

Investigation into Risk Factors for Progressive Inflammatory Neuropathy Among Swine Abattoir Workers in the United States

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Outbreak Detection

- **Minnesota Department of Health was notified of a cluster of 10 persons with neurologic illness in late October 2007**
- **All worked at Quality Pork Processors in Austin, MN**

Outbreak Investigation

- **Patients interviewed**
 - All had worked in warm room
 - 7 had worked where the heads were processed (head table)
- **Medical charts reviewed**
 - All had similar illness
 - Progressive Inflammatory Neuropathy

Illness Characteristics

- Numbness, tingling, weakness, or pain in the extremities
- No antecedent illness
- 1 had rapid onset of paraplegia
- 2 were hospitalized
- Time from illness onset to symptom plateau
 - 29.5 days (8 – 213 days)

QPP

- **Employs ~ 1300 workers**
 - **846 cases per 100,000**
- **Far exceeds background rate of:**
 - **CIDP: 0.5 – 2 cases per 100,000**
 - **AIDP: 1.2 – 1.9 cases per 100,000**

Helmar C. et al. J Peripheral Nerv Sys 2007 12 (4), 285–285.

Kohler H. N Engl J Med 2005;352:1343-56.

Initial Environmental Investigation

- **QPP used compressed air device to remove brains from pig skulls**
 - **Device attached to compressed air line**
 - **Pass stainless steel tube through foramen magnum**
 - **A wire trigger mechanism**
- **Operator and nearby workers had brain material on clothes**
- **Mist of brain material was in air around work station**

Initial Recommendations

- **After discussion with MDH:**
 - **The plant discontinued brain removal**
 - **Workers at head table required to wear additional personal protective equipment**

Epidemiologic Case Definition

- **Used to describe an affected individual in order to determine risk factors associated with illness**
 - **Maximize positive predictive value of the case definition**
 - **Include epidemiology, clinical, and diagnostic components**
- **Epidemiologic case definition has a different purpose than a clinical case definition**

Case Definition

- **Confirmed case**
 - **Participation in swine-slaughtering operations**
 - **Clinical and diagnostic findings not attributable to alternative diagnosis**
 - **Signs and symptoms of new onset peripheral neuropathy**
 - **Electrodiagnostic testing**
 - **Axonal and/or demyelinating neuropathy in affected limbs**

Case Definition

- **Probable case**
 - **Participation in swine-slaughtering operations**
 - **Clinical and diagnostic findings not attributable to alternative diagnosis**
 - **Signs and symptoms of new onset peripheral neuropathy**
 - **Neuroimaging consistent with radiculitis, myelitis, or encephalitis, or an elevated CSF protein (>45 mg/dL)**

Case Definition

- **Possible case**
 - **Participation in swine-slaughtering operations**
 - **Clinical and diagnostic findings not attributable to alternative diagnosis**
 - **Signs and symptoms of new onset peripheral neuropathy**

Case - Control Study

- All current or recently employed confirmed and probable cases
- 2 control groups:
 - Randomly selected warm room workers
 - Initial design of 5 controls : 1 case
 - All current non-ill head table workers

Case - Control Study Design

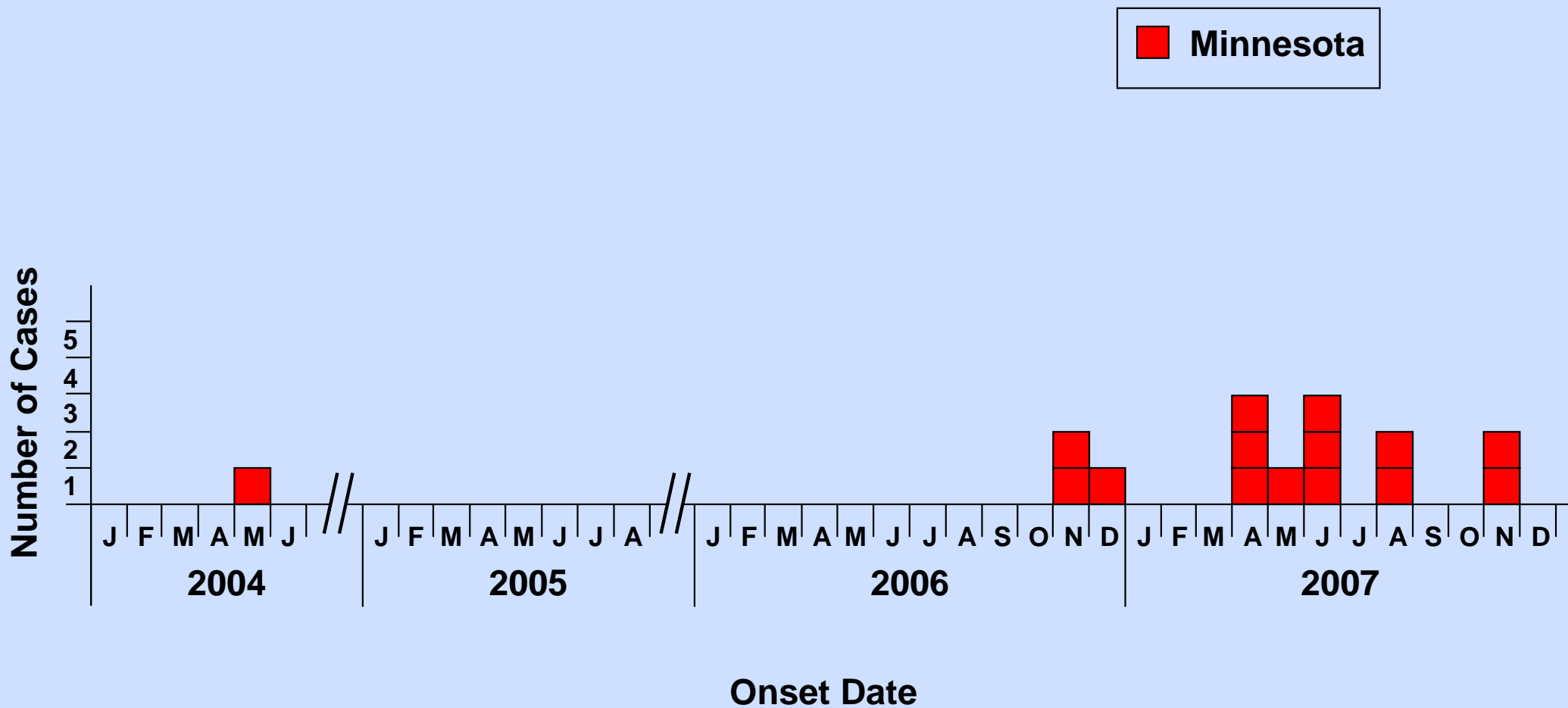
- **Standardized questionnaire (30-45 minutes)**
 - **Clinical - Neurologic and infectious symptoms, personal and family health history**
 - **Work related exposures – job type, PPE, toxin/chemical**
 - **Non-work related exposures – travel, outside work/hobbies, animal contact, medications, supplements, herbals, home chemicals**

