“When The Bite is Worse Than The Bark”
Rabies and Animal Bites

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The Views are our own opinions, and not those of the US Army/Air Force, WRAIR, or USUHS. We have no financial relationships with any of the products/companies discussed.
The Most Common Story ...
A 3 Year Old Girl - Dog Bite:

• Out in yard with other children
• “Unknown” small dog approaches group
• Nips her palm, then runs off
• No one can identify dog’s location, after an extensive search...
Risk Factors Quiz:

• Common age and sex of those exposed (US)
• Location on body
• Most common animals
• Animal behavior
• Geographic Region
• Post-exposure handling
Animal Bites and Zoonoses: Overview

• **Bite Infections**: mix of anaerobes and aerobes from the patient’s skin and the animal’s oral cavity – direct inoculation

• **Zoonosis**: (1) disease that is transmissable from animals to human (2) spread by aerosols, feces, urine, insects, and direct contact

• **Zooanthroponosis**: Reverse zoonotic disease transmission – primarily human disease, can bridge over in animals
## Animal Bites and Zoonoses: Overview

<table>
<thead>
<tr>
<th>Location of Wound</th>
<th>Dog Bite % of Patients</th>
<th>Cat Bite % of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face, scalp, or neck</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Trunk</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Shoulder, arm, or forearm</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>Hand</td>
<td>50</td>
<td>63</td>
</tr>
<tr>
<td>Thigh or leg</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>Feet</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

*Figure 1. Location of Wound Infections in 50 Patients Bitten by Dogs and 57 Patients Bitten by Cats.*
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...
- (Refused photograph)
Animal Bites and Zoonoses: *Dogs*

- 4.5 million people are bitten each year (United States)
  - Dogs more likely to bite: male (6.2x), chained (2.8x), intact (2.6x)
  - Pit bulls, Rottweiler's, Presa canarios, Cane corsos, Mastiffs, Dogo argentinos, fila brasileiro, Sharpeis, boxers

- Age of victim
  - 5–9 year old boys
Animal Bites and Zoonoses: Dogs
• **Aulus Cornelius Celsus** (Not MD):
  – Roman historian, 25 BC to 50 AD
  – “Rubor, Dolor, Calor, Turgor”

• **To prevent infection and rabies:**
  “Cleanliness and washing wounds with solutions such as vinegar”

• Hold the victim underwater to relieve thirst and cure rabies

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**Table – Common bacteria in animal bites**

<table>
<thead>
<tr>
<th>Dog bites</th>
<th>Cat bites</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pasteurella</em> (both <em>canis</em> and <em>multocida</em>)</td>
<td><em>Pasteurella</em> (primarily <em>multocida</em>)</td>
</tr>
<tr>
<td>Streptococci</td>
<td>Streptococci</td>
</tr>
<tr>
<td>Staphylococci</td>
<td>Staphylococci</td>
</tr>
<tr>
<td>Neisseria</td>
<td>Moraxella</td>
</tr>
<tr>
<td>Corynebacterium</td>
<td>Corynebacterium</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>Neisseria</td>
</tr>
</tbody>
</table>

*Listed in order of most common to least common.*
Animal Bites and Zoonoses: *Dogs*

- **Bacteria:** mix of dog oral flora & bacteria on the skin victim
  - Aerobic: *Pasteurella spp, Streptococcus spp, Staphylococcus spp, Neisseria*
  - Anaerobic- wide variety: *Fusobacterium, Bacteriodes, Porphyromonas, Prevotella, Capnocytophaga canimorsus* *Capno - Commonly found in healthy dog & cat saliva; bites; licking; Immunocompromised are typically infected*
- Most Treat only infection (redness, swelling, warmth, excess pain)
- Post-Injury prophylaxis if primary closure; who have sustained severe crush, devitalized tissue, tendons, ligaments, and joints; for those with deep puncture wounds, facial bites, hand or foot bites, and genital area; or those who are immunocompromised or asplenic
- Treatment:  
  - **Augmentin** (Amoxicillin & Clavulanic acid)  
    - (Allergy or Bacterial Resistance: 3rd gen CP; TMP/SMX (trimethoprim-sulfamethoxazole) + clindamycin; quinolones; aminoglycosides
- **Virus:** **RABIES** Dogs account for 90% of rabies transmission to humans in developing countries; more later
Animal Bites and Zoonoses: *Cats*
Animal Bites and Zoonoses: Cats
Animal Bites and Zoonoses: *Cats*

