ZOONOSES: PAST AND PRESENT

PART 1

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Objectives

01

Detail multiple zoonotic infections from the distant past through the present time

02

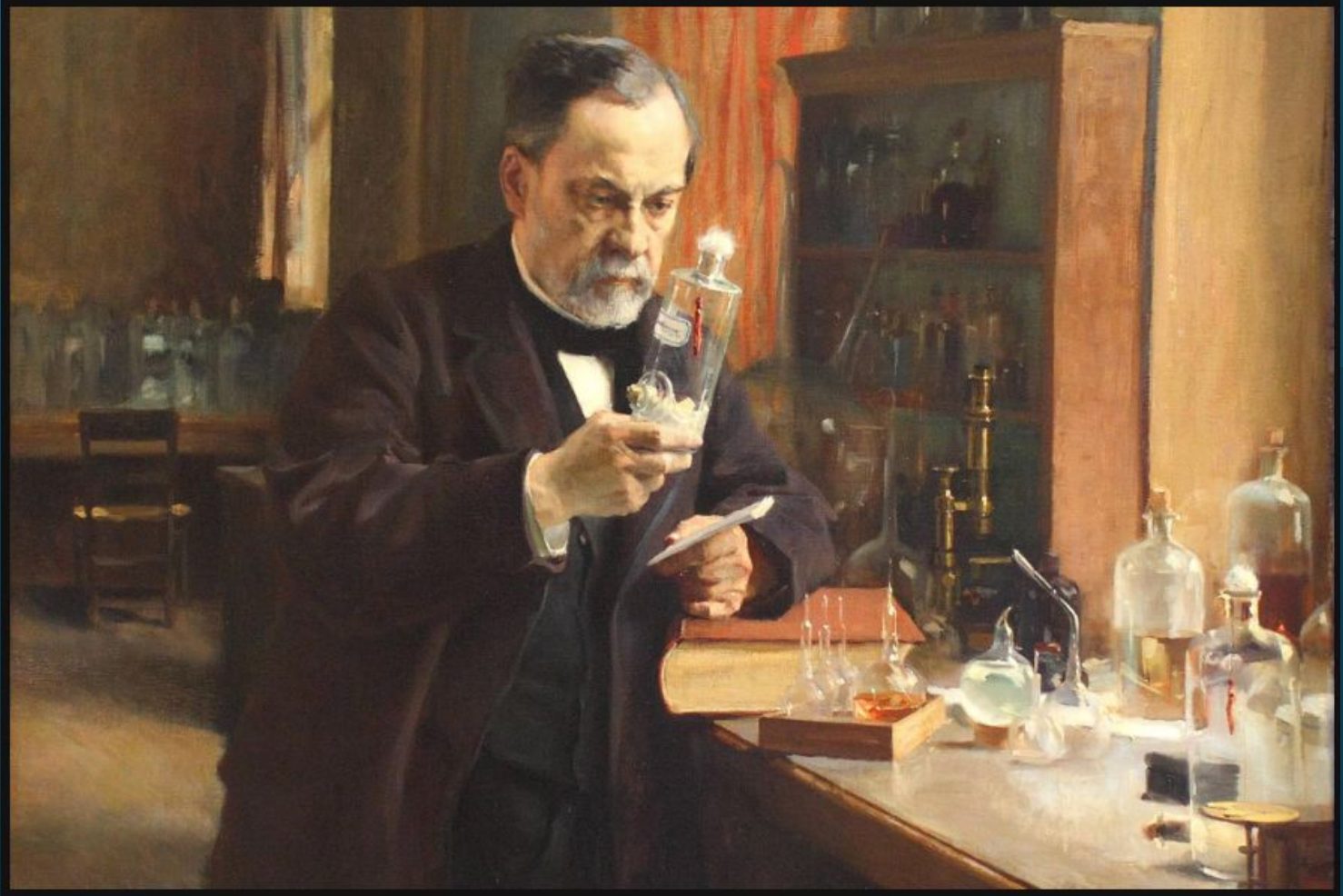
Discuss both viral and bacterial pathogens with variable acuity and geographic reach

03

Appreciate the historical aspects of the outbreaks

History of Rabies (*Lyssavirus*)

- Lyssa in Greek means, “frenzy or madness”
  - Lyssa was the goddess of rage
- Virus in Latin means, “poisonous secretion”
- Homer (8th century BCE)
  - Thought to have referred to rabies in the Iliad, when he mentioned Sirius (brightest star in Canis Major) and its malignant influence (heat causing aggression); also used the term, “raging dog”
- Aristotle (4th century BCE)
  - “Dogs suffer from the madness. This causes them to become irritable and all animals they bite to become diseased.”
- Hippocrates (4th century BCE)
  - Thought to have referred to rabies: “persons in a frenzy drink very little, are disturbed, and frightened…”
- Ancient Romans believed that clipping the tail of the dog that bit you may help stave off illness

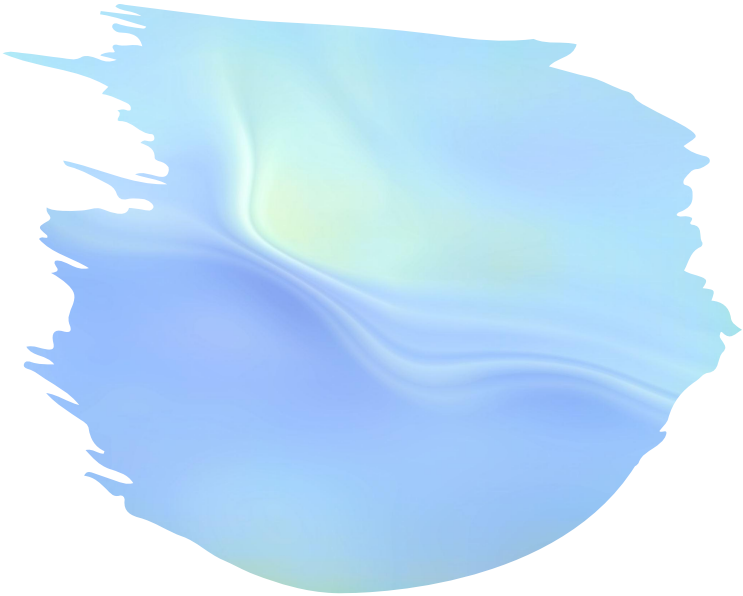


Dr. Louis Pasteur
Dr. Louis Pasteur, who gives the first rabies vaccine, in his lab.

1885

Dr. Louis Pasteur injects a series of a new rabies vaccine into a boy who had been bitten by a rabid dog. The boy survives. This is the first vaccine to protect against rabies in people. Before the rabies vaccine, nearly all people infected with rabies died.

Rabies



- Family: *Rhabdoviridae*
- Genus: *Lyssavirus*
  - 17 species
    - *rabies* species is the most commonly known, upon which vaccination is based (for humans and animals), with good cross protection against many of the other species (but these infections are rare in animals and do not occur in humans)
    - Only *rabies* species is endemic to the Americas
- Disease: Fatal encephalomyelitis

Rabies

- Virions are bullet-shaped, enveloped, ssRNA (negative-sense), non-segmented

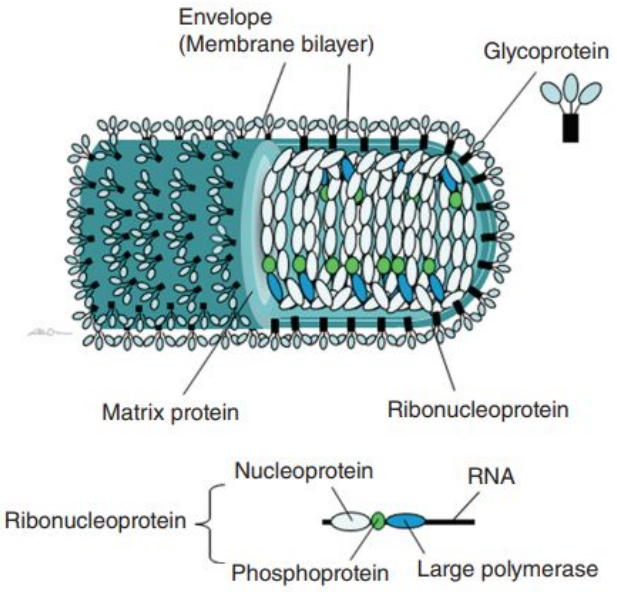


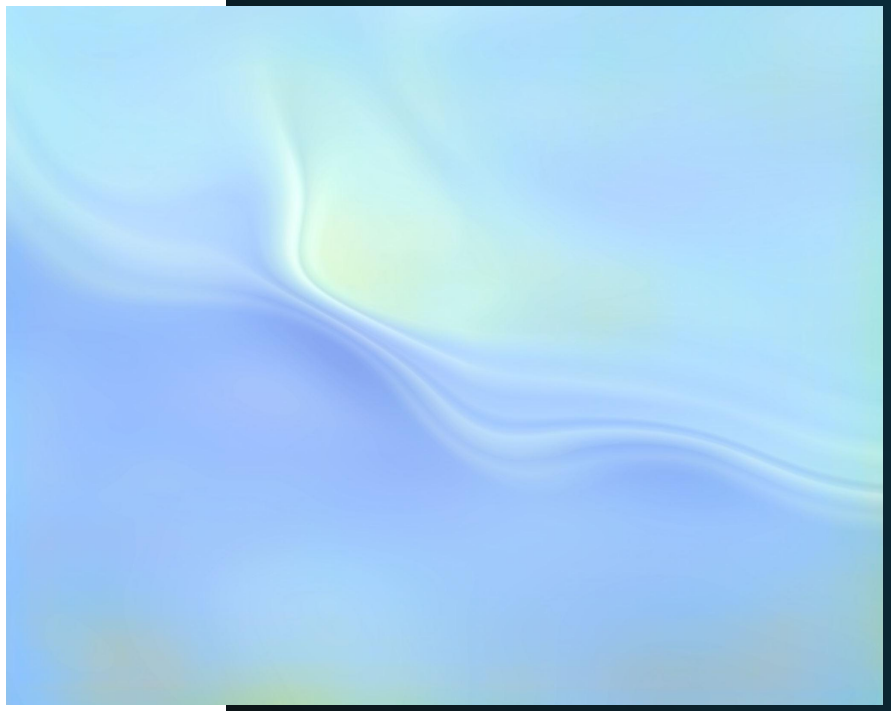
FIGURE 2 Diagram of lyssavirus morphology and structural proteins.

Rabies virus, purified from an infected cell culture. Negatively stained virions: note their characteristic "bullet shape." Magnification approximately x70,000.

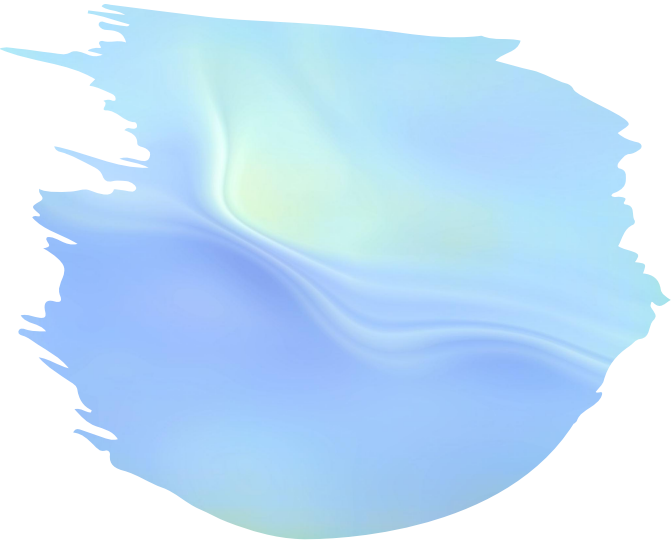
Micrograph from F. A. Murphy, University of Texas Medical Branch, Galveston, Texas.

Epidemiology

- >6000 animal cases are diagnosed each year in the United States
  - Racoons, skunks, foxes, mongooses, bats
- Human cases in the US are rare (<4 cases per year)
  - Worldwide estimates are up to ~70,000 cases
    - >90% of which are caused by dogs
    - Lack of access to PEP and public health resources
- Every year, ~60,000 Americans receive PEP following an exposure



Transmission



- All mammals are susceptible
- Infected saliva (bite)
- Nonbite exposures are rare (scratches, open wounds, mucous membranes, transplanted corneas / organs)
  - No known transmission of rabies from autopsies
- Not via fomites (virus susceptible to sunlight, drying, standard disinfectants like bleach and 70% ethanol)
- Cleansing of wound (essential), PEP (life-saving)
- The virus travels slowly along nerves to the brain
  - The closer the bite is to your CNS, the shorter the incubation period

Clinical

- Incubation period: several weeks to months (average timing is 45 days)
- Initially, non-specific symptoms (prodrome)
- Then, acute neurological phase ➡ coma, death
  - Encephalitic / furious form (~80%)
    - Hyperexcitability, confusion, hallucinations, agitation / aggression
      - Can have lucid moments
    - Dysphagia, hypersalivation, lacrimation, diaphoresis, hydrophobia (painful throat spasms), aerophobia (painful diaphragmatic spasms)
  - Paralytic form (~20%)
    - Ascending muscle flaccidity, cranial nerves (including deafness), laryngeal weakness, urinary incontinence, cardiopulmonary compromise
- One of the highest case fatality rates by an infectious pathogen (>99%)
  - 29 known cases of survival; most had some form of PEP

Diagnosis (antemortem)

- All four samples below must be collected for definitive rule out:
  - Saliva
    - 4+ samples; reverse transcription (RT) PCR
  - Skin biopsy
    - 5-6mm (diameter) section from nuchal region, containing hair follicles (at a depth to include cutaneous nerves that lie at the base of the follicles); RT-PCR and immunofluorescent staining for viral antigens in frozen sections
  - Serum
    - Fluorescent antibody (Ab) test and virus neutralization test
    - The presence of Abs can be diagnostic of infection if patient was not vaccinated
  - CSF
    - Fluorescent Ab test and virus neutralization test
    - The presence of Abs in the CSF (even if patient was vaccinated) suggests infection

Treatment

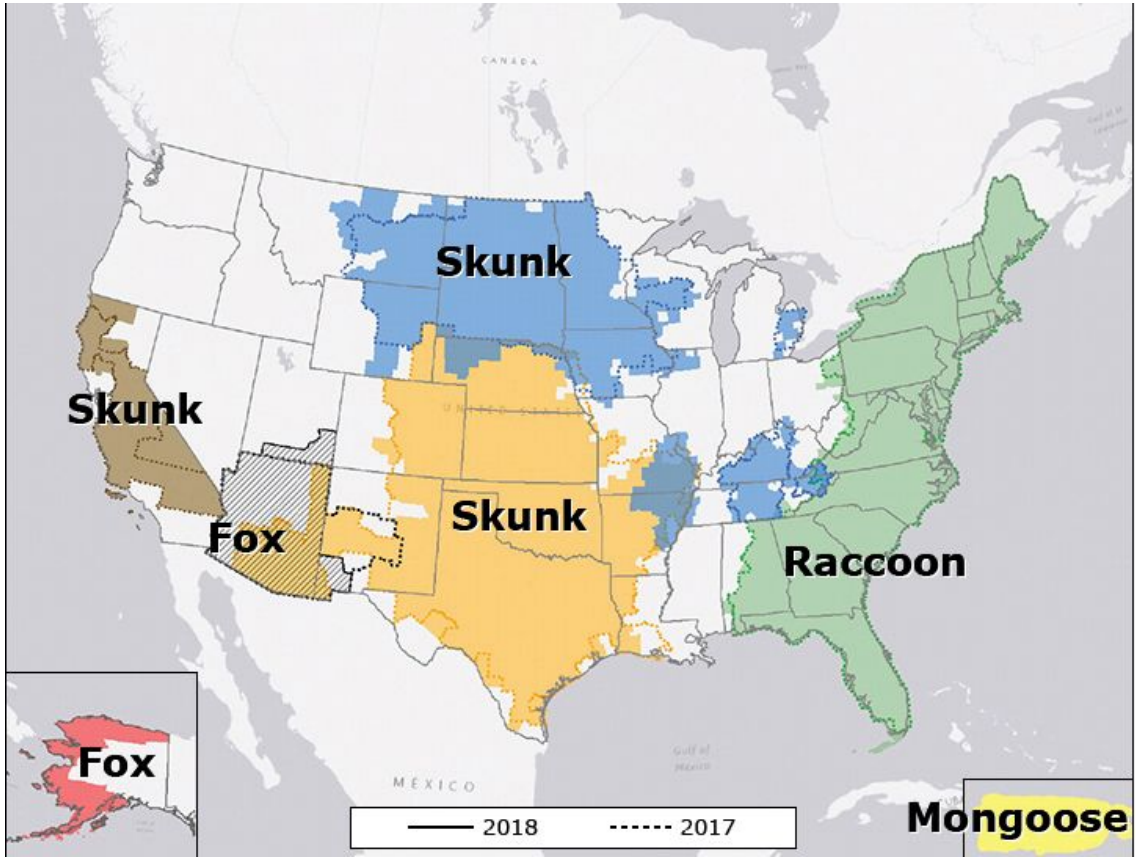
- After symptoms appear, no proven medicinal interventions
- Supportive (sedation, intubation, intracranial pressure monitoring)
- Vaccination and human rabies immune globulin (HRIG) does not impact survival rate and in fact may hasten death

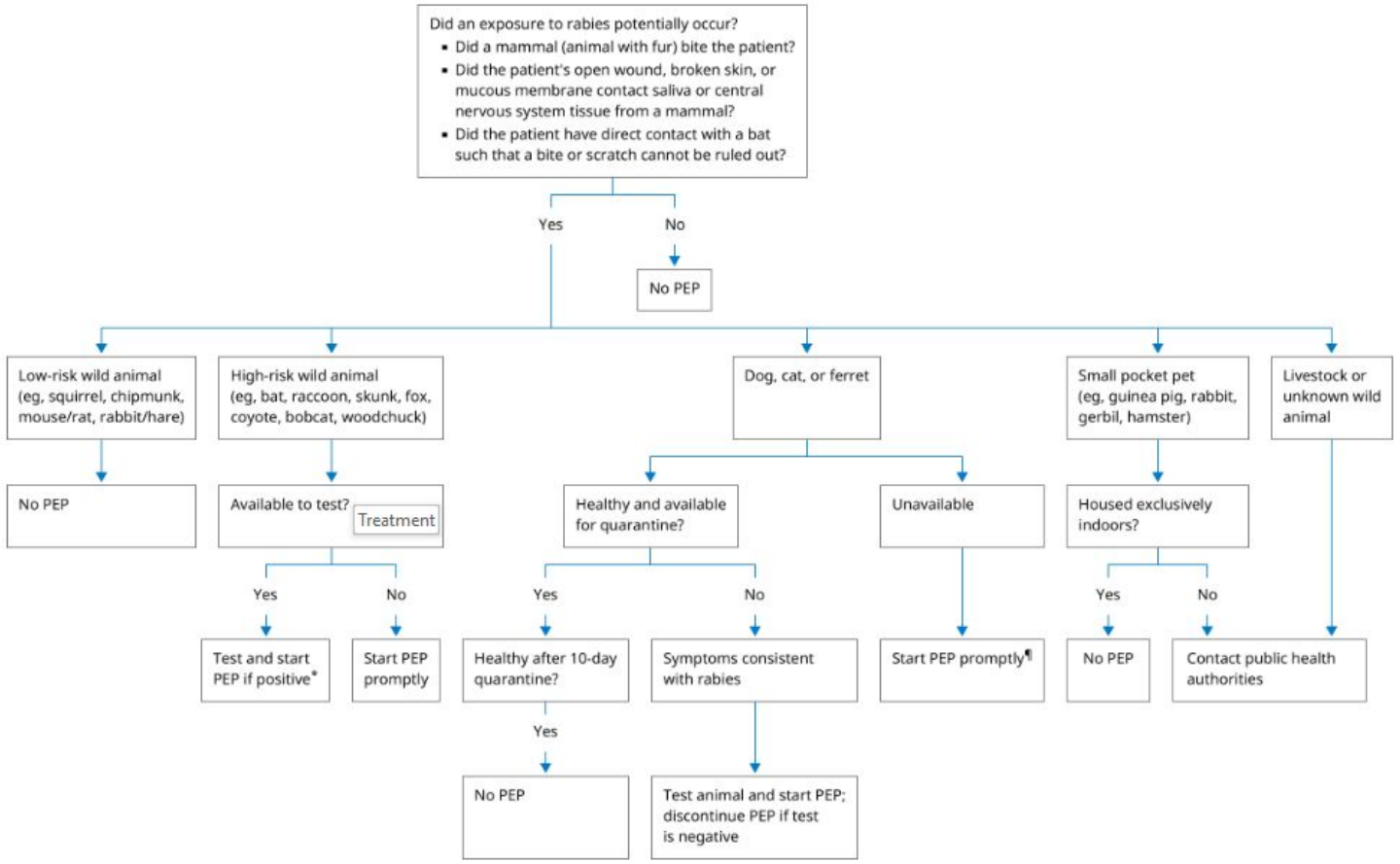
Treatment (experimental)

- Milwaukee Protocol:
  - Aggressive sedation
  - Steroids
  - Maintain hypernatremia (145-155 mEq/L; cerebral edema)
  - Insulin drip (to maintain euglycemia)
  - Maintain body temp to 35-37 ºC
  - Amantadine (neuroprotective in rabies; PD drug = antidyskinetic)
  - Vitamin C (vasospasms)
  - No ribavirin (immunosuppressive; antiviral)

PEP Indications

- Consider:
  - The epidemiology of animal rabies in the region
  - Species of animal in question
    - Behavior (unprovoked attack)
    - Absence of appropriate vaccination
    - Bite wound(s) on animal
    - Observation / quarantine of animal
  - Exposure / contact type





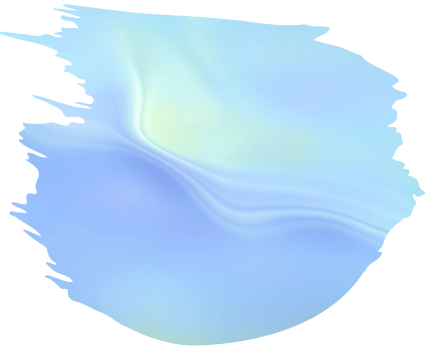
PEP: postexposure prophylaxis.