Case Characteristics

(n=15)

Age, median (range)	34 years (21–54)
Female	8 (53%)
Hospitalized (range, days)	2 (2–42)
Time employed at Plant A, median (range)	13 months (3–252)
Worked in Warm Room	15 (100%)
Worked at Head Table	9 (60%)

Epidemiologic Confirmed and Probable Cases by Month of Illness Onset



Case-Control Study

- **13 confirmed cases**
- **49 warm room controls**
- **56 head table controls**

Univariate and Multivariate Analysis using Warm-room Controls

Risk Factors	Cases N=13	Controls N=49	OR (95% CI)	P
Female, N (%)	7 (54)	12 (24)	3.6 (0.9 – 15.5)	0.09
Median age, yrs (range)	32 (21-51)	27 (18 – 59)		0.23
Total time at Plant A, months Median (range)	18.3 (3 – 251)	15 (2 – 190)		0.84

Univariate and Multivariate Analysis using Warm-room Controls

Risk Factors	Cases N=14	Control s N=49	OR (95% CI)	Adjusted OR (95% CI)
Work at head table, N (%)	9 (69)	12 (24)	6.9 (1.8 – 26.6)	6.6 (1.6 – 26.7)
Backing heads or removing brain, N (%)	5 (38)	2 (4)	14.7 (2.4 – 89.1)	10.3 (1.5 – 68.5)

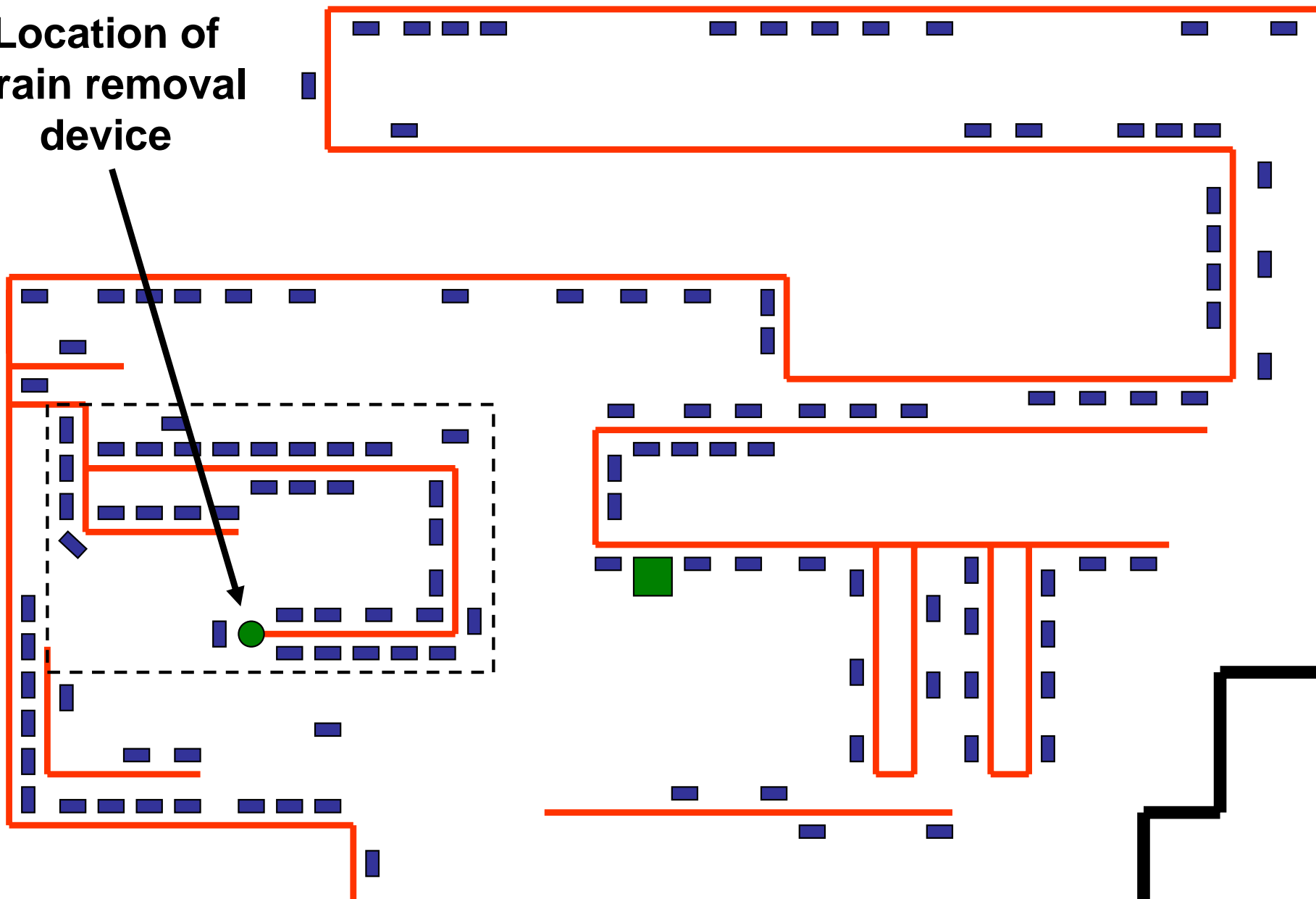
Univariate and Multivariate Analysis using Warm-room Controls

Risk Factors	Cases N=14	Controls N=49	OR (95% CI)	Adjusted OR (95% CI)
0 to 10 feet, N (%)	5 (38)	2 (5)	17.5 (2.5 – 122.2)	9.9 (1.2 – 80.0)
11 to 20 feet, N (%)	4 (29)	10 (25)	2.8 (0.6 – 13.4)	2.7 (0.5 – 13.4)
> 20 feet, N (%)	4 (29)	28 (70)	ref	ref