• Bacteria:
  – Aerobic
    • High rates of *Pasteurella, Streptococcus spp, Staphylococcus spp, Neisseria, Bartonella henselae*
  – Anaerobic
    • *Fusobacterium, Bacteriodes, Porphyromonas, Prevotella*
  – Bacteria located on the skin of person bitten

• Again, Augmentin is #1 choice

• Virus: RABIES (cats > dogs in US!)
Animal Bites and Zoonoses: Cats

(*Pasteurella multocida*)
Animal Bites and Zoonoses: Cats

(*Pasteurella multocida*)

Gram-negative, non-spore-forming bacilli consistent with *Pasteurella multocida*
Animal Bites and Zoonoses:  
*(Cat Scratch Fever)*

- *Bartonella henselae*; gram-negative, argyrophilic, bacilli.
- Cats are the major reservoir, but arthropods (fleas) and other animals may also play a role in the pathogenesis; Worldwide
- **Transmission**: bites; scratches; licks
- **Clinical signs/lesions**: Single-node / regional lymphadenopathy; fever; fatigue; muscle/joint pain; weight loss; and splenomegaly
- **Treatment**: Azithromycin (Consider penicillin; tetracycline; cephalosporins; aminoglycosides; fluoroquinolones
The Plain Stupid Story...

A 21 Year Old (ND) Student:

• Out at a party with the other students – consuming large amounts of beer
• Fell asleep in a chair on the porch – intoxicated, with beer spilled on his bare feet
• Wakes to an “unknown” raccoon licking and chewing his toes
• Waits a week, then told his father
• No one can identify raccoon’s location, after an extensive search...
Regional Situation:

• 2009: 384 positive animal specimens in Maryland
• 2/3 are raccoons
• Domestic #1 – cats (3-7%)
• Occasional horses and cows
• Very Rare for pet dogs (≤ 1/year)
Animal Bites and Zoonoses: NHP

(Herpes B)

NEW WORLD MONKEYS

- Nostrils are far apart and open to the side
- Some species have prehensile tails
- Thumb orientation lies in line with other digits
- Some species have fingernails on big toe
- Live in trees

(Examples: marmosets, tamarins, squirrel monkeys)

OLD WORLD MONKEYS

- Nostrils are closer together and open downward or forward
- Tail is not prehensile
- Thumbs are opposable
- Fingernails and toenails present on digits
- Live mostly on the ground

(Examples: macaques, baboons, African green monkeys)
Animal Bites and Zoonoses: NHP (*Herpes B*)

- **Herpes B Virus**
  - Macaquesine (formerly, Cercopethicine) herpes virus 1
  - **Distribution:** Worldwide
  - **Transmission:** *rhesus macaques* (via bites/scratches/contact w/tissue fluids)
  - **80 – 90% of adult macaques infected; ASYMPTOMATIC**
    - Virus is shed throughout life in oral, genital and ocular secretions
  - **3 patterns of disease:**
    - Vesicular/ulcerative
    - Influenza like illness
    - Neurologic with nausea and vomiting

**Human disease (encephalitis) is usually fatal (80%) if untreated or results in severe neurologic impairment**
Animal Bites and Zoonoses: NHP  
(\textit{Herpes B})

Post exposure treatment:

• **Wash wound** for 15 minutes
  – Skin: antiseptic (betadine; chlorohexidine; or bleach 1:20)
  – Eyes, mucous membranes: flush with sterile saline

• **Cultures of wound** (post wash): **viral transport media** (refrigerate)

• Draw blood (5 mls. of serum)

