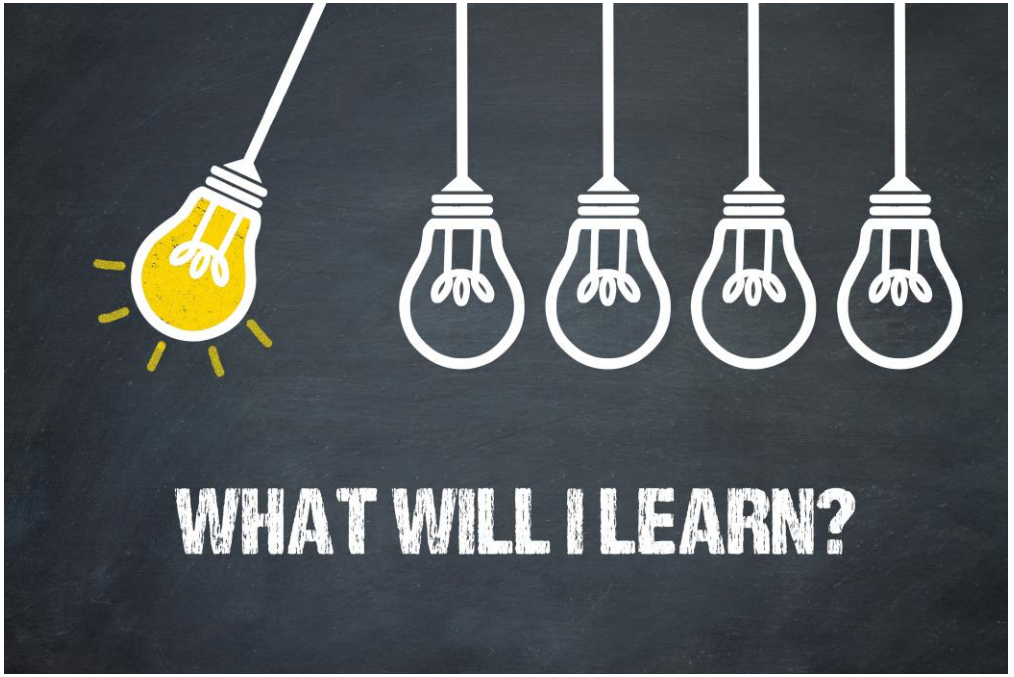
Rabies, Brucellosis, Tularemia, Q Fever, Anthrax….Oh My!!

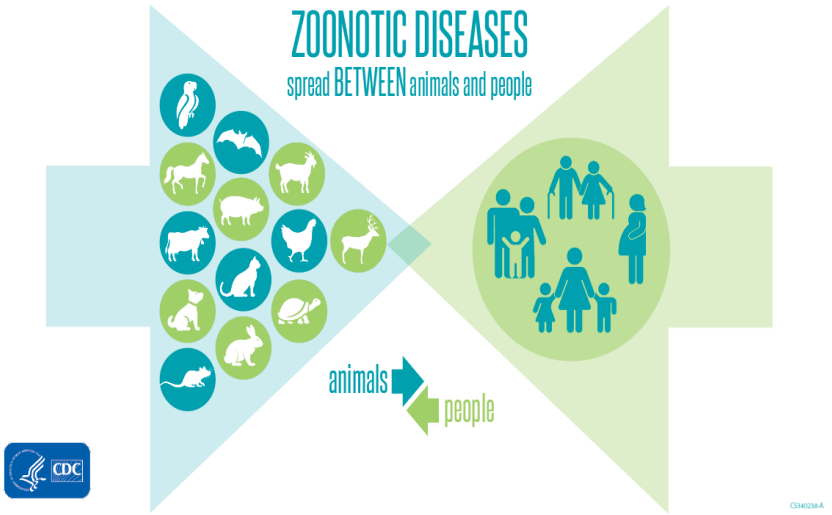
Objectives

- Understand zoonotic disease importance
- Understand history, modern context, human and animal disease process, treatment and prevention of:
  - Rabies
  - Brucellosis
  - Q fever
  - Tularemia
  - Anthrax
  - Leptospirosis
  - Plague



Zoonotic Disease Importance

- ~60% of human pathogens are zoonotic
- >70% of emerging infectious diseases in people are zoonotic
  - MERS, SARS, Ebola, H1N1, COVID-19
- Category A and Category B bioterrorism agents, select agents
- ~50% of livestock losses worldwide are because of zoonotic diseases



Nipah virus's brief but deadly reign of terror

PHEI BICKSON. When Kampung Baru Sungai Nipah residents began dying mysteriously, the authorities were at a loss until mistakenly labelled the outbreak as a Japanese Encephalitis epidemic.

A research team led by Professor Emeritus Datuk Dr Lam Sai Kit and assisted by Associate Professor Chua Kaw Bing of Universiti Malaya's Medical Faculty was formed to study the virus.

Lacking the necessary equipment here, Dr Chua took samples with him to the Centers for Disease Control and Prevention in Atlanta, the United States, where it was confirmed that the Nipah virus, named after the village, was new and not a mutation of the JE virus.

The Nipah virus shared 82 per cent of its DNA sequence with a virus called Hendra, which killed 14 racehorses and their trainer in Queensland, Australia, in 1994.

The discovery led to the conclusion that close contact with pigs was the main mode of transmission to humans, unlike JE, which is spread from animals to humans by mosquitoes.

It also proved that fogging (as the wrong presumption that the virus was a JE virus variant) and vaccination against JE would not work.

NST LIVE
OUR HEALTH CONCERNS
Japanese Encephalitis, bird flu, and now, swine flu. Health Minister Datuk Seri Liow Tiong Lai will answer your questions about health "live" at 3.30pm tomorrow. Visit nst.com.my

Pigs in the village were culled and this finally brought the outbreak under control.

A species of fruit bat known as the Island flying fox, or *Pteropus hypomelanus* is found in many islands off Malaysia, Myanmar, Thailand, Cambodia, Vietnam, Indonesia and Papua New Guinea, and it often roosts close to rivers, an coconut trees or other palm trees and feeds on tropical fruits.

It was discovered that the Nipah virus was transmitted from the fruit bats to pigs, horses and goats through direct contact with the saliva and urine.

This occurred when the animals ate remnants of fruits which the bats had partially eaten or came into contact with the bats' urine.

Humans who came into contact with the neutral fluids of the infected animals were thus infected.

The disease did not spread further as the virus died quickly when exposed, unlike the JE virus, which was spread by the Culex mosquito after biting infected pigs.

The Nipah and JE virus outbreak occurred from 1996 to March 1999, causing 106 human deaths.

FROM THE DECEMBER 1993 ISSUE

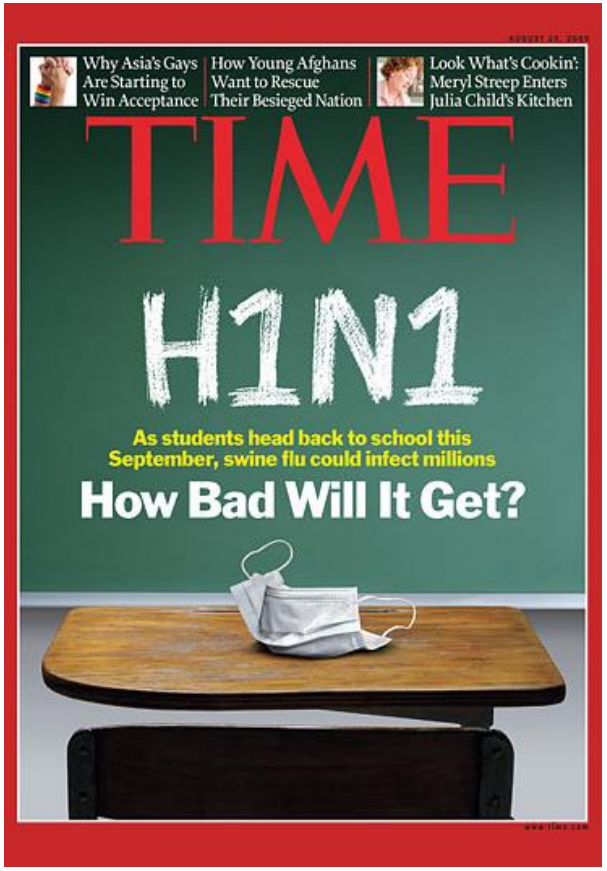
Death at the Corners

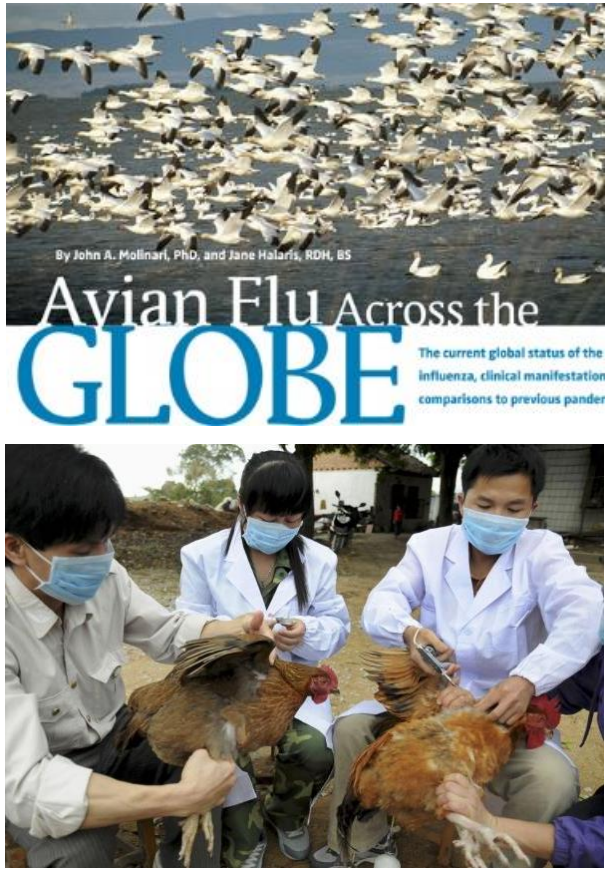
A spate of sudden deaths in the Southwest has revealed a new viral villain. But is the virus really new--or an old one we've flushed out of hiding?

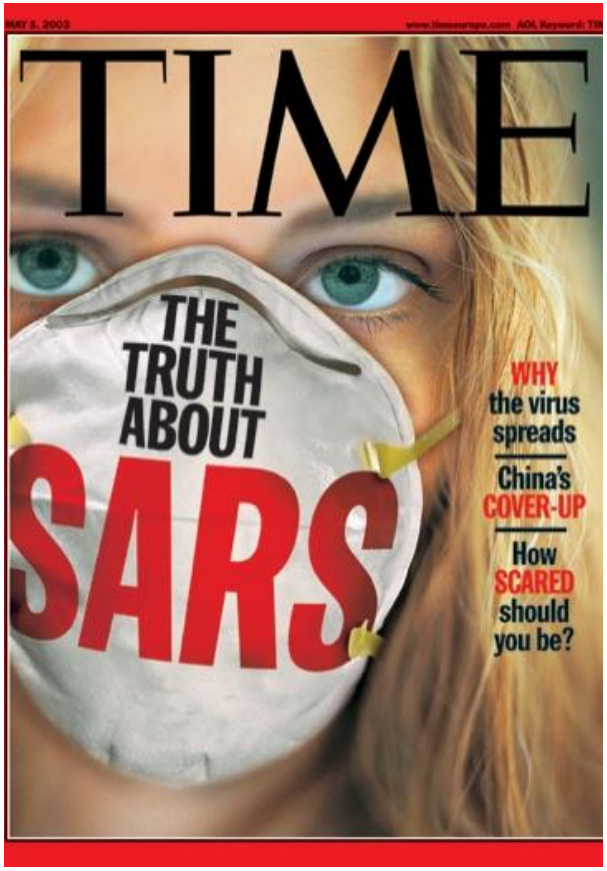
By Denise Grady | Wednesday, December 01, 1993

RELATED TAGS: INFECTIOUS DISEASES

Zoonotic Disease Outbreaks, 1990s







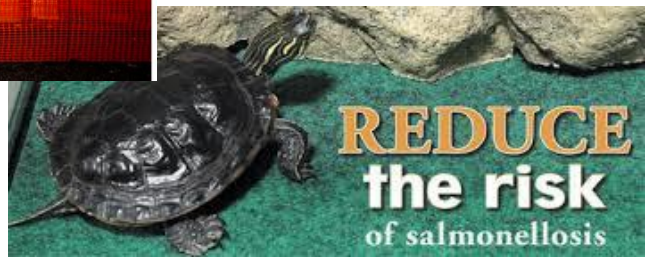
By SUE CHAN / CBS/AP / *February 10, 2003, 6:44 PM*

Prairie Dogs And Monkeypox

Zoonotic Disease Outbreaks, 2000s

Zoonotic Disease Outbreaks, 2010s

Ebola spread in the Democratic Republic of Congo, causing the second-largest outbreak in history.



CDC Warns People (Again) Not To Drink Raw Milk After 19 States On High Alert For Deadly Bacteria

9.9K SHARES Share on Facebook Share on Twitter

The deadly, bat-borne Nipah virus spread in India.

Zoonotic Disease Outbreaks, 2020s

Infectious Diseases, Viruses

Monkeypox Outbreaks: What Do You Need to Know? Do You Need to Worry?

Author Chandana Balasubramanian , 15-May-2022

A police volunteer is disinfected to prevent the spread of coronavirus COVID-19, in Pamplona, northern Spain. March 22, 2020 - Alvaro Barrientos/AP Photo

BREAKING | Aug 27, 2021, 08:18pm EDT | 7,960 views

Oh, Deer: Whitetails In Ohio Have Covid-19

World Health Organization announces novel coronavirus

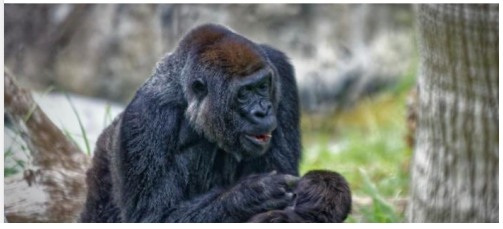
A man wears a mask while walking in the street on Jan. 22 in Wuhan, Hubei province, China. A new infectious coronavirus known as "2019-nCoV" has been discovered in Wuhan. (2020 Getty Images)

On Jan. 9, the World Health Organization first announced news about the deadly coronavirus that had emerged in Wuhan, China.

ANIMALS

Gorillas in San Diego Test Positive for Coronavirus

By Olivia Rosane | Jan. 13, 2021 01:13PM EST ANIMALS



The first US case of an animal testing positive for COVID-19 was a tiger at a New York zoo.

Role of DPHHS with Zoonotic Diseases

- Assists local health departments with investigating zoonotic diseases in humans
- Works closely with Department of Livestock and Department of Fish, Wildlife, and Parks to monitor and treat humans who were exposed to zoonotic diseases by Montana wildlife
- Works with Montana Public Health Lab (MTPHL) and the Montana Veterinary Diagnostic Lab (MVDL) to coordinate testing of human and animal specimens to aid in the care coordination of humans exposed to zoonotic conditions (e.g., rabies, tularemia, brucellosis)

Role of DPHHS with Zoonotic Diseases

- Coordinates with the Bacterial Special Pathogens Branch (BSPB) and the Viral Special Pathogens Branch (VSPB) of the CDC when unique situations arise related to zoonotic disease (e.g., individual exposed to *B. canis* after administering mouth-to-mouth to a stillborn pup)
- DPHHS follows standardized case definitions created by the Council for State and Territorial Epidemiologists (CSTE) when enumerating cases of zoonotic disease in Montana
  - Providers may consider someone a case of a zoonotic disease even if DPHHS cannot due to differences in case definition

Example of Case Definition

Laboratory Criteria For Diagnosis

Definitive

- Culture and identification of *Brucella* spp. from clinical specimens
- Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart

Presumptive

- *Brucella* total antibody titer of greater than or equal to 160 by standard tube agglutination test (SAT) or *Brucella* microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms
- Detection of *Brucella* DNA in a clinical specimen by PCR assay

Case Classification

Probable

A clinically compatible illness with at least one of the following:

- Epidemiologically linked to a confirmed human or animal brucellosis case
- Presumptive laboratory evidence, but without definitive laboratory evidence, of *Brucella* infection

Confirmed

A clinically compatible illness with definitive laboratory evidence of *Brucella* infection

Category A Bioterrorism Agents

- Easily disseminated or transmitted person-to-person
- High mortality rates
- Potential for major public health impact
- Might cause public panic and social disruption
- Require special action from public health preparedness

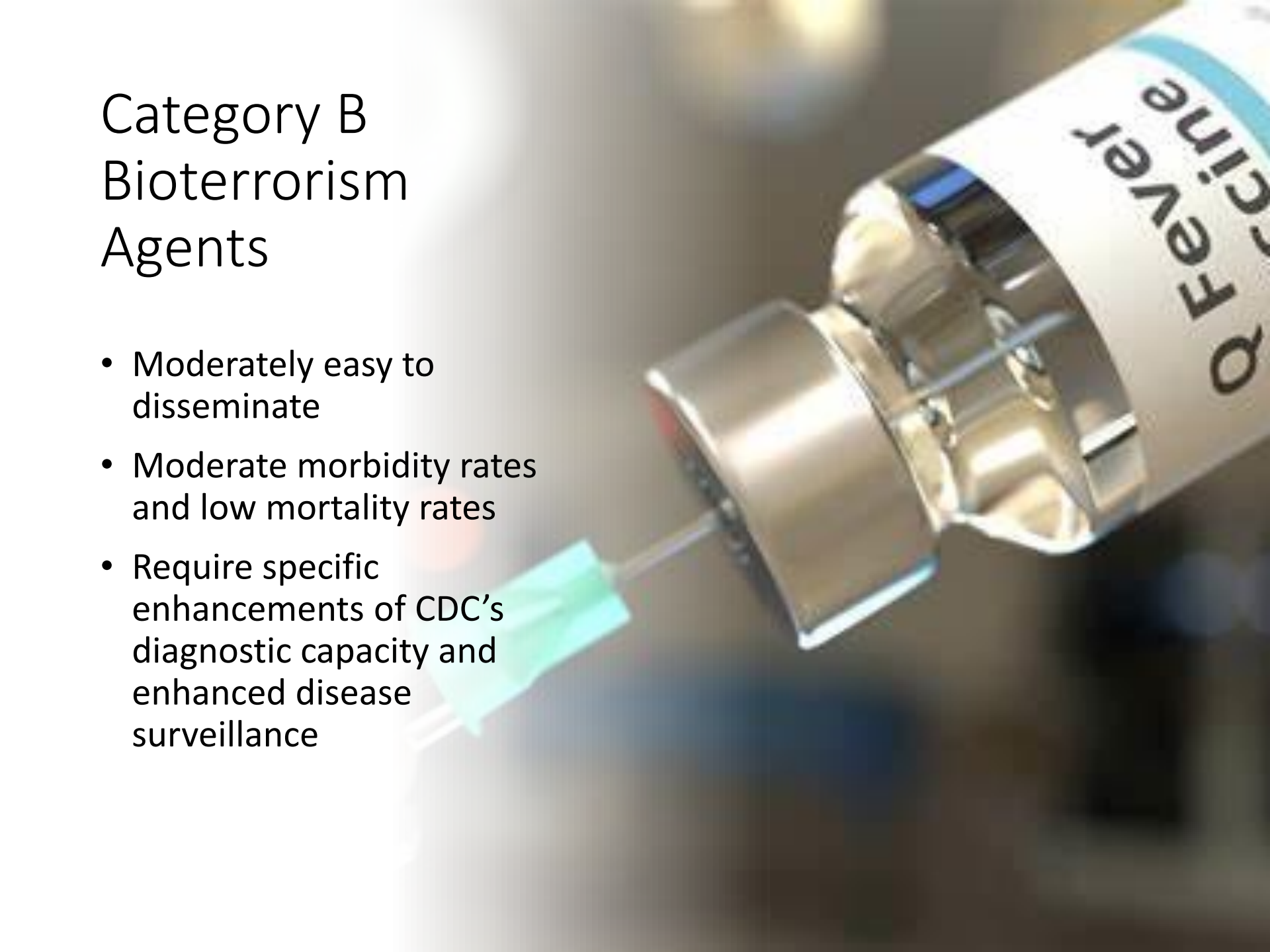
Category A Bioterrorism Agents

- Anthrax*
- Botulism
- Plague*
- Smallpox
- Tularemia*
- Viral hemorrhagic fevers

(Ebola, Marburg, Lassa, Machupo)*

Category B Bioterrorism Agents

- Moderately easy to disseminate
- Moderate morbidity rates and low mortality rates
- Require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance



Category B Agents

- Brucellosis (*Brucella* species)*
- Epsilon toxin of Clostridium perfringens
- Food safety threats (*Salmonella* species*, *Escherichia coli* O157:H7*, Shigella)
- Glanders (*Burkholderia mallei*)*
- Meloidosis (*Burkholderia pseudomallei*)*
- Psittacosis (*Chlamydia psittaci*)*
- Q fever (*Coxiella burnetii*)*
- Ricin toxin from *Rininus communis*
- Staphylococcal enterotoxin B
- Typhus fever (*Rickettsia prowazekii*)*
- Viral encephalitis (VEE, WEE, EEE)*
- Water safety threats (*Vibrio cholerae, Cryptosporidium parvum**)

Select Agents (n=68)

- Select agents are biological agents and toxins that have been determined to have the potential to pose a severe threat to public health and safety.
- The Federal Select Agent Program is jointly comprised of the Centers for Disease Control and Prevention/Division of Select Agents and Toxins and the Animal and Plant Health Inspection Service/Division of Agricultural Select Agents and Toxins.
- Oversees the possession, use, and transfer of biological select agents and toxins which have the potential to pose a severe threat to public, animal, or plant health or to animal or plant products.

Select Agents- HHS (n=36)

Abrin	Omsk hemorrhagic fever virus
Bacillus cereus Biovar *anthracis*	Reconstructed 1918 Influenza virus
Botulinum neurotoxins	Ricin
Botulinum neurotoxin producing species of *Clostridium*	*Rickettsia prowazekii*
Conotoxins	SARS-associated coronavirus (SARS-CoV)
Coxiella burnetii	SARS-CoV/SARS-CoV-2 chimeric viruses resulting from any deliberate manipulation of SARS-CoV-2 to incorporate nucleic acids coding for SARS-CoV virulence factors
Crimean-Congo hemorrhagic fever virus	Saxitoxin
Diacetoxyscirpenol	South American Hemorrhagic Fever viruses (Chapare, Guanarito, Junin, Machupo, Sabia)
Eastern Equine Encephalitis virus	Staphylococcal enterotoxins (subtypes A,B,C,D,E)
Ebola virus	T-2 toxin
Francisella tularensis	Tetrodotoxin
Kyasanur Forest disease virus	Tick-borne encephalitis complex (flavi) viruses (Far Eastern subtype and Siberian subtype)
Lassa fever virus	Variola major virus (Smallpox virus)
Lujo virus	Variola minor virus (Alastrim)
Marburg virus	*Yersinia pestis*
Mpox virus	

Select Agents- USDA Veterinary Services (n=14)

African horse sickness virus	*Mycoplasma capricolum*
African swine fever virus	*Mycoplasma mycoides*
Avian influenza virus	Newcastle disease virus
Classical swine fever virus	Peste des petits ruminants virus
Foot-and-mouth disease virus	Rinderpest virus
Goat pox virus	Sheep pox virus
Lumpy skin disease virus	Swine vesicular disease virus

Select Agents- USDA Plant Protection and Quarantine (n=7)

Coniothyrium glycines (formerly *Phoma glycinicola and Pyrenochaeta glycines)*	*Sclerophthora rayssiae*
Peronosclerospora philippinensis (Peronosclerospora sacchari)	*Synchytrium endobioticum*
Ralstonia solanacearum	*Xanthomonas oryzae*
Rathayibacter toxicus	

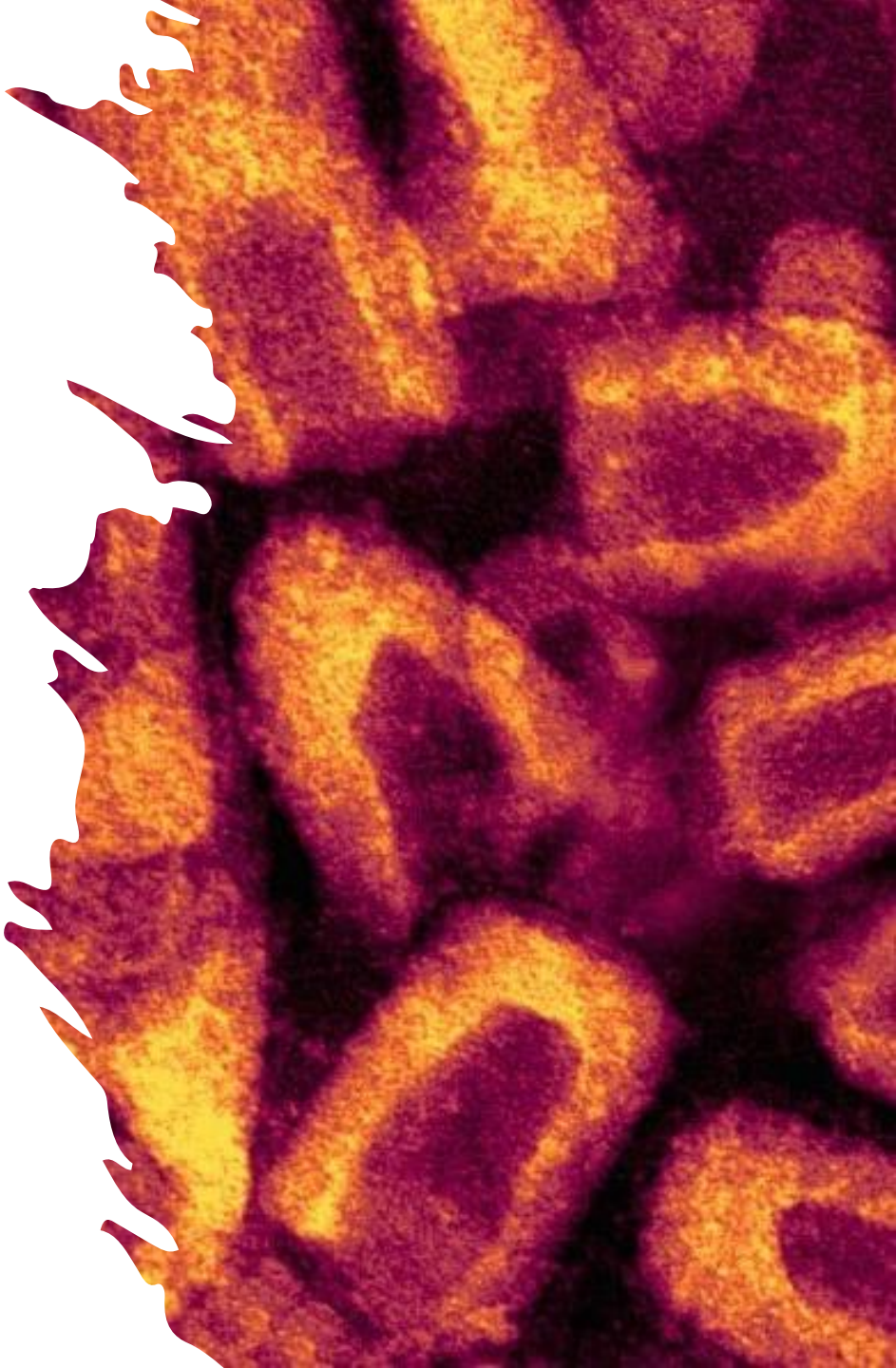
Select Agents- Overlap HHS & USDA (n=11)

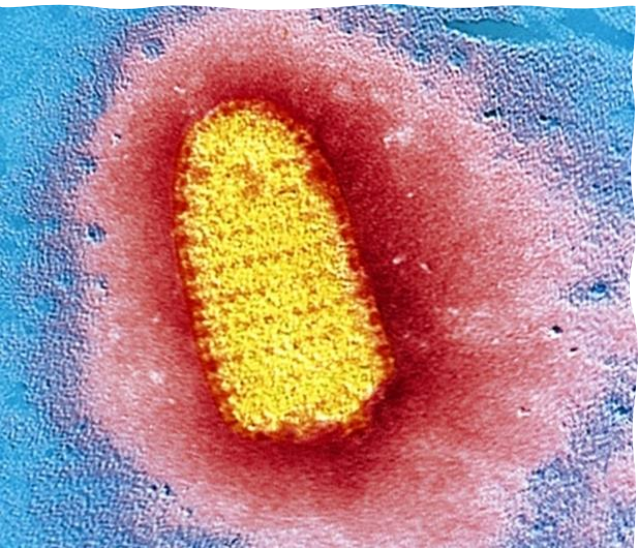
Bacillus anthracis	*Burkholderia pseudomallei*
Bacillus anthracis Pasteur strain	Hendra virus
Brucella abortus	Nipah virus
Brucella melitensis	Rift Valley fever virus
Brucella suis	Venezuelan equine encephalitis virus
Burkholderia mallei	

Rabies

Rabies Virus

- Family *Rhabdoviridae*, genus *Lyssavirus* (Lyssa means frenzy or madness)
- Bullet-shaped
- Single-stranded RNA virus
- Affects only mammals
  - Highest case fatality rate of any etiologic agent
  - Leading viral zoonosis of public health significance
- 90% of cases occur in wildlife in U.S.

