“Tails” from the CDC

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Division of State and Local Readiness

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CDC Career Epidemiology Field Officer

- Assigned to the NYC Department of Health and Mental Hygiene
- Director of Informatics, Data, and Outbreak Response team in the Division of Disease Control
Epidemic Intelligence Service

http://www.imdb.com/title/tt1598778/
Zoonosis

- A human pathogen with a non-human animal source

Emerging infectious diseases (EID)

- Infectious diseases whose incidence in humans has increased...or threatens to increase in the near future.

http://wwwn.cdc.gov/eid/pages/background-goals.htm
The purpose of this study was to analyze the global temporal and spatial patterns that contribute to EIDs.
Temporal trends in EID events

- The incidence of EID events has increased since 1940
- 60.3% of EID events were due to zoonoses
- >70% of emerging zoonoses originated from wildlife
Bats as a reservoir for emerging pathogens & pathogen discovery

- Bats provide major ecological services

- Bats have been implicated as reservoirs for:
  - Lyssaviruses
  - Filoviruses
  - Henipaviruses

- Factors that contribute to bats’ role in hosting viruses:
  - High population densities
  - Flight

Idanre, Nigeria

- Under consideration to become a UNESCO World Heritage Site
- Located 3000 ft above sea level
Nigerian bats

- Known reservoirs to a number of viruses, including Lagos bat virus and pegiviruses
- Caves are home to *Rousettus aegyptiacus*, a known reservoir for Marburg virus (related to Ebola virus) in Central Africa
Annual bat festival

- Local population holds a festival once per year
- Consumption of bats is very popular
- Many direct contacts with bats occur

Photo by Ivan Kuzmin.
Photo of a bat hunter
CAUTION: DO NOT TOUCH BATS
Photo of bat hunters and their catch
CAUTION: DO NOT TOUCH BATS
Results from 2013 human survey

- Interviews conducted with 54 persons who participated in the festival as bat hunters revealed that:
  - 43 (80%) had a history of bat scratches
  - 39 (72%) had a history of bat bites
  - 1 (1.9%) reported having ever received rabies vaccine
Concluding thoughts

- How come there were no reports of outbreaks?

- Public health interventions in this high-risk setting

- One Health is more than just having animal and human health experts working together → disease ecology model
  - Environmental science
  - Anthropology

- Building local capacity

- West African Ebola outbreak → what was the inciting event?
Rabies basics

- Rabies is an acute, progressive encephalomyelitis
- High case fatality rate
- Caused by RNA viruses in the Family *Rhabdoviridae*, Genus *Lyssavirus*
- Typically transmitted through the bite of an infected animal

Global burden of human rabies

- >55,000 human deaths/year
- Most cases are canine variant
- Most deaths occur in Africa and Asia

Kidney transplant

Day 0

2011

2013
Kidney transplant

*Day 0*

Right hip pain

*Day 509 (17 months)*

2011

2013
Kidney transplant
Day 0

Right hip pain
Day 509 (17 months)

Bilateral lower extremity weakness
Day 515

Admitted to hospital
Day 514

Altered mental status
Day 519
Kidney transplant Day 0

Right hip pain Day 509 (17 months)

Bilateral lower extremity weakness Day 515

Admitted to hospital Day 514

Altered mental status Day 519

Death Day 536

2011

2013
Diagnosis in the deceased kidney recipient

- Autopsy was performed
- Specimens were sent to CDC for rabies diagnostics
- Rabies virus antigens detected in brain tissues
- Sequence analysis implicated the raccoon rabies virus variant
Distribution of rabies virus variants among terrestrial reservoirs
Rabies in the United States

- Approximately 2 human deaths/year from rabies

- During 2000–2010, all but 2 domestically acquired human cases were associated with bats
  - Puerto Rico: Mongoose rabies virus variant
  - Virginia: Raccoon rabies virus variant (first documented human rabies case from this rabies virus variant)

- There are more rabid raccoons reported in the USA every year than rabid bats

MMWR. Nov 2003.
How was the deceased kidney recipient exposed to rabies virus?

- No reported exposures to potentially rabid animals
- No reported international travel
- No occupational risk identified
How was the deceased kidney recipient exposed to rabies virus?

