
Spinal spookiness



CID conference
Hunter Ratliff
10/31/2024

*Ages, dates, and other identifying information may have been changed
I have no conflict of interest in relation to this presentation*

Shortcuts



Case 1: [Start](#) | [Summary slide](#)

Case 2: [Start](#) | [Summary slide](#)

Takeaway slide

The plague

- **Geography** | transmission | bioterrorism?
- **Syndromes** | Bubonic | septicemic | pneumonic
- **Diagnosis** | subtopic | subtopic
- **Treatment** | isolation & PEP

Elsberg Syndrome

- **Clinical manifestations** & etiologies
- Savoldi et al (2017)
- Petersen et al (2023)

Case #1

Case 1: HPI



A **60 y/o female** p/w **altered mental status** after being found down

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38.2°C | 110 bpm | 121/60 | SpO2 **80%** (ambient air)

Pulm: **crackles** at the left base

Abd: soft, normal bowel sounds

Neuro: **A&O x1**, no focal deficits

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Case 1: A little more

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Abd: soft, normal bowel sounds

Neuro: **A&O x1**, no focal deficits



Diagnosed with CAP → Unasyn & levofloxacin

WBC: **46.8** CXR: LLL atelectasis

AST: **336** ALT: 59

Case 1: Even more

A **60 y/o female** p/w **altered mental status** after being found down. She was febrile to 38.2, hypoxic to 80%, and A&Ox1. Tx for CAP w/ Unsayn & levaquin

By day 3,

Intubated for resp failure & AKI → transferred

Plts: **54** **Developed DIC** w/ schistocytes → **PLEX** for TTP



WBC: **46.8** LDH: **3300**

AST: **336** ALT: 59

Questions? DDx?

Case 1: The micro data



A **60 y/o female** p/w **altered mental status** after being found down. She was febrile to 38.2, hypoxic to 80%, and A&Ox1. Tx for CAP w/ Unsayn & levaquin.

By day 3, intubated for resp failure & developed DIC w/ thrombocytopenia. Received PLEX for possible TTP

OSH BCx: gram-positive rods (1/2 bottles)

OSH UCx: Pseudomonas aeruginosa

- Switched to Merrem & gentamicin

WBC: **46.8** LDH: **3300** Plts: **54**

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Case 1: Summary

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By day 3, intubated for resp failure & developed DIC w/ thrombocytopenia. Received PLEX for possible TTP.

Switched to Merrem & gent for UTI w/ PsA



WBC: **46.8** LDH: **3300** Plts: **54**

AST: **336** ALT: 59 Cr: 1.2

OSH BCx: gram-positive rods (1/2 bottles)

OSH UCx: Pseudomonas aeruginosa

Case 1: Hospital course

- Receiving hospital calls to ask about blood culture. Tech reviews it and changes it to **gram-negative rod**
 - Vitek: *Yersinia pestis*
 - bioMérieux's API: poorly viable *E. coli* or *Proteus spp*
- Community hospital sends subculture to the academic hospital

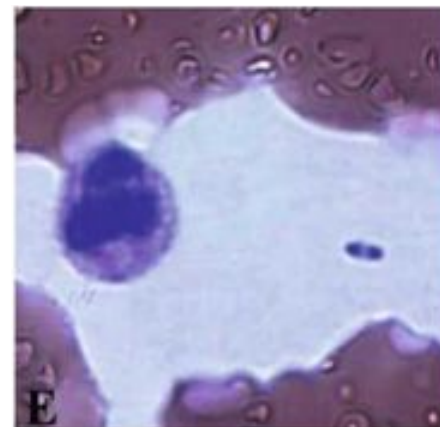


Case 1: Hospital course

- Receiving hospital calls to ask about blood culture. Tech reviews it and changes it to **gram-negative rod**
 - Vitek: ***Yersinia pestis***
 - bioMérieux's API: poorly viable *E. coli* or *Proteus spp*
- Community hospital sends subculture to the academic hospital

They send isolate to San Diego health department

- Confirmed ***Yersinia pestis*** on PCR
- Review of **blood smear** on admission showed **bipolar-staining bacteria**



Discussion



Links to articles discussed
here



The plague

Objectives:

- Describe the **geographic distribution** of *Yersinia pestis*
- Identify **vectors** and **routes of transmission**
- Review **microbiology** and **pathogenesis**
- Compare the **clinical manifestations** of the plague
- Discuss **diagnostic modalities** & **treatment options**

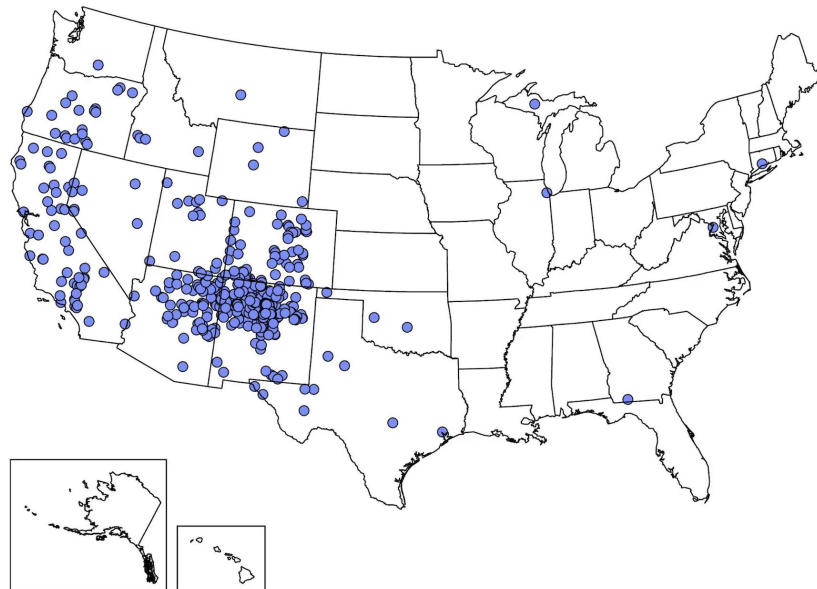
Geographic distribution

- Mainly **southwest US & former soviet union**
 - Plague is **endemic** in western portion of US
 - Some outbreaks in Africa, Asia, South America
- Most human cases this century have been in Africa

WHO cases

- 2000-2009: 21,700 with 1612 deaths
 - **Case fatality rate of 7.4%**
- 2010-2018: 4420 with 751 deaths