* PEP should be initiated immediately in patients with severe bites to the head, neck, or trunk after an unprovoked attack from a high-risk animal. PEP can be discontinued if testing proves the animal was not rabid.

¶ In areas without an endemic, terrestrial strain of rabies (eg, dog, raccoon, skunk, fox, mongoose), contact local public health authorities for risk assessment.

Courtesy of Alfred DeMaria Jr, MD and the Massachusetts Department of Public Health.

Fun (?) facts

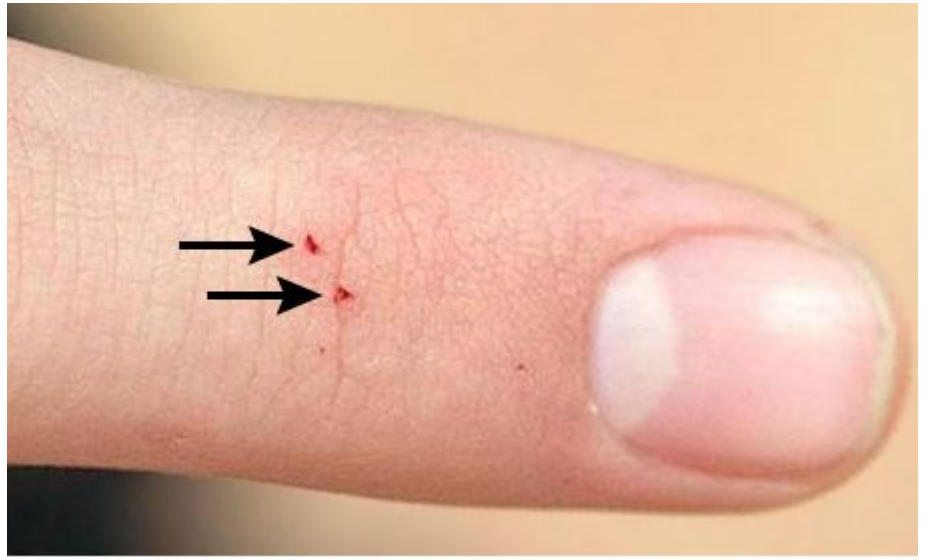


- Human-to-human transmission of rabies can theoretically result from bite and nonbite exposures, but reports are very rare, poorly documented, and occur in places where it is difficult to rule out potential animal exposures

- No transmission of rabies has been documented from rabies-infected patients to health care providers or to household contacts in the United States

- However, human-to-human transmission arising from transplantation (corneas, organs) is well documented

Bats



- No rabies in Hawaii
- Between 1990 and 2018:
  - 51/56 human cases were from bats
- If bat can be tested, can delay PEP for several days
  - >90% submitted bats are negative
- If bat cannot be tested, or if bat is positive ➡ PEP
- PEP is also needed:
  - For patients with bites, scratches, or mucous membrane exposure
  - If the above contact mechanisms cannot be ruled out (sleeping, intoxication, child, person with a disability)
- PEP is not needed if the person was aware of the bat at all times and can definitively state there was no contact

TABLE 3. Rabies postexposure prophylaxis (PEP) schedule — United States, 2010

Vaccination status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area†), 1 each on days 0,§ 3, 7 and 14.¶
Previously vaccinated**	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area†), 1 each on days 0§ and 3.

* These regimens are applicable for persons in all age groups, including children.
† The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.
§ Day 0 is the day dose 1 of vaccine is administered.
¶ For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.
** Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

Prevention

- When traveling, avoid unfamiliar animals (dogs, cats)
- Higher risk with some outdoor activities:
  - Camping, spelunking, hunting
- Veterinary medicine professionals, animal control workers, laboratory workers (working with live rabies virus)
  - Vaccination
- Vaccinate pets
- Cleansing any wounds from animals and seeking medical care

History of Plague

- *Yersinia pestis* DNA detected in remains of humans (4500-2000 BCE)
- Roman Empire
  - “Justinian Plague” 541-546 CE
  - Emperor was infected but lived
  - Buboes and high death toll were described
  - Mass burials outside of city walls

“The Pestilence”

- 1347-1352 CE
- Originated in Asia, spread to Russia, Europe
- Described in a book by Italian author Boccaccio in 1348:
  - “…it first betrayed itself by the emergence of certain tumours in the groin or armpits... After which the form of the malady began to change, black spots or livid making their appearance.”
- The term, “Black Death,” was not used until the 18th century
  - Septicemia → limb ischemia → gangrene
- In revenge for losing a siege, the Tartar armies of Khan Janibeg catapulted corpses over the city walls, further spreading disease
- Bodies into pits, or decayed at home / on streets
  - “The sexton and the physician were cast into the same deep and wide grave…”
- At least 25 million people died in both Europe and Asia
- Death within 4 days
- “Quarantena” (patient isolation for 40 days; Italian) = derivation of the word, quarantine

History of Plague

- Used by physicians treating patients in the early 17th century (Italy and France)
- Hood with crystal eye pieces
- Beak filled with herbs and compounds:
  - Cinnamon, pepper, turpentine, roast copper, powdered viper flesh; all thought to ward off poison air “miasma” (Greek)
- Robe, boots, gloves
- “Ring Around the Rosie”

American children playing "Ring Around the Rosie" in an illustration by Jessie Willcox Smith from The Little Mother Goose (1912)

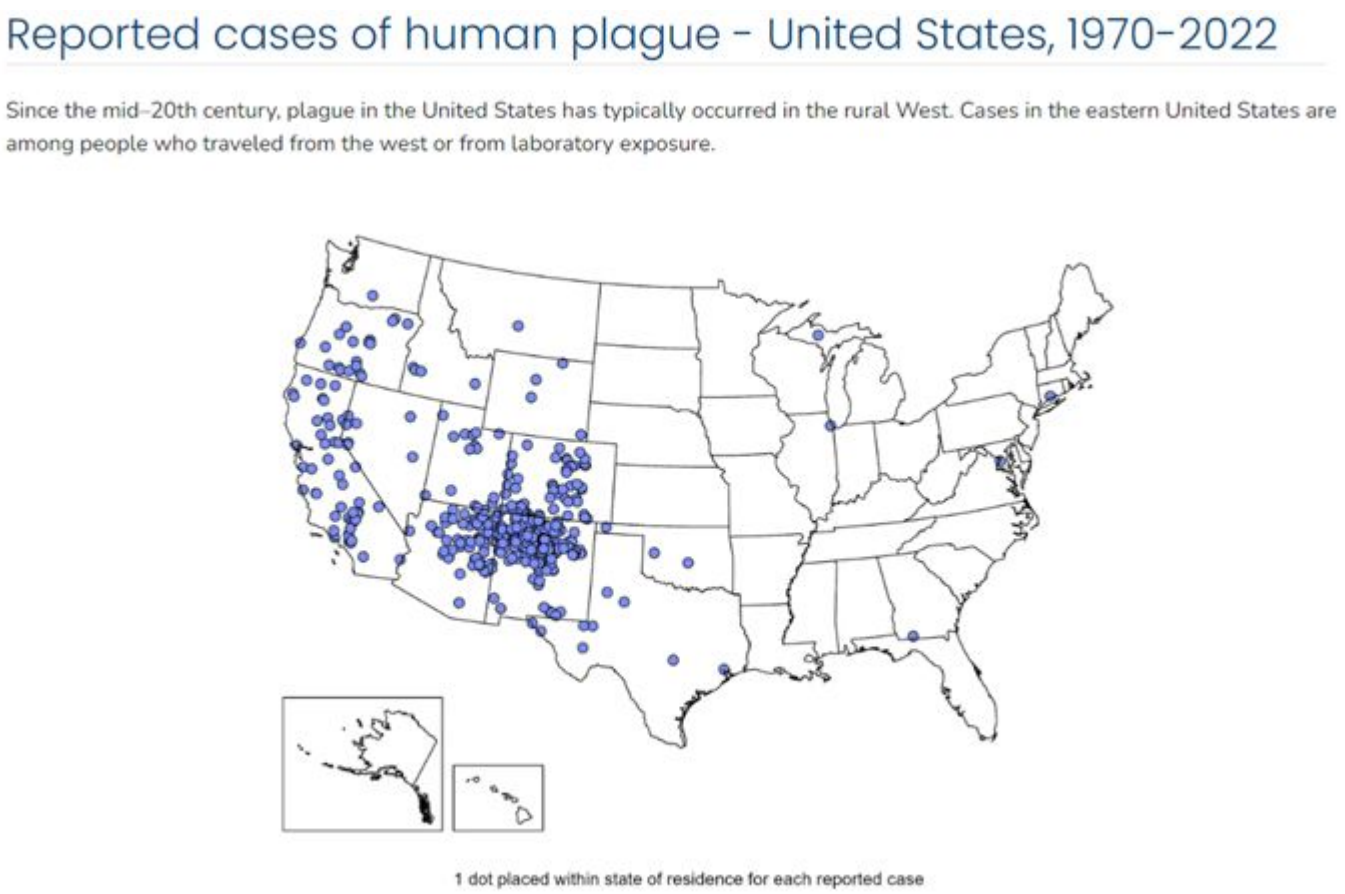
The “Third Pandemic”

- 1894 CE
- Originated in Asia
  - By 1900 CE, had reach ports on every continent
- Causative agent discovered during this time by Alexandre Yersin
- Followed soon by the discovery that the primary host was the brown rat, with the rat flea as the vector
- Waxed and waned until 1959
  - 15 million deaths total

Plague

- Currently there are about 2,000 plague cases that occur annually, mostly in Africa > Asia and S. America

- In North America
  - ~7 cases per year
  - Most cases occur in New Mexico, Arizona, Colorado, California, Oregon



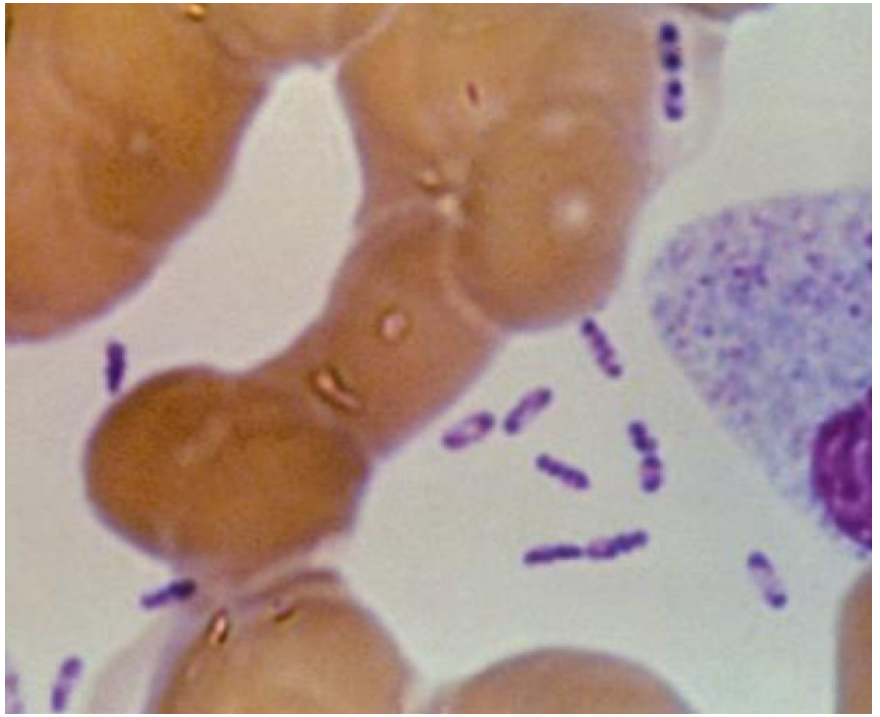
Epidemiology / Transmission

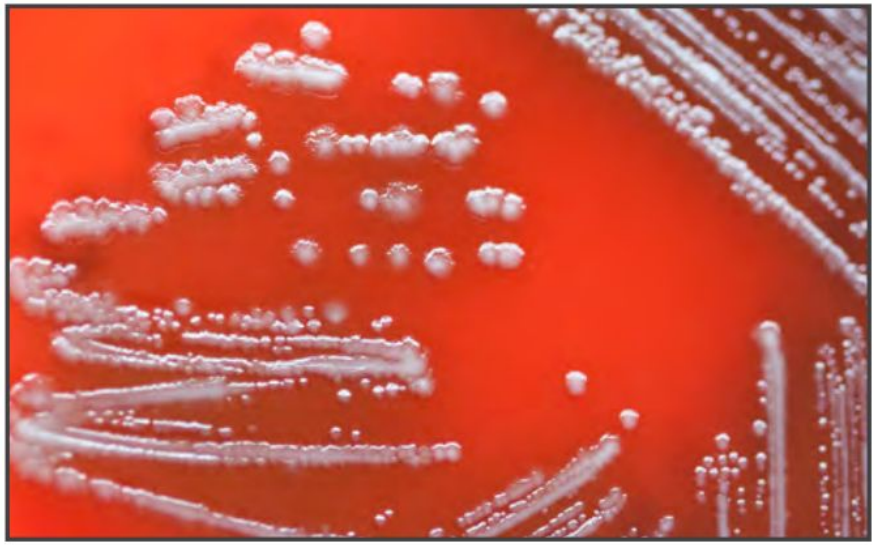
- 80% of plague cases in the US since 2000 were of the bubonic form
  - Septicemic: 10-20%
  - Pneumonic: rare
- Endemic in indigenous rodents and some wild animals in N. America
  - Humans and some domestic animals are incidental hosts
- Flea bite
- Scratches or bites from infected animals (rodents, rabbits, prairie dogs, cats)
- Less commonly from handling infected tissues, person-to-person (pneumonic form), and lab-acquired

Microbiology

- *Yersinia pestis*
  - *pestis* atra (pestilence / plague; terrible or dreadful)
  - atra mors (black; death)

- Plump GNR, in singles or pairs
  - Safety pin appearance (better seen on Giemsa or Wright stain)
- Facultative anaerobe
  - Best growth at 25-28 ºC
- Gray/white pinpoint colonies at 24h; 1-2mm after 48h (may have slight yellow hue)
  - Little to no hemolysis on BAP
  - NLF on MAC
- Catalase positive; oxidase / urease / indole negative
- Work up in Class II BSC using BSL-3 practices
  - Category A bioterrorism agent

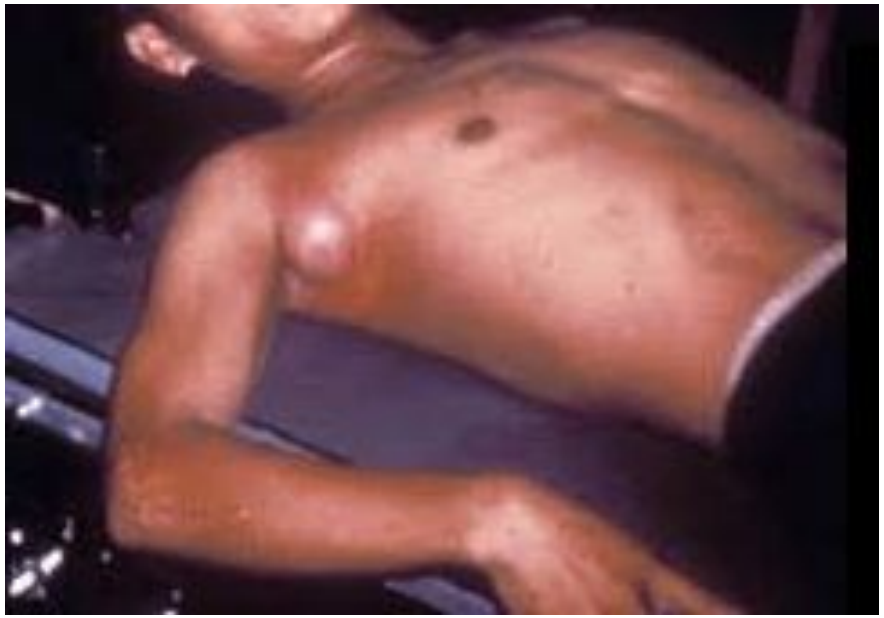




48h growth on BAP

Clinical

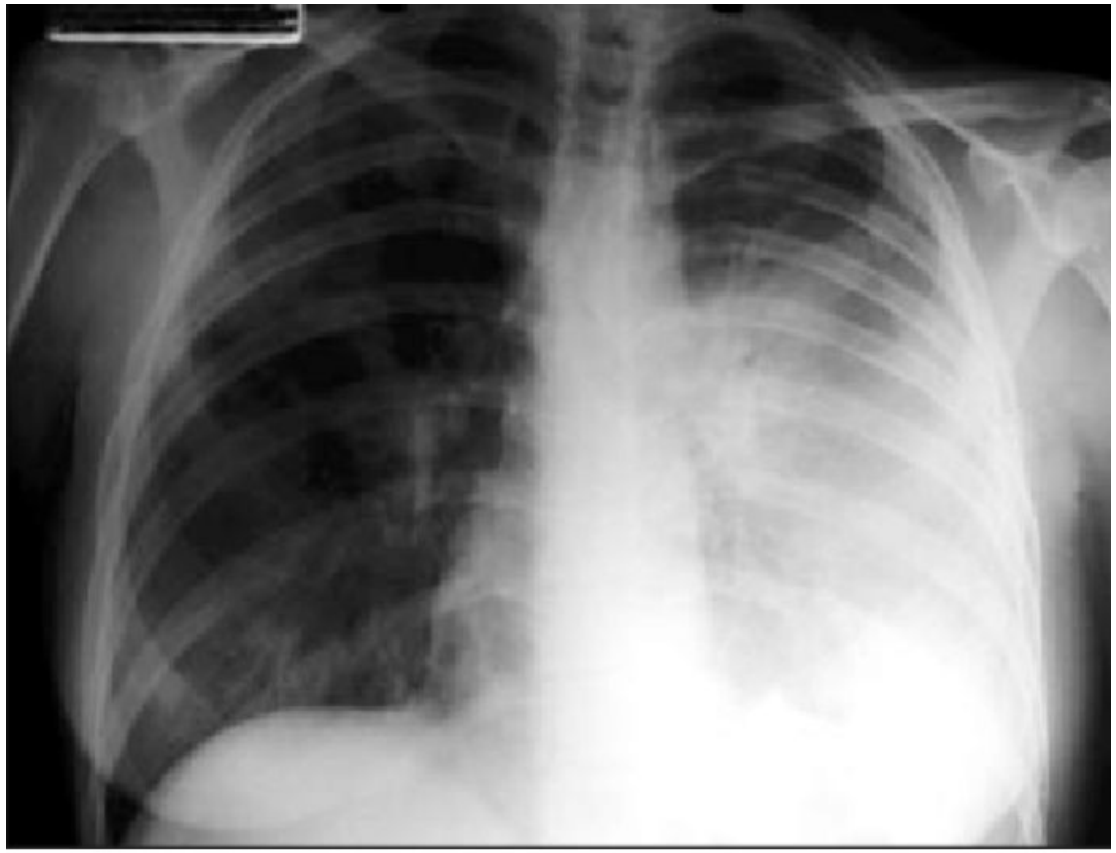
- Buboes → "Bubonic Plague"
  - Painful and purulent abscesses of lymph nodes
  - Fever, chills, headache, followed by the buboes
  - Can be complicated by bacteremia, pneumonia, and meningitis
  - Incubation period 2-8 days



- Septicemic
  - Occurs without preceding buboes
  - Fever, very ill, non-specific symptoms (nausea, diarrhea, abdominal pain)
  - Septic shock and multiorgan failure
  - Can also be complicated by meningitis
  - Incubation period poorly defined (likely days)

