

Animal Bites and Zoonosis



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Disclosures

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- ❧ Views are my own opinion, and not those of the US Army or WRAIR
 - ❧ I have no financial relationships with any of the products / companies discussed

Outline



- ❧ Dogs
- ❧ Cats
- ❧ Other pets
- ❧ Exotics
- ❧ Review

A few cases along the way...



☞ Bite Infections

- ☞ mix of anaerobes and aerobes from patient's skin and animal's oral cavity

☞ Zoonosis

- ☞ Animal disease that is transmissible to humans (humans are usually an accidental host)
- ☞ Spread by aerosols, feces, urine, insects, and direct skin contact

Bites



- ❧ 1% of all ER visits
- ❧ 60% related to dogs, 10% -20% cats
- ❧ Dog bites account for \$1 Billion/year in USA
- ❧ Age and gender
 - ❧ Age <20 and males more frequent victims for all bites
 - ❧ Females and elderly more common in cat bites
- ❧ Exotic animals

Dogs



Dogs



Risk of Bite injury

- ❧ Type of dog
 - ❧ Working dogs and aggressive breeds at higher risk
 - ❧ Pit bull terrier, Rottweiler, German shepherd, Akita
- ❧ Age of victim
 - ❧ Young boys (age 5 – 9)

Area of bite

- ❧ Children: face, head and neck
- ❧ Adults: hand, face, scalp, neck, thigh, leg

Type of bite

- ❧ Severe crushing injury can cause depressed skull fracture, severe scalp and intracranial bleed, facial disfigurement, damage to the great vessels and nerves



Dog Bites - organisms



☞ Aerobic

- ☞ *Pasteurella canis*.
- ☞ *Streptococcus* spp.
- ☞ *Staphylococcus* spp.
- ☞ *Neisseria* spp.

☞ Anaerobic

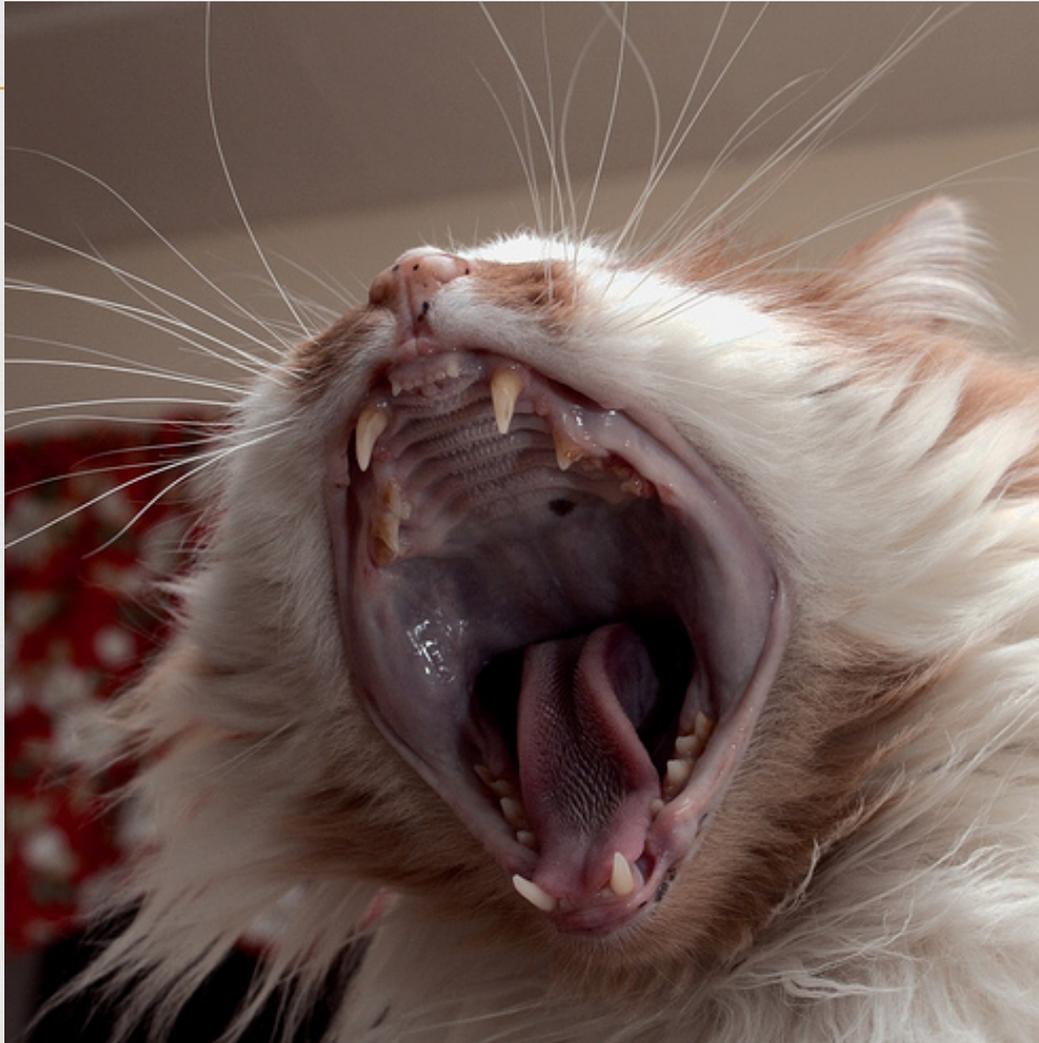
- ☞ *Fusobacterium* spp.
- ☞ *Bacteroides* spp.
- ☞ *Porphyromonas* spp.
- ☞ *Prevotella* spp.
- ☞ *Capnocytophaga canimorsus*

Dog Bites



- ❧ Only 2 – 10% get infected-Augmentin is drug of choice (Unasyn IV)
- ❧ *Pasteurella spp.*
 - ❧ Resistant to: cephalixin, clinda, diclox, erythro
 - ❧ Susceptible to: PCNs/cephalosporins, FQs, Doxy, TMP/SMX
- ❧ *Capnocytophaga spp.* (very bad in asplenic patients)
 - ❧ Resist to: TMP/SMX, ? vancomycin
 - ❧ Susceptible to: Amox/Clav, PCN G, clindamycin
- ❧ *Staphylococcus aureus*
 - ❧ MSSA > MRSA

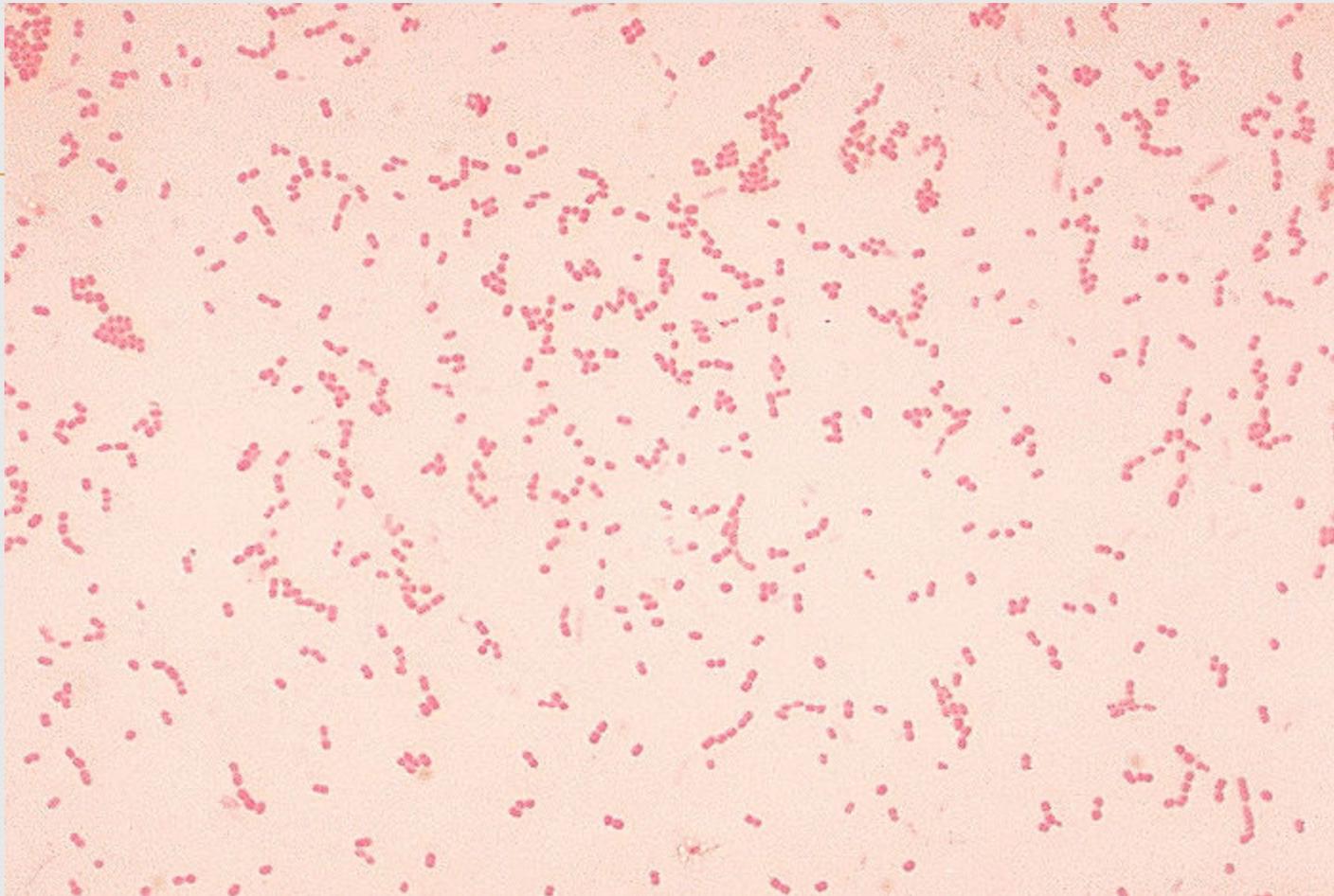
Cat Bites



Pasteurella multocida



- ❧ In saliva of >90% of cats, over 80% of wounds get infected
- ❧ Different species, *Pasteurella canis*, in saliva of 50% dogs, only 2 – 8% get infected
- ❧ Small aerobic GN bacilli
- ❧ Amoxicillin-sensitive



