

GALLUP INDIAN MEDICAL CENTER

Epidemiology and Ecology
of Hantaviruses in the Americas

HANTAVIRUS PULMONARY SYNDROME OUTBREAK CHRONOLOGY

May 14	REPORT OF A CLUSTER OF ARDS CASES
June 4	PRELIMINARY LABORATORY TESTS INDICATE SEROLOGIC CONNECTION TO HANTAVIRUSES
June 4	FDA APPROVED RIBAVIRIN OPEN LABEL PROTOCOL
June 7	SIX CASES SEROLOGICALLY POSITIVE FOR HANTAVIRUSES
June 8	FIRST PCR POSITIVE FROM PATIENT MATERIAL
June 8	FIRST PATIENT ENROLLED IN RIBAVIRIN PROTOCOL
June 9	FIRST SEQUENCE FROM PATIENT MATERIAL, IDENTIFYING UNIQUE HANTAVIRUS
June 9	FIRST RODENTS TRAPPED
June 13	30% OF 40 RODENTS TRAPPED AT ONE CASE RESIDENCE ARE SEROLOGICALLY POSITIVE FOR HANTAVIRUSES
June 14	FIRST POSITIVE PCR FROM RODENT TISSUES
June 16	FIRST SEQUENCE FROM RODENT TISSUES, IDENTIFYING A DIRECT GENETIC LINK WITH VIRUS SEQUENCE FROM CASES
June 18	9 CASES CONFIRMED



NEW MEXICO LAST ELISA NEWS June 4, 1993

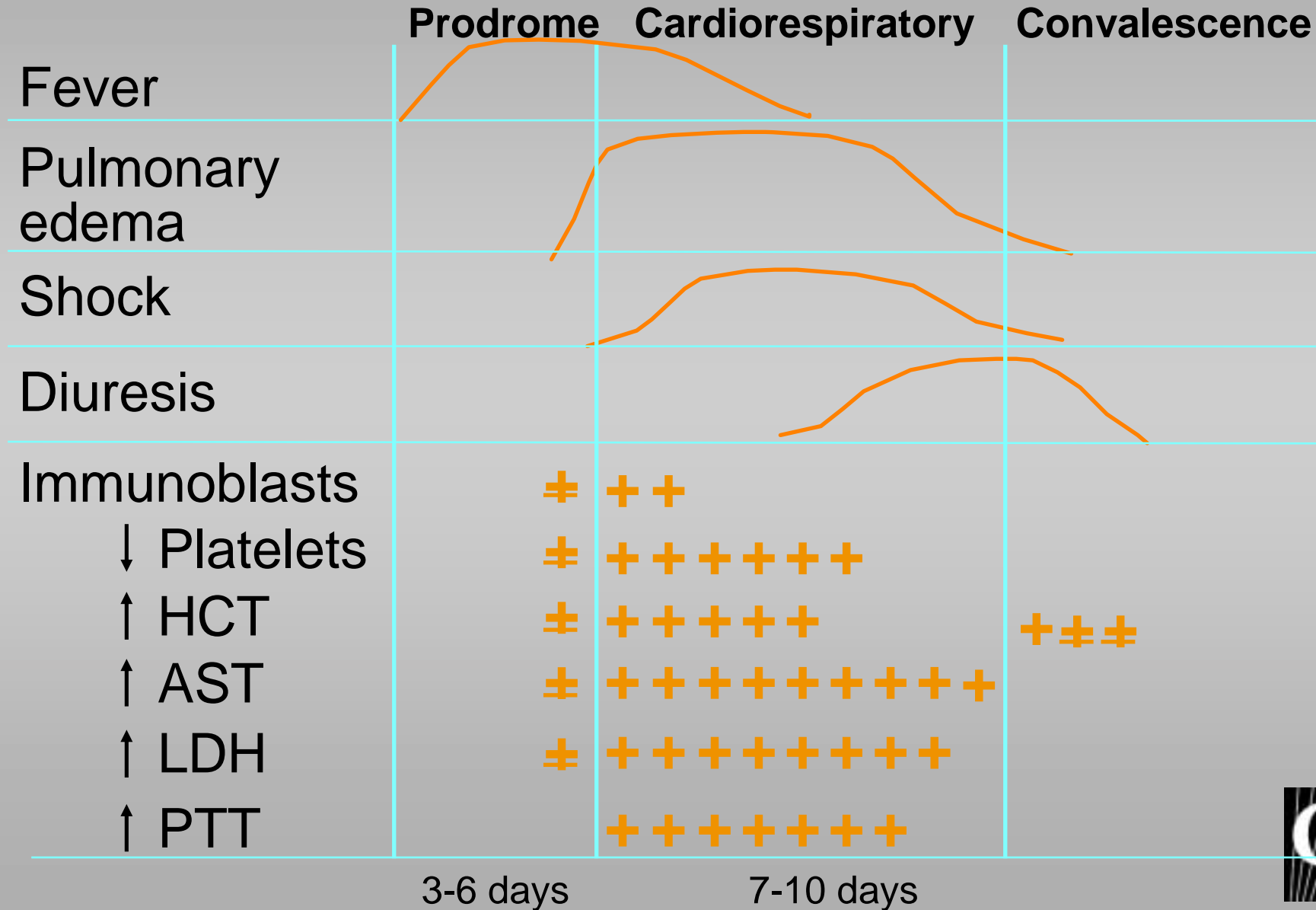
HANTAAN

PUUMALA

SEOUL

Serum #	IgG	IgM	IgG	IgM	IgG	IgM
1121	-	-	-	100	100	400
1122	100	-	1600	-	400	-
1124	-	-	-	-	-	-
1125	-	-	-	-	-	-
1129	-	-	-	1600	400	1600
1134	-	-	-	-	-	-
1148	-	-	-	-	-	-
1154	-	1600	-	-	-	6400

Clinical Progression of HPS



Hantavirus Pulmonary Syndrome

Radiographic Findings

Bilateral interstitial infiltrates

Bilateral alveolar infiltrates

Pleural effusion



Histopathology (Lung)

Interstitial Pneumonitis

Interstitial infiltrates of enlarged mononuclear cells

Congestion

Intra-alveolar and septal edema

Loads of viral antigen in the macrovascular endothelium

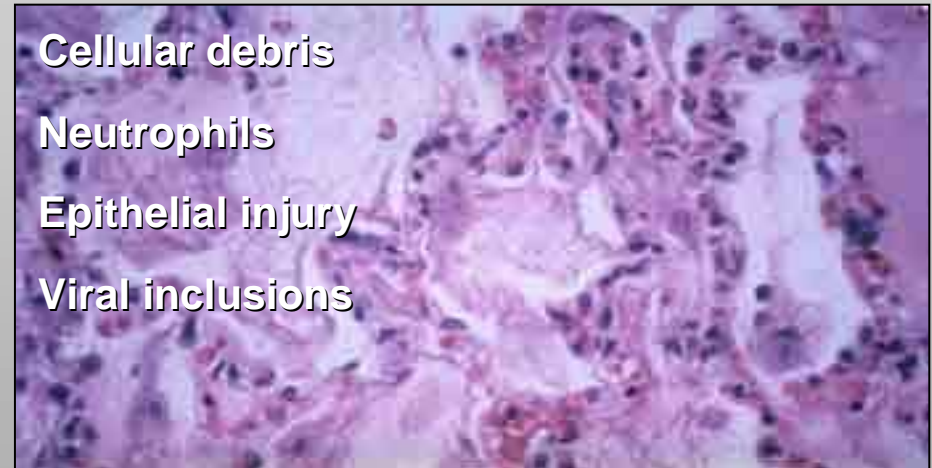
Absence or minimal evidence of:

Cellular debris

Neutrophils

Epithelial injury

Viral inclusions



The current working hypothesis is that HPS is immunomodulated disease

Presence of large immunoblasts seen in the circulation at the onset of the pulmonary edema or in the necropsy lung tissues

Despite prominent accumulation of viral antigen in the infected vascular endothelium, no evidence of cell destruction has been observed

High levels of cytokine producing cells in lung tissue from HPS fetal cases

Recently, specific HLA alleles are linked to either mild or severe HPS



Criteria for inclusion in the Registry

- Fever >101 F or >38.3
- Thrombocytopenia (platelets 150,000 mm³):
- Elevated Hematocrit (Hct):
- Elevated WBC: _____
- Total Neutrophils: _____ (%)
- Banded Neutrophils: _____ (%)
- Lymphocytes
- CXR with unexplained bilateral interstitial infiltrates or suggestive of Respiratory compromise requiring supplemental oxygen? Yes No Unk.
- Oxygen saturation <90% at any time? Yes No Unk.
- Was the patient intubated? Yes No Unk.
- Has the patient received ribavirin?

