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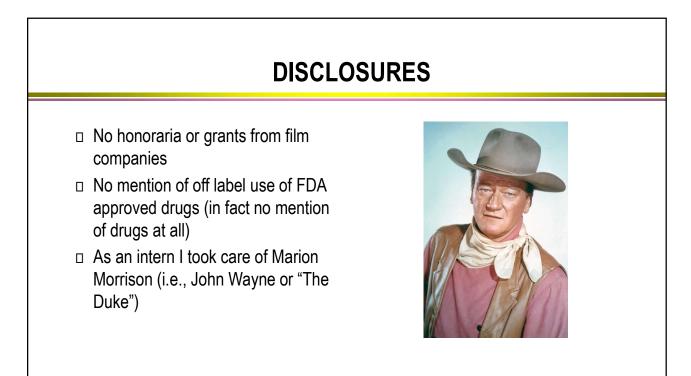
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LECTURE GOALS

- □ Provide entertainment (learning medicine should be fun)
- Provide trivia for your next cocktail party or Jeopardy appearance
- Develop an appreciation for classic movies
- Place infectious diseases in historical perspective

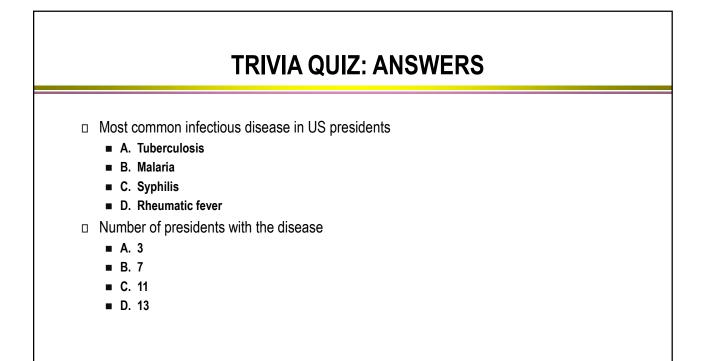
DISCLOSURES

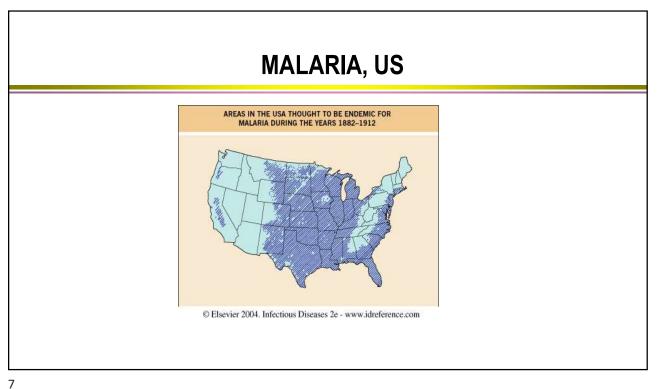
- □ No honoraria or grants from film companies
- No mention of off label use of FDA approved drugs (in fact no mention of drugs at all)
- □ As an intern I took care of Marion Morrison





- Most common infectious disease in US presidents
 - A. Tuberculosis
 - B. Malaria
 - C. Syphilis
 - D. Rheumatic fever
- Number of presidents with the disease
 - A. 3
 - B. 7
 - C. 11
 - D. 13







INFECTIOUS DISEASES IN THE MOVIES Historical movies-overcoming adversity Infectious diseases as natural hazards □ Miracle Worker, 1962: scarlet fever □ African Queen, 1951: Mosquitoes, leeches D Tombstone, 1993: Tuberculosis D To Kill A Mocking Bird, 1962: Rabies Period movies – overcoming adversity Motorcycle Diaries, 2004: Leprosy □ Five Pennies, 1959: Polio Scary movies D Philadelphia, 1993: AIDS □ War Of The Worlds, 1953: "Common" bacteria **D** Finding Neverland, 2004: Tuberculosis Dutbreak, 1995: Ebola Tear jerkers □ Cujo, 1983: Rabies Little Women, 1949: Scarlet fever Did Yeller, 1957: Rabies

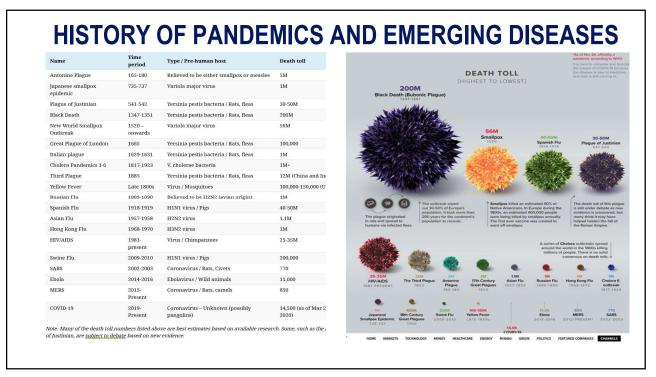


NEW DISEASES: THE FACTS

- □ Mars is the most earth-like of the planets
- Many recent epidemics have been due to microbes jumping species lines
- □ We live in a sea of "organisms"
- Fortunately, our host defenses, in general, prevent us form acquiring infections from most environmental microbes (most infections come from endogenous flora)