• Seek medical attention!!!!
Animal Bites and Zoonoses: NHP

*Herpes B (Post exposure treatment)*

**Post exposure treatment:**
- **Prophylaxis**
  - Acyclovir: (800 mg po qid) x 2 weeks, if 1 day post exposure
  - Valacyclovir: (1g po tid) x 2 weeks
- **Clinical signs**
  - If no CNS/PNS findings: IV Acyclovir
  - If CNS/PNS findings: IV Gancyclovir
- Additional treatment:
  - Antimicrobials
  - Tetanus verification/vaccination
  - Rabies post exposure prophylaxis (PEP)
Animal Bites and Zoonoses: Herpes B

Herpes B (Potential Cases in Afghanistan)

- 126 animal bite exposures in Afghanistan
- 10 monkey bites
- 5 received appropriate B virus prophylaxis

Combined Joint Task Force–1 in eastern Afghanistan. We evaluated these records to identify and describe monkey bites and high-risk exposures among US military members serving in eastern Afghanistan during September–December 2011. For this study, eastern Afghanistan refers to North Atlantic Treaty Organization Regional Command East, which covers ~43,000 square miles (110,000 km²). The US military population in eastern Afghanistan during the study period was ~23,500 persons. Case information obtained included patient age, sex, rank, branch of military service, animal exposures, and treatment details.

We evaluated the cases for the 5 parameters that comprise appropriate initial treatment according to the literature. The parameters are wound care (appropriate cleansing of the wound) (7), antiviral medications for B-virus (valacyclovir) (8), antimicrobial drugs for oral bacteria (amoxicillin/clavulanic acid or clarithromycin plus sulfamethoxazole/trimethoprim) (9), verification of up-to-date tetanus vaccination status or vaccine administration in accordance with Advisory Committee on Immunization Practices guidelines (9), and rabies postexposure prophylaxis (PEP). US military policy advised that rabies PEP should adhere to World Health Organization guidelines (10), which recommend giving human rabies immunoglobulin plus 5 doses of rabies vaccine. In accordance with the same policy, adherence to Advisory Committee on Immunization Practices guidelines for rabies PEP with human rabies immunoglobulin plus 4 doses of rabies vaccine was also acceptable (11).

When appropriate initial treatment was not administered, subsequent follow-up was conducted to ensure that patients received required treatment. Appropriate treatment was accomplished by contacting and coordinating with the responsible provider, the patients, and their commanders.

During the study period, we identified 126 cases of animal bites or serious exposures (involving animal neural tissue or saliva affecting the mucosal surfaces or open wounds of the patient). Among these cases, 10 were cases of monkey bites.

Among the 10 military members who had been bitten by monkeys, age range was 22–44 years (Table); most (7) were <30 years of age, and 8 were male. All were junior enlisted or noncommissioned officers; 8 were members of the Army, and 2 were members of the Air Force (Table).
Rabies Post-Exposure Prophylaxis?

"We'll have to clean that out immediately... there's nothing dirtier than a lawyer bite."
The Incredibly Sad Story ...

- 24 year old Ft Drum Soldier deployed to Afghanistan as a cook, also duties with base dogs
- “Reportedly” Bit on hand by stray dog in Afghanistan in Jan, 2011:
- Soldier “reported” that the treatment was possibly incomplete (Partial PEP, expired vaccines, dog tested? – all this is hearsay from family; quoted in the common press, all that is unofficial)
- August 14, 2011 – weird tingling in left arm, followed by GI issues
- Aug 17 – trouble drinking
- Aug 18 – checked into Ft Drum
- Aug 19 – collapsed; immediate question of rabies – transfer to Syracuse, induced Coma, ECMO, experimental rabies protocol
- Aug 31 – brain hemorrhage and death
- Investigation – possible other exposures/other animal contact without PEP?
ALARACT/Facts - Army PHC: (All Army Activities ...)

- Follow General Order 1: **Do not keep mascots or pets** when deployed!
- Do **not** approach, feed, or **handle animals**.
- If bitten or if saliva contacts your broken skin, eyes or mouth, immediately wash the area with soap and water and **seek medical attention**.
- **Report** animal exposures immediately.
- Rabies vaccines.... must be **stored and handled correctly**.
- ... may include what is known as **post-exposure prophylaxis (PEP)**
- Should all deployed receive the primary (0-7-21/28) 3 dose rabies series?
  - Costs - $600 for primary series
  - **Not enough vaccine in the world**
  - Inflaming the “Anti-Immunization” press/league
- > 600 known bites per year in deployed – So, “Follow The Rules For PEP”
- Logistics of PEP are difficult for “select units” – consider for high risk groups (Current practices)
Rabies Background Quiz:

• How far back in history have we recorded rabies?
• When did they recognize the common modes of transmission?
• What are they?
• Any “good“ historic preventive medicine practices?
• Any favorite “quack” cures?
• How could they control rabies?
An Old, Old Disease ...