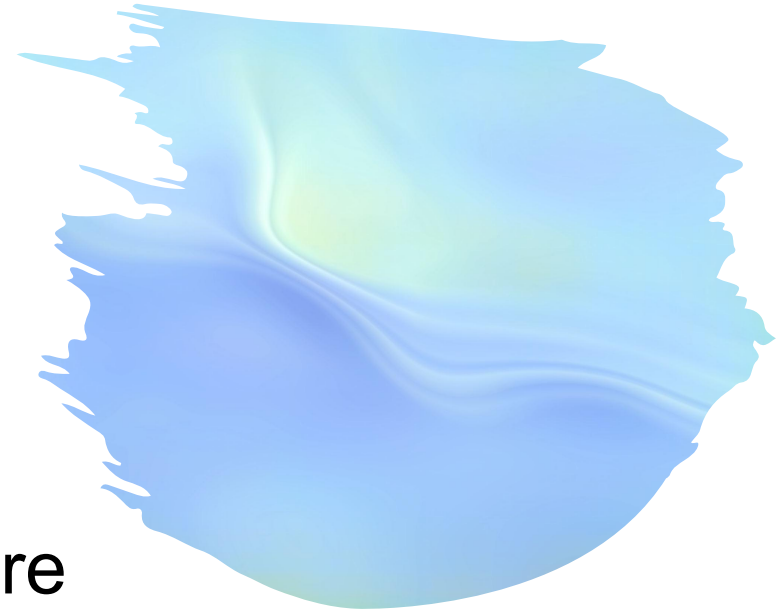
Clinical

- Pneumonic
  - Primary (inhalation of droplets)
  - Secondary (hematogenous spread from a bubo or other source)
  - Only form that can be spread person-to-person
  - Very short incubation period (a few hours to a few days)
  - Shortness of breath, high fever, pleuritic chest pain, cough, bloody sputum
  - Meningitis can occur
  - Fatal unless treatment starts ~first day of illness



Chest Radiograph of Patient With Primary Pneumonic Plague

Diagnosis



- Bubonic: tissue or aspirate for culture
- Septicemic: blood culture
- Pneumonic: bronchial wash / lavage for culture
- General lab work:
  - Leukocytosis up to 100,000 cells per microliter
  - Thrombocytopenia
- Symptom report, clinical exam, travel / exposure history
- Radiographic chest imaging is non-specific (similar to other bacterial pneumonias)

Diagnosis

- Serology
  - Requires acute and convalescent serum; fourfold rise in antibody titers
- PCR and WGS
  - Detection in (very old) human remains
- Rapid antigen F1 test
  - Sputum or serum
  - Not widely available

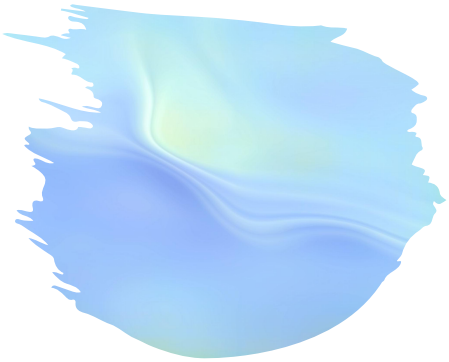
Treatment

- Prompt!
- Bubonic
  - Aminoglycoside, fluoroquinolone, or doxycycline
  - Fluctuant buboes warrant incision and drainage
- Septicemic or pneumonic
  - Aminoglycoside or fluoroquinolone
- In general, naturally-occurring disease needs single coverage
  - Bioterrorist attack, a combination is recommended until susceptibility testing is performed
- Duration is 10-14 days
- Untreated, mortality rate is 60-100%
- Treated, mortality rate is <15%

Prevention

- In endemic areas, avoid handling sick / dead animals
- Rodent and flea control
- Avoid close contact with those suspected to have pneumonic plague
- Droplet precautions in the hospital (gown, mask, eye protection, gloves)
  - Continued for at least 48h and there is evidence of clinical improvement
- In crisis settings, PrEP with antibiotics for first responders may be considered

Prevention



- PEP is suggested if unprotected face-to-face contact (~6’) with someone infected with pneumonic form (received <48h therapy)
  - Doxycycline, fluoroquinolones
  - Seven days

- Inactivated vaccine was developed
  - Not commercially available in the United States
  - Military used previously
  - Concern for BT event has led to new vaccine development, which is undergoing clinical testing

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Thank you!

ZOONOSES: PRESENT

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Oropouche

Introduction

- Orthobunyavirus (one of the most common)
- Arbovirus: has a sylvatic cycle (part of its cycle involves non-human animals and vectors) and urban cycle
- 3 RNA segments (most insect-borne viruses have one) negative sense, single stranded
  - Can lead to increased mutations- Helps virus evade immune system, cause disease, increase spread etc.
- 4 known genotypes
  - Infection with one, may generate antibodies for others

BBC Watch

Oropouche: The mysterious 'sloth virus' with no treatment

29 August 2024

Onur Erem, André Biernath and Richard Gray

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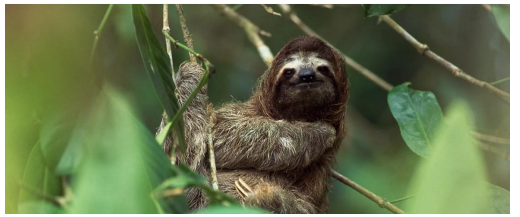


Healthcare & Pharmaceuticals | Public Health

Cuba faces uphill battle as Oropouche virus spreads

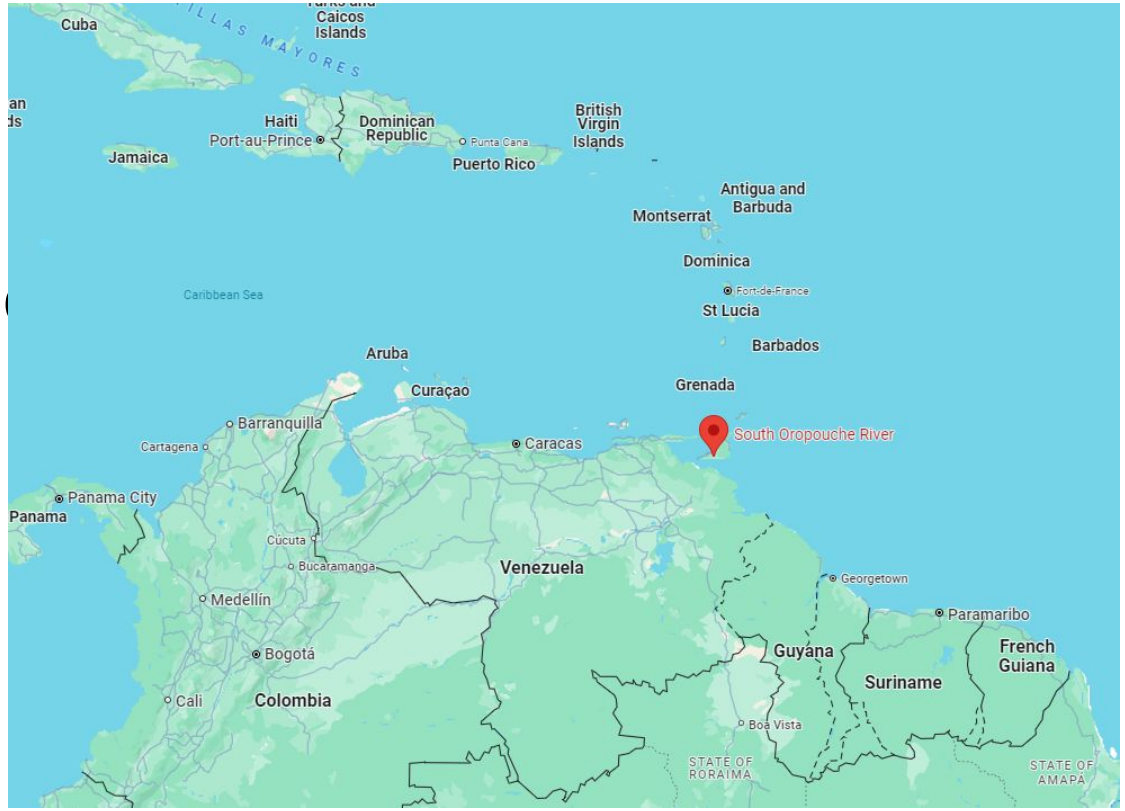
By **Reuters**

August 30, 2024 7:37 PM EDT · Updated 23 days ago

Aa

Epidemiology

- First detected in 1955 in Trinidad and Tobago near the Oropouche River.
  - 500,000 cases since its discovery
- Before 2000: Brazil, Panama and Peru an cases in animals (Colombia and Trinidad)
- Since 2000: Argentina, Bolivia, Brazil Colombia, Ecuador, French Guiana, Panama, Peru and Haiti
- In 2023 and 2024, large outbreaks in S. America and isolated cases in Cuba



Vectors and hosts

- Some mosquitoes (*Culex quinquefasciaticus, Coquillettidia venezuelensis,* and *Aedes serratus*)
- Mostly midges (*Culicoides paranesis)*
  - Worldwide distribution
  - Small (2.5mm)
  - Less affected by repellants
- Animal reservoirs: sloths, non-human primates and birds

Pictures: cdc.gov

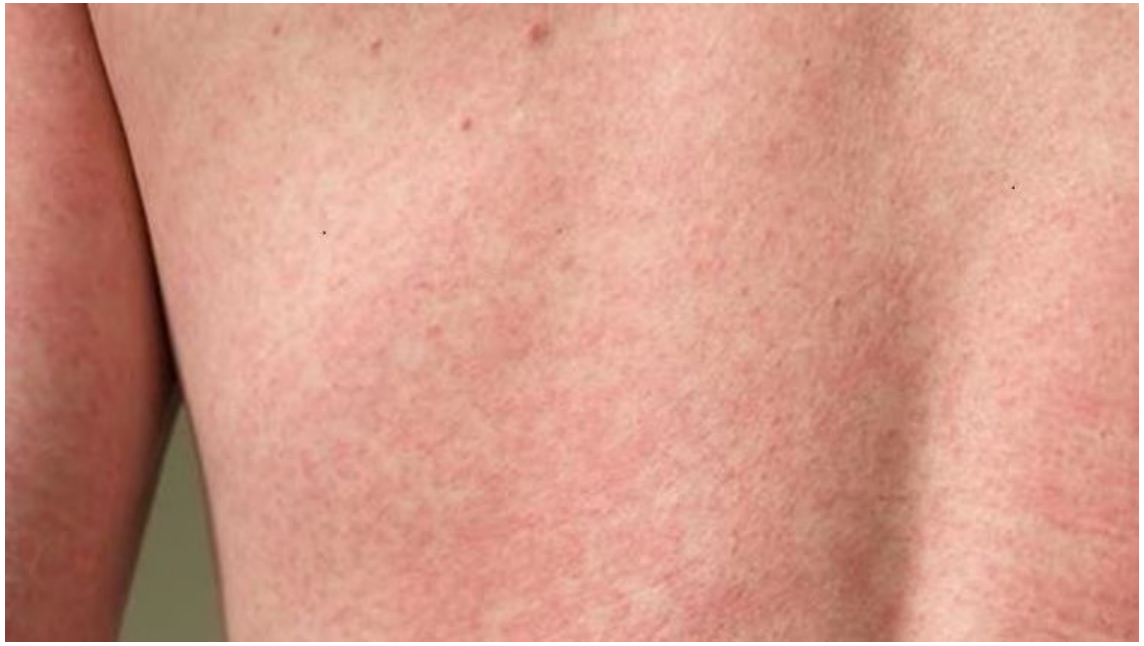
Clinical Features

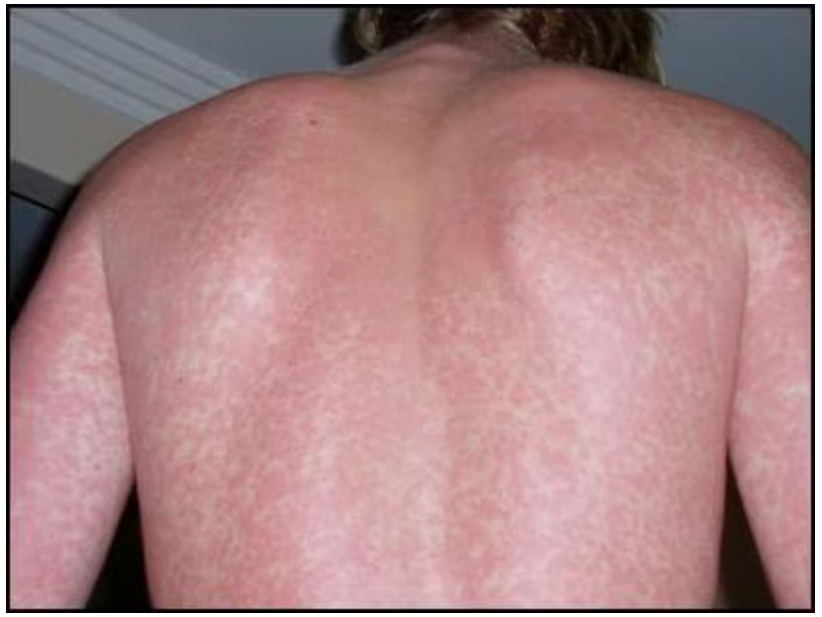
- Incubation period: 3-10 days

- Abrupt onset of:
  - Fever and chills
  - Severe headache
  - Myalgia and arthralgia

- Can include: retro-orbital eye pain, nausea and vomiting, and maculopapular rash that starts on the trunk and spreads to the extremities

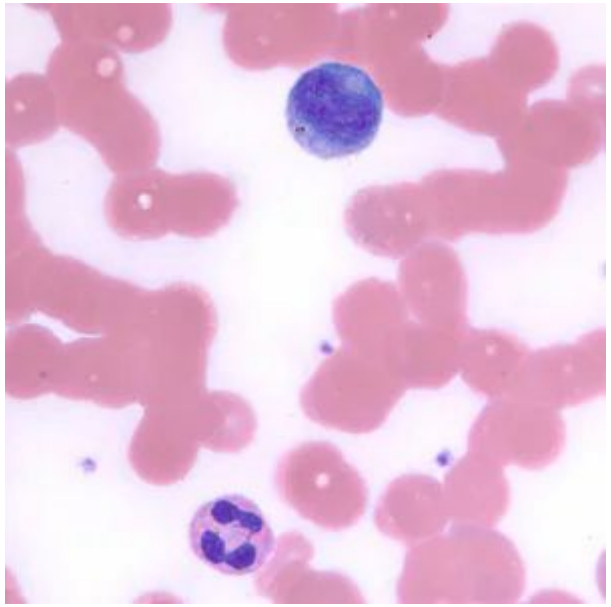
- similar to dengue, chikungunya, zika and even malaria.

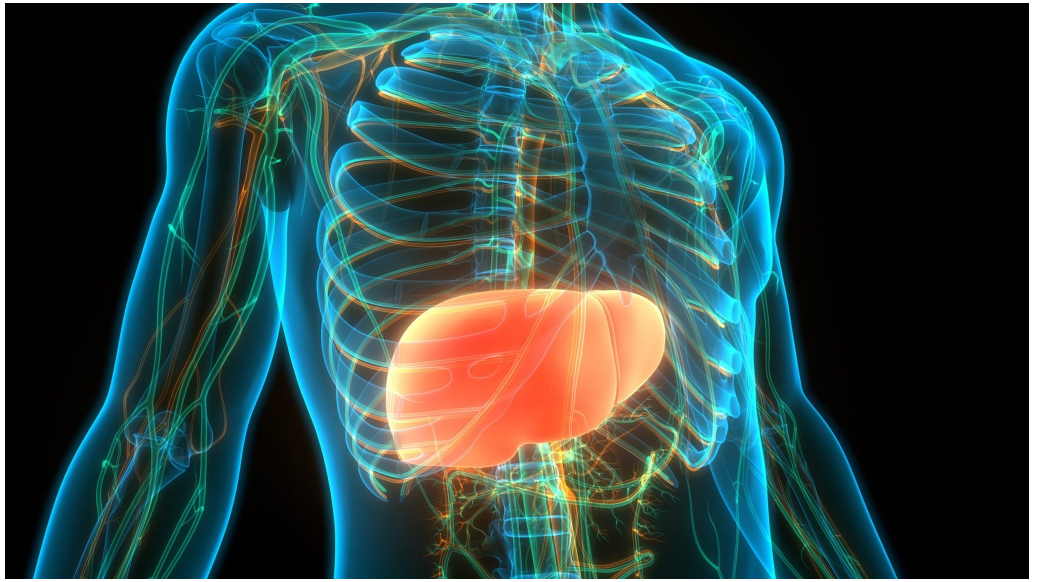




Abnormal Laboratory Values

- Lymphopenia and leukopenia (low white count)
- Elevated C-reactive protein (CRP)
  - Indicator of inflammation
- And elevated liver enzymes

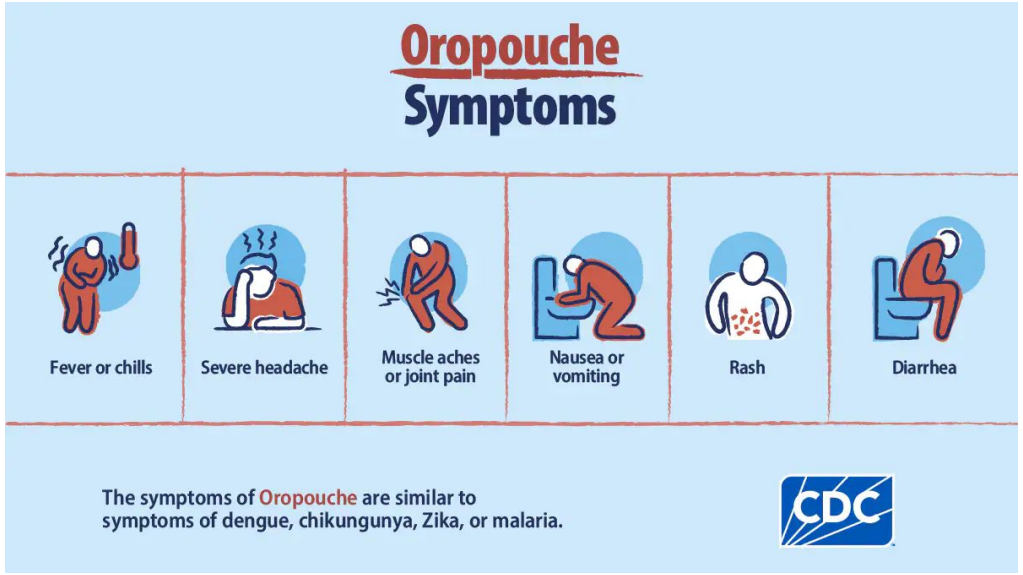




Pictures: cdc.gov

Progression and Prognosis

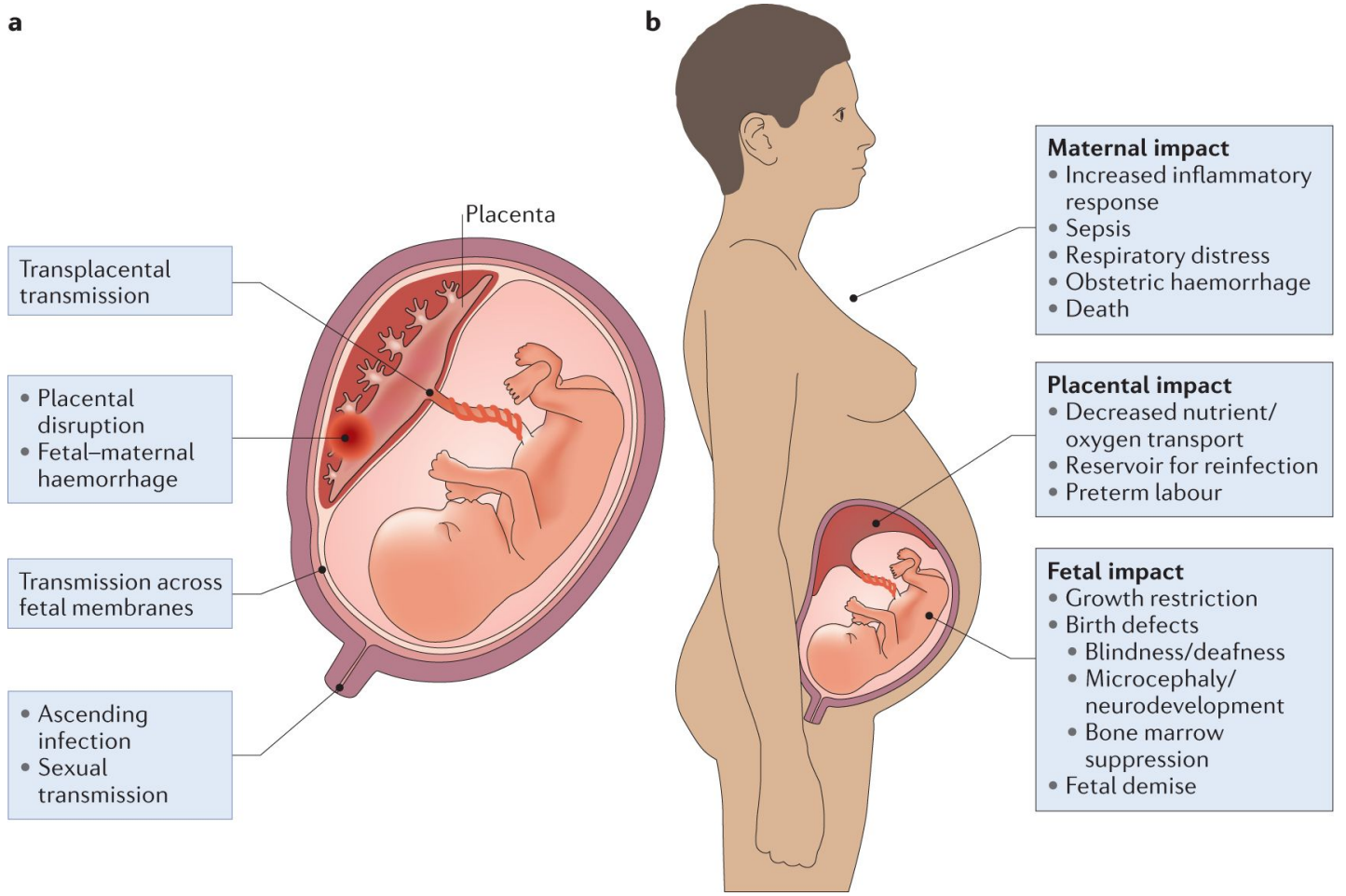
- Can cause neuro-invasive disease in up to 4% of patients
  - CSF= pleocytosis and elevated protein
- Symptom persistence for weeks, even months has been documented
  - Weakness and malaise
- Very few deaths



