hungary and Germany.
- Late 1831, England via port of Sunderland, and London in spring of 1832 (22K deaths).



# 2<sup>nd</sup> Cholera Pandemic (2)

(1826-1837)

- Between 1832 and 1834, the disease reached Quebec, NYC, Nova Scotia, Ontario, Detroit, and spread to the Pacific Coast.
- In mid-summer 1832, 57 Irish immigrants were contracted to lay a stretch of railroad 30 miles west of Philadelphia; 2 months later they had all died of cholera.



In NYC, blacks and Irish living in 5 Points, were blamed.

# 2<sup>nd</sup> Cholera Pandemic

## (1826-1837)

- Irish immigrants fleeing poverty and the Great Famine carried the disease from Europe to North America.
- Soon after the immigrants' arrival in Canada in the summer of 1832, 1,220 people died in Montreal and another 1,000 across Quebec.
- The disease entered the U.S. by ship traffic through Detroit and New York City.
- Spread by ship passengers, it reached Latin America by 1833.

# 3<sup>rd</sup> Cholera Pandemic

(1846-1860)

- 3<sup>rd</sup> outbreak (most deadly!) originated in India and researchers believe it may have started in 1837 and lasted until 1863:
  - in Russia, more than one million people died
  - In London, during 1853-1854, more than 100K died and 23K in the rest of Great Britain
- Another outbreak across England and Wales began in 1848, killing 52K over 2 years.

# Dr. John Snow

- In 1854, identified contaminated water in transmission of cholera.
- After the 1854 Broad St. outbreak, he mapped the cases in the Soho area, and noted many were near a neighborhood water pump.
- He convinced officials to remove the pump handle, and the number of cholera cases in the area immediately decreased.



John Snow's map 1854

# 4<sup>th</sup> Cholera Pandemic

(1863-1875)

- Mecca: 30K dead pilgrims
- Zanzibar: 70K dead
- Netherlands: 20K dead
- London: 6K dead
- North America: 50K dead
- Hungary: 30K dead
- Belgium: 30K dead
- Algeria: 80K dead
- Russia: 90K dead
- Italy: 113K dead

# 5<sup>th</sup> Cholera Pandemic

(1881-1896)

- Russia: 200K dead.
- Japan: 90K dead.
- Hamburg, Germany: 9K dead.
- Sanitary measures based on the findings of John Snow kept cholera out of Britain and the United States.
- This was the last serious European cholera outbreak of the 19<sup>th</sup> century.

# 6<sup>th</sup> Cholera Pandemic

(1899-1923)

- India: 800K dead.
- By 1923, cholera had receded from most of the world, although many cases were still present in India.
- Overlapped with part of WWI. (1914-1918)

# 7<sup>th</sup> Cholera Pandemic

(1961-Present)

- Only one that originated in Indonesia, not India:
  - 1991: Peru, 10K dead
  - 1994: Rwandan refugee camp, 30K dead
  - 2008: Zimbabwe, 500 dead
  - 2010: Haiti 800K ill, 10K dead (UN)
- 100K/year still die worldwide nowadays.



# Cholera in Haiti

## United Nations



- On January 12, 2010, a magnitude 7.0 earthquake killed over 250K and displaced over 1M people.
- In October, 2010, Haiti had an epidemic of cholera (1<sup>st</sup> in >100 years).
- UN peacekeepers were found to be the source because sewage from their base contaminated a major river water supply.
- Nearly 820K Haitians were infected by cholera, and more than 10K died; cholera is now endemic in Haiti.
- Another minor outbreak in 2022.

# Cholera in the US <sup>(1)</sup>

- New York had outbreaks in
  - 1832: 3,515 dead
  - 1849: 5,000 dead
  - 1866: 1,137 dead
- Cincinnati: 8K dead
- Chicago: 3.5K dead
- New Orleans: 3K dead

# Cholera in the US (2)

- Spread throughout the Mississippi river system, killing over 4,500 in St. Louis.
- Thousands died in New York, a destination for Irish immigrants.
- Nashville outbreak in 1849–1850 took the life of former U.S. President James K. Polk.

# Cholera in the US <sup>(3)</sup>

- During the California Gold Rush, it followed the California, Mormon and Oregon Trails.
- 6K to 12K are believed to have died on their way to Utah and Oregon in 1849–1855.
- Cholera claimed more than 150K victims in the US between 1832 and 1849.