Seroprevalence of SNV IgG Antibodies in Select Populations

Risk group	Positive/tested (%)	Location/time
Forest workers	0/143	SW US, 1993
Health care workers	0/396	SW US, 1993
Prodromal HPS	3/300 (1.0%)	SW US, 1993
Contacts	3/239 (1.3%)	SW US, 1993
Rural OCC	1/522 (0.2%)	SW US, 1994
Rodent workers	8/932 (0.9%)	US, 1994
Total	15/2501 (0.6%)	

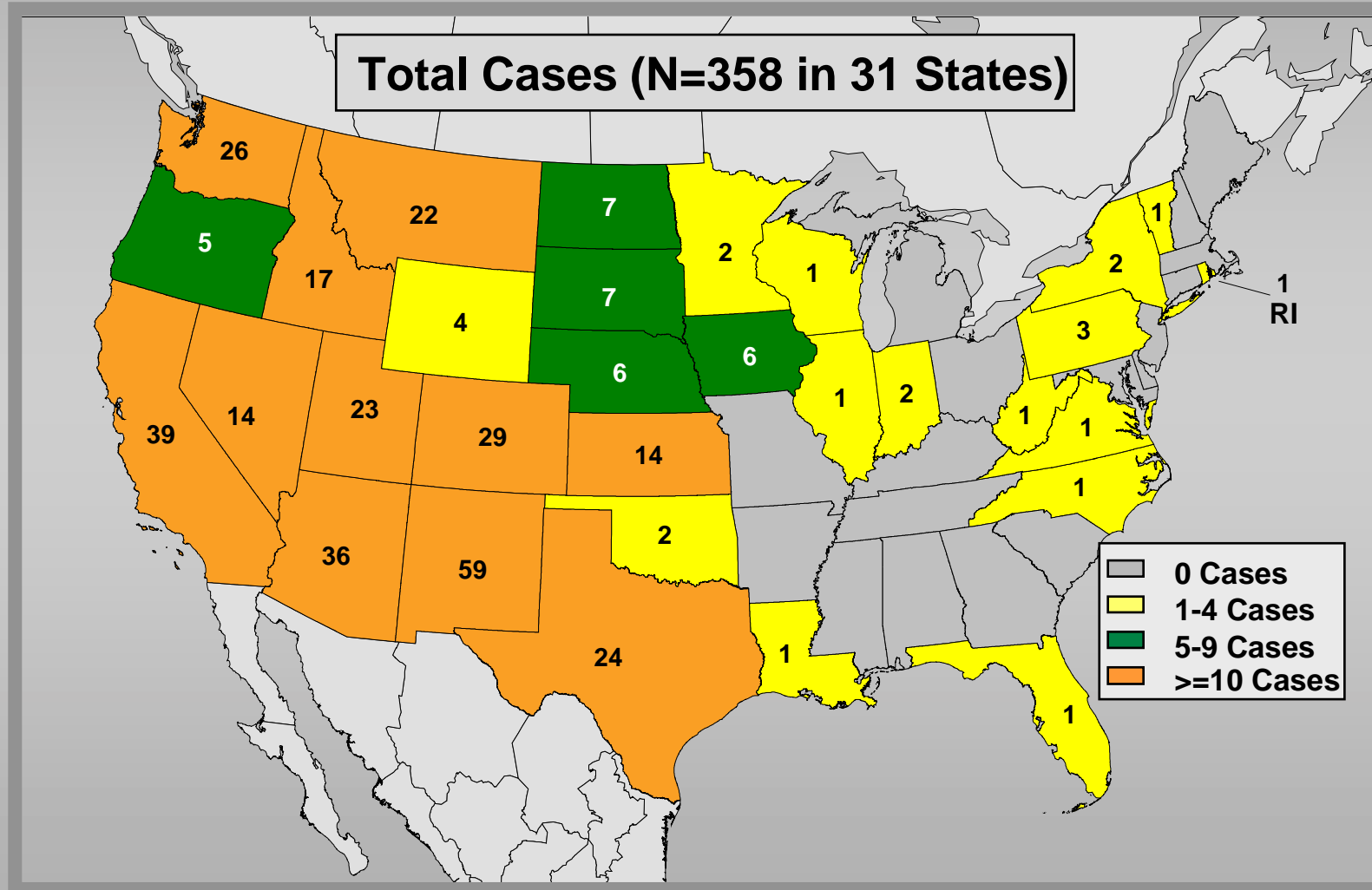


Hantavirus Pulmonary Syndrome, United States Descriptive Demographic Statistics, January 6, 2004

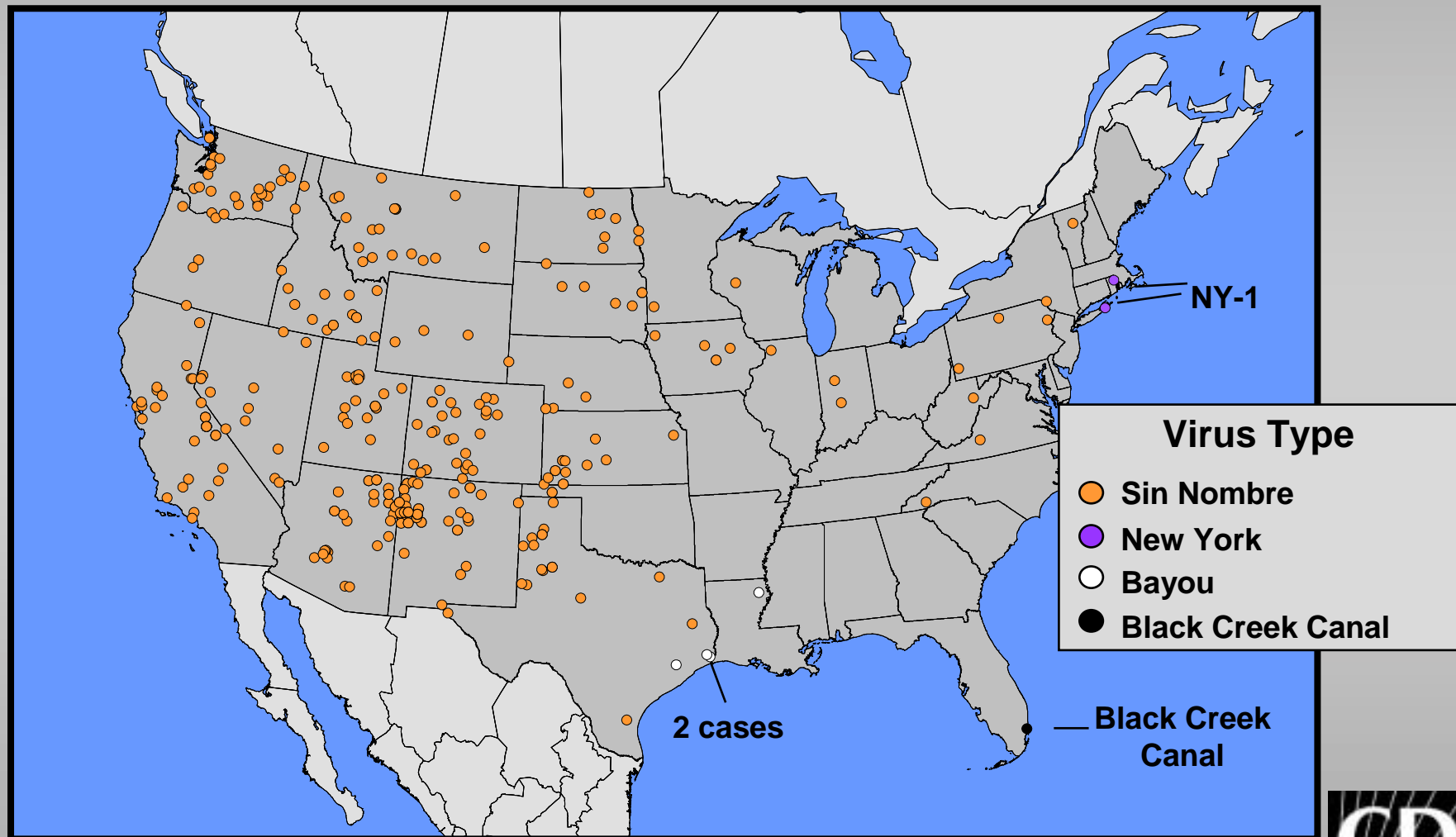
Characteristics	Total	Up to 1/94	Up to 1/04
N		79 (100 %)	362 (100 %)
Gender			
Male		47 (59 %)	223 (62 %)
Female		32 (41 %)	139 (38 %)
Race			
White		51 (65 %)	277 (77 %)
American Indian		26 (33 %)	73 (20 %)
Black		2 (2 %)	6 (2 %)
Asian		0	3 (1 %)
Ethnicity			
Hispanic		7 (9 %)	48 (13 %)
Case Fatality			
Dead		45 (57%)	134 (37%)
Age (years)		Mean=33 [12-69]	Mean=37 [10-75]