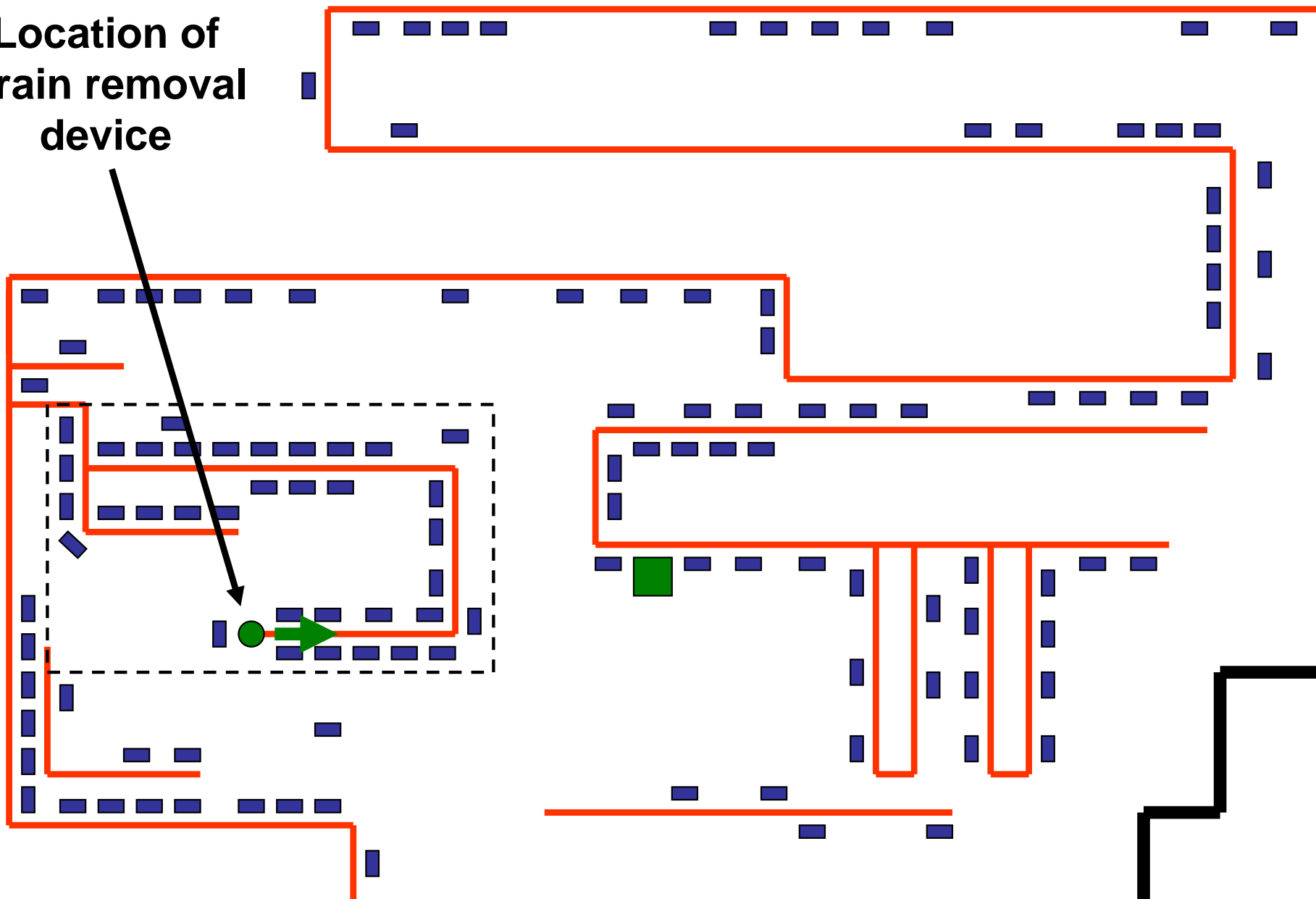
Univariate and Multivariate Analysis using Head-table Controls

Risk Factors	Cases n=9	Control s n=56	OR (95% CI)	Adjusted OR (95% CI)
0-10 feet from brain operation, N (%)	5 (56)	8 (15)	7.2 (1.6 – 32.7)	12.7 (1.8 – 91.4)
>10 feet from brain operation, N (%)	4 (40)	46 (85)	ref	ref

