Zoonotic Infections

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Outline

- Overview of Zoonoses
- Potpourri of topics
- Case presentation of different zoonotic disease cases with different:
  - Mode of transmission
  - Reservoir hosts
  - Severity of illness
- Illustrates the diversity of zoonotic diseases
- Emerging topics

What is a Zoonosis?

A zoonosis (also zoonotic disease) is an infectious disease that is transmitted between species (sometimes by a vector) from animals to humans or from humans to other animals. It is sometimes called reverse zoonosis or anthrozoosis. In direct zoonosis the agent needs only one host for completion of its life cycle, without a significant change during transmission.

- From Wikipedia

Companion animals

<table>
<thead>
<tr>
<th></th>
<th>Dogs</th>
<th>Cats</th>
<th>Birds</th>
<th>Horses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of households owning</td>
<td>36.5%</td>
<td>30.4%</td>
<td>3.1%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Number of households owning</td>
<td>43,348,000</td>
<td>36,617,000</td>
<td>3,671,000</td>
<td>1,700,000</td>
</tr>
<tr>
<td>Average number owned per household</td>
<td>1.6</td>
<td>2.1</td>
<td>2.3</td>
<td>2.7</td>
</tr>
<tr>
<td>Total number in United States</td>
<td>68,936,000</td>
<td>74,858,000</td>
<td>8,300,000</td>
<td>4,858,000</td>
</tr>
</tbody>
</table>

**Specialty and Exotic Animals**

![Households and Population Table](https://www.avma.org/KB/Resources/Statistics/Pages/Market-research-statistics-US-pet-ownership.aspx#exotic)

**Zoonosis: General**
- Many are missed because of vague clinical presentation – ‘viral’
- Lack of awareness
- Diagnosis is often problematic
  - Tests not widely available
  - Orphan diseases
  - “new twists”

- Handout slightly different > PowerPoint

**When you hear hoof beats…**

- **Bacterial Zoonoses**
  - Anthrax
  - Brucellosis
  - Campylobacteriosis
  - Cat Scratch Disease
  - Ehrlichiosis
  - E. coli 0157:57
  - Glanders
  - Leptospirosis
  - Listeriosis
  - Lyme Disease
  - Melioidosis
  - Plague
  - Psittacosis
  - Q Fever
  - Rat-bite Fever
  - Relapsing Fever
  - Rocky Mountain Spotted Fever
  - Salmonellosis
  - Tularemia
  - Typhus Fever
  - Yersiniosis
  - Zoonotic Tuberculosis

- **Viral Zoonoses**
  - Arenaviruses (LCMV, Lassa, S. American hemorrhagic fevers)
  - Bat lyssaviruses
  - Colorado tick fever
  - Ebola
  - Equine encephalitides (WEE, EEE, VEE)
  - Hantaviruses (Hantaan, Sin Nombre)
  - Hendra

- **Parasitic Zoonoses**
  - Babesiosis
  - Cryptosporidiosis*
  - Leishmaniasis*
  - Giardiasis*
  - Toxoplasmosis*
  - Trypanosomiasis
  - Protozoa
  - Helminths: (roundworms, tapeworms, flukes)*

- Anisakiasis
- Cysticercosis
- Hydatidosis
- Mesocoeostoidiasis
- Schistosome Dermatitis (Swimmer’s itch)
- Trichinosis*
- Visceral Larval Migrans*
Emerging infectious diseases

- Estimated that 75% are zoonotic
  - Many viral
  - Many vector borne (e.g., West Nile virus)

-Chomel et al., Emerg Inf Dis 2006

Case 1

Girl with Fever & Rash

- 8 year old female
  - Developed headache, fever, sore throat
  - 4 days later: macular rash on hands/feet—later petechial
  - 1 week: severe arthralgias, refusal to walk
  - Seen by several physicians; primary MD, rheumatologist, oncologist, dermatologist
  - Pediatric ID consulted just before bone marrow

Girl with Fever & Rash

- CBC, urinalysis: normal
- Blood / urine culture negative
- Unremarkable PMH except allergy to PEN
- No recent travel
- No tick bites, denied pet ownership
- No unusual dietary history