- Sanskrit “rabhas” = "to do violence"
- Latin “rabere” = to rage
- Greek “lyssa” = violence/madness (Source of virus family)
- Mesopotamian “Laws of Eshnunna” - 2300 BC (4K ago)
  - North of Ur, near Diyala River, tributary of Tigris (Near Balad)
- Fines for dog owners allowing spread of rabies by bites

Bridges near “FOB Warhorse”
Middle Ages - St Hubert:

• 656-727 (est); Patron of the Hunter
• His wife died, depressed – he “escaped by hunting”
• Had a vision - a stag with a cross in its horns told him to “shape up!”
• He became the Bishop of Liege
• Given a Metal Key by St Peter to “cauterize wounds and stop rabies”
• Europeans traveled to his shrine at Liege, Belgium, to help cure rabies
Rupprect – Rabies in the New World:

• “Bat related illness” in the tribal legends of the Pacific Northwest
• California, 1703 – Rabies reported by a Spanish priest
• Late 1700’s Rabies in the Colonies:
  – Fox hunting
  – 1753 – outbreaks in Virginia
  – 1890’s eruption in LA; treated by muzzling, +/- impact
• Madstones common in the Ozarks
  – 1860’s – lay against bites
  – Burnt animal horn; bezoars
  – Natural risk without PEP is 1 in 6 bites – effectiveness?
Louis Pasteur 1822-1895
Vaccines:

• **Dr. Emile Roux** – “killed” rabies vaccine
  - Desiccating the spinal cords of infected rabbits.
  - Tested only in eleven dogs

• **Joseph Meister:**
  - Age 9 in July 1885 - Mauled by a rabid dog - Alsatian region

• **Roux:** “vaccine is not ready for humans”

• **Pasteur:** Go ahead – use it! (This was a big risk for Pasteur who was not a physician!)
  - “M. Pasteur does not cure hydrophobia; he gives it!”

• Some unpleasant manipulation of results by all involved (Pro and anti-vaccine groups)

• Wide use by 1900; in 1950’s RIG added
Genera: Lyssavirus: “Rabies, and Rabies-like” viruses

- Lyssavirus species (- RNA)
  - Main Serotype = Rabies virus (RABV) “Classic Rabies”
    - bats/mammals
  - At least 10 additional – most bat associated
- Bites are the most common route – virus in saliva
- Mucous membrane contact with virus – saliva?
  - Respiratory mucosa (bat strains) – not well-defined
  - WRNMMC renal transplant case
- Global: dogs, dogs, dogs > bats > other mammals (skunk, fox, raccoon)
- Peak in summer; # 1 young males
- No racial, genetic differences in susceptibility
Unfair Focus on Dogs?

Does Dr. O Hate Dogs?
(Accused by tropical medicine and other students)
Hillbilly Hound (Ottolini Family Member)

AKC – Registered Black Mouthed Cur
Petty Officer (Seal) Jon Tumilson - his dog Hawkeye

Aug 19, 2011; Rockford, Iowa
(CNN) -- A Maryland man recently died of rabies that he contracted from a *tainted kidney he received in a transplant* operation a year and a half ago, the Centers for Disease Control and Prevention said Friday. (*Raccoon Rabies - 18 Month incubation*)

Anti-rabies shots to three other patients who received organs from the same donor as the patient (per the CDC) *Good AB response in all 3 (kidney, heart, liver)*

The Maryland man and three other people -- in Florida, Georgia and Illinois -- received organs from a person who died in Florida in 2011 – thought to be *Ciguatera toxin severe enteritis*.