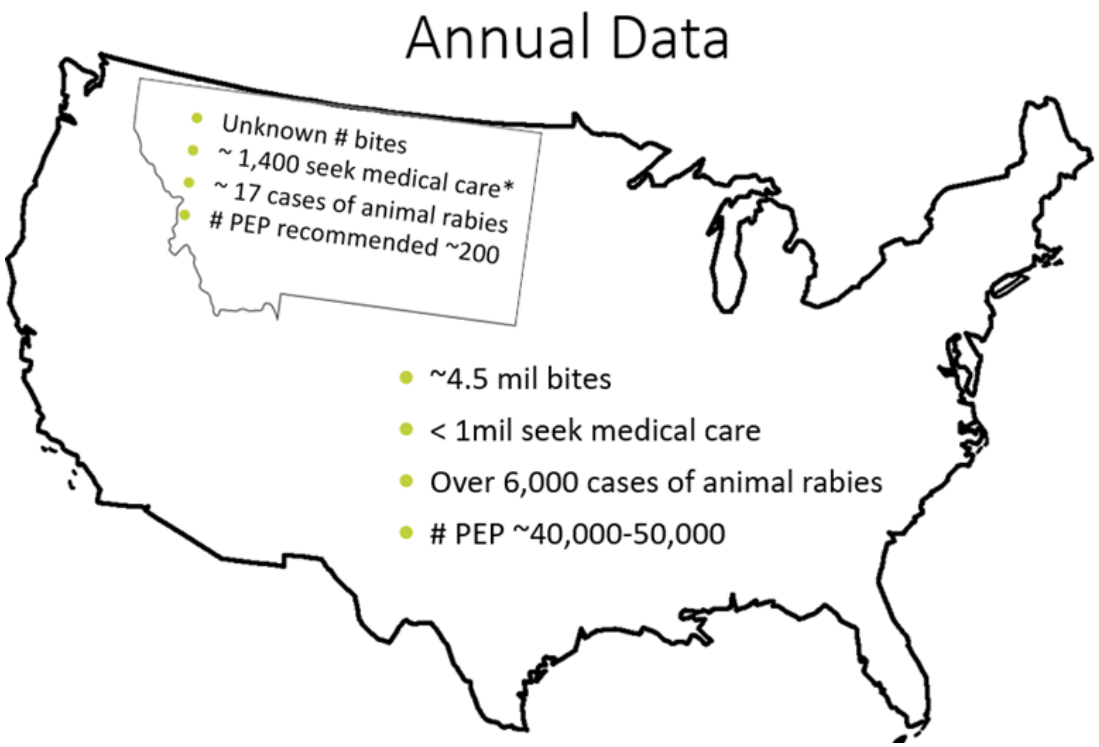


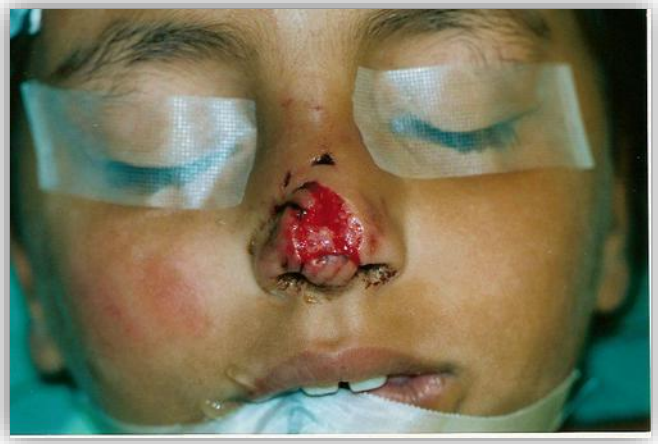


History

- Ancient disease
  - Described as early as 2300 B.C.
  - "Hair of the dog that bit you"
  - Dog owners in Babylon fined for deaths caused by dogs biting people
- Louis Pasteur developed the first vaccine
  - Dried spinal cords of infected rabbits
  - Tested in dogs
  - 1885 used successfully in a child in a child bitten by a rabid dog and the child survived

Modern Problem



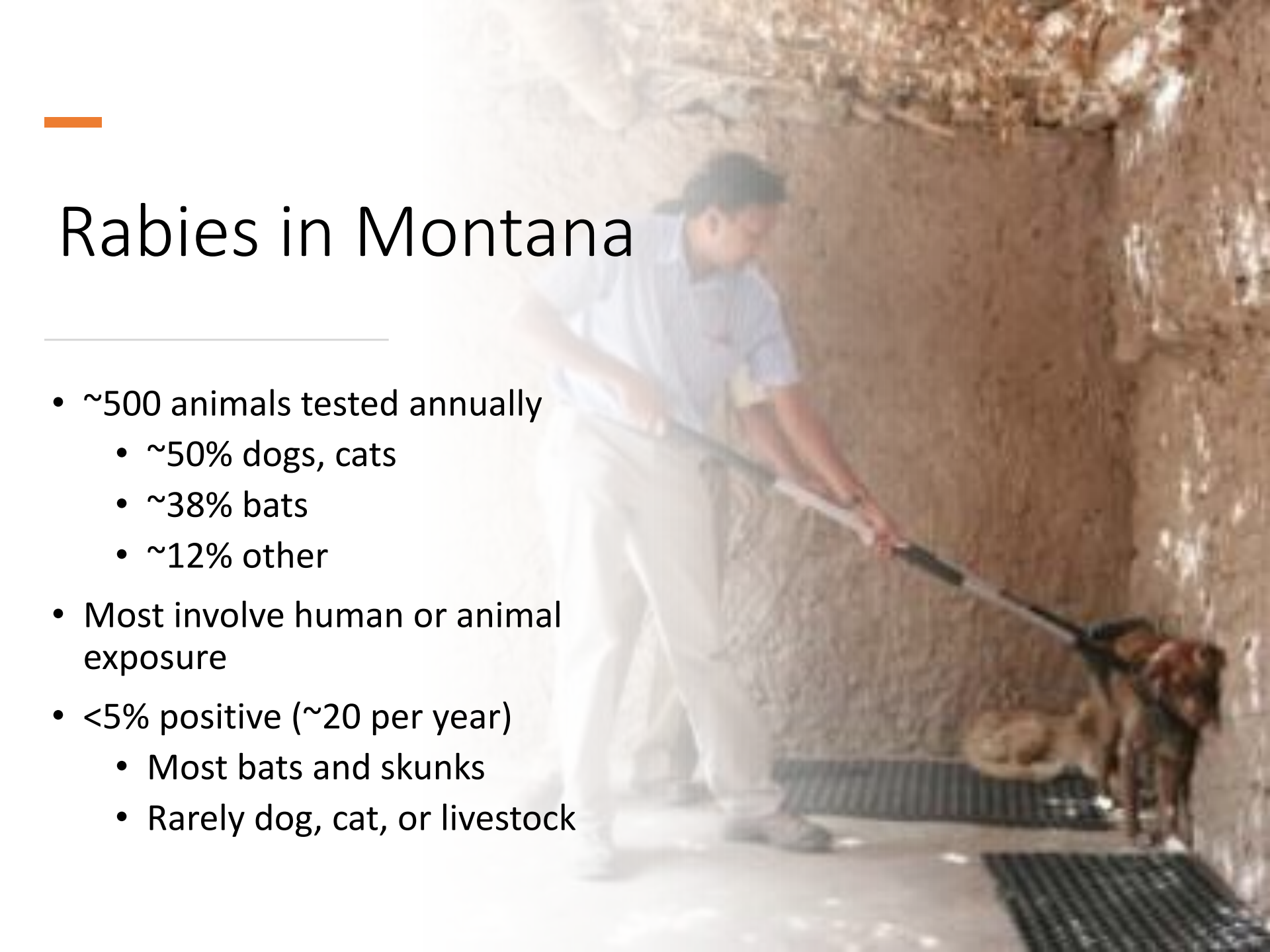


Human Rabies Deaths

World	United States	Montana
• ~55,000 deaths • 40-70% <15years old • One death every 15 minutes	• Avg. 3 deaths/yr • 70% domestic (bats, organ transplant, raccoon) • 30% imported (mainly dog bites) • Deaths often due to unawareness of exposure and lack of seeking medical attention	• No deaths in 23 years! • 2 deaths: 1996 & 1997 • Both bat variant • Unaware of exposures (one case reportedly chased bats out of house one month prior illness onset) • Missoula & Blaine County

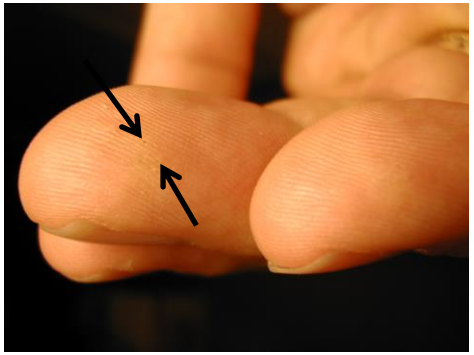
Rabies in Montana

- ~500 animals tested annually
  - ~50% dogs, cats
  - ~38% bats
  - ~12% other
- Most involve human or animal exposure
- <5% positive (~20 per year)
  - Most bats and skunks
  - Rarely dog, cat, or livestock



Transmission

- Most often by bite
- Saliva, CSF, & CNS tissues of rabid mammal
- Blood, urine, feces- are **NOT** infective
- Contamination of mucous membranes, open wounds
- Aerosol transmission
- Corneal & other organ transplant
- Special considerations for bats



Bats

- ~92% of bats tested in Montana are NOT rabid
- ~ 7 out of 10 cases of human rabies in U.S. are bat-associated strains (2019)
- Bat acquired rabies
  - ~23% bite
  - ~44% physical contact, no bite
  - ~32% no bat contact

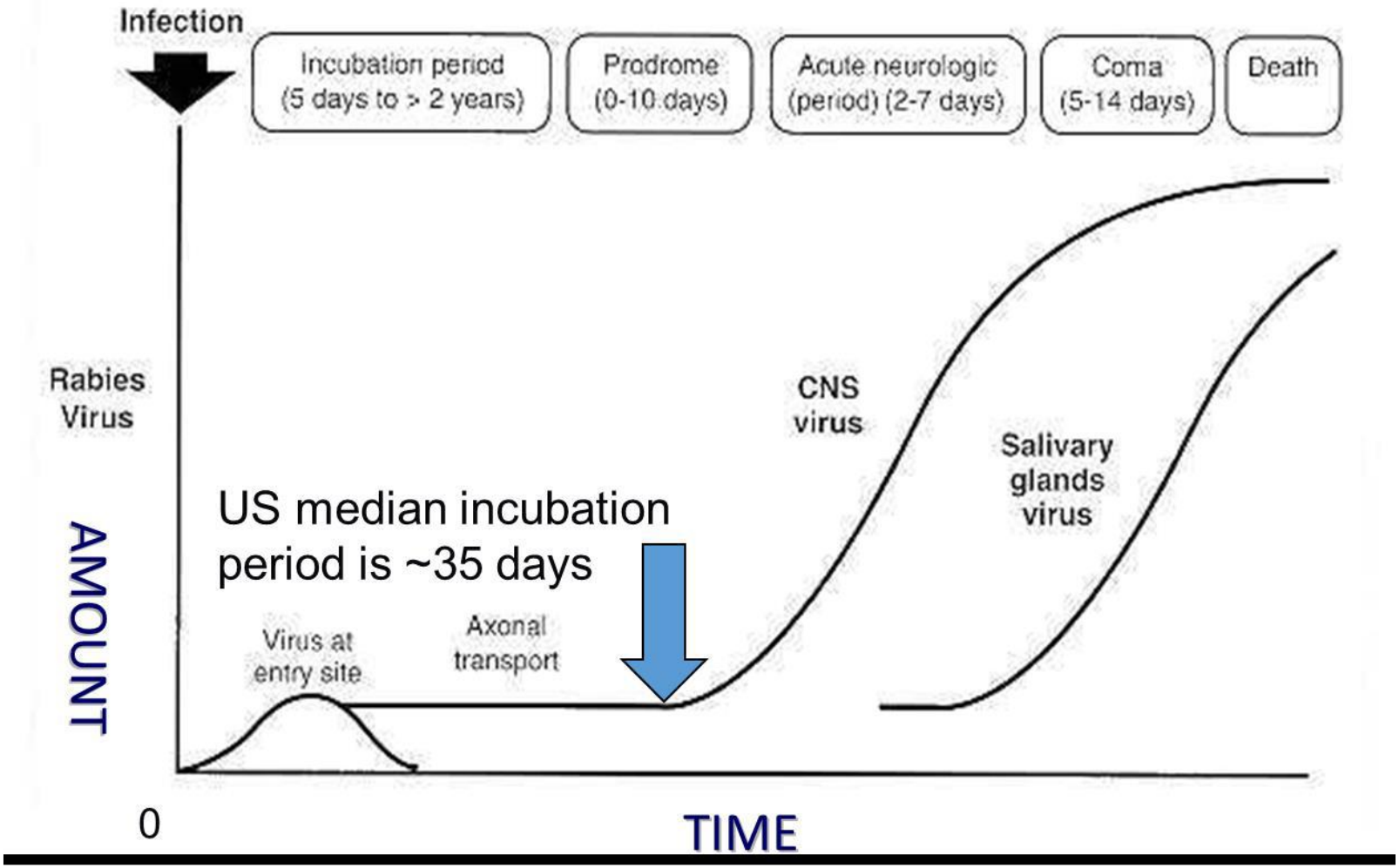
Preferred Management of the Animal

Risk Categories for Animals in Montana

HIGH RISK	MEDIUM RISK	LOW RISK	ALMOST NO RISK
• Bat • Skunk	• Fox • Dog – feral • Wolf Hybrid • Cat - feral • Other non-rodent wild animals species (raccoon, opossum, bear, deer, coyote) • Groundhog*	• Dog - owned • Cat – owned • Livestock	• Squirrel, chipmunk • Rat • Mouse, vole • Indoor small caged pet rodent • Lagomorph

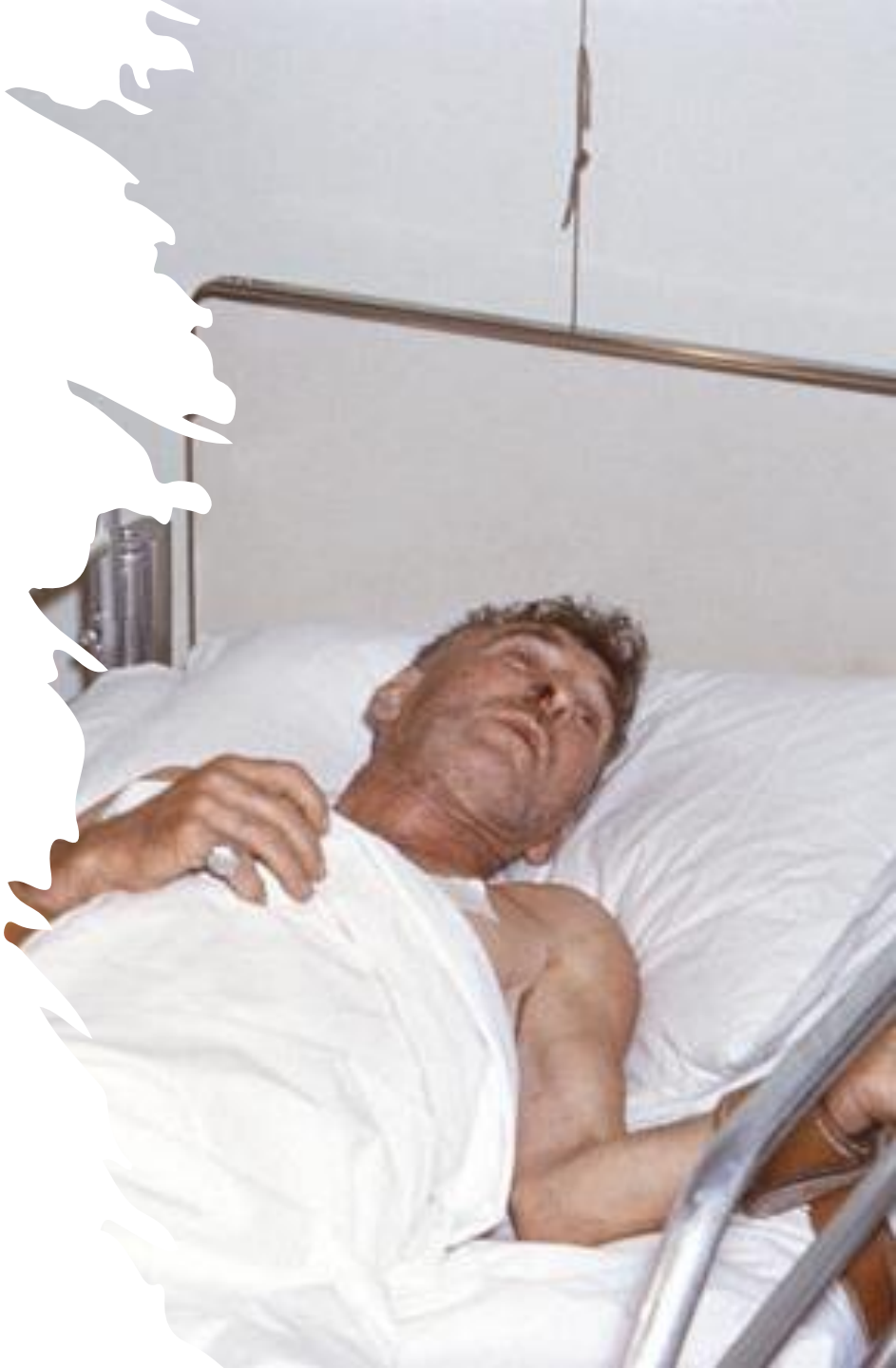
Disease in Humans

- Incubation: 30 – 50 days (US average is 35 days)
  - Range: 5 days–>2 years
- Direct relationship between location of bite and length of incubation period
- Outcome of exposure affected by
  - Virus variant
  - Dose of inoculum
  - Route and location of exposure
  - Individual host factors (age and immune status)


Infection
Incubation period (5 days to > 2 years)
Prodrome (0-10 days)
Acute neurologic (period) (2-7 days)
Coma (5-14 days)
Death
Rabies Virus
AMOUNT
US median incubation period is ~35 days
Virus at entry site
Axonal transport
CNS virus
Salivary glands virus
0
TIME

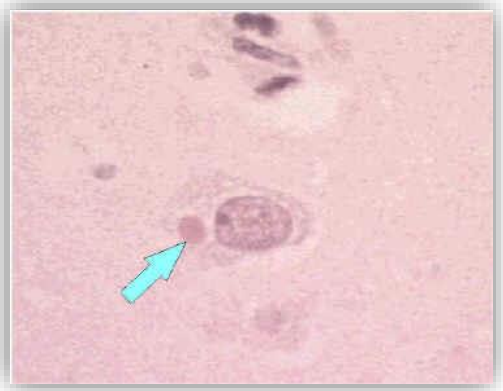
Signs and Symptoms in Humans

- Early symptoms non-specific
  - Fever, headache, and general malaise
- Progresses to encephalitis or myelitis with worsening neurologic signs
- Once symptoms appear…
  - ***<u>It's too late</u>***
- Highest case fatality rate of any infectious disease

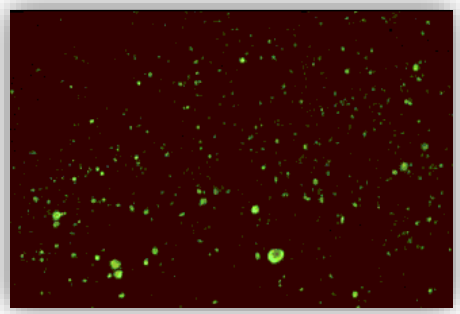


Diagnosis and Treatment — Humans

- Ante-mortem — multiple tests
  - RT-PCR, antibody, antigen tests
  - Saliva, serum, CSF, nuchal biopsy



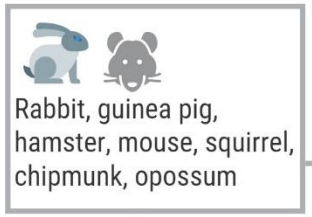
- Post-mortem
  - Immunofluorescent testing of brain
- **Reportable** disease to local, state, and federal health officials
- No single effective treatment
  - Palliative supportive care
  - Milwaukee protocol



Considerations for Rabies PEP

- Medical urgency, not emergency
- Consult with public health
- Animal species, behavior, and risk of infection
- Exposure evaluation
- Likelihood and timing for animal capture for confinement or testing
- Epidemiology of rabies in the area

Montana Rabies Exposure Assessment Tree



Rabbit, guinea pig, hamster, mouse, squirrel, chipmunk, opossum

Was the person bitten, or was there saliva contact from the animal to an open cut or mucous membrane of the individual? [1]

NO → Did the incident involve a bat? [4]

NO →

YES → Was the bat found indoors?

NO →

YES → Did the bat have access to a room where a person was:
- sleeping
- intoxicated
- mentally disabled
- a child

NO → Can the person be reasonably sure that a bite, scratch or contact to saliva has not occurred?

NO →

YES → **No PEP is recommended**

YES → What type of mammal was involved in the exposure?

Bites from small rodents seldom, if ever, require PEP. Consult if animal exhibits extremely unusual behavior.

Dog, cat, ferret

Livestock: Horse, cow, pig, goat

Wildlife: Bats, skunks, fox, raccoon, coyote, wolf-hybrid

Is the animal available for a 10-day observation period?

NO → Can the animal be euthanized for rabies testing?

NO →

YES → Can the animal safely be captured for rabies testing?

YES →

NO → **Recommend PEP [3]**

YES → Test animal for rabies.[2] What is the result?

- Negative (−) → NEGATIVE → **No PEP is recommended**
- Unsuitable (?) → **Consider all factors: Nature of contact, rabies epidemiology, animal species and animal behavior. May need to recommend PEP.**
- Positive (+) → POSTIVE → **Recommend PEP [3]**

YES → Does the animal show any signs of illness?

NO →

YES → Evaluate health by veterinarian.

Sick → Test animal for rabies.[2] What is the result?

Healthy → **No PEP is recommended**

[1] All bites and wounds should receive proper wound care. Assess the need for a tetanus booster.

[2]The animal should be taken to a facility to have the head removed (except bats). Submit specimen to the Veterinary Diagnostic Laboratory in Bozeman (406-444-4885). There is a charge for this testing. Please call for current testing fees.

[3] Refer to the Advisory Committee on Immunization Practices for guidance on post-exposure prophylaxis (PEP) recommended to prevent rabies infection.

[4] Bats pose a particular risk of rabies in Montana. PEP should be considered when contact between a human and a bat has occurred, and assessment may go beyond this assessment tree depending on the complexity of the situation.

Prepared by the Communicable Disease Epidemiology Program
406-444-0273
dphhs.mt.gov/publichealth/cdepi

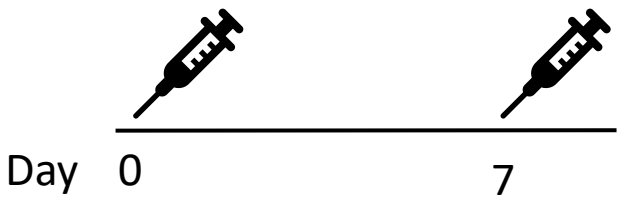
MONTANA DPHHS

Rev. 3/2017

100% Preventable

- Avoid animal bites
- Recognize signs of rabies in animals
- Vaccinate animals and humans
- Seek immediate wound care and post-exposure prophylaxis (PEP)
- PEP 100% effective in preventing rabies in humans
- No validated or recommended PEP for animals

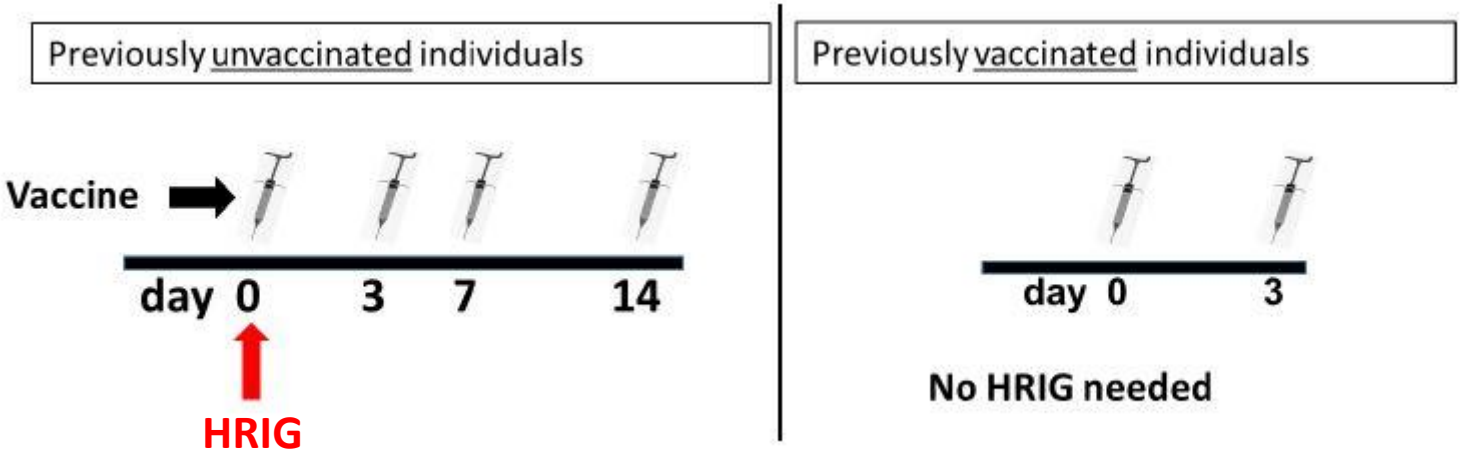
Pre-Exposure Rabies Vaccination for Humans



- New 2-dose series
  - Must align with ACIP recommendations to be considered previously vaccinated
- Intended to simplify the post-exposure prophylaxis
- Not universally effective without PEP after recognized rabies exposure
- Recommended for veterinarians and support staff
  - Other risk categories, can consult with DPHHS/LPH

Post-Exposure Prophylaxis

- Recommended when exposed to a positive rabid animal or when rabies exposure can not be ruled out
- Can be delayed while observing or testing the animal