# Questions? (2)



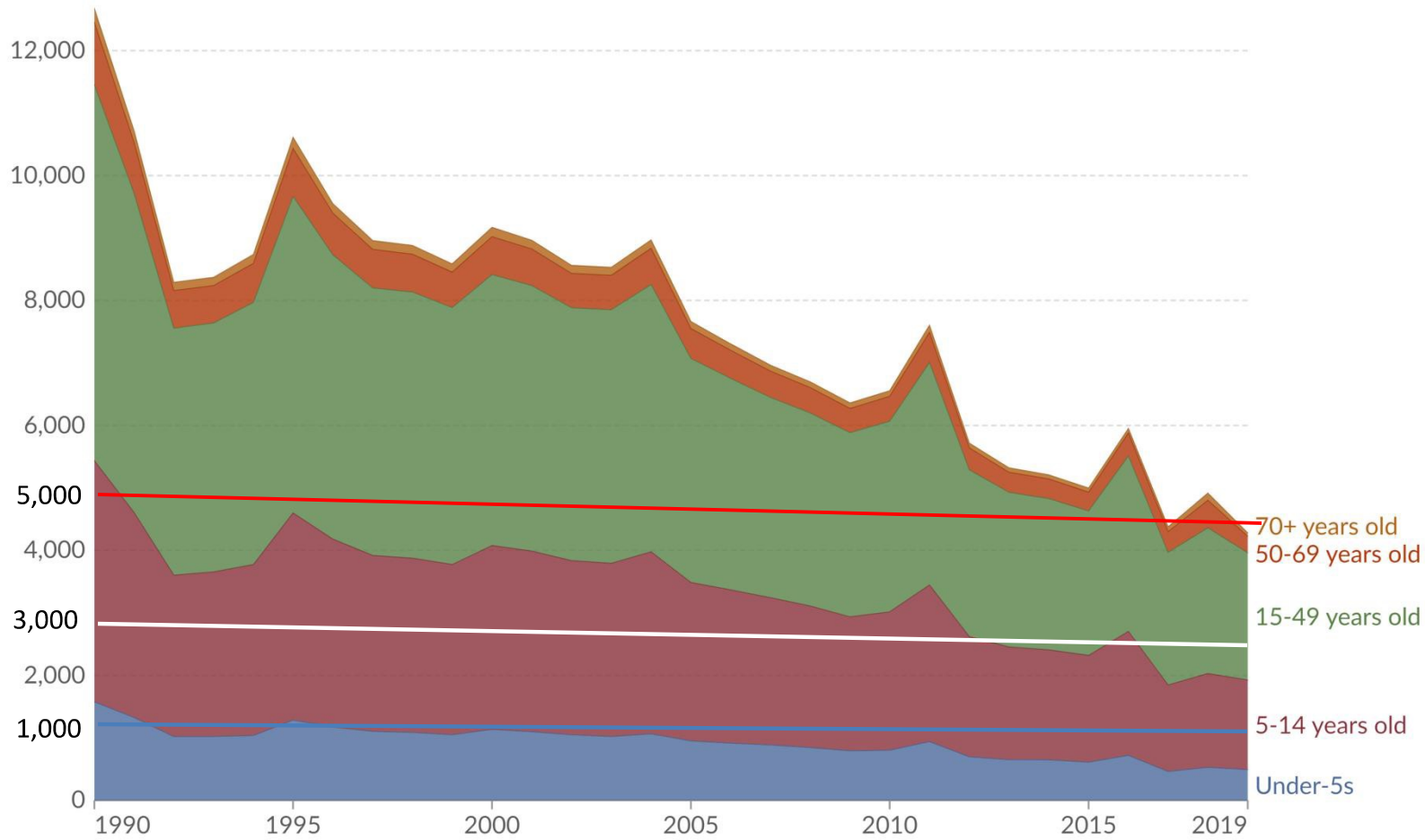


Viral With Vector

# YELLOW FEVER

# Deaths from yellow fever, by age, World, 1990 to 2019

Annual number of deaths from yellow fever



Data source: IHME, Global Burden of Disease (2019)

[OurWorldInData.org/causes-of-death](https://OurWorldInData.org/causes-of-death) | CC BY

# Name and Meaning

- Yellow fever, Fièvre jaune : from the yellow skin color (jaundice, French *jaune*=yellow) caused by liver illness.
- *Fiebre amarilla, vómito negro, yellow plague, yellow jack, bronze john.*
- Also called *xekik* (black vomit) by Mayans.



# Nature of Infection

- acute febrile viral disease
- bite of female *Aedes aegypti* mosquito
- flavivirus, renamed orthoflavivirus in 2023
- Not contagious

# Transmission



- bite of an infected female *Aedes* mosquito
- infected or carrier mosquito injects the virus into host when biting and sucking blood
- NO person-to-person transmission