When asked specifically about rodents - patient owned a rat but no bite history (mother didn’t consider it a “pet”)

Blood culture repeated with RBF diagnosis in mind (micro lab can optimize isolation of organism with special techniques):
  - Blood culture positive for *Streptobacillus moniliformis*
Rat Bite Fever: Microbiology

- Two distinct disease syndromes
  - *Streptobacillus moniliformis*: most cases in US
    - Incidence unknown since not a reportable disease
    - Probably rare but likely underdiagnosed
    - Relatively difficult to isolate
  - *Spirillum minor*: not generally found in US
    - Mostly in Asia
    - Different syndrome
    - Sodoku or relapsing fever

Rat Bite Fever: Epidemiology

- Typically transmitted by bite or scratch of rats, mice, squirrels, carnivores that prey on rodents
- Can be acquired through handling of dead rats
- 50-100% wild and lab rodents harbor organism
- Food/water contaminated with infected rat excreta (cases called Haverhill)
- 40% of cases no history of bite

Rat Bite Fever: Clinical

- Incubation: ~ 7 days (range 1-10 days)
- Abrupt onset fever (irregular relapsing fever)
- Chills, headache
- Migratory arthralgias, myalgias
- Clinical features similar to other diseases
- Diagnosis usually requires high index of suspicion

Rat Bite Fever

- Complications
  - Endocarditis, myocarditis, pericarditis
  - Meningitis
  - Pneumonia
  - Abscesses in “virtually every organ”
- Untreated: 7-13% mortality
- Treatment
  - Penicillin or Doxycycline

Case 2

*Elliot et al., Clin Microbiol Rev, 2007
Dijkmans et al., Infection, 1984
Pins et al., Clin Inf Dis, 1996*
11 m/o male with Encephalopathy

- History of present illness
  - 5 days PTA: developed irritability
  - 2 days PTA: unable to sit
- Other history
  - no major illnesses; vaccines UTD
  - 1 older sibling, both parents healthy
  - travel to Sierra Nevada 4 weeks PTA
  - lives in Pacific Grove
  - spends much time outdoors; occasional pica noted

11 m/o male with Encephalopathy

- Examination findings
  - Right eye
    - deviated medially
    - diffuse serpiginous lesions
  - Hypertonicity extremities
- Lab findings
  - CBC: 18K WBCs, 50% lymph, 17% eosin
  - CSF: 50 WBCs, 45% eosin
- Cranial MRI
  - “patchy” disseminated white matter

11 m/o male with Encephalopathy

- Hospitalized for workup and treatment
- Serology/PCR: negative
  - Toxocara, Coccidioides, Varicella, HSV
- Cultures: negative
  - blood, CSF, urine
- Treatment
  - acyclovir, erythromycin, steroids, clonazepam, albendazole

11 month old male with Encephalopathy

- Serum sent to Purdue University:
  - Positive for Baylisascaris procyonis

Balamuthia vs. Baylisascaris

- Balamuthia: Free-living amoeba
- Baylisascaris: a worm

- Both can cause CNS illness but very different

Baylisascaris procyonis

- Intestinal nematode
- Natural hosts
  - adult raccoons
- Transmission
  - eggs shed in feces (millions of eggs shed)
  - require 3-4 weeks to become infectious
  - ova extremely resistant to dessication/destruction; may remain viable in the environment for years
Baylisascaris procynosis

Human infections rare
- Despite high potential for exposure, few cases reported
- Infected animals shed millions eggs/day, ~90% juvenile raccoons infected in some areas
- ~20 human cases reported

Risk factors for infection
- Contact with raccoon feces or an environment contaminated by infected feces and geophagia or pica
- “Suspect vehicles” include soil, wood, leaves and other vegetation, bark, and stone

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Baylisascaris procynosis

3 forms
A. organs: visceral larva migrans (VLM) [only one documented case]
B. brain: neural larval migrans (NLM) [typically young children, but case reports of older individuals]
C. eye: Ocular larva migrans (OLM) [adults]

Gavin et al., Clin Microbiol Rev 2005
Wise et al., Microbes and Infection 2005

Baylisascaris procynosis

An emerging parasite..