Hantavirus Pulmonary Syndrome Cases by State of Residence United States – January 6, 2004

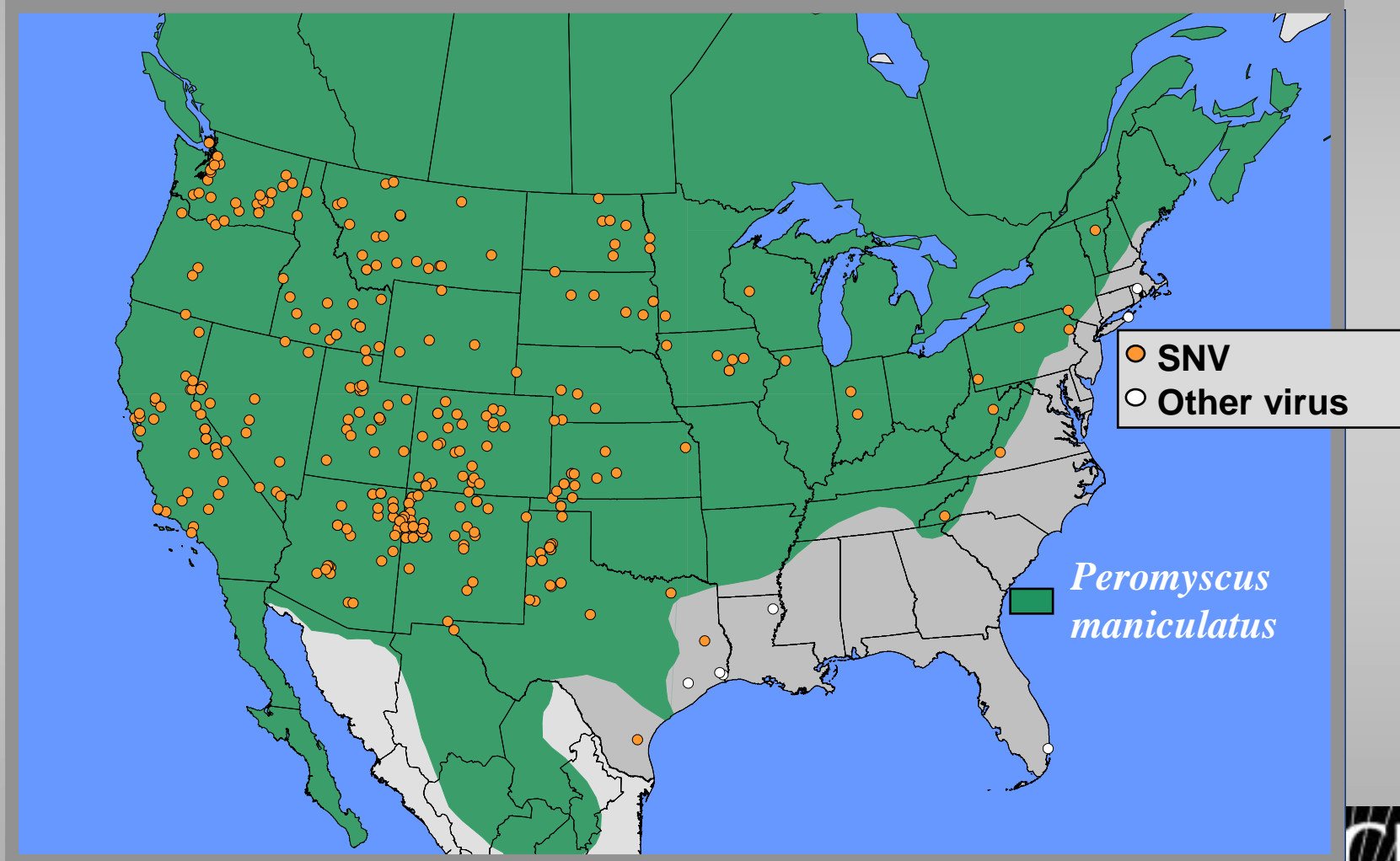


Location of HPS Cases by Virus Type as of January 6, 2004 *Total Cases (N=358 in 31 States)*



Although serologically confirmed as HPS, sequence data are not available for all cases. For non-sequenced cases, the specific infecting hantavirus is assumed to be that corresponding with the known rodent reservoir in the area of probable exposure.

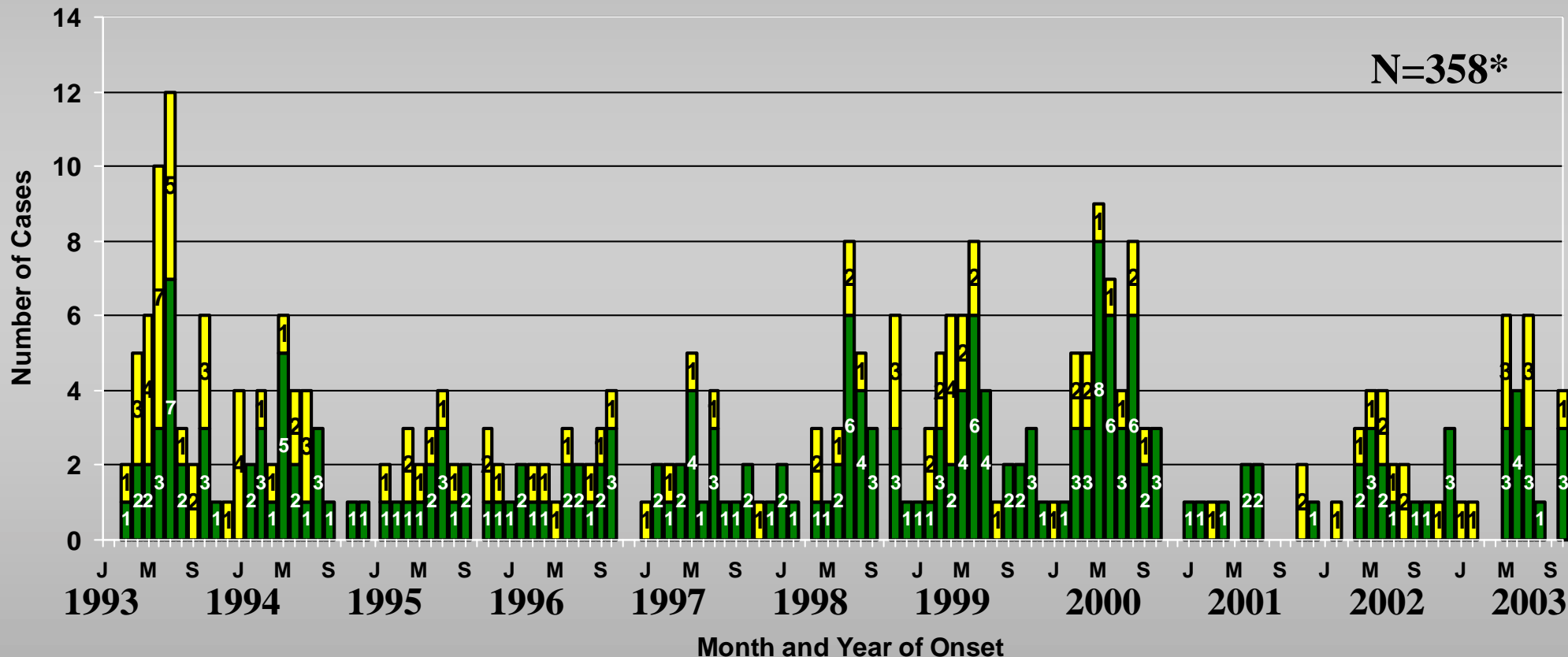
Distribution* of *Peromyscus maniculatus* and Location of HPS Cases as of January 6, 2004 Total Cases (N=358 in 31 States)



*Rodent distributions from: Burt WH, Grossenheider RP. A Field Guide to the Mammals. 3rd ed. New York, New York. Houghton Mifflin Company. 1980

Hantavirus Pulmonary Syndrome Cases by Outcome United States, as of January 6, 2004

■ Alive ■ Dead



*Thirty-two additional cases (nineteen deceased) with onset before 1993 not shown.