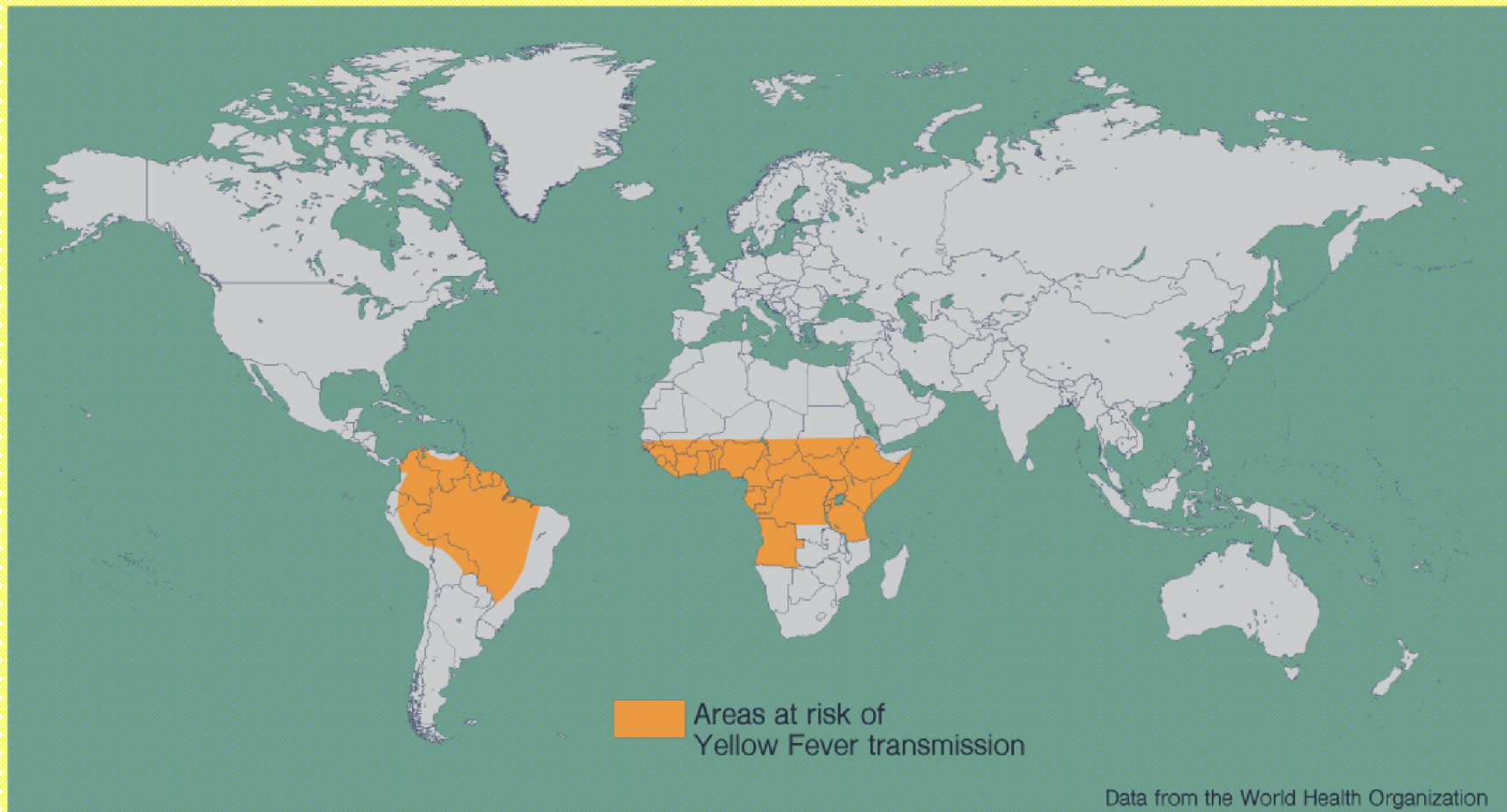
# Morbidity and Mortality

- fever, headaches, chills, back pain, nausea, and loss of appetite start 3-6 days after bite
- 85% get better in 3-4 days
- 15% go to 2<sup>nd</sup> phase with recurring fevers, jaundice, bloody vomit, bleeding from eyes & mouth
- if jaundice present, mortality = 20-50%
- overall fatality rate is 3-7%

# Distribution

- as of 2023, 34 countries in Africa and 13 countries in Central and South America are endemic for, or have regions that are endemic for yellow fever
- ~600 million people live in endemic areas
- **No** natural cases in Asia, only imported cases
- requires adequate habitat for *Aedes* mosquitoes

# Yellow Fever Distribution



Data from the World Health Organization

La Jolla Institute for Immunology 2023

# Yellow Fever Worldwide

The burden of yellow fever during 2013 was 84K to 170K severe cases and 29K to 60K deaths globally .

## Africa

Dates	Probable	Confirmed	Deaths	CFR
Jan to Dec 2022	147	65	8	12.3%

CFR= case fatality rate

# Prophylaxis/Prevention <sup>(1)</sup>

- avoid bites, use repellent
- repellent-impregnated clothing, long sleeves
- vaccine works after 10 days in 95% of people
- a single dose of yellow fever vaccine is sufficient to grant life-long protection (WHO 2023)

# Prophylaxis/Prevention (2)

- vaccination recommended for visitors to an active area (locals have some immunity)
- *Aedes* bites during daylight hours, but insecticide-impregnated mosquito nettings are helpful at night
- vector control: larvicides, insecticides, eliminate breeding areas, use larvae-eating fish and copepods
- *Aedes* also carries dengue and chikungunya.



# Treatment

- no cure known, no antiviral is effective
- hospital care, hydration, pain relief
- isolation not required
- No aspirin: interferes with blood clotting

# Looking to the future?

- Asia could become an endemic focus.
- *Aedes* mosquitoes are already in Asia.
- Eradication is only possible if vector is eliminated.

# Major Yellow Fever Epidemics in the USA



# USA Yellow Fever Epidemics

City	Dates	Dead	Comments
Philadelphia	August-November 1793	5,000	10% population
New York	July-October 1795	730	Refused PA refugees
Boston, NYC, Philadelphia	Summer of 1798	>5,000	Concurrent
Baltimore	Summer of 1800	1,200	
New Orleans	Summer of	>8,000	7.4% white; 0.2% black
Norfolk	June-October 1855	2,000	Ship from West Indies
Mississippi River Valley	May-October 1878	20,000	Memphis data next slide
New Orleans*	May-October 1905	>900	Last epidemic in USA

