Hantavirus Disease

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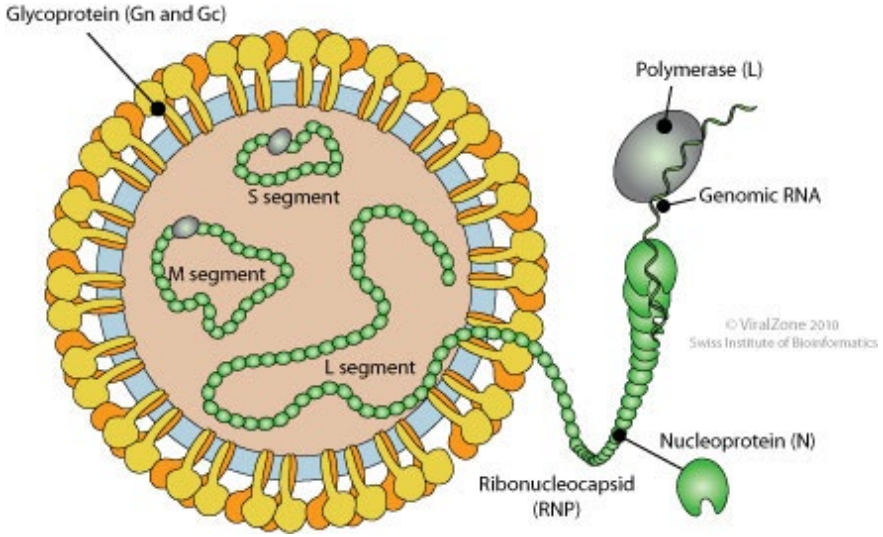
Outline

- Hantavirus overview
- Epidemiology of hantavirus disease in the U.S.
- Clinical presentation of hantavirus cardiopulmonary syndrome (HCPS)
- Laboratory testing
- Treatment
- Hantavirus 5-point screen

Hantavirus – General Features

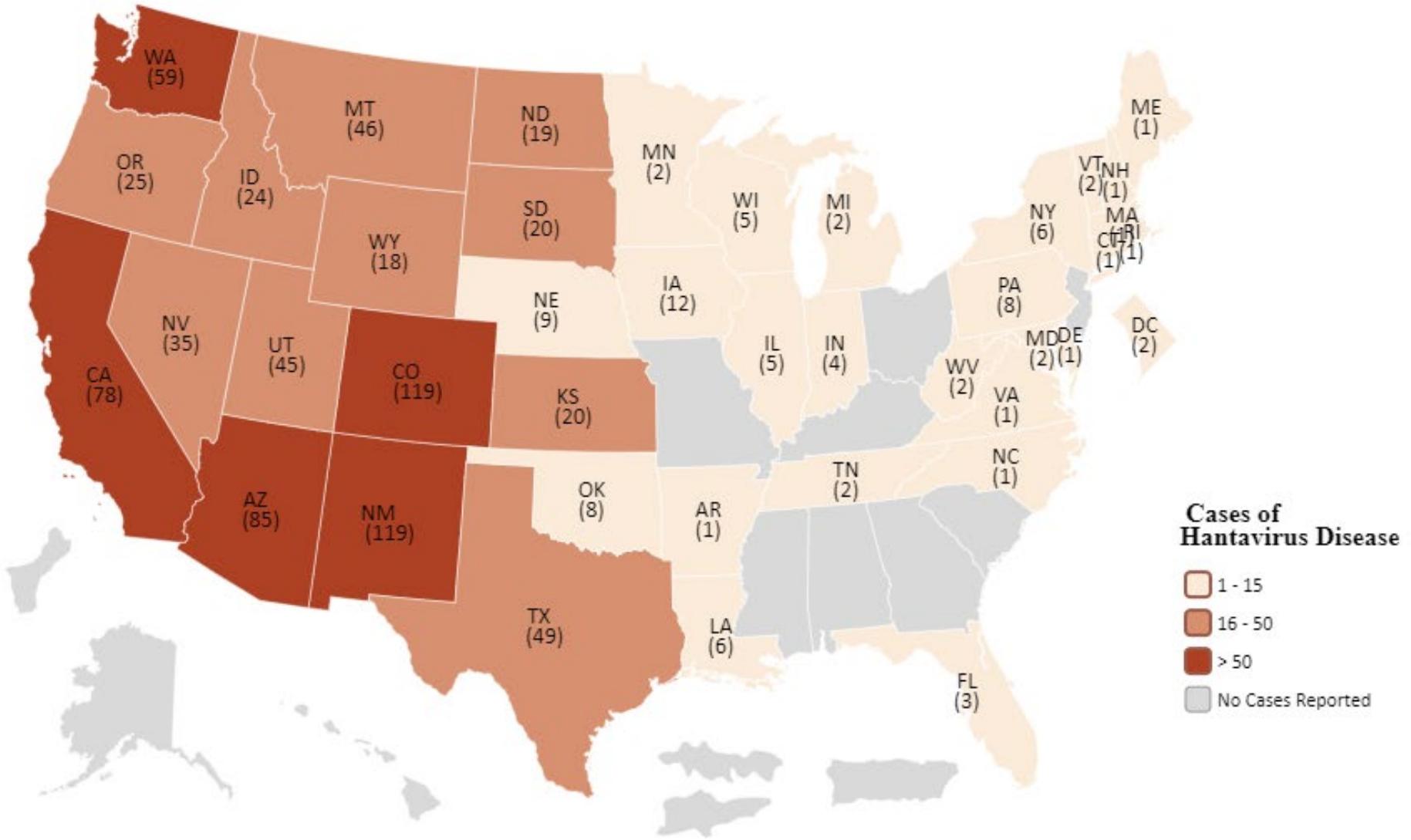
- Member of the *Bunyavirales* order
- Enveloped virus; easily killed by bleach, detergents, soap, disinfectants
- Rodents are the natural reservoir
- In the Four Corners region, cases of HCPS are due to Sin Nombre virus (SNV)



