The Investigation Begins

- May 15, 2015
- Electronic laboratory report received from commercial laboratory
- Positive for Hantavirus IgM
  - 7.44 (Ref: <2.00)
- Positive Lyme disease IgM serologies
  - Western Blot, 23KD, 39KD, 41KD bands
- Initial patient interview
  - Female, nurse, 58 years
  - Onset May 2, 2015
  - Not hospitalized
  - Fever, mild respiratory illness (cough), myalgia, fatigue, N/V, rash all over body

Hantavirus vs. Lyme Disease

Hantaviruses

- Dozens of different viruses
  - Specific rodent reservoirs for each
- 2 clinical syndromes
  - Hemorrhagic fever with renal syndrome (HFRS) – Old World viruses
  - Hantavirus pulmonary syndrome (HPS) – New World viruses
Patient History/Background

- Lives in rural area of central NY with husband
- Home is a basement with a roof, plywood for a door
  - Built 2 years ago, plans to build rest of home delayed for lack of funds
- Have had mouse infestations “off and on”
- Developed a rat infestation over the winter
  - Jan 2015 they poisoned the rats, which died in walls and ceilings
  - Soon “dead rats began falling from the bathroom ceiling”
- ~ April 1, insulation and dead rats removed, gloves and dust masks worn
- May 1, swept up storage area without mask
- No history of tick bites

Clinical Presentation

- Illness onset May 2
  - Self-reported fever to 103.5°F, body aches, cough, congestion
- Sought care May 11
  - PMH: Obesity, HTN, hyperglycemia, anxiety, atrial fibrillation
  - Symptoms mostly resolved, but fatigue persisted
  - Rash developed and worsening, now all over body
  - Look like petechiae to patient
  - Described by PCP as multiple, large, non-raised, blanchable, erythematous, irregular in shape but circular. No purpura/petechiae.
  - Patient concerned about hantavirus
  - Bloodwork/UA/hantavirus serology ordered. Lyme disease serology ordered after consult with another provider at practice.

Lab Findings

- CBC normal, no thrombocytopenia
- UA normal, no renal dysfunction
- Chem panel unremarkable, no renal dysfunction
- Coagulation studies normal
- Elevated CRP, LDH, sedimentation rate
- Lyme disease screen, WB, all 3 bands positive
- Hantavirus serology at a commercial laboratory
  - IgG screen: <2.0 (ref 2.0), Negative
  - IgM screen: 7.44 (ref 2.0), Positive
  - Sin Nombre virus IgM Confirmation test: Positive
3 Days Later – Results Available, More Symptoms Develop (May 14)

- Right flank pain, worsening cough, rash persists
- Further testing
  - Urine culture – negative
  - Renal ultrasound – no abnormalities found
  - Chest X-ray – no abnormalities found
  - Repeat UA and bloodwork normal (↑ CRP)
- Started on doxycycline
  - Delayed
- Referred to ID

ID Consult – May 21

- Had been on doxycycline for 1 week
- Rash and other symptoms had resolved
  - Notes rash consistent with disseminated EM from photos
- Only complaint fatigue
  - ID physician concludes
    - Rash and other symptoms consistent with Lyme disease (doxy to 21 d)
    - Hantavirus serology false positive
- One more PCP visit... May 27
  - Chief complaint dyspnea, several episodes of shortness of breath
  - Normal enhanced CT scan of chest

Hantavirus Acute Specimen Confirmatory Results (collection date May 11)

- CDC Special Pathogens branch (prelim results June 11)
  - Sin Nombre virus
    - IgM and IgG negative
  - Seoul virus
    - IgM Positive
    - IgG negative
- Lab information matches epi information
- Reminder: commercial laboratory results positive for Sin Nombre IgM 7.44 (IgG neg)

Hantavirus Pulmonary Syndrome (HPS)

- Sin Nombre, Monongahela, and New York viruses in NY
  - Peromyscus spp. reservoir
- Primarily respiratory involvement
- Fever, myalgia, GI → cough, pulmonary edema, ARDS
- Thrombocytopenia, left shift, hemoconcentration
- CFR ~35%
- Mild illness possible
- Extremely rare in Northeast
  - 5 cases with exposure in NY

Hemorrhagic Fever with Renal Syndrome (HFRS)

- Seoul virus (in North America)
  - Rattus norvegicus reservoir
- Primarily renal involvement
- Fever, myalgia, hemorrhage (GI, urinary, brain, conjunctiva)
- Acute renal failure with oliguria
- Thrombocytopenia, fluid overload
- CFR <1% (worldwide)
- Extremely rare in North America
  - Travel-related cases
  - Few locally acquired (~5 total)
Seoul Virus as a Public Health Concern in Rural New York?