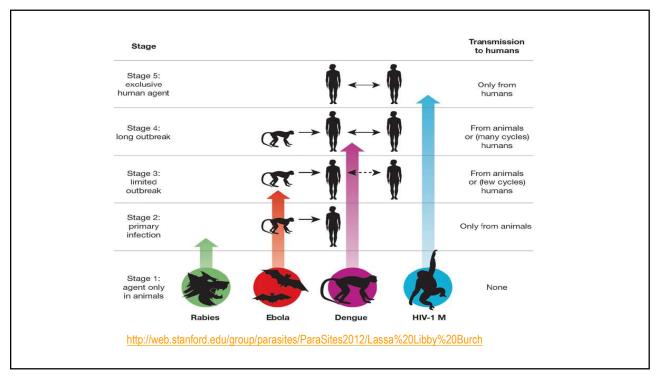
NEW DISEASES: FICTION

- No life on mars
- Most microbes that have jumped species lines and caused recent epidemics have been viruses (not bacteria)
- Host resistance varies; implausible that an entire species would be killed by a single microbe simultaneously



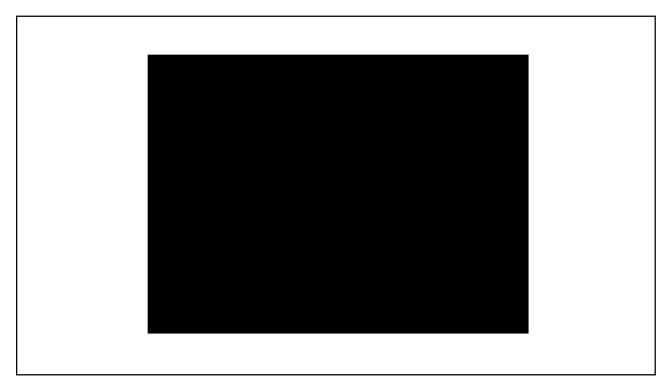
EMERGING DISEASES IN THE US

DISEASE (source)	CASES	OUTCOME	YEAR
West Nile virus (Israel)	Thousands	Endemic (US)	1999
SARS (China)	8096 (8 US, 1 UNC)	Controlled	2003
Monkeypox (Africa)	71	Controlled	2003
Novel flu, H1N1 (Mexico)	Thousands	Endemic (Worldwide)	2009
MERS-CoV (Arabian Peninsula)	Hundreds	Epidemic (Arabian area)	2014
Enterovirus D68	Hundreds (13 UNC)	Epidemic (US)	2014
Ebola	Thousands (1 US)	Epidemic (West Africa)	2014-15
SARS-CoV-2	Millions	Endemic (Worldwide)	2019-present



BASIC CONCEPTS IN DISEASE EMERGENCE

- □ Emergence of infectious diseases is complex
- □ Infectious diseases are dynamic
- □ Most new infections are not caused by genuinely new pathogens
- Agents involved in new and reemergent infections cross taxonomic lines
- □ The concept of the microbe as the cause of disease is inadequate and incomplete
- □ Human activities are the most potent factors driving disease emergence
- Social, economic, political, climatic, technologic, and environmental factors shape disease patterns and influence emergence
- Understanding and responding to disease emergence require a global prospective, conceptually and geographically
- The current global situation favors disease emergence



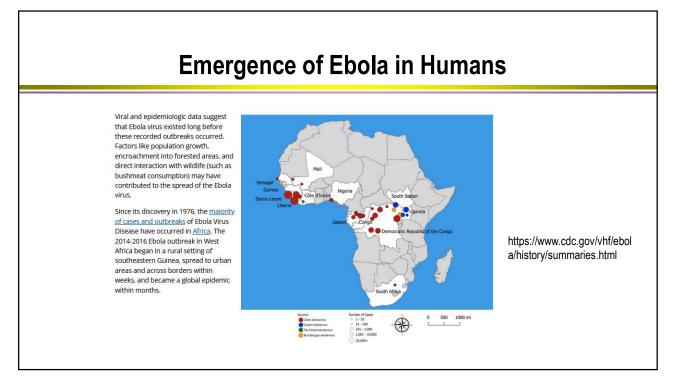
EBOLA: THE FACTS

- □ Multiple outbreaks described in Africa; first outbreak in Zaire 1967
- Acquisition from monkeys
- □ High mortality
- Derson-to-person transmission; healthcare personnel at high risk
- Therapy has advanced from supportive to monoclonal antibodies approved in 2020 (Inmazeb, Ebanga)
- Pre-exposure prophylaxis now also available with rVSV-ZIBOV (Ervoba), approved by FDA in 2019