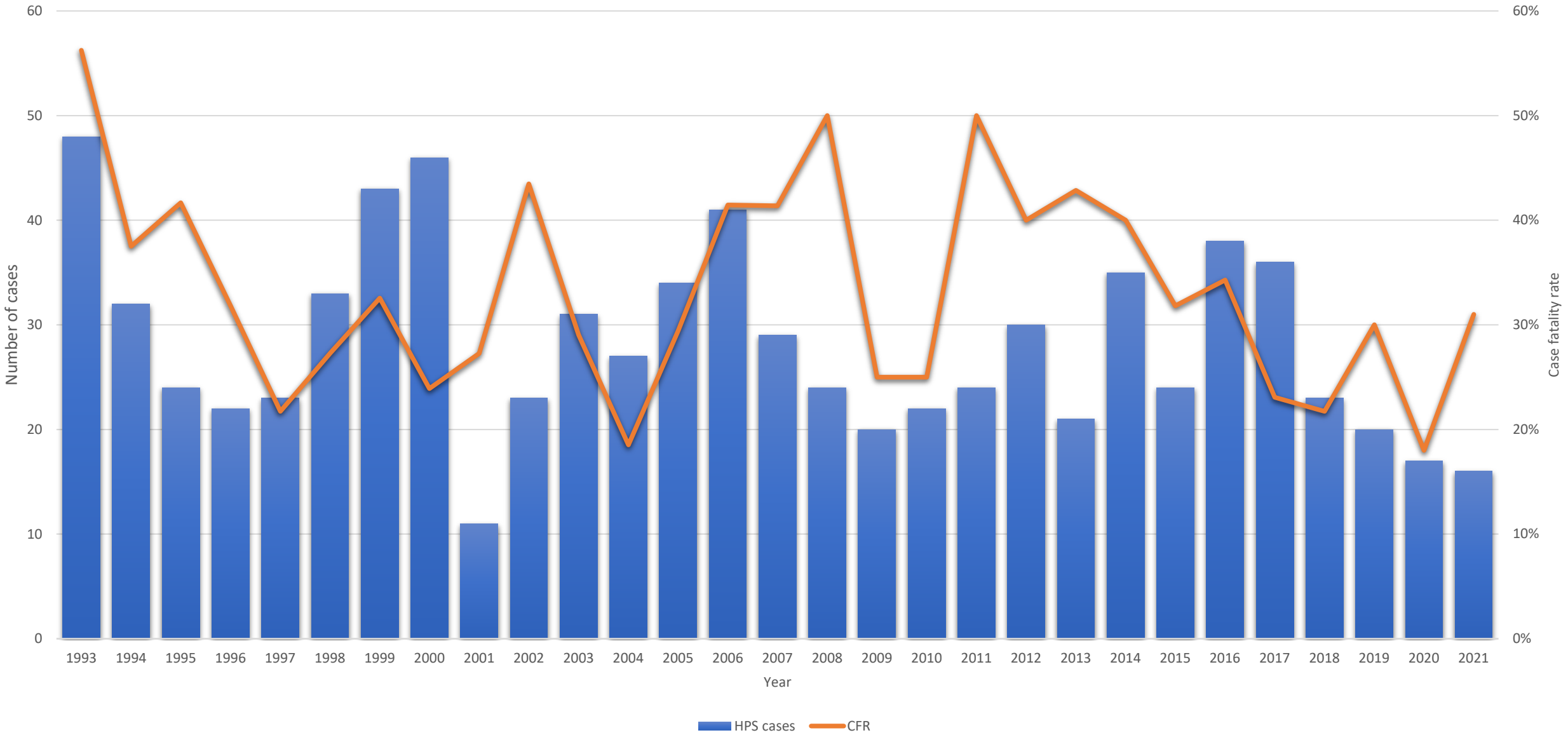
Rodent Host – Sin Nombre Virus

- Deer mouse (*Peromyscus maniculatus)*
  - Found throughout North America
  - Approximately 10% of deer mice tested have shown evidence of infection with SNV
- Hantavirus infection does not cause illness in the rodent
- Infected rodents shed the virus in saliva, urine, feces

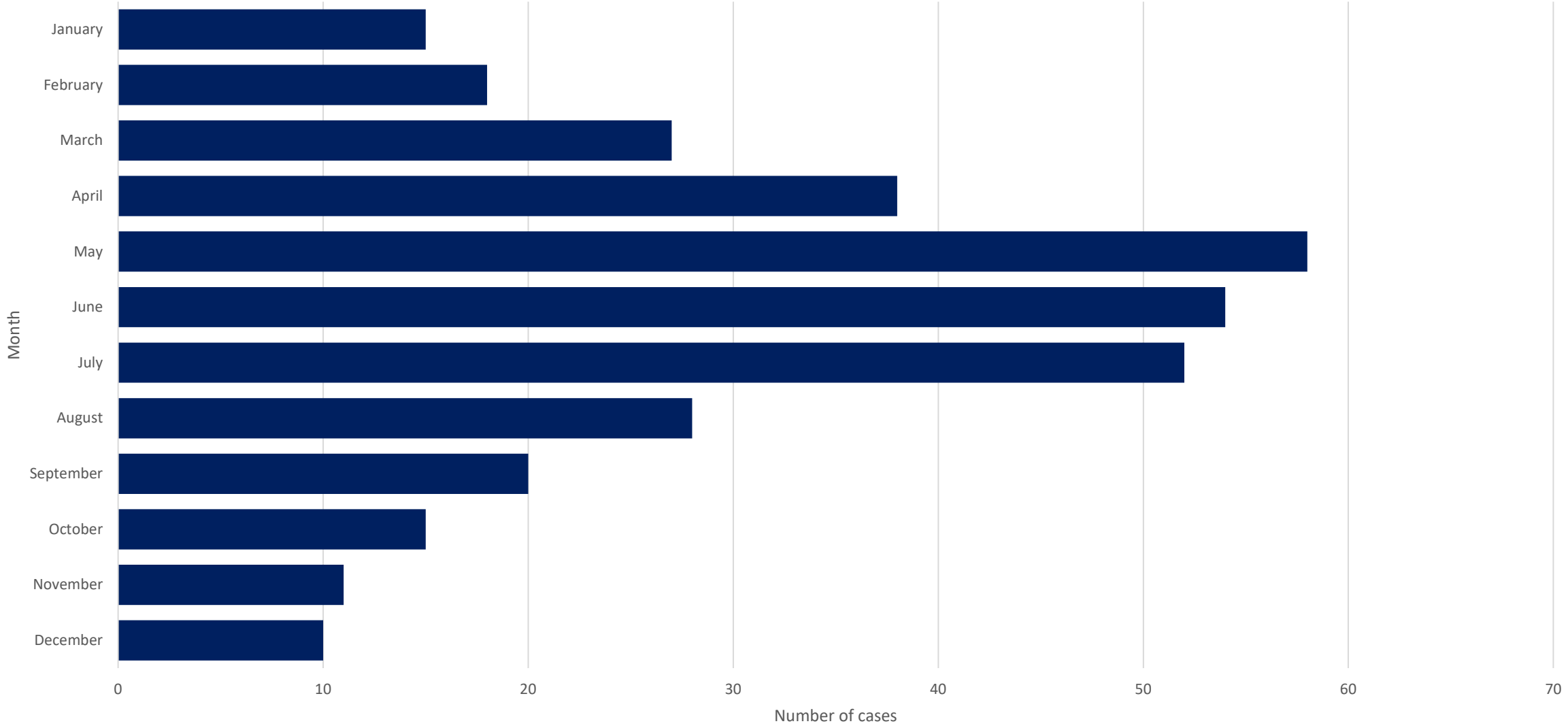
Map of US Cumulative Cases of Hantavirus by State through 2021



Annual U.S. Hantavirus Cases and Case Fatality Rate 1993-2021



Hantavirus cases reported in the Four Corners region from 1993-2021, by month of symptom onset



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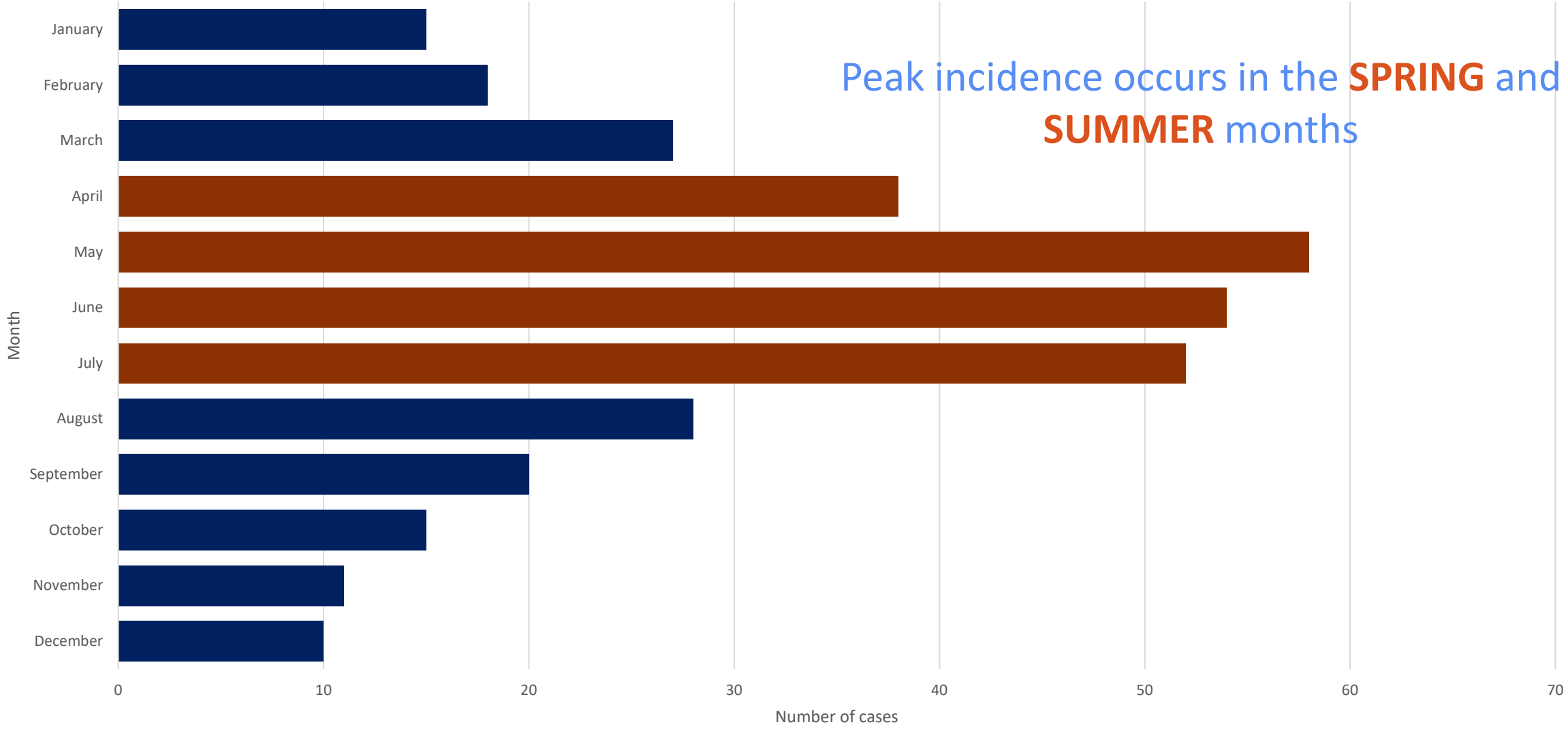