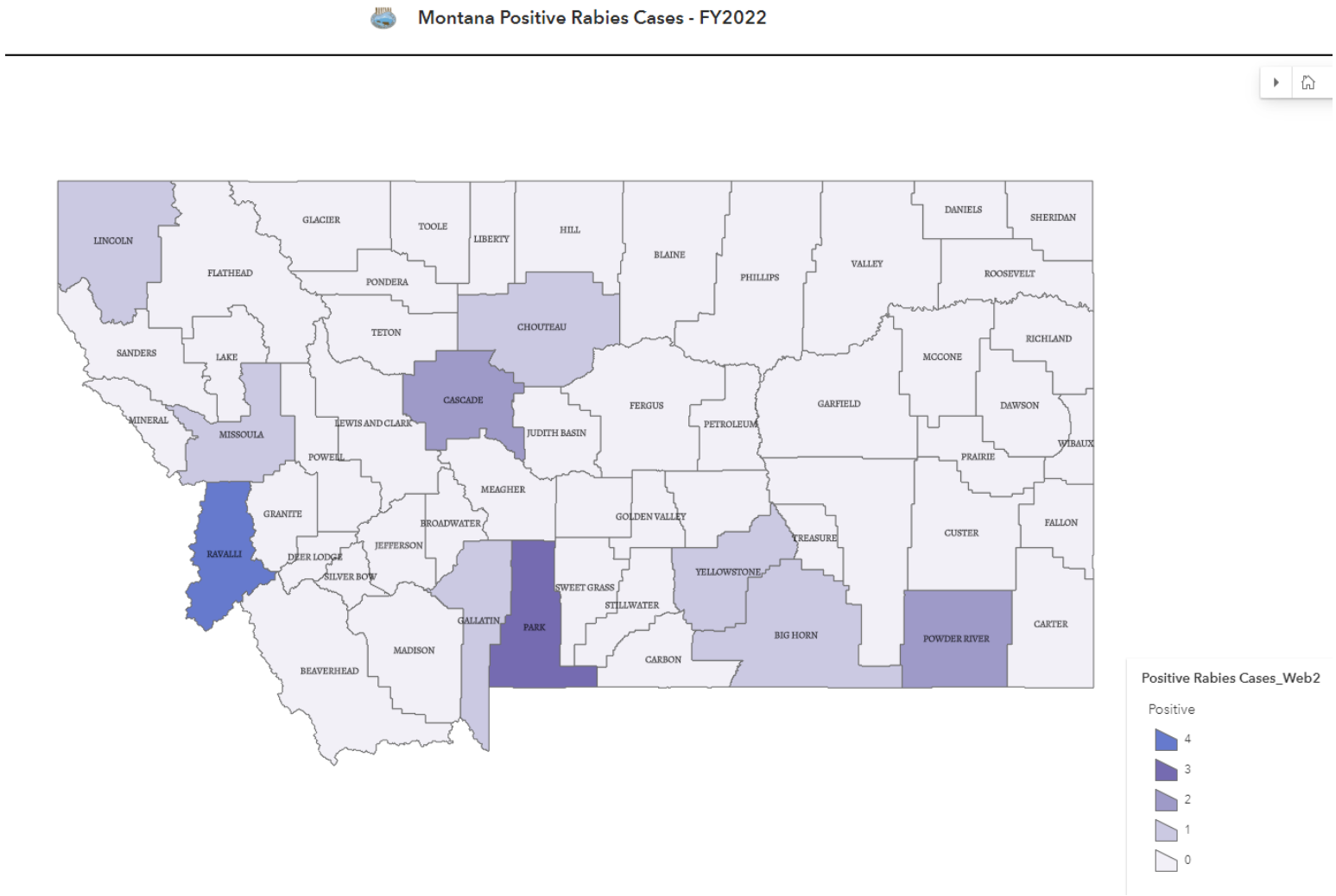
Disease in Animals

- All mammals are capable of being infected with and transmitting rabies
- Transmission occurs most commonly from the bite of an infected animal
  - Virus is contained in saliva
- Signs/symptoms include:
  - Changes in behavior: unusual aggression, friendliness, or fearfulness
  - Difficulty swallowing, increased drooling, voice change, paralysis, seizures, death
- Dogs, cats, and ferrets can secrete rabies virus in saliva for up to 10 days before showing signs of disease

Rabies in MT

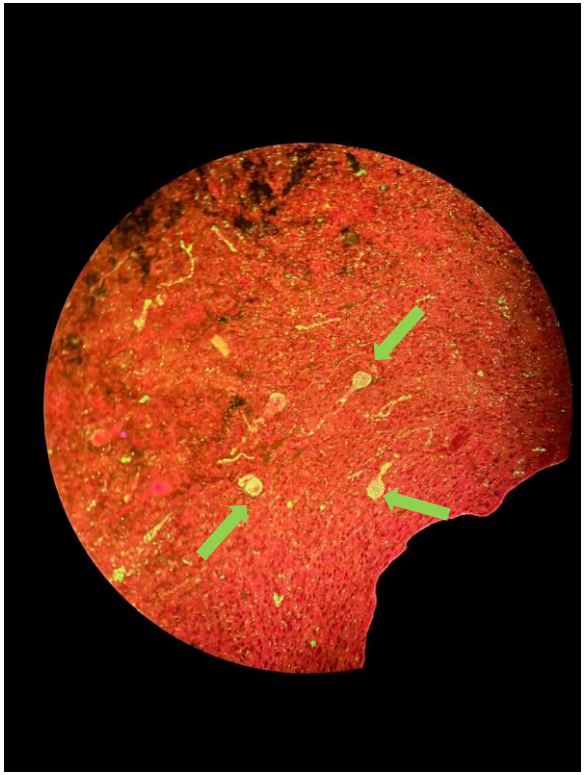
- 436 rabies tests completed in FY22
  - Positive rabies results:
    - 13 bats
    - 2 skunks
    - 1 cat
    - 1 dog
    - 1 horse
- When a terrestrial rabies case is identified the county is issued a 60-day quarantine

Montana Positive Rabies Cases - FY2022 (arcgis.com)



Diagnosis in Animals

- Post-mortem
  - Direct Fluorescent Antibody (DFA)
    - CDC approved method
    - Must be an approved laboratory
    - Must have appropriate anatomical sites present
    - Positive vs Unsuitable vs. Negative
  - Confirmatory Diagnostics
    - PCR – only performed by CDC
    - Variant typing
      - Combination of PCR and specific DFA sub-testing
    - IHC – not routinely performed by non-reference labs



Apple-green fluorescence of rabies virus in bovine neuron bodies (MVDL)

Diagnosis in Animals

- No ante-mortem testing options for definitive diagnosis
- Serology
  - Only for titers
    - Cannot differentiate between exposure or vaccination
  - Fluorescent Antibody Virus Neutralization (FAVN)
    - Response to vaccination (>0.5 IU/mL is sufficient)
    - May be required for international travel
    - Performed by Kansas State
  - Rapid Fluorescent Foci Inhibition Test (RFFIT)
    - Endpoint titer vs. Vaccine potency
    - Performed by Kansas State
  - Remember that with either test, a titer of >0.5 IU/mL indicates robust immune response but does not give assurance of complete protection against disease in <u>every</u> individual animal!

Post-Mortem Testing: Lab Submissions

- Bats and very small mammals (e.g., rodents)
  - Humane euthanasia
    - Inhalant: isoflurane, sevoflurane, CO2 (paired with injectable)
    - Injectable: barbiturates, dissociative agent combos (e.g., Ket/Val), 70% ethanol IP (only in bats smaller than mice)
    - Unacceptable: cervical dislocation/decap, exhaust fumes, lighter fluid, blunt force, drowning, freezing, etc.
  - Packaging
    - Send whole animal – do not remove head!
    - Refrigerate and do not freeze
      - Autolysis happens quickly
      - Freeze-thaw can damage tissue
    - Hard sided primary container (deli cup, jar, etc.), ice pack in leak proof secondary container
    - Place paperwork in separate plastic ziploc bag, place on top of packaged animal
    - Send overnight to lab, if possible
  - MVDL: DFA performed same day if received before 2pm
    - $36.00/specimen

Post-Mortem Testing: Lab Submissions

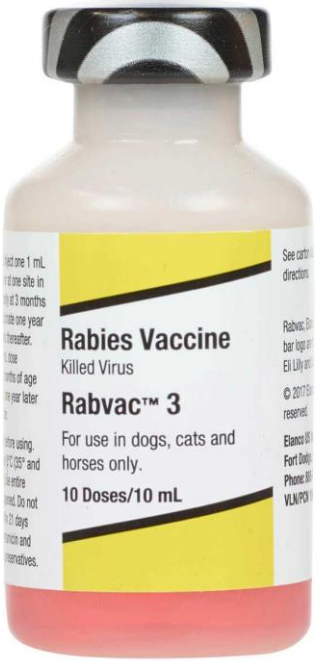
- Small mammals: cats, dogs, raccoons, skunks, etc.
  - Sampling and Packaging
    - Disarticulate head (if very small, can send whole carcass)
      - Necessary anatomic sites: brain stem, cerebellum, hippocampus
      - No need to remove brain from calvarium or remove skin from skull
      - Refrigerate but do not freeze
    - Leakproof primary container or ziploc bag, absorbant material, leakproof secondary container with icepack
    - Place paperwork in separate clean ziploc and place on top of packaged specimen inside secondary container
    - Send overnight if possible
  - MVDL: DFA performed same day if received before 2pm
    - $36.00/specimen

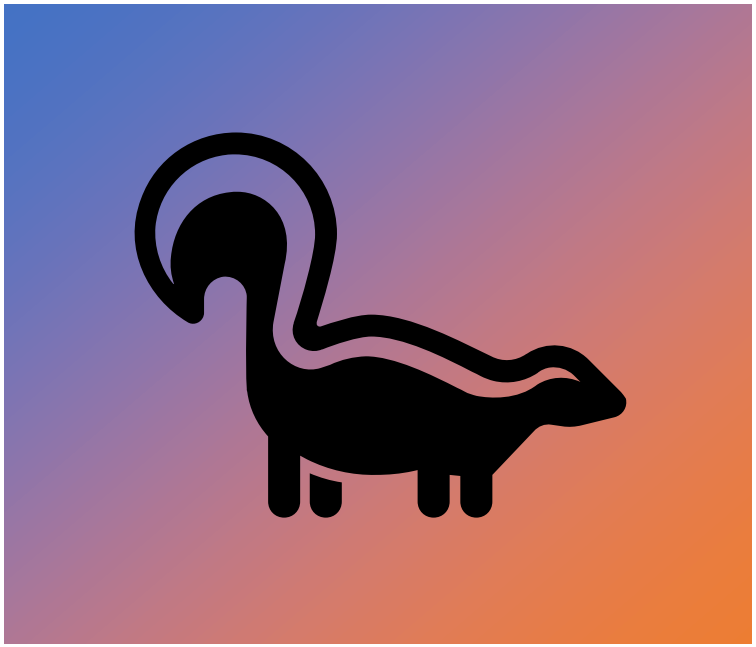
Post-Mortem Testing: Lab Submissions

- Large mammals: horses, cattle, goats, sheep, etc.
  - Sampling and Packaging
    - Disarticulate head, may remove brain or send in whole skull
      - If removing the brain, be careful not to damage necessary sites: brain stem, cerebellum, hippocampus
        - Send whole brain
      - Do not place half of the brain in formalin! Send whole brain FRESH!
      - Place whole brain in leakproof primary container, place in leakproof secondary container with icepack, include paperwork in a separate clean ziploc bag and place on top of primary container
  - MVDL: DFA performed same day if received before 2pm
    - $67.00/specimen, includes histopathology

Prevention in Animals

- Approved rabies vaccines are available for cats, dogs, ferrets, horses, cattle, and sheep
- Domestic animals should be vaccinated according to the Rabies Compendium
- Keep pets away from wildlife
  - If an interaction/exposure occurs with a wild mammal (especially bats, skunks, raccoons, foxes, coyotes) an attempt should be made to safely collect the wild animal for rabies testing
  - If an exposure occurs, pet needs to receive rabies vaccine booster immediately

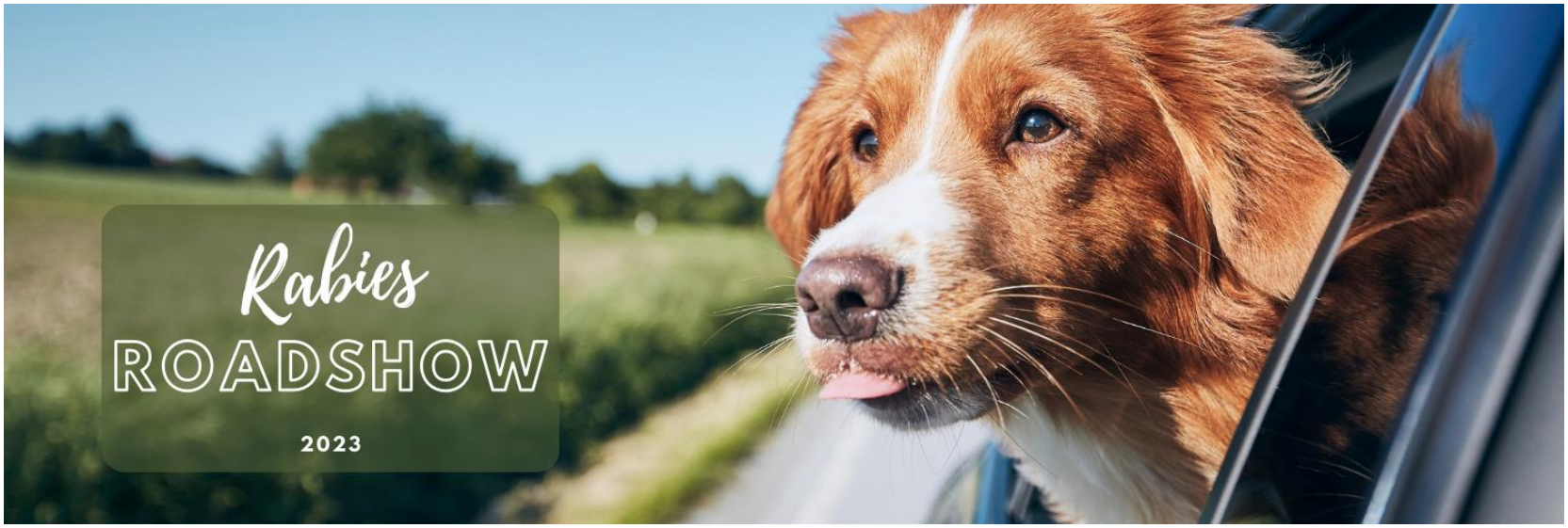




Wildlife Concerns

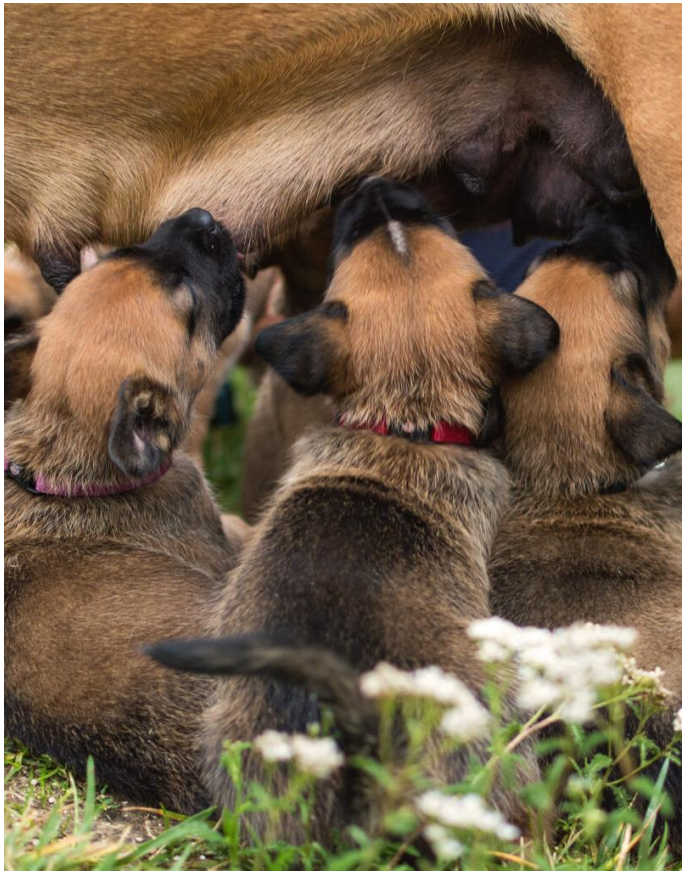
- Most cases of rabies in the U.S. occur in wild animals
  - Bats, skunks, raccoons, coyotes, and foxes
- Successful use of oral vaccine distributed to control fox rabies in Europe and Canada
- Use of rabies vaccine eliminated coyote rabies in southern Texas and limited expansion of raccoon rabies from the east

Rabies Management Training



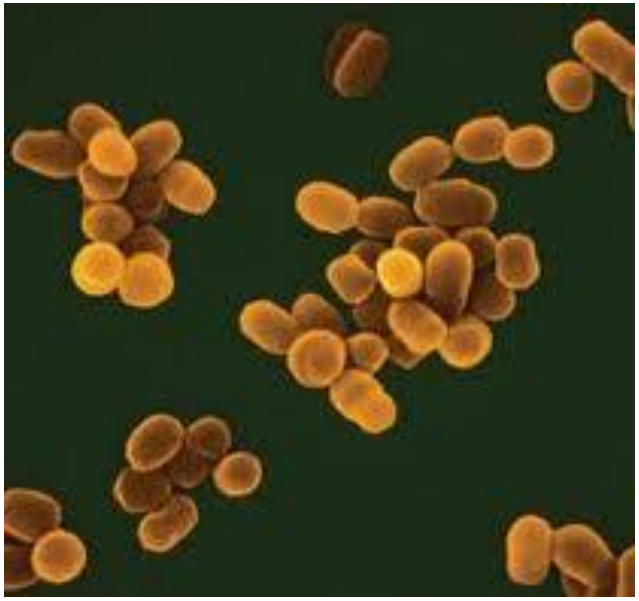
1 remaining training: July 11, 2023 9am – 4 pm
VIRTUAL!
Sign up here: https://form.jotform.com/231206644467153
Or contact Jessica Lopeman for more information
Jessica.Lopeman@mt.gov 406-444-3165

Brucellosis



Brucella Genus

- Gram-negative, non-motile coccobacilli
- Multiple species associated with certain hosts
- Withstands drying, especially when organic material present
- Viable for months in optimal conditions (high humidity, low temperatures, and no sunlight)
- Survival times of years in frozen meat
- **Select Agent**: *B. abortus*, *B. melitensis*, and *B. suis* isolates/cultures
- **Category B Bioterrorism Agent**

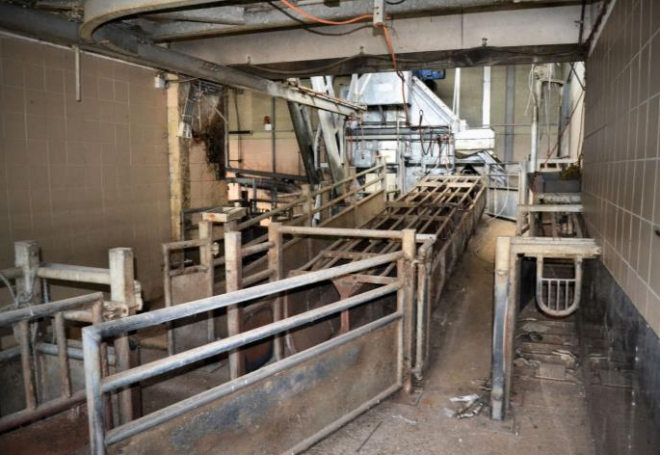


History

- 450 BC — Hippocrates referenced disease in his *Epidemics* writings
- 429 BC — Believed to be the plague described in Sophocles' *Oedipus Rex*
- 60 AD — Apostle Paul considered to be infected following shipwreck on Island of Malta
- 1887 — British physician David Bruce isolated organism from spleen samples of fatal cases in Malta
    - Surgeon Captain M. Louis Hughes assisted David Bruce with his studies and first named the disease 'undulant fever', *Micrococcus melitensis.*
- 1887 — Bernard Bang isolated organism causing abortions in cattle in Denmark, *Bacillus abortus*
- 1905 — Introduced into the U.S. through 65 Maltese goats
- 1918 — Alice Evans showed *Bacillus abortus* caused human brucellosis

Brucella Species and Reservoirs

- *B. abortus* — primarily cattle, bison, buffalo
  - Elk, camels, deer, dogs, horses, sheep
- *B. suis* — primarily pigs
  - Wild hares, reindeer, wild caribou, rodents
- *B. melitensis* — primarily goats and sheep
  - Cattle
- *B. ovis* — sheep, primarily rams
- *B. canis* — dogs
- *B. maris, B. pinnipediae, B. cetaceae* — marine mammals (seals, sea lions, walruses, dolphins, porpoises, whales, otters



Transmission

- Ingestion
  - Raw milk, unpasteurized dairy products
  - Undercooked meat
- Contact with Mucous Membranes and Breaks in the Skin with Infected Materials
  - Animal abortion or reproductive tract tissues/fluids
  - Vaccine splashes
- Aerosolization
  - Laboratory, abattoirs
  - Pens, stables, slaughterhouses
- Accidental Self-Inoculation with Vaccines
  - Strain 19, RB-51, Rev-1
  - Needle sticks (injections), conjunctival splashes, wound splashes
- Person-to-person (rare)
  - Breast milk from an infected mother to her child
  - Transplacental transmission
  - Contaminated tissue transplant
  - Sexual contact

People at Highest Risk for Exposure

- Occupational disease
  - Livestock producers
  - Veterinarians
  - Abattoir workers
  - Meat inspectors
  - Lab workers
- Hunters
- Travelers
- Consumers
  - Unpasteurized dairy products

Epidemiologic Trends in Diseases

- ~100 reported human cases per year in the U.S.
- Montana has not reported a case in a human since 2017.
  - Note: we have had **two** individuals clinically diagnosed with brucellosis this year (2023), but infection is believed to be linked to international travel to areas where unpasteurized milk products are more common. Montana is not officially reporting these as cases as they do not meet reporting requirements established by CSTE.
- Higher incidence reported worldwide, especially in Mediterranean countries, the Middle East, Africa, central Asia, central and South America, India, and Mexico.
- Likely underreported due to it being difficult to recognize clinically.
- Among most common laboratory-acquired bacterial infections.

Disease Manifestation in Humans

- Incubation period variable: usually 5–60 days
  - Lac[illegible]
- Acute
  interm
  weakn[illegible]lgia,
  fatigu[illegible]
- Can b[illegible]
- Multi-systemic
- Can last days, months, or years if not adequately treated

Nonspecific symptoms can make it difficult to include as part of a differential, especially if the patient doesn't appear to have any obvious exposures.

Diagnosis in Humans

- Isolation of organism- **GOLD STANDARD FOR DIAGNOSIS!**
  - Most commonly isolated from blood
  - Also, may be isolated from bone marrow, cerebrospinal fluid, urine wounds, purulent discharge, joint fluid, or tissue
- Serum agglutination test
  - *B. abortus, B. melitensis, B suis*
  - NO serological test available for *B. canis* or RB51
- Immunofluorescence, ELISA
- PCR
  - Available for isolates to identify *Brucella* species
- **Reportable** disease to local, state, and federal health officials

Treatment

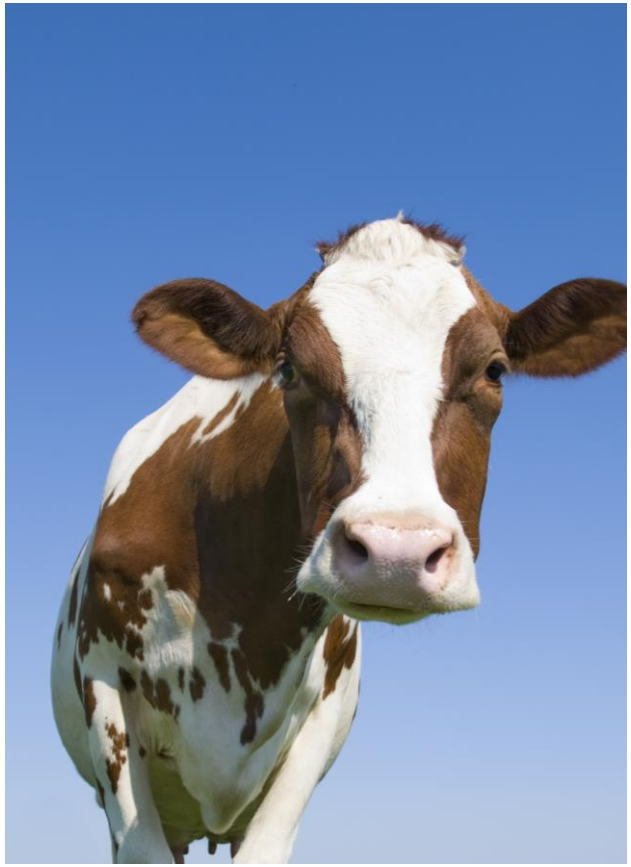
- Antibiotic Therapy
  - Treatment of choice: combination doxycycline and rifampicin, or streptomycin, for at least 6 weeks
  - Rifampicin not effective in treating brucellosis caused by exposure to RB51
- ~5%–15% uncomplicated cases treated with doxycycline and rifampicin will experience a relapse in disease
  - Sequestered bacteria
  - Treat with same regimen
- ~50% of cases treated with monotherapy will relapse

Prevention in Humans

- Do not consume:
  - Undercooked meat
    - Note: freezing, smoking, drying, and pickling do not kill *Brucella* species
  - Unpasteurized dairy products (e.g., milk, cheese, ice cream), especially in endemic countries
    - Note: If you are unsure if the dairy product is pasteurized, do not eat it
- PPE for hunters when handling viscera of animals
- PPE for at-risk occupations (veterinarians, laboratorians)
  - Rubber gloves, goggles, gowns or aprons

Disease in Animals

- In its principal host brucellosis causes spontaneous abortion (usually between 5-7 months of gestation) or birth of weak offspring, reduced milk production, and infertility
  - Infected animals may appear normal
- Transmission
  - Direct contact with or ingestion of infected blood, placenta, fetus, or uterine secretions
- Incubation period is from 2 weeks to 1 year



Diagnosis in Domestic Animals

- Smooth-type Brucellae (*B. abortus, B. melitensis, B. suis*)
  - Serology is primary method of diagnosis
    - Bedside:
      - Card test (Rose Bengal)
    - Methods used for DSA testing (used standalone or in series):
      - Fluorescent Polarization Assay (FPA)
      - Buffered Antigen Plate Assay (BAPA/BPA)
      - Complement Fixation (CF) test
    - Other methods (export, etc)
      - Standard Tube Agglutination Test (STT)
      - Standard Plate Agglutination Test (SPT)
      - ELISA (not yet approved in the USA)

- Rough-type Brucellae (*B. ovis* and *B. canis)* - ELISA only
  - Card test in small ruminants is not for Dx of *B. ovis*
- All of these are antibody tests and will not detect reactions to rough-type Brucellae
- Cannot distinguish between antibodies to different smooth-type brucellae species

