# 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

# 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)

<u>Pulm</u>: **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

A



*Diagnosed with CAP → Unasyn & levofloxacin* 

WBC: 46.8 CXR: LLL atelectasis

<u>AST</u>: **336** <u>ALT</u>: 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





<u>WBC</u>: **46.8** <u>LDH</u>: **3300** 

<u>AST</u>: **336** <u>ALT</u>: 59

**Questions? DDx?** 







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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

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Switched to Merrem & gent for UTI w/ PsA





WBC: 46.8 LDH: 3300 Plts: 54

<u>AST</u>: **336** <u>ALT</u>: 59 <u>Cr</u>: 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
  - <u>Vitek</u>: Yersinia pestis
  - bioMérieux's API: poorly viable E. coli or Proteus spp
- Community hospital sends subculture to the academic hospital





## Case 1: Hospital course

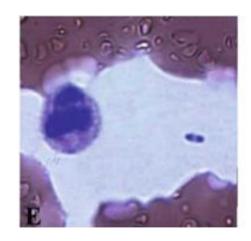
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- Community hospital sends subculture to the academic hospital

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

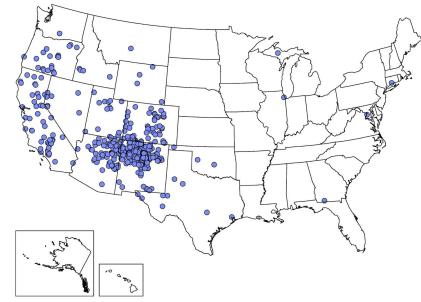
## Geographic distribution

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

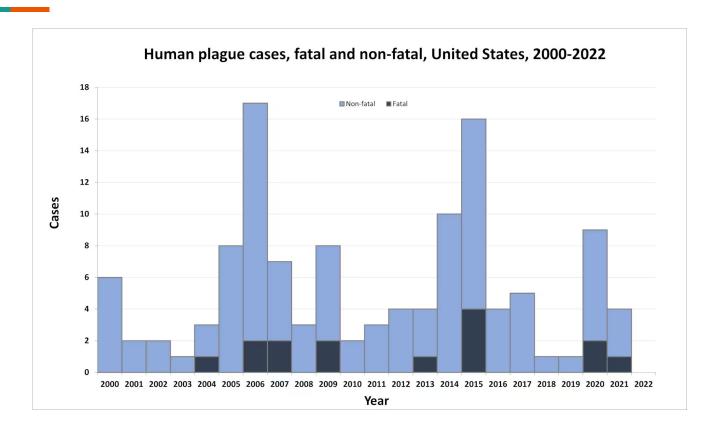
#### **WHO** cases

- <u>2000-2009</u>: 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]

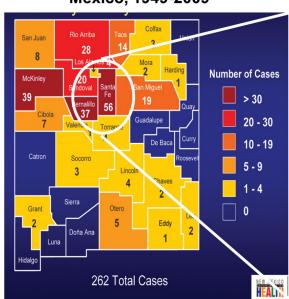


1 dot placed within state of residence for each reported case



## **New Mexico**

## Human Plague cases in New Mexico, 1949-2009



#### **Locations of Plague Isolates, 2009**

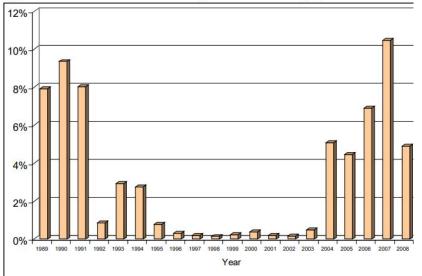


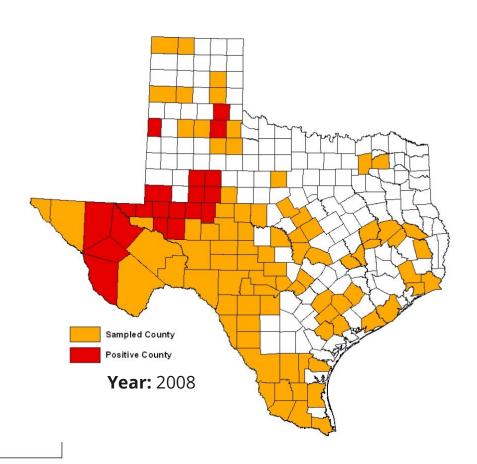
PLOS One - Gibson (2012) [1.1]

## **Texas**

Texas DHSH data [1.2]