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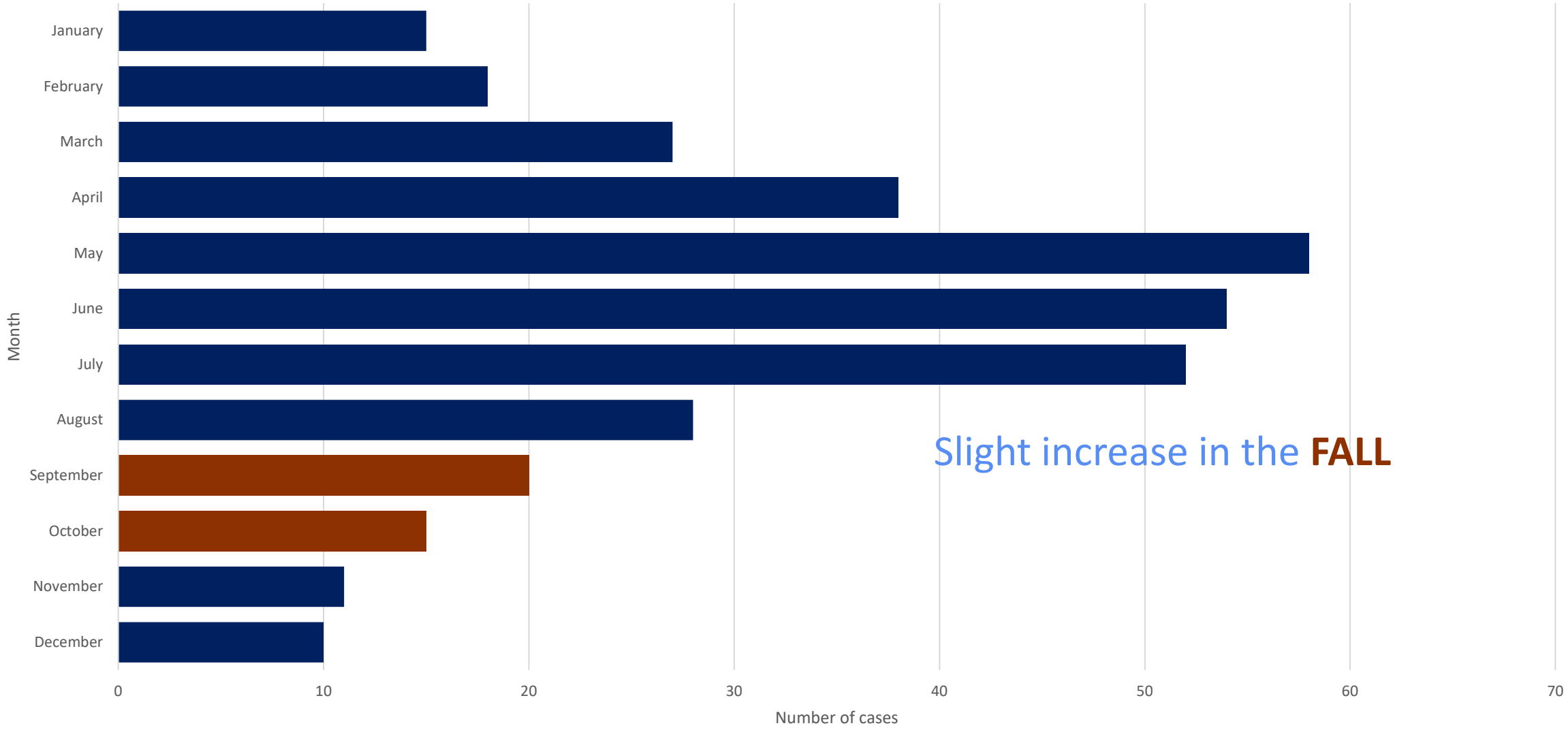
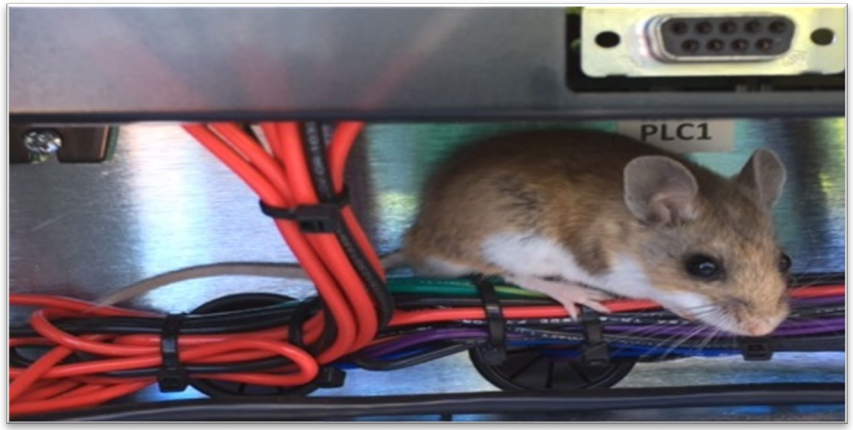


Virus Transmission

- Humans can become infected when they breathe in aerosolized virus
- Infected rodents shed hantavirus in their urine, saliva, and feces
- When fresh rodent urine, droppings, or nesting materials are stirred up, tiny droplets containing the virus get into the air
- Humans can also become infected through bites from infected rodents
- There is NO human to human transmission of Sin Nombre virus

Risk Factors for Hantavirus

- Outdoor occupations: farming/ranching/construction/forestry
- Outdoor activities: camping/hiking
- Opening and cleaning previously unused buildings (cabins, sheds, cars)
- Cleaning rodent infested areas
- Living in proximity to rodent infestation



Clinical Presentation

- Incubation period: 9-49 days* (median = 14-17 days)
- Febrile prodrome: 3-6 days of flu-like illness
- Cardiopulmonary Stage
  - Cough, shortness of breath, hypoxemia, rapid onset hypotension
  - Without treatment, almost all deaths occur within 24-48 hrs of the onset of this phase
  - Most deaths result from cardiogenic shock
- Diuretic Stage: 3-7 days; polyuria
- Convalescence: may have residual fatigue, poor exercise tolerance

*Nunez et al. Hantavirus infections among overnight visitors to Yosemite. Emerg Infect Dis 2014; 20(3): 386-93.

Diagnosis

- No rapid test available
- Confirmatory diagnosis by enzyme-linked immunosorbent assay (ELISA) capable of detecting IgM and IgG antibodies
- ~ 12 hours required to complete antibody testing, not including transport of the specimen to the laboratory

Treatment

- Treatment is supportive
- Administer inotropes early for hypotension
  - Avoid fluid resuscitation, may exacerbate pulmonary edema
- Supplemental oxygen as needed
- Caution with intubation (hemoconcentration + sedation/intubation can decrease venous return and have led to instances of cardiac arrest)
- Immediate transfer to a center capable of extracorporeal membrane oxygenation (ECMO)

Challenges

- Patients developing HCPS often initially present with clinical features similar to other viral or flu-like illnesses (e.g., influenza, COVID-19)
- HCPS patients may deteriorate rapidly
- Prompt recognition and rapid transfer to an ECMO center critical for survival
- No rapid test available

Hantavirus 5-Point Screen

Hantavirus 5-point Screen

- Developed at the University of New Mexico
- Identified 5 findings on a CBC/peripheral blood smear commonly seen in patients with confirmed HCPS
- Presence of 4/5 criteria most clinically useful
  - 96% sensitivity, 99% specificity for HCPS*
  - Retrospective review of 10-years of cases (158 patients) found 89% sensitivity, 93% specificity**

*Koster et al. “Rapid Presumptive Diagnosis of Hantavirus Cardiopulmonary Syndrome by Peripheral Blood Smear Review” *Am J Clin Pathol* 2001;116:665-672