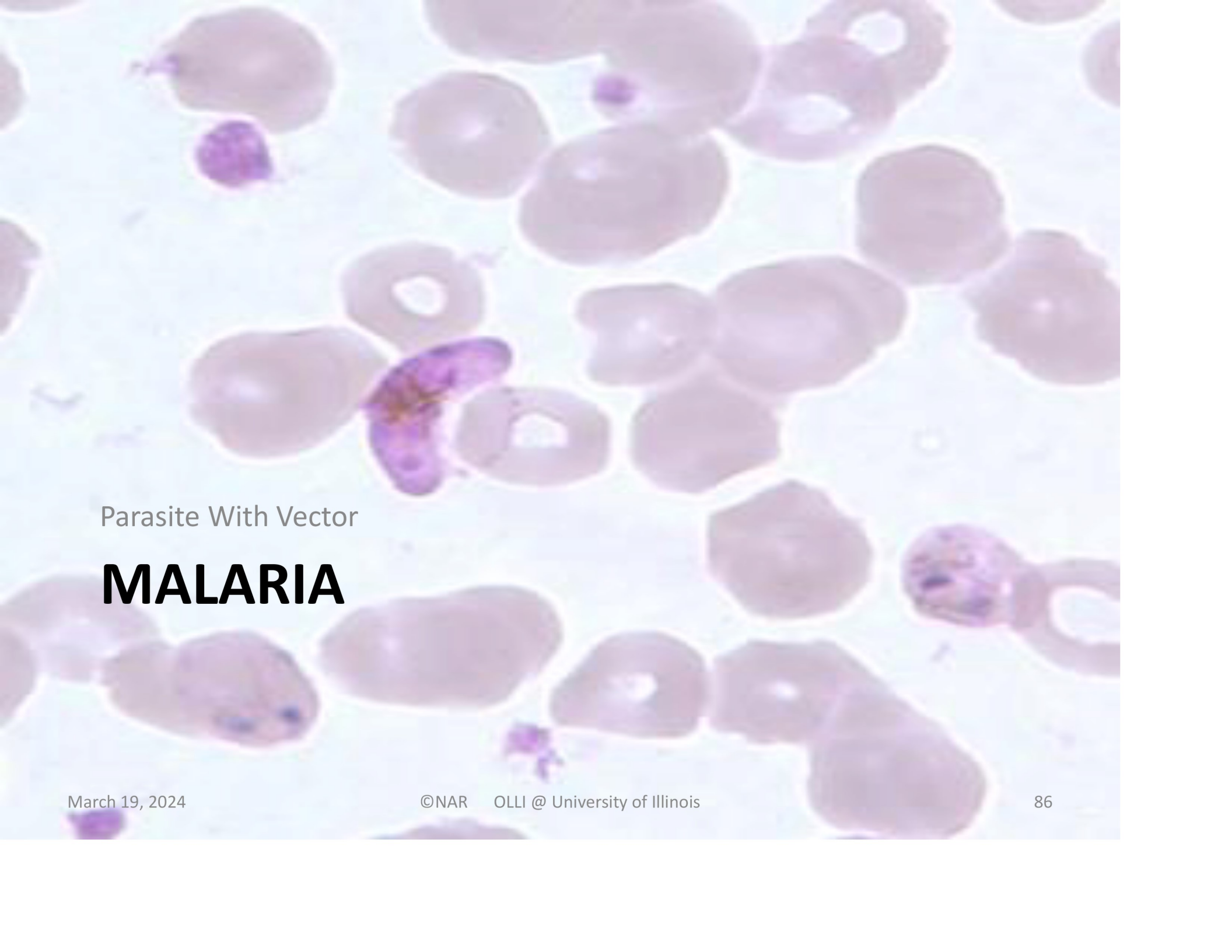
\*NOLA 1817-1905: >40,000 deaths

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# Yellow Fever in USA

## Memphis Epidemics

Year	Epidemic #	Cases	Deaths	%
1828	First	650	150	23.1%
1855	Second	1,250	220	17.6
1867	Third	2,500	550	22
1873	Fourth	5,000	2000	40
<b>1878</b>	<b>Fifth</b>	<b>17,000</b>	<b>5000+</b>	<b>29.4</b>
1879	Sixth	2,000	600	30