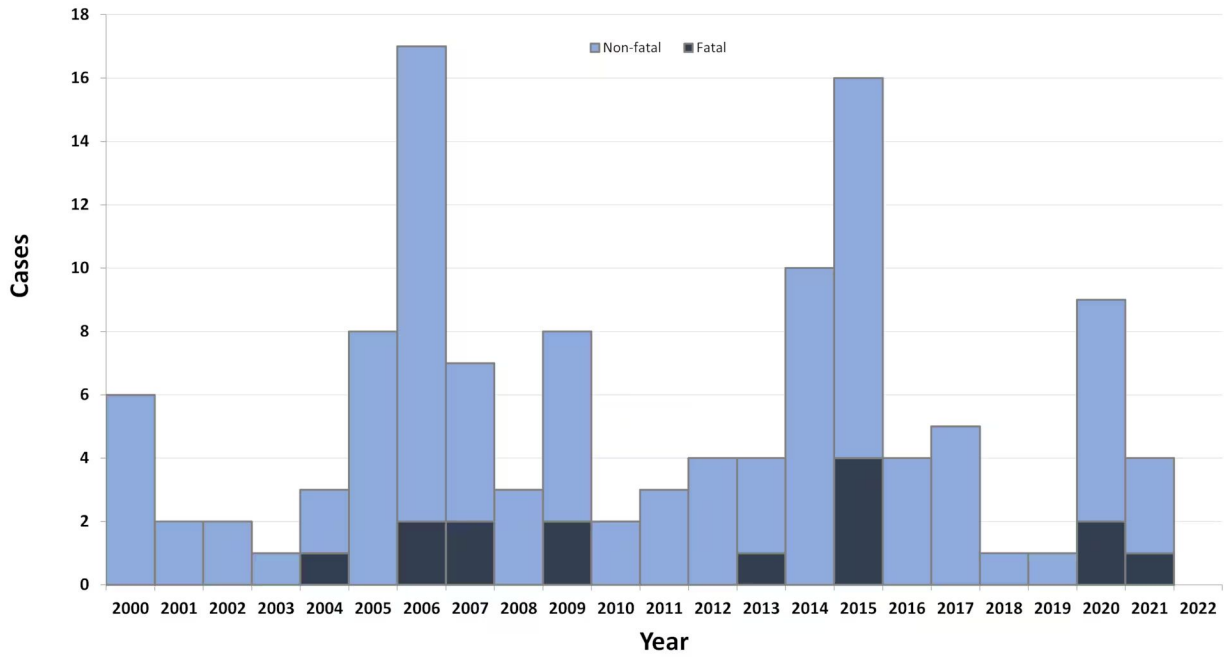
CDC: reported human plague cases, 1970-2022 [3.1]



1 dot placed within state of residence for each reported case

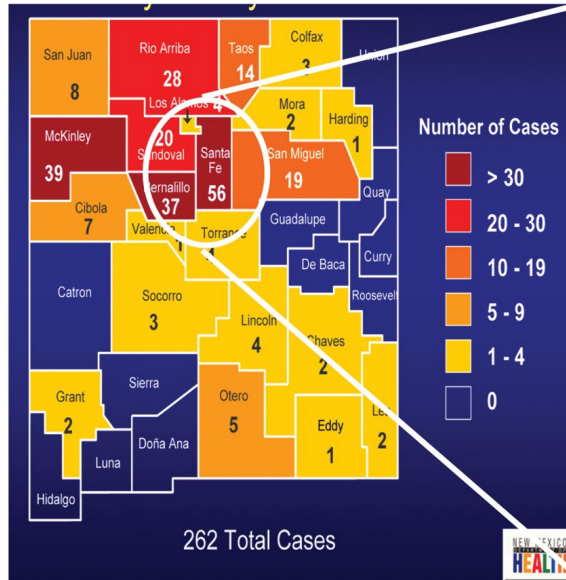


Human plague cases, fatal and non-fatal, United States, 2000-2022



New Mexico

Human Plague cases in New Mexico, 1949-2009



Locations of Plague Isolates, 2009

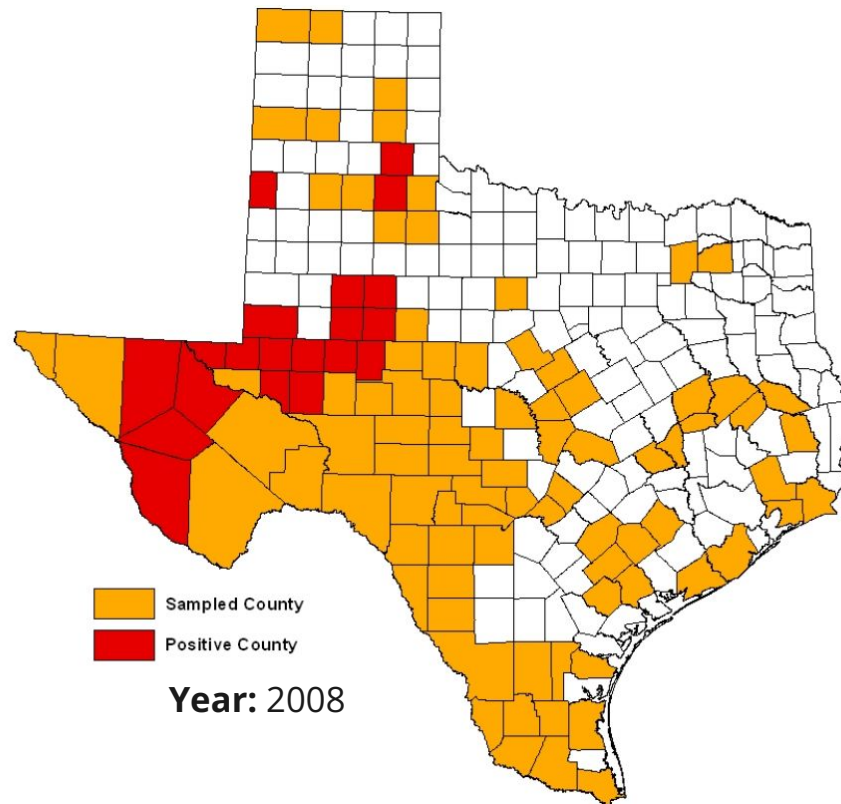
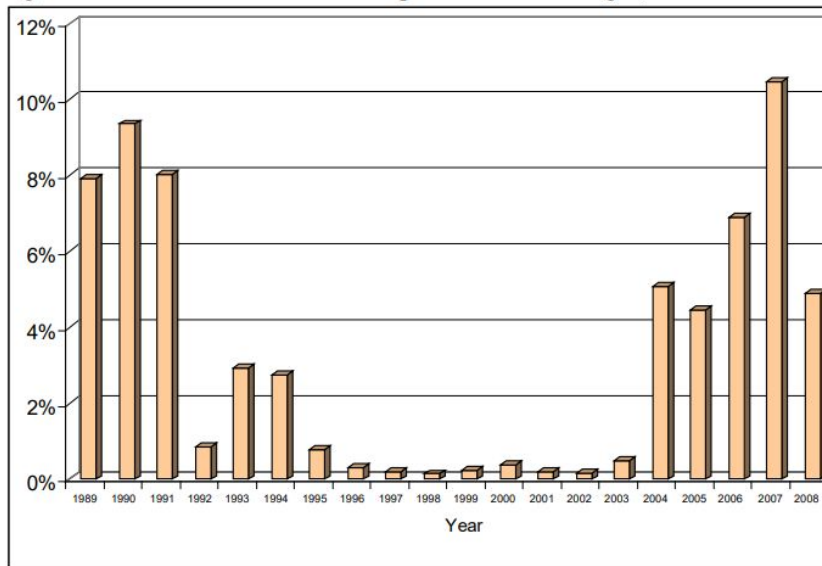


Texas



Texas DSHS data [1.2]