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







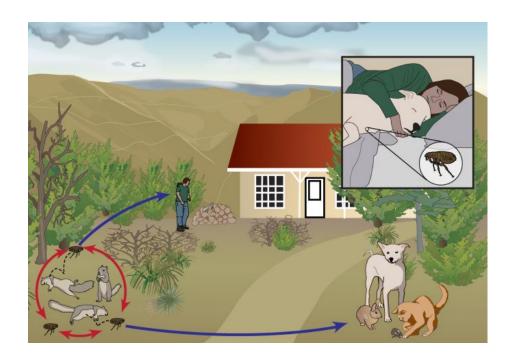
## **Transmission**

#### **Objectives:**

- Describe the geographic distribution of Yersinia pestis
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## **Ecology & Transmission**

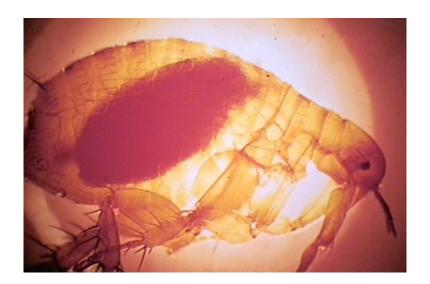
- Transmitted by fleas among wild rodents (squirrels, prairie dogs, rats)
- If ↑↑ among rodents ⇒ rodents die ⇒ fleas get hungry ⇒ fleas find other food
  - May bite humans directly
  - Cats get very sick and may cough droplets that infect humans
  - Dogs can carry fleas that bite humans



#### 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
  - o Regurgs up to 24k CFUs!
  - Infectious dose (for SQ) may be <10 CFUs</li>



The Oriental rat flea (Xenopsylla cheopis) engorged with blood

https://en.wikipedia.org/wiki/Black\_Death

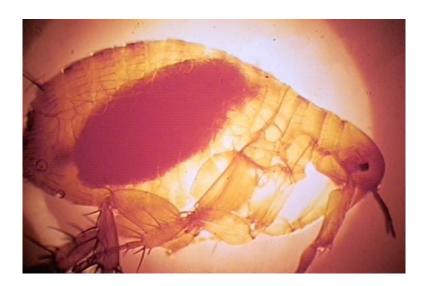
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- ⇒ Flea gets very hungry so ↑ feeds
- ⇒ Also vomits infected blood into new host
  - Regurgs up to 24k CFUs!
  - o Infectious dose (for SQ) may be <10 CFUs

Later studies showed transmission <u>without</u> GI obstruction.

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

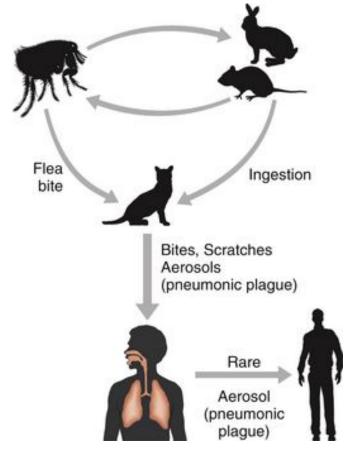


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#### Other transmissions

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



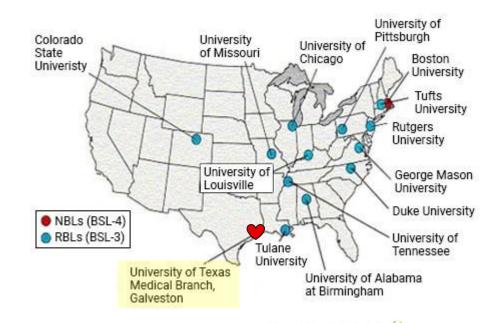
https://veteriankey.com/yersinia-pestis-plague-and-other-yersinioses/

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#### Possible agent of bioterrorism

- PPE: N95, googles, 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)







# Microbiology & clinical presentation

#### **Objectives:**

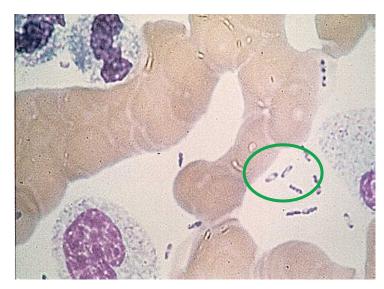
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## Microbiology

#### *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

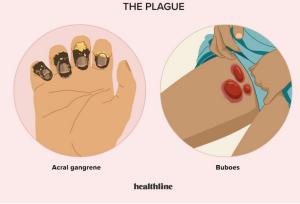
#### **Bubonic plague** (80-95%)