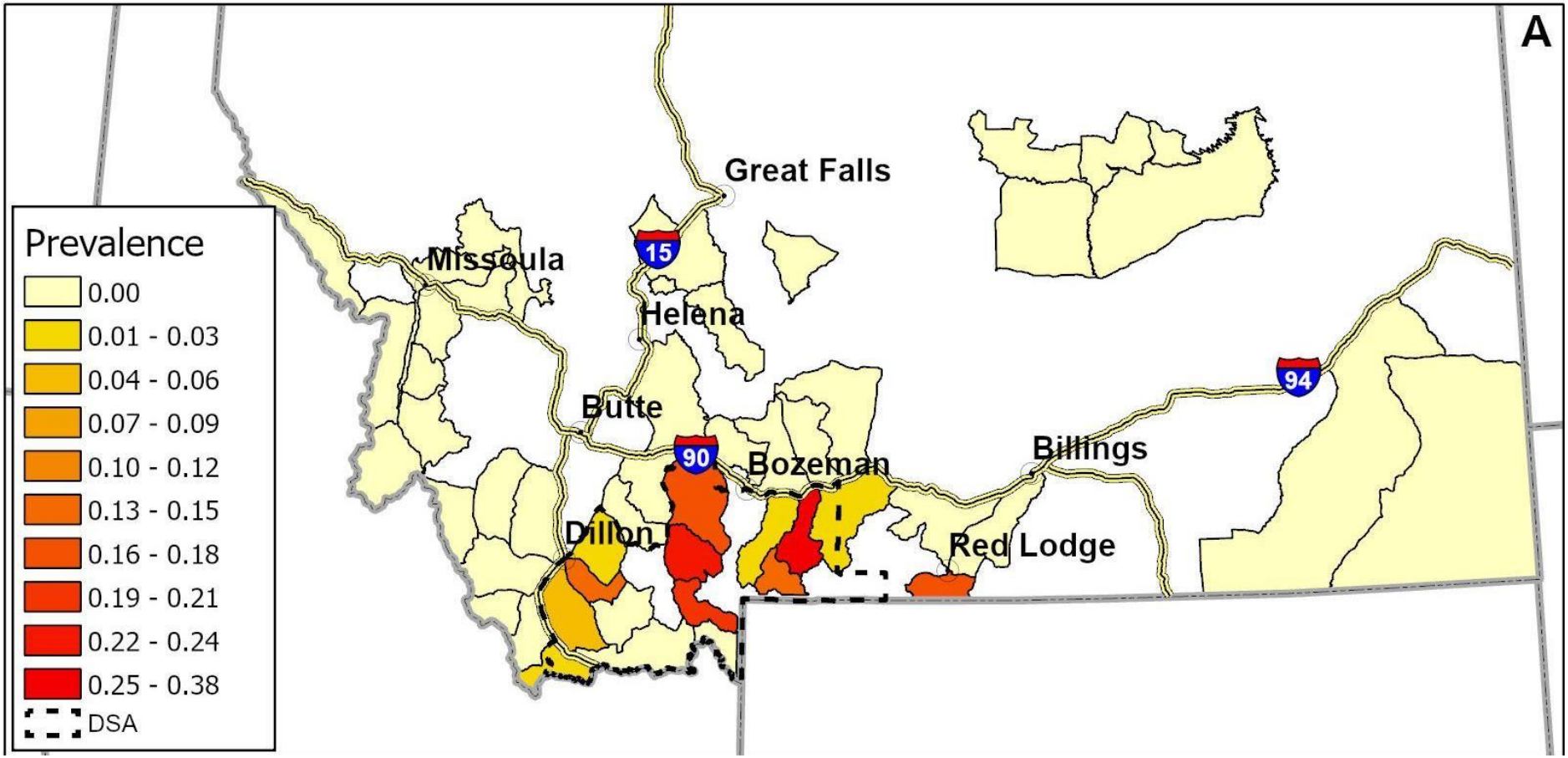
Treatment in Livestock

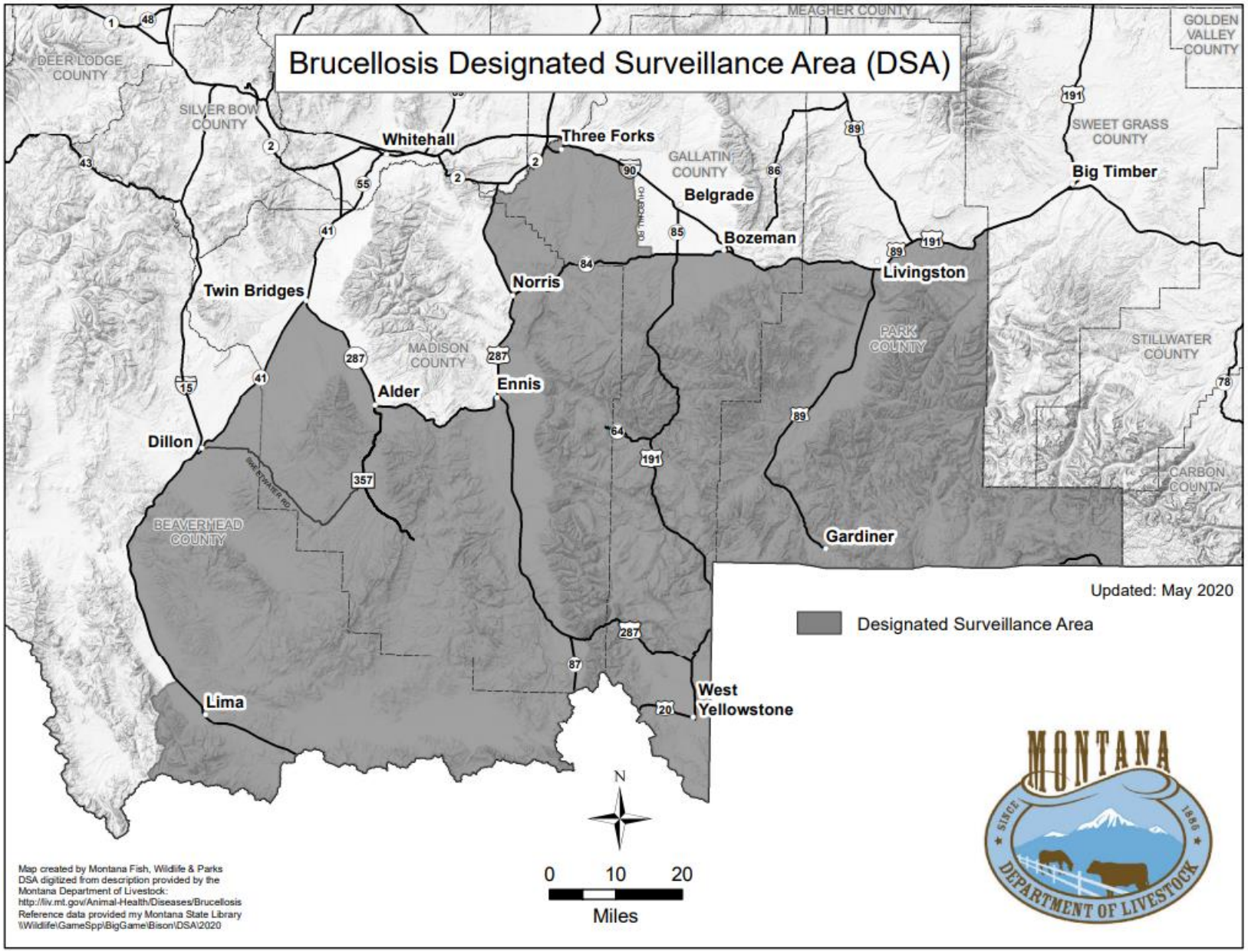
- No economically practical treatment for brucellosis in livestock
- Control relies on detection of infected herds and prevention of disease in non-infected herds
- Eradication program = repeat testing and culling of reactors

Prevention in Domestic Animals

- RB51 strain developed for vaccination of cattle
  - Effective at decreasing rate of abortion (~85-90%)
  - Less effective at preventing colonization
- Heifer calves should be vaccinated between 4-12 months old
- Montana: all sexually intact female or domestic bison and cattle >12 months or older in the DSA (designated surveillance area) and surrounding region must be official vaccinates

Estimated Seroprevalence in elk in SW Montana ranges from 0-38%.
-Targeted Elk Brucellosis Surveillance Project




Brucellosis Designated Surveillance Area (DSA)
MEAGHER COUNTY
GOLDEN VALLEY COUNTY
DEER LODGE COUNTY
SILVER BOW COUNTY
SWEET GRASS COUNTY
Whitehall
Three Forks
GALLATIN COUNTY
Big Timber
Belgrade
Bozeman
Livingston
Norris
Twin Bridges
PARK COUNTY
STILLWATER COUNTY
MADISON COUNTY
Alder
Ennis
Dillon
CARBON COUNTY
BEAVERHEAD COUNTY
Gardiner
Lima
West Yellowstone
Updated: May 2020
Designated Surveillance Area
N
0 10 20
Miles
Map created by Montana Fish, Wildlife & Parks
DSA digitized from description provided by the
Montana Department of Livestock:
http://liv.mt.gov/Animal-Health/Diseases/Brucellosis
Reference data provided my Montana State Library
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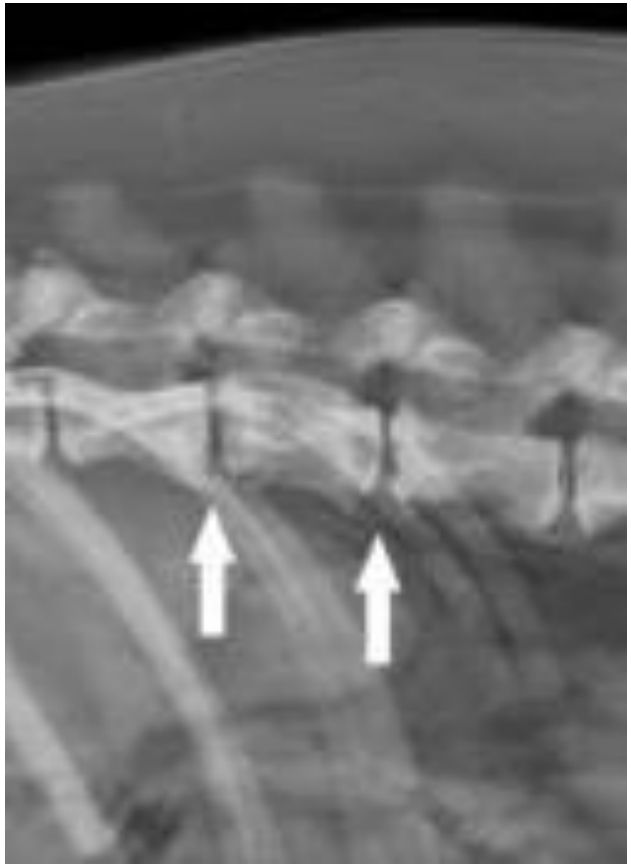
MONTANA
SINCE 1865
DEPARTMENT OF LIVESTOCK

Brucella canis

- Canine brucellosis is caused by the bacteria *Brucella canis (B. canis)*
- Domestic dogs are the only significant host
  - Dogs rarely become infected with the other *Brucella* sp.
- Transmission typically occurs through reproduction but can also be spread via ingestion or mucous membrane contact with contaminated bodily fluids, especially birthing fluids. Can be passed in utero
- Endemic in areas with large populations of intact, stray animals

B. canis Disease in Dogs

- Incubation period: variable, bacteriemia typically begins 1-4 weeks after infection
  - Abortions occur in the last trimester
- Clinical symptoms:
  - Reproductive abnormalities: abortion, still born or weak puppies, infertility
  - Genital abnormalities: epididymitis, orchitis, scrotal edema
  - Other: Discospondylitis, uveitis, lymphadenitis, unexplained lameness or pain, ADR



Diagnosis in Domestic Animals

- Rough-type Brucellae (*B. ovis, B. canis*)
  - Serology is primary screening method, may confirm with culture or PCR (not always reliable)
    - ELISA – *B. ovis* and *B. canis*, MVDL (other labs starting to bring online)
    - Indirect Fluorescent Antibody (IFA) - *B. canis* only, MVDL & many other labs
    - Tube Agglutination Test (TAT) - *B. canis* only, NVSL
    - Multiplex Assay – *B. canis* only, Cornell
    - AGID – *B. canis* only, Cornell
    - RSAT/2ME - permanently discontinued, no longer offered by any lab
  - Antibody tests
    - The above serology tests will not detect antibodies to smooth-type Brucellae
    - Positive - Infection vs. Exposure vs. Cross-reaction; retests may be necessary
  - Cannot distinguish between *B. ovis* and *B. canis* infection by antibody test, but host animal species implies infecting brucella species
    - *Important to keep in mind with working sheep dogs
  - DOL website has *B. canis* information, case definitions, testing recommendations, veterinarian resources, etc.

B. canis Treatment in Dogs

- *B. canis* is considered an incurable and lifelong infection in dogs
    - Bacteria can sequester in areas such as the prostate, uterus, lymph nodes, or spleen making it difficult for antibiotics to penetrate and eliminate the bacteria fully
- Treatment/management: Euthanasia recommended
        - Alternative option: Spay/neuter, combination of medically important antibiotics used long-term, periodic serologic retesting/monitoring, lifelong isolation

B. canis Prevention in Dogs

- No vaccine available
- Spay/neuter decreases risk for transmission from breeding
  - May decrease bacterial shedding in urine
- Testing prior to adoption
  - Euthanasia of all positive dogs
- Yearly testing of breeding groups
  - Breeding only non-infected dogs
- Purchasing dogs from rescues or breeders that require testing

B. canis- Implications for Human Health

- *B. canis* requires a large infectious dose (10^6 organisms/mL organisms) to cause infection in a human
  - **Reminder**: other *Brucella* species have a far lower infectious dose
- Risk of *B. canis* infection in humans appears low due to the infectious dose required, however the CDC estimates that the disease is likely underdiagnosed and under-reported
  - Immunocompromised people and children are at higher risk
- Symptoms are vague, flu-like, and wax-wane
- Diagnosis in humans difficult, requires blood culture
- Humans concerned with exposure should consult a physician
- DPHHS Q&A available on DOL webpage for animal caretakes with human health concerns

B. canis Prevention: Humans

- The risk of *B. canis* exposure in a household setting from simply touching a dog bowl or toy is low, especially if the owners practice good hand hygiene following contact with potentially contaminated items.
- Parents should encourage good hand hygiene with their children after interacting with household pets and ensure that items like food bowls and toys are kept out of reach of children who may mouth these objects.

B. canis Prevention: Humans

- When assisting with whelping:
  - Use proper PPE when handling animal bodily fluids, especially reproductive fluids
  - Avoid mucous membranes or abraded skin contact with all animal bodily fluids
  - Wear face mask, gloves, and eye protection when helping with whelping to prevent splash exposures
  - Do not give mouth to mouth resuscitation to still born puppies
  - Keep children away from birthing animals to prevent exposure
- Wash hands after interacting with animal bodily fluids even if you were wearing gloves and even if you do not suspect the animal to have *B. canis*.

Wildlife

- *B. canis* seropositive wildlife are uncommon
- Seropositive wildlife are occasionally detected (foxes, coyotes, raccoon, others).
- Yellowstone National Park survey of coyotes (1989-1993) - 0/100 seropositive
- Chile (2021) - 10.9% of 46 fox samples seropositive for B. canis but negative on PCR and culture
- MT FWP – 0/353 animals tested

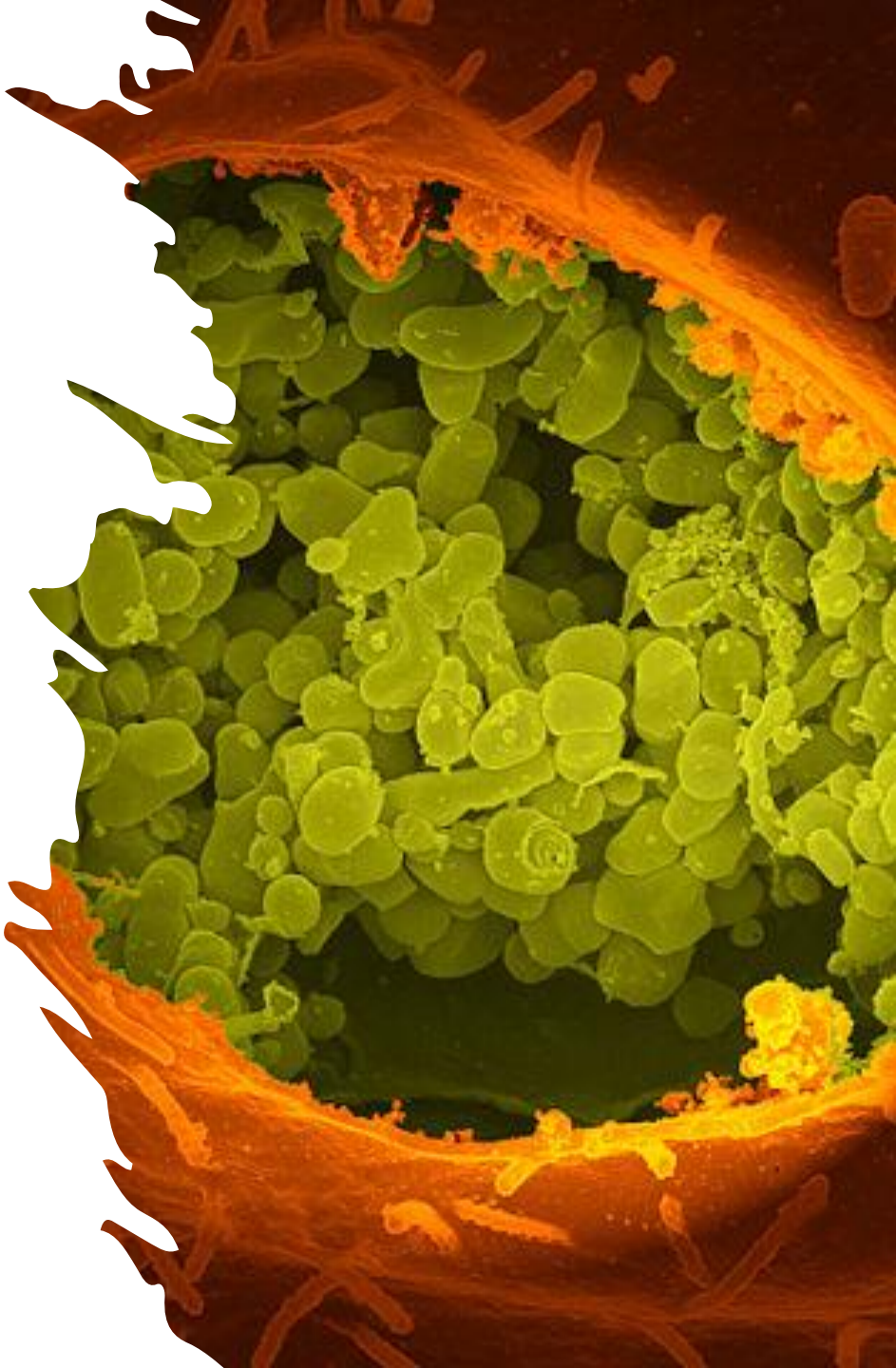
Wildlife Implications

- Brucellosis can affect bison and elk (*B. abortus*)
  - Has been found in moose, Dall sheep, caribou, and deer
- Eradication effort started in 1935 eliminated disease in cattle, however a reservoir of *B. abortus* remains in the Greater Yellowstone Area
- Transmission occurs through ingestion of bacteria from aborted fetuses, fetal membranes, and vaginal discharge
- In elk, abortion is most common during the late stages of the first pregnancy following infection. Normal pregnancies often occur after.
- Seropositive cow elk have reduced pregnancy rates compared to seronegative cow elk.
- In 82 seropositive "elk-years", 4 abortions, 61 live births, 17 undetermined.
- Not a population limiting disease

Q Fever

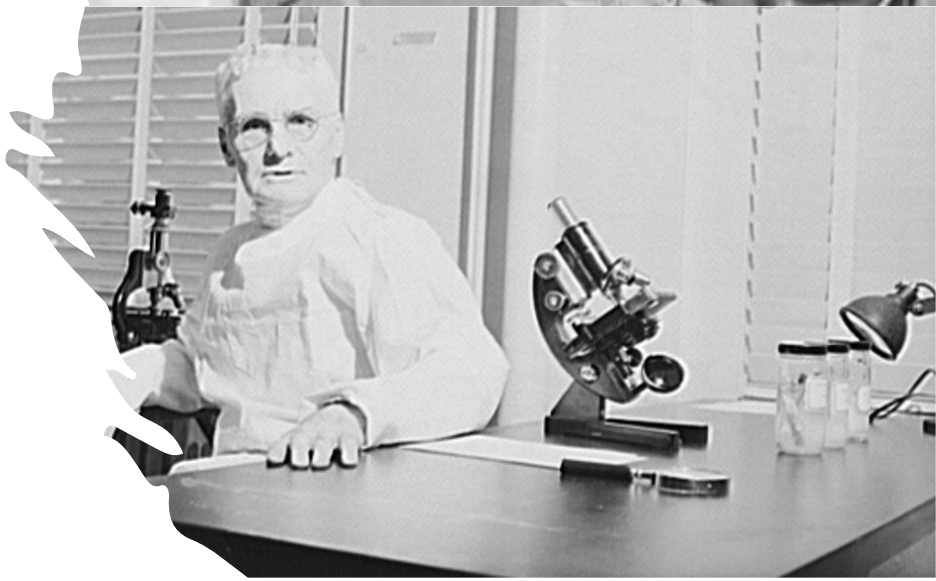
Coxiella burnetii

- Small, gram-negative coccobacillus
- Obligate intracellular pathogen
- Forms spore-like structures that are highly resistant to environmental conditions
- Bacteria can survive outside of a host for weeks to months
- Killed by pasteurization
- “Q” stands for “query”, which was applied when the causative agent was unknown
- Highly infectious, low infectious dose (<10 bacteria can make you sick)
- **Select Agent**
- **Category B Bioterrorism Agent**



History

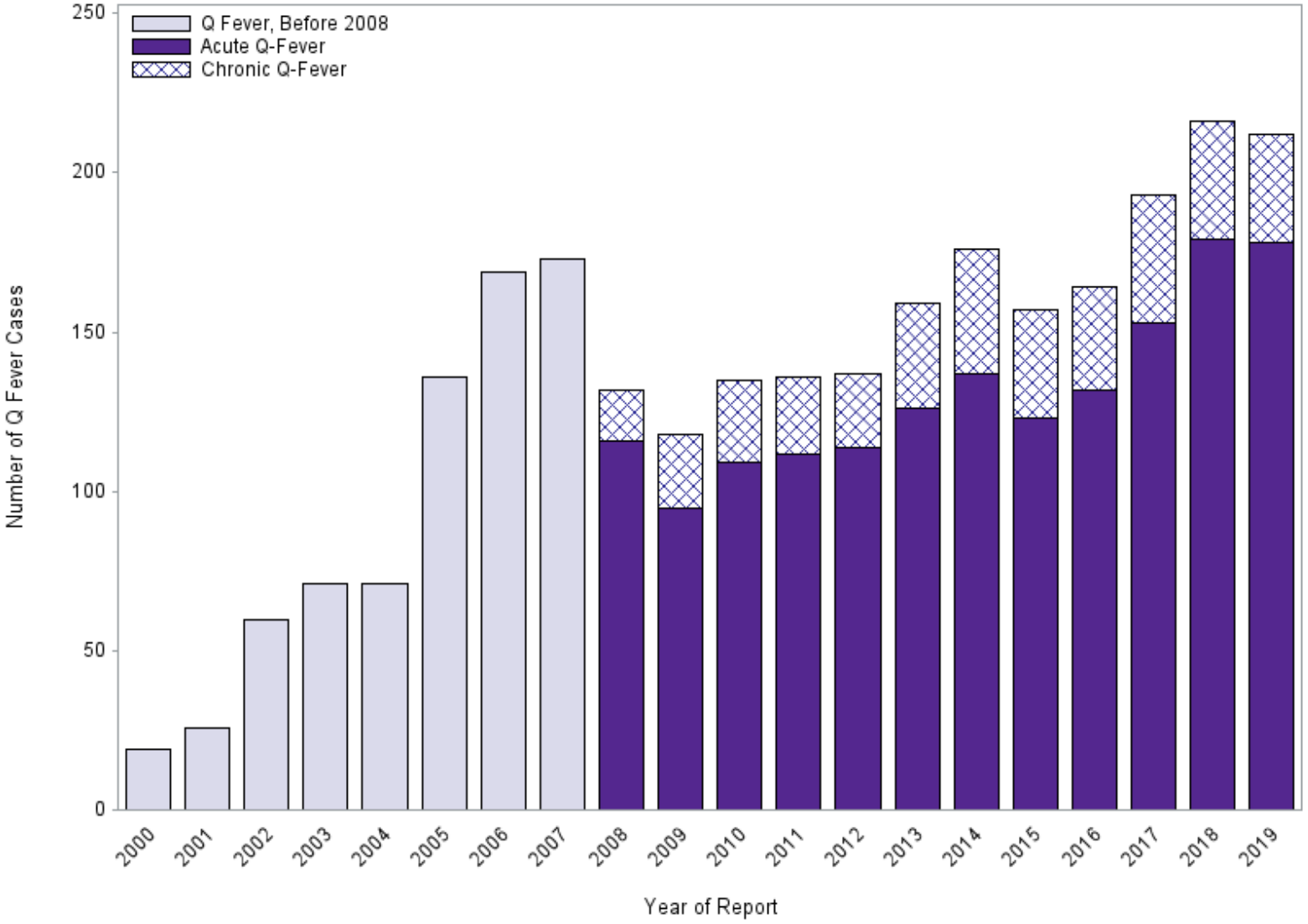
- 1935 — Q fever described by Edward Holbrook Derrick in abattoir workers in Queensland, Australia
- 1937 — Frank Macfarlane Burnet and Mavis Freeman isolated organism from one of Derrick's patients
- 1938 — H.R. Cox and Gordon Davis at **Rocky Mountain Laboratories** isolated the organism from ticks collected in Nine Mile, Montana.
  - Initially named "*Rickettsia burnetii*" since they believed it to be related to *Rickettsia rickettsia* (Rocky Mountain Spotted Fever).
  - Cornelius B. Philip proposed the creation of a new genus called "*Coxiella*" after H.R. Cox.
  - Renamed after Frank Mcfarlane Burnet and H.R. Cox to be *Coxiella burnetii*.



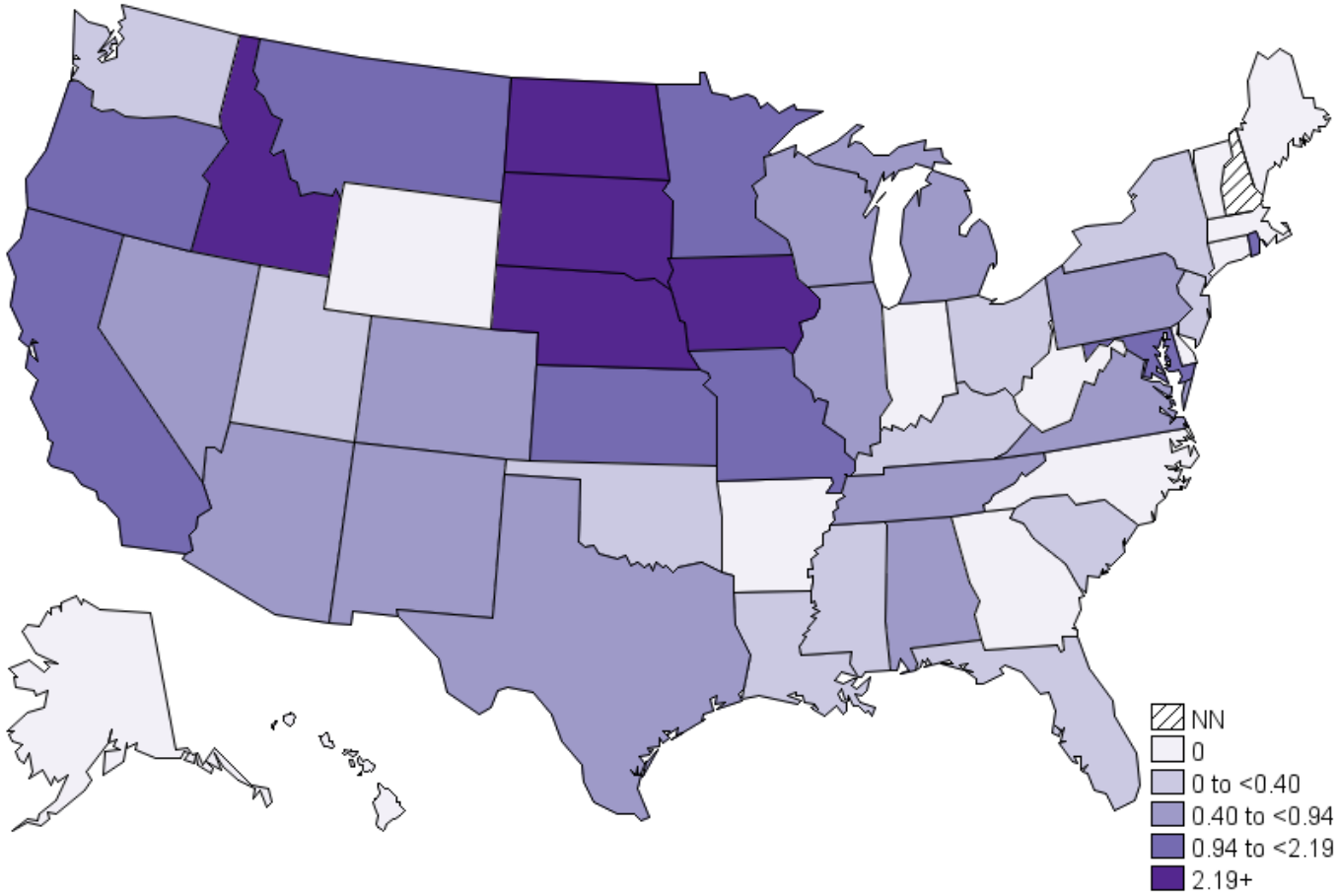
Modern Context

- Occurs worldwide (except New Zealand)
- Became a nationally notifiable disease in the United States in 1999.
- ~3 human cases annually in Montana, ~200 annually in the United States
- 2011 — Montana and Washington experienced one of largest Q fever outbreaks in U.S. (21 cases total, 15 in Montana alone)
- 2007–2010 — Netherlands experienced the largest outbreak ever reported (~4,000 cases)

Number of reported cases of Q fever –United States, 2000–2019



Annual incidence (per million population) of reported Q fever–United States, 2019. (NN= Not notifiable)



Reservoirs

- Domestic animals
  - **Most common**: cattle, sheep, goats
  - Also found in dogs and cats
    - A recent study showed seroprevalence in brown rats in Oxfordshire, United Kingdom. Cats, as frequent predators of rats, are important in maintaining the transmission cycle of *C. burnetii*.
- Ticks (Arthropods)
  - Important in maintaining the transmission cycle of *C. burnetii* between wildlife
  - Vector is not required to transmit the bacteria from host to host
- Birds
- Reptiles
- Wild mammals (e.g., wild rabbits)