Hantavirus Pulmonary Syndrome

Number of cases by date

¹PAHO December 02 ²May 02

³October 02 ⁴January 04

Canada
(36)²

United States
(358)⁴

Brazil (240)¹

Panama (31)³

Paraguay (95)¹

Bolivia (19)¹

Uruguay (38)¹

Chile (340)⁴

Argentina (530)¹

Countries with
reported cases
of HPS
(no of cases)

Countries with
no reported
cases of HPS



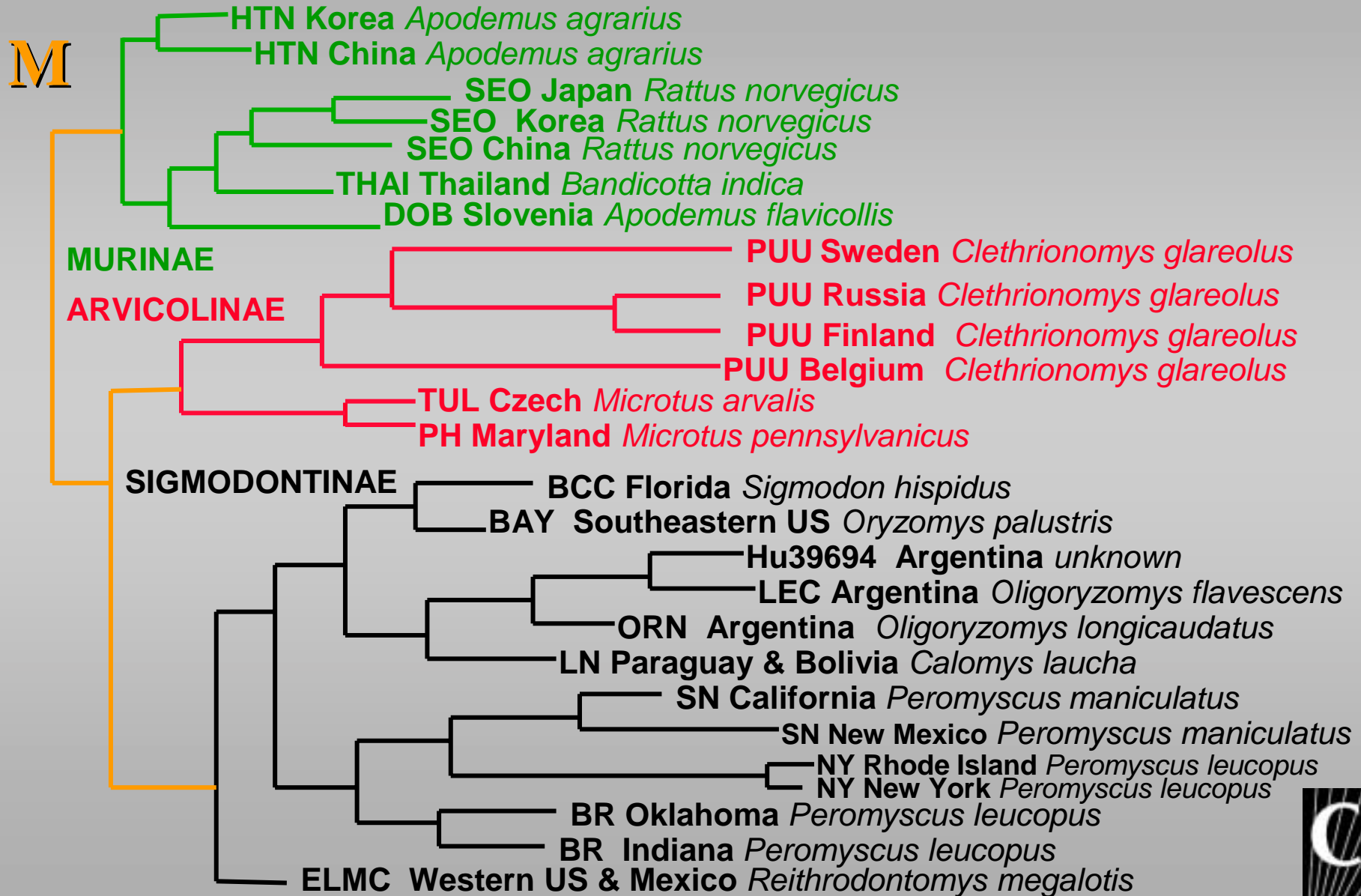
New World Hantaviruses



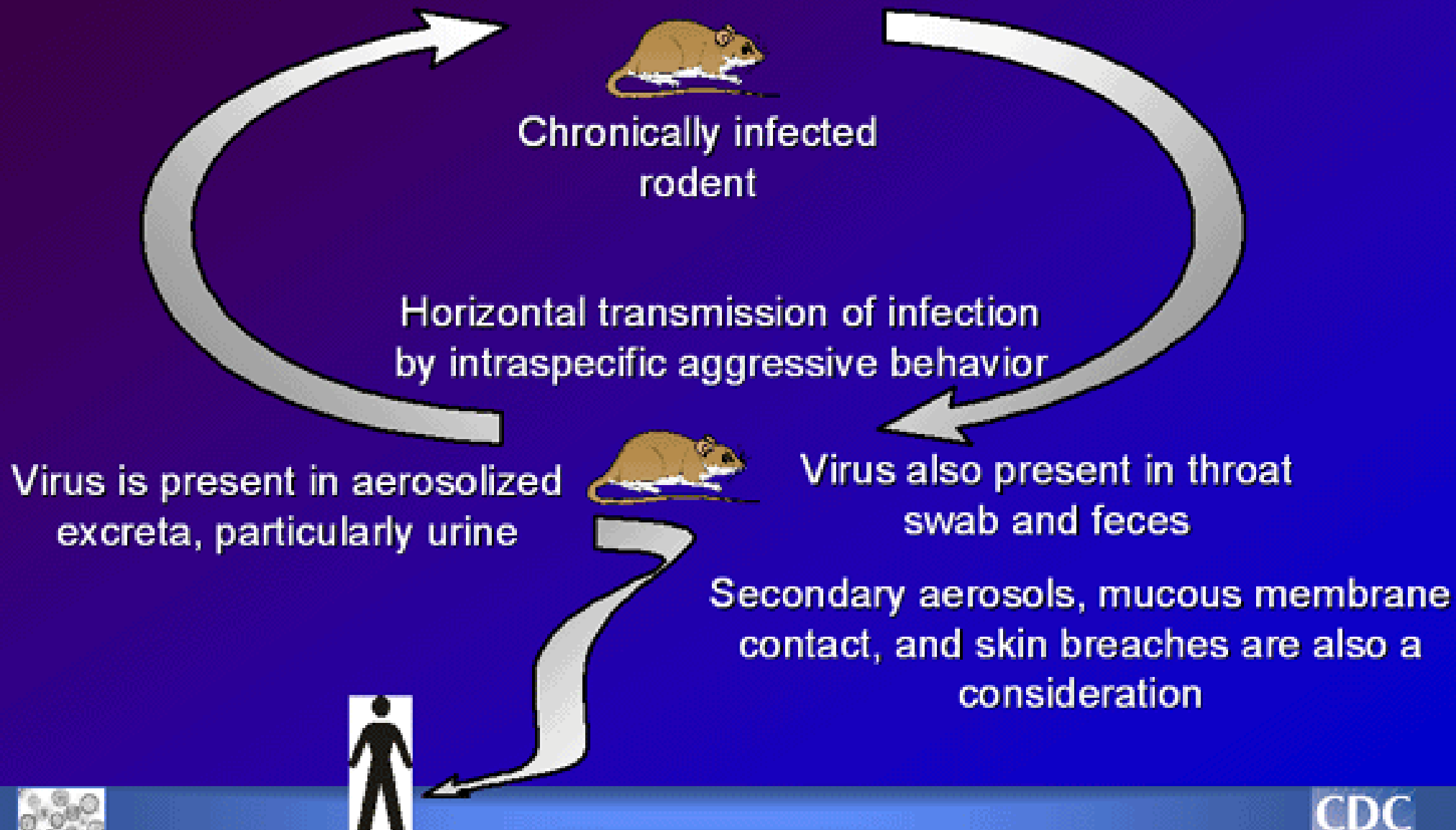
New World Hantaviruses



Phylogeny of Hantaviruses: Based on Sequence of M Segment (Subfamily, Hantavirus, Location, Host)