- 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





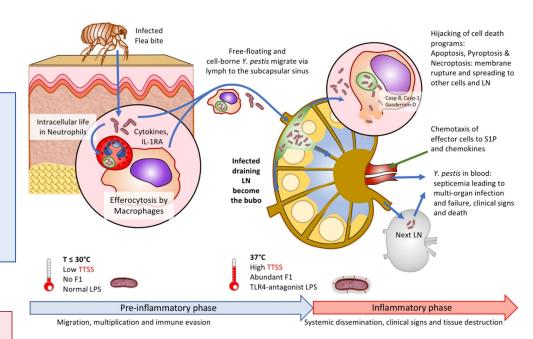
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- Sepsis and immune evasion **mediated by temp**
- at 37 C  $\Rightarrow \uparrow$  **F1 antigen expression** &  $\uparrow$  LPS

Nature Gene - Demeure (2019) [1.3]

## Clinical syndromes

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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
- 10-20% of **septicemic** have no preceding bubos



# Diagnosis & management

#### **Objectives:**

- Describe the geographic distribution of Yersinia pestis
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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
  - o 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:
  - o 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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<u>-17 days</u>: 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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<u>-13 days</u>, **(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**.

- <u>-2.5 weeks</u>: 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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- <u>-1 day</u>: 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% NФ)
- 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

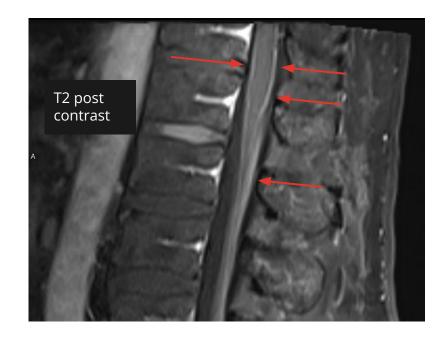
## Workup

#### 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



## Workup

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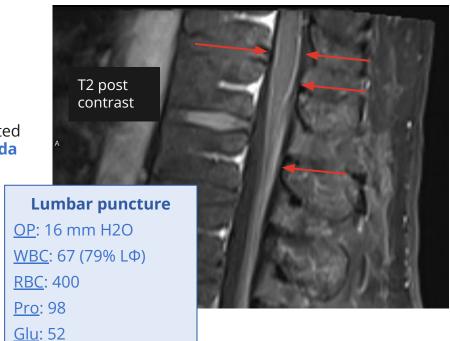
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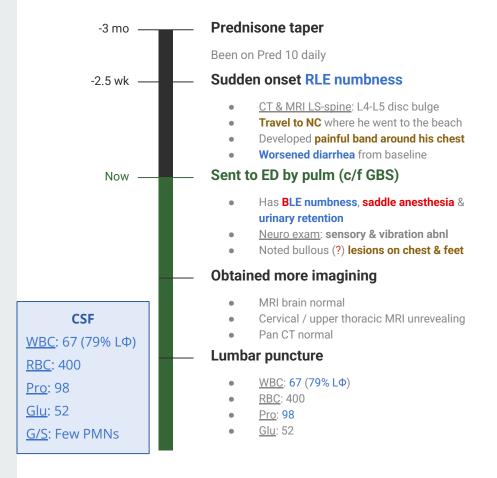


G/S: Few PMNs

## 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



## 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**

<u>OP</u>: 16 mm H2O

<u>WBC</u>: 67 (79% LФ)

RBC: 400

<u>Pro</u>: 98

<u>Glu</u>: 52

G/S: Few PMNs

#### **CSF** studies

<u>Cultures</u>: Neg

Biofire: HSV-2

West Nile: Neg

Crypto Ag: Neg

Flow cytometry: Neg

Pathology: Neg

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- Initial c/f leptomeningeal carcinomatosis
- Normal CT  $\rightarrow$  c/f autoimmune  $\rightarrow$  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

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## **Discussion**



Links to articles discussed here



## **Elsberg Syndrome**

#### **Objectives**

- Recognize the clinical manifestations of lumbosacral myeloradiculitis
- Review <u>both</u> 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.
- <u>Distinction</u>: 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
  - Likely more, because under recognized