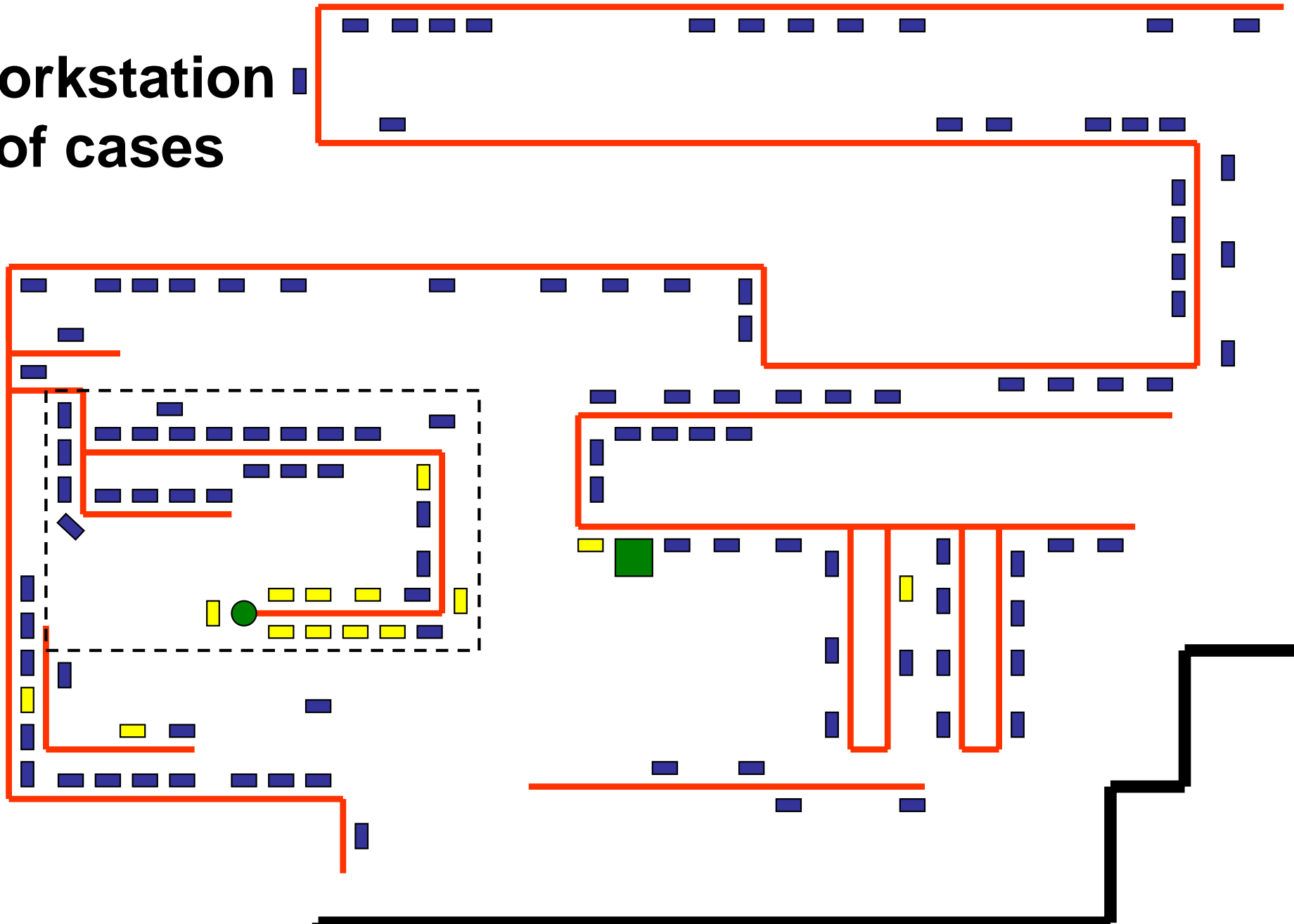
Location of
Brain removal
device



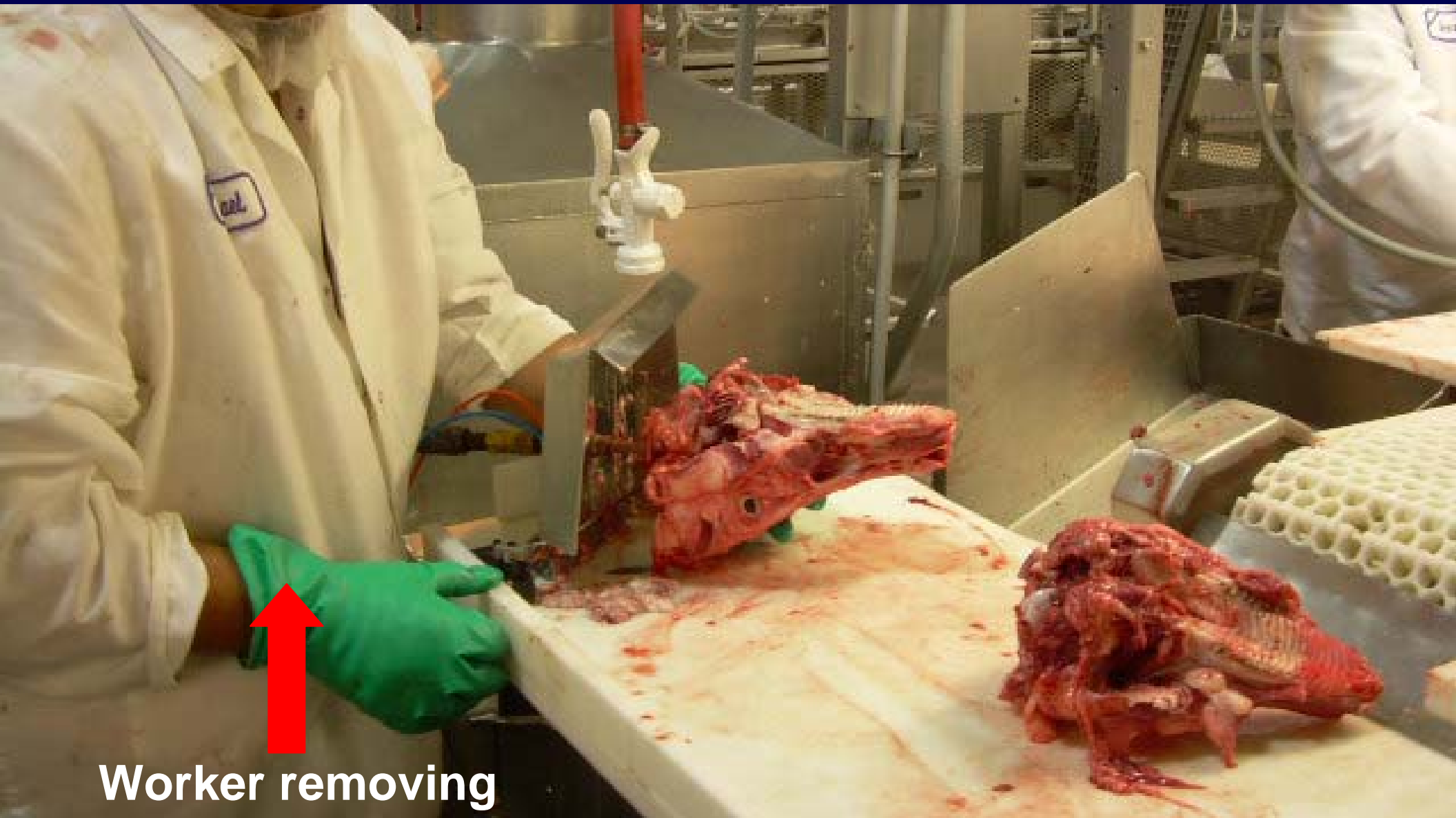
Location of
Brain removal
device



Workstation of cases

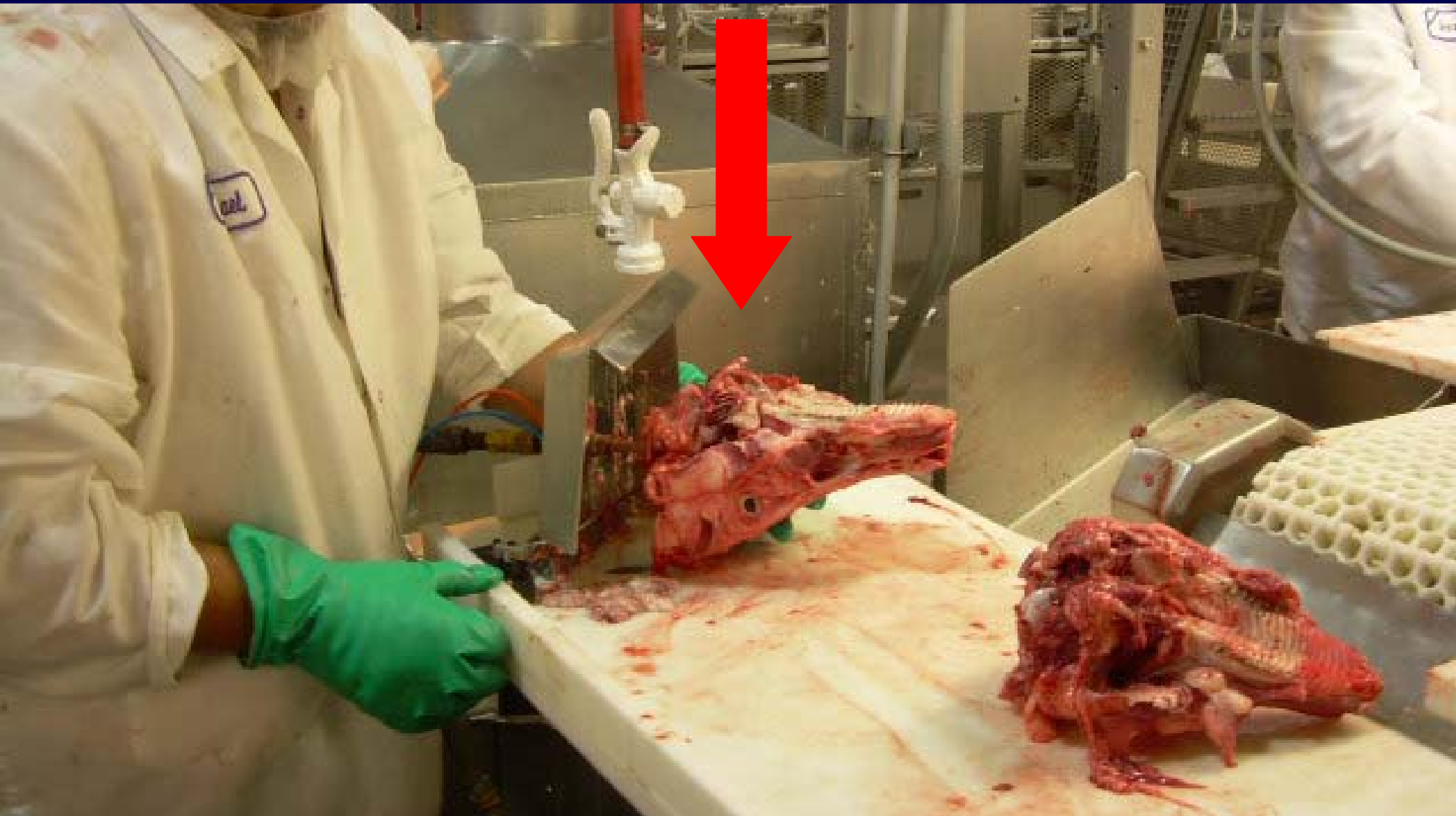






**Worker removing
brains**

**Porcine skull placed on
brain removal device**



**Worker backing
heads**



Environmental Investigation

- **National Institute for Occupational Safety and Health**
- **Inspected plant over 2 day period**
 - **Reviewed maintenance records**
 - **Measured airflow**
 - **Measured particulate size**
 - **Reviewed all MSDS sheets**

Environmental Investigation

- **NIOSH**
 - **No evidence for a toxicosis**
 - **Too much variability to establish a clear effect of air movement**

Additional Case Ascertainment

- 1. All electrodiagnostic tests performed at Austin Medical Center from 2005-2007**
- 2. ICD-9 Code search - CIDP (357.81), AIDP/GBS (357.0), Idiopathic progressive polyneuropathy (356.4) 1997-2007**
 - All Austin Medical Center matches**