Vertical Transmission

- The Pan-American Health Organization published a report highlighting concerns of possible mother to child transmission

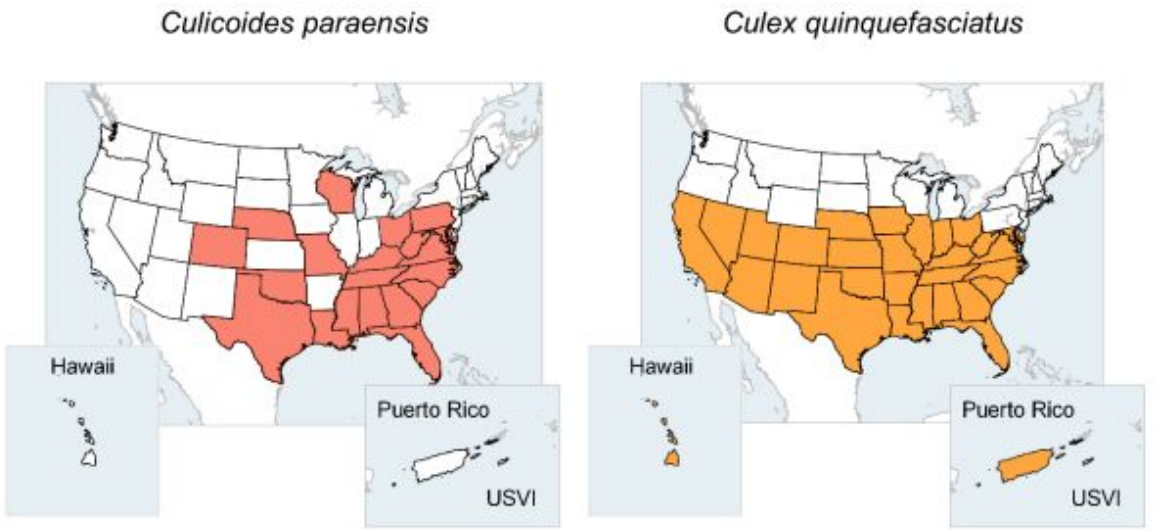
- Associated with adverse pregnancy outcomes
  - Congenital abnormalities
    - microcephaly, miscarriage
  - Fetal death



Infections at the maternal–fetal interface: an overview of pathogenesis and defence | Nature Reviews Microbiology

What if Oropouche is suspected?

- Contact state laboratory
  - They will assist in determining if samples need to be tested for Oropouche
- Then samples get sent to CDC Arbovirus Diagnostic Laboratory
  - Through the state health departments
- Results get sent from CDC back to the state health departments



Laboratory Diagnostics

- Evidence of the virus can be detected in serum during the first week of infection
  - Detection of viral RNA
- After that, IgM followed by IgG

- CDC performs real-time RT-PCR to detect viral RNA in serum and CSF during the acute phase
  - Can also perform plaque reduction neutralization tests
- Acute and convalescent samples needed (4-fold or greater change in antibody titers)

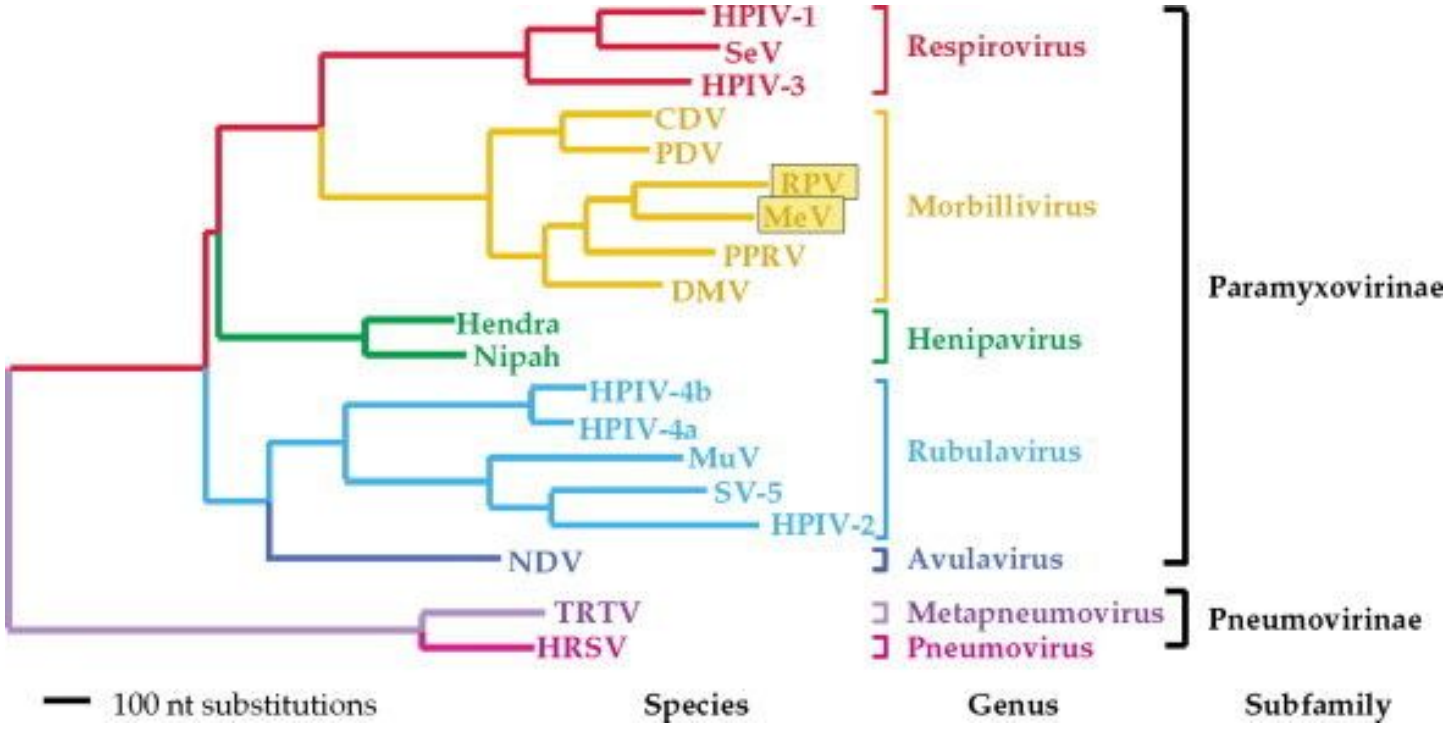
Treatment and Prevention

- No vaccine
- No approved medicine
  - Supportive care
  - Avoid aspirin and NSAIDs until Dengue is ruled out (bleeding).
- Prevention: protect from insect bites
  - Easier said than done. Midges are small and can pass through nets
  - Midges are less affected by common insect repellants
- Protection from aerosolization/ingestion:
  - Seven laboratory workers are known to have been accidentally infected; all developed symptoms.

NIPAH

Nipah Virus

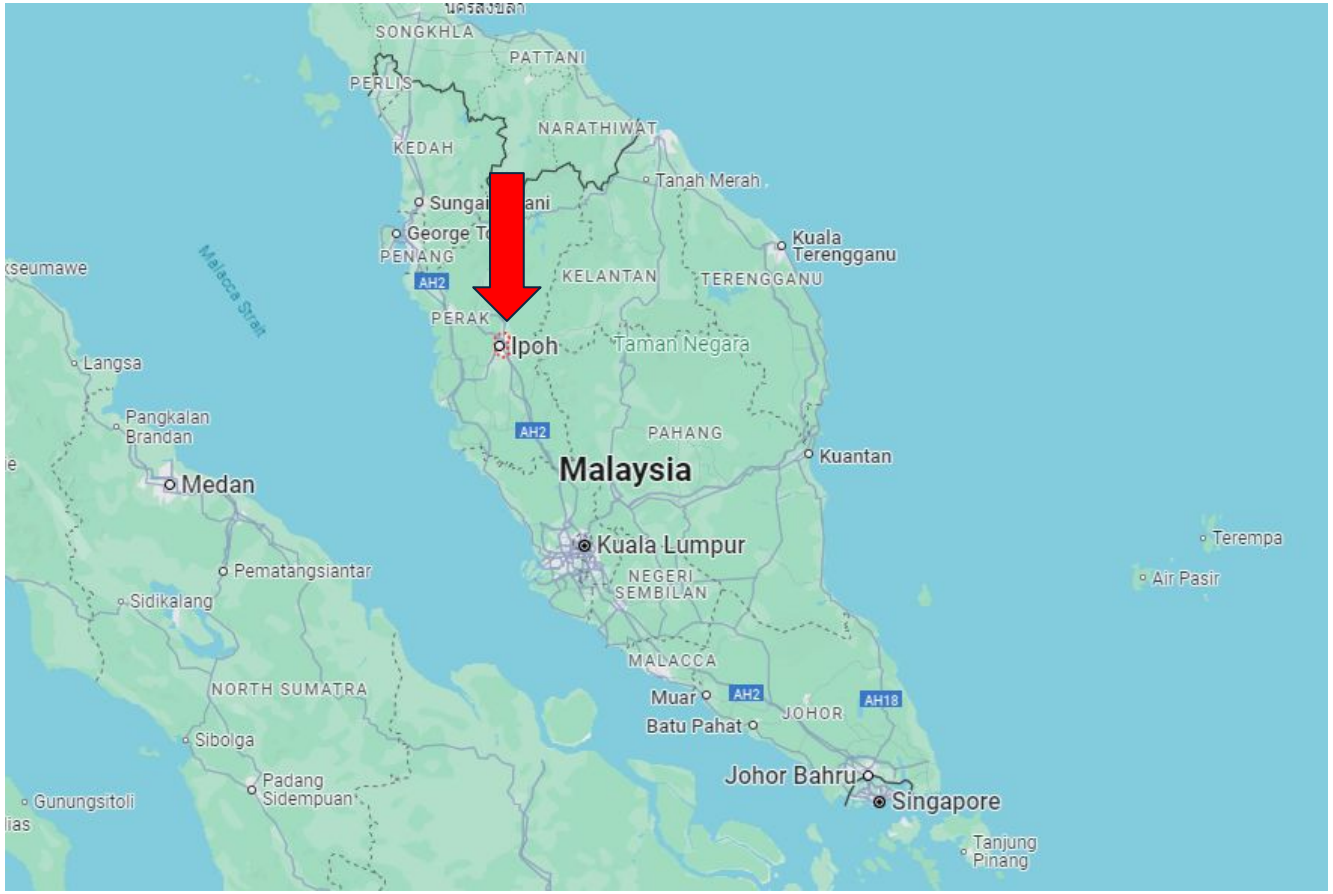
- *Paramyxoviridae* (family)
  - *Henipavirus nipahense*
  - Similar to the Hendra virus
  - Single stranded, negative sense, RNA
- The (−)RNA viruses are major causes of human morbidity and mortality



Minus-Strand RNA Viruses - PMC (nih.gov)

Emergence of Nipah

- First recognized in 1998
  - Closely related to Hendra Virus
  - First discovered in Ipoh, Malaysia
  - Outbreak among pig farmers in Malaysia
  - Close contact with sick pigs



Natural host

- Pteropodidae of the Pteropus genus (FRUIT BATS!)
  - Can carry the virus, but show no signs of disease.
- Other genera of fruit bats have found to be positive for antibodies to Nipah, indicating that these viruses may be present in other parts of the world (Africa)

Epidemiology

- Case fatality rate ~40-75%
- Broad species tropism
- Transmitted to humans from animals, or contaminated foods
  - Also human to human transmission
- Recent outbreaks in Bangladesh and India
  - Consumption of fruits or fruit products (raw date palm juice) contaminated with urine or saliva from infected fruit basts
  - Human-to-human transmission (hospital staff and family of those infected)

Epidemiology

- Annual outbreaks in Bangladesh since 2001
- Outbreaks have occurred in: Singapore, India
- 2 genetic lineages
  - NiV-BD (more pathogenic), NiV-MY

Yellow= fruit bats
Red= Nipah outbreaks

cdc.gov

Exposure risk

- People working with pigs
- Families, caregivers, and healthcare workers caring for patients with Nipah
- Exposure to or ingestion of food or drinks contaminated by infected animals (bat saliva and urine)
- Those who climb trees where fruit bats roost

Fao.org

Npr.org, courtesy of Dr. Emily Gurley from EcoHealth Alliance

Clinical Presentation

- Incubation 4-14 days
- From acute respiratory infection to fatal encephalitis
- Fever, headaches, myalgia, sore throat, vomiting
  - Can be followed by: dizziness, altered mental status, and neurological symptoms
  - And/or severe respiratory complications including acute respiratory distress

Laboratory Diagnosis

- PCR from bodily fluids
- Antibody detection from serum via ELISA
- Viral culture
  - Requires BSL-4 facilities
- Not widely available and affected by quality, quantity, type, transport time and timing of sample collection.

Treatment

- No vaccines
- No specific drugs for treatment
- WHO has identified Nipah as a "priority disease" for the WHO Research and Development Blueprint

https://www.who.int/publications/m/item/pathogens-prioritization-a-scientific-framework-for-epidemic-and-pandemic-research-preparedness

Family	2017 Priority Pathogens	2018 Priority Pathogens	2024 PHEIC risk	2024 Priority Pathogens	2024 Prototype Pathogens
Adenoviridae			Low-Medium		Recombinant Mastadenovirus
Adenoviridae			Low-Medium		Mastadenovirus blackbeardi serotype 14
Anelloviridae			Low		
Arenaviridae	Arenaviral hemorrhagic fevers including Lassa Fever	Lassa Fever virus	High	Mammarenavirus lassaense	Mammarenavirus lassaense
Arenaviridae			High		Mammarenavirus juninense
Arenaviridae			High		Mammarenavirus lujoense
Astroviridae			Low		Mamastrovirus virginiaense
Bacteria			High	Vibrio cholerae serogroup O139	
Bacteria			High	Yersinia Pestis	
Bacteria			High	Shigella dysenteriae serotype 1	
Bacteria			High	Salmonella enterica non typhoidal serovars	
Bacteria			High	Klebsiella pneumoniae	
Bornaviridae			Low		Orthobornavirus bornaense
Coronaviridae	Middle East Respiratory Syndrome Coronavirus	Middle East Respiratory Syndrome Coronavirus	High	Subgenus Merbecovirus	Subgenus Merbecovirus
Coronaviridae	Other highly pathogenic coronaviral diseases such as Severe Acute Respiratory Syndrome	Severe Acute Respiratory Syndrome	High	Subgenus Sarbecovirus	Subgenus Sarbecovirus
Filoviridae	Filoviral diseases Ebola	Ebola virus disease	High	Orthoebolavirus zairense	Orthoebolavirus zairense
Filoviridae	Filoviral diseases Marburg	Marburg virus disease	High	Orthomarburgvirus marburgense	
Filoviridae			High	Orthoebolavirus sudanense	
Flaviviridae	Zika virus	Zika virus	High	Orthoflavivirus zikaense	Orthoflavivirus zikaense
Flaviviridae			High	Orthoflavivirus denguei	Orthoflavivirus denguei
Flaviviridae			High	Orthoflavivirus flavi	
Flaviviridae			High		Orthoflavivirus encephalitidis
Flaviviridae			High		Orthoflavivirus nilense
Hantaviridae			High	Orthohantavirus sinnombreense	Orthohantavirus sinnombreense
Hantaviridae			High	Orthohantavirus hantanense	
Hepadnaviridae			Low		Orthohepadnavirus hominoidei genotype C

Family	2017 Priority Pathogens	2018 Priority Pathogens	2024 PHEIC risk	2024 Priority Pathogens	2024 Prototype Pathogens
Hepeviridae			Low		Paslahepevirus balayani genotype 3
Herpesviridae			Low		
Nairoviridae	Crimean Congo Haemorrhagic Fever	Crimean Congo Haemorrhagic Fever	High	Orthonairovirus haemorrhagiae	Orthonairovirus haemorrhagiae
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H1	Alphainfluenzavirus influenzae H1
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H2	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H3	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H5	Alphainfluenzavirus influenzae H5
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H6	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H7	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H10	
Papillomaviridae			Low		
Paramyxoviridae	Nipah and related henipaviral diseases	Nipah and henipaviral diseases	High	Henipavirus nipahense	Henipavirus nipahense
Parvoviridae			Low		Protoparvovirus carnivoran
Peribunyaviridae			Low		Orthobunyavirus oropoucheense
Phenuiviridae	Severe Fever with Thrombocytopenia Syndrome		High	Bandavirus dabieense	Bandavirus dabieense
Phenuiviridae	Rift Valley Fever	Rift Valley Fever	High		Phlebovirus riftense
Picobirnaviridae			Low		Orthopicobirnavirus hominis
Picornaviridae			Medium	Enterovirus coxsackiepol	
Picornaviridae			Medium		Enterovirus alphacoxsackie 71
Picornaviridae			Medium		Enterovirus deconjucti 68
Pneumoviridae			Low-Medium		Metapneumovirus hominis
Polyomaviridae			Low		
Poxviridae			High	Orthopoxvirus variola	
Poxviridae			High		Orthopoxvirus vaccinia
Poxviridae			High	Orthopoxvirus monkeypox	Orthopoxvirus monkeypox
Retroviridae			Medium	Lentivirus humimdef1	Lentivirus humimdef1
Rhabdoviridae			Low		Genus Vesiculovirus
Sedoreoviridae			Low		Genus Rotavirus
Spinareoviridae			Low		Orthoreovirus mammalis
Togaviridae			High	Alphavirus chikungunya	Alphavirus chikungunya
Togaviridae			High	Alphavirus venezuelan	Alphavirus venezuelan
Pathogen X	Pathogen X	Pathogen X		Pathogen X	

[4] https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts

A WHO tool distinguishes which diseases pose the greatest public health risk due to their epidemic potential and/or whether there is no or insufficient countermeasures.

At present, the priority diseases are:

- COVID-19
- Crimean-Congo haemorrhagic fever
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipaviral diseases
- Rift Valley fever
- Zika

Possible agent of bioterrorism?

Nipah has many characteristics which make it a potential agent

- highly virulent
- high mortality
- spreads easily

“Poses a severe threat to both human and animal health, to plant health, or to animal and plant products”

Overlap Select Agents and Toxins

37. *Bacillus anthracis* [1]
38. *Bacillus anthracis* Pasteur strain
39. *Brucella abortus*
40. *Brucella melitensis*
41. *Brucella suis*
42. *Burkholderia mallei* [1]
43. *Burkholderia pseudomallei* [1]
44. Hendra virus
45. Nipah virus
46. Rift Valley fever virus
47. Venezuelan equine encephalitis virus [4][5][8]

selectagents.gov

Reasons for re-emergence

- Human, ecological and viral factors
  - Climate change
  - Population growth and urbanization
  - human and animal mobility and behavior
  - deforestation
  - land use
  - habitat fragmentation (especially of reservoir animals)
  - Genetic evolution of viruses (considered a minor factor)

cdc.gov

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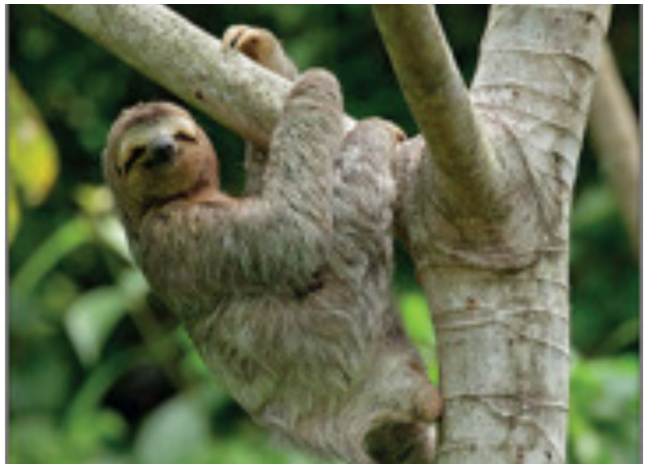
Thank you!