- “Suspect vehicles” include soil, wood, leaves and other vegetation, bark, and stone

Baylisascaris NLM

Often devastating outcome with death or severe neurologic sequelae
- 14 month old boy with NLM from MA, some residual deficits and moderate speech delay but overall good
- 4 year old boy from New Orleans, LA with NLM, “full recovery”
- Both treated with steroids and anti-helminthic

Peters et al., Pediatrics, 2012
Pai et al., Emerg Infect Dis, 2007

Epidemiology

- Raccoon defecate in “latrines” - outside or inside:
- Eggs of Baylisascaris very hardy
  - Highly resistant to desiccation
  - Viability not affected by freeze/thaw
  - However relatively low thermal death point (≤62 C)

Who is at risk?
- Contact with raccoon feces or an environment contaminated by infected feces and geophagia or pica
  - Typically young children, males > female
  - Other cases;
    - Developmental delay with history of pica
    - Teenager with substance abuse
    - 73 year old with Alzheimer-type dementia

- Hung et al., Emerg Infect Dis, 2012
- Chung et al., Pediatr Infect Dis J, 2009

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Baylisascaris NLM

- Often devastating outcome with death or severe neurologic sequelae

- However, a few ‘promising’ case reports
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Baylisascaris procyonis

- More severe than Toxocara
  - larger larvae (1-2 mm)
  - extensive migration (brain, eye, heart)
- Clinical
  - eosinophilic meningoencephalitis
  - death or long-term DD in children
- Pathology
  - deep cerebral white matter granulomas

Other potential hosts

- Olingos
- Kinkajous
- Opossums
- Clingos

Case 3

72 y/o male with lethargy and ascending paralysis

- Onset of headache/fever
- 5 days later hospitalized with lethargy, somnolence and ascending paralysis
- Clinician thought it was probably a stroke but wanted to rule out encephalitis
Exposure history:
- Born and raised in the Philippines and had been there 10 months prior to onset of illness
- US resident for 10 years
- No known mosquito bites
- No known animal exposures

Admit labs/Neuroimaging:
- LP: WBC = 10 WBCs/mm³, Protein = 172 mg/dL, Glucose = 60 mg/dL
- MRI: mild atrophy (appropriate for age), otherwise normal
- Died 11 days after hospitalization
- No autopsy, cause of death: "cerebral vascular accident"

Rabies antibody positive and rabies PCR positive from "throat swab" (contaminated with saliva)
- Sequenced strain: canine strain/Philippines
- Patient originally from Philippines, was there 10 months prior to onset of illness

Causes a severe acute progressive encephalitis
- One of the ‘oldest’ infectious disease known to man
- The world’s “most deadly virus”
- Latin for: to “be mad”/“madness”

Etiology
- Family: Rhabdoviridae
  - Negative-stranded RNA genome
- Genus: Lyssavirus
- Envelope virus, bullet-shaped
Epidemiology
• Only 1-2 recognized cases/year in the United States...so why is it so important?
  • "uniformly fatal" without vaccine [until recently]
  • Tremendous 'angst': ~40,000 persons receive post-exposure prophylaxis (PEP) in the US
  • Many encephalitis cases are 'rule out' rabies ...on the other hand, cases are missed
  • World: 50,000-100,000 cases/year

Rabies Reservoirs
• All mammals are susceptible
• However some species much more important > others, e.g., canine rabies, raccoon rabies, bat rabies, skunk, etc.
• Humans generally "dead-end" hosts

Bats (non-terrestrial) and Rabies
• Most common source of human infection in US
• Since 1990, > 90% of endemically acquired rabies in the US
• Exposure to bat not always recognized, especially bites

Clinical
• Incubation period ranges from few days to >1 year
  • Most cases present between 2 and 16 weeks
  • Pleomorphic manifestations, often mistaken for other CNS diseases [e.g., case 2]
  • Initial symptoms are nonspecific:
    • Fever, malaise, fatigue, anxiety, headache
    • Half of patients have pain, itching or paresthesias at site of the bite
    • Lasts 2-10 days