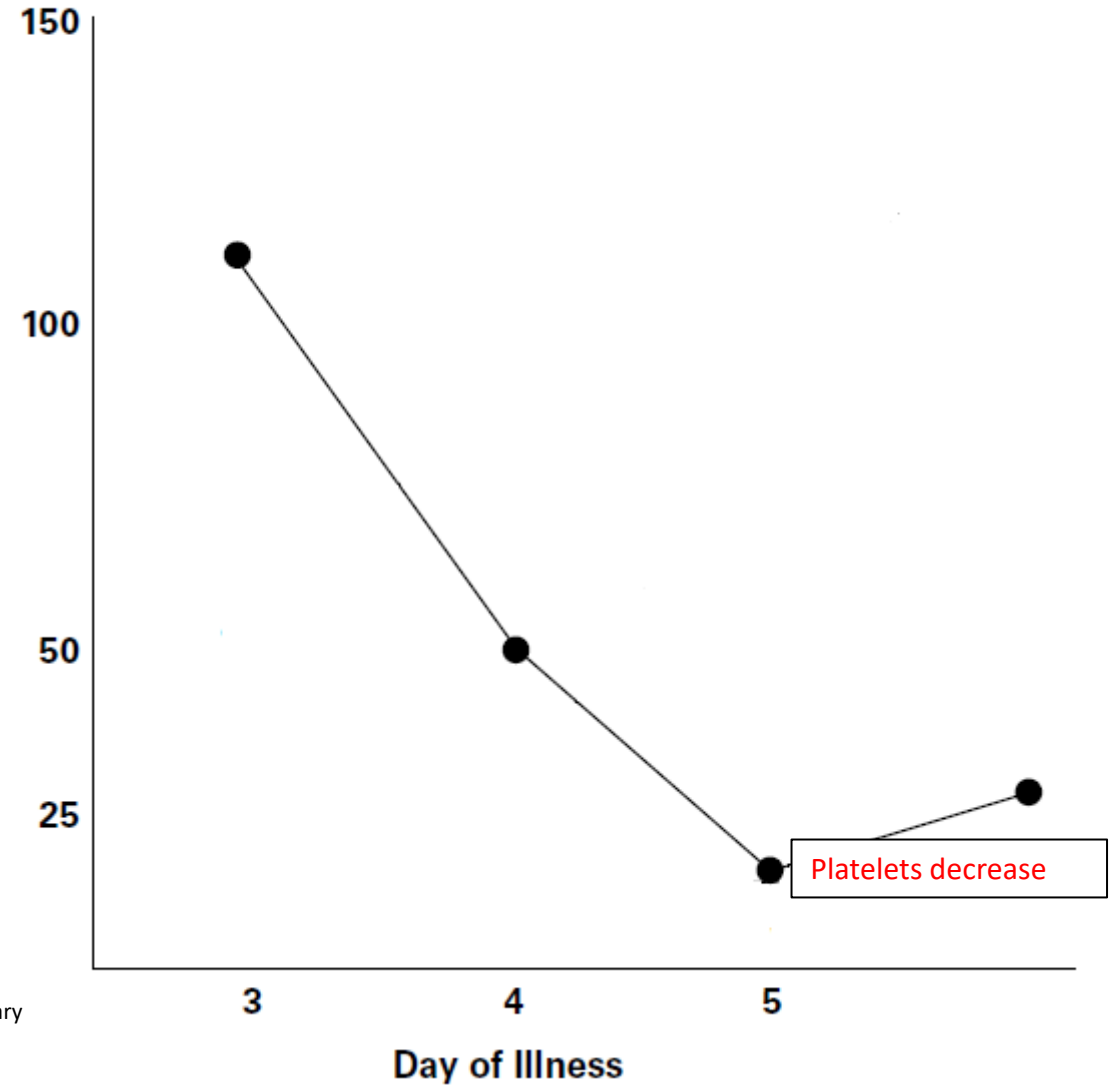
**Dvorscak et al. “Successful Triage of Suspected Hantavirus Cardiopulmonary Syndrome by Peripheral Blood Smear.” *Am J Clin Pathol* 2014;142:196-201.

CBC/Blood Smear Findings in the Cardiopulmonary Phase

Five criteria used to evaluate patients for hantavirus disease

1. Low platelet count (<150,000)
2. Elevated white blood cell count with left shift
3. Increased immunoblasts (>10% of lymphocyte population)
4. Lack of significant toxic changes in neutrophils
5. Hemoconcentration

Laboratory results in patients with HCPS



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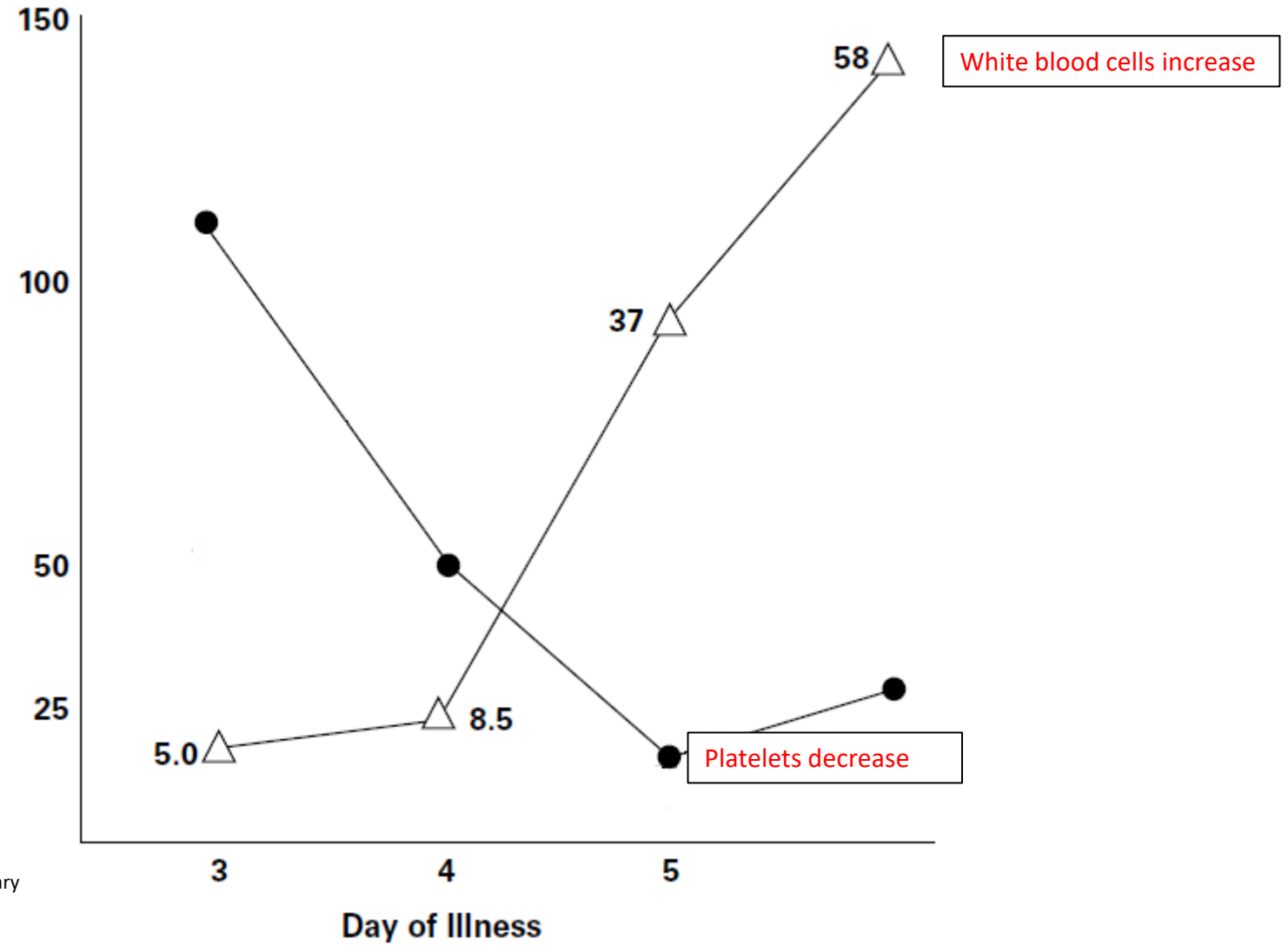