 - IA and MN residents – Mayo clinic**

Additional Case Ascertainment (cont.)

3. Cross match

- All QPP employees + Hormel Rendering workers**
- List of all Mayo and Austin Medical Centers EMG's**
- 1997-2007**
- All matches had an expanded chart review**

Additional Case Ascertainment (cont.)

- 4. Formal queries of neurologists and primary care providers in Worthington, MN and referral area – SD Dept of Health as partners**
- 5. More than 100 independent contacts to MDH**
 - 32 with components of case definition**
 - 8 considered potential cases with chart reviews**

Additional Case Ascertainment - Results

- **Reported cases were identified from multiple data sources**
- **No new cases identified**

Survey of Swine Abattoirs in United States, 2007

26 swine abattoirs

Survey of Swine Abattoirs in United States, 2007

26 swine abattoirs

9 extracted brains

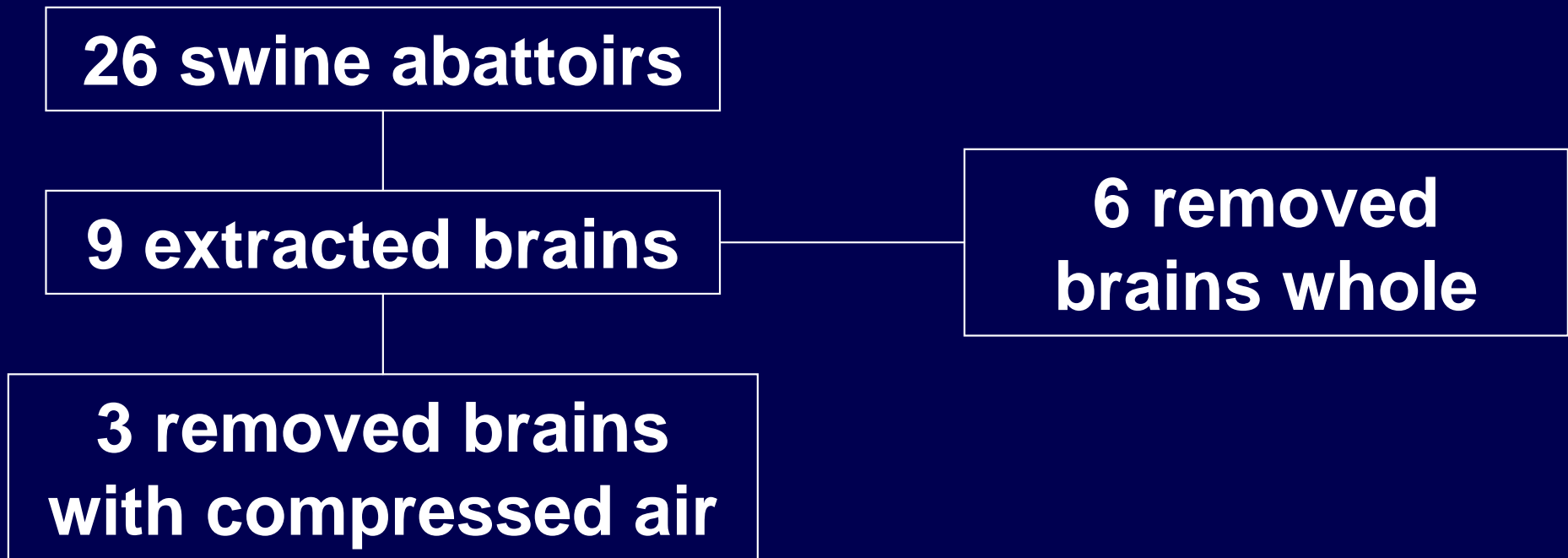
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26 swine abattoirs