Parasite With Vector

# MALARIA

# Name and Meaning

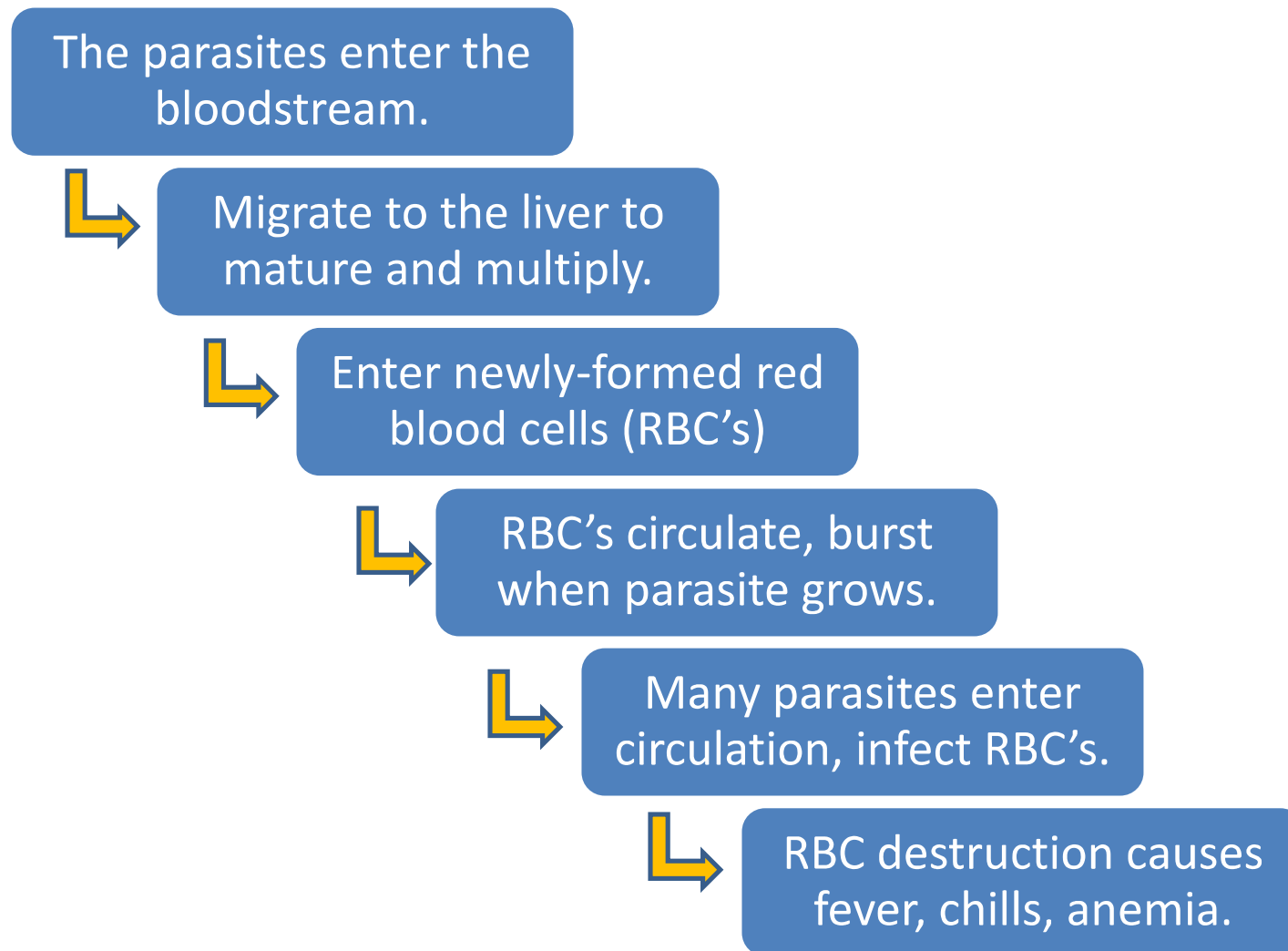
- Malaria: from the Italian *mal'aria*= bad air.
- English call it “the ague”.
- French call it *le paludisme*, Spanish *paludismo*, literally “the paleness”.
- Many cultures call it “Swamp fever”.
- In Mali the word means “sickness of the green season” because it comes with the rains.

# Nature of Infection <sup>(1)</sup>

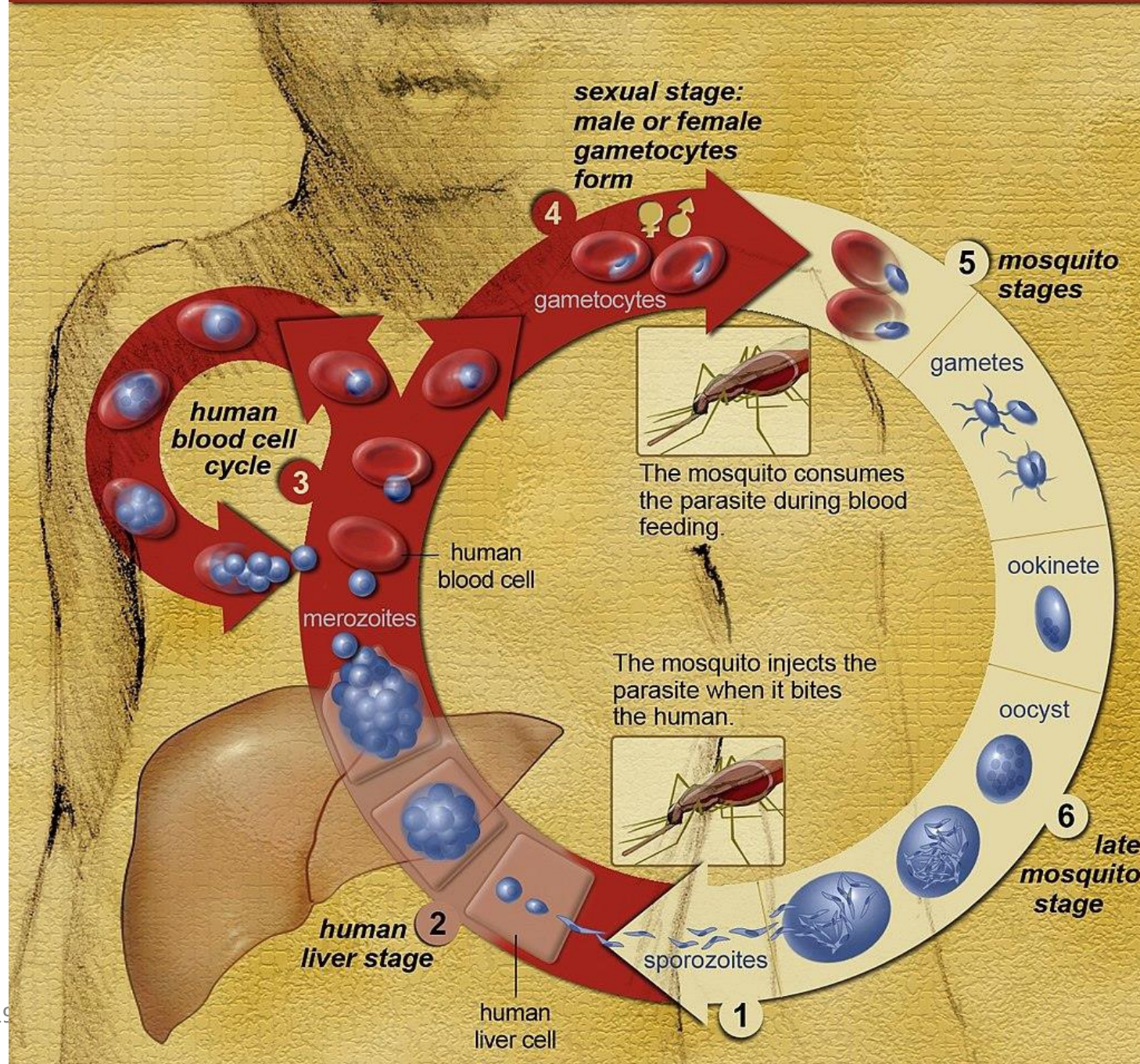
- Acute/chronic febrile parasitic blood disease.
- Bite of female *Anopheles* mosquito injects the victim with the *Plasmodium* parasite.
- Five types:
  - *Plasmodium vivax*: Asia and Latin America
  - ***Plasmodium falciparum***: most serious, commonly fatal
  - *Plasmodium malarie*: mild symptoms
  - *Plasmodium ovale*: mild, rare, Africa & Pacific islands
  - *Plasmodium knowlesi*: SE Asia, mostly severe