Figure 2. Percent of Surveillance Samples Positive for Plague, 1989-2008





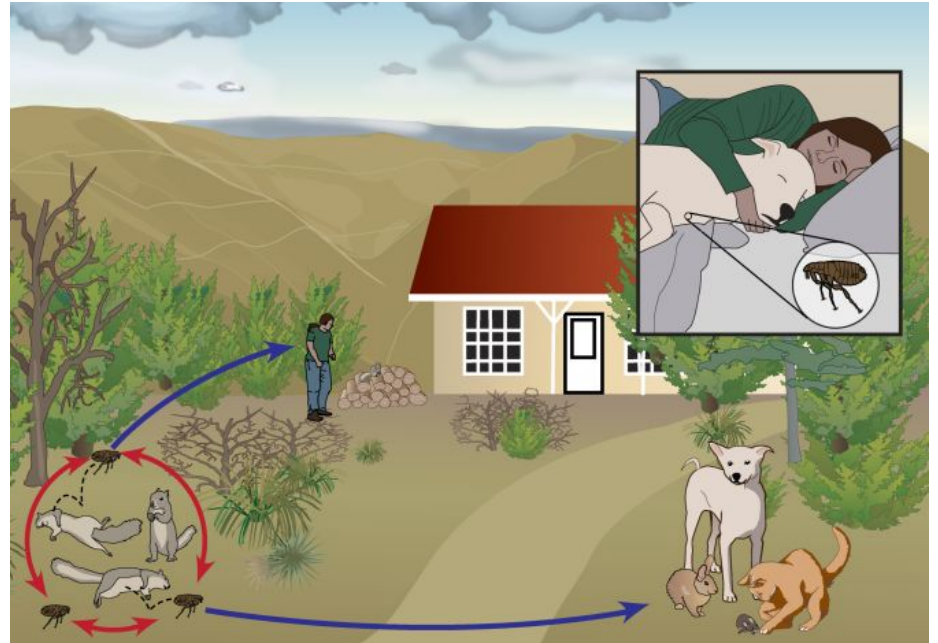
Transmission

Objectives:

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- Compare the **clinical manifestations** of the plague
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Ecology & Transmission

- Transmitted by fleas among wild rodents (squirrels, prairie dogs, rats)
- If $\uparrow\uparrow$ among rodents \Rightarrow rodents die \Rightarrow fleas get hungry \Rightarrow fleas find other food
 - May bite humans directly
 - Cats get very sick and may cough droplets that infect humans
 - Dogs can carry fleas that bite humans

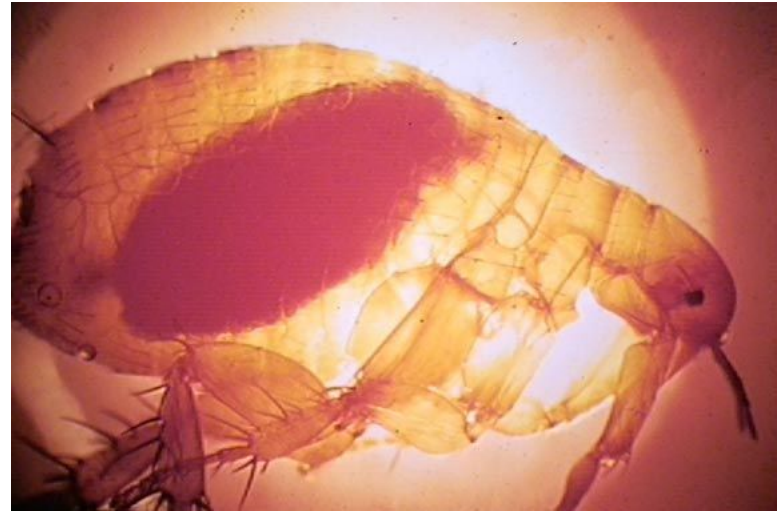


CDC [3.2]

Flea transmission

High amounts of bacterial replication within the flea's digestive tract ⇒ **Blocks flea gut**

- ⇒ Flea gets **very hungry** so ↑ **feeds**
- ⇒ Also **vomits infected blood** into new host
 - Regurgs up to 24k CFUs !
 - Infectious dose (for SQ) may be <10 CFUs



The Oriental rat flea (*Xenopsylla cheopis*) engorged with blood

https://en.wikipedia.org/wiki/Black_Death

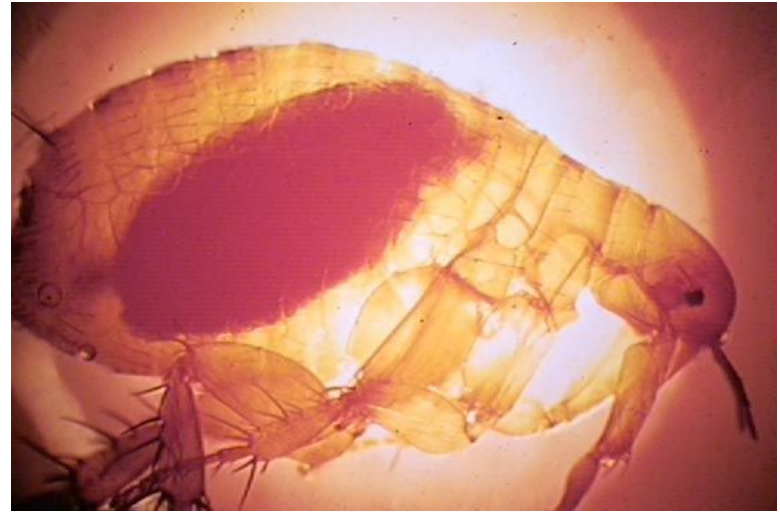
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Later studies showed transmission without GI obstruction.

- Hgb poorly soluble ("pseudo-obstruction")
 - Occurs with rats & guinea pigs
 - Not with mice or gerbils
- Gives flea GERD ⇒ reflux when feeding

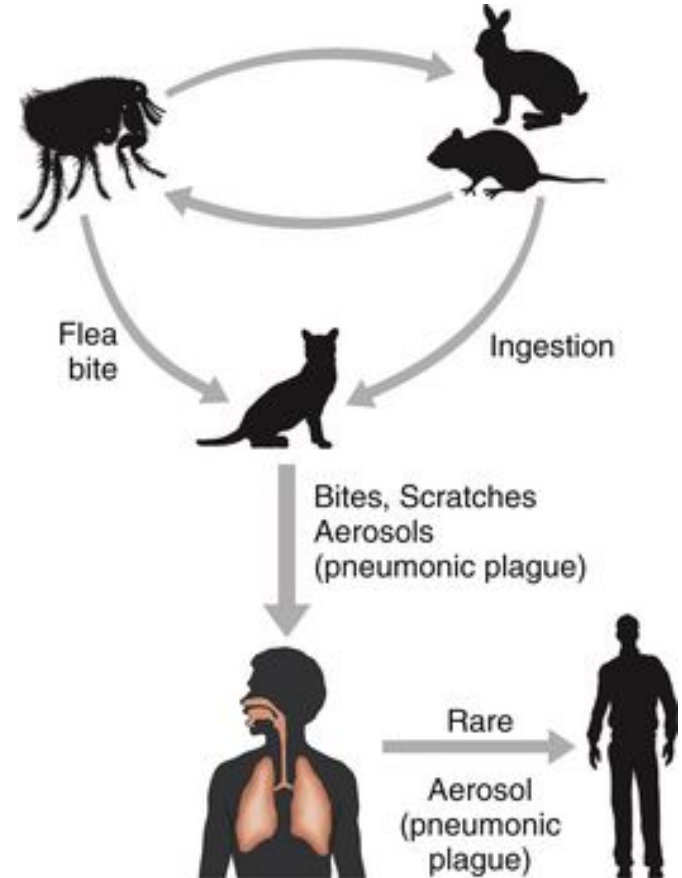


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Other transmissions

- Transmitted with **direct contact** with infectious fluids
- Biggest concern is **airborne transmission**
 - Infectious dose somewhere between **100 and 15,000 cfu** when inhaled