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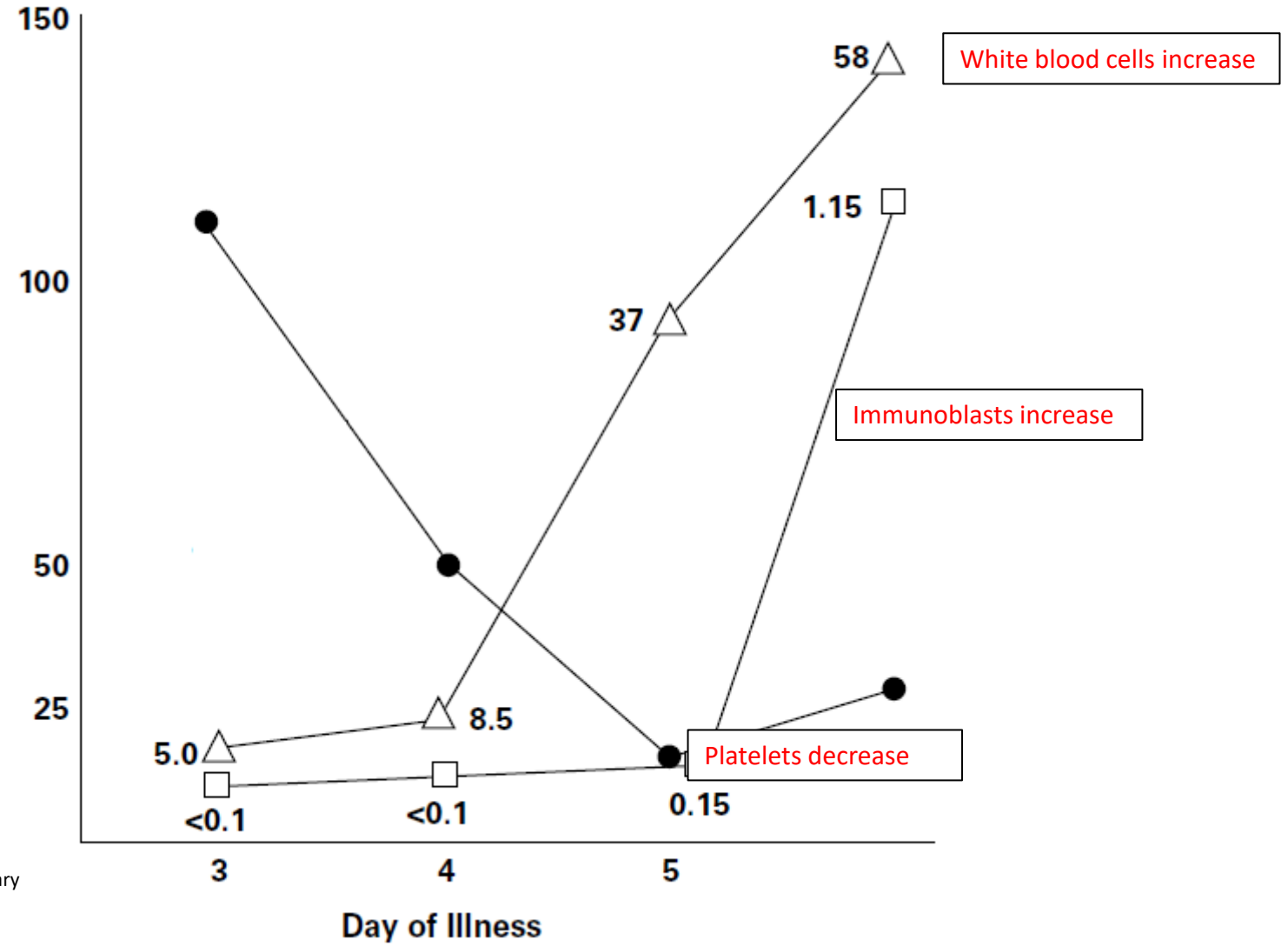

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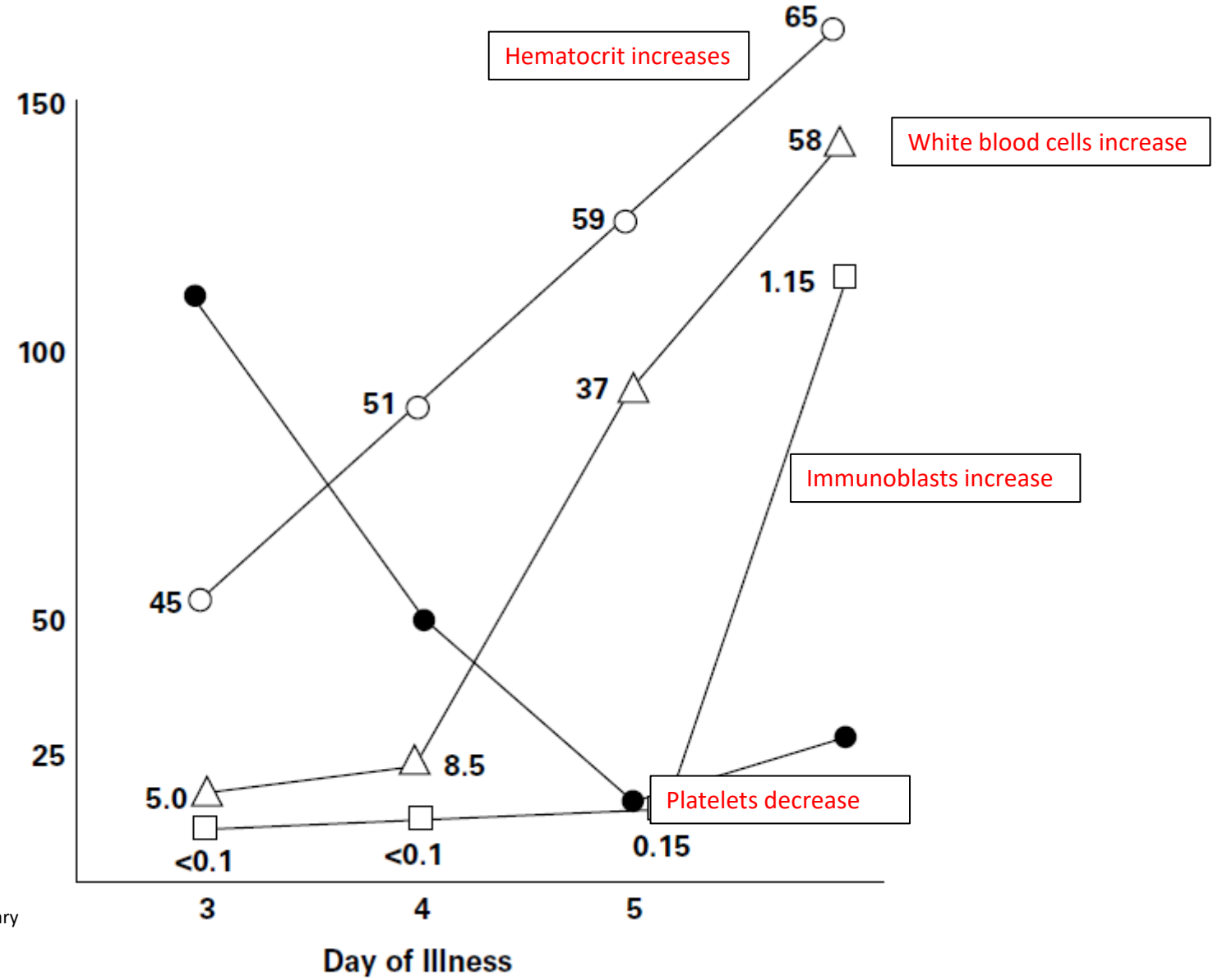

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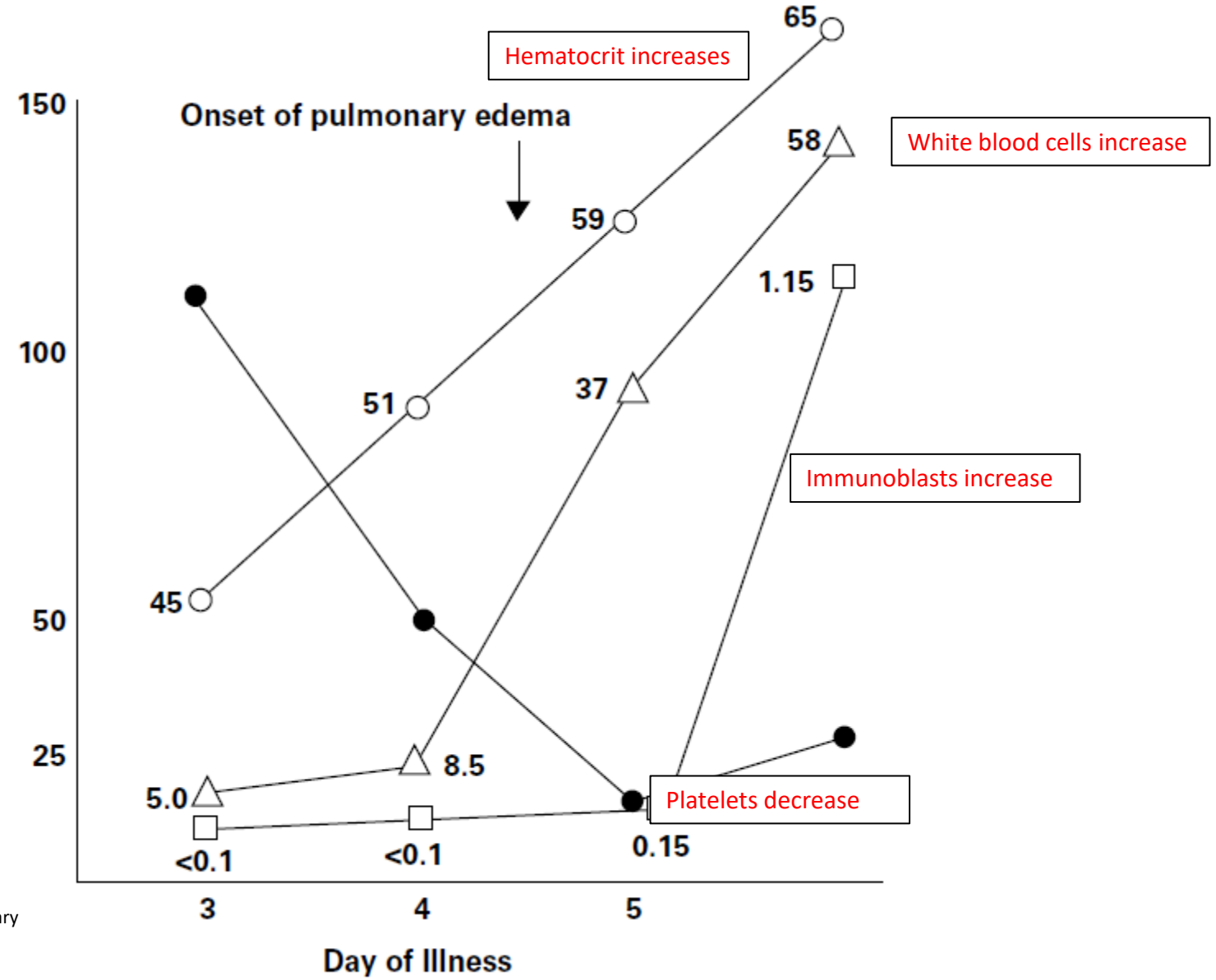