Questions?



ZOONOSES: PAST AND PRESENT

PART 1

Sara W. F. Geffert, MD, MS, D(ABMM), M(ASCP)
Lifespan Academic Medical Center
The Warren Alpert Medical School of Brown University

Objectives

01

Detail multiple zoonotic infections from the distant past through the present time

02

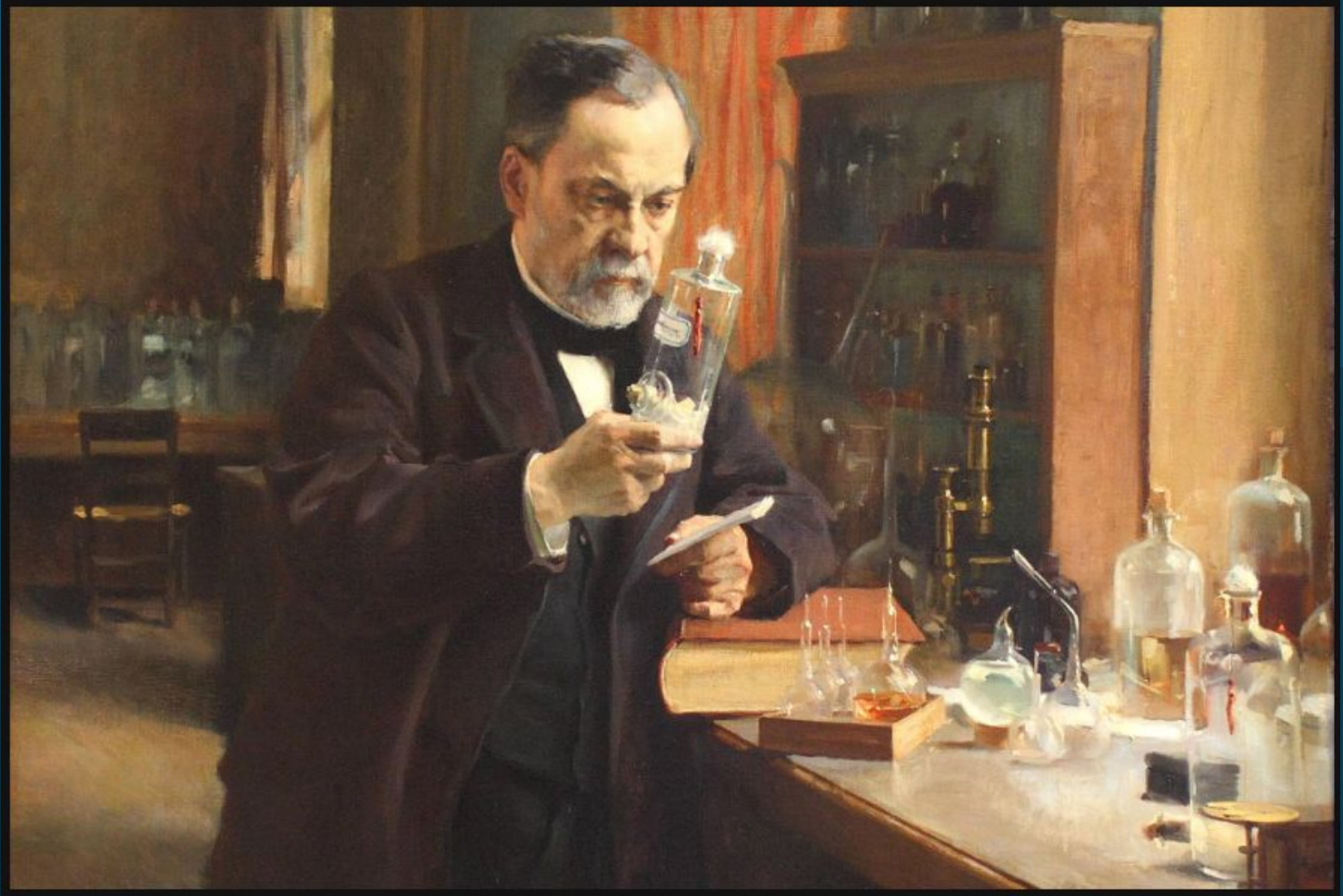
Discuss both viral and bacterial pathogens with variable acuity and geographic reach

03

Appreciate the historical aspects of the outbreaks

History of Rabies (*Lyssavirus*)

- Lyssa in Greek means, “frenzy or madness”
  - Lyssa was the goddess of rage
- Virus in Latin means, “poisonous secretion”
- Homer (8th century BCE)
  - Thought to have referred to rabies in the Iliad, when he mentioned Sirius (brightest star in Canis Major) and its malignant influence (heat causing aggression); also used the term, “raging dog”
- Aristotle (4th century BCE)
  - “Dogs suffer from the madness. This causes them to become irritable and all animals they bite to become diseased.”
- Hippocrates (4th century BCE)
  - Thought to have referred to rabies: “persons in a frenzy drink very little, are disturbed, and frightened…”
- Ancient Romans believed that clipping the tail of the dog that bit you may help stave off illness

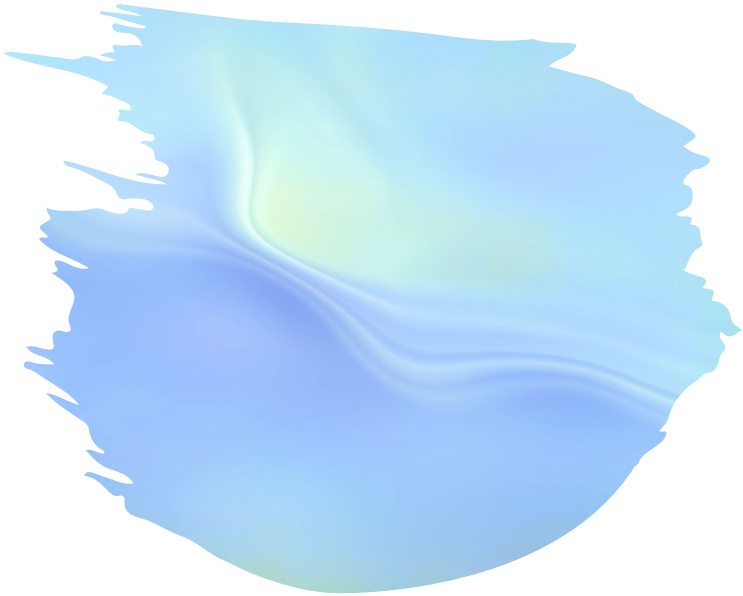


Dr. Louis Pasteur
Dr. Louis Pasteur, who gives the first rabies vaccine, in his lab.

1885

Dr. Louis Pasteur injects a series of a new rabies vaccine into a boy who had been bitten by a rabid dog. The boy survives. This is the first vaccine to protect against rabies in people. Before the rabies vaccine, nearly all people infected with rabies died.

Rabies



- Family: *Rhabdoviridae*
- Genus: *Lyssavirus*
  - 17 species
    - *rabies* species is the most commonly known, upon which vaccination is based (for humans and animals), with good cross protection against many of the other species (but these infections are rare in animals and do not occur in humans)
    - Only *rabies* species is endemic to the Americas
- Disease: Fatal encephalomyelitis

Rabies

- Virions are bullet-shaped, enveloped, ssRNA (negative-sense), non-segmented

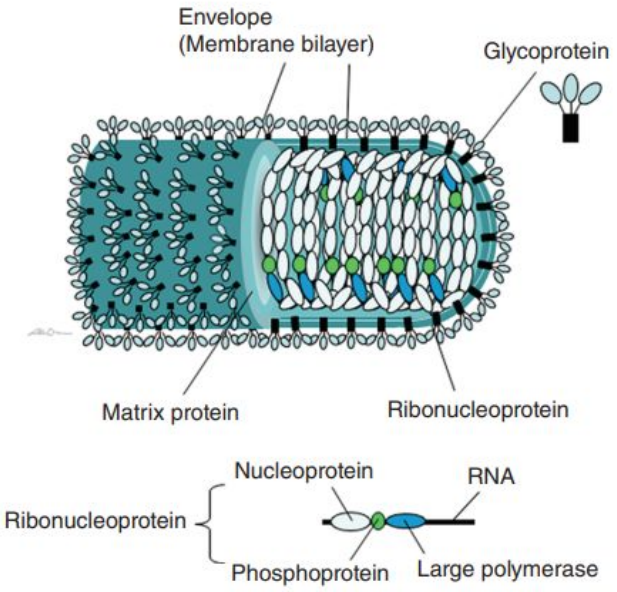


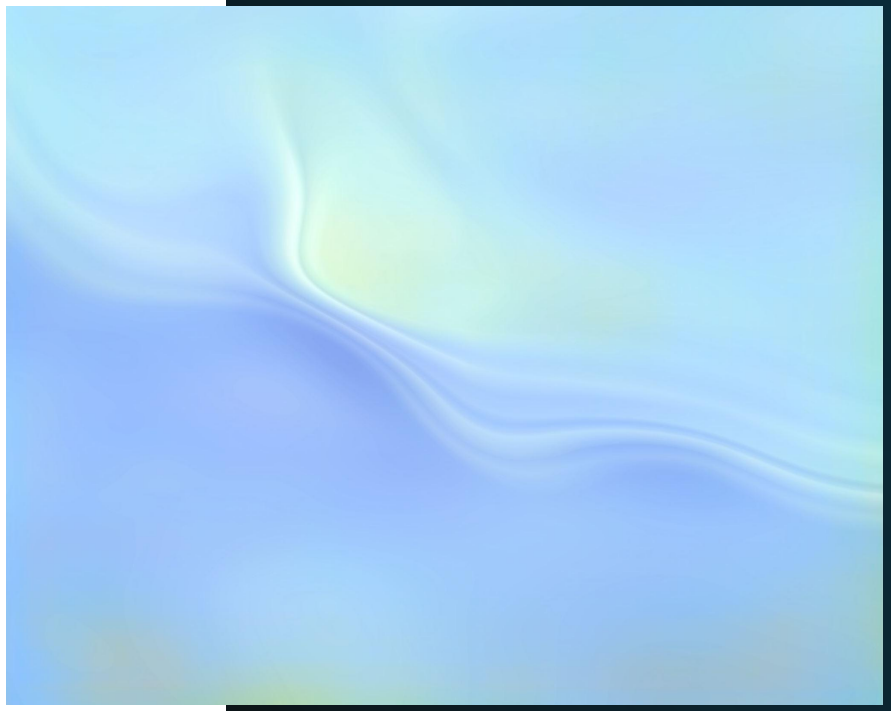
FIGURE 2 Diagram of lyssavirus morphology and structural proteins.

Rabies virus, purified from an infected cell culture. Negatively stained virions: note their characteristic "bullet shape." Magnification approximately x70,000.

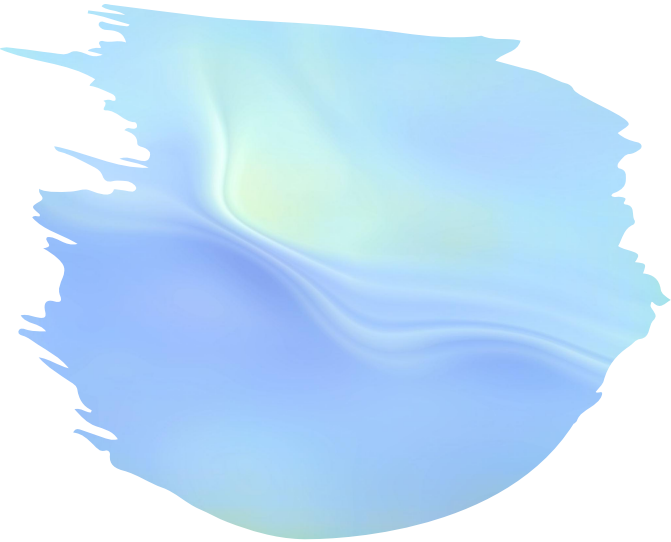
Micrograph from F. A. Murphy, University of Texas Medical Branch, Galveston, Texas.

Epidemiology

- >6000 animal cases are diagnosed each year in the United States
  - Racoons, skunks, foxes, mongooses, bats
- Human cases in the US are rare (<4 cases per year)
  - Worldwide estimates are up to ~70,000 cases
    - >90% of which are caused by dogs
    - Lack of access to PEP and public health resources
- Every year, ~60,000 Americans receive PEP following an exposure



Transmission



- All mammals are susceptible
- Infected saliva (bite)
- Nonbite exposures are rare (scratches, open wounds, mucous membranes, transplanted corneas / organs)
  - No known transmission of rabies from autopsies
- Not via fomites (virus susceptible to sunlight, drying, standard disinfectants like bleach and 70% ethanol)
- Cleansing of wound (essential), PEP (life-saving)
- The virus travels slowly along nerves to the brain
  - The closer the bite is to your CNS, the shorter the incubation period

Clinical

- Incubation period: several weeks to months (average timing is 45 days)
- Initially, non-specific symptoms (prodrome)
- Then, acute neurological phase ➡ coma, death
  - Encephalitic / furious form (~80%)
    - Hyperexcitability, confusion, hallucinations, agitation / aggression
      - Can have lucid moments
    - Dysphagia, hypersalivation, lacrimation, diaphoresis, hydrophobia (painful throat spasms), aerophobia (painful diaphragmatic spasms)
  - Paralytic form (~20%)
    - Ascending muscle flaccidity, cranial nerves (including deafness), laryngeal weakness, urinary incontinence, cardiopulmonary compromise
- One of the highest case fatality rates by an infectious pathogen (>99%)
  - 29 known cases of survival; most had some form of PEP

Diagnosis (antemortem)

- All four samples below must be collected for definitive rule out:
  - Saliva
    - 4+ samples; reverse transcription (RT) PCR
  - Skin biopsy
    - 5-6mm (diameter) section from nuchal region, containing hair follicles (at a depth to include cutaneous nerves that lie at the base of the follicles); RT-PCR and immunofluorescent staining for viral antigens in frozen sections
  - Serum
    - Fluorescent antibody (Ab) test and virus neutralization test
    - The presence of Abs can be diagnostic of infection if patient was not vaccinated
  - CSF
    - Fluorescent Ab test and virus neutralization test
    - The presence of Abs in the CSF (even if patient was vaccinated) suggests infection

Treatment

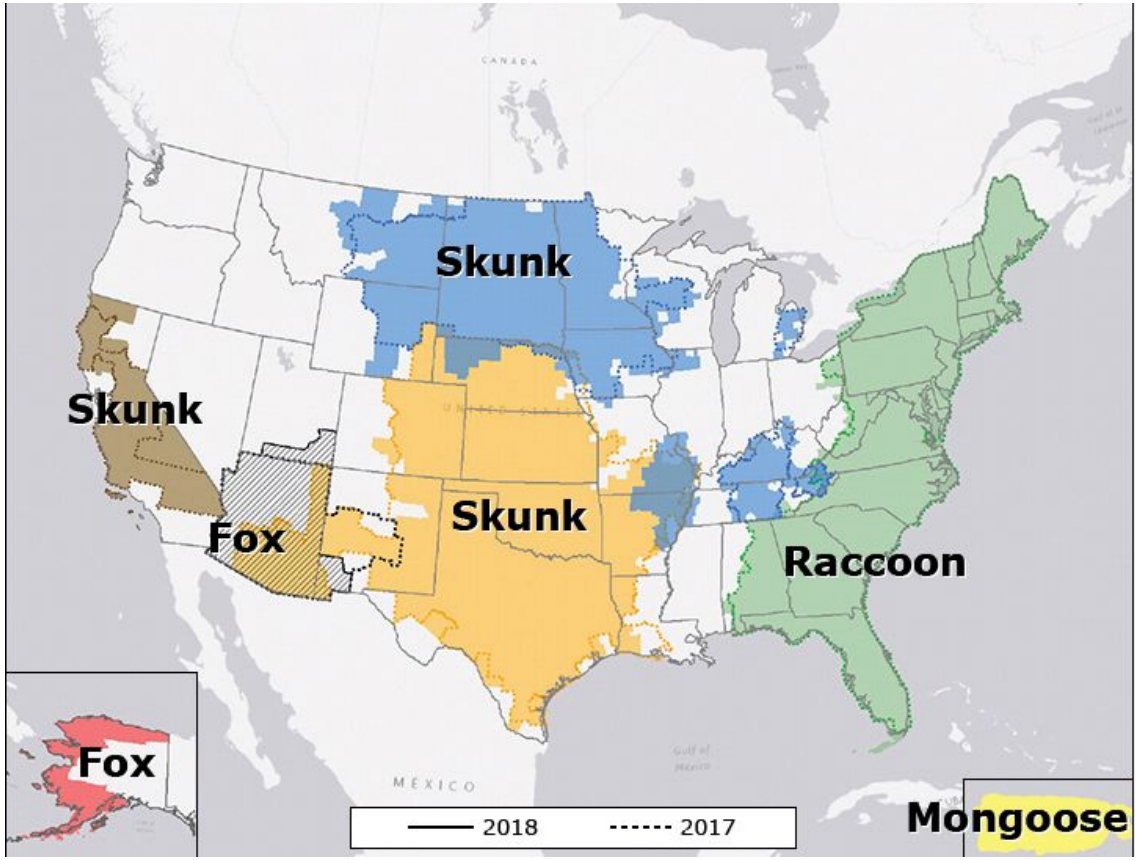
- After symptoms appear, no proven medicinal interventions
- Supportive (sedation, intubation, intracranial pressure monitoring)
- Vaccination and human rabies immune globulin (HRIG) does not impact survival rate and in fact may hasten death

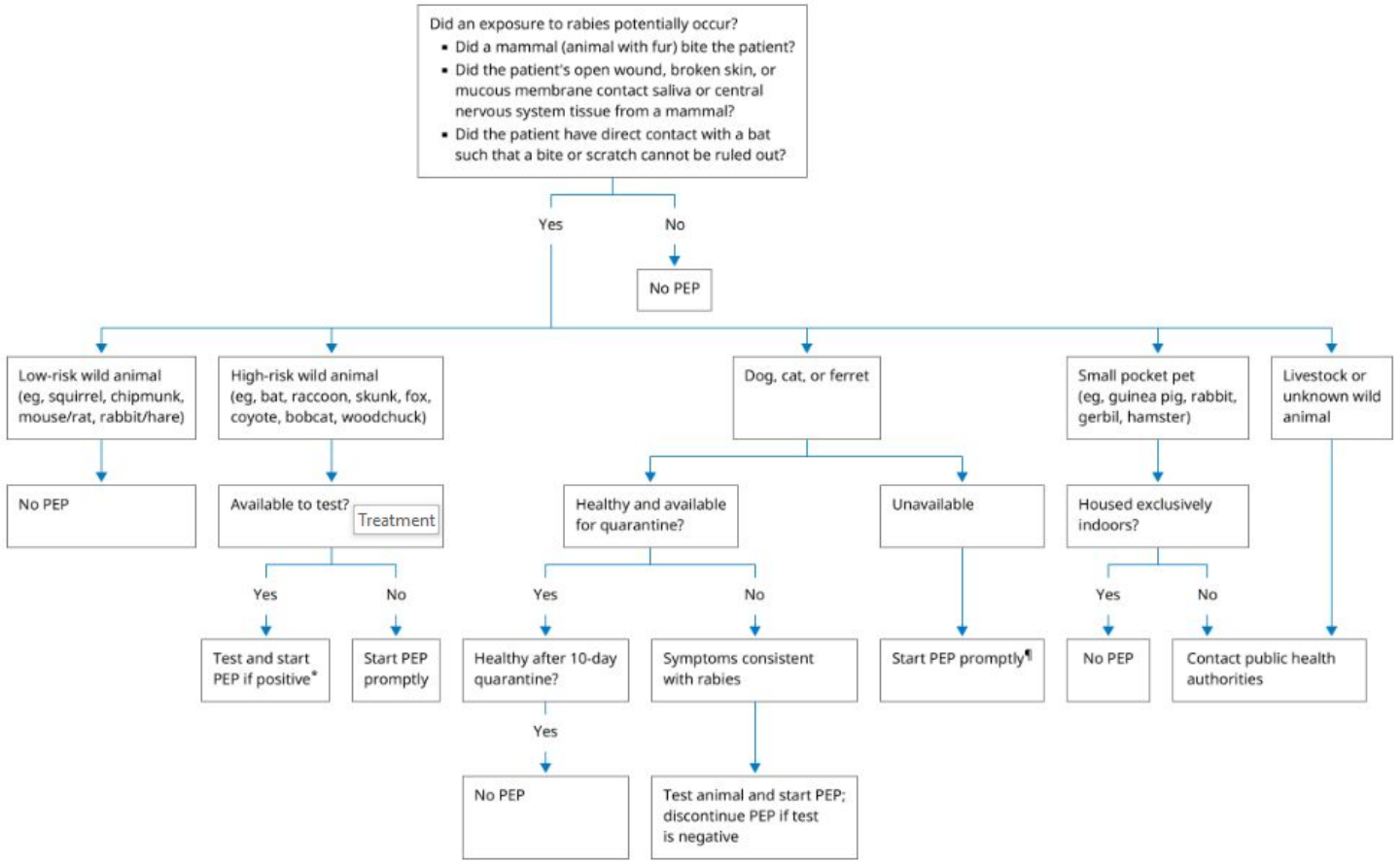
Treatment (experimental)

- Milwaukee Protocol:
  - Aggressive sedation
  - Steroids
  - Maintain hypernatremia (145-155 mEq/L; cerebral edema)
  - Insulin drip (to maintain euglycemia)
  - Maintain body temp to 35-37 ºC
  - Amantadine (neuroprotective in rabies; PD drug = antidyskinetic)
  - Vitamin C (vasospasms)
  - No ribavirin (immunosuppressive; antiviral)

PEP Indications

- Consider:
  - The epidemiology of animal rabies in the region
  - Species of animal in question
    - Behavior (unprovoked attack)
    - Absence of appropriate vaccination
    - Bite wound(s) on animal
    - Observation / quarantine of animal
  - Exposure / contact type





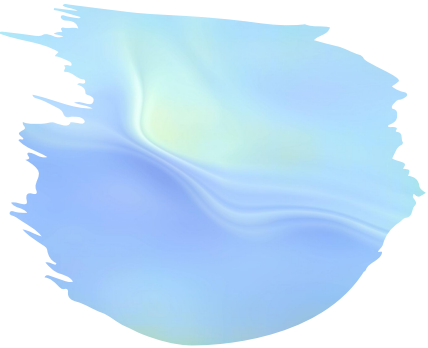
PEP: postexposure prophylaxis.