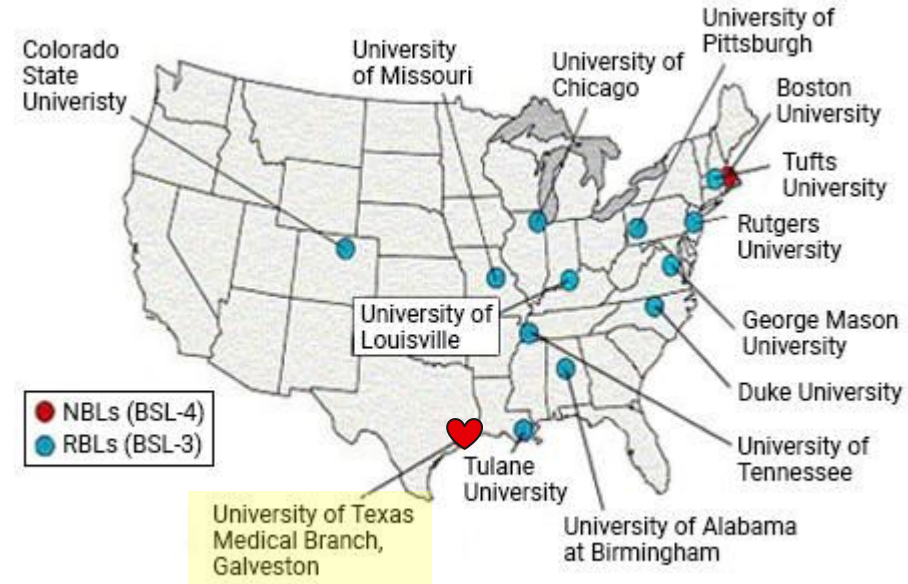
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Possible agent of **bioterrorism**

- PPE: N95, goggles, gown, gloves
- **Risk group 3** pathogen
 - DHS says should be handled with BSL-3 practices
 - American Society for Microbiology says minimum BSL-2 (for diagnostic)

DHS [3.3]





Microbiology & clinical presentation



Objectives:

- Describe the **geographic distribution** of *Yersinia pestis*
- Identify **vectors** and **routes of transmission**
- Review **microbiology** and pathogenesis
- Compare the **clinical manifestations** of the plague
- Discuss **diagnostic modalities & treatment options**

Microbiology

Yersinia pestis is **gram negative (cocco)bacillus**

- Bipolar staining on Giemsa, Wright's, or Wayson staining ("**safety pin**")
- Automated identification systems may **misidentify** (e.g. *Acinetobacter*, *PsA*)

Once again, **tell the lab** if there is concern for *Y pestis* (for multiple reasons)



https://en.wikipedia.org/wiki/Wayson_stain

Clinical syndromes

Bubonic plague (80-95%)

- Sudden onset of fever +/- headache ⇒ severe *nonfluctuant* **painful lymphadenopathy**
 - Often inguinal
 - Epitrochlear buboes a/w cats
- Untreated, 50% develop to **septicemic plague**

Septicemic plague (10-20%)

- AKA *Yersinia pestis* bacteremia
- Very sick w/o localizing symptoms
- Progresses to DIC w/ multiorgan failure



THE PLAGUE



Acral gangrene



Buboes

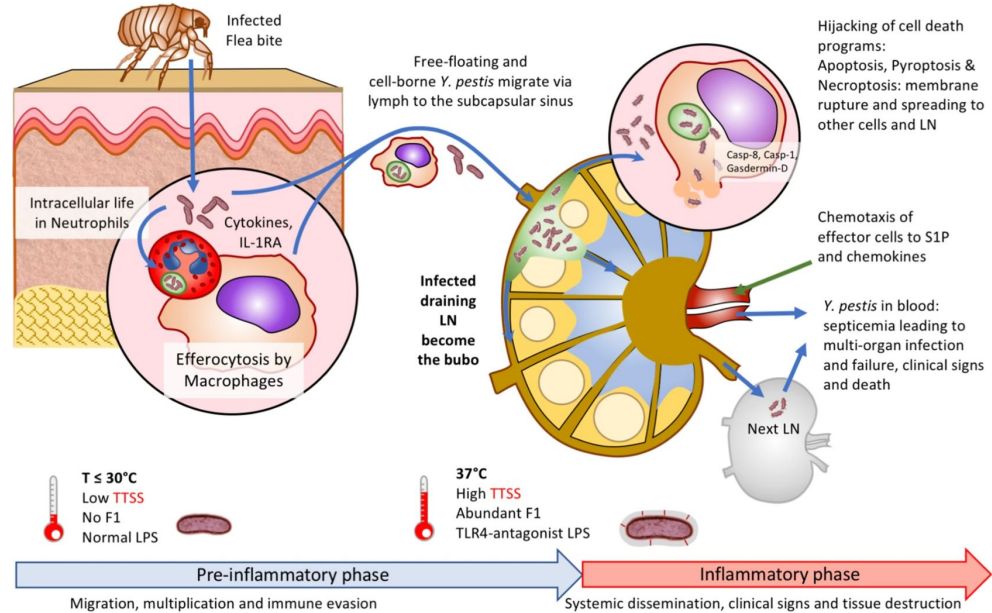
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- Sepsis and immune evasion **mediated by temp**
- at 37 C ⇒ ↑ **F1 antigen expression** & ↑ **LPS**

Nature Gene - Demeure (2019) [1.3]

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Pneumonic plague

Primary: from inhalation, luckily is rare

- Rapid onset of severe pneumonia
 - High fever, cough, hypoxemia, hemoptysis
- If untreated, death within days

Secondary: (develops in 10% of cases)

- Often 2/2 untreated **bubonic plague** w/ hematologic seeding
- Similar manifestations to primary

Other / Misc

- Any type can have +/- meningitis
- Can develop **septicemic** or **pneumonic** without bubos (must have ↑↑↑↑↑ index of suspicion)
- 10-20% of **septicemic** have no preceding bubos



Diagnosis & management

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Diagnosis

- Often will **grow on culture**, either of blood or pus / buboes
- 40% of cases of **peripheral blood Giemsa-Wright stains** were positive
- Rapid tests
 - Mostly in case of bioterrorism
- Serologic tests
 - Mostly helpful after the fact

Diagnostic clues

- WBC >20k & ↓ platelets (50% of cases)
- **Painful, nonfluctuant, lymphadenopathy**
 - Esp. fever + hypotension + regional lymphadenitis
- Fever after contact with dead rodents
- Hilar or mediastinal adenopathy in what otherwise appears to be bacterial pneumonia

Treatment

First line options: **Aminoglycosides** (Streptomycin, Gent), **fluoroquinolones**, **tetracyclines**