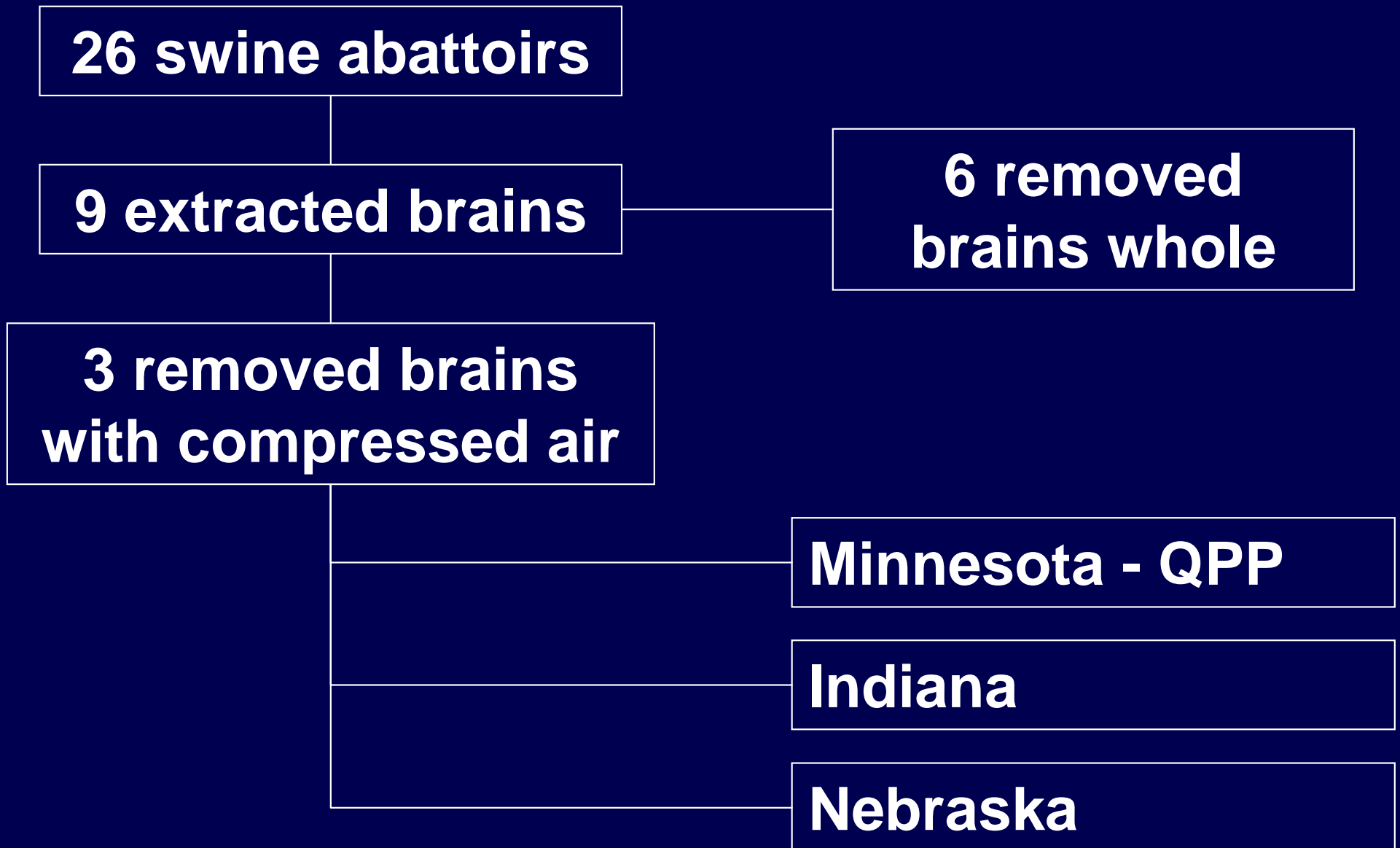
9 extracted brains

**6 removed
brains whole**

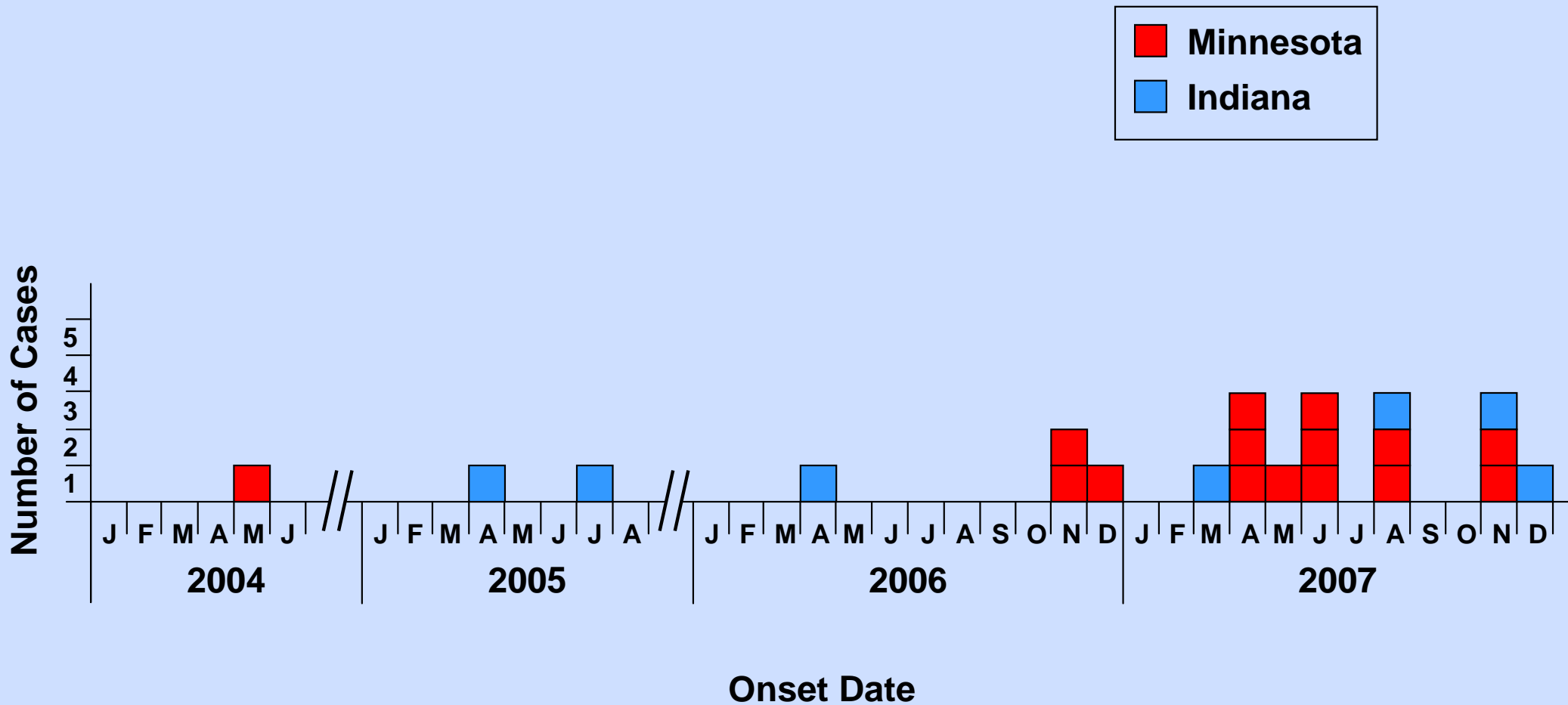
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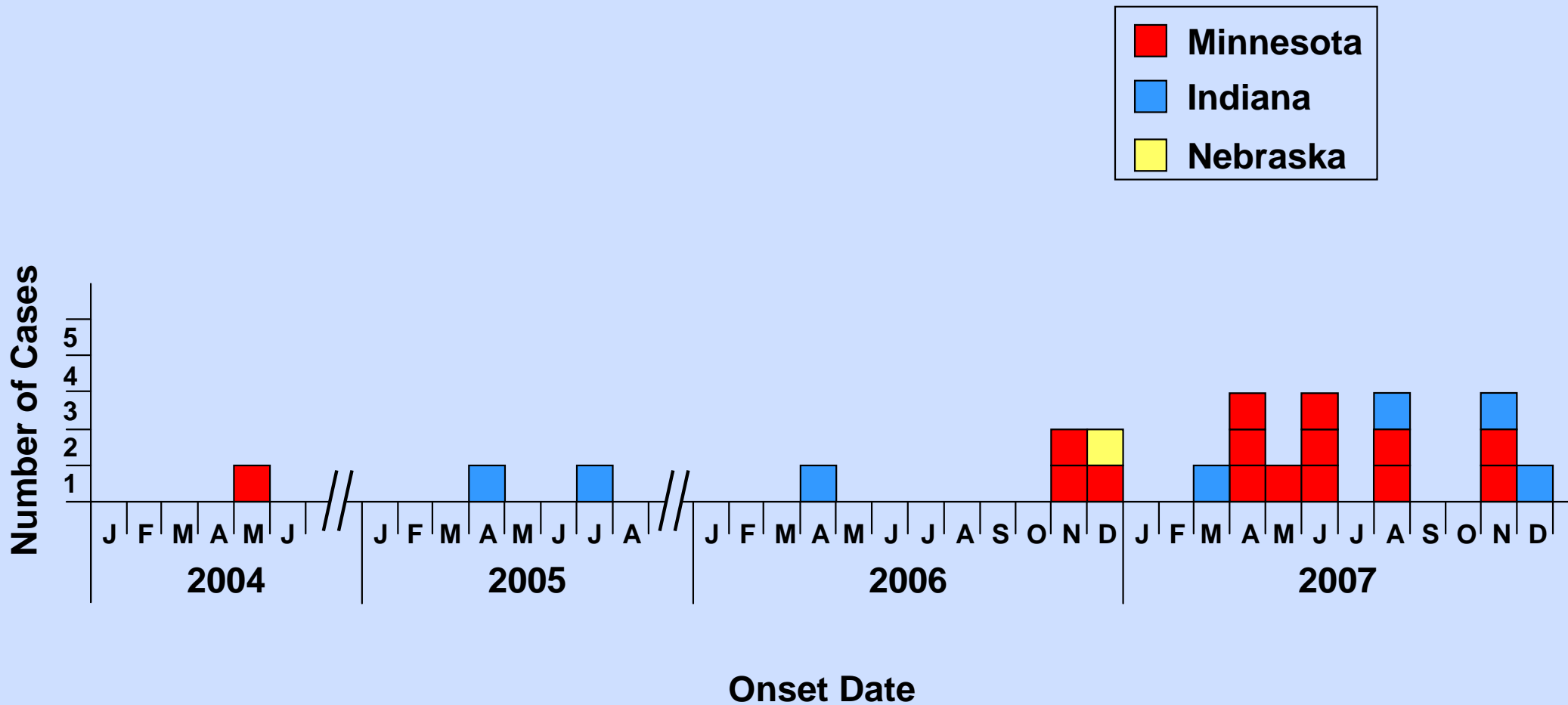
Epidemiologic Confirmed and Probable Cases by Month of Illness Onset