Coincidentally, both the donor and the recipient who died are members of the military. The donor was a 20-year-old airman who was training to be an aviation mechanic in Pensacola, and the recipient was a retired Army veteran, according to the Department of Defense.
Bats as a Reservoir for Rabies:

- 1953 – Florida – Identification of Human Rabies
- NOW = 2/3 of endogenous rabies - **BAT SEROTYPES**
- Transmission– **Still Mysterious ??**
  - Frequent “lack” of a significant (Bite or MM) exposure
  - 2 of 24 bat rabies cases had a **definitive bite** from 1990-2001
  - Silver haired bats >>> brown bats (Still, only 0.5-1% of bats test pos.)
- What explains “Bat to Human”
  - Are bat bites nearly invisible?
  - Do people “minimize” contact with a bat vs. a mean mammal?
  - “Aerosol” transmission not likely
    - Do we overdo the “bat in a bedroom”

Gibbons, RV (WRAIR), Ann Em Med, 2002
Varied Practices/Environments - Result in Distinctly Regional Epidemiology

• Most rabies may have originated in bats, but, most human spillover occurs from intermediate mammalian reservoirs - Dogs

• 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
Clinical Rabies Quiz:

• What are the two forms of clinical mammalian rabies? (Think Dogs)
• How does rabies go from the site of exposure to the CNS?
• When and how can we diagnose rabies in humans?
• What is the incubation period in humans?
• What is the standard Post-Exposure Prophylaxis?
• Can we cure rabies once established?
• Best ways to prevent rabies?
Understand Rabies: Pathogenesis

• After bite occurs:
  – virus localized in wound area ... then long latent period ... then spread up neurons to CNS

• After CNS - rapid spread
  – salivary glands infected shortly after CNS
  – Faster in dogs? Effective Transmitters

Russian Website: Russia-IC.com
LOCAL – NERVE – CNS - SALIVA
Understand Rabies: Incubation

• In humans, typically 1 – 3 months
  – 84% within 90 days, **99% < 1 year**
  – Wide range of 4 days to 19 years
  – Shorter period if bites to face/neck – close to brain (Virus travels up nerves)

• We try to give vaccine and RIG ASAP for head and neck bites!!
Understand Rabies: Prodromal Phase for Clinical Disease, then CNS

• “Prodrome” early illness for 2-10 days
  – Pain and \textit{paresthesia} at bite site in \(\sim 1/2\); lots of itching
  – malaise, fatigue, HA, anorexia, GI complaints, fever
  – apprehension, anxiety, insomnia, depression
    • Early encephalitis – \textbf{the game is over} at this point!

• Two clinical states for animal CNS:
  – Furious/classical \(\sim 80\%\) (MADNESS)
    • “Odd behavior” night animal seen in daytime
  – Paralytic / dumb \(\sim 20\%\)
    • Sick, lethargic
Human Rabies?

- "Hydrophobia" - Violent spasm of diaphragm and accessory muscles triggered by attempts to swallow
- Fever 100°F – 104°F, seizures, hallucinations
- Neurological deterioration to coma over days – week
- Cardiac or respiratory arrest (Parasympathetic instability) – 100% fatal
- Commonly “Misdiagnosed” prior to CNS infection
  - No antibody while “immunologically protected” at bite or in neurons
  - AB begins after CNS infection (Game is Over) avg. 6th day of illness
  - CSF Ab may not appear for another week (VERY SLOW)
  - Steroids, interferon may delay antibody development
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; Do **RT-PCR; Virus isolation**

2. **Neck biopsy:** 5-6 mm diameter punch from nape; minimum 10 hair follicles-deep to include **cutaneous nerves** at base On moist sterile gauze; **RT-PCR** and fluorescent staining for viral Ag in frozen sections

3 & 4. **Serum and CSF serology:**
   - Fluorescent Focus Inhibition Test (RFFIT) – WHO gold standard = in vitro cell cx assay that measures neutralizing Ab (highly sensitive and specific)
   - rare reports of unimmunized humans with Ab
   - If no vaccine or RIG (No PEP), 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 (1903 Pathologist) – very specific, lower sensitivity – cerebellum or basal ganglia (post mortem)


“Babes Node”
- focal demyelination
- lymphocyte collections
Back to the 3 Year Old Girl - Dog Bite:

- What are the common aspects of this case?
- Rabies Prophylaxis? – Y or N
- If so, what sequence (March, 2010, ACIP)
- 4 Doses of vaccine (HDCV or:
  - Days 0 – 3 – 7 – 14
    - Prior Vaccine – 2 doses; days 0, and 3 (no HBIG)
    - Plus HRIG (Days 0 to 7, if no prior immunizations) full dose around wound; NOT near 1st Vaccine
    - Plus wound cleansing (Don’t underestimate this!)
- The 5th dose added “nothing” to protection (Critical 28 days), same antibody response
  - But, is given if Immunosuppressed; or “on anti-malarials”
- NO breakthroughs in the USA if at least 4 doses
Why 4 Shots?

Exception for those on anti-malarial drugs! Still need 5 doses.
Rabies prevention:
Post-Exposure Prophylaxis (PEP)

• 1st CLEANSE the WOUND (After Celsus)
• Evaluate exposure -- assess risk:
  – Can the animal’s vaccination be verified?
  – Can the animal be watched for illness (if it's an extremity bite)?
  • Stray dog that ran away – Must Prophylax
  • Bat found flying clumsily in sleeping child’s bedroom?
  ...... More late
• Antibiotics? – usually Augmentin
• Post-exposure prophylaxis
  – Initiate vaccination
  – Administer passive immunization: RIG
Rabies Vaccines: Try to use U.S. lots, but lots of recent shortages:

- Many inferior vaccines available outside the USA, **US uses two:**
  - **HDCV- Human Diploid Cell Vaccine** (MRC-5 cells)
    - Product: **Imovax Rabies** Manufacturer: Sanofi Pasteur, licensed **1980**
  - **PCEC - Purified Chick Embryo Cell Vaccine**
    - Product: **RabAvert** Manufacturer: Novartis, licensed **1997**
- **Standard use = 1.0 cc IM** (Intradermal use discouraged)

http://www.cdc.gov/rabies/virus.html

- **40,000/yr in US receive 4 post-exposure vaccines (0, 3, 7, 14):**
  - **Add day 28 if immune suppressed**
    - **18,000/yr in US receive 3 pre-exposure series (0, 7, 21/28):**
      - If pre-vaccinated, 2 boosters (days 0 and 3) and **no HRIG**
      - Booster every 2 years (High risk – check RFFIT titer Q-6 to 24 mo)
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 7 days until patients 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
Understand Rabies Mortality

• Patients usually die of **respiratory arrest**
• ICUs duration from onset to death averages 25 days—
  – patient may survive in a coma for months
  – usual complications of ICU/ventilated patients
• Most uniformly fatal infection in humans – 100%
  – Yet, NO massive necrosis/NO dramatic inflammation; MILD changes in basal ganglia, caudate nuclei, cerebellum, brainstem (Awasthi, et al, AJNR, May, 2000)
  – If it is not so destructive, could people survive?
• And then....
October 2004: 15 year old female in Fond du Lac County, WI:

- “Fatigue, tingling and numbness (L) hand,” headache, diplopia, nausea and vomiting, and partial CN VI Palsy
- Brain MRI/MRA normal, sent home
- Admitted on day #4
- LP: Viral Meningitis?
  - WBC = 23 cells/uL, 93% lymph
  - RBC = 3 cells/uL
  - Protein = 50 mg/dL (nl: 15-45)
  - Glucose = 58 mg/dL (nl: 40-70)
- Fever 102.9, tremors, deterioration

Jeanna Giese
Rabies Treatment: Case Report, 2004

• On Illness day #6: a bat-bite history was now recalled:
  – 31 days prior, picked up a bat in church, bit on tip of left index finger, washed at home
• Dx studies: serum, CSF, nuchal skin, saliva
  – Rabies-specific Ab (+) in serum and CSF
    Game Over?
  – DFA staining of nuchal skin biopsies negative
  – Rabies virus isolation from saliva negative
  – Rabies RNA not detected by RT-PCR
• Option of induced coma and drugs:
  “it has never been done before, and he doesn't know if it will work or if I would come out brain dead.”
Rabies Treatment: Case Report, 2004