- Most experience has been with aminoglycosides (namely streptomycin)
- Someone managed to do a RTC with 65 patients. Cure rates were similar at 7 days
 - Gentamicin (94%)
 - Doxycycline (97%)
- Resistance rates are low
 - Mostly thought to **horizontal exchange** from other Enterobacteriaceae plasmids
 - Still, CDC suggests **dual therapy** for **severe cases** and if from **bioterrorism**
- Meningitis: Chloramphenicol **and** moxi or levoflox

Isolation, PEP, vaccines

- **Best advice:** Don't be around rats, especially dead ones!
- **Isolation:**
 - Droplet precautions for 48h of antibiotics (& improvement) or pneumonia ruled out
 - Standard precautions if no pneumonia
 - Eye/face shield & mask if lancing buboes
- **PEP:** 7 days of doxy or a quinolone
- **Immunizations:**
 - No longer available in the US
 - Some vaccines under development

Case #2

Case 2: HPI

A **57 y/o M** with PMH including ILD, remote SCC of tongue, prior C-spine Sx p/w **3 weeks of RLE>LLE numbness**

Background:

- **ILD:** Biopsy confirmed on PRN O2. Has been on Nintedanib (Ofev) for two years, and prednisone 10 for the past 3 months
- **SCC of tongue:** Over 30 years ago s/p resection and in remission

Case 2: HPI

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-17 days: Woke up with **sudden onset** numbness from **R hip down to R foot**. Maybe some numbness in left foot. Seen by chiropractor next day who said go to ED as this isn't normal

- Seen in the ED, CT LS-spine showing L4-L5 disc bulge
- D/C with steroids & spine referral

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- Seen in the ED, CT LS-spine showing L4-L5 disc bulge
- D/C with steroids & spine referral

-13 days, (ED #2): Spine center reviews ED notes and finds patient also c/o perirectal numbness, so tells him to return to ED

- Gets MRI LS-spine *without contrast* with same findings as CT
- PVR normal
- Ortho notes numbness is not dermatomal and have low c/f cauda equina
- Discharged (without a diagnosis, just that it's not CES)

Case 2: HPI

A **57 y/o M** with PMH including ILD, remote SCC of tongue, prior C-spine Sx p/w **3 weeks of RLE>LLE numbness**.

-2.5 weeks: Woke up with **sudden onset** numbness from **R hip down to R foot**. Maybe some numbness in left foot. LS-spine CT & MRI (w/o) **showing L4-L5 disc bulge**. Got steroids (ED #1) & ortho consult (ED #2)

-1 day: Pulm sees in clinic and he looks unwell. Now with saddle anesthesia, BLE numbness, and worsening of baseline diarrhea. They are worried about GBS so send him to the ED for neuro.

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-1 day: Pulm sees in clinic and he looks unwell. Now with saddle anesthesia, BLE numbness, and worsening of baseline diarrhea. They are worried about GBS so send him to the ED for neuro.

- **Afebrile**, vitals normal
- Decreased **sensation** to pin prick in BLE length dependent fashion
- Hypersensitive to pinprick in plantars
- Decreased **vibratory** sense knees, ankles, and toes
- **Strength normal**

Labs

- WBC 11.2 (63% NΦ)
- CMP normal
- HIV screen negative
- Blood cultures negative

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-1 day: Pulm sees in clinic and he looks unwell. Now with saddle anesthesia, BLE numbness, and worsening of baseline diarrhea. They are worried about GBS so send him to the ED for neuro. Neurology finally does a history and finds...

- Recent travel to **North Carolina** where he went to the beach
- He also had burning sensation across upper chest and back (bandlike, ?b/l)
- But has **scattered bullous lesions** on his skin with a red base
 - Rash is on his feet and his chest (unclear if the same area where he has burning sensation)
 - Now they order **MRI whole spine** with contrast

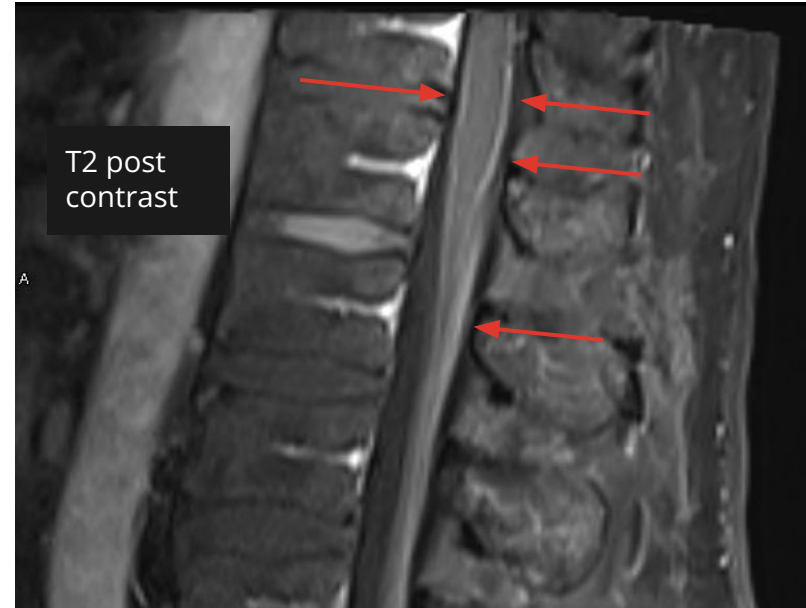
Workup

MRI whole spine (with contrast):

- There is no abnormal enhancement identified within the cervical and upper thoracic spine.
- There is however suggestion of **mild diffuse non-nodular enhancement** noted to the **conus and extending to the cauda equina nerve roots**
- Could be artifactual, however with the clinical history this could be seen with Guillain-Barre syndrome

MRI brain: Normal

Pan CT: Normal



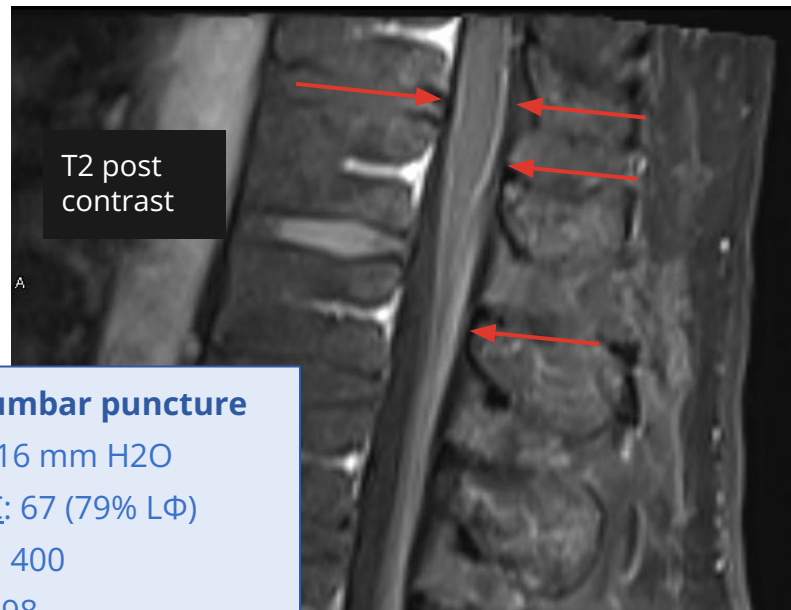
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MRI brain: Normal

Pan CT: Normal



Lumbar puncture

OP: 16 mm H₂O

WBC: 67 (79% LΦ)