Transmission of Hantaviruses





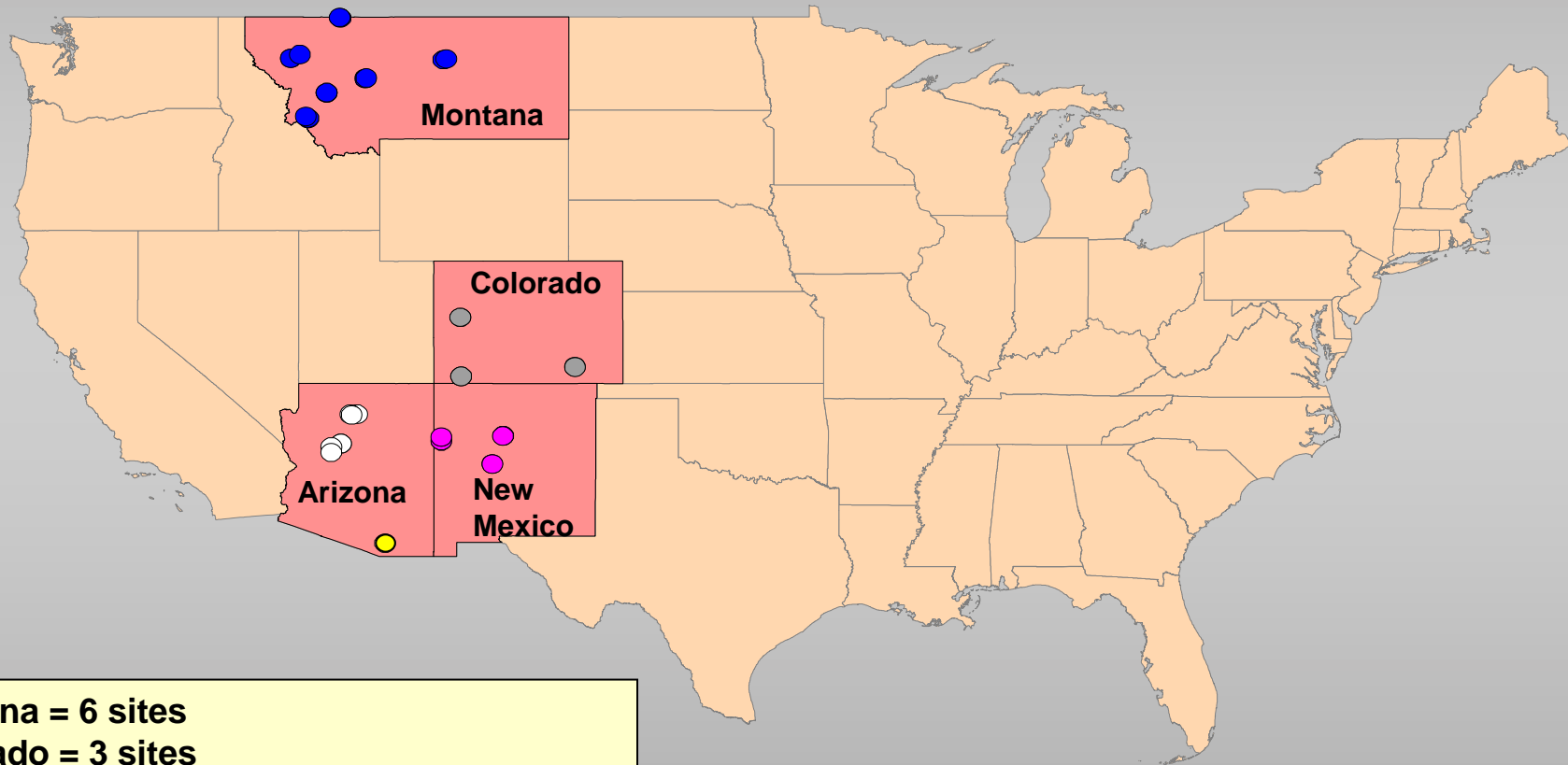
CDC-initiated Longitudinal Rodent Study

Purpose of the longitudinal rodent study:

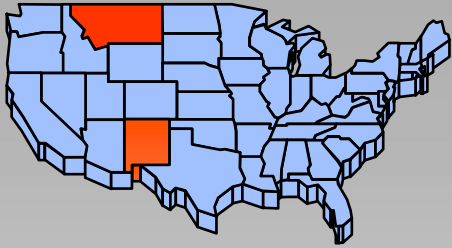
- ✓ Describe/monitor Δ s in deer mouse populations.
- ✓ Describe/monitor Δ s in the # of SNV-infected deer mice.
- ✓ Ecological factors associated with Δ s in deer mouse populations.
- ✓ Meteorological factors associated with Δ s in deer mouse populations.
- ✓ Conditions associated with disease transmission to humans (risk of infection).



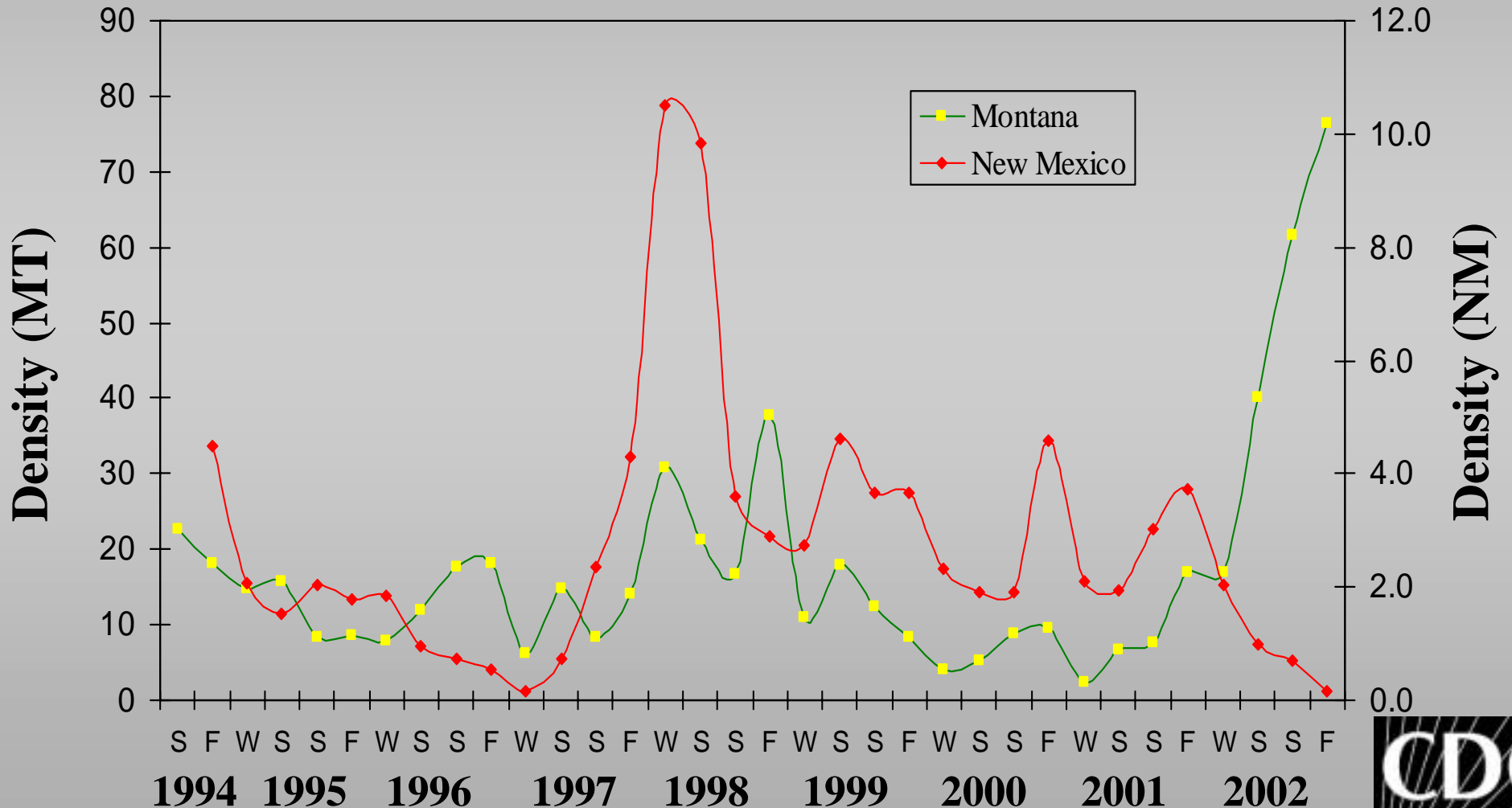
Longitudinal Study of Hantavirus (Rodent Trapping Sites)