# Nature of Infection (2)



# Life Cycle of the Malaria Parasite



# Transmission

- The *Anopheles* female bites, sucks blood, injects saliva with parasites into host.
- The mosquito bites at night, goes to a vertical surface to rest and digest after biting.
- Mosquito absorbs the blood cells, eliminates the fluid of the blood as urine.

# Morbidity and Mortality <sup>(1)</sup>

- Symptoms appear 8-25 days after bite.
- Initially headache, fever, joint pain, vomiting, jaundice, blood in urine, retinal hemorrhage.
- Cardinal sign is the paroxysm of fever & chills:
  - Quotidian (daily): *Falciparum*
  - Tertian (every third day): *Vivax* and *Ovale*
  - Quartan (every fourth day): *Malariae*

# Morbidity and Mortality <sup>(2)</sup>

- *P falciparum* (and *P knowlesi*) can produce:
  - cerebral malaria with encephalopathy
  - severe anemia
  - kidney failure
  - enlarged spleen and liver
  - blackwater fever (hemoglobin in urine)
- Can affect pregnant mothers and cause stillbirth, prematurity, neonatal malaria.

# Distribution 2022

249M Cases

- WHO African Region (233M or 94%)
- WHO SE Asia Region (7.75M or 3.4%)
- WHO E. Mediterranean Region (4.79M or 2.1%)
- WHO Region of the Americas (597K or 0.24%)
- 19 countries in sub-Saharan Africa and India had ~85% of the total

6 countries accounted for more than ½ of all malaria cases:

- Nigeria: 25%
- DR of the Congo: 12%
- Uganda: 5%
- Côte d'Ivoire: 4%
- Mozambique: 4%
- Niger: 4%

# Global Morbidity & Mortality

Year	Cases	Deaths	% Mortality
2015	231 M	586 K	2.53 %
2016	232 M	582 K	2.51 %
2017	237 M	580 K	2.45 %
2018	232 M	581 K	2.50 %
2019	233 M	576 K	2.47 %
2020	244 M	633 K	2.59 %
2021	224 M	610 K	2.72 %
2022	249 M	608 K	2.44 %

Ramírez from WHO 2023  
World Malaria Report data

Children under 5 years are the most vulnerable group, with 78% (468K ) of all deaths in 2022.

# CDC Yellow Book 2024

- *Health Information for International Travel* is a resource for healthcare professionals providing care to international travelers.
- It compiles the US government's most current travel health guidelines, including pre-travel vaccine recommendations, destination-specific health advice, and easy-to-reference maps, tables, and charts.



# Malaria Vaccine

- The malaria parasite is a complex organism with a complicated life cycle, and the human immune response is still incompletely understood.
- *Plasmodium* can evade human's immune system by constantly changing its surface, so development of a vaccine is very difficult.
- Other methods of fighting malaria (insecticides, drugs, and treated bed nets) have not succeeded.

# Incidence

- The Institute of Health Metrics and Evaluation (IHME) provides estimates of malaria deaths from the year 1990 onwards.
- Over this period there is a clear rise-peak-fall trend, increasing from around 850K deaths in 1990, peaking at around 965K in 2004; and then declining to around 650K in 2019.
- These estimates are notably higher than those of the WHO, but both the IHME and WHO estimate that more than 90% of deaths are from the African region.

# Prophylaxis/Prevention

- vector control is A#1 priority
- community education
- preventive medication indicated only for people traveling or working in endemic areas
- vaccine effective in 40% of children over 24 months but requires 4 doses

# Malaria Vaccines

- The 1<sup>st</sup> approved vaccine for malaria is *RTS,S* (**Mosquirix**), which as of April 2023, has been given to 1.5M children living in areas with moderate-to-high malaria transmission.
- It requires at least 3 doses in infants by age 2, and a 4<sup>th</sup> dose extends protection for 1–2 more years.
- The vaccine reduces hospital admissions from severe malaria by around 30%.