RBC: 400

Pro: 98

Glu: 52

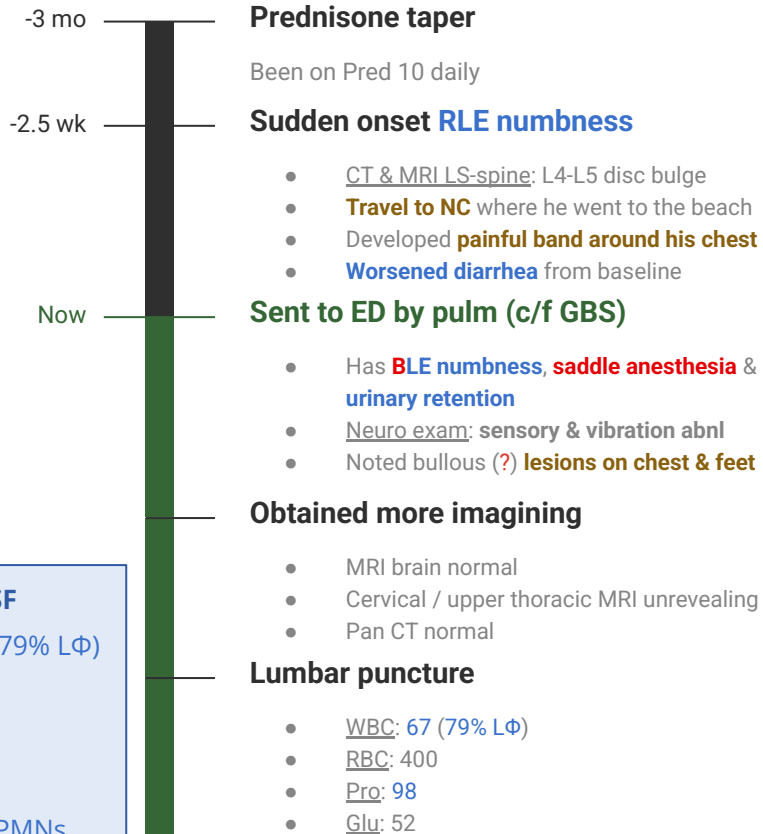
G/S: Few PMNs

Case 2: Summary

A **57 y/o M** with PMH including ILD (on Ofev & pred), remote SCC of tongue, prior C-spine Sx p/w **3 weeks of progressively worsening** RLE>LLE numbness and was admitted for **cauda equina syndrome like symptoms** despite **no evidence of cord compression** radiographically

MRI: Lumbosacral w/ contrast
Mild **diffuse non-nodular enhancement** noted to the conus and extending to the cauda equina nerve roots

CSF
WBC: 67 (79% LΦ)
RBC: 400
Pro: 98
Glu: 52
G/S: Few PMNs



Case 2: Hospital course

- Initial c/f leptomeningeal carcinomatosis
- Normal CT → c/f autoimmune → did LP
- Dx: **Elsberg Syndrome**
 - AKA **HSV lumbosacral radiculitis**
 - Given solumedrol (x5 days) & acyclovir (x14 days) → OPAT

Lumbar puncture

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G/S: Few PMNs

CSF studies

Cultures: Neg

Biofire: **HSV-2**

West Nile: Neg

Crypto Ag: Neg

Flow cytometry: Neg

Pathology: Neg

Case 2: Hospital course

- Initial c/f leptomeningeal carcinomatosis
- Normal CT → c/f autoimmune → did LP
- Dx: **Elsberg Syndrome**
 - AKA HSV lumbosacral radiculitis
 - Given solumedrol (x5 days) & acyclovir (x14 days) → OPAT
- Discharged w/ OPAT
- Got volume overload so readmitted
 - This is when ID saw him for the first time
- Diarrhea improved with holding Ofev

Lumbar puncture

OP: 16 mm H₂O

WBC: 67 (79% LΦ)

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Discussion



Links to articles discussed
here



Elsberg Syndrome

Objectives

- Recognize the clinical manifestations of lumbosacral myeloradiculitis
- Review both of the retrospective cohort studies on PubMed

Elsberg syndrome (ES)

- Described in 1914 by a neurosurgeon (Dr Elsberg)
- Five younger adults (37-45 y/o) with syndrome of
 - Urinary retention
 - Constipation
 - Radicular pain
 - Paraesthesia
 - Paresis of the lower limbs
- He presumed an infectious or toxic etiology

“During the past five years in a large number of spinal operations under our observation... we have met with 5 cases so alike in their histories, in their clinical findings, and in the morbid appearances on the operating table that we have been led to class them together, in the belief that we have here a definite clinical and pathological entity”

- Charles Elsberg, 1914

Elsberg syndrome (ES)

Neurotropic viruses (namely **HSV-2**), were later identified as a cause of **lumbosacral radiculitis** or **myeloradiculitis**

- Can present as **cauda equina syndrome**, as it causes lumbosacral radiculopathy &/or myelopathy.
- Distinction: ES is an **-itis** (which causes the **-opathy**)
 - Thus easily missed on routine evaluation

Neurotropic viruses causing ES
HSV-2, VZV, CMV, WNV, Cv19

Annual incidence

1.2 episodes / million adults

- Likely more, because under recognized

Elsberg syndrome (ES)

Neurotropic viruses (namely **HSV-2**), were later identified as a cause of **lumbosacral radiculitis** or **myeloradiculitis**

- Can present as **cauda equina syndrome**, as it causes lumbosacral radiculopathy &/or myelopathy.
- MRI findings are nonspecific and may be negative
 - Savoldi et al (2017) [2.1] is an excellent review of radiographic findings
- In most case reports, CSF has lymphocytic pleocytosis
 - Negative CSF PCR does not rule out the diagnosis, especially if delayed diagnosis

Neurotropic viruses causing ES
HSV-2, VZV, CMV, WNV, Cv19

Annual incidence

1.2 episodes / million adults

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Treatment

- Acyclovir or valacyclovir
- Not well established degree of benefit
- Unclear if role for steroids

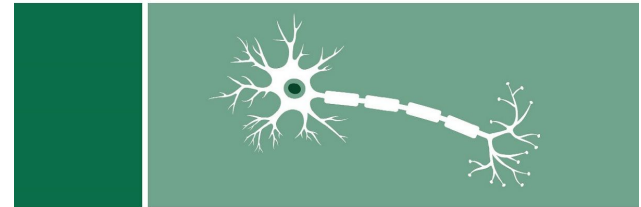


Article #1

AMERICAN ACADEMY OF
NEUROLOGY.