Indiana Case-control Results

- 5 cases
- 106 controls
- Case-patients were more likely to report having had pig brain material entering their eyes, nose, or mouth during work
(OR, 12.8; 95% CI: 1.4 to 119.3)

Epidemiologic Confirmed and Probable Cases by Month of Illness Onset



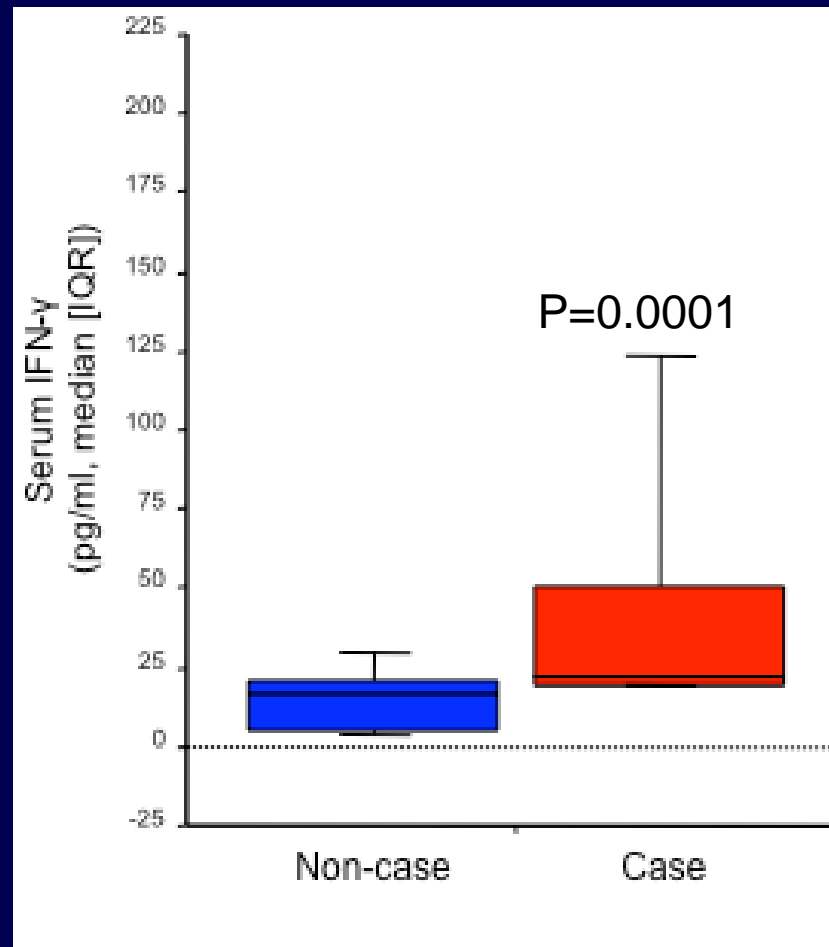
Laboratory Investigation

- Porcine hemagglutinating encephalomyelitis virus
- Encephalomyocarditis virus
- Porcine circovirus Type 2
- Porcine enterovirus subtype 1-8
- Porcine reproductive and respiratory syndrome (PRRS) virus
- *Mycoplasma hyopneumoniae*
- New (H2) swine influenza virus strain
- Encephalomyocarditis virus
- Hepatitis E
- Transmissible gastroenteritis virus
- Porcine adenovirus
- Porcine rotavirus
- Porcine reovirus
- Swine influenza virus
- Porcine teschovirus
- Porcine enterovirus A
- Pseudorabies virus
- Porcine parvovirus
- *Campylobacter sp.*
- *C. perfringens*
- *C. difficile*
- Hepatitis A
- Adenovirus
- Norovirus
- Astrovirus
- Rotavirus
- Sapovirus
- *Edwardsiella sp.*
- *Yersinia sp.*
- *Aeromonas sp.*
- *Vibrio sp.*
- *Hafnia sp.*
- *Shigella sp.*
- *Plesiomonas sp.*
- *Salmonella*
- *Microsporidium*
- *Entamoeba coli*
- *Cryptosporidia*
- *Giardia*
- *Blastocystis hominis*
- Coccidian parasites
- *E. coli* O157:H7

No clear pathogen identified

Serum IFN- γ Levels – Luminex Multiplexed Immunoassay

IFN- γ level	Cases	Controls	p-value
Median (IQR) pg/mL	22.3 (38.4)	16.6 (15.6)	0.0001



Biologically Plausible?