# Malaria Vaccines

- The most effective other malaria vaccine is the *R21/Matrix-M*, with a 77% efficacy rate shown in initial trials and significantly higher antibody levels than with the RTS,S vaccine.
- It is the 1<sup>st</sup> vaccine that meets the WHO goal of at least 75% efficacy, and only the 2<sup>nd</sup> vaccine to be recommended by the WHO.

# Treatment

- Historically *Chinchona* bark (contains quinine).
- *Choroquine* (**Aralen**) was used during WWII, and its worldwide use dramatically reduced the incidence of malaria.
- *P. falciparum* has become resistant and other new drugs and combinations (*artemisinin, primaquine, mefloquine, doxycycline, proguanil*) have become necessary.
- *Artemisinin* Combination Therapy (ACT) is now the standard, especially for *P. falciparum*.

# Looking to the Future

- In some parts of Africa, malaria cases are decreasing due to prevention measures and also to the effects of climate change on rainfall.
- Countries must move individually supported and encouraged by WHO to progress as quickly as possible towards elimination and, eventually, eradication:
  - achieve better vector control measures without negative environmental impact
  - improved therapeutics to compensate for drug resistance by *falciparum*

# New Strategies

- Development of mosquitoes that are resistant to the malaria parasite and then spread these resistance traits in other mosquito populations.
- Eventually, all the mosquitoes in an area would become resistant to the parasite and would not be able to transmit it.
- The main advantages of this strategy:
  - no one has to do any work with compliance in using bed nets
  - no spraying insecticides
  - no taking drugs
  - everyone gets protected, not only those who can afford the drugs or have access to the bed nets



# *Anopheles* that can't get Malaria

- A naturally occurring bacterium and a chemical it secretes inhibit the development of *Plasmodium* in mosquitoes—so they can't transmit the parasite to humans.
- A strain of *Delftia tsuruhatensis*, which was named *Tres Cantos 1*, or *TC1*, was present in all mosquito samples that couldn't be infected with *Plasmodium*.
- An important discovery is that once the mosquito gets the bacterium, it stays with the mosquito for its life.

# *Anopheles* that can't get Malaria

- The chemical was identified as *harmaline*, which can easily be purchased from chemical companies.
- The researchers dried the *harmaline* on a glass plate, let the mosquitoes sit on that plate for one hour, and then fed infected blood to the mosquitoes.
- They found that the mosquitoes that sat on *harmaline* had strongly impaired development of the parasites.

# Anopheles that can't get Malaria

- **Attractive Toxic Sugar Baits (ATSBs)** are toxic floating traps for mosquitoes.
- A proposal is that instead of mixing the sugar baits with an insecticide, mix them with the bacteria so the mosquitoes can feed on it.
- Another possibility is to incorporate *harmaline* into bed nets or spray it on walls.

# Genetic Modification

- A long-term goal is to develop mosquitoes that are resistant to the *Plasmodium* through genetic engineering of specific genes and then spread this resistance in natural mosquito populations.
- Eventually, all the mosquitoes would become resistant to the parasite and would not be able to transmit it.

# Malaria in the USA

## Current Conditions

- About 2K to 2.5K cases/year, most of whom have recently traveled to an infected region.
- CDC reported 63 outbreaks in the US between 1957 and 2011.
- Local mosquitoes are infected by people who acquired the parasite in endemic areas.