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EBOLA: FICTION

- The US doesn't destroy villages suffering an outbreak of Ebola
- The reservoir is probably bats
- Pandemic unlikely; high mortality and short incubation period



Chronology of Previous Ebola Virus Disease Outbreaks, WHO

Year	Country	EVD	Cases	Deaths	Case fatality	2011	Uganda	Sudan	1	1	100%
2021	Guinea	Zaire	Ongoing				Democratic				
	Democratic					2008	Republic of the	Zaire	32	14	44%
2021	Republic of the	Zaire	Ongoing				Congo	_			
	Congo					2007	Uganda	Bundibugyo	149	37	25%
	Democratic		100			2007	Democratic Republic of the	7.1.	201	107	7404
2020	Republic of the Congo	Zaire	130	55	42%	2007	Congo	Zaire	264	187	71%
	Democratic					2005	Congo	Zaire	12	10	83%
2018-2020	Republic of the	Zaire	3481	2299	66%	2004	Sudan	Sudan	17	7	41%
	Congo					2003 (Nov-Dec)	Congo	Zaire	35	29	83%
2018	Democratic Republic of the	Zaire	54	33	61%	2003 (Jan-Apr)	Congo	Zaire	143	128	90%
2010	Congo	2.010		55	01/8	2001-2002	Congo	Zaire	59	44	75%
	Democratic					2001-2002	Gabon	Zaire	65	53	82%
2017	Republic of the	Zaire	8	4	50%	2000	Uganda	Sudan	425	224	53%
100000	Congo	78075		2.22		1996	South Africa (ex-	Zaire	1	1	100%
2015	Italy	Zaire	1	0	0%		Gabon)				
2014	Spain	Zaire	1	0	0%	1996 (Jul-Dec)	Gabon	Zaire	60	45	75%
2014 2014	UK	Zaire	1	0	0% 25%	1996 (Jan-Apr)	Gabon	Zaire	31	21	68%
2014	Senegal	Zaire	4	0	25%		Democratic			254	
2014	Mali	Zaire	8	6	75%	1995	Republic of the Congo	Zaire	315	254	81%
2014	Nigeria	Zaire	20	8	40%	1994	Côte d'Ivoire	Tai Forest	1	0	0%
2014-2016	Sierra Leone	Zaire	20 14124*	o 3956*	28%	1994	Gabon	Zaire	52	31	60%
2014-2016	Liberia	Zaire	10675*	4809*	45%	1994	Sudan	Sudan	34	22	65%
2014-2016	Guinea	Zaire	3811*	2543*	67%	1010	Democratic	Judun	37	44	00.0
2011 2010	Democratic	2010	0011	2010	0.10	1977	Republic of the	Zaire	1	1	100%
2014	Republic of the						Congo				
	Congo					1976	Sudan	Sudan	284	151	53%
	Democratic						Democratic				
2012	Republic of the Congo	Bundibugyo	57	29	51%	1976	Republic of the Congo	Zaire	318	280	88%
2012	Uganda	Sudan	7	4	57%		Congo				
2012	Uganda	Sudan	24	17	71%	* Include Sugner	t. Probable and Cont	med EV/D cases			

EBOLA VIRUS DISEASE, KEY FACTS, WHO

- □ Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a rare but severe, often fatal illness in humans.
- □ The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission.
- □ The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks.
- Community engagement is key to successfully controlling outbreaks.
- Good outbreak control relies on applying a package of interventions, namely case management, infection prevention and control practices, surveillance and contact tracing, a good laboratory service, safe and dignified burials and social mobilization.
- Vaccines to protect against Ebola have been developed and have been used to help control the spread of Ebola outbreaks in Guinea and in the Democratic Republic of the Congo (DRC).
- Early supportive care with rehydration, symptomatic treatment improves survival. Two monoclonal antibodies (Inmazeb and Ebanga) were approved for the treatment of Zaire ebolavirus (Ebolavirus) infection in adults and children by the US Food and Drug Administration in late 2020.
- Pregnant and breastfeeding women with Ebola should be offered early supportive care. Likewise vaccine prevention and experimental treatment should be offered under the same conditions as for non-pregnant population.

https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease

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KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Pathogen
 - Taxonomy (provides clues regarding transmission routes, environmental stability, germicide susceptibility)
 - Hosts
- Epidemiology
 - Locations of endemicity (i.e., locations in the world where sources or reservoirs reside)
 - Incubation period
 - Transmission routes
 - Infectivity (i.e., communicability)
 - Duration of infectivity

- Clinical
 - Symptoms
 - Signs
 - Risk factors for acquisition of infection
 - Morbidity
 - Mortality
 - Risk factors for morbidity and mortality
 - Diagnostic methods (sensitivity, specificity, biosafety)
 - Therapy (availability, efficacy, safety)