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5-pt Screen Implementation Study

- Téhootsooi Medical Center adapted and implemented the 5pt screen in 2016
- Trained 20 medical technologists to perform the test
- Testing triggered by:
  - Physician request
  - Reflex testing for thrombocytopenia for all patients seen in the emergency department
- 189 screens performed from May 2016 – September 2020

5-pt Screen Implementation Study: Methods

- 4 or 5 out of 5 criteria present:
  - Positive screen for hantavirus cardiopulmonary syndrome (HCPS) if consistent with clinical and history findings
  - Serum specimen for serologic confirmation is indicated
- 3 out of 5 criteria present:
  - Blood features are non-diagnostic currently for HCPS
  - If an early hantavirus infection is still a clinical consideration, repeat peripheral blood screening in 12 hours
- 1 or 2 out of 5 criterial present:
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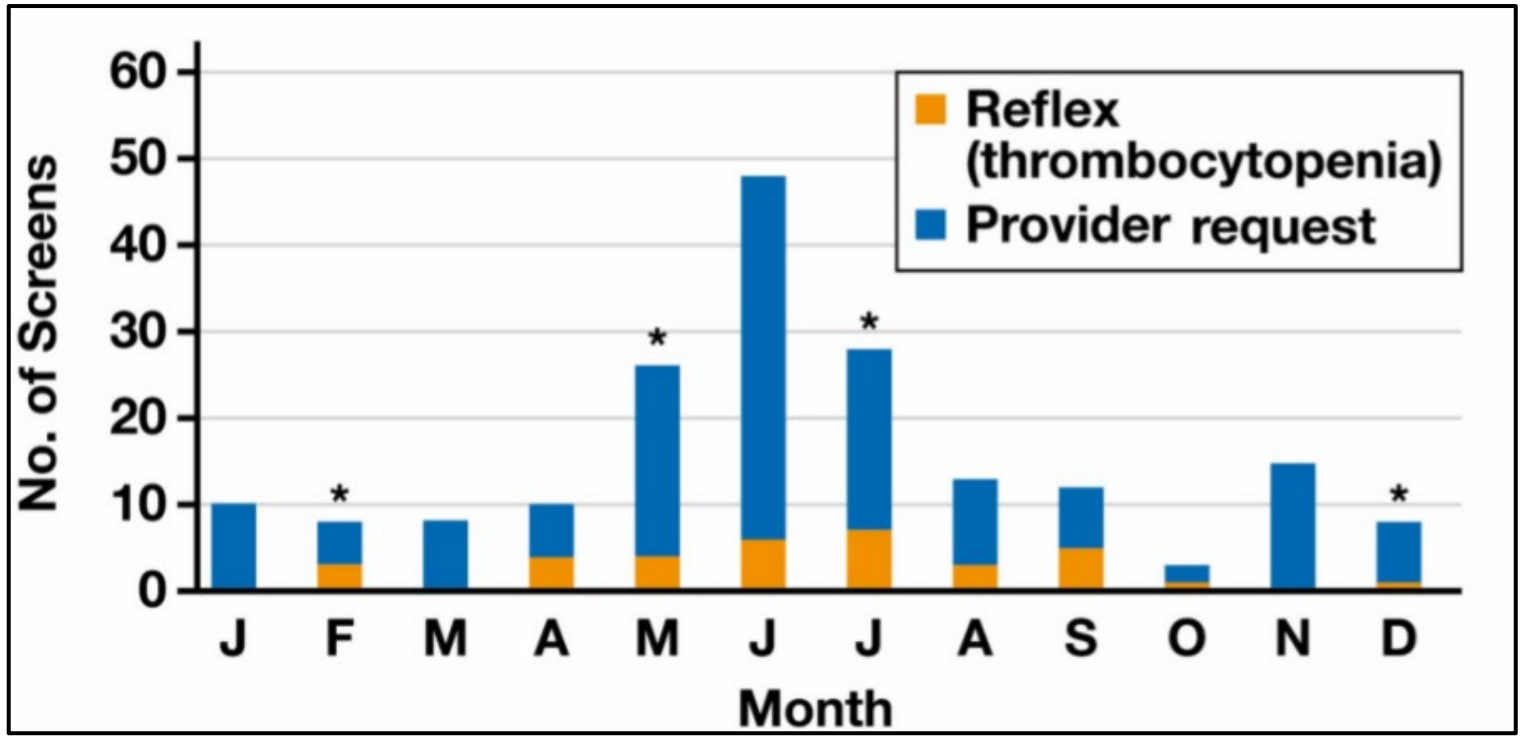
5-pt Screen Implementation: Results

- 4 confirmed cases of HCPS detected
- 2 of 4 confirmed cases detected in February & December, both through reflex testing
- 1 of the confirmed cases detected through repeat testing after 12 hours when initial score was 3/5



* Confirmed HCPS

Limitations of 5-point Screen

- Screening test; not diagnostic
- Most accurate when performed during the cardiopulmonary phase
- Estimates of sensitivity and specificity from the UNM study were determined on a patient population with high pre-test probability of HCPS
- This screen would not be appropriate to perform in non-endemic areas

Hantavirus 5-pt Screen and COVID-19

Rationale

- Signs and symptoms of COVID-19 overlap with those of HCPS
- Outcomes of COVID-19 infection and HCPS differ greatly
  - Most healthy adults with COVID-19 experience mild to moderate disease
  - Clinical course of HCPS is often severe, with many requiring ICU-level care/ECMO
- May 2020: a mother and son died after a brief, severe respiratory infection
  - COVID-19 was initially suspected
  - Autopsy findings confirmed HCPS

Question

- Can the hantavirus 5-point screen distinguish between COVID-19 and HCPS?