Occupational and Environmental Hazard

- Farmers
- Livestock producers
- Veterinarians and technicians
- Meat processors/abattoir workers
- Laboratory workers

Transmission

- Aerosol
  - Primary method of transmission
- Direct contact (e.g., touching, being licked)
  - Infected animals or contaminated materials
- Ingestion
  - Unpasteurized dairy products
- Rare:
  - Tick-bite transmission
  - Person-to-Person through sexual intercourse, from a pregnant woman to her fetus, blood transfusions, bone marrow transplants

Disease in Humans

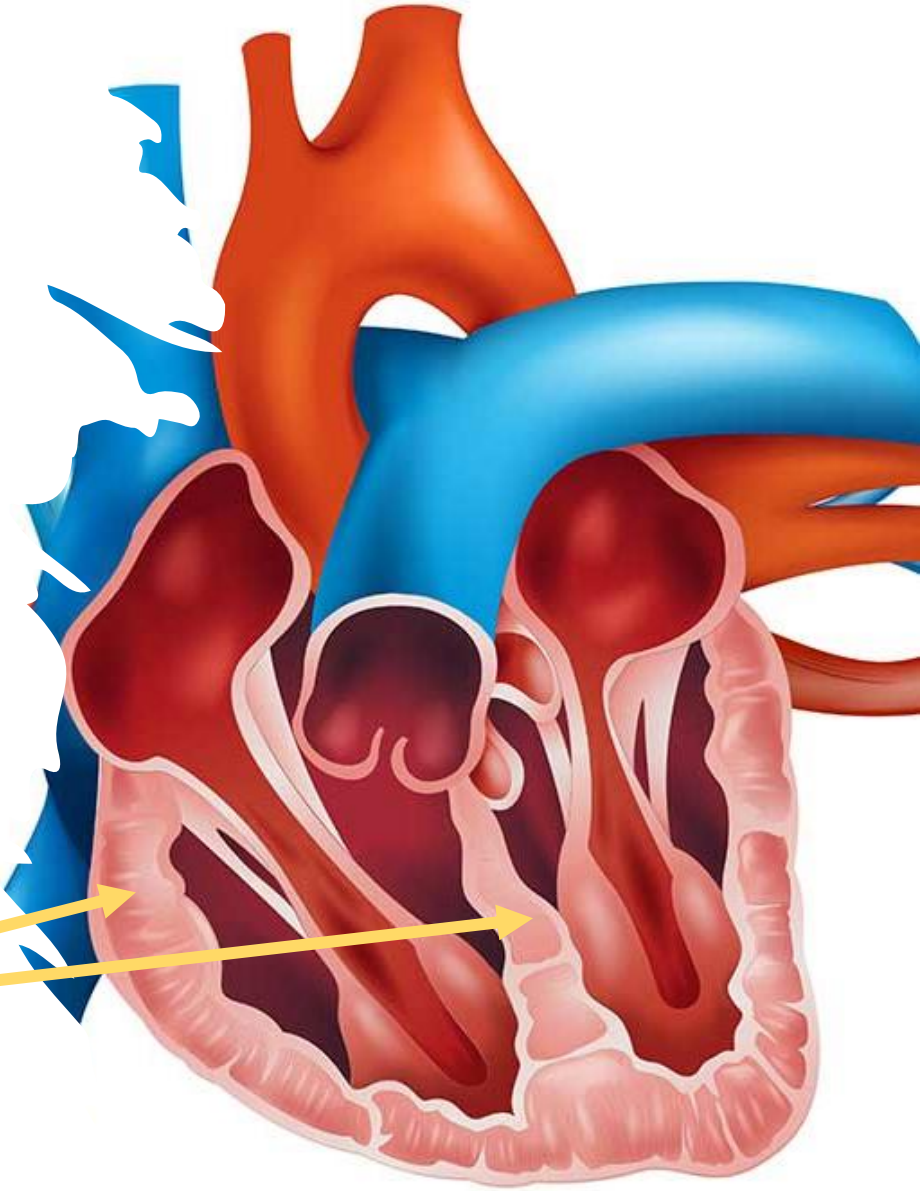
- Incubation is dose dependent, typically 2–3 weeks (range: 3–30 days)
- Q fever is highly infectious, and as few as 1-10 *C. burnetii* organisms may cause disease in a susceptible person
- Clinical manifestations extremely variable
  - Asymptomatic in 50%–60% of cases
  - Acute
  - Chronic

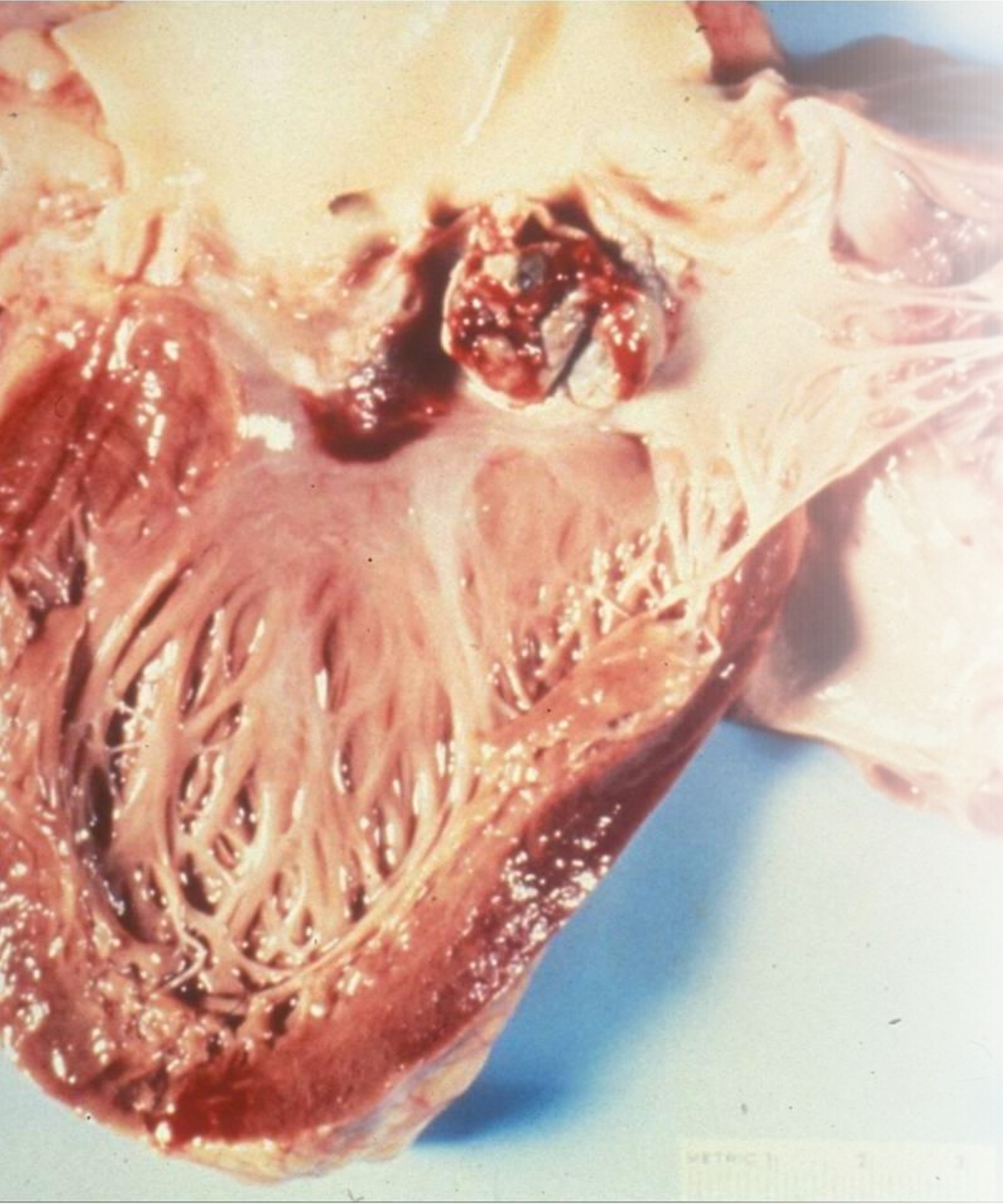
Acute Disease

- Self-limiting flu-like illness
  - High fevers (up to 104–105°F) lasting up to 2 weeks
- Atypical pneumonia (30%–50%)
- Hepatitis
- Mortality rate 1%–2%
- Pregnant women
  - 98% asymptomatic
  - Linked to premature delivery, miscarriage, placentitis, and low birth weight

Chronic Q Fever

- <5% of acutely infected persons
- Persistent focalized infection
- Variable with presentation: may present as early as 6 weeks after an acute infection or years later
- Persons at highest risk:
  - Pregnant women
  - Immunocompromised persons
  - Persons with a pre-existing heart valve defect
- Manifestations
  - Endocarditis
  - Aortic aneurysms
  - Osteoarthritis and osteomyelitis



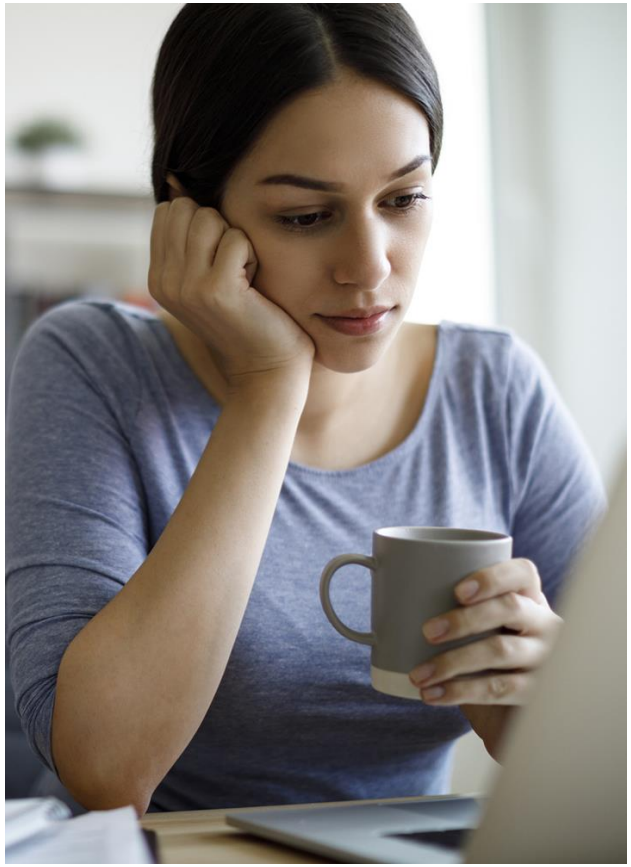


Endocarditis

- 60%–70% of all chronic Q fever manifestations
- Case fatality rate in untreated cases 25%–60%
- Requires early diagnosis
- Long-term antibiotic therapy (≥18 months)
- 50%–60% need valve replacement

Q Fever Fatigue Syndrome (QFS)

- 1996 — first recognized by researchers in Australia and Great Britain
- ~20% of acutely infected persons develop protracted debilitating fatigue syndrome lasting 5–10 years
- Long-term fatigue following acute Q fever infection, different than chronic Q fever infection
    - Similar to chronic fatigue syndrome (CFS)
- Organism remnants persist in host after initial infection causing cell-mediated hypersensitivity
- Associated with musculoskeletal complaints, neurocognitive problems, sleeping problems, headache, respiratory tract problems, and mood disorders
    - Low-grade inflammatory component



Q Fever Diagnosis in Humans

- Acute phase (phase II antigen)
  - Serology
  - PCR- most sensitive during first week of illness
  - ELISA
  - Immunohistochemistry
  - Culture
- Chronic phase (phase I antigen)
  - Serology
  - PCR
  - Immunohistochemistry
  - Culture
- Post Q-fever fatigue syndrome
  - Complex diagnosis with medical exam and Chronic Fatigue Syndrome questionnaires
- **Reportable** disease to local, state, and federal health officials

Diagnosis in Humans
Phase I? Phase II? Antibodies? ELISA?

Type of Test Performed	Test Result	Case Status	Classification
IFA to Detect Antibodies to *C. burnetii* antigens	IgG antibody to **phase I** antigen ≥ 1:800 (**phase II** IgG titer may be elevated, but **phase I** is higher)	Confirmed	**Chronic**
	IgG antibody to **phase I** antigen ≥ 1:128 and < 1:800	Probable	**Chronic**
	Serological evidence of a fourfold change in IgG antibody to **phase II** antigen between paired serum samples (first sample taken during the first week of illness and then a second sample taken 3-6 weeks later)	Confirmed	**Acute**
	Single IgG titer of ≥ 1:128 to **phase II** antigen (**phase I** titers may be elevated as well)	Probable	**Acute**
Enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination	Elevated **phase II** IgG or IgM antibody reactive with *C. burnetii* antigen	Probable	**Acute**
Polymerase Chain Reaction (PCR) Assay	Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by PCR assay	Confirmed	**Chronic** if patient has evidence of endocarditis **Acute** if no evidence of endocarditis
Immunohistochemistry (IHC) Methods	Demonstration of *C. burnetii* antigen in a clinical specimen by IHC		
Culture	Isolation of *C. burnetii* from a clinical specimen by culture		

Treatment in Humans

- Acute
  - Doxycycline for 14 days
    - If patient is a child, they should receive cotrimoxazole for 14 days (if the case was severe, doxy is the preferred treatment)
    - If patient is pregnant, they should receive cotrimoxazole for the remainder of the pregnancy
  - Most effective against severe disease if started within 3 days of symptom onset
- Chronic
  - Doxycycline in combination with hydroxychloroquine for 18-24 months
    - Surgical replacement of infected heart valve may be necessary
- Q Fever Fatigue Syndrome
  - **NO** evidence-based treatment with proven efficacy
  - Anecdotal positive effects with long-term doxycycline
  - Cognitive behavior therapy (CBT) has shown efficacy in treating chronic fatigue caused by other diseases
    - Clinical trial occurring in the Netherlands

Prevention in Humans

- Reduce the potential for exposure to infected tissue and fluids
- PPE for high-risk occupations
- Consume only pasteurized dairy products
- No commercially available vaccine in the U.S.

Disease in Animals

- Affects cattle, sheep, and goats
- Infected animals are often not visibly ill, but can shed bacteria in bodily fluids
- Infection causes late abortion and reproductive disorders (stillborn or weak offspring), mastitis, and metritis
  - Non-pregnant animals do not show clinical signs
- Transmission: aerosols of body fluids (esp reproductive fluids) or direct contact with infected materials (shed in milk and feces)
  - Persistent in the environment and can be spread from the environment

Diagnosis in Domestic Animals

- Primary screening/presumptive diagnosis by serology - not nearly as many options as in human diagnostics
  - ELISA (MVDL)
  - Complement Fixation (NVSL)
- PCR
  - Often multiplexed with Chlamydophila/Chlamydia in ovine abortion panels (many labs, also in development at MVDL)
  - Better used for confirmatory diagnosis with tissue (e.g., abortions)
  - May result in false negatives if used for screening
- Culture
  - Very difficult
  - Obligate intracellular organism, requires extensive purification and enrichment
  - Not routinely performed for diagnostic testing due to Select Agent status/BSL-3 requirements, lab worker risk, technical difficulty

Treatment in Domestic Animals

- No approved treatments for livestock
- Animals may recover without treatment or have no signs of disease
    - However, reproductive losses can recur and cause financial losses and culling of animals from the herd

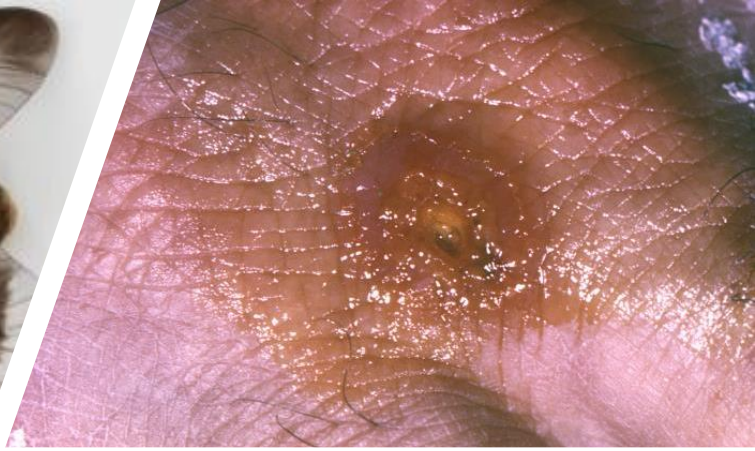
Prevention in Domestic Animals

- No vaccine available
- Carcasses, aborted fetuses, and placentas should be removed quickly to minimize spread from potentially infected materials
- Pregnant, infected females should be isolated from the herd
- Barns/birthing pens should be thoroughly cleaned
  - 10% bleach, 5% hydrogen peroxide, or 1% Lysol solution
- Proper composting of manure
- Minimizing exposure to dust and avoid spreading manure when windy

Wildlife Implications

- *C. burnetii* can spread between wildlife through ticks
  - The bacterium has been isolated from hard and soft-shelled tick species, bed bugs, flies, and mites
- Minimize contact of livestock with wildlife and practice tick and vector control on farms
- Very broad potential host range
- Australia found seroprevalence in deer ranging from 3-4%, typically lower than local small ruminants
- Seropositive wildlife generally asymptomatic



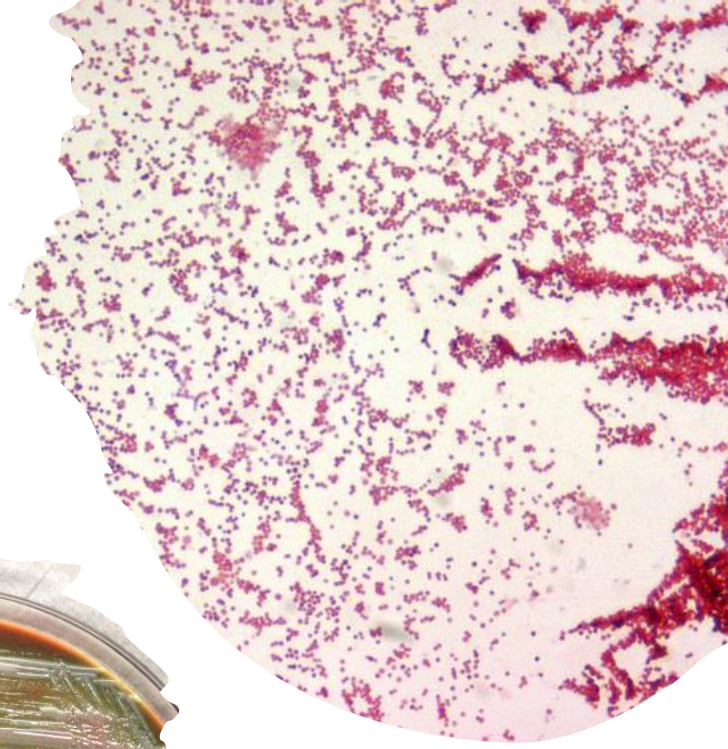


Tularemia

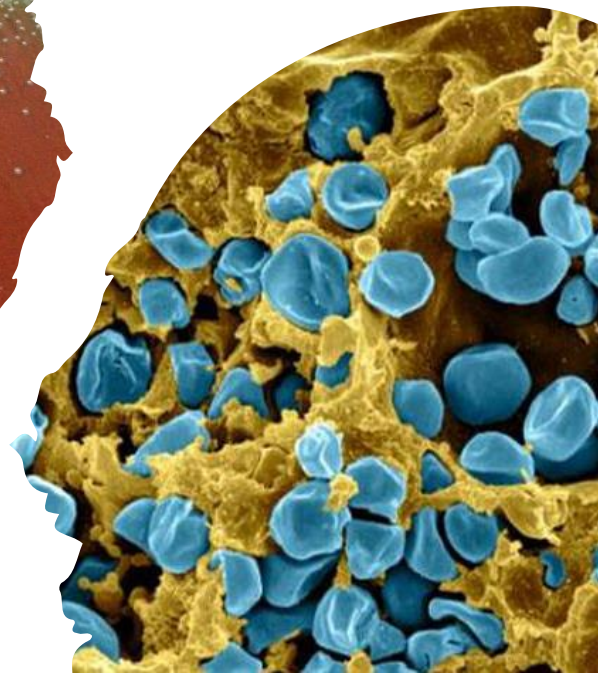
a.k.a "Rabbit Fever"



Francisella tularensis

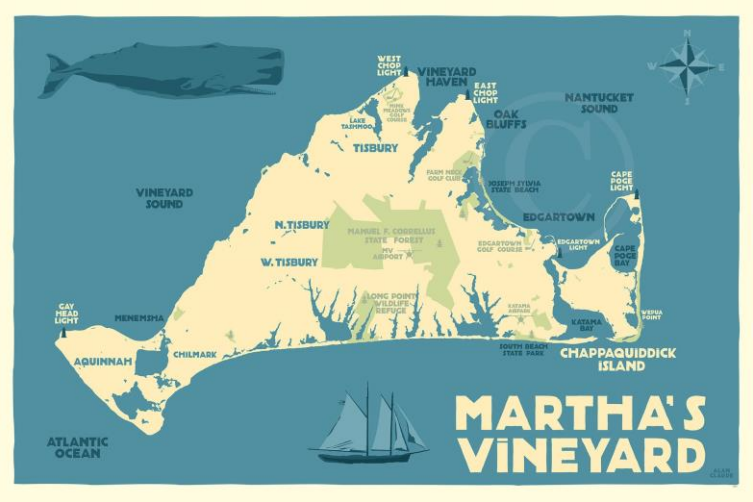


- Small, gram-negative coccobacillus
- Capsule allows survival for several months in water, mud, and decomposing materials
- **Category A bioterrorism agent**
- **Select Agent**



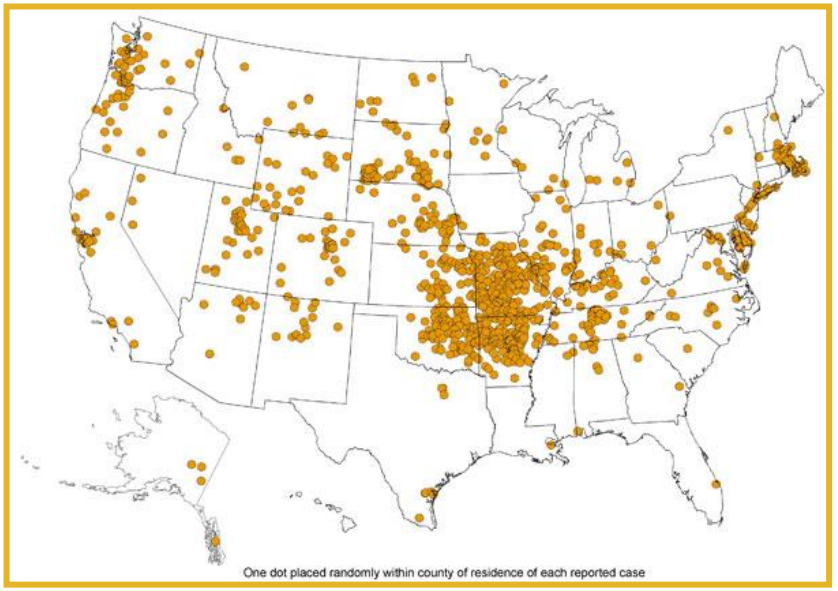
History

- 1907 — First described in humans
- 1930s–40s — Large waterborne outbreak in Europe and Soviet Union
- 1950s–60s — Organism used in U.S. biologic warfare program
- 1967–68 — Sweden experienced the largest airborne outbreak with ~600 cases
- 1978 — First U.S. pneumonic cases (7) occurred at Martha's Vineyard
- 2000 — Second cluster of pneumonic cases occurred at Martha's Vineyard



Modern Context

- Northern hemisphere most commonly
- Reported in all states, except Hawaii
- <200 human cases per year in the U.S.
- ~4 human cases per year in Montana



Reservoirs

- Wild rabbits, hares, rodents
- Pheasants, quail
- Ticks
  - American dog tick (*Dermacentor variabilis)*
  - Wood tick (*Dermacentor andersonii)*
  - Lone star tick (*Amblyomma americanum)*
- Deer flies (*Chrysops spp.)*

Transmission

- Tick bite
  - Most common
  - Can be infective for life
- Deer fly bite
  - Less common
  - Infective for ~14 days
- Direct contact with an infected animal
- Inhalation
  - Aerosolization of the bacteria
- Ingestion
  - Undercooked meat, contaminated water, raw milk

Disease in Humans

- Incubation period: 1 – 14 days, 3 – 5 days average
- Infectious dose
  - Small for inoculation or inhalation (10-50 organisms)
  - Large for oral (10^8 organisms)
- May have **non-specific symptoms** and resemble:
  plague, brucellosis, Q-fever, community-acquired pneumonia, anthrax, and tick-borne relapsing fevers
  - Fever, fatigue, chills, headache, severely swollen lymph nodes

Disease in Humans

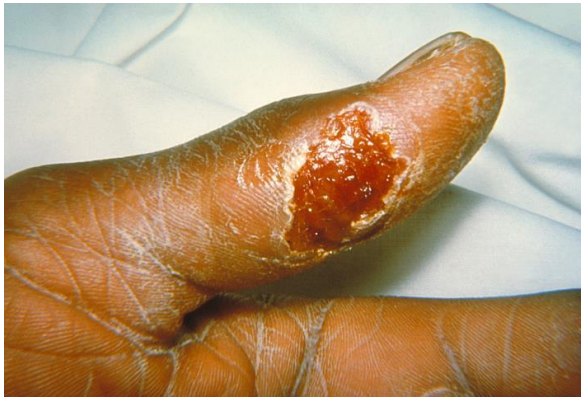


Image: Ulceroglandular tularemia. Credit: CDC Public Health Image Lab

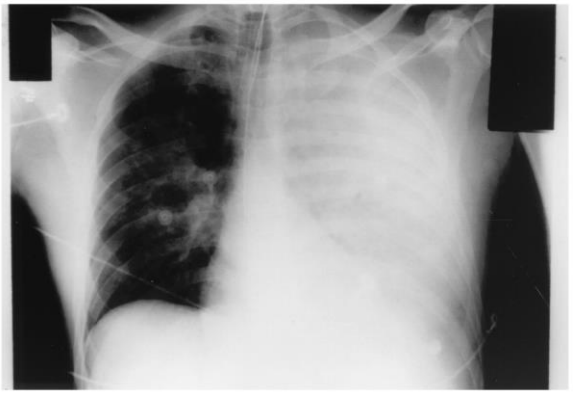


Image: Pneumonic tularemia X-ray. Credit:Shapiro, D. S., & Schwartz, D. R. (2002). Exposure of laboratory workers to Francisella tularensis despite a bioterrorism procedure. *Journal of clinical microbiology*, *40*(6), 2278-2281.

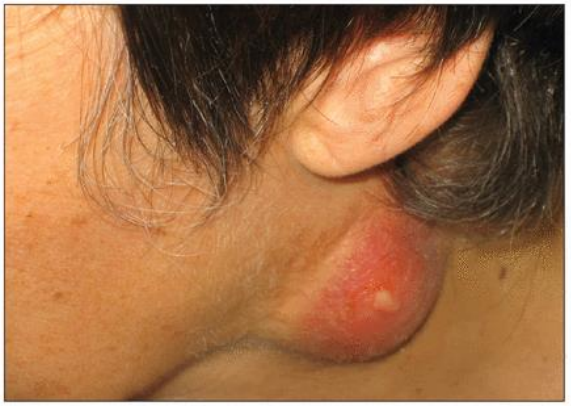


Image: Oropharyngeal tularemia. Credit: Steinrücken, J., & Graber, P. (2014). Oropharyngeal tularemia. *CMAJ*, *186*(1), E62-E62.