• Most cases of rabies in India, China, SE Asia, Iran, Africa and South America
• Most are canine rabies
• Estimated 50,000 cases/year
Clinical

After prodrome:
- Furious form (aka "mad dog") Increasing agitation, hyperactivity, seizures, hallucinations, aggressive behavior, hydrophobia (spasm of respiratory muscles when attempting to drink)
  - Coma develops, then death
- Paralytic form (aka dumb rabies) Progressive lethargy, incoordination and ascending paralysis
  - Respiratory muscle paralysis may occur
  - Coma, then death

Diagnosis of Rabies

- Always consider in case of acute onset, rapidly progressive encephalitis
- Diagnosis before death is 'tricky', testing includes:
  - Testing for viral antigen by DFA in nuchal skin or corneal cells
  - Testing for viral RNA by PCR of saliva, neural tissue, or CSF
  - Serology for antibodies in the blood
  - Growing virus isolated from saliva or CSF in cell culture
- Testing after death includes:
  - Testing for viral antigen by DFA in brain tissue

Prevention and Treatment issues these issues often confused…note the differences

- Rabies Pre-exposure prophylaxis
  - Given to 'high risk' individuals such as veterinarians, animal control workers, splenekers before exposure
  - 3 doses vaccine
- Rabies Post-exposure prophylaxis (PEP)
  - Given following a bite from rabid (or suspected rabid) animal
  - Rabies Immune globulin (RIG) and 4 doses vaccine (day 0,3,7,14)
  - Highly effective for prevention
- Rabies "Treatment"
  - No known effective Rx; once symptoms develop; vaccine and RIG of no benefit
  - Experimental treatment

PEP - Yes or No?

- Type of exposure (bite, non-bite)
  - If bite: provoked vs. unprovoked
  - Assess other circumstances of exposure, e.g., behavior of animal
- Severity of wound
- Animal species involved
- Animal health and vaccination history
- Local animal rabies epidemiology
- Animal available for observation / testing
- Urgent but not "emergency", consult local public health

“Treatment”

Human Rabies Survivors - Prior Experiences in US

- Recovery without rabies PEP
  - 15 year old female, Wisconsin, 2004 → Milwaukee protocol
  - 17 year old female, Texas, 2009 ("Abortive Case")
- Both met case definition for human rabies based on clinical manifestations and rabies virus specific antibodies in serum and CSF
- Rabies virus, antigen, nucleic acid not detected from these patients
- Antibody identified “early”

Controversial whether this was really a case or not...
Case 4

Adult female with ARDS
- 38 year old female, physician
- Flu-like illness in September 2000
- Rapid progression of illness
  -> ventilator and critically ill
- Laboratory: Elevated WBC (marked left shift, many atypical lymphocytes), elevated hematocrit and low platelets

Adult female with ARDS
- Lived in residential area
- Owned dog and cat
- No international travel
- Reported rodent dropping in attic
- Camping trip ~ 5 weeks prior to onset illness
- Hantavirus ELISA testing done
  - IgM +, IgG +

Hantavirus
- Bunyaviridae family
- Many hantaviruses worldwide
- Hantavirus Pulmonary syndrome (HPS) first identified in 1993 in humans in US with unexplained respirator illness
- Sin Nombre Virus (aka "Four Corners virus") in United States
  - West J Med 1994

HANTAVIRUS 1993
FOUR CORNERS
Hantavirus

- No arthropod vector established *unique* among genera of Bunyaviridae
- Rodent hosts: *genus and possibly species specific*

**Reservoir**
- Deer mouse: *Peromyscus maniculatus*
- Humans accidental host
- Aerosol transmission from rodent excreta
- Incubation period: typically 2-4 weeks (few days-6 weeks)
- Most cases: adults

**Transmission**
- Chronically infected rodent
- Horizontal transmission of infection by aggressive intraspecies behavior
- Virus is present in aerosolized excreta, particularly urine
- Virus also present in throat and feces
- Secondary aerosols, mucous membrane contact, and skin breaches