fastidious gram-negative bacillus

Pasteurella multocida



- ❧ Cause serious infections
 - ❧ Necrotizing fasciitis
 - ❧ Septic arthritis
 - ❧ Osteomyelitis
 - ❧ Less commonly, sepsis, septic shock, pneumonia, and meningitis
- ❧ High risk groups for severe infection:
 - ❧ Infants
 - ❧ Pregnant women
 - ❧ Patients with evidence of notable liver disease
 - ❧ Patients on chronic steroids
 - ❧ HIV-positive individuals
 - ❧ Organ-transplant recipients
 - ❧ Other immunocompromised patients
- ❧ Mortality with severe infection remains substantial at 25%

Cats



Septic arthritis of left first proximal interphalangeal joint

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Girl vs Cat



- ❧ 15 y/o female with wound from cat on forearm
- ❧ Seen in ED, wound cleaned, treated with amox/clav orally
- ❧ Wound slowly became worse, somewhat ulcerative. Patient now back in ED for further evaluation.
- ❧ Upon further questioning, she had a history of recurrent infections



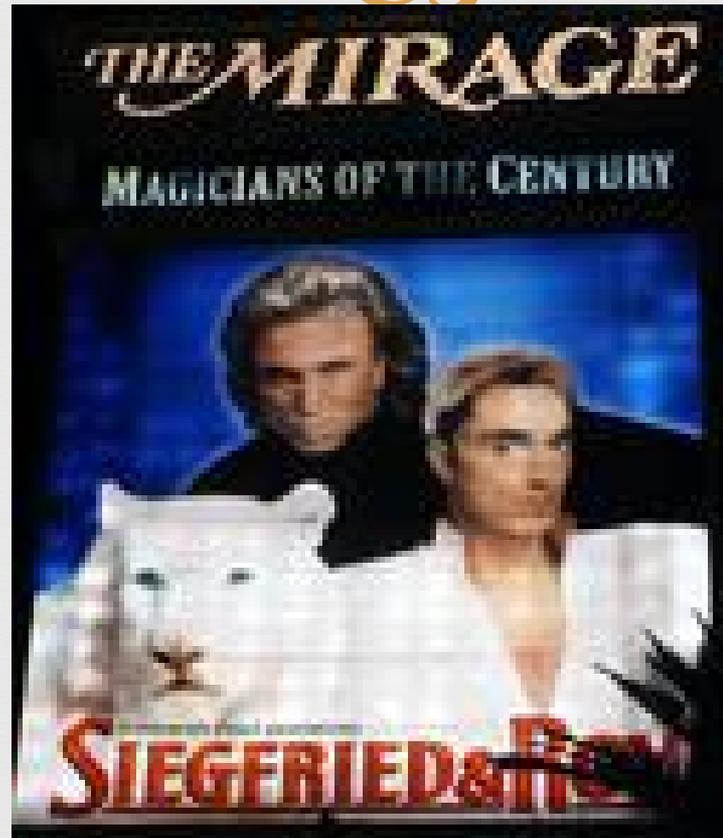
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infection of the left forearm of a 15-year-old



cat had developed recurrent MRSA culture-positive skin lesions of the perineal area 18

Roy Horn of Siegfried and Roy Roy attacked by tiger



Don't try this at home...or abroad



Tiger Bite



- ❧ September 18, 2003, a group of U.S. Army Reserve soldiers and Iraqi police were patrolling in the zoo after it had closed.
- ❧ A soldier had his right arm severely mauled by a male Bengal tiger; he had reportedly attempted to feed the tiger a chicken kabob
- ❧ Bystanders, seeing the attack, shot and killed the animal
- ❧ Bleeding was stopped, wound debrided, placed on broad spectrum ABX and patient medevac'd to WRAMC for further debridement and therapy

Acinetobacter baumannii

- ❧ Environmentally present
- ❧ Occurs in many of the wounded coming in from theater
- ❧ Treated with further wound revision, broad spectrum ABX to include Amox/Sulbact and colistin, wound eventually healed
- ❧ Sustained a substantial amputation of arm in sequential surgical revisions

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*"We'll have to clean that out immediately...
there's nothing dirtier than a lawyer bite."*

Human Bites



- ❧ 52 y/o male suffers a hand injury in brawl at tailgate party in Baltimore
- ❧ Presents 12 hrs later with a swollen, red, painful fist. X-ray shows bony fragments. Wound cleaned and given cephalexin, ice, rest.
- ❧ Returns to ER 5 days later with tachycardia, hypotension, fever, confusion
- ❧ Small wound with minimal serous secretions on the dorsum proximal 3rd phalanx of left hand; warmth, edema, painful movement of phalanx, decreased sensation, no crepitation detected





- ❧ As soon as clinical evaluation was finished, anti-tetanic immunization was performed, and patient transferred to surgery room
- ❧ Pressure in dorsal compartment was (20mm Hg) and in palmar compartment (42 mm Hg)
- ❧ Purulent material (about 120 ml) drained from pre-retinacular space
- ❧ 1 g amox-sulbact IV q 6 hours



Eikenella corrodens



- ❧ Anaerobic small GN bacilli
- ❧ Common in human oral flora
- ❧ Resistant to:
 - ❧ cephalexin, clindamycin, erythromycin, Flagyl
- ❧ Susceptible to:
 - ❧ PCN, FQs, TMP/SMX, Doxy, ESC



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Clinically significant Viral Zoonotic diseases

Pathogen

Borna disease virus
California serogroup viruses

Chikungunya virus

Cowpox virus
Crimean–Congo
haemorrhagic fever virus

Ebolavirus

Hantaviruses

Hendra virus

Hepatitis E virus

Influenza viruses

Japanese encephalitis virus

Kyasanur forest disease virus
Lassa virus

Lymphocytic
choriomeningitis virus
Marburg virus

Monkeypox virus
Nipah virus

Omsk haemorrhagic fever virus
Oropouche virus
Rabies and lyssaviruses

Rift Valley fever virus

Ross River virus

SARS coronavirus
Sindbis virus
Tick-borne encephalitis

Venezuelan equine
encephalitis virus
West Nile virus (WNV)

Yellow fever virus

Zika virus

Clinically significant Bacterial Zoonotic Infections

Pathogen

Anaplasma phagocytophilum

Bacillus anthracis
Bartonella sp.

Borrelia sp.

Brucella sp.

Burkholderia mallei and
Burkholderia pseudomallei
Campylobacter sp.

Capnocytophaga canimorsus and
Capnocytophaga cynodegmi
Chlamydochyta psittaci

Clostridium sp.

Corynebacterium ulcerans

Coxiella burnetii

Ehrlichia chaffeensis and
Ehrlichia ewingi
Escherichia coli

Francisella tularensis

Helicobacter sp.

Leptospira sp.

Listeria sp.

Mycobacterium sp.



Orientia tsutsugamushi

Pasteurella sp.

Rickettsia sp.

Salmonella sp.

Shigella sp.

Staphylococcus aureus

Streptococcus sp.

Vibrio sp.

Yersinia sp.