Ulceroglandular	Glandular	Oculoglandular	Oropharyngeal	Pneumonic	Typhoidal
Tick, deer fly, handling an infected animal	Tick, deer fly, handling an infected animal	Bacterial aerosolization contact with eyes (e.g. animal butchering)	Ingesting contaminated food/water	Breathing in aerosolized bacteria	--
Ulcer at bite site, regional lymph gland swelling (groin, armpits common)	No ulcer, regional lymph gland swelling	Eye irritation and inflammation, swelling of lymph glands at the front of ears	Sore throat, mouth ulcers, tonsillitis, swelling of lymph glands in neck	Cough, chest pain, difficulty breathing, pneumonia	Febrile, non-localized

Persons Most at Risk

- Hunters and Trappers
- Veterinarians and veterinary technicians
- Livestock producers
- Laboratory workers
- Persons working with wildlife

Diagnosis in Humans

- Diagnosis method varies with symptom presentation
- Serology: most common
  - Can cross-react with *Brucella* spp., *Y. Pestis*, *Legionella* spp. at low titers
    - Elevated antibody titers reflex to agglutination
    - Montana Public Health Lab (MTPHL) runs brucella serology with all tularemia requests
  - Acute & convalescent serums needed for confirmation
- Culture and isolation
  - Not routinely done, slow growing
  - Requires biological safety level III procedures
- PCR
- **Reportable** disease to local, state, and federal health officials

Treatment

- Can be fatal if not treated
- Antibiotics
  - Streptomycin, gentamicin, doxycycline, and ciprofloxacin*
- Treatment usually lasts 10 – 21 days
- <1% mortality in treated cases

Prevention

- No vaccine
- Tick control most important including for pets
- PPE when handling, skinning, or dressing rabbits, hares, rodents, pheasants, and quail
- Cook rabbit and other wild game thoroughly
- Do not drink untreated water, especially in endemic areas
- PPE when working in soil, mowing lawn, clearing weeds, excavating in endemic areas

Practice

All exposed persons should be on **fever watch** for at least 14 days following the day of exposure. Fever watch means self-monitoring for fever and reporting for medical care should fever occur. Fever should be regularly monitored with a thermometer.

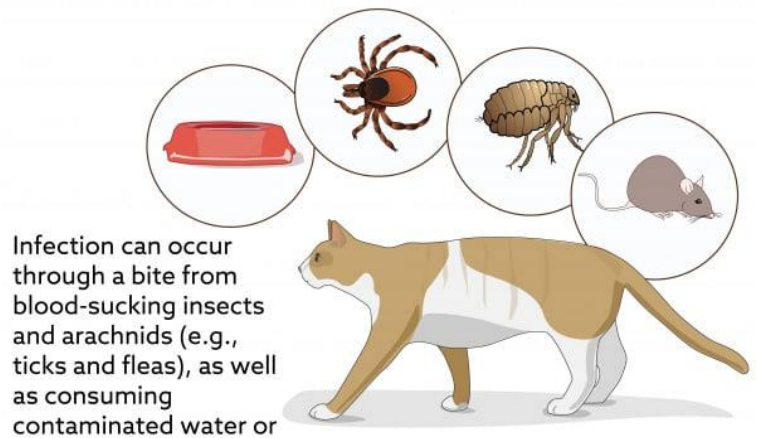
A post-exposure prophylactic prescription of **doxycycline** may also be recommended following physician consult.

Remember – Tularemia is reportable. Loop in MT DOL & DPHHS for further guidance!

What now?

Disease in Domestic Animals

- Has been reported in sheep, cats, dogs, pigs, and horses
  - Cats at increased risk due to predation on small mammals
- Transmission occurs through inhalation of aerosolized organism, direct contact, ingestion, or arthropods
- Incubation period is 1-10 days



Infection can occur through a bite from blood-sucking insects and arachnids (e.g., ticks and fleas), as well as consuming contaminated water or infected animals, such as rodents or rabbits.

Disease in Animals

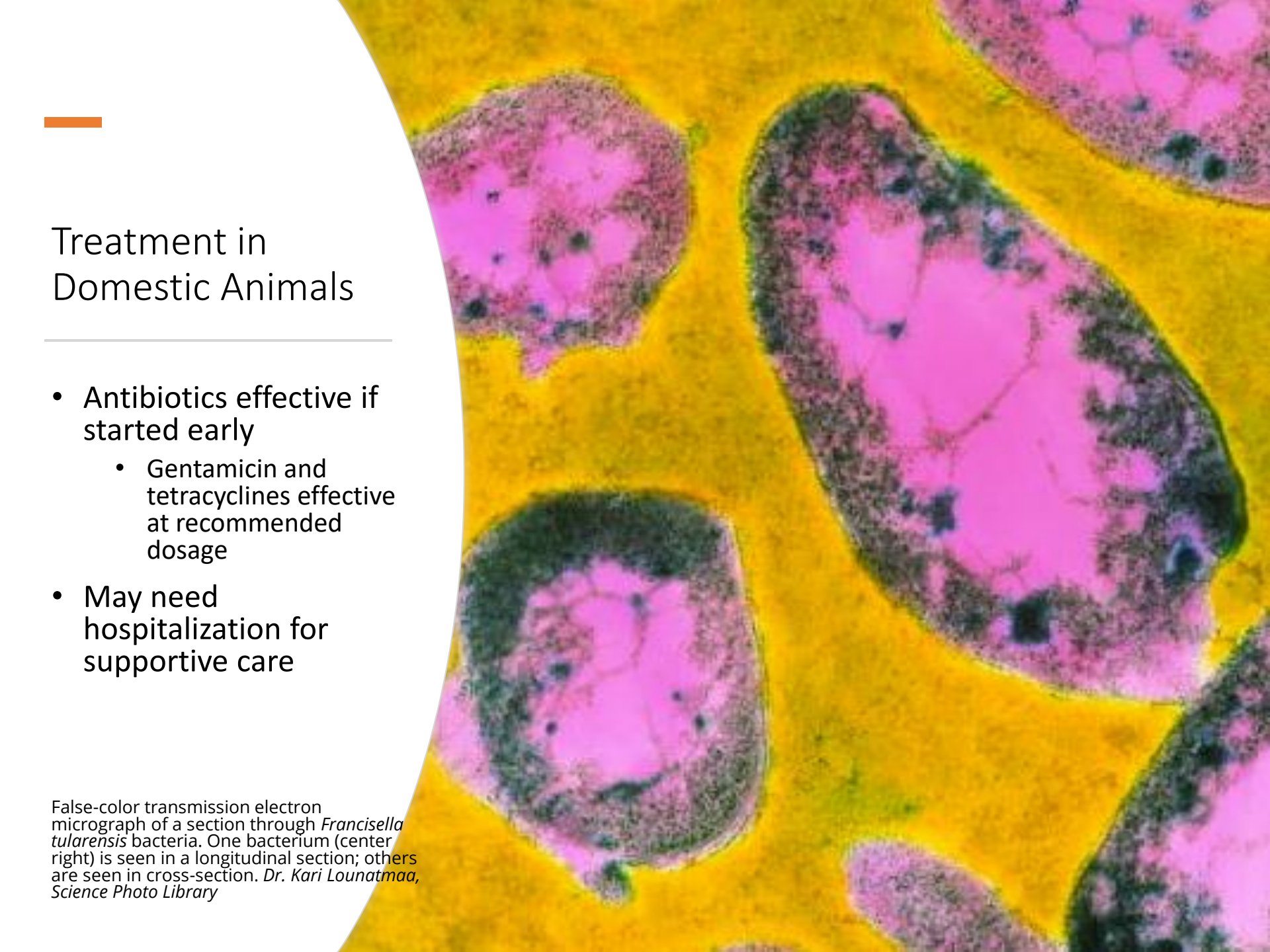
- Clinical presentation depends on host species, subspecies of the bacteria, and route of infection
- Signs may include fever (cats 104-106F), tachycardia and tachypnea, coughing, diarrhea, oral ulceration, pollakiuria, lymphadenopathy, hepatosplenomegaly, and death
- Cats seem to be more susceptible than dogs
  - Cats can be asymptomatic or have ulceroglandular or oropharyngeal signs due to ingestion
- Lesions include miliary, white foci of necrosis in the liver and sometimes spleen, lung, and lymph nodes

Diagnosis in Domestic Animals

- Rule-out cultures (*F. tularensis* is a Select Agent)
  - Sentinel Laboratories (e.g., MVDL) can perform cultures to "rule out" organism
    - Once suspect colonies are isolated, must stop culture and refer isolate to reference lab for identification
    - MVDL usually has ~2-3 cases per year, most frequently in wildlife and cats
  - Acceptable samples for submission: lymph node aspirates (ante-mortem), fresh tissue (spleen, lymph node, liver – post-mortem)
  - **If you are clinically concerned for tularemia and the patient is deceased, recommend sending the whole animal for necropsy and tissue collection to reduce exposure risk during collection**
    - If sending to MVDL, always note that tularemia is a differential on the submission sheet, as this helps us protect our staff and ensure we are working with tissue at the appropriate biosafety level
      - Tularemia is a concern for lab-acquired infections due to low infectious dose!
- PCR
  - Recently added by Kansas State for ante-mortem diagnosis
    - Lymph node aspirates or biopsies, pharyngeal swabs, respiratory fluids, swabs/scrapings of ulcers
      - Fresh tissue (post-mortem)

Treatment in Domestic Animals

- Antibiotics effective if started early
  - Gentamicin and tetracyclines effective at recommended dosage
- May need hospitalization for supportive care



False-color transmission electron micrograph of a section through *Francisella tularensis* bacteria. One bacterium (center right) is seen in a longitudinal section; others are seen in cross-section. *Dr. Kari Lounatmaa, Science Photo Library*

Prevention in Domestic Animals

- No vaccine available
- Reduce exposure to wildlife and ticks
- Keep cats indoors to prevent ingestion of and exposure to wildlife

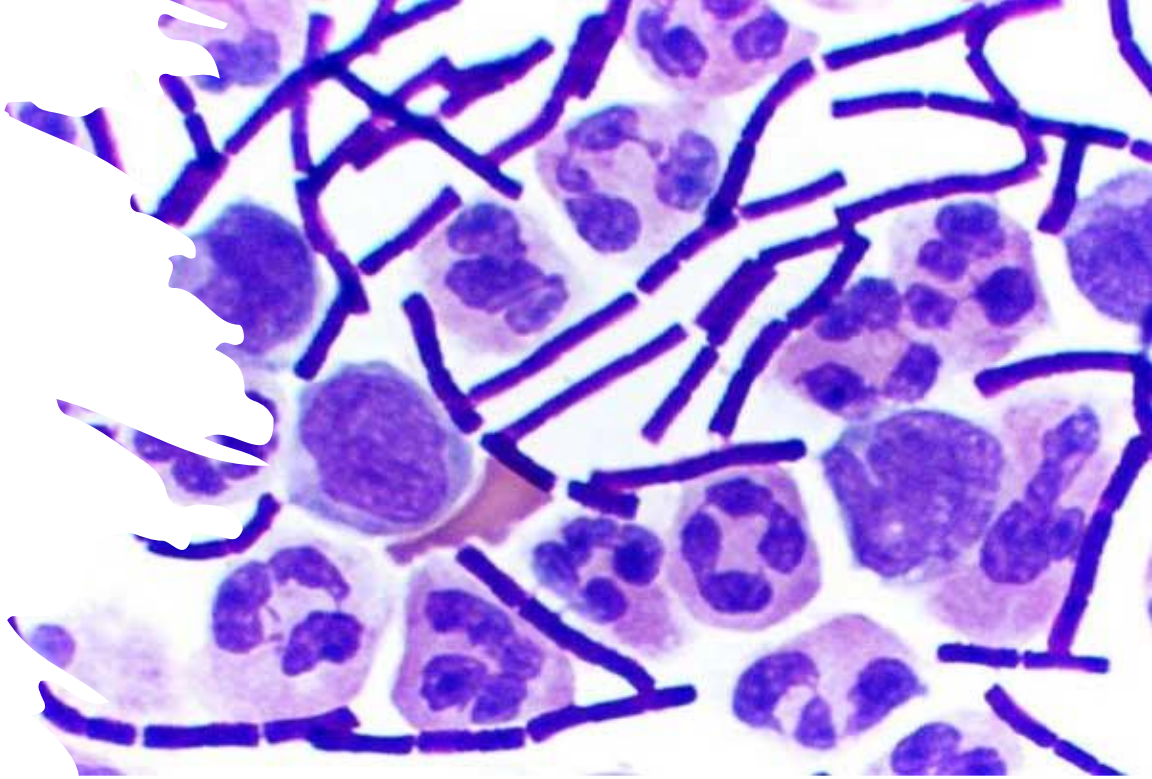
Wildlife Implications

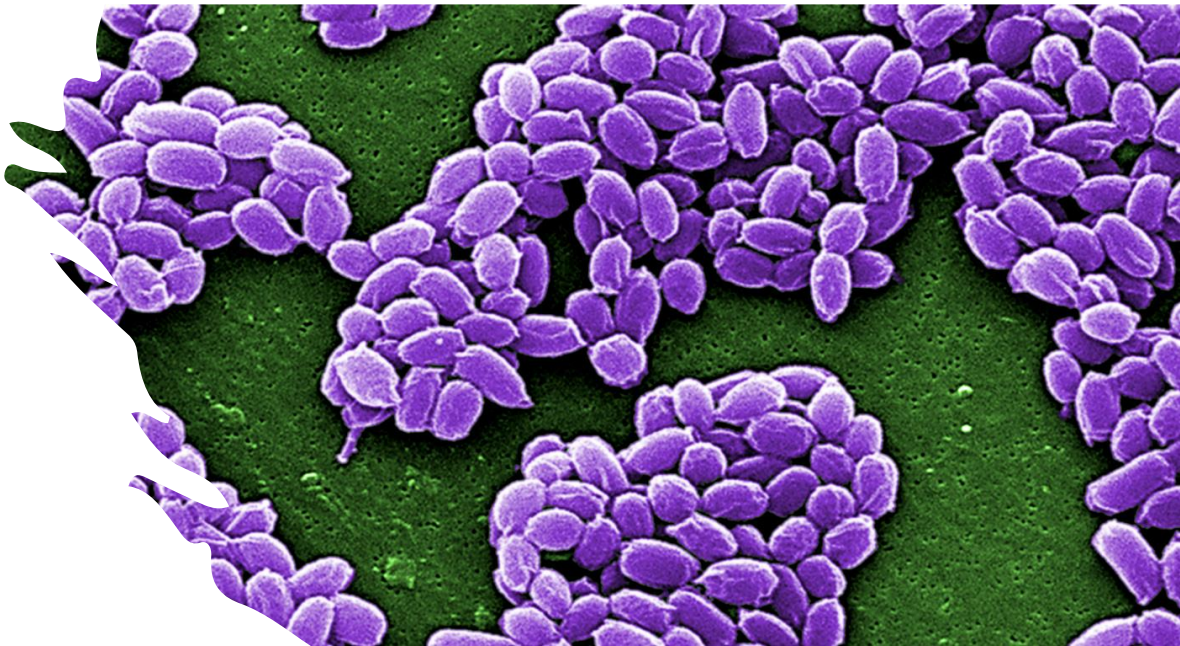
- *F. tularensis* can infect a variety of species including several species of mammals, birds, amphibians, and invertebrates
- In the US, cottontail rabbits, jackrabbits, squirrels, beaver, moles, voles, and muskrats are most commonly infected
- In Montana, wildlife cases are most frequently detected in beavers and cottontail rabbits. Can eliminate local populations.
- Serological survey has detected seropositive in 2 wolves

Anthrax

Bacillus anthracis

- Gram-positive, non-motile rod
- Two forms, vegetative and spore
- Spores
  - Very resistant
  - Survive for decades
  - Taken up by host and germinate
  - Lethal dose 2,500 to 55,000 spores
- **Category A bioterrorism agent**
- **Select Agent**





History

- 700 B.C. — Moses' time might have caused the fifth plague of Egypt
- 1752 — first clinical descriptions of cutaneous anthrax given by Maret
- 1877 — Rober Koch used *B. anthracis* to develop his famous Koch Postulates
- 1881 — Louis Pasteur developed first vaccine for anthrax
- 1937 — Max Sterne developed anthrax live spore vaccine for humans
- 1944 — Penicillin used to treat anthrax
- 1950s — First human anthrax vaccine developed

Anthrax as Biological Weapon

- 1914 — first deliberate used of anthrax as a weapon in World War I
- 1932 — Japan produced anthrax as weapon to use on prisoners and Chinese cities
- 1942 — bioweapons programs expanded
- 1972 — treaty signed to prohibit biologic and toxic weapons
- 1979 — deadly anthrax outbreak Sverdlovsk Russia
- 2001 — Anthrax attacks U.S.

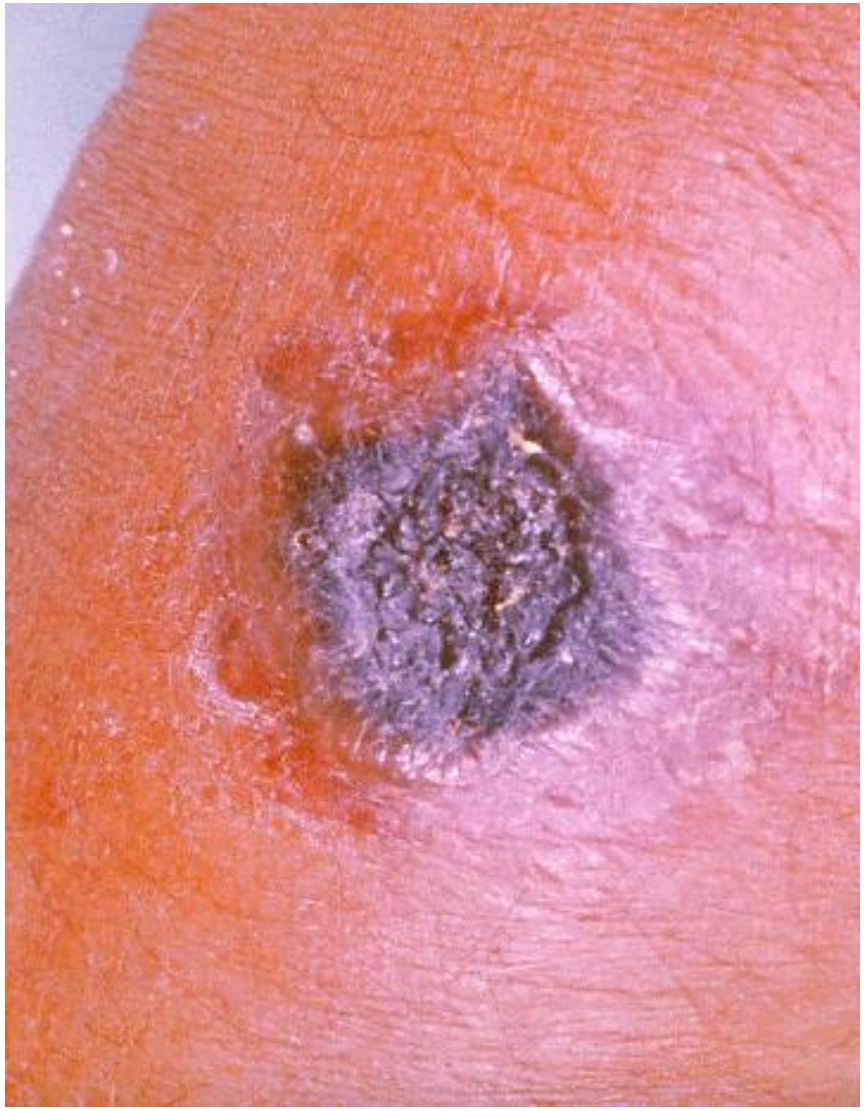
Modern Context

- Worldwide distribution
- <1 human case per year in the U.S., rare
- 0 human cases per year in Montana
- Recent situation in southern Ukraine (April 2023)
  - Russian troops unearthed a cattle burial site
  - 2 soldiers were infected with anthrax
  - Remainder of their unit is quarantined

https://www.msn.com/en-us/news/world/russian-troops-digging-trenches-in-ukraine-reportedly-infected-with-anthrax/ar-AA1anUDX

Cutaneous Anthrax in Humans

- ~95% of all cases globally
- Incubation 5 to 7 days (Range 1-12)
- Spores enter skin through open wound or abrasion
  - Typical sites include head, neck, forearms and hands
- Initially may be itchy at the affected site
- Progresses from papule to vesicle to ulcer to eschar over 2-6 days
- Case fatality rate 5 to 20%
- Untreated leads to septicemia and death



Inhalation Anthrax in Humans

- Incubation can widely vary, range 1-43 days
- Initially nonspecific clinical signs (fever, malaise, fatigue, mild cough, chest pain)
- Progresses to severe respiratory distress over 3-4 days
  - Dyspnea, stridor, cyanosis, mediastinal widening
  - Death within 24 to 36 hours
- Case fatality rate greater than 85% when untreated

Ingestion Anthrax in Humans

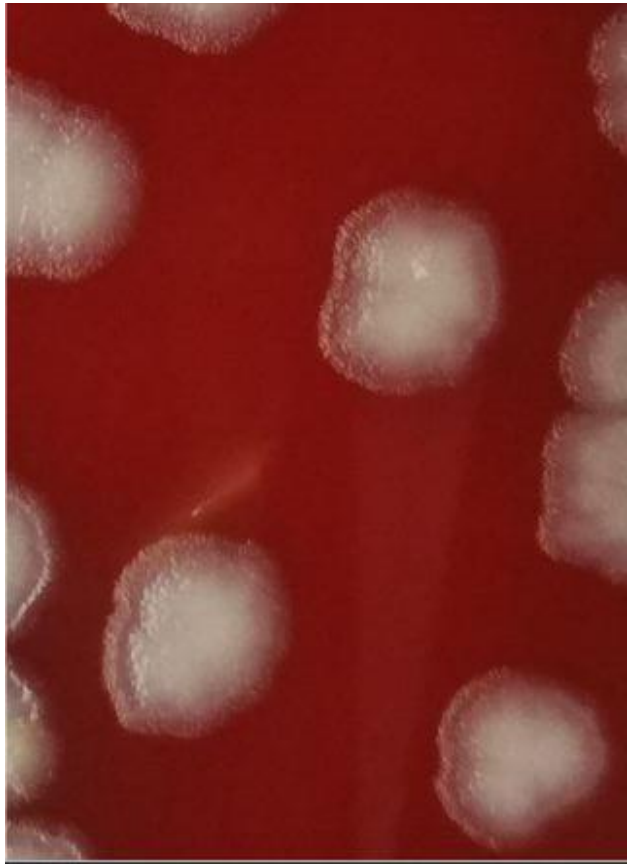
- Two subtypes:
  - Oropharyngeal (spores germinate in upper GI)
  - Gastrointestinal (spores germinate in lower GI)
- Incubation 1 to 6 days
- Symptoms depend on type
  - Sore throat, difficulty swallowing, swelling of neck
  - Nausea, vomiting, fever, abdominal pain
  - Progresses rapidly to severe, bloody diarrhea
- Case fatality rate: 40%

Transmission

- Usually by bacterial endospores
- Contact with infected animals, their parts, or products made from them
- Cutaneous
  - Contact with infected tissues, skins, hides, bones, bone meal, wool, soil
  - Biting flies
  - Person-to-person transmission is rare
- Inhalation
  - Risky industrial processes in poorly ventilated areas
  - Tanning hides, processing wool or bone
- Ingestion
  - Undercooked meat of infected animals
  - No evidence of milk transmission from infected animals

Diagnosis in Humans

- Identification of B. anthracis
  - Blood, skin, secretions
- Culture is gold standard for diagnosis
  - May be difficult after antibiotic initiation
- Other methods allow for quick detection
  - PCR
  - Antigen detection using immunohistochemistry (IHC)
  - Antigen toxin detection using mass spectrometry of serum
- Serology
  - ELISA



Treatment in Humans

- 3 antimicrobial agents for all types
  - Except localized cutaneous cases
- Ciprofloxacin is recommended first line drug
  - Levofloxacin and moxifloxacin are equivalent
- 1-2 additional agents
  - Meropenem, doripenem, and imipenem/cilastatin have good CNS penetration and should be included
  - Linezolid, clindamycin, or doxycycline inhibit protein synthesis to reduce toxin production
- Monoclonal antibodies or anthrax immune globulin can be used as adjuncts
- Duration of therapy should be 10-14 day and is dependent on patient condition
- Patient may require supportive treatment (ICU care) and/or drainage of effusions or ascities
- Localized cutaneous treatment is 7-10 days of oral ciprofloxacin or doxycycline
  - Treatment is extended to 60 days if related to a biological attack to prevent inhalation anthrax

Prophylaxis in Humans

Depends on exposure route -

- Contact with infected animals, animal products, or ingestion of contaminated meat
  - Ciprofloxacin and doxycycline for 10-14 days
- Inhalation exposure of spores
  - 3 doses of cell-free vaccine at 0, 2, and 4 weeks AND
  - 60 days of antimicrobial (either ciprofloxacin or doxycycline)

* The US cell-free vaccine has not been evaluated for safety and efficacy in children younger than 18 years or in adults 60 years or older.

Prevention in Humans

- Preventing disease in animals
- Improved industry standards
- Monitoring of imported goods
- Safety practices in laboratories
- Post-exposure prophylaxis
- Vaccine available for risk groups

Public Health Implications

Suspected or confirmed anthrax is an immediately notifiable condition

- Must notify local and/or state public health department with 4 hours

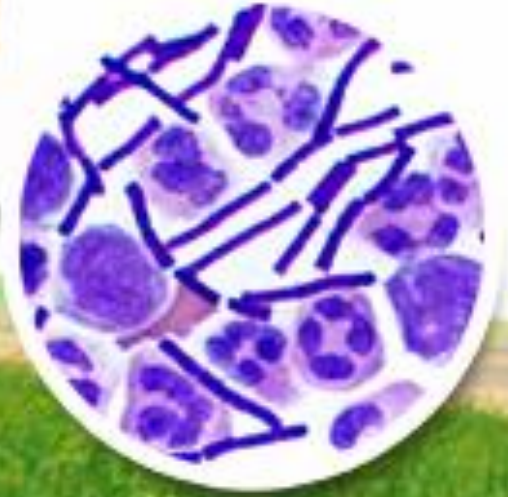
Law requires lab confirmation of human specimens at MT Public Health Lab in Helena

Disease in Animals

- Most common in herbivores
  - Cattle, sheep, and goats
- Transmission occurs when grazing animals ingest spores from the soil
- Transmission may also occur from biting flies, ingestion of contaminated feed (bone meal from infected animals), raw or undercooked contaminated meat ingestion (pigs, dogs, cats, mink, wild carnivores)
- Classic presentation = downpour followed by hot weather, usually mid-late summer
- Clinical signs range from acute to chronic

1 The bacteria known as *Bacillus anthracis* produce dormant spores (not active) that can live in the environment, like soil, for a long time, even decades.

2 When spores get into the body of an animal or person (a place rich with waters, sugars and other nutrients), they can be "activated" and turn into **active growing cells**.



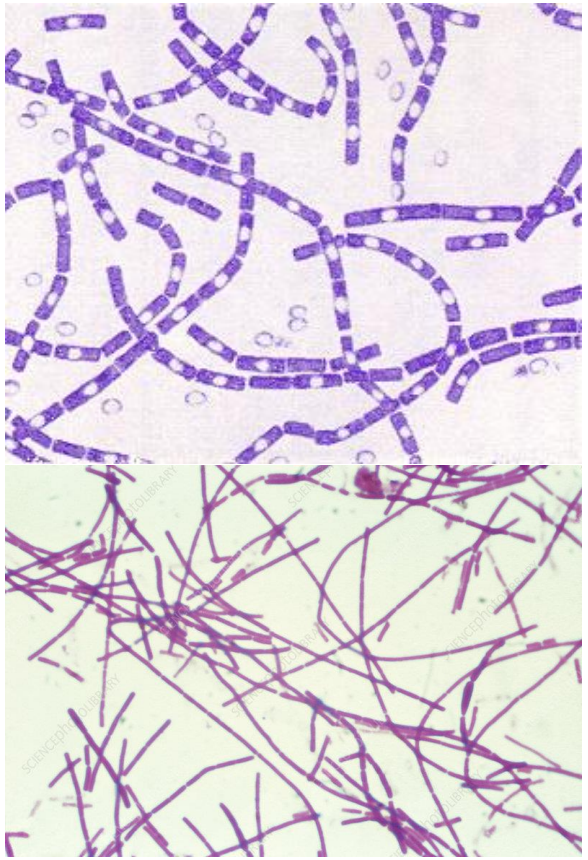
3 When they become active, the bacteria can multiply, spread out in the body, produce toxins (poisons) and cause severe illness and death.