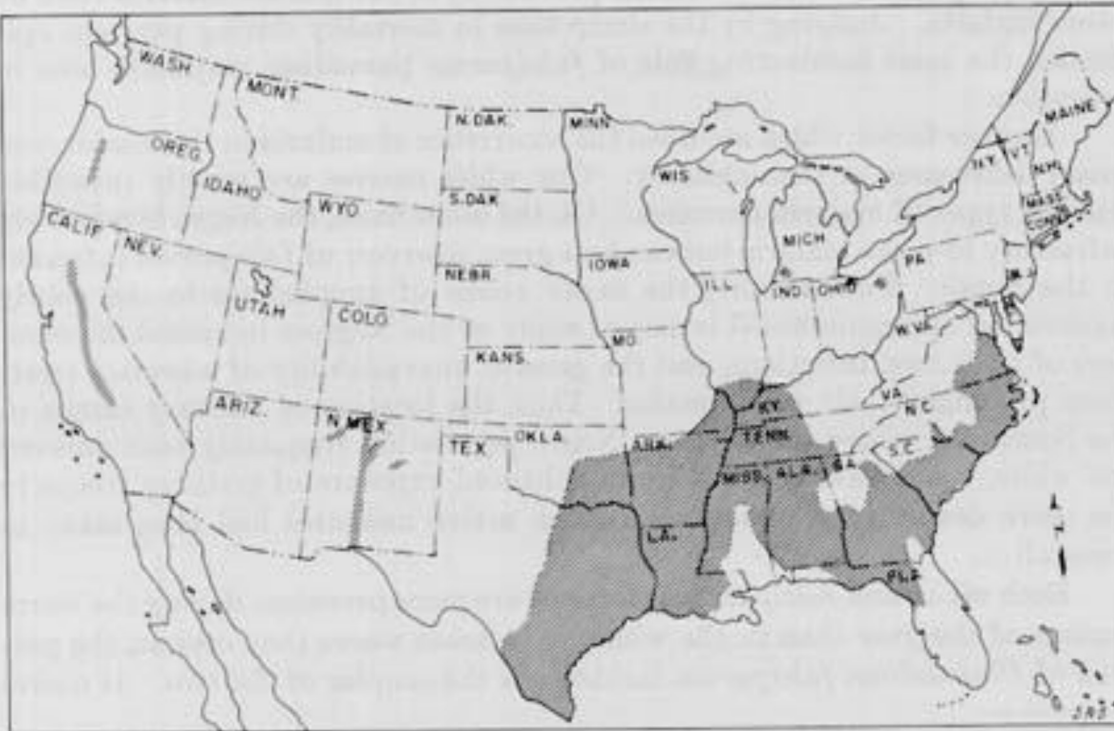
# Malaria in the USA

## Past History

- Malaria did not exist in the Americas until colonists started arriving.
- Spanish colonists brought *vivax* to the Caribbean and Portuguese brought it to Brazil.
- Need for cheap (free) labor resistant to malaria (African slaves) brought *falciparum* to North America.
- Slave work in plantations, mines and other tasks opened up Carolinas and Virginia.

# Malarious Area in US

(1934-1935)



MAP 4.—Areas of the continental United States believed to be malarious in 1934-35.

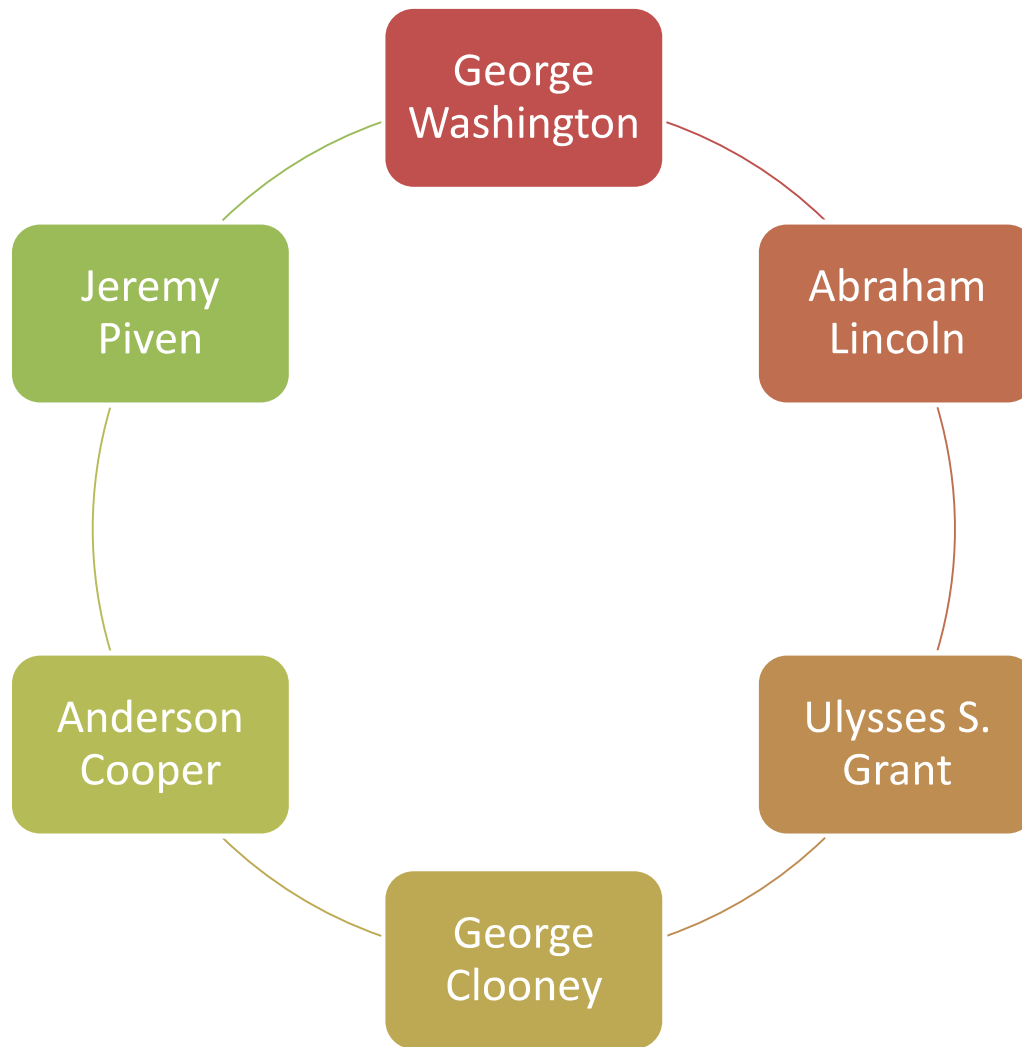
At some time, every state except Alaska was malaria endemic.

500,000 soldiers in WWII got malaria.

Malaria affected 30% of the TVA region in 1933. By 1947, the disease was essentially eliminated.

In 1947, 15,000 malaria cases were reported. By 1950, only 2,000 cases were reported; by 1951, malaria was considered eliminated from the United States.

# Famous Malaria Patients





# 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: 20<sup>th</sup> Century Pandemics, Past & Current
- Session 6 April 2: HIV/AIDS
- Session 7 April 9: 20<sup>th</sup> and 21<sup>st</sup> Century Viruses
- Session 8 April 16: Looking into the crystal ball (?)