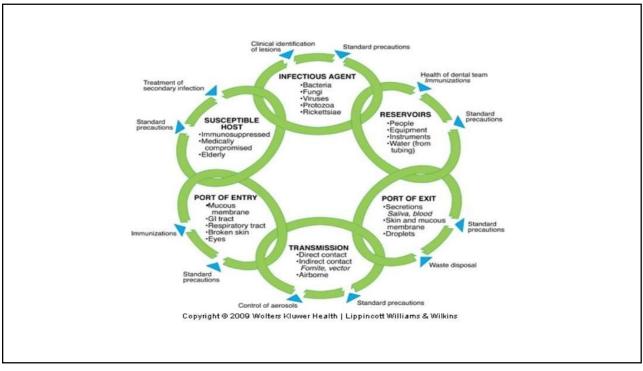
KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

Infection Prevention

- Environmental survival
- Germicide susceptibility
- Isolation recommendations
- Recommended personal protective equipment
- Pre-exposure prophylaxis (availability, efficacy, safety)
- Postexposure prophylaxis (availability, efficacy, safety)
- Recommended biosafety level in the laboratory
- Recommended waste disposal (liquids and solids

- Managing a pandemic
 - Sensitive and specific (ideally rapid) diagnostic test
 - Early identification of patients
 - Protecting our healthcare personnel (PPE, donning, doffing)
 - Sufficient staff, inpatient/ICU beds, ventilators
 - Managing shortages

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RABIES: EPIDEMIOLOGY

- Agent: Rhabdoviridae (genus Lyssavirus)
- Reservoir: Small mammals, bats
 - Bat species include silver-haired bats and eastern pipistrelles
- □ Transmission
 - Animal bite or scratch (contact with infectious saliva)
 - Airborne: Spelunking (rare) or laboratory generated aerosol
 - latrogenic: Corneal transplants (8 cases), transplanted organs (2 outbreaks) or improperly inactivated vaccines
- Deaths, US
 - From 1960 to 2018, 127 human rabies cases were reported in the United States, with roughly a quarter resulting from dog bites received during international travel. Of the infections acquired in the United States, 70% were attributed to bat exposures.
- □ Prevention (or post-exposure therapy)
 - Rabies vaccine + RIG

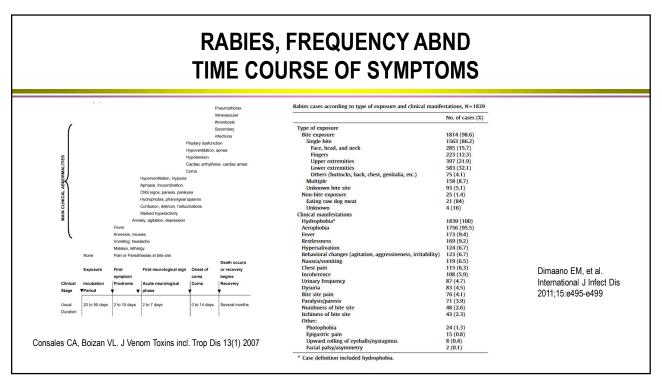
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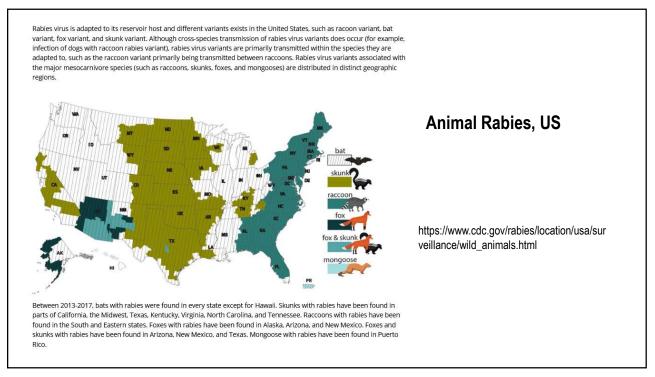
Estimated Incubation Period (days) per Bite Site

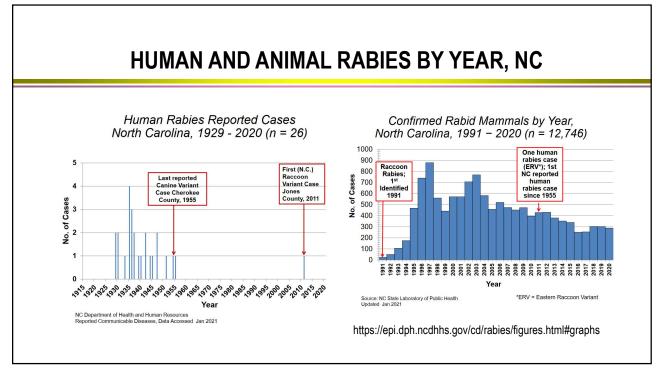
Bite site	<7 (%)	8-14 (%)	15-21 (%)	22-30 (%)	31-90 (%)	91-365 (%)	>365 (%)
Face, head, neck	5 (0.3)	32 (1.8)	49 (2.8)	57 (3.3)	84 (4.8)	46 (2.6)	12 (0.7)
Fingers	0	0	13 (0.7)	21 (1.2)	44 (2.5)	106 (6.1)	39 (2.2)
Upper extremities	0	0	3 (0.2)	8 (0.5)	76 (4.4)	225 (12.9)	85 (4.9)
Lower extremities	0	0	0	5 (0.3)	58 (3.3)	369 (21.2)	151 (8.7)
Other sites (buttocks, back, chest, genitalia)	0	0	1 (0.1)	6 (0.3)	23 (1.3)	31 (1.8)	14 (0.8)
Multiple bite	2 (0.1)	5 (0.3)	16 (0.9)	24 (1.4)	69 (4.0)	34 (2.0)	8 (0.5)
Non-bite (eating raw dog meat)	0	0	0	3 (0.2)	7 (0.4)	11 (0.6)	0
Total cases ^b	7 (0.4)	38 (2.1)	92 (5.0)	155 (8.4)	498 (27.1)	785 (42.8)	251 (13.7