Horses

- ❧ Fecal transmission unlikely, but considered in those with close equine contacts
 - ❧ Salmonella
 - ❧ Usually mild, self limited disease
 - ❧ Severe cases (septicemia, meningitis) in immunocompromised
 - ❧ Campylobacter
 - ❧ Incubation 1 - 7 days
 - ❧ Abdominal pain and bloody diarrhea
 - ❧ Cryptosporidium
 - ❧ Rarely from healthy horses
 - ❧ Intracellular protozoan parasite
 - ❧ *C. parvum* and *C. hominis* are the likely human pathogens
 - ❧ *Giardia lamblia*-
 - ❧ directly or thru contaminated water
 - ❧ *Clostridium difficile*-
 - ❧ no horse-to-man transmission

Horses



❧ Aerosol

❧ *Rhodococcus equi*

- ❧ GP pleomorphic coccoid
- ❧ Found in the soil contaminated with herbivore manure
- ❧ Horses have lung disease, UC and mesenteric adenitis
- ❧ Humans - pulmonary infection most common occurs in immunocompromised

❧ Pathogens also found in sheep and cattle:

❧ *Brucella suis* and *abortus*

- ❧ exposure to blood and body fluids

❧ *Coxiella burnetti*

- ❧ Q fever
- ❧ Generally flu-like illness, pneumonia, hepatitis
- ❧ Chronic infection results in endocarditis

Horses



☞ Mosquito-borne disease

- ☞ EEE, WEE, West Nile virus: low/undetectable viremia; no reservoir for further spread
- ☞ VEE: horse is primary amplification host
 - ☞ Prevent by immunizing horses
 - ☞ Found in FLA to South America
 - ☞ Incubate 1-6 days in man
 - ☞ 0.5% adults and 4% children develop encephalitis

☞ Infected saliva

- ☞ Rabies unlikely but possible

Rabbits?



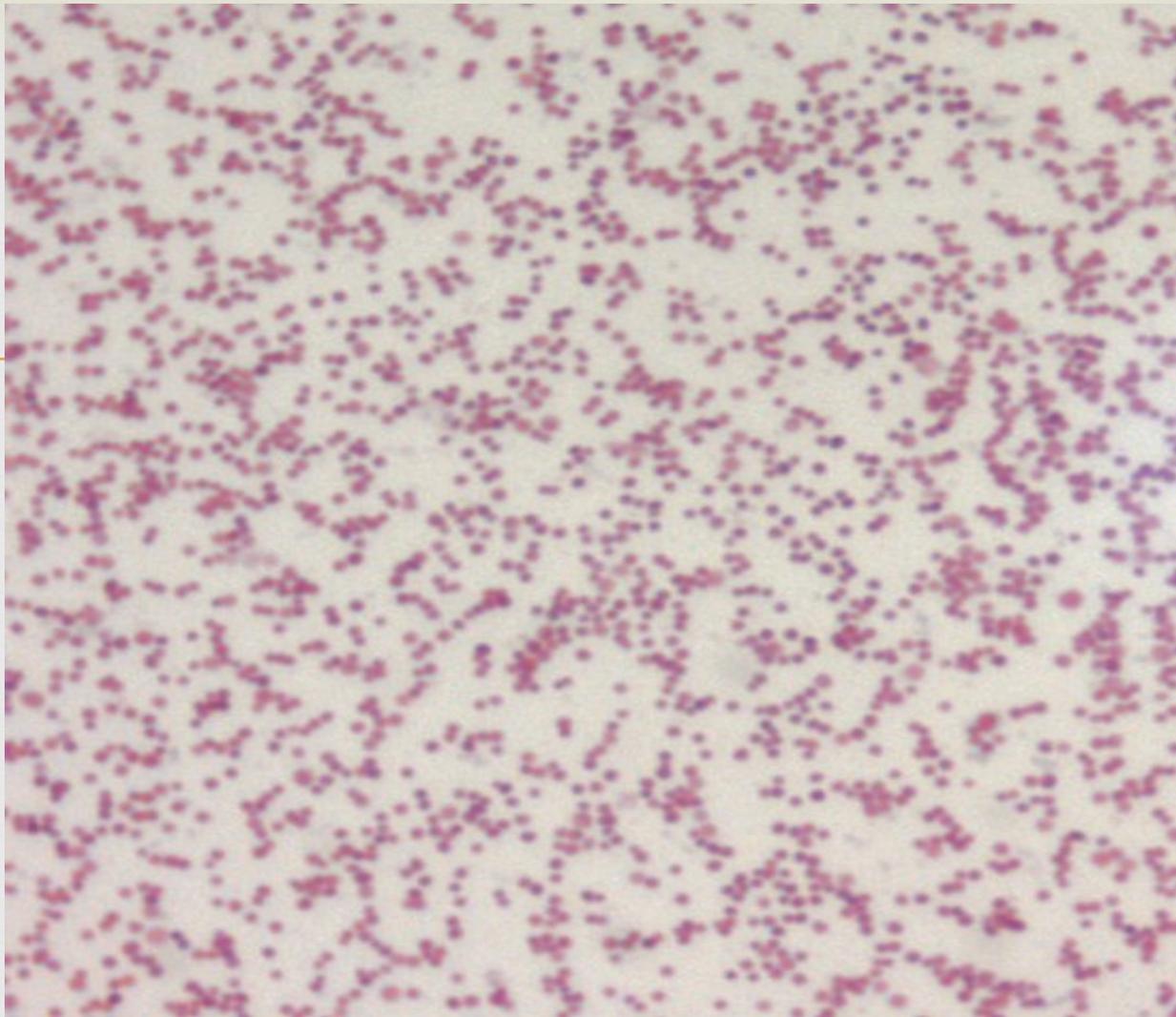
- ❧ 22 y/o male acute fever, lymphadenopathy, malaise, and dry, non-productive cough in Martha's Vineyard
- ❧ 5 pack-year smoker, mows lawns at the Golf club. No reports of running over any animals nor handling animal carcasses
- ❧ CXR showed RLL pneumonia, with some findings on LLL (Bilat?)

Engl J Med 2001; 345:1601-1606 [November 29, 2001](#)

Differential



- ❧ Typhoidal syndromes such as salmonellosis or rickettsial infections should be included in the differential diagnosis.
- ❧ Other causes of pneumonia such as infection with *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Coxiella burnetii*, or *Chlamydia psittaci*, as well as exposure to *staphylococcal* enterotoxin B
- ❧ In fulminant pneumonias, plague and inhalational anthrax



Tiny, pleomorphic, poorly staining gram-negative coccobacillus (0.2 to 0.5 by 0.7 to 1.0 microns). In clinical specimens, these forms can be found intracellularly.

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Rabbits

❧ GI

❧ ~~*Salmonella, Yersinia pseudotuberculosis, cryptococcus spp.*~~

❧ Respiratory

❧ *Pasteurella multocida* (no bunny-to-man trans) causes eye infections and snuffles in rabbits

❧ *Bordetella bronchiseptica* respiratory infection that can transmit to man

❧ Neurologic

❧ Rabies reported in 7 rabbits (chance encounter, generally doesn't happen)