• Avoid respiratory complications, supportive care
  – “Neuroprotective Measures”: drug-induced coma - midazolam, phenobarbital
  – Initially IV ribavirin (IND protocol) plus amantadine

• CSF IgG increased from 1:32 to 1:2,048

• Coma for nearly 1 month, extubated on day #33, 2 months after bite; transferred to rehab

“I was slowly taken out of the coma. It was unknown whether I was actually alive, or if my soul had left my body.”
Case Report, 2004

- Was “No Vaccine” better than partial prophylaxis?
  - Less inflammation?
- Bit on tip of finger = better systemic immunity?
- Weaker form of virus? (bat viruses vary)
- Bit in church - role of St Hubert!

2nd survivor – 2009:
  - 17 yo girl, aseptic meningitis months after visiting bat cave
  - Serum rabies IgG = 1:8,192
Bats in the Bedroom! What do you do?

• 55 US/Canadian bat associated cases of human rabies in 2 generations (1950-2007):
  – 22 (39%) cases a bite was reported
  – 9 (16%) cases contact but no bite detected
  – 6 (11%) cases bats in the home but no known contact
  – 2 (4%) in their bedroom – PEP?
  – 19 (34%) no history of any bat exposure – can’t prevent

• Case: Bat found flying in upstairs
  - One room with sleeping 8 yo boy
Bats in the Bedroom! What do you do?

- Median incubation period 7 weeks
- If bat is available, send it for rabies testing
- **Consider PEP** if bat is unavailable, and persons were unaware that a bite or direct contact occurred – one decision factor: if sleeping in the room
  - But, **only 2 “probable” cases** in 20 years
  - Number needed to treat and cost benefit analysis ????
FIGURE. Assessment of risk for bat exposure in a volunteer facility — Kentucky, 2012

**Abbreviation:** PEP = postexposure prophylaxis.

* Had direct contact with a bat or slept in a room where a bat was sighted.
† Had direct contact with the mouth or head of a bat or was unable to rule out such contact.
§ Had direct contact with a bat other than the mouth or head or was unable to rule out contact with bat while sleeping.
In Summary …

• Rabies Vaccine and RIG Works – must be used exactly as recommended

• Animal immunization programs – work, but expensive

• Bat Risk – Is the sleeping/bedroom risk exaggerated? What is the source of most exposures?

• Therapy – has “worked” a few times – are these unusual circumstances?
  – Still > 99% Fatal

• Prevention !!!
Animal Bites and Zoonoses: *Snakes*

- Worldwide: > 5 million people bitten annually (majority in Africa and South-East Asia)
- ~2.4 million envenomation
- 400,000 severe health consequences (i.e.; amputation)
- 94,000-125,000 death annually
- Poisonous snakes (North America): *Rattlesnake*, *Cottonmouth (water moccasin)*, *Copperhead*, and *Coral Snakes*
Animal Bites and Zoonoses: *Snakes*

*Pit vipers:* rattlesnakes; copperheads; water moccasin (cotton mouth)

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**Pit vipers**
- Rattlesnakes
- Copperheads
- Water moccasin (cotton mouth)

**Visual Features**
- Elliptical pupils
- Small, hooked teeth
- Two large hollow fangs
- Tongues of all snakes are harmless

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**Diagram:**
- Illustration of a Rattlesnake showing the nostril, pit, and elliptical pupil.
Animal Bites and Zoonoses: *Snakes*

- **Snake toxins:**
  - **Cytotoxins:** causes local tissue damage
  - **Hemotoxins:** damages blood vessels/cells
  - **Neurotoxins:** affects the nervous system
  - **Cardiotoxins:** act directly on the heart

- **History (Hx):**
  - Time of bite
  - Description of the snake
  - Type of field therapy
  - Underlying medical conditions
  - Allergy to horse or sheep products
  - Hx of previous venomous snake bites & therapy

- **Physical examination:**
  - Complete physical exam performed; plus baseline measurements of limb circumference proximal & distal to site
  - **Pit vipers:** local effects; coagulopathy (specifically, Rattlesnakes); other systemic effects
  - **Coral snakes:** primarily neurotoxic effects