Neurology®

The most widely read and highly cited peer-reviewed neurology journal



MS AND CNS INFLAMMATORY DISEASE EPOSTER SESSION

| April 18, 2017 | 

 Check for updates

Elsberg syndrome: A rarely recognized cause of cauda equina syndrome and lower thoracic myelitis (P2.074)

Filippo Savoldi, Timothy Kaufmann, Eoin Flanagan, and Brian Weinshenker

[AUTHORS INFO & AFFILIATIONS](#)

Savoldi et al (2017)

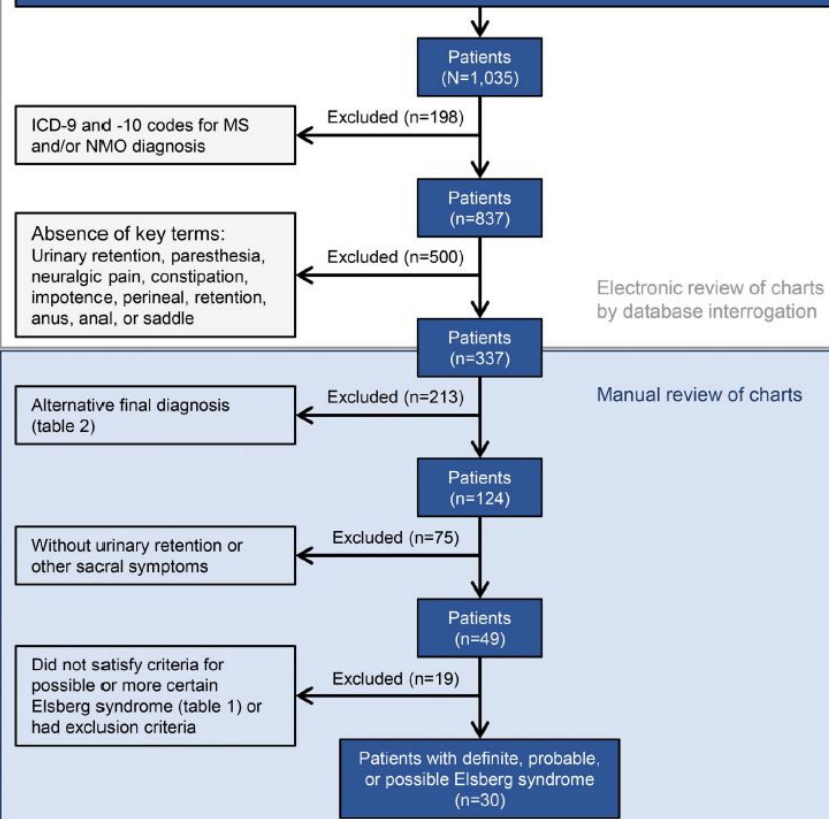
Methodology: Retro review @Mayo (2000 to 2016)

- Patients seen by neuro, urology, gyn, or ID
- Pretty robust & conservative electronic search
 - 1,035 → 337 chart reviewed
 - Identified 49 patients meeting inc/exc criteria
- Developed diagnostic criteria (definite, probable, possible, excluded)
 - Total of 30 patients had at least possible Elsberg syndrome

Inclusion criteria: Patients with both myelitis and radiculitis since 2000 identified by one or more of these search strategies that identified overlapping groups of patients:

- Search #1: n=831 (myelitis OR myelopathy OR radiculomyelitis OR myeloradiculitis) AND (radiculitis OR radiculopathy OR radiculomyelitis OR myeloradiculitis)
- Search #2: n=555 (conus OR cauda equina) AND (radiculomyelitis OR myeloradiculitis OR myelitis)
- Search #3: n=168 (conus AND radiculitis)
- Search #4: n=4 (Elsberg syndrome)

All searches were restricted to patients evaluated in the neurology, urology, gynecology, and infectious disease departments.



Savoldi et al (2017)

Results: 80% male, median age of 53

- Only **one patient** (3.3%) **immunosuppressed**
- Only **10% had skin manifestations** before onset
- Only 60% of patients had any kind of viral testing (PCR or serology from lesions, serum, or CSF)
 - **PCR positive in 17%** of patients (3 / 17)
- Most had LP done (83%)
 - But **median delay** from symptoms to CSF collection **32 days**

CSF cell count, median (range)	9 (0 - 1057)
Mean % lymphs (among those w/ >5 WBCs)	69%
Mean CSF protein	143

Symptom	N (%)
Urinary retention	23 (77%)
Catheter required for retention	21 (70%)
Urinary incontinence	7 (23%)
Bowel incontinence	3 (10%)
Saddle anesthesia	15 (50%)
Constipation	13 (43%)
Loss of limb sensation	24 (80%)
Leg weakness	15 (50%)
Lower extremity hyporeflexia	10 (33%)

Savoldi et al (2017)

- **Acyclovir was given to 20% of patients** (ES was on the DDx for only 10% of patients)
- Half of patients got some form of steroids

Of the patients with follow up data (**n=13**):

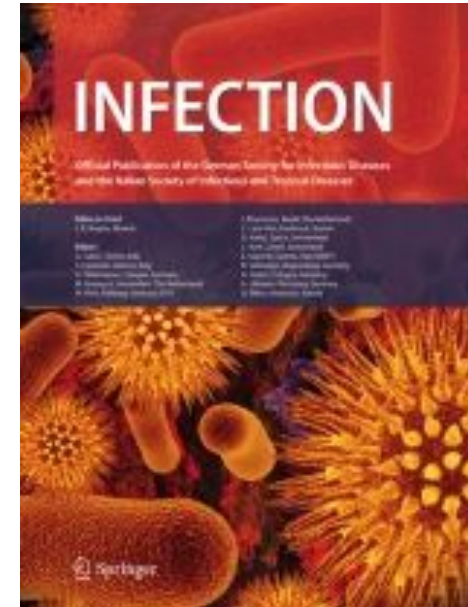
- One patient (**7.7%**) **died** of encephalomyelitis
- Three (**23%**) had **no neurologic recovery**
- Eight (**44%**) had **moderate recovery**
- One (**7.7%**) had **complete recovery**
- Two patients **relapsed (15%)** at 33 & 82 months

Viral lumbosacral radiculitis (Elsberg syndrome) in Denmark

Research | [Open access](#) | Published: 02 November 2023

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Petersen et al (2023)



Methods: Danish **nationwide population-based** observational cohort study used data from the Danish Study Group for Infections of the Brain (DASGIB) database from **2015 to 2020**

- DASGIB includes patients admitted for CNS infections at departments of ID in Denmark

Petersen et al (2023)

Methods: Danish **nationwide population-based** observational cohort study used data from the Danish Study Group for Infections of the Brain (DASGIB) database from **2015 to 2020**

- DASGIB includes patients admitted for CNS infections at departments of ID in Denmark

Stricter inclusion criteria: Urinary retention --AND-- (at least one) of below:

- Positive **CSF PCR**
- **CSF WBC > 10** --AND-- (at least one) of below:
 - Viral lumbosacral radiculitis considered the **most likely diagnosis** ---or---
 - **Evidence of neurotropic virus**, including:
 - Positive intrathecal antibody index
 - Positive serology
 - Positive PCR of other samples

Petersen et al (2023)



Methods: Danish **nationwide population-based** observational cohort study used data from the Danish Study Group for Infections of the Brain (DASGIB) database from **2015 to 2020**

- DASGIB includes patients admitted for CNS infections at departments of ID in Denmark

Outcomes:

- DASGIB database has **Glasgow Outcome Scale** assessed at **discharge** and at **outpatient follow-up** visits (at 30, 90, and 180 days)
- They did chart review for additional sequelae (including persistent urinary retention) at 30 days