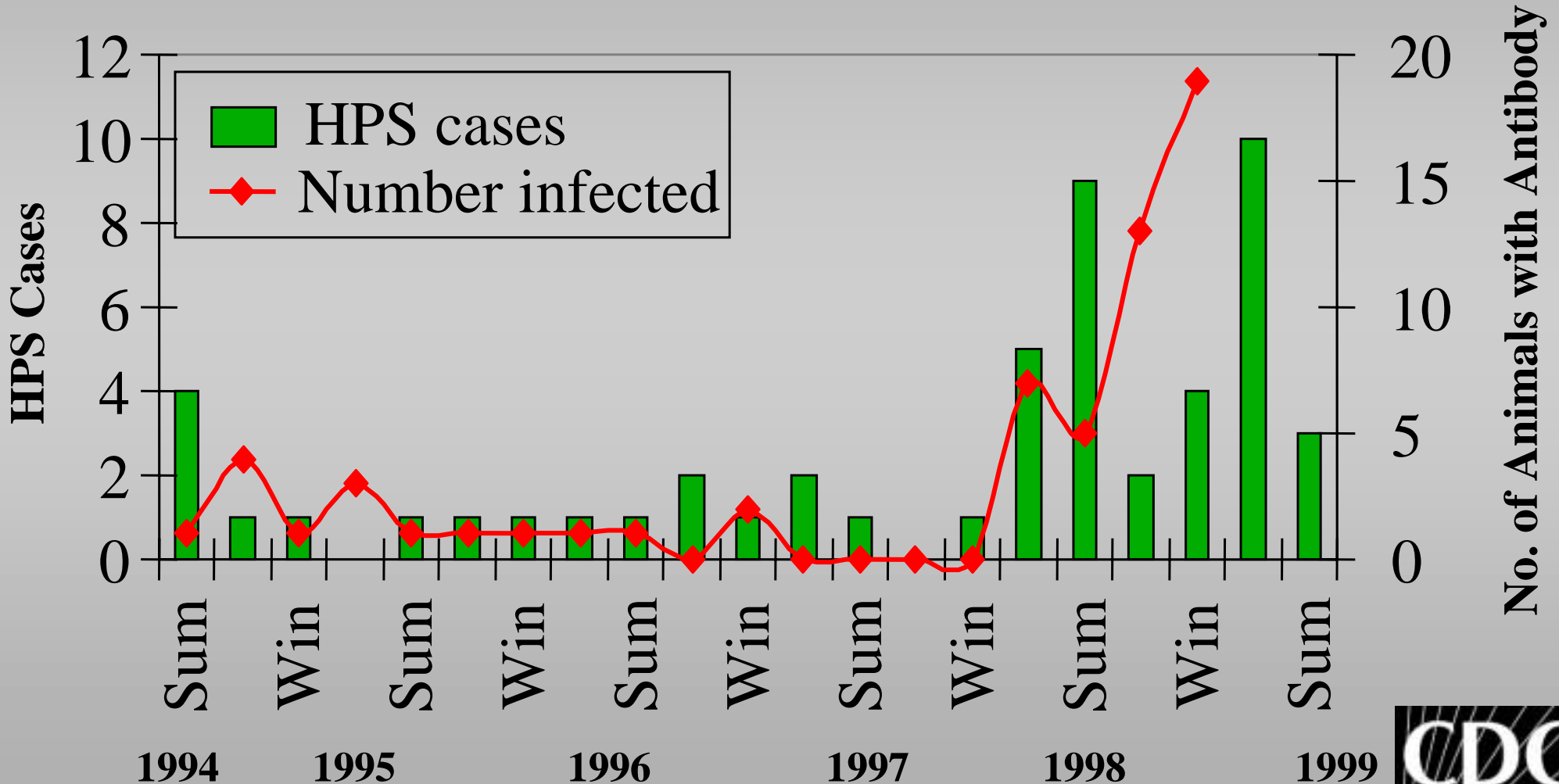
Montana = 6 sites
Colorado = 3 sites
AZ (Yavapai) = 3 sites
AZ (UAZ) = 1 site (discontinued 2000)
New Mexico = 4 sites



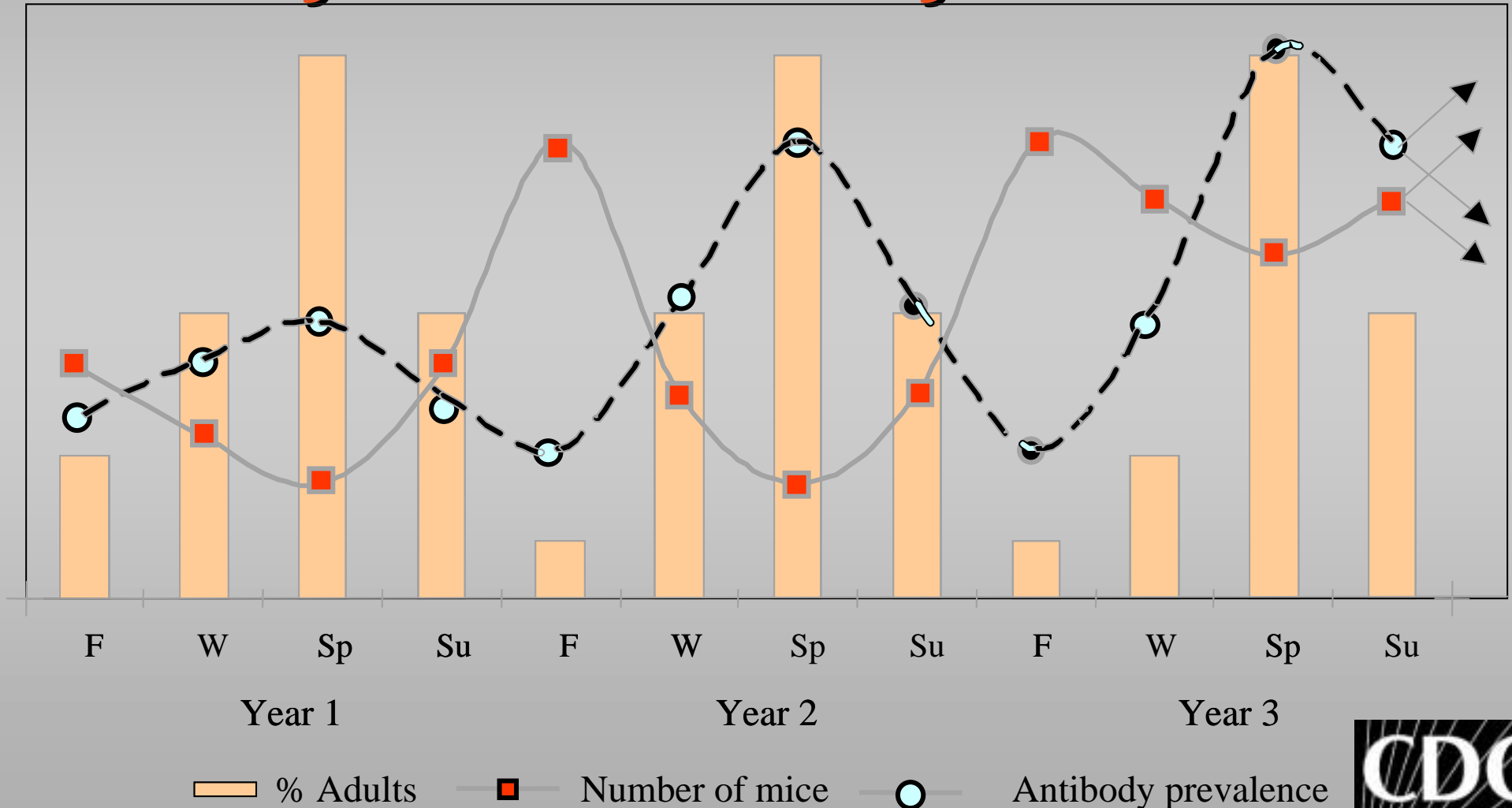
P. maniculatus Population Density by Season, 1994-2002: New Mexico and Montana