❧ Cutaneous

❧ Dermatophytes (ringworm) transmitted by direct skin contact

❧ Zoonoses

❧ Tularemia

❧ Babesiosis

AN OUTBREAK OF PRIMARY PNEUMONIC TULAREMIA ON MARTHA'S VINEYARD

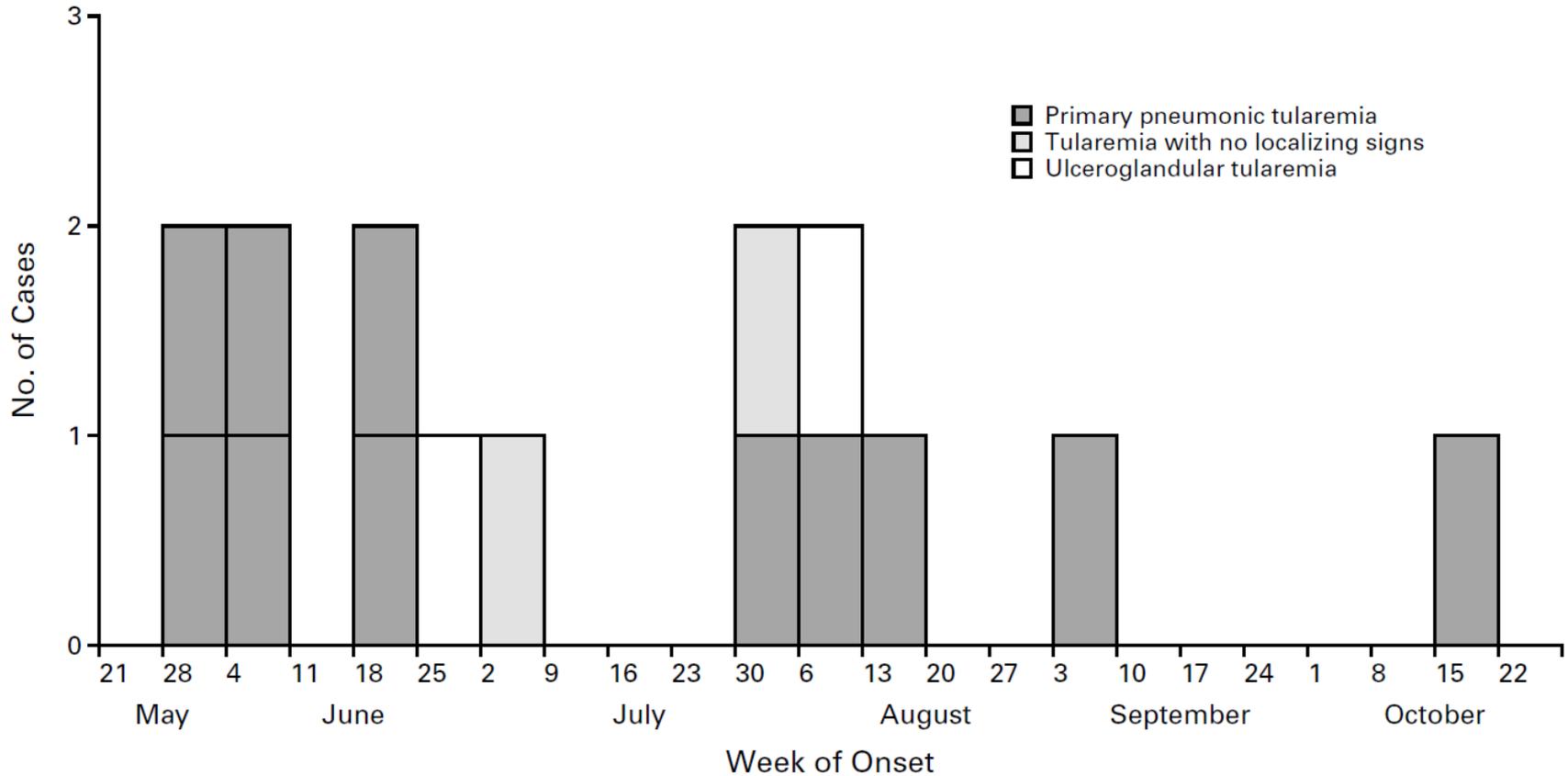


Figure 1. Cases of Primary Pneumonic Tularemia, Tularemia with No Localizing Signs, and Ulceroglandular Tularemia on Martha's Vineyard, May 21 through October 28, 2000, According to the Week of Onset of Illness.

Tularemia



- ❧ Although *F. tularensis* does not form spores, it can survive in water, soil, and decaying animal carcasses
- ❧ The organism persists in water and mud for as long as 14 weeks, in straw for 6 months, and in oats for 4 months
- ❧ *F. tularensis* was shed in animal excreta, persisted in the environment, and infected people after being mechanically aerosolized and inhaled

Tularemia: 6

Presentations



☞ *Typhoidal*

- ☞ Bacteremia with fever, chills, headache, myalgias, malaise, sore throat, and anorexia.
- ☞ Abdominal pain, nausea, vomiting, and diarrhea may be present

☞ *Pneumonic*

- ☞ Dry, non-productive cough, dyspnea, pleuritic chest pain, and fever.
- ☞ Physical examination may reveal rales, consolidation, and a friction rub or signs of effusion

☞ *Oculoglandular*

- ☞ painful, often purulent, conjunctivitis with lymphadenopathy especially in the periauricular, submandibular, and cervical areas

Tularemia: 6

Presentations (cont'd)



❧ *Oropharyngeal*

- ❧ painful sore throat; there may also be abdominal pain, nausea and vomiting

❧ *Ulceroglandular*

- ❧ Regional lymphadenopathy with a papule that develops into an ulcer at the site of entry. Fever, chills, headache, malaise, anorexia, and fatigue usually are the first symptoms

❧ *Glandular*

- ❧ similar to the ulceroglandular form, but without skin or mucous membrane lesions

Diagnosis



- ❧ *F. tularensis* is difficult to culture on standard media
 - ❧ Send early post-exposure (<24 hrs) nasal swabs, sputum, induced respiratory secretions for culture, DFA
- ❧ Definitive diagnosis is usually made retrospectively by serology
 - ❧ Titers are usually negative during the first week

Tularemia



☞ Treatment:

☞ Streptomycin 30 mg/kg qd IM for 10-14 days, or gentamicin 3-5 mg/kg qd IV for 10-14 days.

☞ Prophylaxis:

☞ A live, attenuated vaccine (available as an IND) is administered once by scarification

☞ Doxycycline 100 mg q12h po for 14 days, or

☞ Tetracycline 500 mg qid po for 14 days.

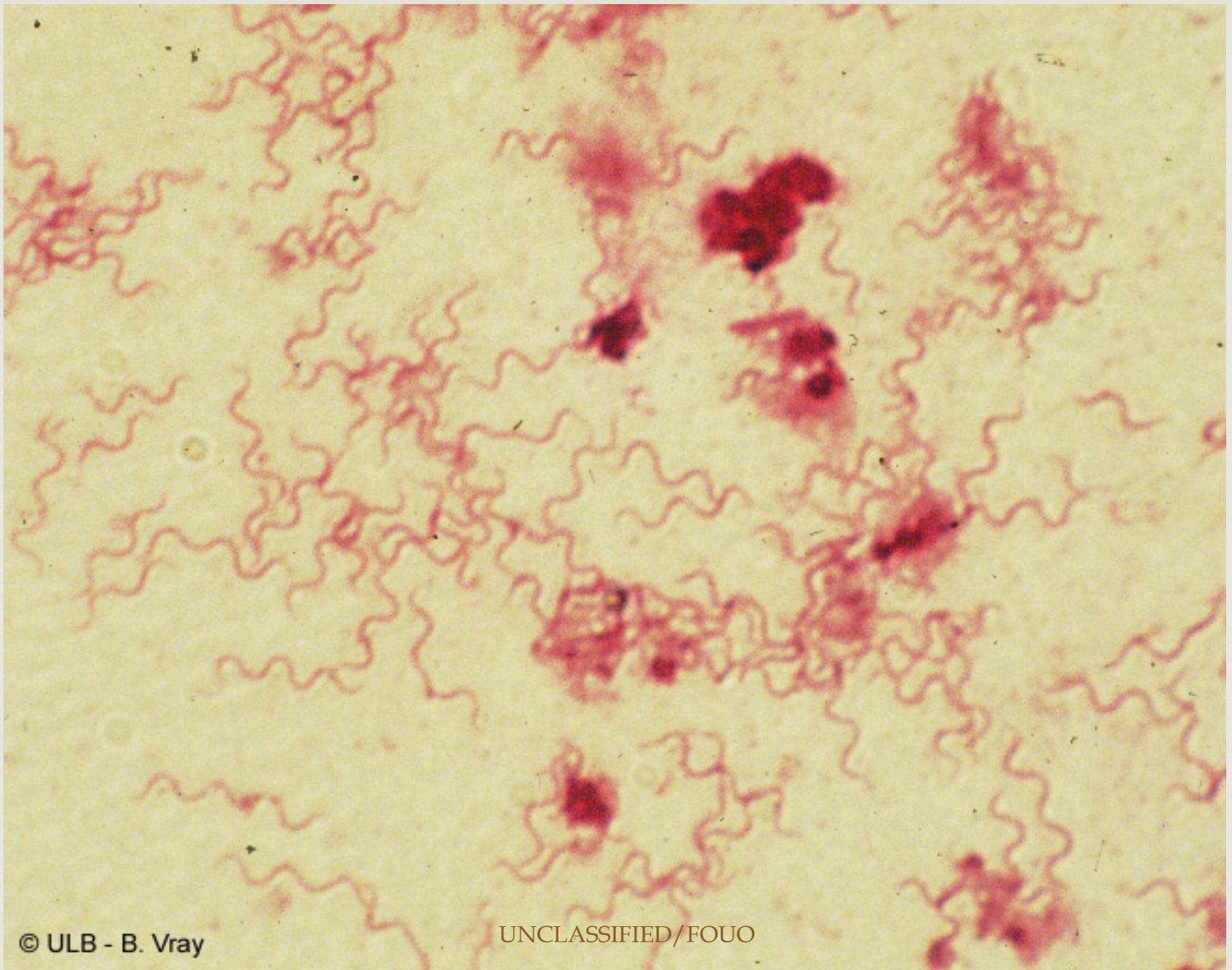
Rodents



- ❧ Infected saliva
 - ❧ Tularemia
 - ❧ Rat bite fever
 - ❧ Rabies (VERY rare): 2005 case report of rabies in guinea pig in NY
- ❧ Direct contact or aerosol
 - ❧ LCMV (lymphocytic choriomeningitis virus)
 - ❧ Transmission to man thru direct contact with fomites or aerosolization of virus
 - ❧ Monkeypox
 - ❧ Prairie dogs in the flea market
 - ❧ Cowpox
 - ❧ Ringworm
 - ❧ Hantavirus

Clubbing with the rat pack

- ❧ 48 y/o male in SE Asia comes to the clinic with fevers and severe myalgias
- ❧ He had been slipped a ruffi while at a club, bushwacked when exiting, roughed up, robbed and left in a back alley, awakening in his own filth, shoes, valuables and ID all stolen
- ❧ No evidence of sexual assault
- ❧ On PE, animal bite marks around right ankle
- ❧ Faint rash on extremities
- ❧ Within 24hrs, blood cultures positive for pleomorphic GNR



Rat Bite fever



- ❧ *Spirillum minus* in Asia
- ❧ *Streptobacillus moniliformis* in USA
- ❧ Children, poor, pet shops, labs
- ❧ Symptoms:
 - ❧ Fever
 - ❧ Rash (mac/pap, pustular, petechial, purpuric)
 - ❧ Polyarthralgias
 - ❧ Haverhill Fever (unpasteurized milk outbreak)
- ❧ Treatment:
 - ❧ PCN, Doxy