**Epidemiology**
- Since 1993, United States;
  - 556 cases HPS nationwide in 34 states
  - California, Arizona, New Mexico, Colorado
  - >45% of cases
  - 63% males
  - Mean age = 37 yrs (6-83 yrs)
  - Case-fatality=36%

- CDC website, Special Pathogens Branch, Aug 2012


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Hantavirus

- Risk factors: handling or trapping rodents, cleaning or entering closed rodent infested structures or animal shelters
- Potential risk groups: mammal workers, utility company, agricultural workers

Deer mouse

[Image of a deer mouse]

[Caption: A deer mouse in a lab setting. The mouse has reddish-brown fur with white fur on its belly, feet, and underside of the tail. It has a blackened ear.]

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Hantavirus Pulmonary Syndrome by State (cumulative)

Hantavirus Clinical
- Hantavirus is distinctive syndrome:
  - prodrome 3-7 days: myalgias, chills, fever, GI complaints
  - later: non-productive cough ---> dyspnea
  - myocardial depression
  - profound capillary leak syndrome: pulmonary edema/pleural effusions
  - hypotension, tachycardia, tachypnea

Khan AS et al., Jour Inf Dis 1996

Hantavirus Laboratory features
- CXR: normal early on, later interstitial pulmonary infiltrates, pleural effusion
- HEMATOLOGY: low platelet count, elevated hematocrit, elevated WBC, left shift, atypical lymphocytes (immunoblasts)
- CHEMISTRY: low albumin, elevated LDH, elevated AST/ALT

Khan AS et al., Jour Inf Dis 1996

Hantavirus Diagnosis
- Serology is both sensitive and specific
  - IgG/IgM tests are excellent;
  - ELISA
  - strip immunoblot
  - Western blot

Hantavirus Treatment
- Supportive care
- early transfer to tertiary care center
- Extracorporeal membrane oxygenation (ECMO) (early data promising)
- Ribavirin; no longer considered effective
- Contact University of New Mexico for clinical consultation

Hantavirus Complications
- Mortality rate for patients with cardiopulmonary leak: 40-45%
- if patients survive leak phase; permanent sequelae are uncommon
Hantavirus Prevention

- Nosocomial—not a problem in US
- No person-to-person transmission in US
- Avoid exposure to wild rodents and excreta especially indoor exposure in closed, poorly ventilated spaces

Khan AS et al., Jour Inf Dis 1996

Hantavirus Outbreak in Yosemite 2012

As of November 1, the National Park Service (NPS) has announced a total of 10 confirmed cases of hantavirus infection in people who recently visited Yosemite National Park.
- The visitors to Yosemite are residents of: California (9), Pennsylvania (1), and West Virginia (1).
- Three of the confirmed cases were fatal.
- NPS public health officials believe that 9 of the 10 people with confirmed hantavirus infection were exposed to the virus while staying at the Signature Tent Cabins in Owens Village in Yosemite National Park.

THE POSSIBILITIES ARE LIMITLESS….

Baylisascaris in Kinkajous

Prairie dogs and Monkeypox

Outbreak Salmonella & reptiles

71 human monkeypox cases linked to prairie dogs; 2003

65 human cases of Salmonella associated with Komodo dragon exhibit, Colorado zoo [1998]
Pet marmosets and rabies


Elephants and MTB

12 circus elephant handlers in Illinois infected with MTB; elephants likely source [1998]

Summary from Cases

- Different case presentations:
  - Different host species; rat, raccoons, mice, cats & hedgehogs
  - Extremely diverse clinical presentation, outcome

Summary from Cases

- Knowing how & when to ask about animal exposure
- Knowing which diseases to consider based on animal exposure but also knowing new twists
- Knowing limitations of laboratory results particularly for “orphan diseases”
- Be cautious around wildlife

- Expect the unexpected…speaking of the unexpected all of these zoonotic issues have just emerged..........
Novel influenza (H7N9)

China reports 4 more H7N9 infections, 1 fatal

Hong Kong to cull 20,000 chickens after H7N9 virus found

Emergence of H7N9 avian flu raises new threat for China

The end

Thank you