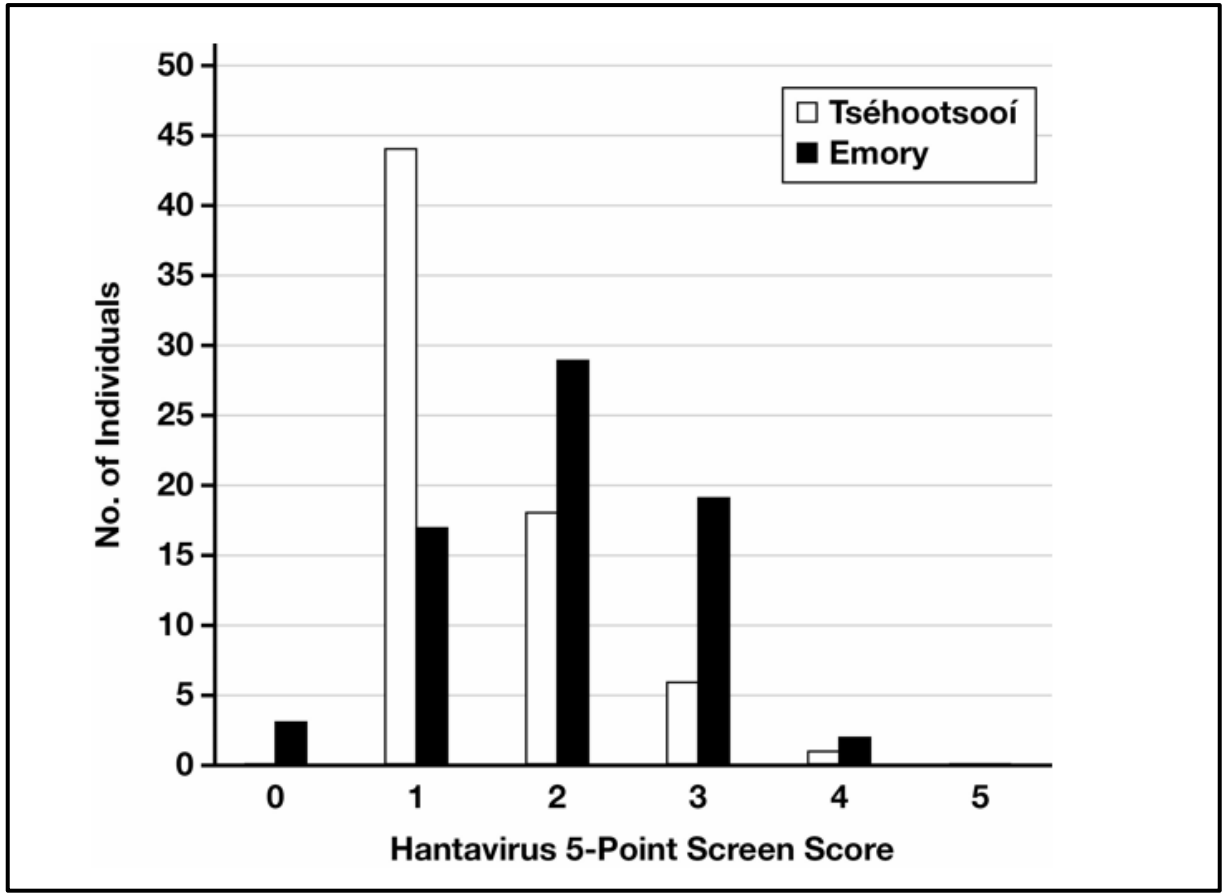
Methods

- Study conducted March – May 2020
- Three study sites
  - Tséhootsooí Medical Center, AZ
  - Emory University Hospital, GA
  - Emory University Hospital Midtown, GA
- All three sites conducted hantavirus 5-pt screens on all confirmed COVID-19 patients presenting with respiratory symptoms

Demographics

- 139 participants enrolled and included in analysis
  - 69 at Tséhootsooí Medical Center (TMC)
  - 70 at Emory (Emory Hospital and Emory Hospital Midtown)
- 100% of participants at TMC were Native American/Alaska Native
- 85% at Emory were African American

Results



*1/69 patient at TMC scored 4/5
**2/70 patients at Emory scored 4/5

Key Points

- Hantavirus 5-pt screen can quickly identify potential cases of HCPS and distinguish it from other diseases
- This can be critical to patient management given key differences in management of HCPS vs. other pulmonary infections/conditions
  - Early recognition is associated with improved survival
- Since 2017, CDC has been coordinating with Navajo Nation to provide training on the hantavirus 5-pt screen
- **If interested in 5-pt screen training, please contact us!**

CDC Resources:

www.cdc.gov/hantavirus

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you!

Viral Special Pathogens Branch (CDC): Spather@cdc.gov

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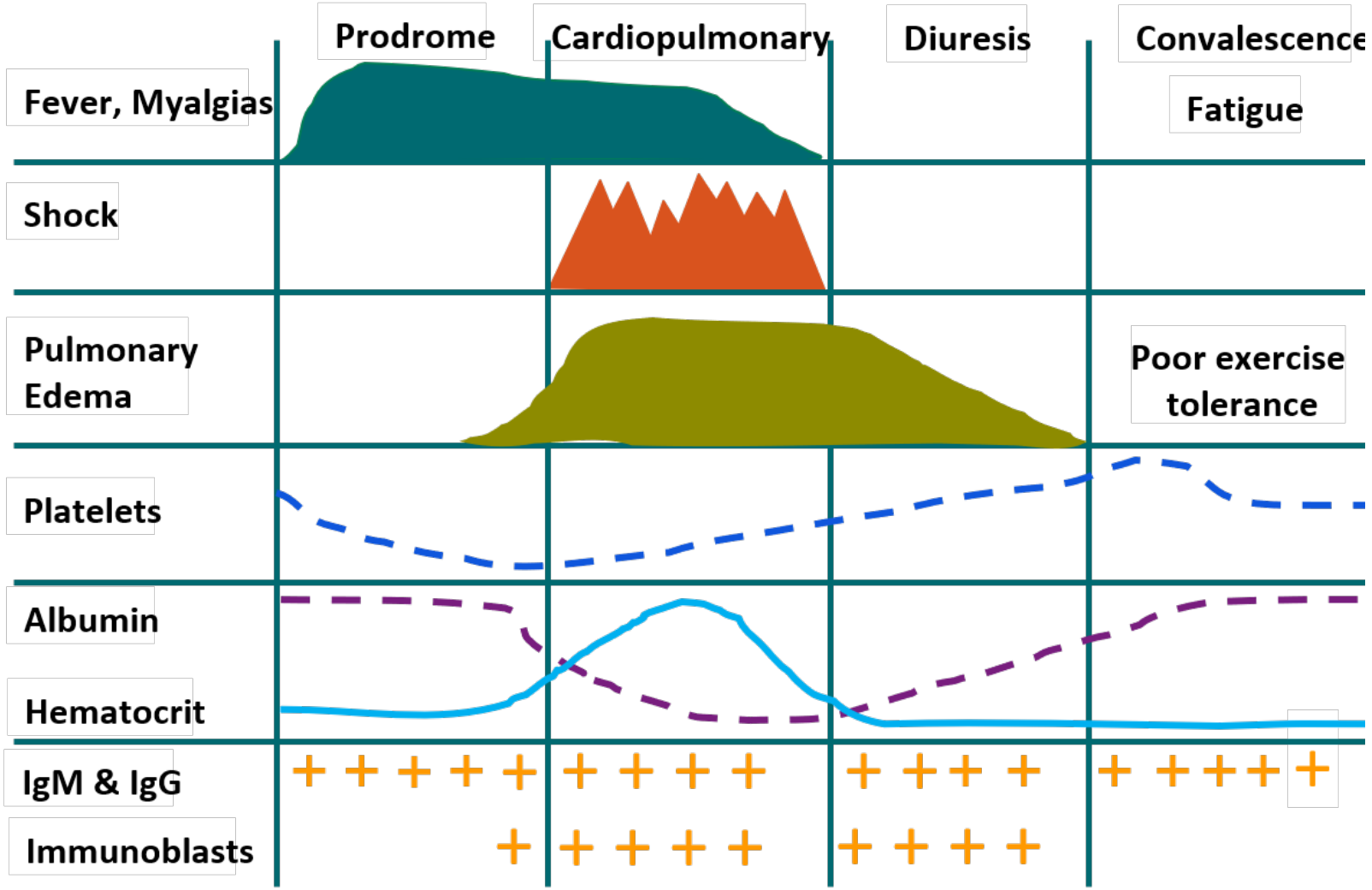
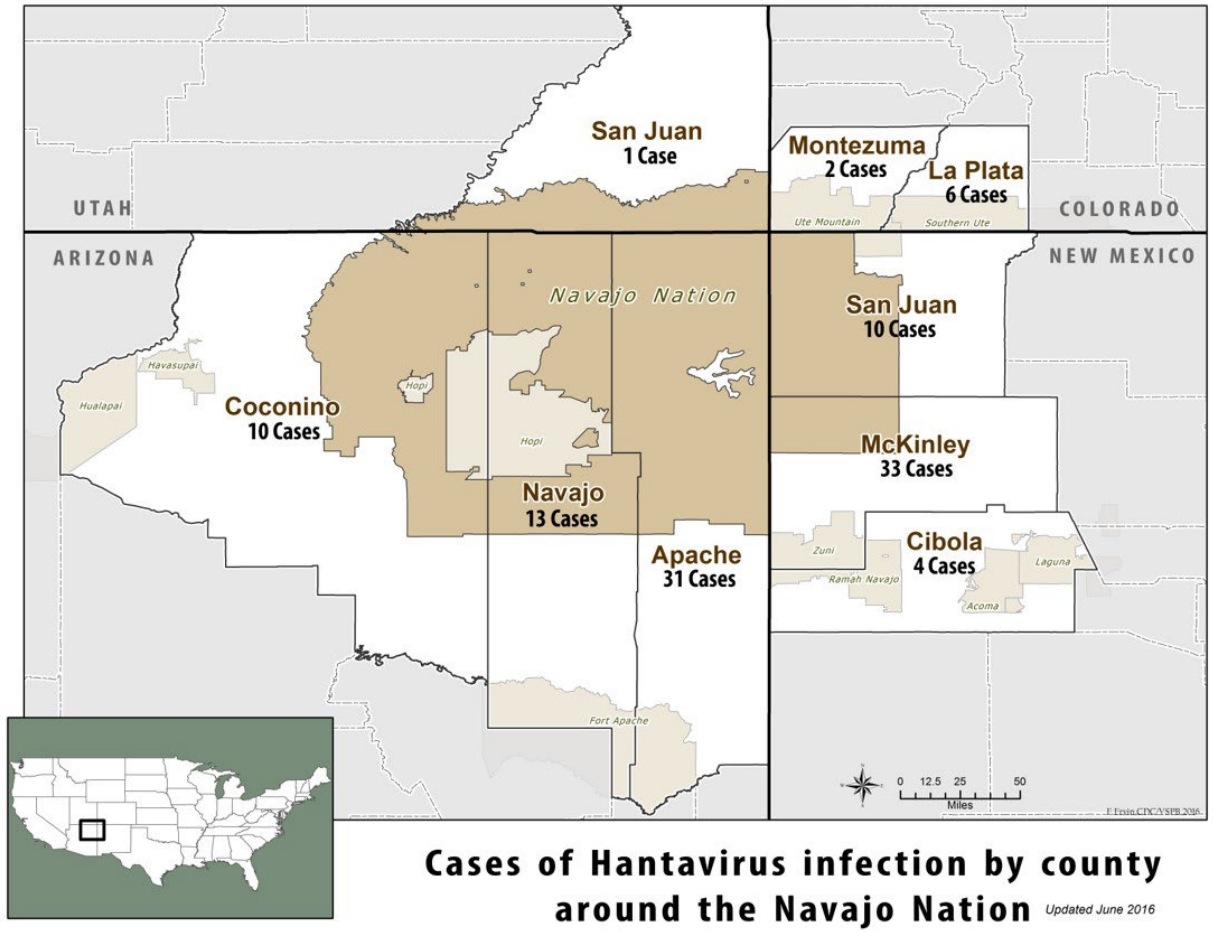