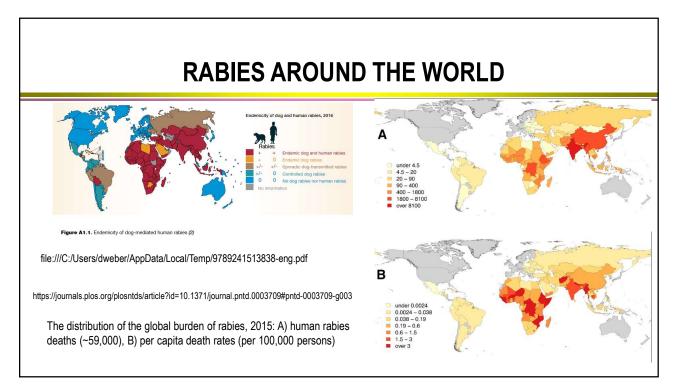
^a Time of exposure to the time of manifest signs and symptoms; eight cases were of 5 years incubation (0.4%) and one case was of 27 years incubation (0.1%). ^b Not all bite locations were recorded, thus *n*=1835 for total cases and *n*=1742 for all cases for which a bite location was recorded.

Dimaano EM, et al. International J Infect Dis 2011;15:e495-e499









RABIES: EPIDEMIOLOGY AND PREVENTION, WHO

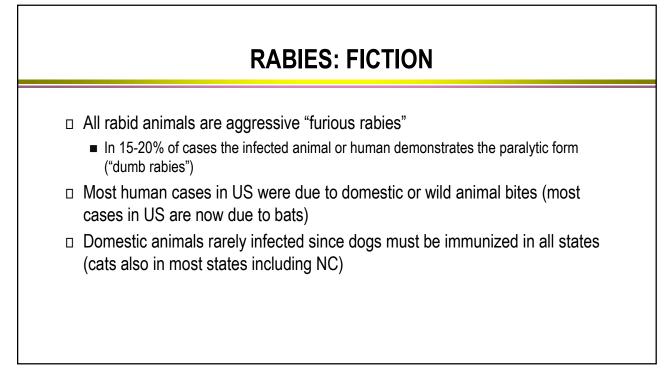
- Rabies is a vaccine-preventable viral disease which occurs in more than 150 countries and territories.
- Dogs are the main source of human rabies deaths, contributing up to 99% of all rabies transmissions to humans.
- □ Interrupting transmission is feasible through vaccination of dogs and prevention of dog bites.
- □ Infection causes tens of thousands of deaths every year, mainly in Asia and Africa.
- □ Globally rabies causes an estimated cost of US\$ 8.6 billion per year
- a 40% of people bitten by suspect rabid animals are children under 15 years of age.
- Immediate, thorough wound washing with soap and water after contact with a suspect rabid animal is crucial and can save lives.
- Engagement of multiple sectors and One Health collaboration including community education, awareness programes and vaccination campaigns are critical.

https://www.who.int/news-room/fact-sheets/detail/rabies



RABIES: THE FACTS

- Rabies endemic throughout the world
- □ Main source of human rabies in the US in the past was dogs
- □ Highly fatal to all mammals (only 6 human survivors)
- No treatment once symptoms appear
- In South America ruminants are a major source of human rabies (due to vampire bats)
- □ Animal saliva is source of infection (dead animals are indeed dangerous)