Birds



❧ Pet birds

❧ *Chlamydophila psittaci*:

- ❧ found in almost all pet birds, shed in feces and nasal discharge
- ❧ 1988-2003, 935 human cases in USA

❧ *Cryptococcus neoformans*

- ❧ Found in soil, from bird feces
- ❧ Inhalation of basidiospores or poorly encapsulated yeast
- ❧ Generally in the immunocompromised

❧ Wild birds

- ❧ Avian influenza
- ❧ West Nile virus



❧ Psittacosis

- ❧ Fever, HA and dry cough with recent bird exposure
- ❧ Pharyngitis, diarrhea and rarely encephalitis
- ❧ DX by serology, DFA, PCR
- ❧ Do NOT culture: grade 3 pathogen
- ❧ Tx with tetracycline; erythromycin (alternative)

❧ Cryptococcus

- ❧ Cough, chest pain, fever, wt loss, hemoptysis
- ❧ Uncommon: dyspnea, rash night sweats
- ❧ DX by histo, fungal cult, serum crypto Ag, x-ray
- ❧ Tx: fluconazole, itra, posi, vori in immunocompetent pt

Exotics



❧ Ferrets

- ❧ Influenza: aerosols from infected ferrets
- ❧ Giardia, Salmonella, Campylobacter, Cryptosporidium
- ❧ *Mycobacterium microte* (vole TB)
- ❧ No rabies transmission documented (vaccinate!)

❧ Hedgehogs

- ❧ Salmonella, Yersinia, dermatophytes (Trichophyton)

❧ Flying squirrels

- ❧ Toxo, Staph, *R. prowazekii* (epidemic typhus)

❧ Chinchillas

- ❧ Dermatophytes
- ❧ Klebsiella and Pseudomonas (no known transmission)

Slow growing ulcer in a Sudanese 10 year-old



Buruli Ulcer



- ❧ *Mycobacterium ulcerans*
- ❧ 3rd most common mycobacterial disease in humans
- ❧ Present in West Africa, East Africa, Papua New Guinea, Indonesia
- ❧ Carried by various animals and insects, including opossums, koalas, African clawed frogs, armadillos, water bugs

Fish



☞ Water exposures:

☞ *Mycobacterium marinum*

☞ Additional occupational exposures:

☞ *Aeromonas hydrophilia*

☞ *Edwardsiella tarda*

☞ *Erysipelothrix rhusiopathiae*

☞ Shellfish insult

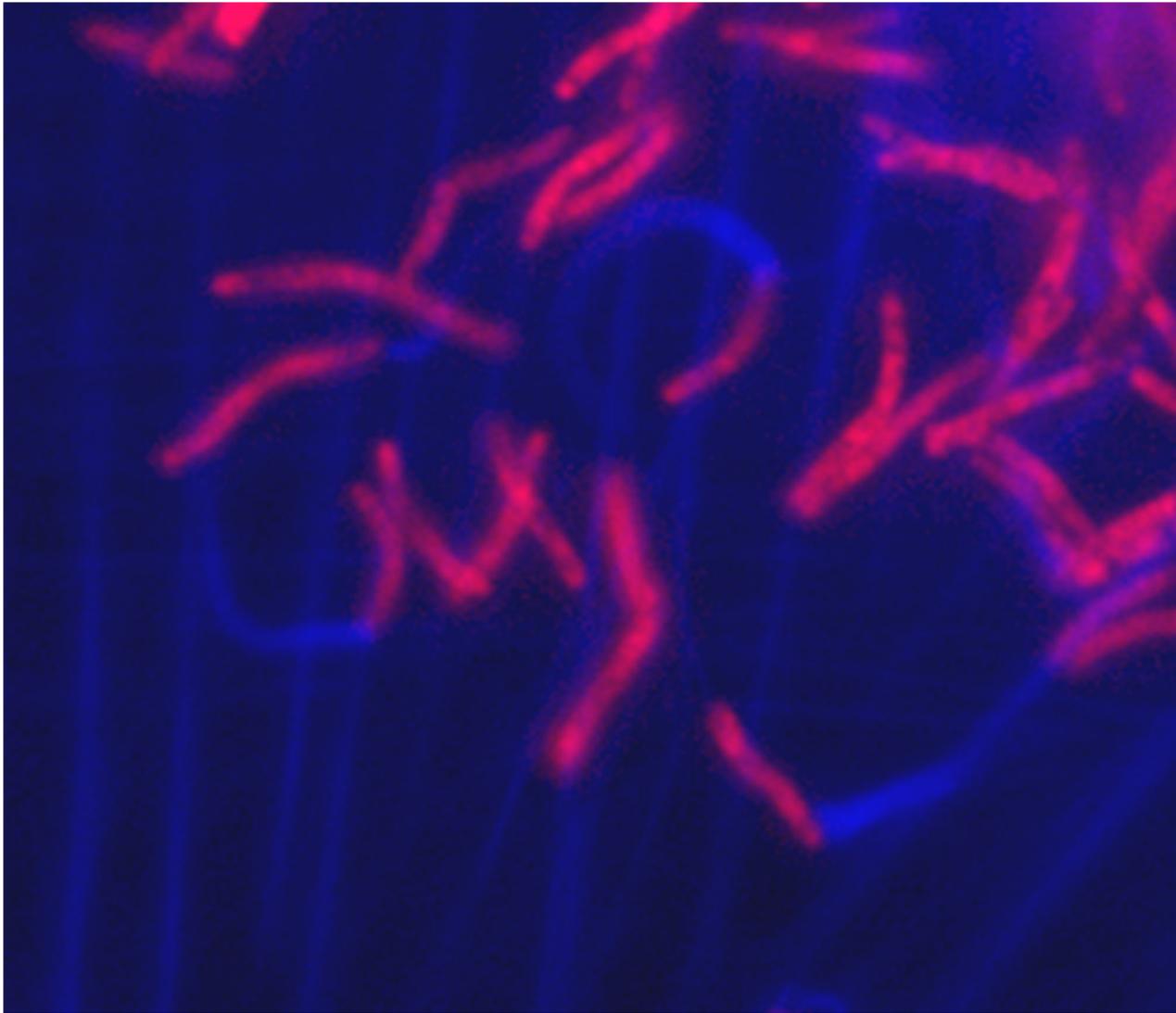
☞ Parasites

Tanks a lot...



- ❧ 22 year old grad student had after-work job at pet shop (fired 3 weeks ago)
- ❧ Sustained minor abrasion on underside of tank/plastic branch, while cleaning aquarium
- ❧ Now with lesion on dorsum of hand, not healing, not responsive to topical antibiotic ointment and cephalexin





Acid fast stain
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Mycobacterium marinum



- ❧ Found in fresh and salt water (swimming pools, fish tanks)
- ❧ “Fish tank granuloma” caused while sustaining minor injury or abrasion while cleaning fish tank
- ❧ Cutaneous lesions: soft skin papules, pustules and ulcers developing weeks after an injury/exposure
- ❧ Treatment options: rifampin plus ethambutol, tetracyclines, TMP-SMX , clarithromycin and fluoroquinolones

fishy case of shellfish?



- ❧ 53 y/o gulf bay fisherman, alcoholic with cirrhosis, has abrasions on arm/leg while harvesting oysters
- ❧ Few hours later, red, painful skin, hemorrhagic bullae begin to develop on legs and hands/arms
- ❧ Comes into the clinic not well 36 hrs later, in pain



Vibrio vulnificus



- ❧ Leading cause of shellfish associated deaths in USA
- ❧ Wound exposure to salt/brackish water in warm summer months
- ❧ Filter-feeding shellfish (i.e. oysters) concentrate bacteria
- ❧ Risk factors for severe disease:
 - ❧ Liver disease, hemochromatosis, alcohol abuse
- ❧ Treatment : doxy + ceftriaxone (or FQ)

Vibrio vulnificus



Preventive measures

- ❧ Avoid exposing open wounds to warm seawater; cover with water-tight wrap.
- ❧ Wear gloves when handling raw shellfish and avoid cross-contamination of raw shellfish with other foods
- ❧ Cook shellfish thoroughly; if considered high risk, do not consume raw oysters or other shellfish

Fear the Turtle



Reptiles



- ❧ 74-90% colonized with Salmonella
- ❧ Intermittently shed in feces
- ❧ Responsible for 6% (74,000 cases) of salmonella cases in US
- ❧ Yersinia, Campylobacter, Aeromonas
- ❧ Sale of turtles with carapace < 4 banned in 1975 resulted in decrease of Salmonella cases in children by 100k



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Monkeys



- ❧ Few reports of disease transmission from pet monkeys
- ❧ Shigella and Salmonella have been transmitted from asymptomatic spider monkeys
- ❧ Herpes B
 - ❧ Cercopethicine herpes virus 1
 - ❧ Transmitted directly from rhesus macaques through bites or scratches or from tissues or fluids
 - ❧ 80 – 90% of adult macaques infected and usually asymptomatic

B virus



- ❧ In monkeys, either no lesions or oral/genital lesions (HSV for monkeys)
- ❧ Viral shed is lifelong in oral and genital secretions, conjunctiva
- ❧ In humans, leads to encephalitis, fatal in 80% without treatment
- ❧ Majority of cases are in those who work with non-human primates

B Virus – Who is at risk?