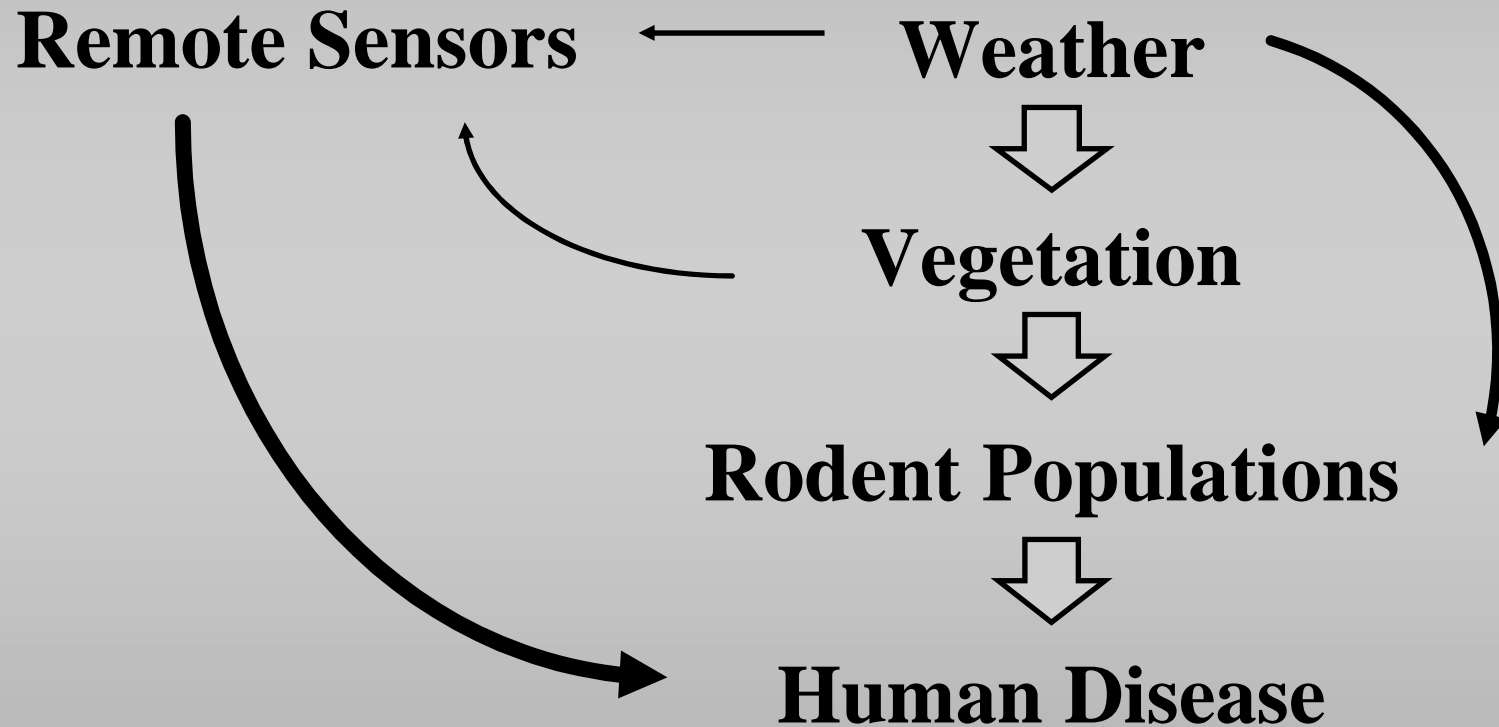
Number of *P. maniculatus* with Ab to SNV and HPS cases by season, 1994-1999



Relationship Between Population Density and Antibody Prevalence



Reservoir Studies → Predictive Model



Time Series Models

for forecasting monthly deer mouse populations in Montana

Kent Wagoner, Northrop Grumman/CDC

Bob Yaffee, New York University

Jim Mills, CDC

Rick Douglass, Montana Tech

Darin Carroll, CDC

Andy Hopkins, CDC



✓ **Site of Interest:**

Cascade, MT (3 Trapping Grids)

Deer mouse data collected monthly from June 1994 - 2001

✓ **Predictor Variables (nearby NOAA weather station):**

Monthly Cooling Degree Days and Heating Degree Days

Monthly Total Precipitation (sum of precipitation)

Cumulative Precipitation (inches since prev. October)

Temperature (mean max, mean min, high, and low monthly)

El Nino (time when SST is $.5^{\circ}\text{C}$ above avg in Eq. Pacific)

✓ **Criterion Variable:**

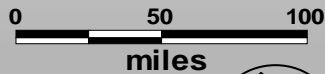
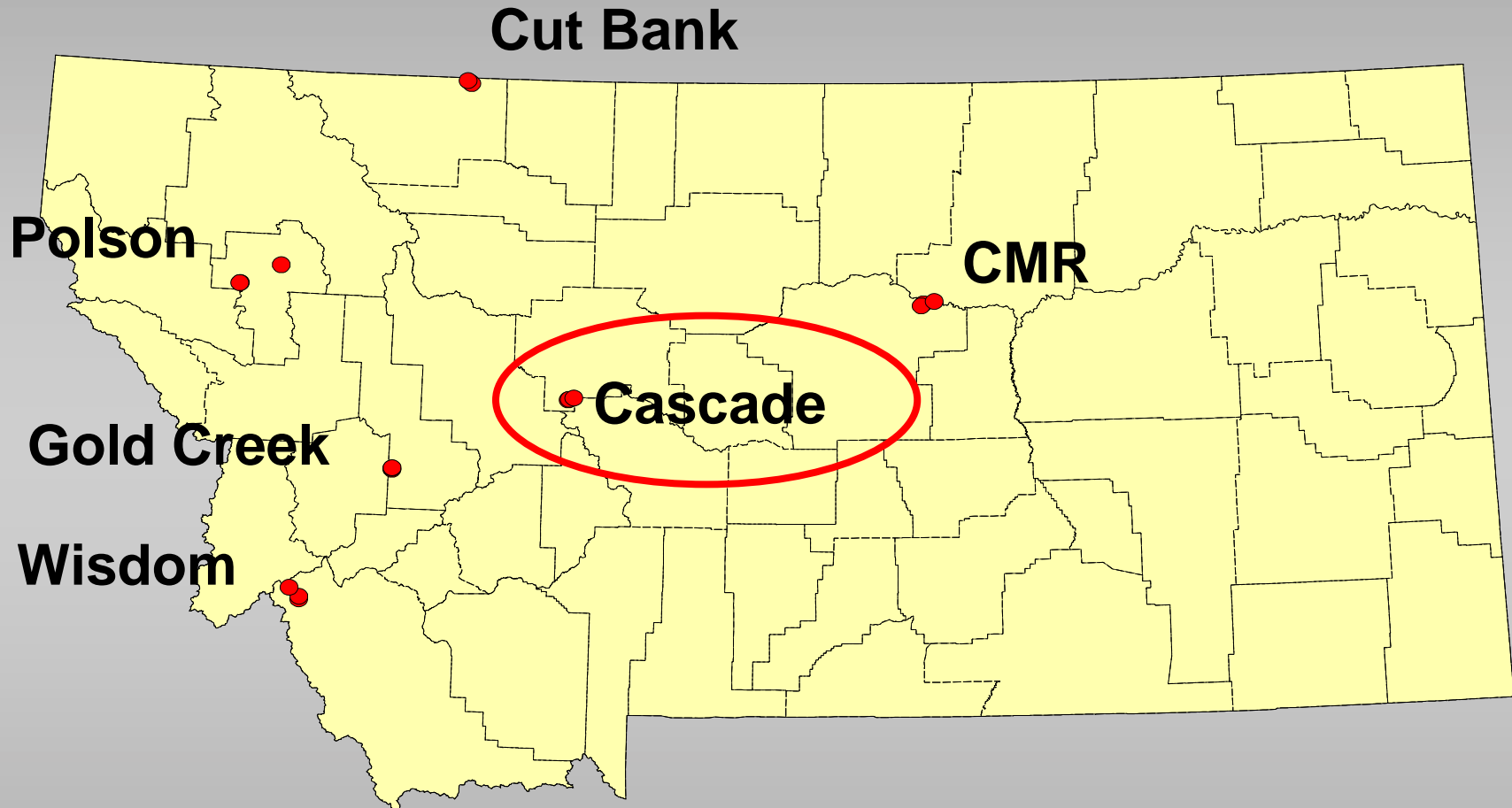
Monthly Minimum Number of Deer Mice Alive ($\text{MNA}_{\text{deer mice}}$)