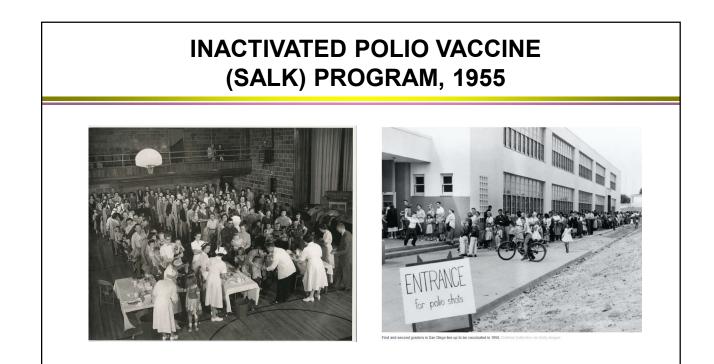


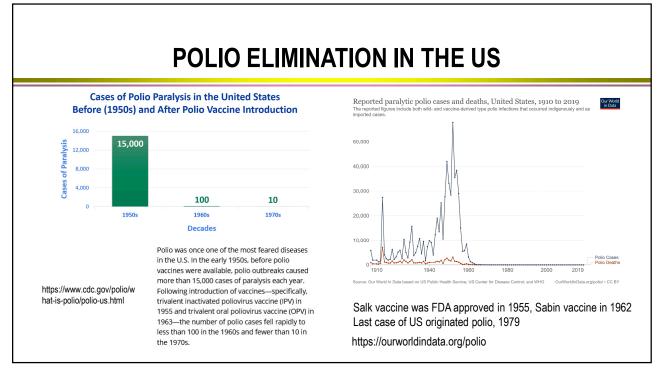


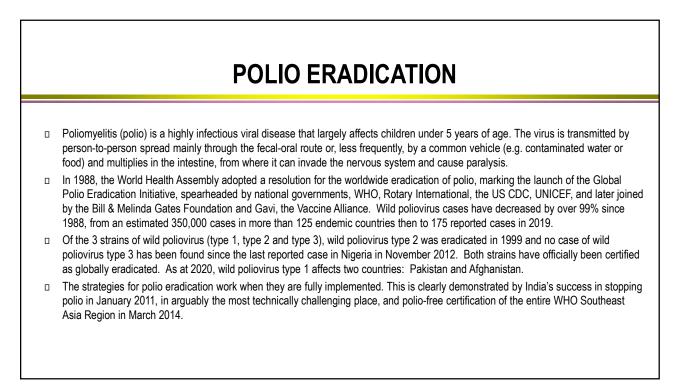
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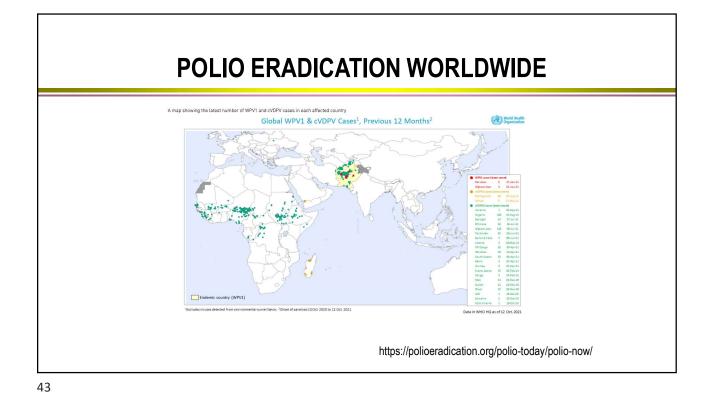
POLIO: FICTION

- Delio not transmitted by respiratory route; masks not necessary (fecal-oral transmission)
- Following acute polio, progressive improvement is the usual course (post-polio syndrome {PPS} affects ~25-40% of survivors, usually 15-40 years after the initial infection; many survivors experience a modest decline in function and muscle strength over many years)
 - Symptoms of PPS: Muscle weakness; mental and physical fatigue; joint pain
 - Some people with PPS have only minor symptoms, while others develop more visible muscle weakness and atrophy (a decrease in muscle size). PPS is rarely life-threatening, but the symptoms can make it difficult for an affected person to function independently.