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**General symptoms of Snakebite**

- **Central**
  - Dizziness
  - Fainting
  - Increased thirst
  - Headache
- **Systemic**
  - Fever
  - Severe pain
- **Respiratory**
  - Breathing difficulty
- **Wound site**
  - Bleeding
  - Fang marks
  - Discoloration
  - Burning sensation
  - Swelling
- **Other skin sites**
  - Bleeding spots
  - Numbness
  - Tingling
  - Sweating

**Systemic manifestations of envenomation**

- **Vision**
  - Blurriness
- **Heart and vessels**
  - Rapid pulse
  - Low blood pressure
  - Severe shock
- **Muscular**
  - Convulsions
  - Loss of coordination
  - Weakness
- **Gastric**
  - Nausea
  - Vomiting
- **Intestinal**
  - Diarrhea
Animal Bites and Zoonoses: Snakes
Animal Bites and Zoonoses: Snakes

Treatment: First: Maintain airway, breathing, and circulation
- Circumferential extremity measurements should be performed on arrival (repeat every 15-20 min)
- Outline the margins of local edema
- Bloodwork: CBC (including platelets); coagulation profile (e.g., PT, APTT, fibrinogen); FDPs, urinalysis, electrolytes, BUN, creatinine
- Moderate-severe envenomation: blood typing; cross matching; ECG; chest x-ray

****Monitor patients closely for at least 8 hours (pit viper bites); 12 hours (coral snakes)****

Watch for infections – dead tissue, lots of gram negatives in snake and other reptile mouths: Quinolones, 3rd generation cephalosporins, aminoglycosides
Animal Bites and Zoonoses: 
*Rodents & Rabbits*

- Rat bite fever
- Tularemia
Animal Bites and Zoonoses: Rodents & Rabbits

*Case 2*

- 48 y/o male in SE Asia arrives at 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 gram negative rods
Gram stain: numerous gram-negative filamentous bacilli with bulbous or sausage-shaped (moniliform) swellings appearing along the filament, resembling a string of beads.
Animal Bites and Zoonoses:

**Case: Rat Bite fever**

- *Spirilium minus* in Asia
- *Streptobacillus moniliformis* in USA
- **Transmission**: bites; scratches; water/food borne
- **Clinical signs/lesions:**
  - Polyarthralgias; headache; rash; vomiting; fever (*Streptobacillary*)
  - Fever; ulcer/swelling @ bite wound; swollen LN; rash (*Spirillary*)
  - Nausea; vomiting; pharyngitis: (“Haverhill Fever” - unpasteurized milk outbreak)
  - Maculo-papular rash (extremities); vasculitis; muscle/joint pain (polyarthritis in approximately 50% of the patients); myocarditis; meningitis; pneumonia
- **Treatment:**
  - Penicillin, Doxycycline
Animal Bites and Zoonoses:

*Case: (Rat Bite fever)*

Purpuric spots on buttocks and thighs due to rat-bite fever
Animal Bites and Zoonoses: Rodents & Rabbits

(*Tularemia*)

- **Condition synonyms:** “Rabbit fever”; Deer fly fever; Ohare’s disease
- **Etiology:** *Francisella tularensis*; Gram negative coccobacillus
- **Wide distribution:** Canada, Mexico, Europe, Russia, Tunisia, Turkey, Israel, Iran, Japan, and China; United States (100-200 cases/annually)
- **Transmission:** vector bite (tick; deerfly); ingestion; aerosolization; direct contact
- **6 forms:**
  - Aerosolization *(pneumonic)*
  - Direct contact/ingestion *(ulceroglandular; oculoglandular; oropharyngeal; glandular; typhoidal)*
- **Clinical signs/lesions:** variable; dermal ulcerations-*lymphadenitis*
- **Treatment:**
  - Streptomycin (30 mg/kg qd IM) for 10-14 days
  - Gentamicin (3-5 mg/kg qd IV) for 10-14 days.
Animal Bites and Zoonoses: Rodents and Rabbits

*(Tularemia)*

**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.
Animal Bites and Zoonoses: Rodents & Rabbits

*(Tularemia)*

Oculo-glandular

Ulcero-glandular

Glandular