✓ **Data Analysis Technique:**

Time Series Analysis



Montana



CDC
Division of Viral and Rickettsial Diseases
Special Pathogens Branch
Created 2003

- ✓ Substantial deer mouse population
- ✓ SNV-infected deer mice
- ✓ Monthly Trapping (1994 – 2001)



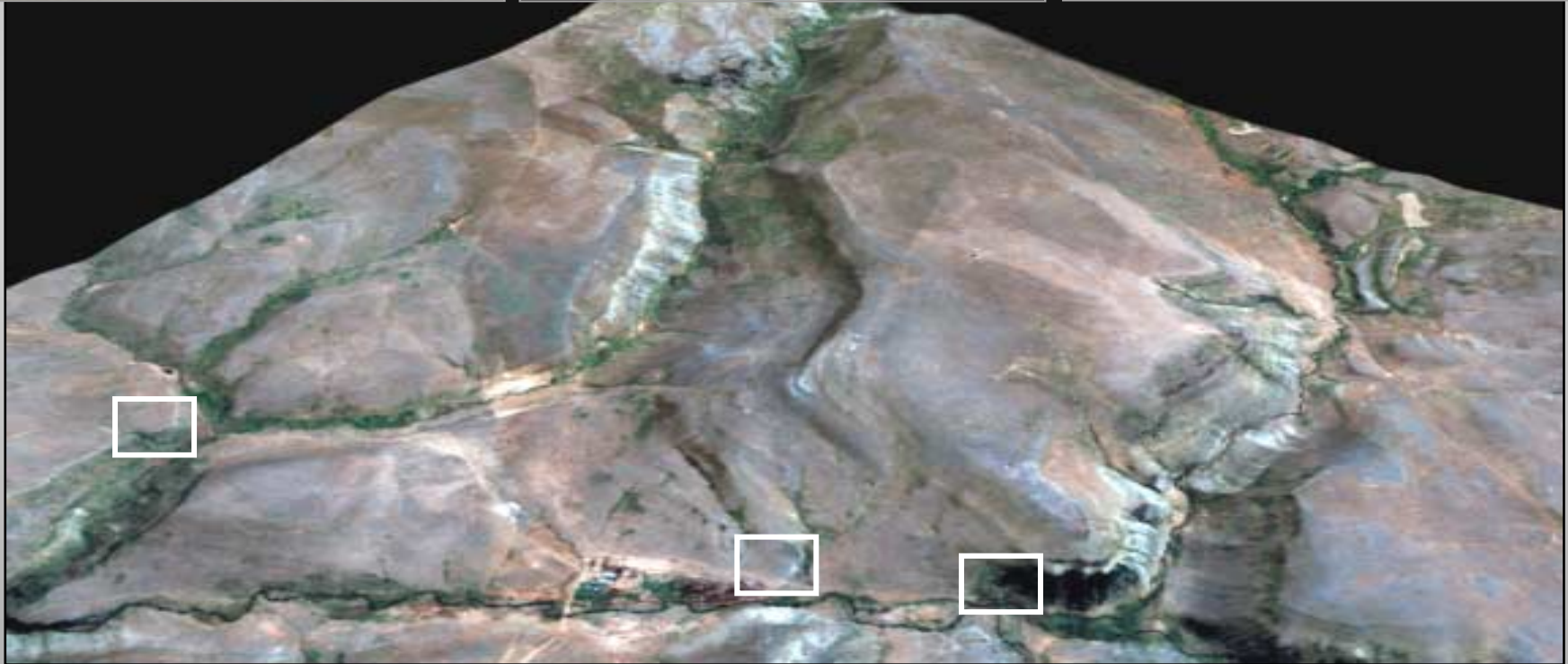
Cascade 12



Cascade 11



Cascade 10



USGS DEM (30m)
IKONOS Geo 1m (Space Imaging)
(August 2003)

Forecasting Total MNA at Cascade

(using meteorological data)

$R^2 = .848$

Adjusted $R^2 = .791$

$$\ln(MNA_{total_t}) = 3.615 - 0.002\text{Time}^2 + 1.18 * 10^{-4}\text{Time}^3$$

$$+ 1.59 * 10^{-6}\text{Time}^4 + 7.179 * 10^{-11}\text{Time}^6$$

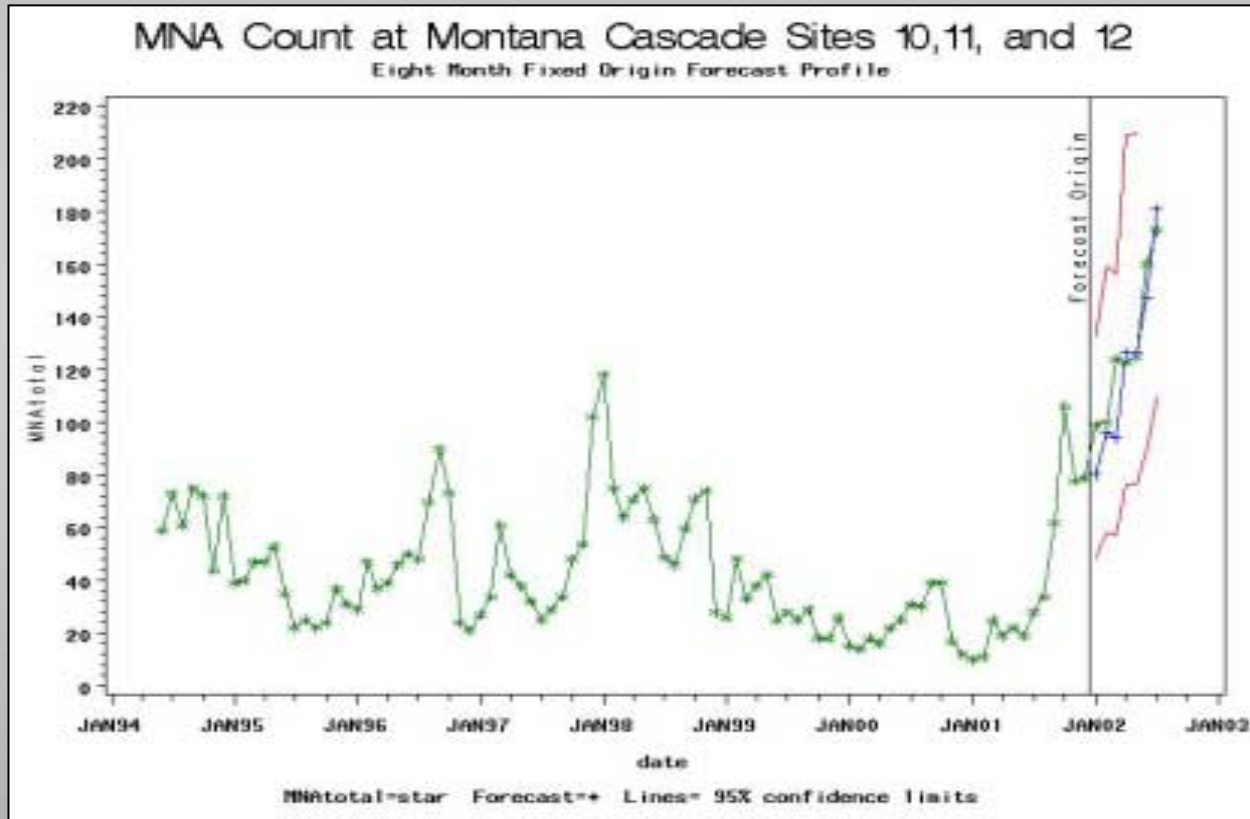
$$- 6.21 * 10^{-3}\text{Cumprecip}_{t-4}^3 + 8.98 * 10^{-3} \text{Sumcdd}_{t-2}$$

$$+ .546\text{ElNino}_{t-7} + .449L^2\text{ElNino}_{t-7} - .827(\text{P199910})$$

$$+ \frac{e_t - .983e_{t-4}}{(1 - .353L + .207L^5 + .457L^{13})}$$



Evaluating Forecast Accuracy (*Mean Absolute Percentage Error*)



Mean absolute percentage error (MAPE)

$$= \frac{100}{n} \sum_{i=1}^n \left| \frac{\text{actual} - \text{forecast}}{\text{actual}} \right|$$

MAPE = .185%

Hantavirus Health Education

www.cdc.gov/ncidod/diseases/hanta/hps/index.htm