Hantavirus Course of Illness

Reported Hantavirus Cases in Navajo Nation by County, 1993 – June 2016



Cases of Hantavirus infection by county around the Navajo Nation *Updated June 2016*

Platelets in HCPS cases

- About 80% of HCPS cases have a platelet count below 150,000
- A dramatic fall in platelet count may signal a transition from the prodromal to the pulmonary edema phase of the illness
- Note: Thrombocytopenia alone is not specific for HCPS. It is commonly seen in other infections (e.g., sepsis, plague, tularemia, borreliosis, Rocky Mountain spotted fever, parvovirus) and noninfectious conditions

Elevated Hb/Hct for age and gender

- A rise in the hematocrit may indicate a fluid shift from the patient's circulation into the lungs in patients with HCPS
- Note: When evaluating the significance of the hemoconcentration, the clinician should be aware of other pre-existing causes of erythrocytosis such as chronic pulmonary disease

Left shift in neutrophils/lack of significant toxic granulation

- In HCPS cases, the white blood cell count tends to be raised with a left shift. Toxic granulation is negligible or absent.
- Note: In bacterial infections with elevated white count and left shift, toxic changes are prominent.

Immunoblasts/plasma cells >10% of lymphocytes

- Immunoblasts/plasma cells are frequently present, usually at the time of onset of pulmonary edema (and numbers tend to decline during convalescence).

- Note: Immunoblasts alone are not specific for HCPS. They are seen in peripheral blood smears in small numbers as the result of transient immune responses due to a number of etiologies.

Hantavirus Peripheral Blood Screen Scoring System

Hgb/Hct elevated for gender/age	Yes	No
Left shift of granulocytic series	Yes	No
Lack of significant toxic granulation	Yes	No
Thrombocytopenia	Yes	No
Immunoblasts and plasma cells > 10% of lymphocytes	Yes	No

Rapid Screening Test for HCPS in Rural Areas - Desired Features

Performed with routinely available laboratory equipment

Performed by non-specialized laboratory technical staff

Feasible to train staff on all shifts and maintain competency

Performed without adversely affecting laboratory workflow

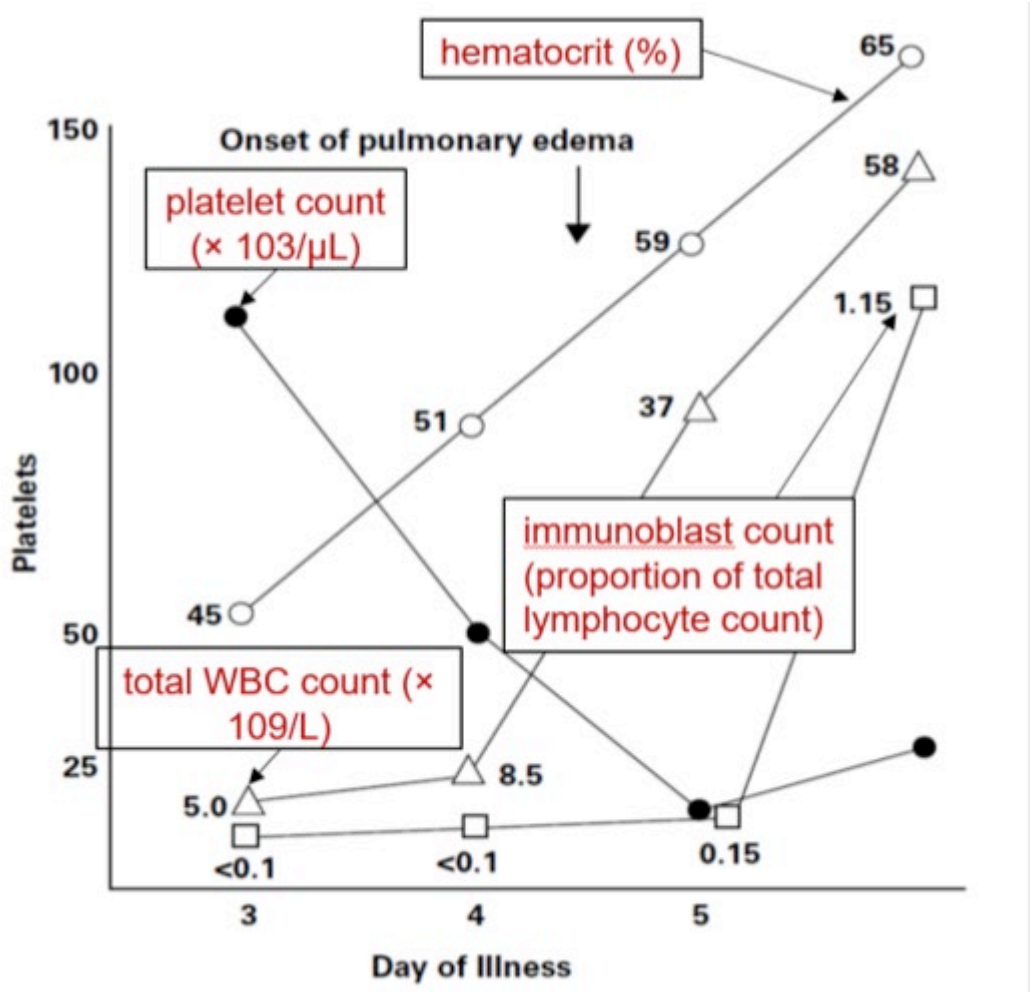
Provides reliable information that supports clinical decision making

Limitations of 5-point peripheral blood screen for HCPS

- **Presumptive diagnosis of HCPS**
  - This scoring system is a screening test for patients who may have HCPS. It is a presumptive diagnosis supported by appropriate clinical and history findings. Confounding chronic clinical conditions may need to be considered when interpreting the significance of a given score
- **Not a test for exposure to hantavirus**
  - Scoring system cannot determine exposure to hantavirus or distinguish milder forms of hantavirus infection from other causes of viral illness
- **Collect a serum sample**
  - Collect a sample for serologic confirmation when performing a hantavirus peripheral blood screen. Positive IgM antibodies for hantavirus suggests acute infection.

Laboratory results in patients with Hantavirus Cardiopulmonary Syndrome

1. Platelets decrease
2. White blood cells increase
3. Immunoblasts increase
4. Hematocrit increases



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