Disease in Animals

- Cattle and sheep = acute
  - Abrupt onset of fever with a period of excitement, then lethargy, stupor, respiratory or cardiac distress, staggering, seizures, and death
  - Often the course of disease is so rapid that illness is not observed
  - Bloody discharge form natural openings, subcutaneous edema, and swelling of the neck/thorax/shoulders
- Horses = acute
  - Fever, chills, severe colic, anorexia, depression, bloody diarrhea, swelling of neck, sternum, abdomen, and genitalia
  - Death occurs 2-3 days after onset of signs
- Pigs
  - Commonly present with a mild, chronic form, can recover with treatment
  - Swelling of the throat and dyspnea can occur
- Dogs and cats
  - Similar to pigs

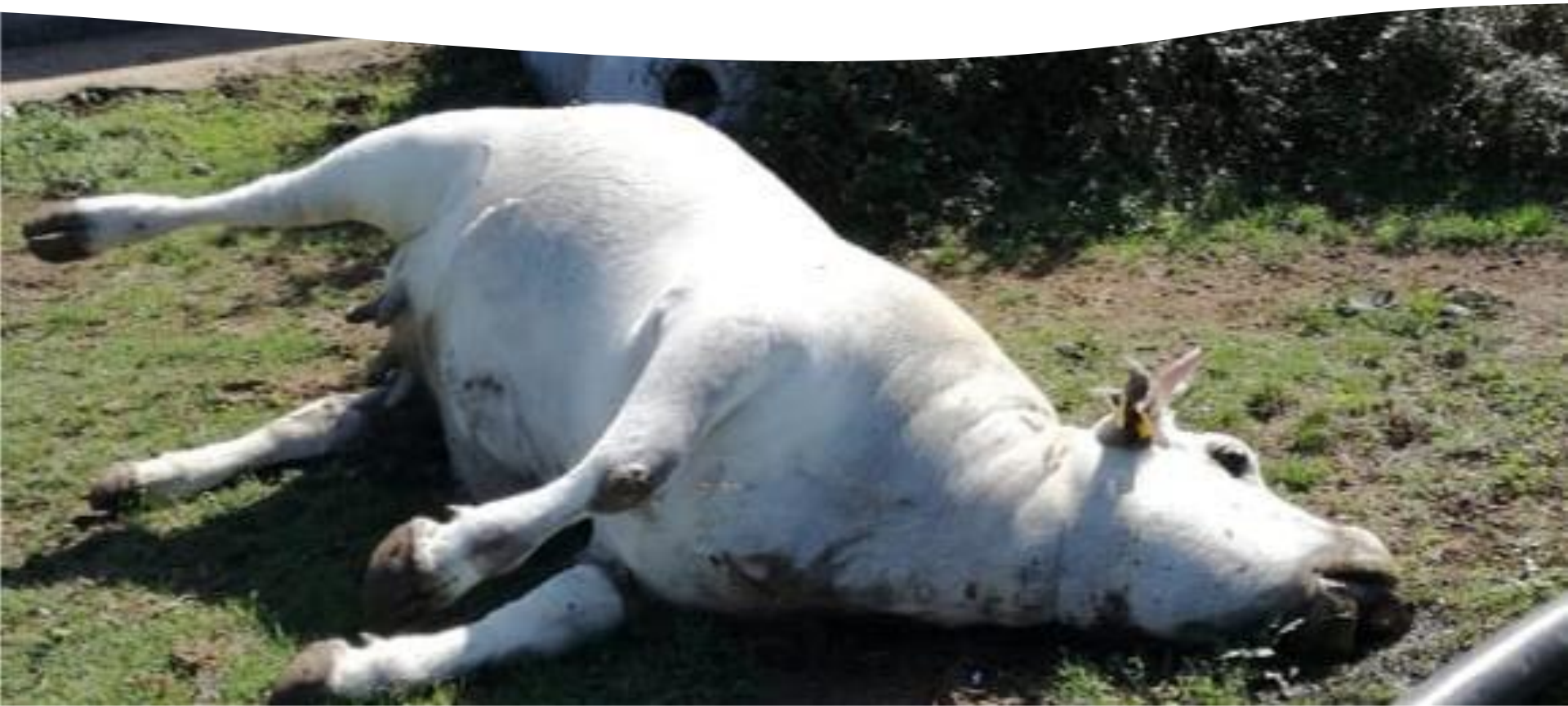
Diagnosis in Animals

- Rule-out culture (*B. anthracis* is a Select Agent)
  - Sentinel Laboratories can provide "rule-out" culture, but must refer suspicious isolates to reference lab for ID
    - Sampling: if there is a clinical suspicion for Anthrax in a deceased animal, recommend that the carcass is not opened in the field
      - Necropsy/tissue collection can be performed at MVDL in containment, but may not be needed
  - Alternatively, blood smear/culture can be performed without the need for tissue collection
    - If unable to transport carcass, pull a peripheral blood sample (ear vein is best in a ruminant)
    - Do not transfer to tube (prevent aerosolization); cap syringe, place in leakproof ziploc bag, and submit to lab as quickly as possible (<4 hours from time of death is optimal)
    - Blood smear gives presumptive result due to characteristic morphology (box-car shaped rods with endospores)
    - Rule out culture and referral of suspicious isolates for ID would follow
  - Notify lab prior to submission if Anthrax is suspected!



Treatment in Domestic Animals

- Early treatment and prevention are essential to limit loss in production animals
- Anthrax is susceptible to abx therapy, but usually clinical course is so rapid there is no opportunity to treat
- Animals at risk should be treated with a long-acting antimicrobial followed by vaccination 7-10 days after treatment



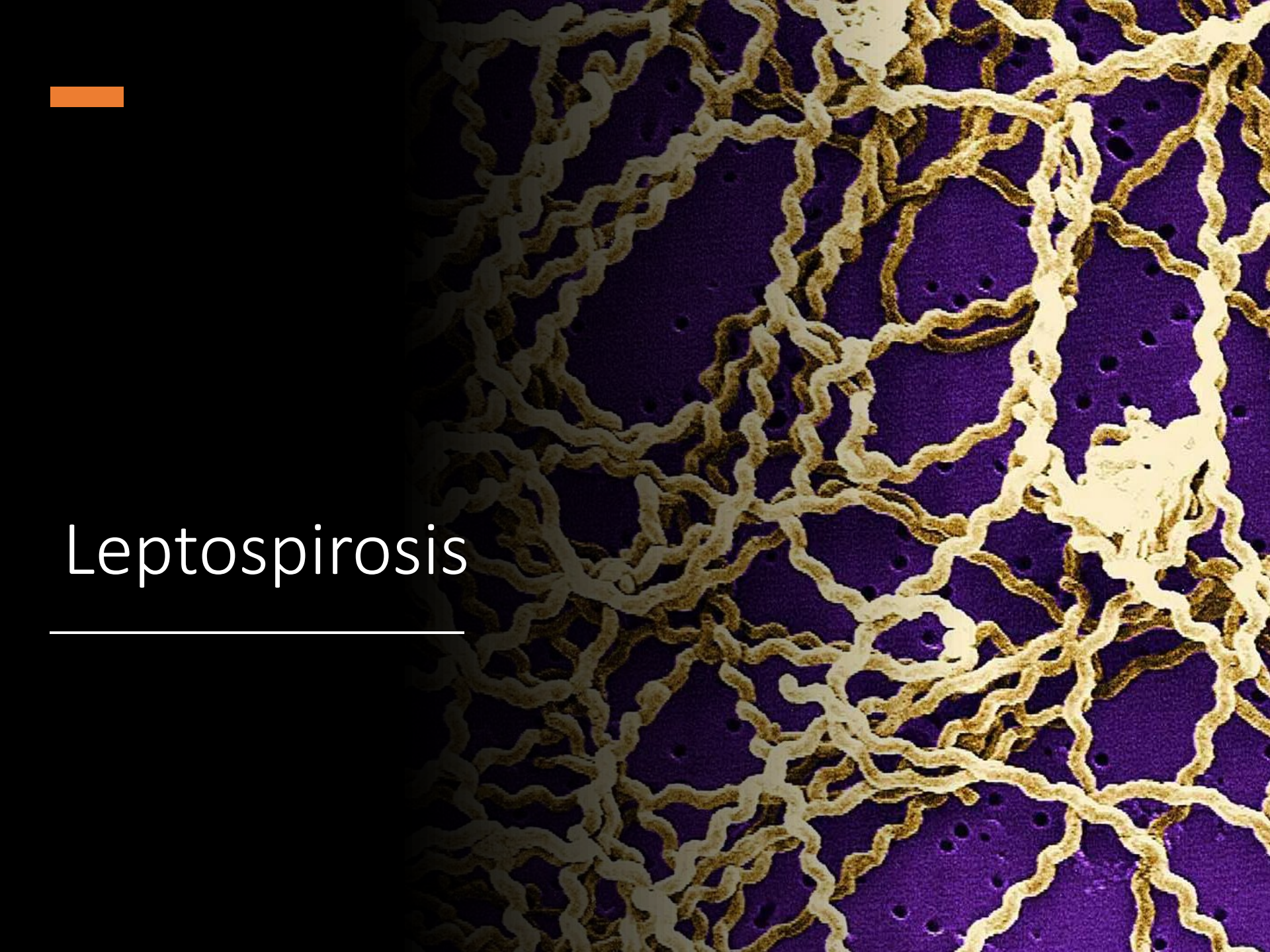
Prevention in Domestic Animals

- Annual vaccination of grazing animals in endemic areas
  - Must be approved by Montana State Veterinarian
- Prompt disposal of dead animals, feces, and other contaminated material by incineration
- Isolation of sick animals
  - Removal of non-sick animals from contaminated area
- Contaminated soils are difficult to decontaminate, but formaldehyde is effective if level of contamination is not excessive

Wildlife Implications

- Wild grazing animals, such as deer, can become infected
- Illness in wild herbivores varies by species, but most commonly results in acute form, as seen in cattle
- History of anthrax in southern and eastern Montana
- Last confirmed outbreak affecting wildlife in Montana in summer 2008. First documented since mid 1950's

Leptospirosis

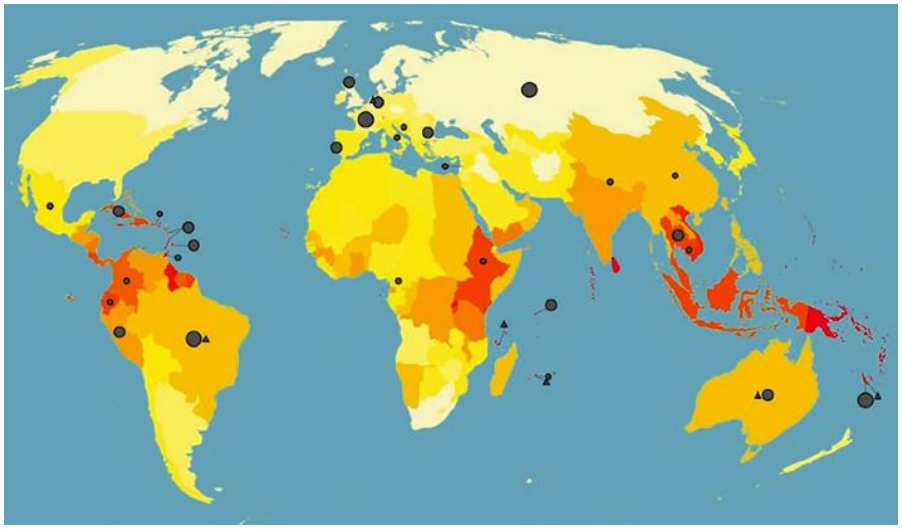


History

- 1886 – First described by German physician Adolf Weil
- 1907 – First observed in post-mortem kidney by Arther Stimson
- 1908 – Japanese research group first identified the bacterium as cause of leptospirosis
- 1917 – rats discovered as carriers of leptospirosis
- 1940s – additional species of leptospirosis identified
- 1980s - >200 serovars identified

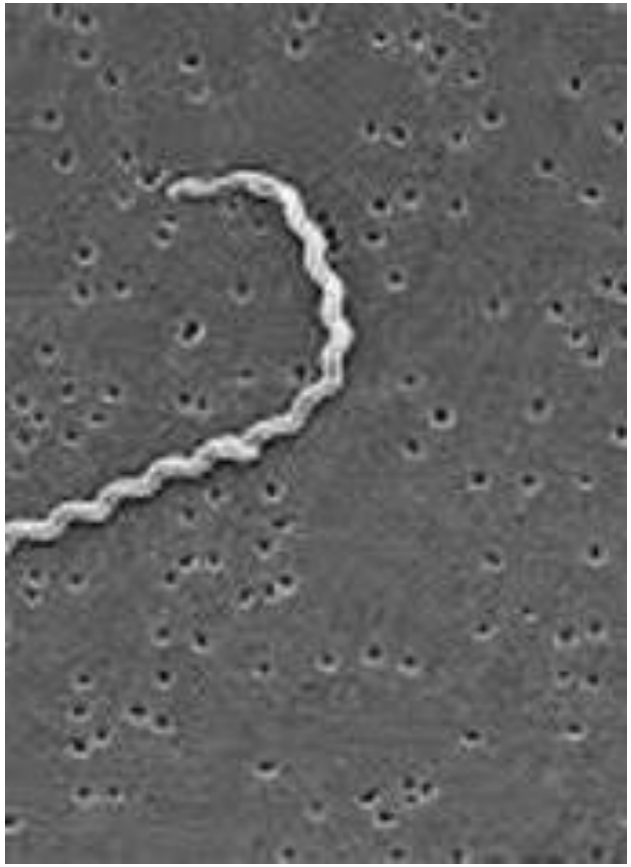
Modern Context

- Occurs worldwide, especially in tropical and sub-tropical climates
- ~1 million cases annually, with close to 60,000 deaths
- <1 human case per year in Montana
- Seasonal disease with most cases occurring in summer and fall in temperate regions



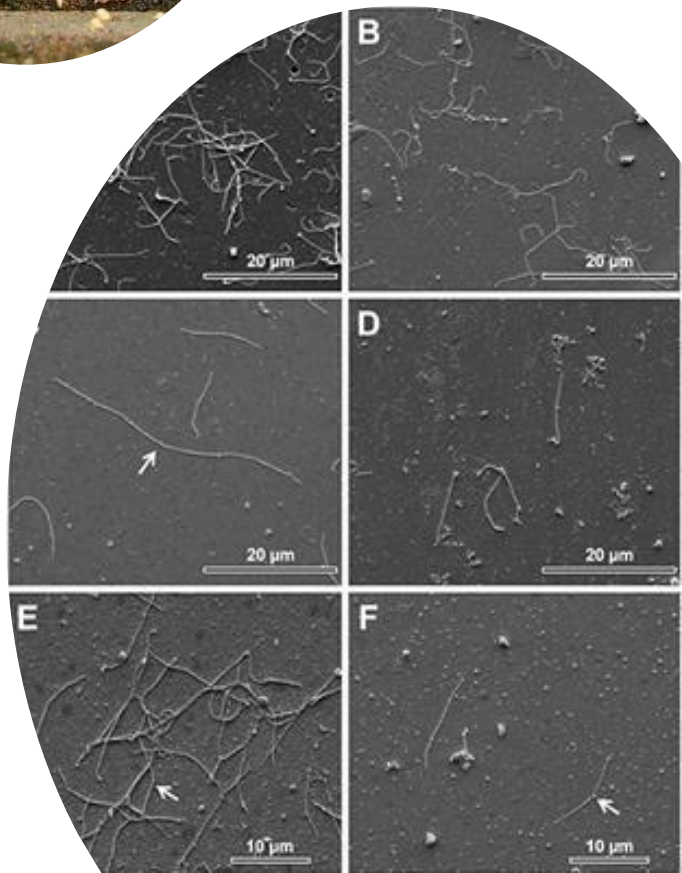
Leptospirosis sp.

- Long, thin, motile spirochetes
- Antigenically complex
- Both harmless saprophytes and some pathogenic
- Categorized by serovars
- Serovars generally adapted to one or more mammalian hosts
- Can survive weeks to months in urine-contaminated soil and water



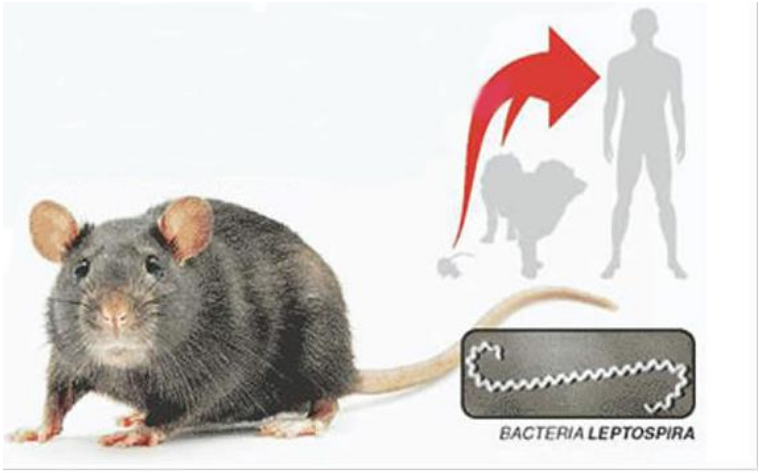
Leptospirosis Serovars and Hosts

- *Canicola* – dog
- *Bratislava* – pigs, horses
- *Pomona* – pigs
- *Hardjo* – cattle
- *Icterohaemorrhagiciae* – rodents and insectivores
- *Grippotyphosa* – rodents and insectivores
- *Sejroe* – rodents and insectivores
- *Autumnalis* – wildlife



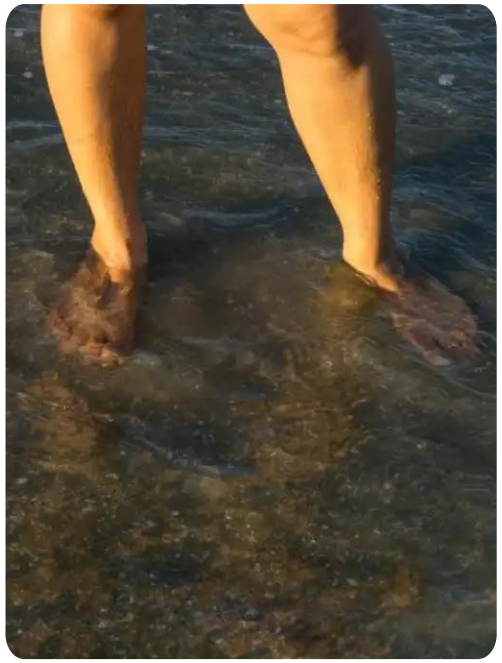
Transmission

- Spread by urine of infected animals
  - Rodents, dogs, livestock, pigs, horses, wildlife
- Direct contact of mucus membranes, conjunctiva, skin cuts, or abrasions
  - Urine or reproductive fluids of infected animals
  - Urine-contaminated water and wet soil
- Ingestion
  - Food or water contaminated by urine or urine-contaminated water
- Human-to-human transmission rare
- Outbreaks tend to occur after heavy rainfall and flooding



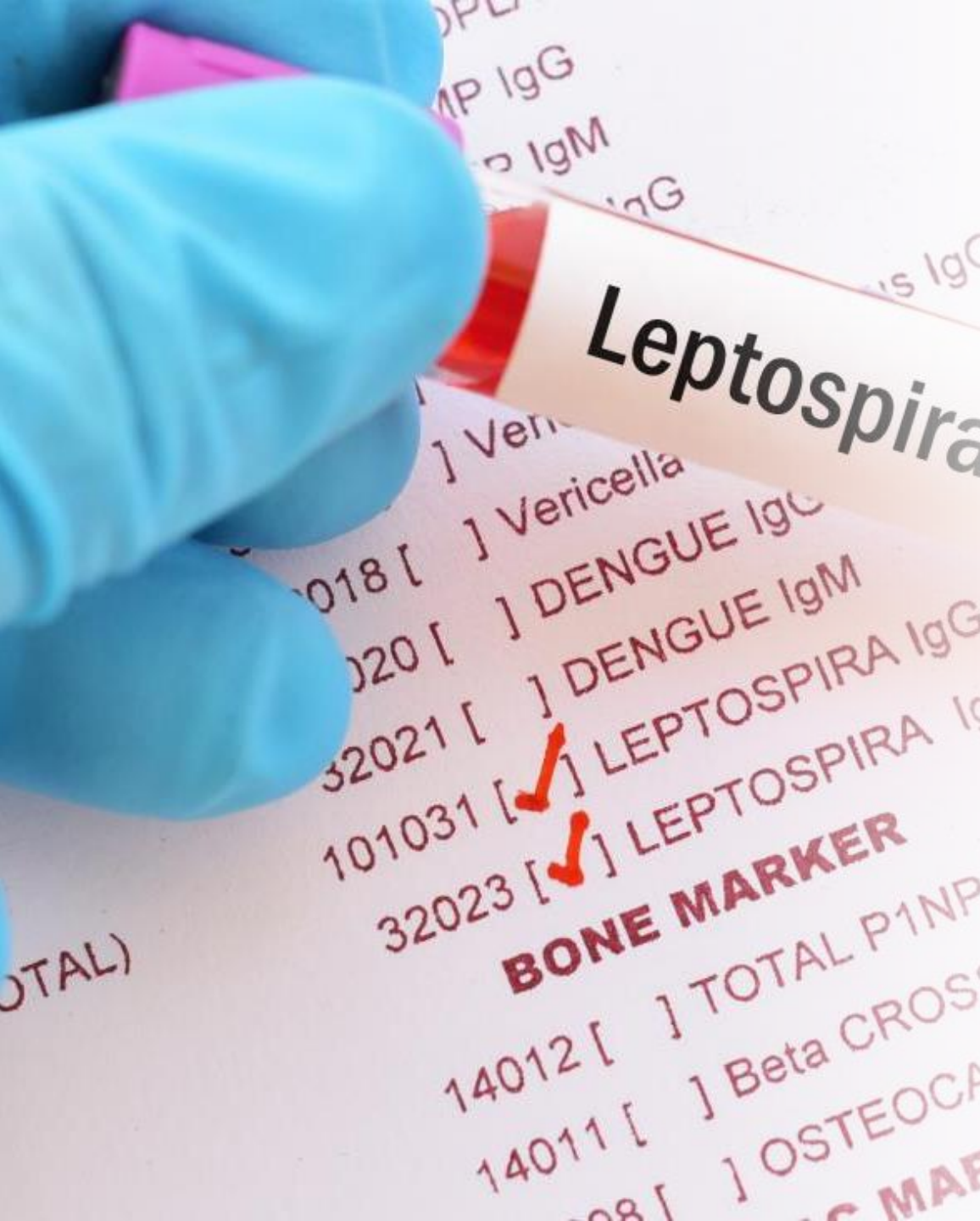
Disease in Humans

- Incubation period 2 to 30 days (most commonly 5-14 days)
- Most infections are thought to be asymptomatic
- 90% clinical illness present as non-specific acute febrile illness
  - Fever, chills, headaches, muscle pain, redness of eyes
- 10% progress to severe, potentially fatal illness with multi-organ dysfunction
- Infection during pregnancy can cause fetal complications including fetal death or abortion
- Case fatality rate for severe illness 5 to 15%



High Risk Occupations and Activities

- Animal contact
  - Farm workers, veterinarians, slaughterhouse workers
- Frequent contact with contaminated environments
  - Sewer workers, coal miners, plumbers, fishing industry
- Recreational activities
  - Gardening and water sports (wading, swimming, or boating)

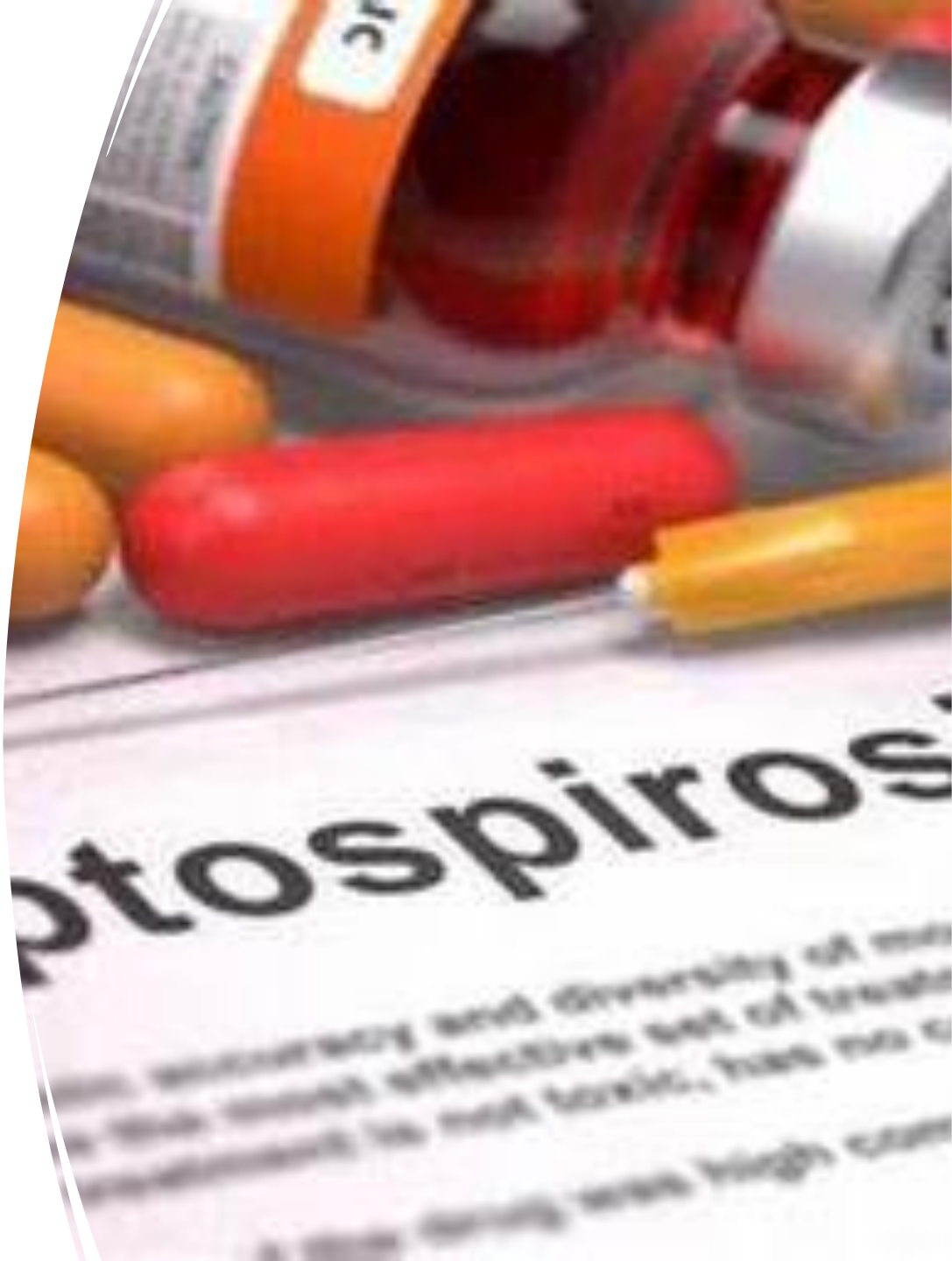


Diagnosis in Humans

- Antibodies develop between 3-10 days after symptom onset
- Culture (fastidious organism)
- Serology
  - ELISA
- PCR
- Immunohistochemistry

Treatment in Humans

- Supportive therapy
- Mild disease
  - Doxycycline drug of choice
  - Other options: azithromycin, ampicillin, or amoxicillin
- Severe disease
  - IV penicillin or ceftriaxone



Prevention in Humans

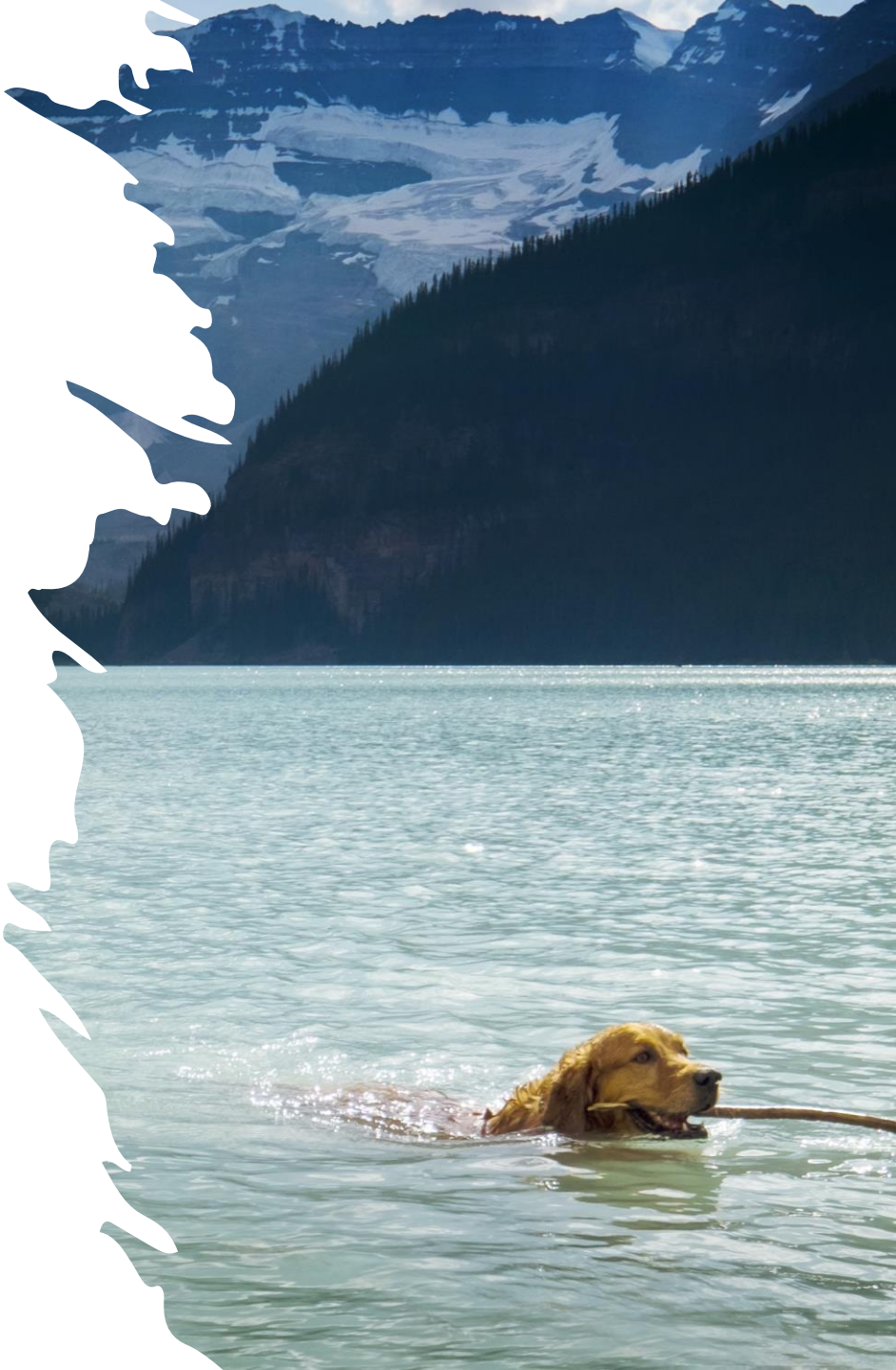
- Controlling infections in livestock and pets
- Rodent control
- Avoid contact with potentially contaminated water
- Protect food from contamination
- Personal hygiene and PPE in high-risk occupations

Disease in Animals

- Almost all mammals are susceptible to leptospirosis infection
  - Affects cattle, swine, dogs, and horses
  - Appears rare and mild in cats
- Risk factors for exposure include swimming in or drinking from rivers, lakes, streams, exposure to wild animals, and contact with rodents
- Transmission occurs through ingestion, mucous membrane contact, or contact with cuts in skin with infected urine, urine-contaminated soil, water, food, or bedding; bite from an infected animal; ingestion of infected carcasses; in utero; rarely through breeding

Disease in Animals - Dogs

- May be asymptomatic, but leptospirosis can be serious and life-threatening
- Acute kidney injury with or without acute liver disease
- Symptoms include fever, weight loss, anemia, muscle pain, hematuria, muscle weakness, icterus, polydipsia/polyuria, vomiting, diarrhea, anorexia, lethargy, and effusions
    - Less commonly – bleeding disorders with prolonged prothrombin time (PT) and prolonged activated partial thromboplastin time (aPPT) or uveitis



Disease in Animals - Livestock

Horses

- Abortions (after 9 months), equine recurrent uveitis, fever, and acute renal failure

Ruminants

- Abortions (anytime), weak offspring, and blood-tinged milk in cows

Swine

- Infertility and sporadic abortions

Diagnosis in Animals

- Serology - "gold standard" for clinical leptospirosis Dx
  - Microagglutination Test (MAT)
    - Functional assay performed on serial serum dilutions to give a titer for various lepto serovars
    - Titer is interpreted in the clinical context of the animal
      - Some cross-reaction between serovars (esp. Pomona and Autumnalis)
        - Individual serovar titer is less important than the whole picture
      - Will detect antibodies due to infection, vaccination, or exposure
    - Recommend submitting an initial and convalescent serum sample together (second sample 10-14 days following first)
      - Results can vary between labs because live bacteria are used for this test and there can be strain variation
        - Always submit acute and convalescent samples to the same lab for consistent results and accurate interpretation
    - Dr. Schwarz loves helping MVDL clients with titer interpretations!