* PEP should be initiated immediately in patients with severe bites to the head, neck, or trunk after an unprovoked attack from a high-risk animal. PEP can be discontinued if testing proves the animal was not rabid.

¶ In areas without an endemic, terrestrial strain of rabies (eg, dog, raccoon, skunk, fox, mongoose), contact local public health authorities for risk assessment.

Courtesy of Alfred DeMaria Jr, MD and the Massachusetts Department of Public Health.

Fun (?) facts

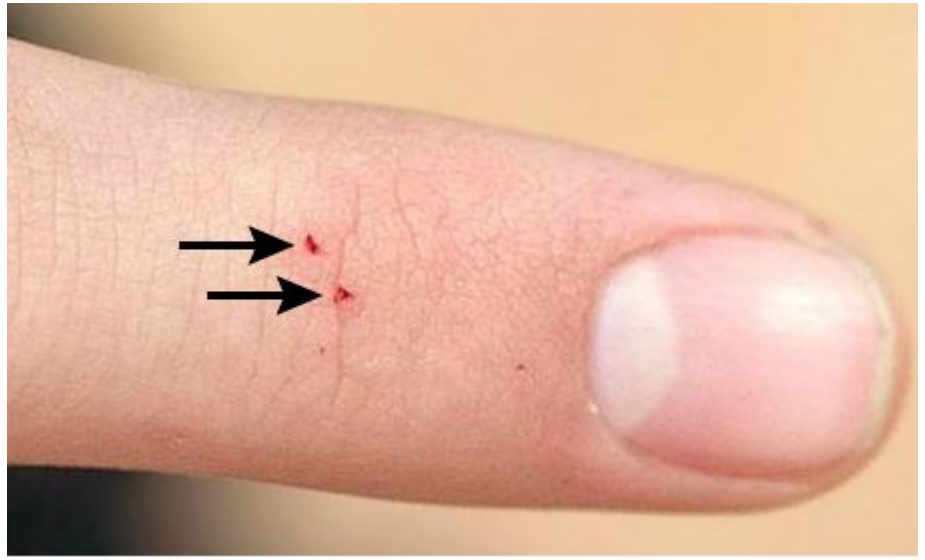


- Human-to-human transmission of rabies can theoretically result from bite and nonbite exposures, but reports are very rare, poorly documented, and occur in places where it is difficult to rule out potential animal exposures

- No transmission of rabies has been documented from rabies-infected patients to health care providers or to household contacts in the United States

- However, human-to-human transmission arising from transplantation (corneas, organs) is well documented

Bats



- No rabies in Hawaii
- Between 1990 and 2018:
  - 51/56 human cases were from bats
- If bat can be tested, can delay PEP for several days
  - >90% submitted bats are negative
- If bat cannot be tested, or if bat is positive ➡ PEP
- PEP is also needed:
  - For patients with bites, scratches, or mucous membrane exposure
  - If the above contact mechanisms cannot be ruled out (sleeping, intoxication, child, person with a disability)
- PEP is not needed if the person was aware of the bat at all times and can definitively state there was no contact

TABLE 3. Rabies postexposure prophylaxis (PEP) schedule — United States, 2010

Vaccination status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area†), 1 each on days 0,§ 3, 7 and 14.¶
Previously vaccinated**	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area†), 1 each on days 0§ and 3.

* These regimens are applicable for persons in all age groups, including children.
† The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.
§ Day 0 is the day dose 1 of vaccine is administered.
¶ For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.
** Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

Prevention

- When traveling, avoid unfamiliar animals (dogs, cats)
- Higher risk with some outdoor activities:
  - Camping, spelunking, hunting
- Veterinary medicine professionals, animal control workers, laboratory workers (working with live rabies virus)
  - Vaccination
- Vaccinate pets
- Cleansing any wounds from animals and seeking medical care

History of Plague

- *Yersinia pestis* DNA detected in remains of humans (4500-2000 BCE)
- Roman Empire
  - “Justinian Plague” 541-546 CE
  - Emperor was infected but lived
  - Buboes and high death toll were described
  - Mass burials outside of city walls

“The Pestilence”

- 1347-1352 CE
- Originated in Asia, spread to Russia, Europe
- Described in a book by Italian author Boccaccio in 1348:
  - “…it first betrayed itself by the emergence of certain tumours in the groin or armpits... After which the form of the malady began to change, black spots or livid making their appearance.”
- The term, “Black Death,” was not used until the 18th century
  - Septicemia → limb ischemia → gangrene
- In revenge for losing a siege, the Tartar armies of Khan Janibeg catapulted corpses over the city walls, further spreading disease
- Bodies into pits, or decayed at home / on streets
  - “The sexton and the physician were cast into the same deep and wide grave…”
- At least 25 million people died in both Europe and Asia
- Death within 4 days
- “Quarantena” (patient isolation for 40 days; Italian) = derivation of the word, quarantine

History of Plague

- Used by physicians treating patients in the early 17th century (Italy and France)
- Hood with crystal eye pieces
- Beak filled with herbs and compounds:
  - Cinnamon, pepper, turpentine, roast copper, powdered viper flesh; all thought to ward off poison air “miasma” (Greek)
- Robe, boots, gloves
- “Ring Around the Rosie”

American children playing "Ring Around the Rosie" in an illustration by Jessie Willcox Smith from The Little Mother Goose (1912)

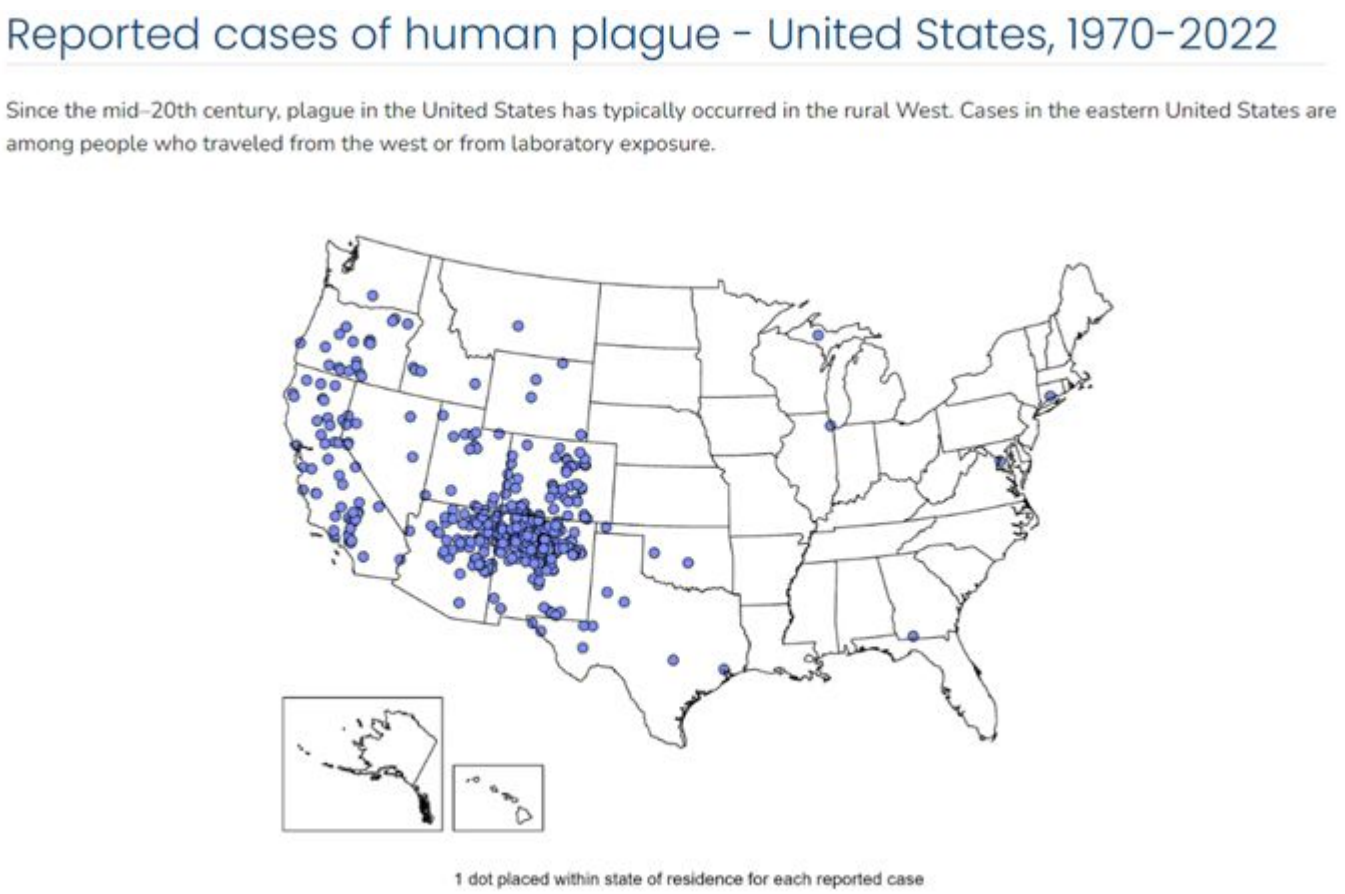
The “Third Pandemic”

- 1894 CE
- Originated in Asia
  - By 1900 CE, had reach ports on every continent
- Causative agent discovered during this time by Alexandre Yersin
- Followed soon by the discovery that the primary host was the brown rat, with the rat flea as the vector
- Waxed and waned until 1959
  - 15 million deaths total

Plague

- Currently there are about 2,000 plague cases that occur annually, mostly in Africa > Asia and S. America

- In North America
  - ~7 cases per year
  - Most cases occur in New Mexico, Arizona, Colorado, California, Oregon



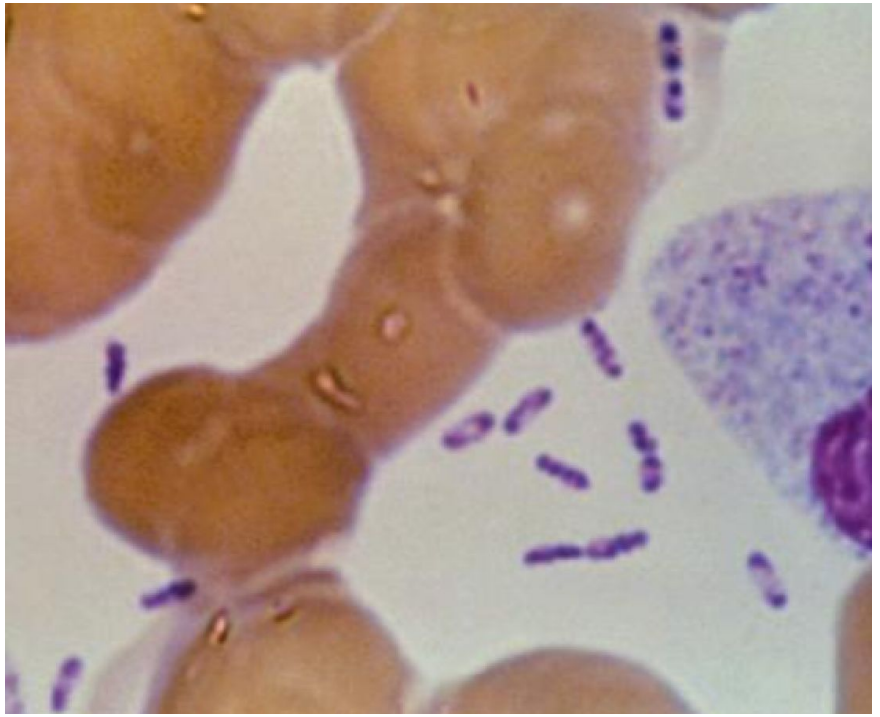
Epidemiology / Transmission

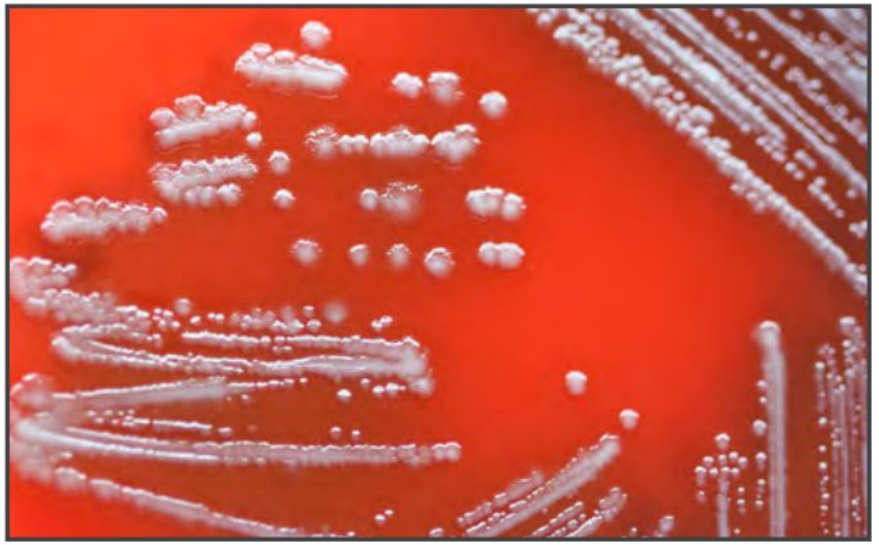
- 80% of plague cases in the US since 2000 were of the bubonic form
  - Septicemic: 10-20%
  - Pneumonic: rare
- Endemic in indigenous rodents and some wild animals in N. America
  - Humans and some domestic animals are incidental hosts
- Flea bite
- Scratches or bites from infected animals (rodents, rabbits, prairie dogs, cats)
- Less commonly from handling infected tissues, person-to-person (pneumonic form), and lab-acquired

Microbiology

- *Yersinia pestis*
  - *pestis* atra (pestilence / plague; terrible or dreadful)
  - atra mors (black; death)

- Plump GNR, in singles or pairs
  - Safety pin appearance (better seen on Giemsa or Wright stain)
- Facultative anaerobe
  - Best growth at 25-28 ºC
- Gray/white pinpoint colonies at 24h; 1-2mm after 48h (may have slight yellow hue)
  - Little to no hemolysis on BAP
  - NLF on MAC
- Catalase positive; oxidase / urease / indole negative
- Work up in Class II BSC using BSL-3 practices
  - Category A bioterrorism agent

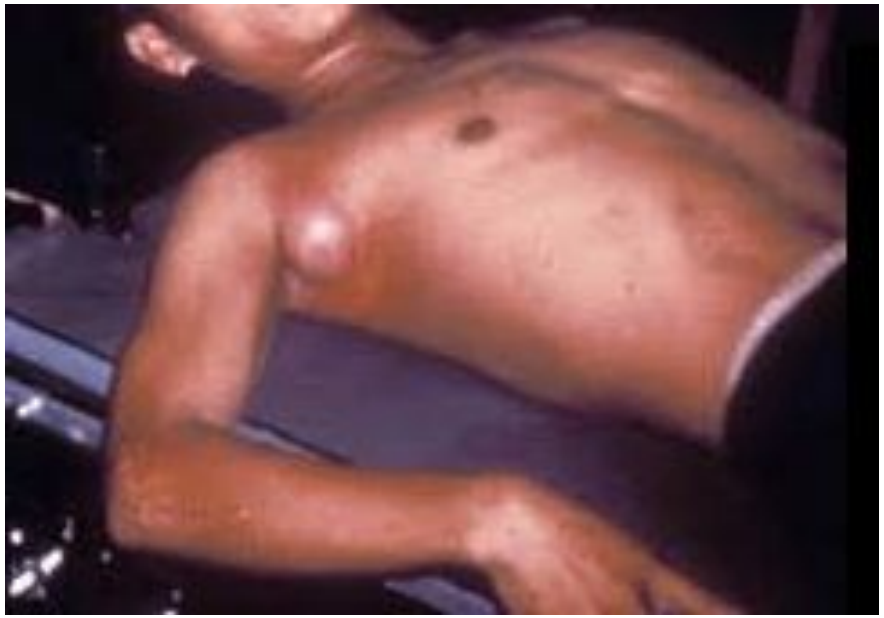




48h growth on BAP

Clinical

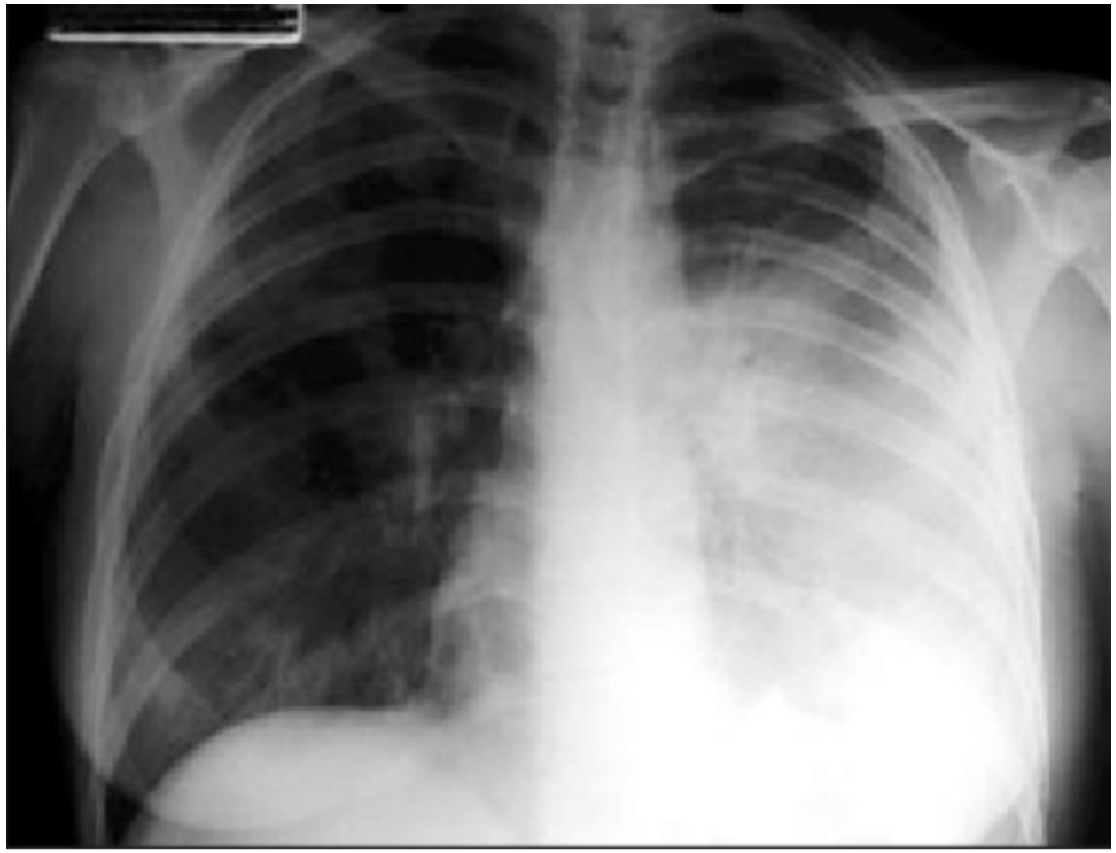
- Buboes → "Bubonic Plague"
  - Painful and purulent abscesses of lymph nodes
  - Fever, chills, headache, followed by the buboes
  - Can be complicated by bacteremia, pneumonia, and meningitis
  - Incubation period 2-8 days