- **Experimental auto-immune neuritis**
 - **Laboratory animal models**
 - **Immunization with peripheral nerve myelin or myelin protein emulsified with Freund's adjuvant**
- **Semple anti-rabies vaccination**
 - **Phenolized sheep brain**
 - **Peripheral neuropathies, encephalitis, myelitis**

ROSE

BRAND



Serving Suggestion

U.S.
INSPECTED
AND PASSED BY
DEPARTMENT OF
AGRICULTURE
EST. 1889

PORK BRAINS

WITH MILK GRAVY

NET
WT.
5 OZ.
(142 g)

Is There Any Risk for Developing PIN from Eating Pork?

- **Cases of PIN have only been identified in persons working in close proximity to pig brain removal**
- **Additional case finding efforts by MDH**
 - **Medical record reviews at multiple hospitals**
 - **No additional cases of PIN in the absence of working in close proximity to pig brain removal**

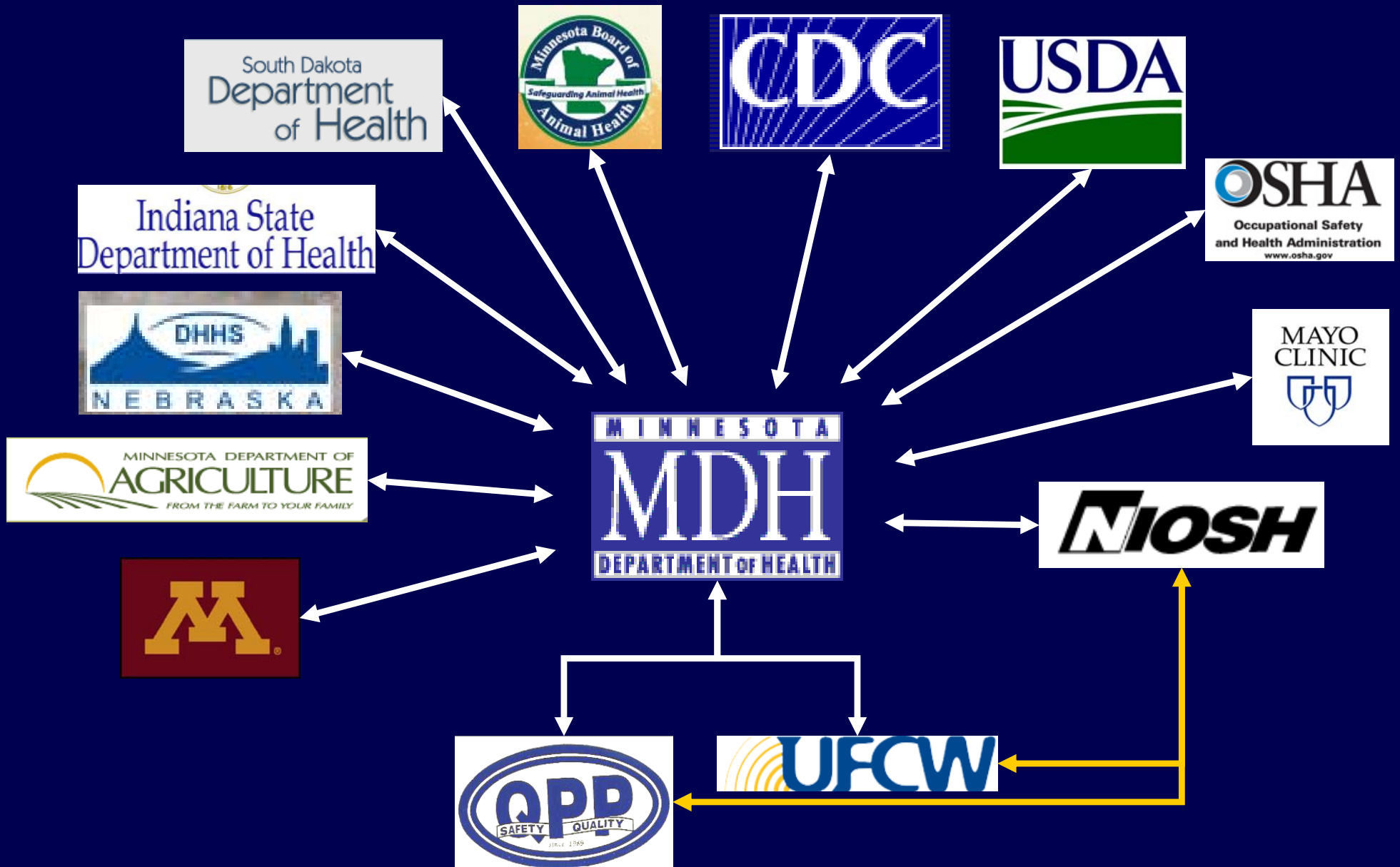
Is This a Prion Disease? (Mad Cow Disease)

	Prion diseases	Progressive Inflammatory Neuropathy
Symptom progression	Only worsen	Stabilize or improve
Affected area	Brain and central nervous system	Primarily peripheral nerves, not central nervous system
Outcome	Typically fatal	No deaths

Conclusions

- **Main risk factor was exposure to brain during removal with compressed air**
 - **Job position**
 - **Distance from brain removal device**
 - **Lack of evidence for an infectious etiology**
 - **Cases found at 2 other plants using this method**
- **Cases are no longer appearing since the discontinuation of the procedure**

Acknowledgements



Questions?

SCRAMBLED BRAINS

1/4 lb. pork brains
1 1/2 tsp. vinegar
3/4 tsp. salt
2 tbsp. butter
4 beaten eggs
1 tbsp. milk



Cover brains with cold water, add vinegar, and soak for 30 minutes. Drain. Remove loose fatty membrane. Cover brains with water, add 1/2 teaspoon salt, and simmer 20 to 30 minutes. Drain and chill in cold water. Finely chop brains. Brown in butter. Combine eggs, milk, and 1/4 teaspoon salt. Add to brains. Turn heat low. Don't disturb mixture until it starts to set on bottom and sides, then lift and fold over with wide spatula so uncooked part goes to bottom. Avoid breaking up eggs any more than necessary. Continue cooking for 5 to 8 minutes, until eggs are cooked throughout, but still glossy and moist. Remove from heat and serve immediately.

Serves 4.

Cooks.com