#### **Treatment**

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

## Article #1







MS AND CNS INFLAMMATORY DISEASE EPOSTER SESSION | April 18, 2017 | 🙃

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

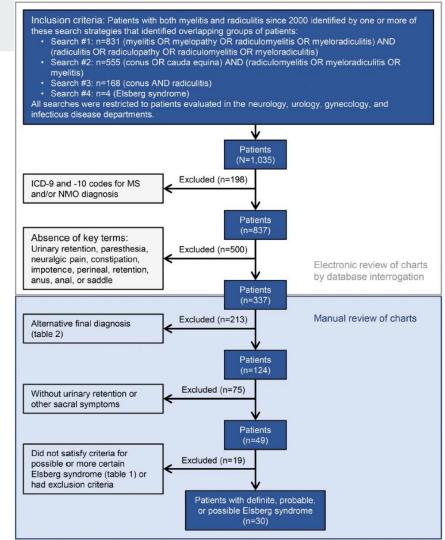
Filippo Savoldi, Timothy Kaufmann, Eoin Flanagan, and Brian Weinshenker

**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
  - $\circ$  1,035  $\rightarrow$  337 chart reviewed
  - o Identified 49 patients meeting inc/exc criteria
- Developed diagnostic criteria (definite, probable, possible, excluded)
  - Total of 30 patients had at least possible Elsberg syndrome



## 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)
  - o **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 ( <b>77%</b> )
Catheter required for retention	21 ( <b>70%</b> )
Urinary incontinence	7 (23%)
Bowel incontinence	3 (10%)
Saddle anesthesia	15 ( <b>50%</b> )
Constipation	13 (43%)
Loss of limb sensation	24 ( <b>80%</b> )
Leg weakness	15 ( <b>50%</b> )
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**):

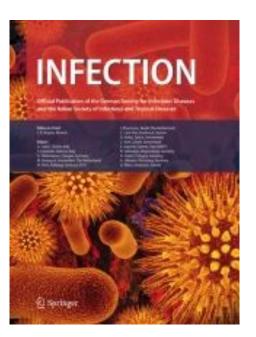
- One patient (**7.7%**) **died** of encephalomyelitis
- Three (23%) had no neurologic recovery
- Eight (44%) had moderate recovery
- One (7.7%) had complete recovery
- Two patients **relapsed (15%)** at 33 & 82 months

# Viral lumbosacral radiculitis (Elsberg syndrome) in Denmark

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

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**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

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#### **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**

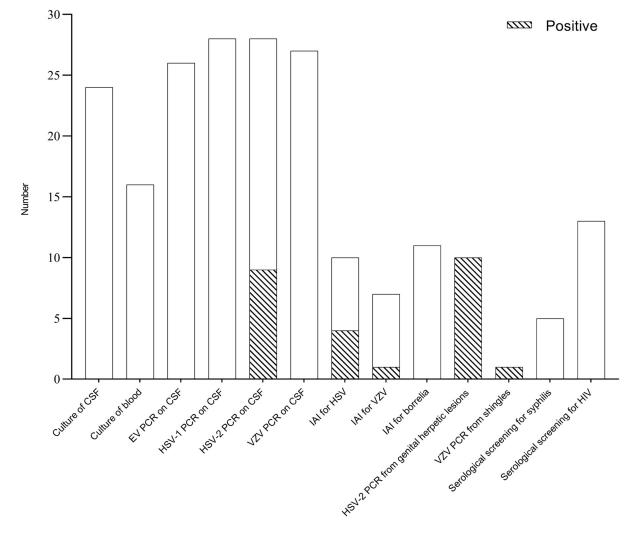
- 1. Death
- 2. Vegetative state
- 3. Severe disability
- 4. Moderate disability
- 5. Good recovery

#### 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)

N (%)
23 ( <b>82%</b> )
6 (23%)
12 <b>(55%)</b>
28 (100%)
17 ( <b>61%</b> )
20 ( <b>71%</b> )
10 (36%)
2 (7%)
13 (46%)

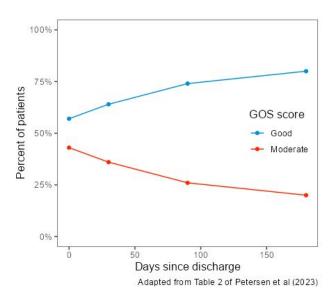
CSF cell count, median (IQR)	153 (31- 514)
CSF % lymphs, median (IQR)	1% (1 - 4)
CSF protein, median (IQR)	70 (46 - 131)



#### 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%)



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:

  - Fever + hypotension + painful, nonfluctuant, regional lymphadenitis
- Treat with aminoglycosides, fluoroquinolones, or tetracyclines



- 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