- Septicemic
  - Occurs without preceding buboes
  - Fever, very ill, non-specific symptoms (nausea, diarrhea, abdominal pain)
  - Septic shock and multiorgan failure
  - Can also be complicated by meningitis
  - Incubation period poorly defined (likely days)

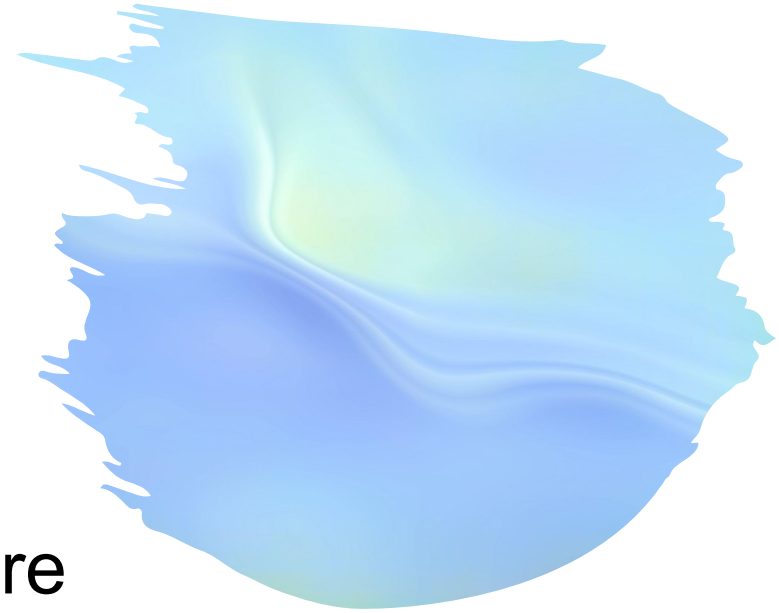
Clinical

- Pneumonic
  - Primary (inhalation of droplets)
  - Secondary (hematogenous spread from a bubo or other source)
  - Only form that can be spread person-to-person
  - Very short incubation period (a few hours to a few days)
  - Shortness of breath, high fever, pleuritic chest pain, cough, bloody sputum
  - Meningitis can occur
  - Fatal unless treatment starts ~first day of illness



Chest Radiograph of Patient With Primary Pneumonic Plague

Diagnosis



- Bubonic: tissue or aspirate for culture
- Septicemic: blood culture
- Pneumonic: bronchial wash / lavage for culture
- General lab work:
  - Leukocytosis up to 100,000 cells per microliter
  - Thrombocytopenia
- Symptom report, clinical exam, travel / exposure history
- Radiographic chest imaging is non-specific (similar to other bacterial pneumonias)

Diagnosis

- Serology
  - Requires acute and convalescent serum; fourfold rise in antibody titers
- PCR and WGS
  - Detection in (very old) human remains
- Rapid antigen F1 test
  - Sputum or serum
  - Not widely available

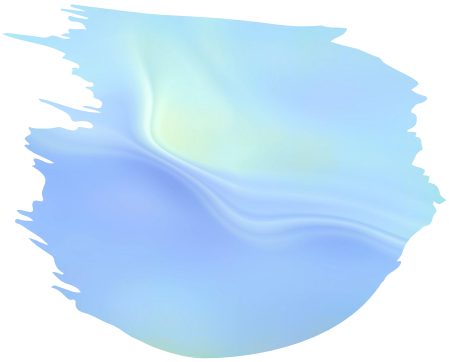
Treatment

- Prompt!
- Bubonic
  - Aminoglycoside, fluoroquinolone, or doxycycline
  - Fluctuant buboes warrant incision and drainage
- Septicemic or pneumonic
  - Aminoglycoside or fluoroquinolone
- In general, naturally-occurring disease needs single coverage
  - Bioterrorist attack, a combination is recommended until susceptibility testing is performed
- Duration is 10-14 days
- Untreated, mortality rate is 60-100%
- Treated, mortality rate is <15%

Prevention

- In endemic areas, avoid handling sick / dead animals
- Rodent and flea control
- Avoid close contact with those suspected to have pneumonic plague
- Droplet precautions in the hospital (gown, mask, eye protection, gloves)
  - Continued for at least 48h and there is evidence of clinical improvement
- In crisis settings, PrEP with antibiotics for first responders may be considered

Prevention



- PEP is suggested if unprotected face-to-face contact (~6’) with someone infected with pneumonic form (received <48h therapy)
  - Doxycycline, fluoroquinolones
  - Seven days

- Inactivated vaccine was developed
  - Not commercially available in the United States
  - Military used previously
  - Concern for BT event has led to new vaccine development, which is undergoing clinical testing

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Thank you!

ZOONOSES: PRESENT

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Oropouche

Introduction

- Orthobunyavirus (one of the most common)
- Arbovirus: has a sylvatic cycle (part of its cycle involves non-human animals and vectors) and urban cycle
- 3 RNA segments (most insect-borne viruses have one) negative sense, single stranded
  - Can lead to increased mutations- Helps virus evade immune system, cause disease, increase spread etc.
- 4 known genotypes
  - Infection with one, may generate antibodies for others

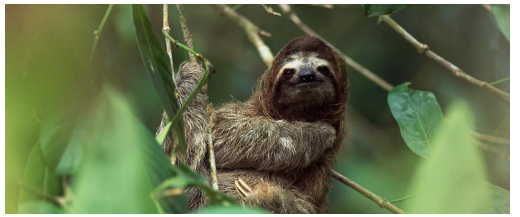
BBC Watch

Oropouche: The mysterious 'sloth virus' with no treatment

29 August 2024

Onur Erem, André Biernath and Richard Gray

Share Save +



Healthcare & Pharmaceuticals | Public Health

Cuba faces uphill battle as Oropouche virus spreads

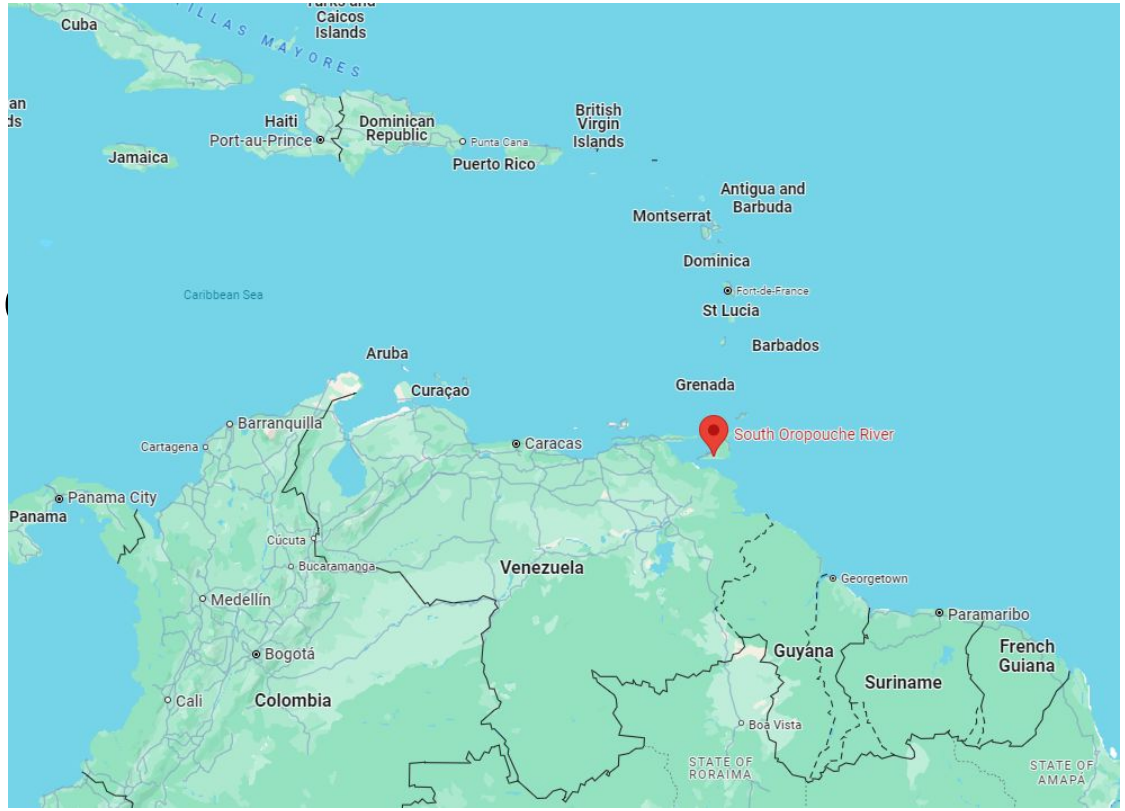
By **Reuters**

August 30, 2024 7:37 PM EDT · Updated 23 days ago

Aa

Epidemiology

- First detected in 1955 in Trinidad and Tobago near the Oropouche River.
  - 500,000 cases since its discovery
- Before 2000: Brazil, Panama and Peru an cases in animals (Colombia and Trinidad)
- Since 2000: Argentina, Bolivia, Brazil Colombia, Ecuador, French Guiana, Panama, Peru and Haiti
- In 2023 and 2024, large outbreaks in S. America and isolated cases in Cuba



Vectors and hosts

- Some mosquitoes (*Culex quinquefasciaticus, Coquillettidia venezuelensis,* and *Aedes serratus*)
- Mostly midges (*Culicoides paranesis)*
  - Worldwide distribution
  - Small (2.5mm)
  - Less affected by repellants
- Animal reservoirs: sloths, non-human primates and birds

Pictures: cdc.gov

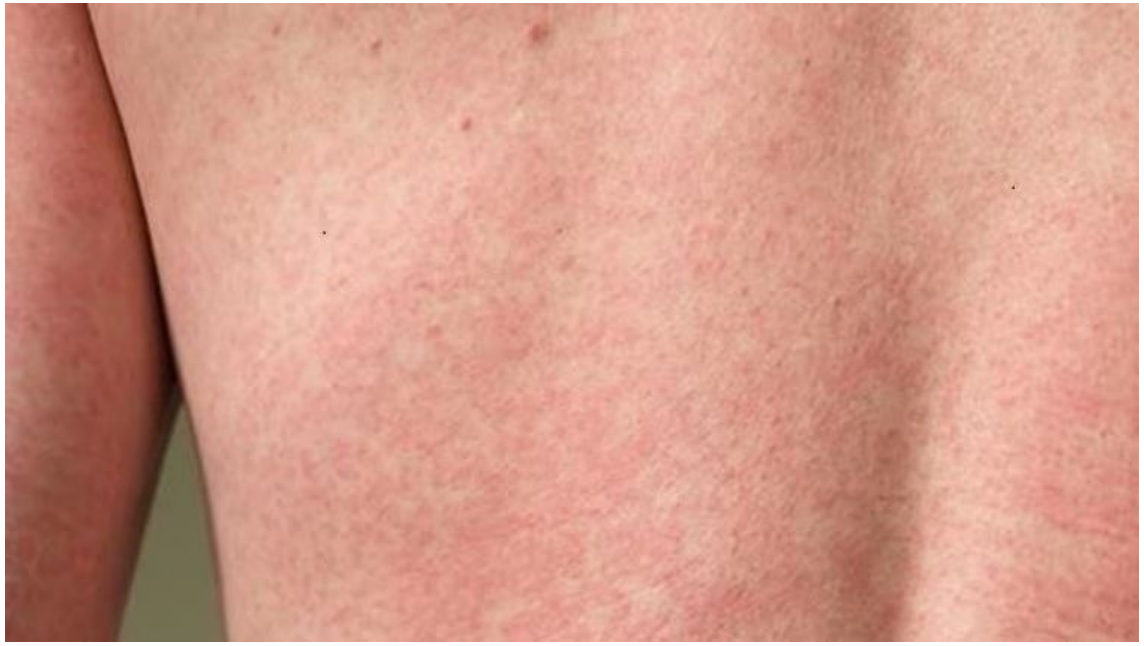
Clinical Features

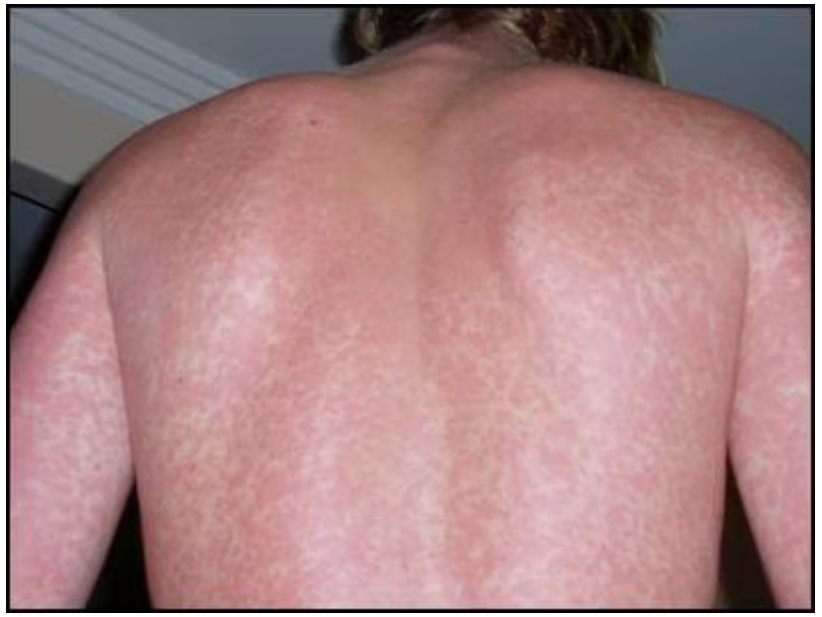
- Incubation period: 3-10 days

- Abrupt onset of:
  - Fever and chills
  - Severe headache
  - Myalgia and arthralgia

- Can include: retro-orbital eye pain, nausea and vomiting, and maculopapular rash that starts on the trunk and spreads to the extremities

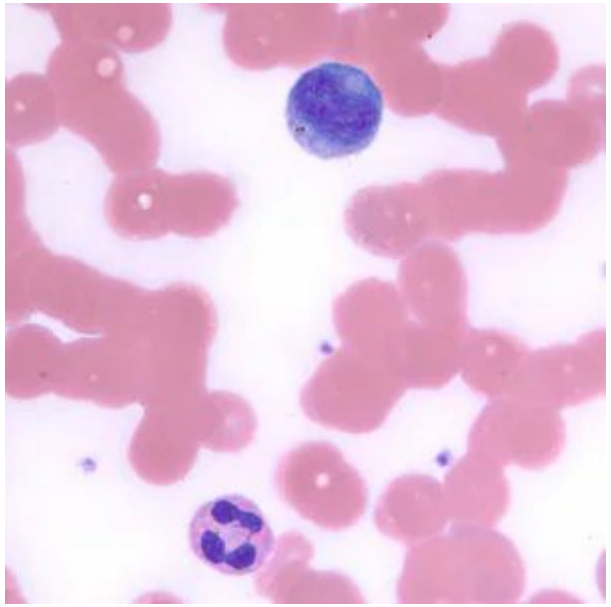
- similar to dengue, chikungunya, zika and even malaria.

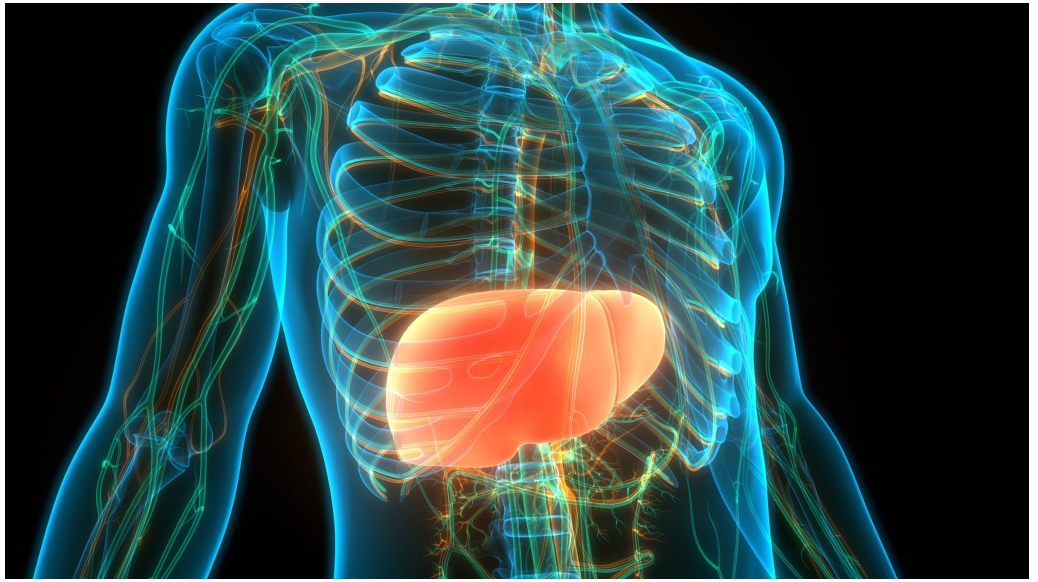




Abnormal Laboratory Values

- Lymphopenia and leukopenia (low white count)
- Elevated C-reactive protein (CRP)
  - Indicator of inflammation
- And elevated liver enzymes

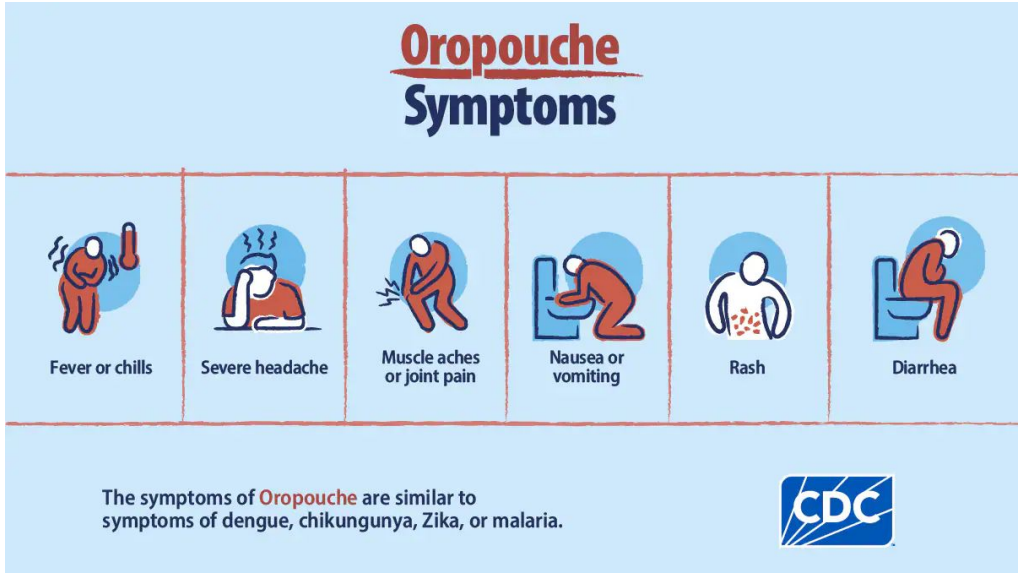




Pictures: cdc.gov

Progression and Prognosis

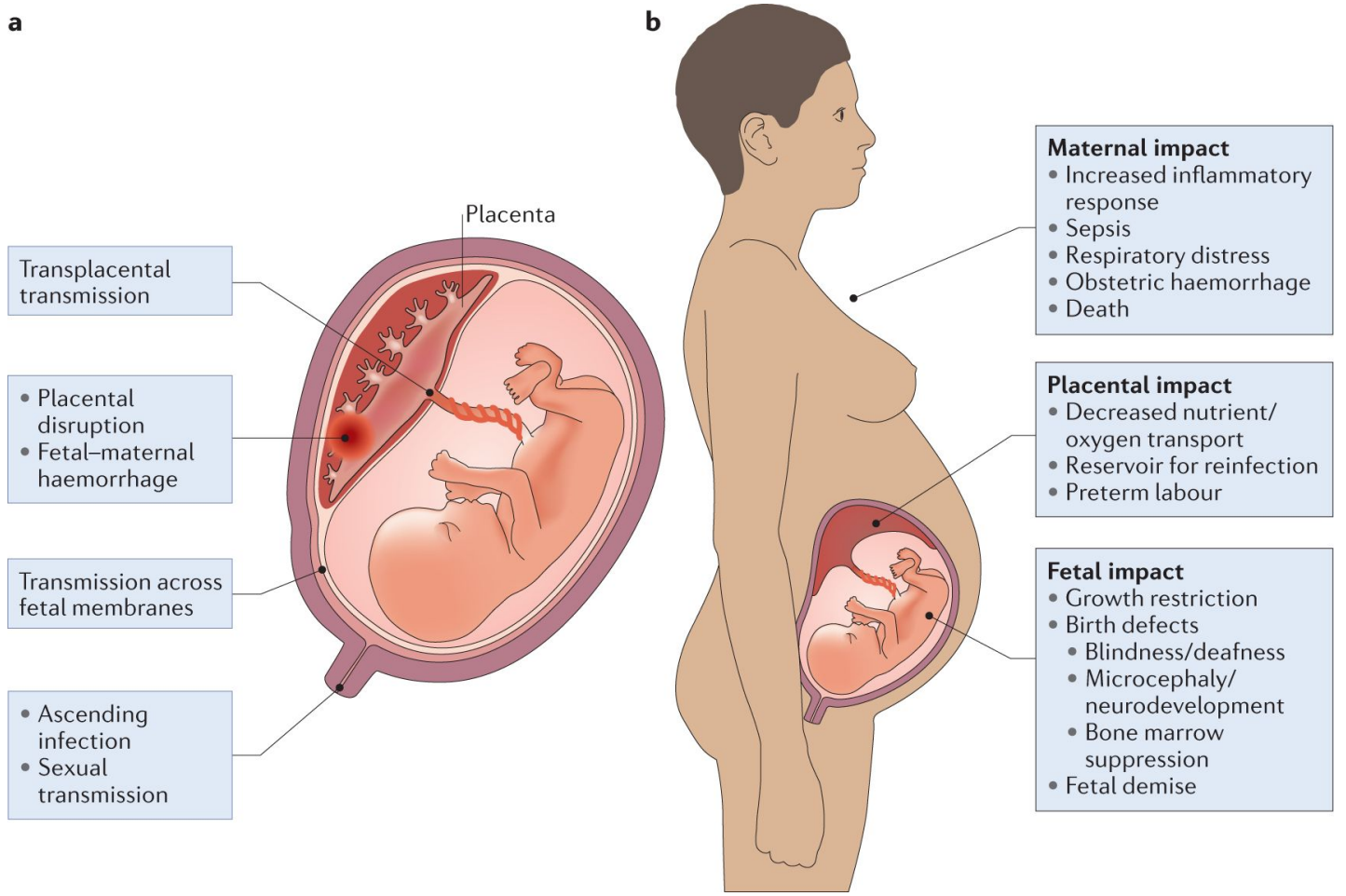
- Can cause neuro-invasive disease in up to 4% of patients
  - CSF= pleocytosis and elevated protein
- Symptom persistence for weeks, even months has been documented
  - Weakness and malaise
- Very few deaths