Diagnosis in Animals

- Serology (continued)
  - Commercial Lepto SNAP test - not extremely reliable in cases that correlate to titers less than 1:3200
    - May be useful for initial in-clinic screening (esp. If positive), but consider confirming with the MAT
    - Interpret negatives with caution – SNAP will miss ~30-50% of clinically significant cases with titers <1:1600 (published by Idexx)
      - Keep in mind that in an animal with clinical signs of leptospirosis, a titer of at least 1:400 is usually significant
      - In reality, we don't see clinically affected small animals with titers at or above 1:1600 all that often...
- Antigen detection
  - Direct Fluorescent Antibody (FA)
    - Primarily used on urine, can also be used on tissue
    - Urine FA can give false negative due to inconsistent shedding
    - Not as good for screening
  - Culture – not typically performed (very difficult)
  - PCR
    - Offered by some labs
    - Can be performed on tissue or urine
    - Can be more sensitive than the FA, but has same limitations as FA for screening purposes

Treatment in Domestic Animals - Dogs

- Chance for recovery is good if antibiotics and supportive care are started early and patient treated aggressively
  - Doxycycline is recommended
  - Fluid therapy, electrolyte supplementation, antiemetics, phosphate binders, hepatic support medication
  - Risk for permanent kidney or liver damage
  - Start antibiotic therapy when leptospirosis is suspected before confirmatory test results

Treatment in Domestic Animals

Horses

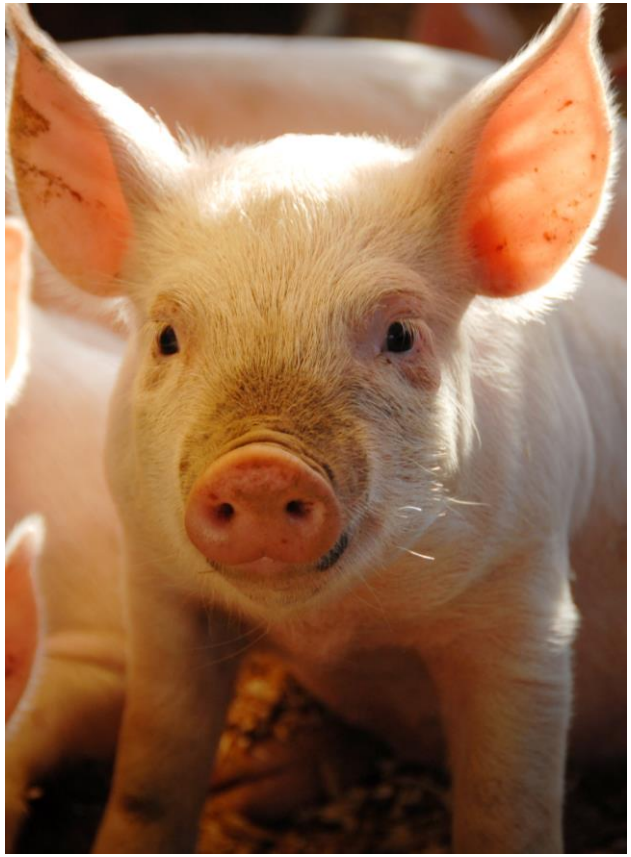
- Systemic antibiotics (enrofloxacin, penicillin, tetracyclines, or aminoglycosides) and topical immunosuppressant agents for uveitis

Ruminants

- Antimicrobial use can prevent abortions

Swine

- Successful use of antimicrobials reported, however this approach is limited to outbreak situations and must comply with regulatory requirements



Prevention in Domestic Animals

- Vaccine available for pigs, cattle, and dogs
  - Annual vaccination recommended for at-risk dogs, but vaccine only protects against most common serovars
- Minimize exposure to sources of bacteria
- Minimize exposure to rodents/wildlife

Wildlife Implications

- Wild animal reservoirs include raccoons, skunks, squirrels, opossums, deer, rodents, buffalo, and marsupials
- Most wildlife cases appear to be self-limiting and asymptomatic. Symptomatic wildlife are rare and very difficult to diagnose.
- Antibodies to the bacteria have also been found in reptiles, amphibians, and fish
- In Montana, low titers to various serovars are common in wildlife, but Lepto serology is difficult to interpret.

Bubonic Plague

(*Yersinia pestis*)

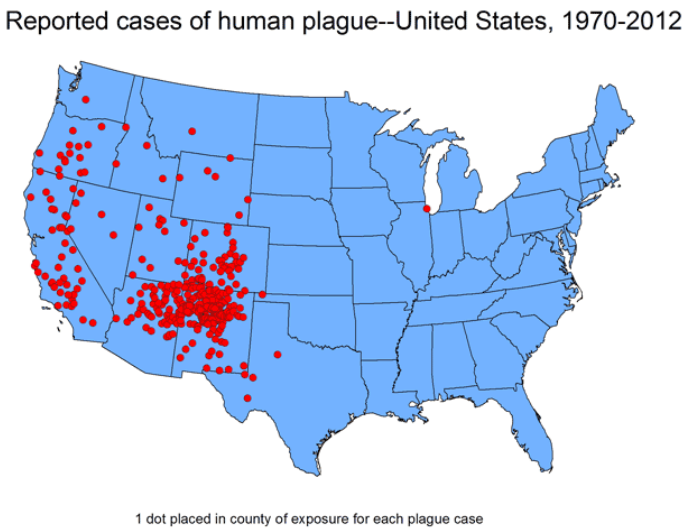
History

- 540–90 — Justinian's pandemic
  - 10,000 deaths per day
  - Fall of the Roman Empire
- 1347–53 — Black Death
  - One of the deadliest pandemics in human history
  - Estimated 25 million died or 1/3 of the world's population
- 1900–04 — first known plague epidemic in North America (San Francisco)
- 1924–25 — last urban plague with person-to-person transmission in the U.S. (Los Angeles)

“Ring Around The Rosy
A Pocket Full Of Posies
Ashes, Ashes
All Fall Down”

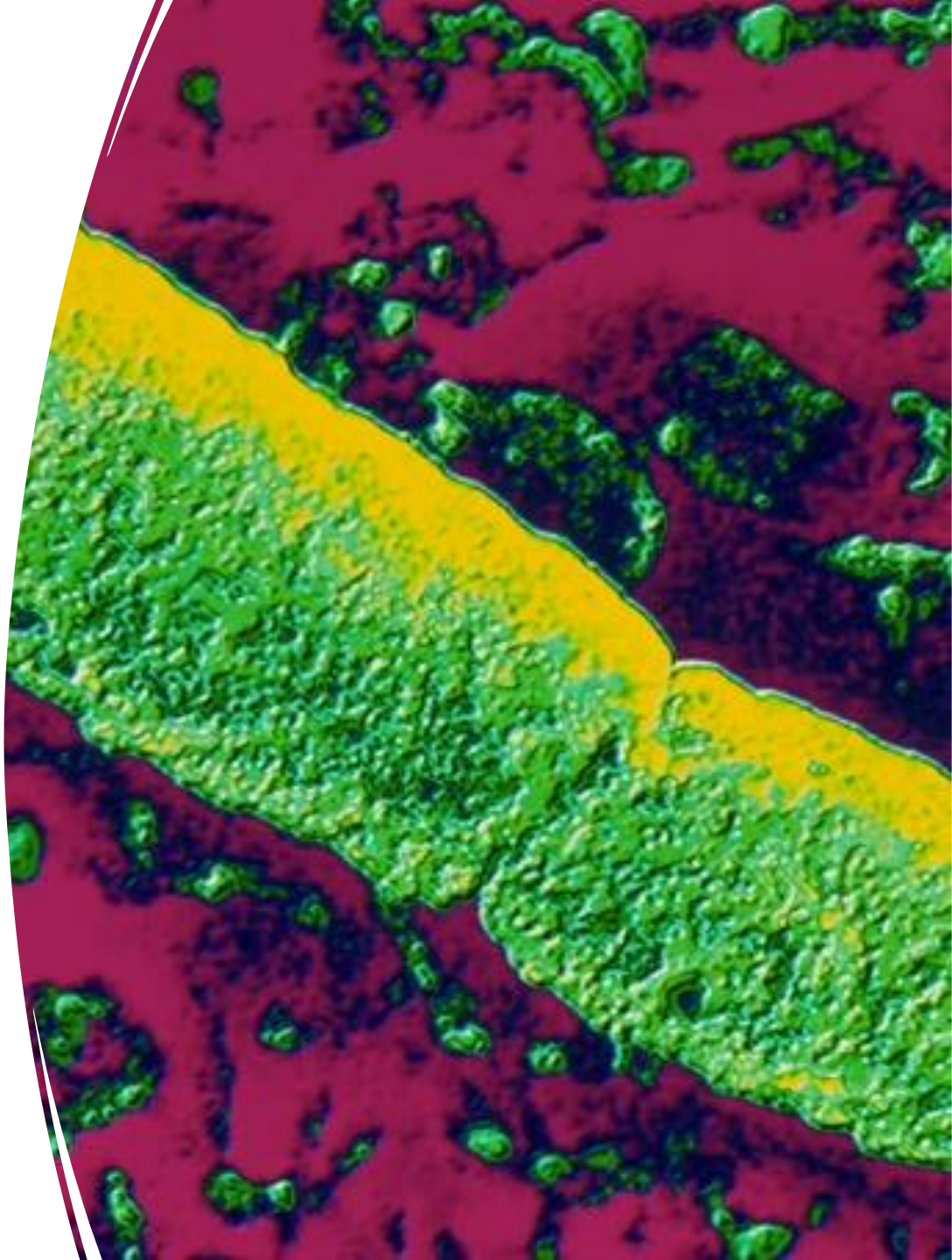
Modern Context

- Average of 7 U.S. per year (range: 1–17)
  - Most in Northern New Mexico, Northern Arizona, Southern Colorado
  - 0 human cases in Montana last 10 years
- Worldwide 1000–2000 per year
  - Most in Africa



Yersinia pestis

- Gram-negative rod
- Easily destroyed by drying or sunlight
- Survive for up to an hour when released into the air
- **Category A bioterrorism agent**
- **Select Agent**

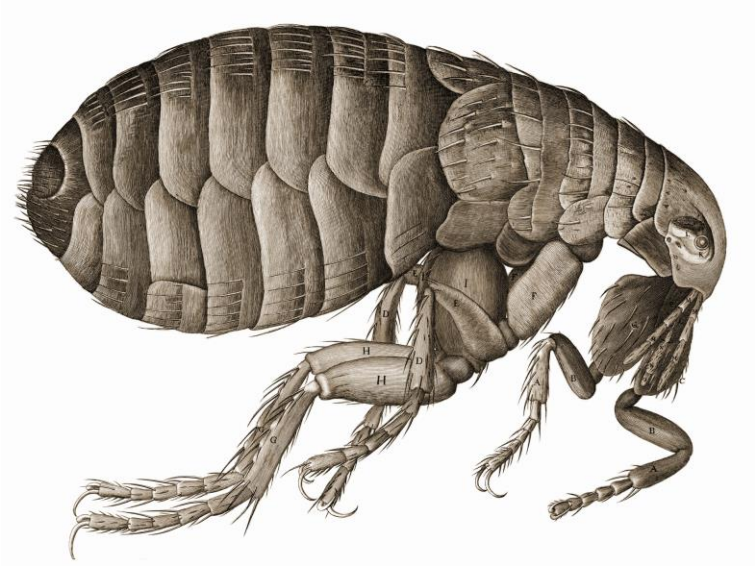


Hosts

- Reservoirs
  - Rats, prairie dogs, rock squirrels, ground squirrels, chipmunks, other burrowing rodents
- Vectors
  - Rat flea
  - Other species of fleas
- Domestic animals
  - Cats, aerosol transmission
  - Cats, dogs, rabbits bring infected fleas to the home

Transmission

- Flea bites
  - Most common
- Contact with contaminated fluid or tissue
- Infectious droplets
  - Pneumonic plague results in the release of droplets containing *Y. pestis*
  - Only way plague can have person-to-person spread
  - Cats with pneumonic plague can transmit to humans



Fleas

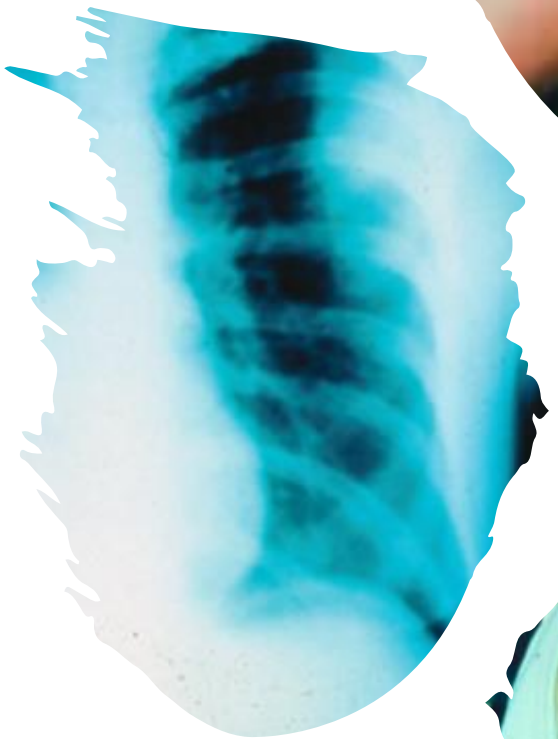
- <80 F
  - Blood clots in gut of flea
  - *Y. pestis* trapped
  - Clotted blood regurgitated
  - Enters wound from flea bite
- >80 F
  - Blood clot in gut of flea dissolves
  - *Y. pestis* passes through

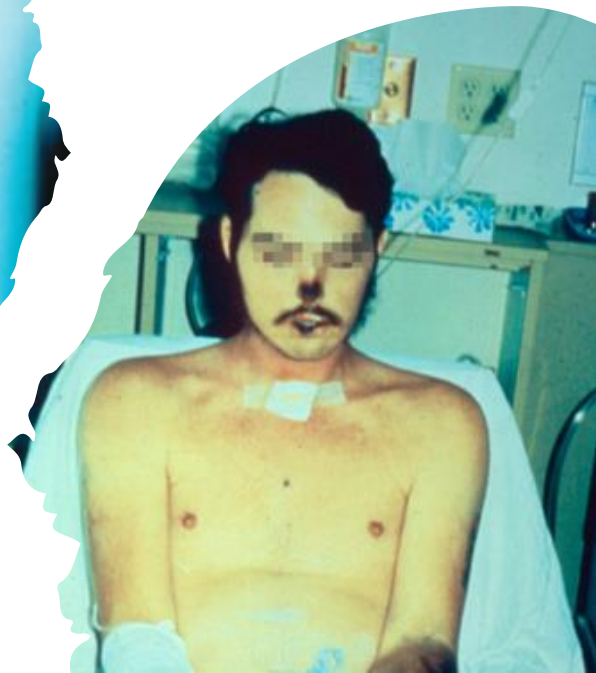
Ecology

- Enzootic cycle
  - Circulates at low rates within population of rodents
  - No excessive rodent die-off
- Epizootic cycle
  - In SW US more likely during cooler summers that follow wet winters
  - Large rodent die-off and fleas change hosts
  - Most likely in areas with multiple types of rodents living in high densities

Human Disease

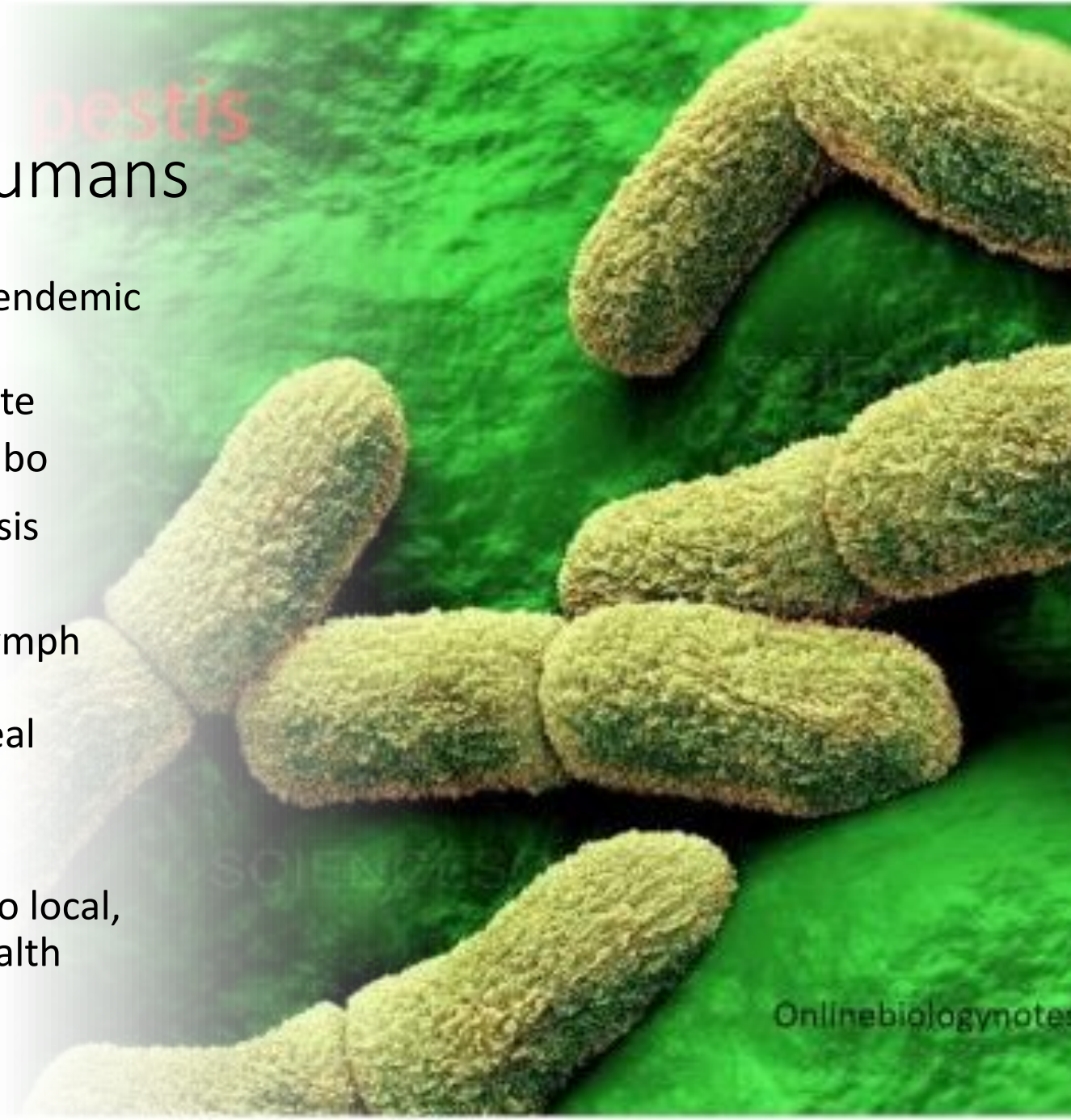
- Three forms
  - Bubonic
  - Septicemic
  - Pneumonic
- Mortality rate in **<u>treated</u>** persons 1%–40%





Diagnosis in Humans

- Tentative diagnosis (endemic areas)
  - History of flea bite
  - Presence of a bubo
- Confirmatory diagnosis
  - Microscopically
  - Culture blood, lymph node, sputum, bronchial/tracheal washing
  - Serology
- **Reportable** disease to local, state, and federal health officials



Treatment in Humans

- Begin appropriate therapy as soon as plague is suspected!
  - Early treatment, survival ~100%
- Antibiotics of choice: streptomycin or gentamicin
- Also effective: tetracyclines, fluoroquinolones, chloramphenicol
- **NOT** effective penicillin and cephalosporins

Prevention in Humans

- Rodent control
  - Eliminate rodent habitat around home
  - Rodent proof buildings
- Prevent roaming or hunting of pets
- Flea preventive for dogs and cats
- Insect repellents for skin & clothes
- Insecticide use in epizootic areas
- PPE when working with or around any potentially infected animal

Disease in Animals

- Carnivores, such as dogs and cats, may become infected and develop clinical signs
  - Canids experience less severe illness
  - ~50% of affected cats will die
  - Infection has been reported in goats, sheep, and camels, but it is uncommon in livestock species
- Transmission often occurs from ingestion of infected animal or flea bite

Disease in Animals - Symptoms

Cats: 50% mortality rate

- abscesses, lymphadenopathy, lethargy, high fever, secondary pneumonia may be present
- Necrotic nodules in spleen and liver, and suppurative pneumonia

Dogs: resistant to infection

- Can present with fever, lethargy, and dyspnea

Diagnosis in Animals

- Rule-out culture (*Y. pestis* is a Select Agent)
  - Sentinel Laboratory (e.g., MVDL) can perform culture to "rule out organism"
    - Suspect isolates must be referred to reference lab for identification and confirmatory testing
  - Sampling – lymph node aspirate (ante-mortem); tissues (lymph node, liver, spleen, lung, bone marrow)
    - If clinical concern for plague, recommend submitting whole carcass for necropsy and tissue collection
      - Always notify the lab prior to submission that plague is a differential so that we can take proper precautions to prevent lab acquire infections!
- PCR – offered by some labs
  - NDSU – whole blood (EDTA), lymph nodes, lung

Treatment in Domestic Animals

- Treat with antibiotics
  - Aminoglycosides, fluoroquinolones, and tetracyclines
- Infected animals should be maintained in isolation and with infection control precautions until at least 48 hours of antibiotic therapy has been completed

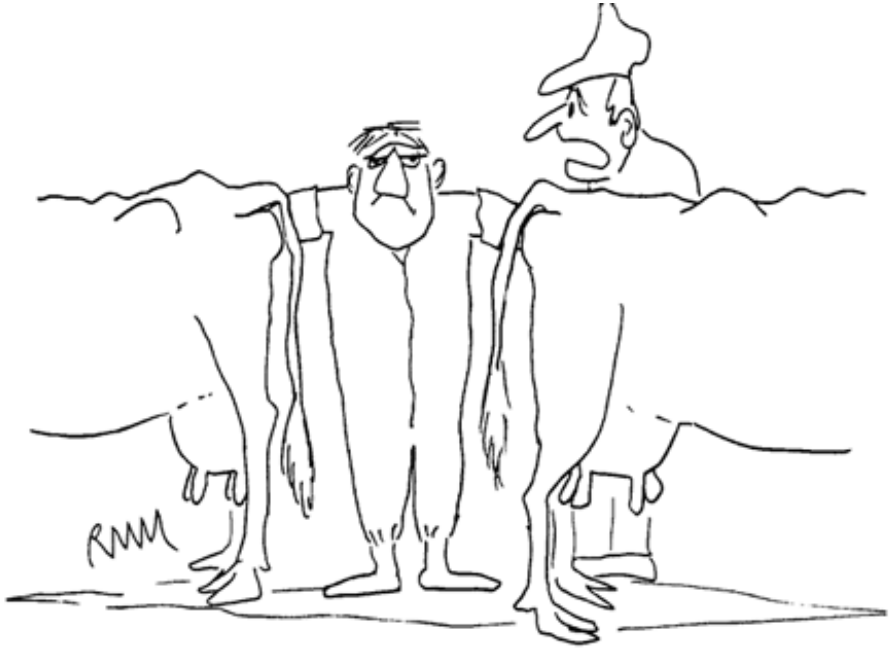
Prevention in Domestic Animals

- Control flea vectors
- Minimize exposure to rodents (alive or dead)
- Eliminate sources of food and nesting places for rodents around homes
    - Attempt to make your home rodent-proof

Wildlife Implications

- Infected wild rodents: disease may be may subacute, mild, or severe with acute high fatality rates
  - Acute form: hemorrhagic buboes and splenomegaly, die within 3-5 days of infection
  - Subacute form: necrotic buboes and necrotic nodules in the liver, spleen, and lungs, die 6 or more days after infection
    - Acute/Subacute – nasal bleeding, petechia, abscess formation, and pneumonitits
  - Resolving form: lymphadenopathy with focal purulent necrosis
- In the US, rodents are very susceptible to infection, having a 90-100% mortality rate
- Significant impact to endangered black-footed ferret recovery
- Also detected in squirrels, mink, marten, bobcats, lynx, rabbits, coyotes, badgers, weasels, skunks
- USDA Wildlife Services serosurvey of coyotes (sentinel species) from 2000-2019 shows that plague is widespread across Montana.

Questions??



"Been really busy, Doctor?"