- ❧ Monkey handlers
- ❧ Travelers exposure to free-ranging monkeys
 - ❧ India, Indonesia and Nepal
 - ❧ Puerto Rico and the Caribbean
- ❧ Those with monkeys kept as pets

B Virus – clinical manifestations

1

- ☞ Vesicular or ulcerative lesions
- ☞ Tingling, pain or itching at site
- ☞ Local lymphadenopathy

2

- ☞ Influenza like illness (fever and myalgias)
- ☞ Numbness, paresthesias, fever, conjunctivitis, abdominal pain, hepatitis, pneumonitis, CNS symptoms

3

- ☞ Nausea and vomiting
- ☞ CNS symptoms including HA, CN deficits, dysarthria, dysphagia, seizures, paralysis, respiratory failure and coma

B Virus: Post exposure Indications

-
- ❧ Skin or mucosal exposures to animals that are at high risk of shedding B virus
 - ❧ ill or immunocompromised macaques, animals with oral or genital lesions, or animals known to be shedding virus)
 - ❧ Inadequately cleaned skin or mucosal exposures
 - ❧ Lacerations of the head, neck, or torso
 - ❧ Deep puncture bites
 - ❧ Needlestick injuries with possibly contaminated needle
 - ❧ Lacerations or puncture wounds with contaminated objects
 - ❧ Exposures in which post-cleansing cultures are positive for B virus

B Virus: Post exposure



- ❧ Wash wound for 15 minutes
 - ❧ Skin: chlorhexidine, detergent or bleach (1:20)
 - ❧ Eyes, mucous membranes: flush with water
- ❧ Post-wash cultures of wound
- ❧ Treatment / prophylaxis
 - ❧ Acyclovir 800 mg po qid x2 weeks (PREGNANCY)
 - ❧ Valacyclovir 1g po tid x2 weeks (preferred for all others)
 - ❧ Suppressive treatment lifelong : valacyclovir 500 qd or acyclovir 400 tid
- ❧ Treatment/disease
 - ❧ If no CNS or PNS findings: IV Acyclovir
 - ❧ If CNS or PNS findings: IV Gancyclovir

Rabies



- ☞ Highest case-fatality rate of any known infectious disease (>99% Fatal)



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The Military Relevant Story ... A 40 yr old Master Sergeant Near Balad Iraq:

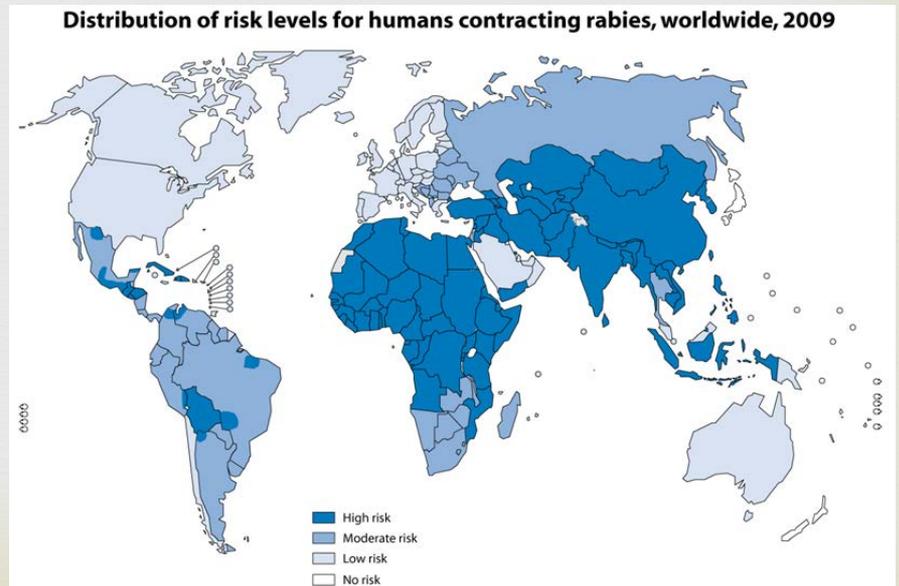


- ❧ Out in FOB with other NCO's
- ❧ "Unknown" small cat appears tangled in the camouflage netting
- ❧ He tries to free up this feral cat
- ❧ Cat bites his palm, then runs off
- ❧ No one can identify cat's location, after an extensive search...