Vertical Transmission

- The Pan-American Health Organization published a report highlighting concerns of possible mother to child transmission

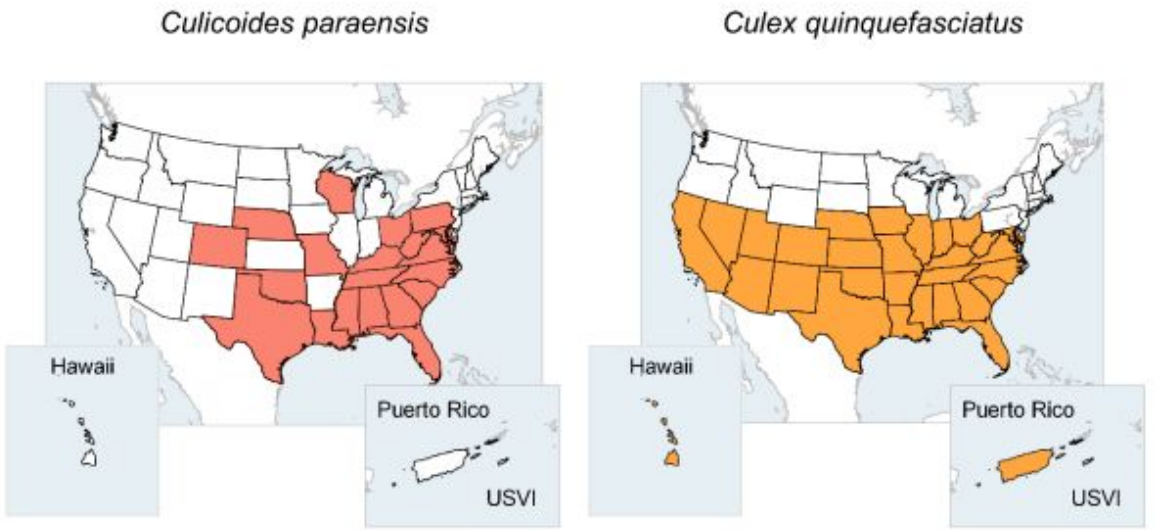
- Associated with adverse pregnancy outcomes
  - Congenital abnormalities
    - microcephaly, miscarriage
  - Fetal death



Infections at the maternal–fetal interface: an overview of pathogenesis and defence | Nature Reviews Microbiology

What if Oropouche is suspected?

- Contact state laboratory
  - They will assist in determining if samples need to be tested for Oropouche
- Then samples get sent to CDC Arbovirus Diagnostic Laboratory
  - Through the state health departments
- Results get sent from CDC back to the state health departments



Laboratory Diagnostics

- Evidence of the virus can be detected in serum during the first week of infection
  - Detection of viral RNA
- After that, IgM followed by IgG

- CDC performs real-time RT-PCR to detect viral RNA in serum and CSF during the acute phase
  - Can also perform plaque reduction neutralization tests
- Acute and convalescent samples needed (4-fold or greater change in antibody titers)

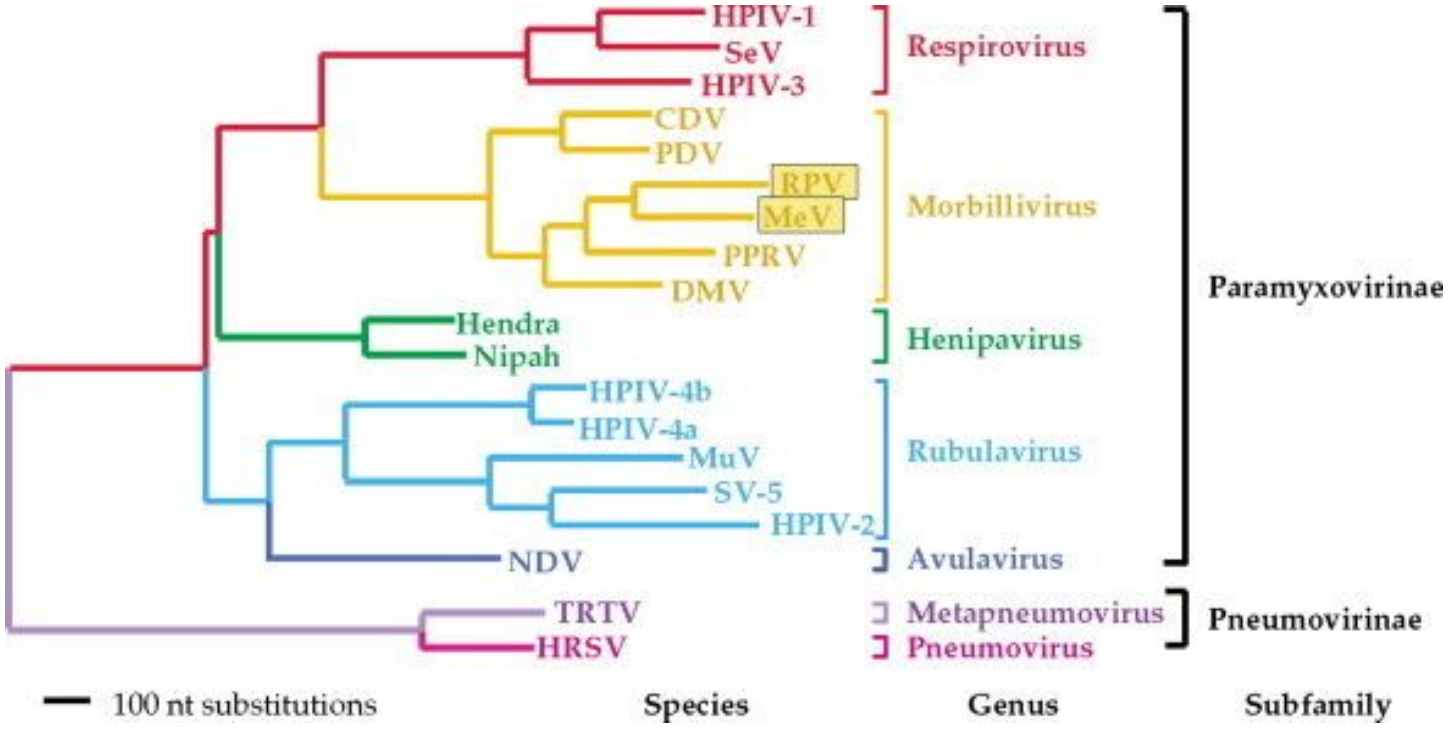
Treatment and Prevention

- No vaccine
- No approved medicine
  - Supportive care
  - Avoid aspirin and NSAIDs until Dengue is ruled out (bleeding).
- Prevention: protect from insect bites
  - Easier said than done. Midges are small and can pass through nets
  - Midges are less affected by common insect repellants
- Protection from aerosolization/ingestion:
  - Seven laboratory workers are known to have been accidentally infected; all developed symptoms.

NIPAH

Nipah Virus

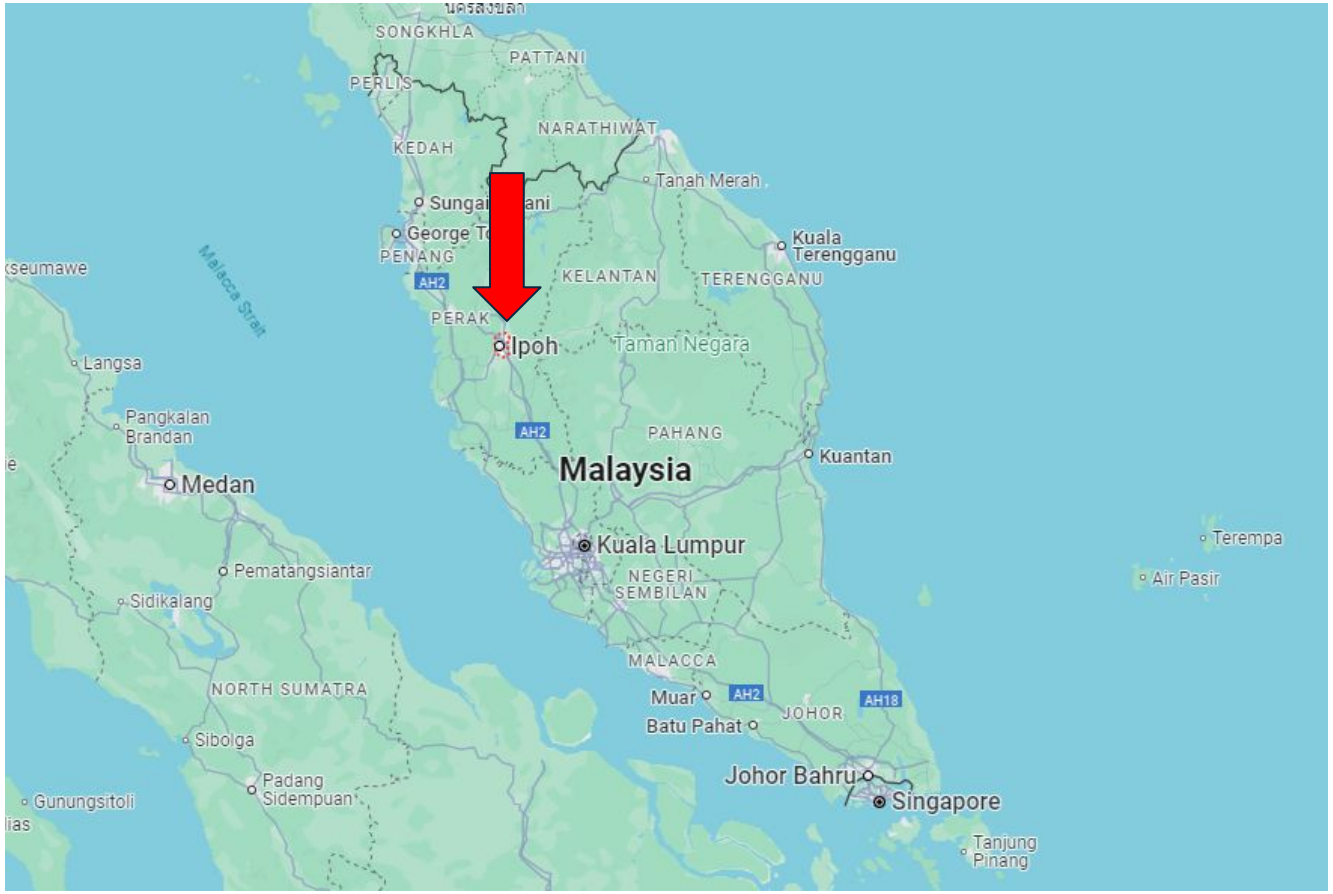
- *Paramyxoviridae* (family)
  - *Henipavirus nipahense*
  - Similar to the Hendra virus
  - Single stranded, negative sense, RNA
- The (−)RNA viruses are major causes of human morbidity and mortality



Minus-Strand RNA Viruses - PMC (nih.gov)

Emergence of Nipah

- First recognized in 1998
  - Closely related to Hendra Virus
  - First discovered in Ipoh, Malaysia
  - Outbreak among pig farmers in Malaysia
  - Close contact with sick pigs



Natural host

- Pteropodidae of the Pteropus genus (FRUIT BATS!)
  - Can carry the virus, but show no signs of disease.
- Other genera of fruit bats have found to be positive for antibodies to Nipah, indicating that these viruses may be present in other parts of the world (Africa)

Epidemiology

- Case fatality rate ~40-75%
- Broad species tropism
- Transmitted to humans from animals, or contaminated foods
  - Also human to human transmission
- Recent outbreaks in Bangladesh and India
  - Consumption of fruits or fruit products (raw date palm juice) contaminated with urine or saliva from infected fruit basts
  - Human-to-human transmission (hospital staff and family of those infected)

Epidemiology

- Annual outbreaks in Bangladesh since 2001
- Outbreaks have occurred in: Singapore, India
- 2 genetic lineages
  - NiV-BD (more pathogenic), NiV-MY

Yellow= fruit bats
Red= Nipah outbreaks

cdc.gov

Exposure risk

- People working with pigs
- Families, caregivers, and healthcare workers caring for patients with Nipah
- Exposure to or ingestion of food or drinks contaminated by infected animals (bat saliva and urine)
- Those who climb trees where fruit bats roost

Fao.org

Npr.org, courtesy of Dr. Emily Gurley from EcoHealth Alliance

Clinical Presentation

- Incubation 4-14 days
- From acute respiratory infection to fatal encephalitis
- Fever, headaches, myalgia, sore throat, vomiting
  - Can be followed by: dizziness, altered mental status, and neurological symptoms
  - And/or severe respiratory complications including acute respiratory distress

Laboratory Diagnosis

- PCR from bodily fluids
- Antibody detection from serum via ELISA
- Viral culture
  - Requires BSL-4 facilities
- Not widely available and affected by quality, quantity, type, transport time and timing of sample collection.

Treatment

- No vaccines
- No specific drugs for treatment
- WHO has identified Nipah as a "priority disease" for the WHO Research and Development Blueprint

https://www.who.int/publications/m/item/pathogens-prioritization-a-scientific-framework-for-epidemic-and-pandemic-research-preparedness

Family	2017 Priority Pathogens	2018 Priority Pathogens	2024 PHEIC risk	2024 Priority Pathogens	2024 Prototype Pathogens
Adenoviridae			Low-Medium		Recombinant Mastadenovirus
Adenoviridae			Low-Medium		Mastadenovirus blackbeardi serotype 14
Anelloviridae			Low		
Arenaviridae	Arenaviral hemorrhagic fevers including Lassa Fever	Lassa Fever virus	High	Mammarenavirus lassaense	Mammarenavirus lassaense
Arenaviridae			High		Mammarenavirus juninense
Arenaviridae			High		Mammarenavirus lujoense
Astroviridae			Low		Mamastrovirus virginiaense
Bacteria			High	Vibrio cholerae serogroup O139	
Bacteria			High	Yersinia Pestis	
Bacteria			High	Shigella dysenteriae serotype 1	
Bacteria			High	Salmonella enterica non typhoidal serovars	
Bacteria			High	Klebsiella pneumoniae	
Bornaviridae			Low		Orthobornavirus bornaense
Coronaviridae	Middle East Respiratory Syndrome Coronavirus	Middle East Respiratory Syndrome Coronavirus	High	Subgenus Merbecovirus	Subgenus Merbecovirus
Coronaviridae	Other highly pathogenic coronaviral diseases such as Severe Acute Respiratory Syndrome	Severe Acute Respiratory Syndrome	High	Subgenus Sarbecovirus	Subgenus Sarbecovirus
Filoviridae	Filoviral diseases Ebola	Ebola virus disease	High	Orthoebolavirus zairense	Orthoebolavirus zairense
Filoviridae	Filoviral diseases Marburg	Marburg virus disease	High	Orthomarburgvirus marburgense	
Filoviridae			High	Orthoebolavirus sudanense	
Flaviviridae	Zika virus	Zika virus	High	Orthoflavivirus zikaense	Orthoflavivirus zikaense
Flaviviridae			High	Orthoflavivirus denguei	Orthoflavivirus denguei
Flaviviridae			High	Orthoflavivirus flavi	
Flaviviridae			High		Orthoflavivirus encephalitidis
Flaviviridae			High		Orthoflavivirus nilense
Hantaviridae			High	Orthohantavirus sinnombreense	Orthohantavirus sinnombreense
Hantaviridae			High	Orthohantavirus hantanense	
Hepadnaviridae			Low		Orthohepadnavirus hominoidei genotype C

Family	2017 Priority Pathogens	2018 Priority Pathogens	2024 PHEIC risk	2024 Priority Pathogens	2024 Prototype Pathogens
Hepeviridae			Low		Paslahepevirus balayani genotype 3
Herpesviridae			Low		
Nairoviridae	Crimean Congo Haemorrhagic Fever	Crimean Congo Haemorrhagic Fever	High	Orthonairovirus haemorrhagiae	Orthonairovirus haemorrhagiae
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H1	Alphainfluenzavirus influenzae H1
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H2	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H3	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H5	Alphainfluenzavirus influenzae H5
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H6	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H7	
Orthomyxoviridae			High	Alphainfluenzavirus influenzae H10	
Papillomaviridae			Low		
Paramyxoviridae	Nipah and related henipaviral diseases	Nipah and henipaviral diseases	High	Henipavirus nipahense	Henipavirus nipahense
Parvoviridae			Low		Protoparvovirus carnivoran
Peribunyaviridae			Low		Orthobunyavirus oropoucheense
Phenuiviridae	Severe Fever with Thrombocytopenia Syndrome		High	Bandavirus dabieense	Bandavirus dabieense
Phenuiviridae	Rift Valley Fever	Rift Valley Fever	High		Phlebovirus riftense
Picobirnaviridae			Low		Orthopicobirnavirus hominis
Picornaviridae			Medium	Enterovirus coxsackiepol	
Picornaviridae			Medium		Enterovirus alphacoxsackie 71
Picornaviridae			Medium		Enterovirus deconjucti 68
Pneumoviridae			Low-Medium		Metapneumovirus hominis
Polyomaviridae			Low		
Poxviridae			High	Orthopoxvirus variola	
Poxviridae			High		Orthopoxvirus vaccinia
Poxviridae			High	Orthopoxvirus monkeypox	Orthopoxvirus monkeypox
Retroviridae			Medium	Lentivirus humimdef1	Lentivirus humimdef1
Rhabdoviridae			Low		Genus Vesiculovirus
Sedoreoviridae			Low		Genus Rotavirus
Spinareoviridae			Low		Orthoreovirus mammalis
Togaviridae			High	Alphavirus chikungunya	Alphavirus chikungunya
Togaviridae			High	Alphavirus venezuelan	Alphavirus venezuelan
Pathogen X	Pathogen X	Pathogen X		Pathogen X	

[4] https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts

A WHO tool distinguishes which diseases pose the greatest public health risk due to their epidemic potential and/or whether there is no or insufficient countermeasures.

At present, the priority diseases are:

- COVID-19
- Crimean-Congo haemorrhagic fever
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipaviral diseases
- Rift Valley fever
- Zika

Possible agent of bioterrorism?

Nipah has many characteristics which make it a potential agent

- highly virulent
- high mortality
- spreads easily

“Poses a severe threat to both human and animal health, to plant health, or to animal and plant products”

Overlap Select Agents and Toxins

37. *Bacillus anthracis* [1]
38. *Bacillus anthracis* Pasteur strain
39. *Brucella abortus*
40. *Brucella melitensis*
41. *Brucella suis*
42. *Burkholderia mallei* [1]
43. *Burkholderia pseudomallei* [1]
44. Hendra virus
45. Nipah virus
46. Rift Valley fever virus
47. Venezuelan equine encephalitis virus [4][5][8]

selectagents.gov

Reasons for re-emergence

- Human, ecological and viral factors
  - Climate change
  - Population growth and urbanization
  - human and animal mobility and behavior
  - deforestation
  - land use
  - habitat fragmentation (especially of reservoir animals)
  - Genetic evolution of viruses (considered a minor factor)

cdc.gov

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Thank you!

Questions?