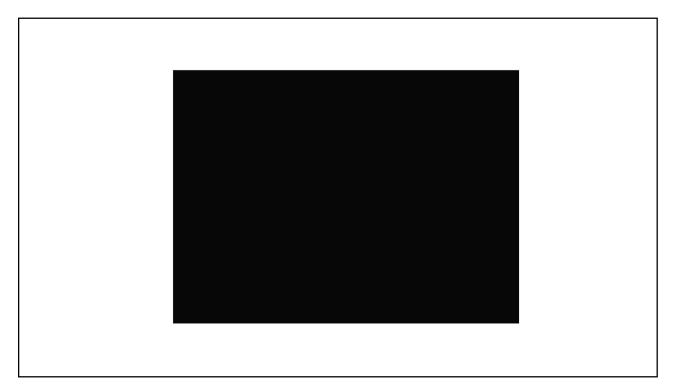


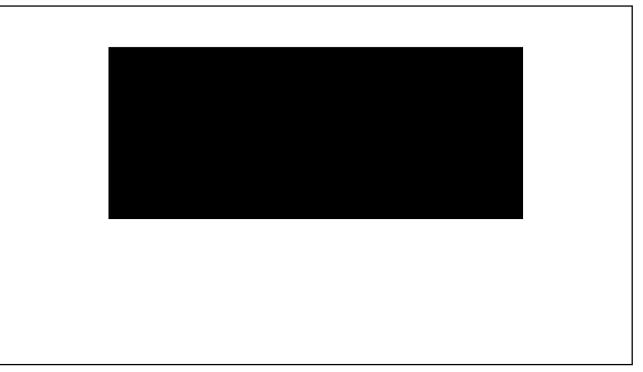


POLIO ERADICATION AND RESURGENCE

- Poliomyelitis (polio) is a highly infectious viral disease that largely affects children under 5 years of age. The virus is transmitted by person-to-person spread mainly through the fecal-oral route or, less frequently, by a common vehicle (e.g. contaminated water or food) and multiplies in the intestine, from where it can invade the nervous system and cause paralysis.
- In 1988, the World Health Assembly adopted a resolution for the worldwide eradication of polio, marking the launch of the Global Polio Eradication Initiative, spearheaded by national governments, WHO, Rotary International, the US CDC, UNICEF, and later joined by the Bill & Melinda Gates Foundation and Gavi, the Vaccine Alliance. Wild poliovirus cases have decreased by over 99% since 1988, from an estimated 350,000 cases in more than 125 endemic countries then to 175 reported cases in 2019.
- Of the 3 strains of wild poliovirus (type 1, type 2 and type 3), wild poliovirus type 2 was eradicated in 1999 and no case of wild poliovirus type 3 has been found since the last reported case in Nigeria in November 2012. Both strains have officially been certified as globally eradicated. As at 2020, wild poliovirus type 1 affects two countries: Pakistan and Afghanistan.
- 2021, cVDPV2 was reported in 2021 in Ethiopia (2), Mali (1), Nigeria (23), Sierra Leone (1), and Tajikistan (1); 2022 cVDP2 reported in Israel, UK (positive wastewater – led to vaccination of London children under 10) and NY (positive wastewater and 1 patient with paralytic polio)
- The strategies for polio eradication work when they are fully implemented. This is clearly demonstrated by India's success in stopping polio in January 2011, in arguably the most technically challenging place, and polio-free certification of the entire WHO Southeast Asia Region in March 2014.

Summary What is already known about this topic? Sustained poliovirus transmission has been eliminated from the United States for approximately 40 years; vaccines are highly effective in preventing paralysis after exposure. PARALYTIC POLIO, US What is added by this report? In June 2022, poliovirus was confirmed in an unvaccinated immunocompetent adult resident of New York hospitalized with flaccid lower limb weakness. Vaccine-derived poliovirus type 2 was isolated from the patient and identified from wastewater samples in two neighboring New York counties. Transmission: Fecal-oral (direct contact, indirect via contaminated) water or food); droplet - infected people can shed virus for weeks What are the implications for public health practice? from GI tract; virus can survive for weeks in the environment Unvaccinated persons in the United States remain at risk for paralytic poliomyelitis if they are exposed to either wild or vaccine-derived poliovirus; all persons in the United States should stay up to date on recommended poliovirus vaccinati Long-term carrier states (>6 mo) may occur in immunocompromised persons Most cases of polio are asymptomatic but 25% develop flu-like FIGURE. Timeline of patient activities, potential poliovirus exposures, shedding, and p linked to a patient with a case of type 2 vaccine-derived poliovirus — New York, May-A symptoms: Pharyngitis, fever, fatigue, nausea, headache, abdominal pain - duration 2-5 days Meningitis = 1% to 5%; Paralysis = 0.5% to 0.05% (Between 2 and 10 out of 100 die) Development of new muscle pain, weakness, or paralysis as adults,15 to 40 years after recovery (25%-40% of patient with hx paralytic polio). Diagnosis: Detection in stool Vaccine: Only inactivated vaccine available in US (risk VAPP with oral vaccine, 1/2.4 million); routine childhood vaccination; effectiveness (3 doses) 99%-100%; >90% have antibody after 25 years Link-Gelles R, et al. MMWR 2022;71:1065





FAMOUS PEOPLE WITH TUBERCULOSIS

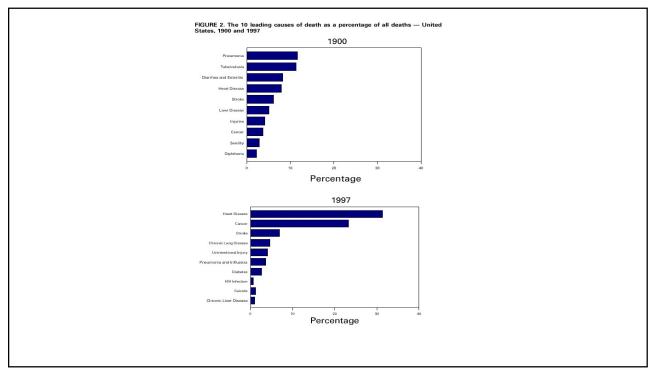
- □ *C. P. E. Bach: Musician
- *Frederic Chopin: Musician
- Noel Coward: Author
- Ralph Waldo Emerson: Writer
- Device Paul Erhlich: Physician
- □ *Doc Holliday: Gunman
- □ *Vivian Leigh: Actress
- D Franklin Pierce: President
- D F. Scott Fitzgerald: Writer