- Norway rats have “worldwide” distribution
- Antibodies to Seoul virus can be found in Norway rats
  - Studies in urban areas
- In the US: rare locally-acquired HFRS, demonstrated antibodies to Seoul virus on serosurveys
- This patient
  - Mild symptoms masked by Lyme disease?
  - Evidence of exposure but not pathogenic?
  - Something completely different?
  - A case?
  - “Get a convalescent sample”

Convalescent Serum Specimen Collected June 23

- Sin Nombre Virus final results reported July 10
  - Acute IgG and IgM Negative
  - Convalescent IgG and IgM Negative
- Seoul Virus final results
  - Waiting…
  - More waiting…
  - Still waiting!
  - Sept 4: Convalescent was negative, acute was falsely positive

Summary

- Lyme disease – yes, hantavirus infection – no
- Patient’s symptoms attributable to lab-confirmed Lyme disease
- Patient’s rash not immediately recognized as multiple erythema migrans
- Treatment with doxycycline was delayed
- False positive hantavirus serology results occurred at both commercial and CDC laboratories
- No abnormalities of CBC, blood chemistries, UA, coagulation studies, or imaging of chest or kidneys consistent with HPS/HFRS
- Substantial rodent exposure in basement home

Conclusions

- Providers should exercise caution when ordering tests without correlating clinical and epidemiologic information
- The patient’s anxiety and medical training might have contributed to progression of hantavirus “symptoms”
- Convalescent specimen testing was necessary for real answers
  - No good explanation why acute specimen false+
Co-Authors and Acknowledgments

- **Co-Authors**
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Hantavirus in New York – Five Previous Cases with Exposure in NY

<table>
<thead>
<tr>
<th>Year</th>
<th>Place of Exposure</th>
<th>Place of Residence</th>
<th>Exposure</th>
<th>Virus</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>Shelter Island (Queens?)</td>
<td>RI</td>
<td>Summer home (warehouse?)</td>
<td>New York</td>
<td>Died</td>
</tr>
<tr>
<td>1999</td>
<td>Catskills</td>
<td>PA</td>
<td>Cabin cleaning, handled rodents</td>
<td>Monongahela</td>
<td>Recovered</td>
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<tr>
<td>2011</td>
<td>South Fork, Long Island</td>
<td>Long Island</td>
<td>Home cleaning</td>
<td>New York or Sin Nombre</td>
<td>Died</td>
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<tr>
<td>2012</td>
<td>Adirondacks</td>
<td>Long Island</td>
<td>Camping in lean-to, mouse bite</td>
<td>Sin Nombre</td>
<td>Mild illness, Recovered</td>
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</tbody>
</table>

Pathogenic Hantaviruses in the United States

<table>
<thead>
<tr>
<th>Virus</th>
<th>Disease</th>
<th>Distribution</th>
<th>Rodent Host</th>
<th>Hosts</th>
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</thead>
<tbody>
<tr>
<td>Sin Nombre virus</td>
<td>HPS</td>
<td>Mostly West, Midwest</td>
<td>Deer mouse, Peromyscus maniculatus</td>
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<tr>
<td>Monongahela virus</td>
<td>HPS</td>
<td>East</td>
<td>Deer mouse, Peromyscus maniculatus</td>
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<tr>
<td>New York virus</td>
<td>HPS</td>
<td>East</td>
<td>White-footed mouse, Peromyscus leucopus</td>
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<tr>
<td>Bayou virus</td>
<td>HPS</td>
<td>South, Southeast</td>
<td>Rice rat, Oligoryzomys palustris, Cotton rat, Sigmodon hispidus, Norway rat, Rattus norvegicus</td>
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</tr>
<tr>
<td>Black Creek Canal virus</td>
<td>HPS</td>
<td>Southeast</td>
<td>Sigmodon hispidus, Norway rat, Rattus norvegicus</td>
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<tr>
<td>Seoul virus</td>
<td>HFRS</td>
<td>Worldwide</td>
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