- No reported exposures to potentially rabid animals
- No reported international travel
- No occupational risk identified
- **However, he did have a history of kidney transplantation**
Transplantation and rabies

- There have been two prior rabies clusters associated with solid organ transplantation (2004 & 2005)

- In these clusters, all solid organ recipients who were unvaccinated for rabies at the time of transplantation developed rabies after an incubation period of <6 weeks

- 100% case fatality rate

Maier, et al. CID. Apr 2010.
Objectives

- To investigate whether organ transplantation was the source of the deceased kidney recipient’s rabies virus infection
- To evaluate for and prevent rabies in other recipients of tissues from the common donor
METHODS
Clinical and epidemiologic review

- Contacted the Organ Procurement Organization that had coordinated recovery and distribution of the donor’s tissues
- Medical providers for donor and recipients were contacted
Laboratory testing

- Laboratory tests were conducted at CDC

- Deceased kidney recipient (autopsy)
  - Brain tissues
  - Transplanted kidney specimens

- Other transplant recipients
  - Available specimens

- Organ donor
  - Archived specimens
FINDINGS/RESULTS
Organ donor

- Organ donor died in 2011

- Heart, liver and both kidneys were transplanted into four recipients
  - No recipient had been vaccinated for rabies at the time of transplantation

- Autopsy attributed death to complications of gastroenteritis

- Chart review revealed that in retrospect the donor’s clinical course was consistent with rabies
Symptom onset, **Day -3**

Donor

**2011**

Symptom onset, **Day -20**

Death, **Day -3**

Organs recovered, **Day 0**

Deceased kidney recipient

Death, **Day 536**

Symptom onset, **Day 509**
• Rabies virus antigen was detected within donor brain tissues by immunohistochemical staining
Rabies viruses infecting the donor and deceased kidney recipient

*N* gene sequences of the rabies viruses infecting the donor and deceased kidney recipient were >99.9% similar, thus confirming organ transplantation as the route of transmission.
Donor’s suspected rabies virus exposure

- Interviews were conducted with the donor’s family members
- The donor was an avid hunter
- He had sustained raccoon bites 18 and 7 months prior to symptom onset
- He never sought medical care for these bites
Symptom onset, Day -3
Death, Day -20

Donor
2011

Symptom onset, Day 509
Death, Day 536

Deceased kidney recipient

Organs recovered, Day 0

Right kidney recipient

Liver recipient

Heart recipient

Postmortem rabies diagnosis, Day 549
PEP started, Day 551

PEP started, Day 549
PEP started, Day 550
Serum results prior to initiation of PEP — surviving organ recipients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Months post-transplant</th>
<th>Rabies virus antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney recipient</td>
<td>18 months</td>
<td>Not detected</td>
</tr>
<tr>
<td>Heart recipient</td>
<td>18 months</td>
<td>Not detected</td>
</tr>
<tr>
<td>Liver recipient</td>
<td>18 months</td>
<td>Not detected</td>
</tr>
</tbody>
</table>
# Evidence of infection within transplanted organs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Specimen</th>
<th>Months post-transplant</th>
<th>RV nucleic acid</th>
<th>RV antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic kidney recipient</td>
<td>Transplanted kidney (biopsies)</td>
<td>2, 12</td>
<td>Not detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>Asymptomatic heart recipient</td>
<td>Transplanted heart (biopsies)</td>
<td>0–18</td>
<td>Not detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>Deceased kidney recipient</td>
<td>Transplanted kidney (autopsy)</td>
<td>18</td>
<td>Not detected</td>
<td>Not detected</td>
</tr>
</tbody>
</table>

RV: Rabies virus
Conclusion

- Human rabies is rare in the United States and likely underdiagnosed

- This is the third documented rabies virus transmission event globally through solid organ transplantation
Raccoon rabies virus variant

- Prior to this investigation, there had only been one reported human rabies case from the raccoon rabies virus variant

- Why are human raccoon rabies cases rare compared with human bat rabies cases?
Survival of three unvaccinated recipients of organs from a donor with rabies

- In the two prior transplant outbreaks, unvaccinated solid organ recipients all developed rabies

- Why was this transmission event different?
  - Three surviving recipients could have been within the incubation period and might have developed clinical illness had they not received PEP
  - Differences in the degree of immunosuppression between these transplant recipients might have had a role
17 month incubation period in the deceased kidney recipient

- This incubation period is longer than the incubation period experienced by most immunocompetent hosts

- In the two prior transplant outbreaks, the incubation period was <6 weeks

- Why was this transmission event different?
  - Perhaps the deceased kidney recipient had exposure to a low dose of virus?
  - Perhaps the natural history of the raccoon rabies virus variant in humans is different from other rabies virus variants?
Concluding thoughts

- PEP is important after a potential rabies virus exposure

- Rabies should be included in the differential diagnosis of unexplained acute progressive encephalitis

- Could PEP enhance transplant safety when a donor is retrospectively diagnosed with rabies?
Concluding thoughts

- Clinicians are the frontlines of public health

- If you have public health concerns, call the NYC Department of Health and Mental Hygiene Provider Access Line:

  1866 692 3641

- Public health is a thrilling career
Questions?
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For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.