- □ *George Orwell: Writer
- □ *Eleanor Roosevelt: Wife of president
- □ *Henry David Thoreau: Writer
- □ Leon Trotsky: Writer
- George Washington: President
- □ *Walt Whitman: Writer

* Died of tuberculosis



- □ 1851: Born in Griffin, Georgia, to a wealthy family
- □ 1870-72: Studied dentistry
- 1873: Found to have tuberculosis (possible nosocomial acquisition) and moved West after being told he had "3 months to live"
- □ 1873: Gave up dentistry due to his chronic cough
- □ 1875-1882: Killed >10 men
- □ 1882: Fought along the Earps at O.K. Corral
- □ 1887: Died of tuberculosis

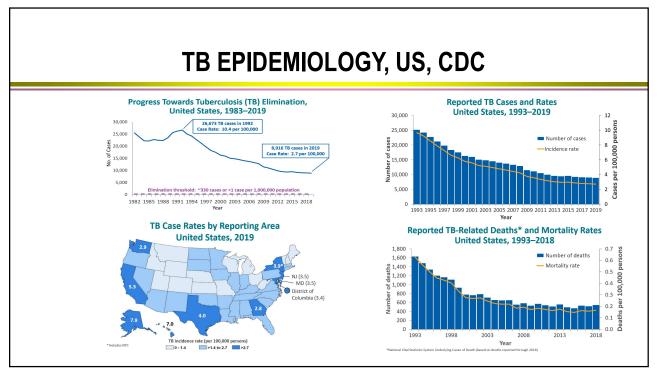


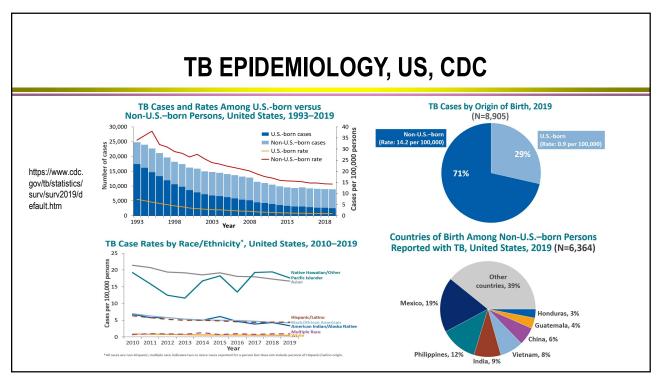
TUBERCULOSIS: THE FACTS

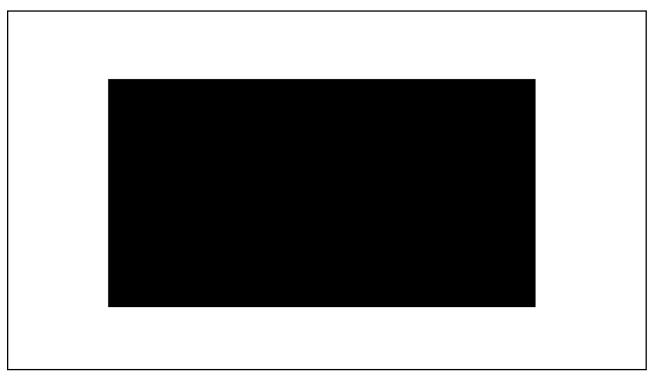
- Tuberculosis primarily a disease of the industrial age
- Common cause of chronic illness
- Well described by term "consumption"
- Transmission via airborne route
 - Coughing in source increases transmission frequency
 - Infection control: Mask on source case, detection & therapy LTBI
- Reactivation TB
 - Hemoptysis, 25%
- □ No effective therapy until mid-20th century
- Highly effective vaccine still lacking

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TUBERCULOSIS TODAY Falling incidence in the U.S. Increasingly a disease of immigrants □ Worldwide concerns of multi-drug resistance (MDR-TB; resistant to INH and rifampin) □ Growing threat of extreme-drug resistance (XDR-TB; resistant to INH, rifampin, and ≥2 classes of injectable treatment) Important cause of death in HIV-infected persons







HIV: THE FACTS

- □ Initial survival of AIDS ~18 weeks
- Wasting a common feature of AIDS
- Kaposi's sarcoma considered an AIDS defining diagnosis
- □ HIV infected persons did in fact face discrimination
- □ Initially no available therapies

HIV: FICTION

- Long term survival of persons with HIV infection now common due to multi-drug treatment
- PrEP and PEP now available
- HIV infected patients protected, in part, from discrimination under the ADA
- Opportunistic infections much less common due to prophylaxis
- Kaposi's sarcoma due to HHV-8
 - Incidence has dropped dramatically
 - But still a major public health concern