Glasgow Outcome Scale

1. Death
2. Vegetative state
3. Severe disability
4. Moderate disability
5. Good recovery

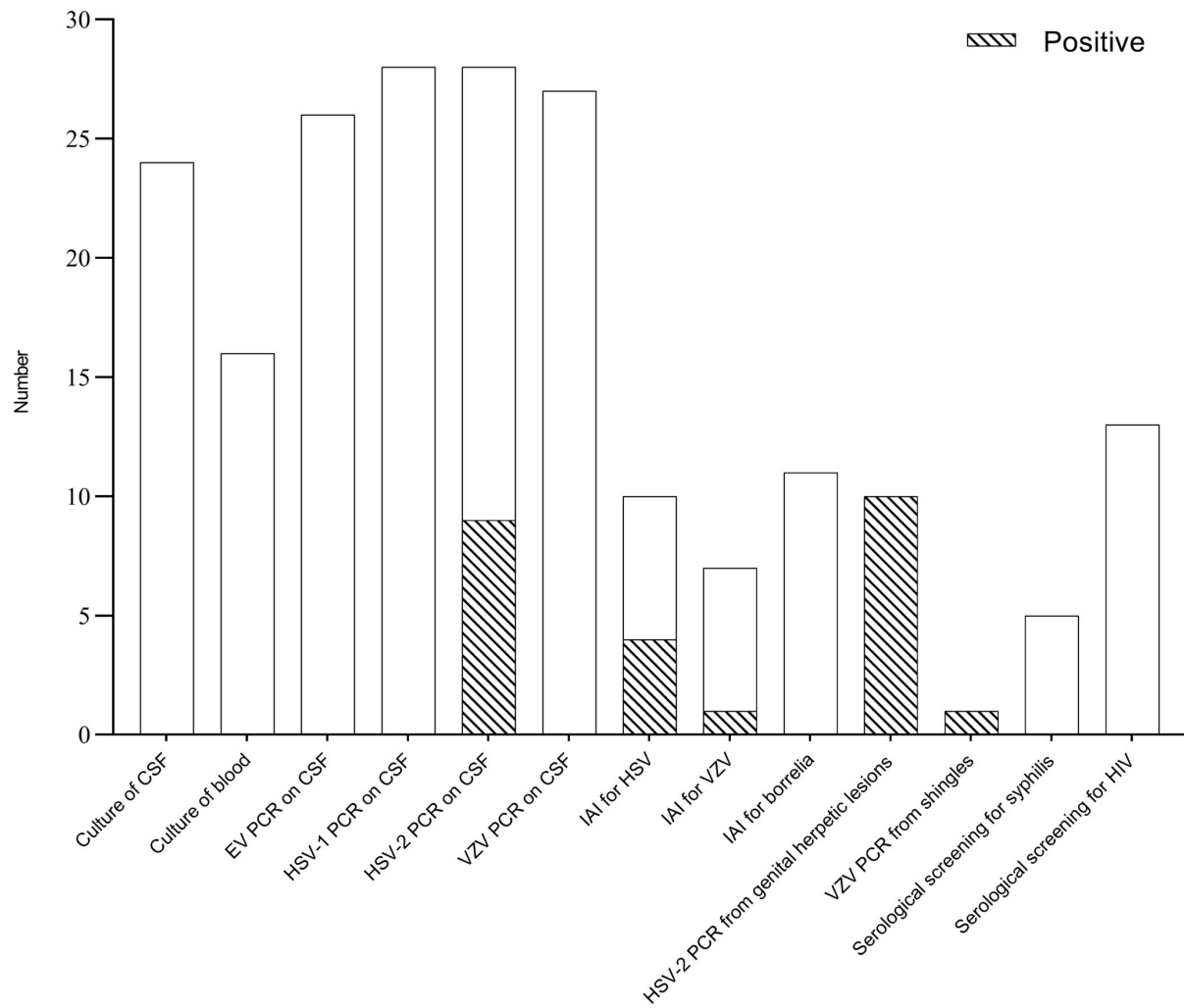
Petersen et al (2023)

Identified 28 cases across five years

- 79% patients female, median age 35 years old
 - Only one patient (4%) was immunosuppressed
- **39%** had **genital herpes**
- Median of **5 days** from symptom onset to admission
 - Many had **febrile illness beforehand**
- **85% of patients** had **another** sign of radiculitis (besides urine retention)
- All but one patient (96%) were treated with acyclovir or valacyclovir
 - Median **duration 14 days** (IQR 7 - 14)

Symptom	N (%)
Headaches	23 (82%)
Neck stiffness	6 (23%)
Photophobia/hyperacusis	12 (55%)
Urinary retention (by def)	28 (100%)
Catheter required for retention	17 (61%)
Constipation	20 (71%)
Leg paraesthesia	10 (36%)
Leg paresis	2 (7%)
Leg radicular pain	13 (46%)

CSF cell count, median (IQR)	153 (31 - 514)
CSF % lymphs, median (IQR)	1% (1 - 4)
CSF protein, median (IQR)	70 (46 - 131)

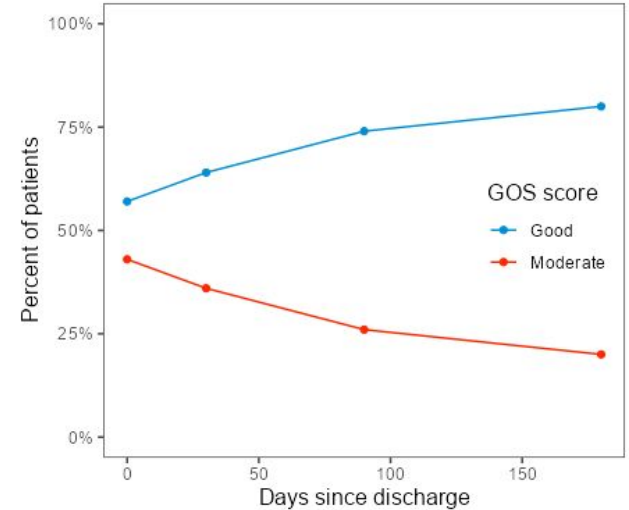


Petersen et al (2023)

Long term outcomes:

- At discharge, 43% had moderate disability
- This improved to 20% by 180 days following discharge

Symptom	Cohort N (%)	30 days N (%)
Headaches	23 (82%)	9 (33%)
Catheter required for retention	17 (61%)	3 (11%)
Leg paraesthesia	10 (36%)	2 (7%)
Leg paresis	2 (7%)	1 (4%)
Leg radicular pain	13 (46%)	2 (7%)



Adapted from Table 2 of Petersen et al (2023)

Learning points & take aways

Learning points & take aways



- **Yersinia pestis** is endemic in **Asia, Africa, & western US** (esp four corners & cali-oregon)
- Ask about **all rodents** & **pet exposure** to rodents
 - The lab likes to know if they have **agents of bioterrorism** so please tell them
- **Diagnostic clues** for the plague:
 - **WBC >20k** + **↓ platelets** +/- DIC
 - Fever + hypotension + **painful, nonfluctuant**, regional **lymphadenitis**
- Treat with aminoglycosides, **fluoroquinolones**, or **tetracyclines**

- **Elsberg Syndrome (lumbosacral myeloradiculitis)** is caused by **HSV-2**
 - Also seen with VZV, CMV, WNV, Cv19
- Elsberg Syndrome is a rare cause of **cauda equina syndrome**
 - **Urinary retention** is common +/- skin lesions
 - Commonly preceded by febrile illness
 - Lymphocytic pleocytosis
- Treatment is not well studied, but often receive **acyclovir** &/or **steroids**