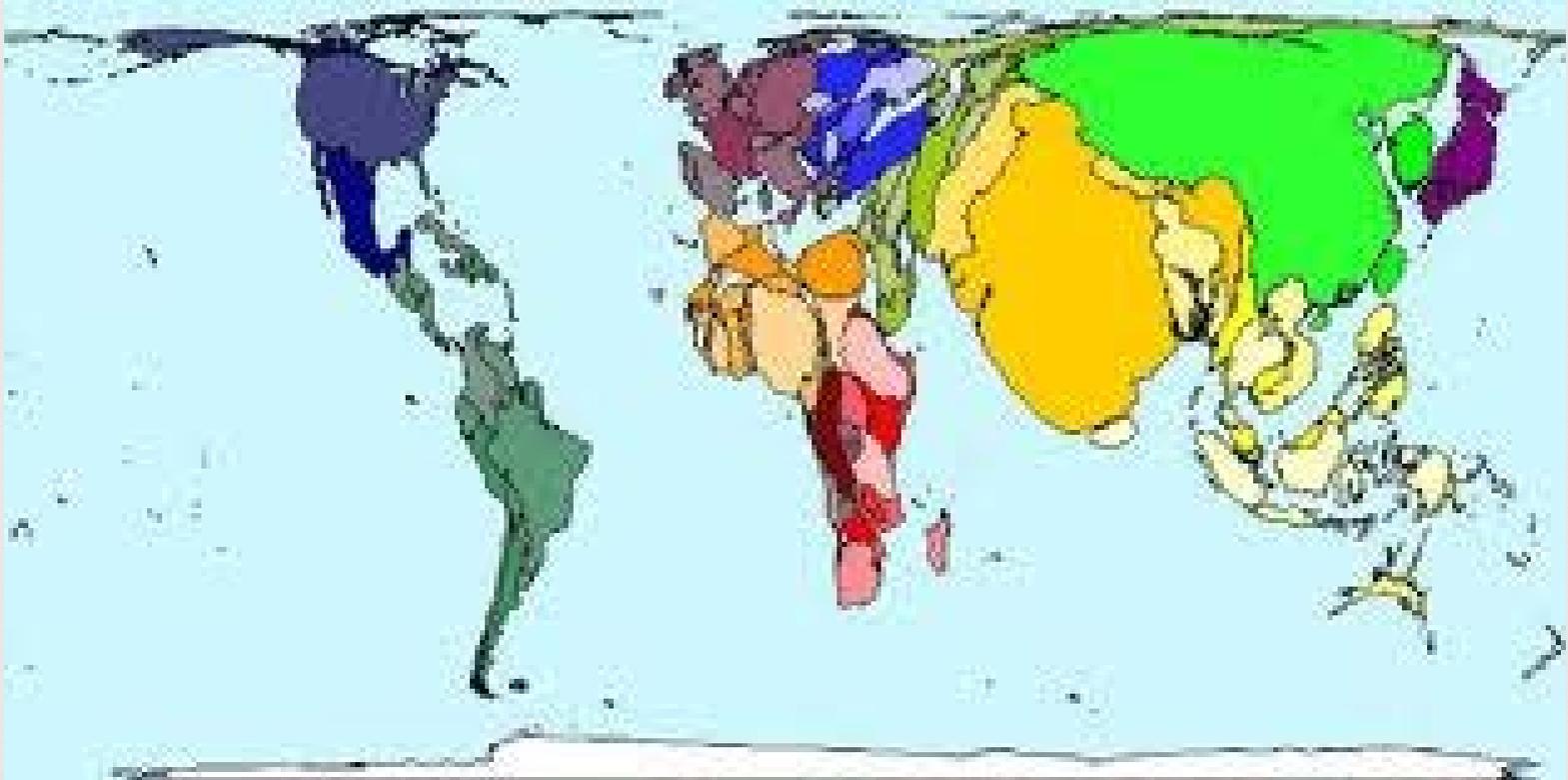


Varied Practices/Environments - Result in Distinctly Regional Epidemiology

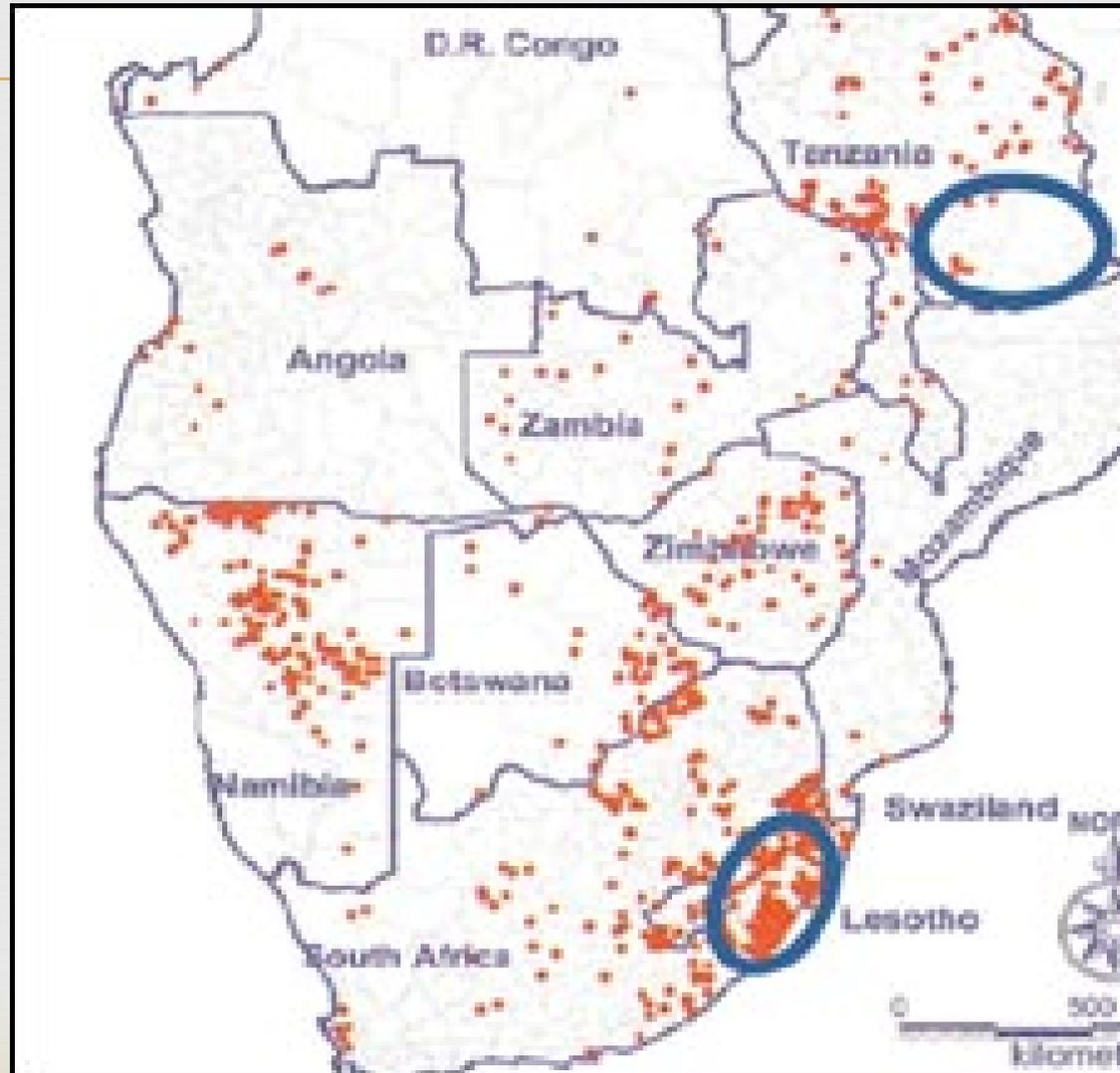
- Probably most rabies may have originated in bats
- But, most human spillover occurs from intermediate mammalian reservoirs
- Worldwide ~40 - 60K human cases *reported* to WHO annually
- Majority of cases are in the developing world -
 - India >30,000 cases/year (Population, unregulated mammals)
 - Often undiagnosed
- 10 million human PEP's yearly
 - 5 million in China
 - 1 million in India
 - 40-60,000 in N. America

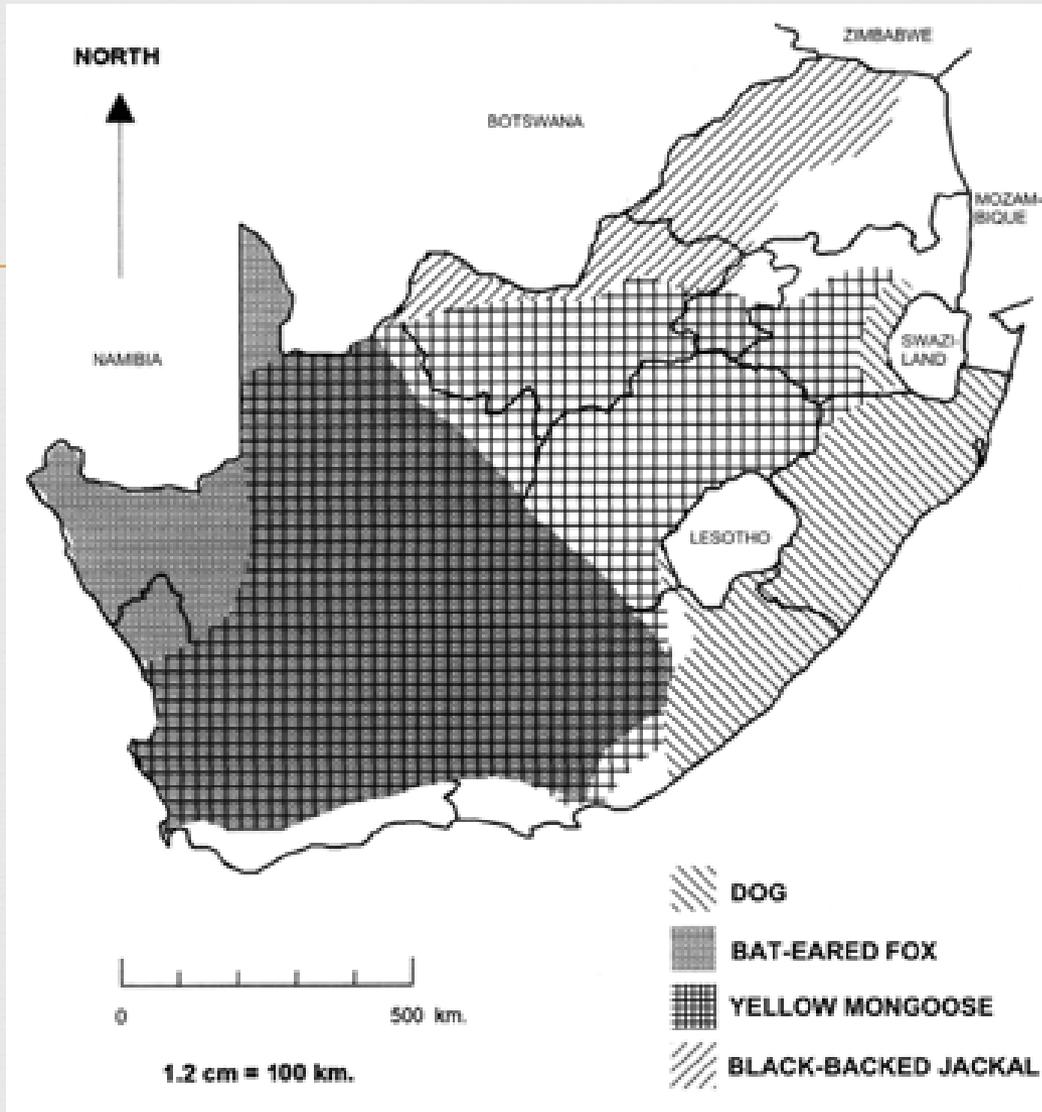


Cases



Africa





Rabies Transmission:



-
- ❧ Bites are the **most common route (high titer in saliva)**
 - ❧ Small abrasions or cuts from animal's teeth –
 - ❧ Mucous membrane contact with virus – saliva?
 - ❧ Including nasal mucosa (bat strains) – **not well-defined**
 - ❧ Corneal/tissue transplants from infected donors
 - ❧ 3 solid organ recipients in Alabama in 2004 – all died
 - ❧ 8 global corneal transplant recipients have died of rabies
 - ❧ Laboratory exposure to aerosols or needle sticks (very rare)
 - ❧ Abrasions/wounds licked by an infected animal
 - ❧ Rabies in saliva a few days before “madness,” lick a cut/wound
 - **Global: dogs, dogs, dogs > bats > other mammals (skunk, fox, raccoon)**
 - Peak in summer
 - # global risk group – young males
 - No racial, genetic differences in susceptibility

Rabies-vectors

COA

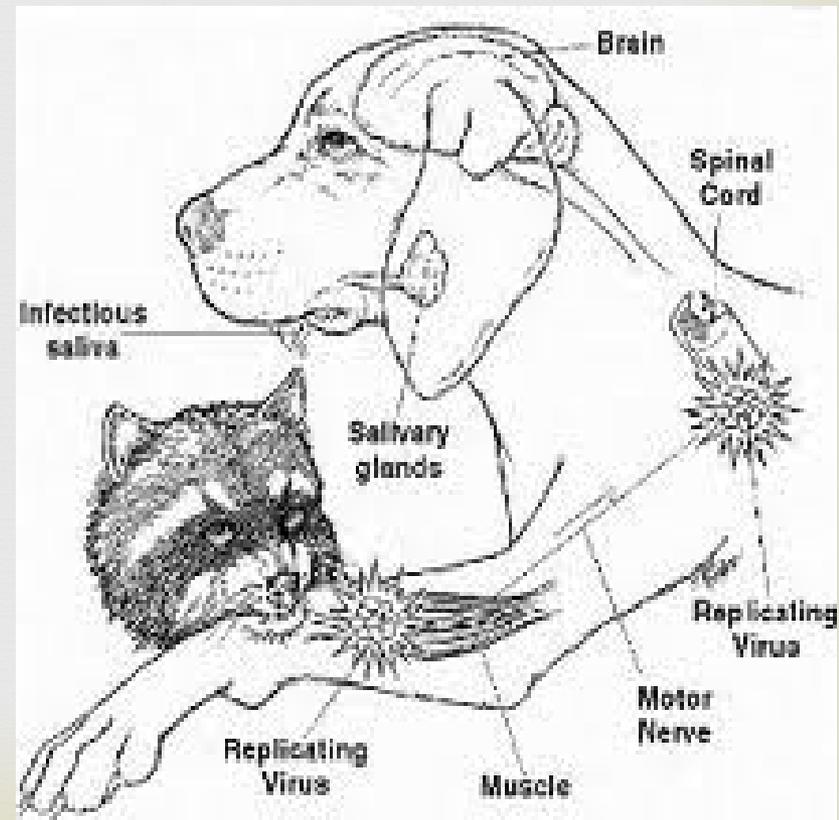


Understand Rabies: Pathogenesis



Russian Website: Russia-IC.com
LOCAL - NERVE - CNS - SALIVA

- After bite occurs:
 - virus localized in wound area – replication in myocytes?
 - latent period: days to years ... then **spread up neurons to CNS**
 - possibly shortened with stress, steroids, large inoculums, etc
- After CNS infection, rapid spread
 - salivary glands infected shortly after CNS (varies)
 - Faster in dogs than humans?



Understand Rabies: Clinical Features



∞ Incubation

∞ Mean: 20 - 60 days, Extremes occur

∞ **Range : 5-6 days to 19+ years**

∞ Prodrome – strange symptoms

∞ Acute neurological phase

∞ Coma

∞ Resolution

∞ Almost universally: death

∞ Anecdotally: recovery with prolonged ICU and antiviral drugs (Approx 6-7 people)



Understand Rabies: Incubation

- ❧ In humans, typically 1 – 3 months
 - ❧ 84% within 90 days, 99% < 1 year
 - ❧ May be as brief as 4 days
 - ❧ Cases documented 19 years post-exposure
 - ❧ Shorter period: little room for delay if ...
 - ❧ Bites to face/neck – close to brain via cranial nerves
(Virus travels up nerves at between 12 and 100 mm/day)
- *We try to give vaccine and RIG ASAP for head and neck bites!!**
- ❧ Younger patients
 - ❧ Multiple bites, high viral dose
- ❧ During incubation:
 - ❧ Clinically silent
 - ❧ No detectable antibody



Understand Rabies - Acute Neurologic Phase

- ❧ Onset with development of objective CNS signs
 - ❧ Typical duration 2 - 7 days
- ❧ Two clinical states
 - ❧ Furious / classical / agitated ~80% (MADNESS)
 - ❧ Look for “Odd behavior” - a night animal seen in daytime
 - ❧ Paralytic / dumb ~20%



Understand Rabies - Serum Diagnosis



- ❧ No technique for diagnosis prior to CNS infection
- ❧ Virus does not stimulate antibody while “*immunologically protected*” at bite site or ascending up neurons
- ❧ Antibody production begins **after CNS infection** (When the Game is Over):
 - ❧ rabies serum neutralizing Ab not detected until 6th day of clinical illness (The **serum** response is **SLOW**)
 - ❧ CSF Ab may be negative as long as 7 days after detection of serum Ab (**CSF** response is **VERY SLOW**)
 - ❧ if no post exposure prophylaxis, 50% show Ab by day 8 and **100% by day 15 of clinical disease**
 - ❧ Steroids, interferon may delay antibody development

5 Rules on How To Deal With Rabies:

1. Understand the disease, know your “region”
 - Rabies is very regional, distinct local vectors (animals)
2. Avoid Getting Bit
4. Low threshold for PEP
3. If “Bit”
 - clean the wound aggressively for “PEP” post-exposure prophylaxis
 - Must have excellent information and full control of risk factors if you decide to “not” give prophylaxis
5. Follow the rules ASAP
 - most rabies due to delays, or not following the recommendations

Rabies Vaccines: Try to use U.S. lots:

-
- ❧ **Many vaccines available outside the USA**
 - ❧ Some less immunogenic, poorly purified –
 - ❧ Increased association with neurologic and other side effects

 - ❧ **Two inactivated US vaccines, ~100% efficacious if correctly used**
 - ❧ **HDCV- Human Diploid Cell Vaccine**
 - ❧ Product: Imovax Rabies (HDCV for pre or post-exposure)
Manufacturer: Sanofi Pasteur, licensed **1980**
 - ❧ **PCECV - Purified Chick Embryo Cell, grown in chicken fibroblasts**
 - ❧ If hypersensitivity to other vaccines, i.e. frequent boosters
 - ❧ Chicken allergy does not preclude use
 - ❧ Product: RabAvert (PCECV for pre/post-exp), Manufacturer:
Novartis, licensed **1997**

 - ❧ **Standard use = 1.0 cc IM**

Rabies Immune Globulin (HRIG):



- ❧ Historically: Used since mid-1950's
 - ❧ Extensive WHO studies in the Middle East
- ❧ All US/Western IG products are very safe!
 - ❧ HyperRab™; and Imogam®
- ❧ Covers the initial 2 weeks for patients to develop their own immunity
- ❧ **Not used** if prior immunization
- ❧ Simple rules:
 - ❧ Give once
 - ❧ Within and including 7 days, *then no benefit afterwards*
 - ❧ **Do not overdose** (may reduce vaccine efficacy)
 - ❧ 20 IU/Kg of body weight
 - ❧ All or most near the wound if possible, remainder IM deltoid or thigh – **NEVER IV**
 - ❧ *Never anatomically close* to the vaccine site



Postexposure Prophylaxis for Non-immunized Individuals

Treatment	Regimen
Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
RIG	If possible, the full dose should be infiltrated around any wound(s) and any remaining volume should be administered IM at an anatomical site distant from vaccine administration. Also, RIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be given.
Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 , 3, 7, and 14.

Postexposure Prophylaxis for Previously Immunized Individuals

Treatment	Regimen
Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
RIG	RIG should not be administered.
Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 and 3.

4 sample sites required by CDC to Rule Out rabies

(To prove you do NOT have rabies)



1. **Saliva for virus:** Collect with dropper and place in sterile container. Tracheal aspirates, sputa not suitable
 - ☞ RT-PCR
 - ☞ Virus isolation
 2. **Neck biopsy:** 5-6 mm diameter punch from nape
 - ☞ Minimum 10 hair follicles
 - ☞ Sufficient depth to include **cutaneous nerves** @ base of follicle
 - ☞ On sterile gauze moistened with sterile water
 - ☞ RT-PCR and IF staining for viral Ag in frozen sections
 - 3 & 4. **Serum and CSF serology:**
 - ☞ Test for Ab with indirect IF and virus neutralization
 - ☞ If no vaccine or RIG has been given, the presence of serum rabies Ab makes dx, CSF testing unnecessary
 - ☞ Ab to RABV in CSF, regardless of immunization hx, suggests rabies infection
- *Brain biopsy** - old histopathology for "Negri" bodies - very specific, lower sensitivity - Best site is the cerebellum or basal ganglia (post mortem)

Rabies specimen submission form: www.cdc.gov/rabies/docs/ror_form.pdf

Summary: Management and Treatment of Animal Bites



Cultures

- Gram stain, aerobic, and anaerobic cultures

Irrigation

- Normal saline; copious high-pressure

Debridement

- remove necrotic tissue and any foreign bodies

Imaging

- Plain radiographs to rule out foreign body
- CT/MRI if concern for osteomyelitis

Wound closure - not usually indicated

Management and Treatment of Animal Bites



Antimicrobial therapy:

- Prophylactic antibiotics in selected cases
- Coverage based on patient type and specific animal involved

Hospitalization Indications:

- fever, sepsis, spreading cellulitis, substantial edema or crush injury, loss of function, immunocompromised status, or noncompliance

Immunizations:

- Tetanus booster and/or immune globulin
- ? Rabies vaccine and/or immune globulin

Empiric oral antibiotic therapy for animal bites

Antibiotic agents	Adults
Agent of choice	
Amoxicillin-clavulanate	875/125 mg twice daily
Alternate empiric regimens include:	
One of the following agents with activity against <i>P. multocida</i>:	
Doxycycline*	100 mg twice daily
TMP-SMX*	1 double strength tablet twice daily
Penicillin VK	500 mg four times daily
Cefuroxime	500 mg twice daily
Moxifloxacin	400 mg once daily
PLUS	
One of the following agents with anaerobic activity:	
Metronidazole	500 mg three times daily
Clindamycin*	150 mg three times daily



QUESTIONS?