

# **Multi-State Fungal Infection Investigation**

## **Epi Rapid Response Team**

### **Annual Conference**

**May 7, 2013**

\* \* \*

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**Kentucky Public Health**

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# Background

- September 18, 2012 Tennessee DPH alerted to unusual case
  - Fungal meningitis - culture-confirmed *Aspergillus fumigatus*
  - Following epidural steroid injection (ESI) at a TN ambulatory surgical center.
- Eight additional meningitis patients identified
  - All received epidural steroid injections of “preservative-free MPA,” and other associated medications
  - 2 patients presented with additional strokes
  - *Exserohilum Rostratum* identified
- September 26 – CDC calls for additional cases nationally



# What is MPA?

- Methylprednisolone acetate
- Steroid used for pain control
- Usually applied into spinal column
  - Into the “epidural space”
- Used for joint pain injections also
- Implicated MPA had no preservative
- Patients can have single or multiple injections



# MPA from NECC



AP Photo



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# New England Compounding Center

- Compounding Pharmacy
  - Licensed to produce individual doses of medication for individual patients
  - Not regulated by FDA
- NECC
  - Located in Framingham, Massachusetts
  - Licensed by Massachusetts Board of Pharmacy
- All MPA produced by a pharmaceutical compounding company – New England Compounding Company (NECC)
- Mass produced and distributed to 23 states nationally



# NECC



(Jared Wickerham/Getty Images)  
(ABCNews.Go.Com)



(60 Minutes)



(Reuters - FoxNews.com)

# NECC Leadership – Barry Cadden



Photo: Joe Brier, Gannett



# NECC Initial Investigation

- NECC facility closed Sept. 20, 2012
- 17,500 vials of MPA (80 mg/ml)
  - Packaged in 1ml, 2ml, and 5ml vials and
  - Distributed to 75 facilities in 23 states.
  - Used to treat both peripheral joint and back pain.
- September 26 - NECC voluntarily recalled the three lots of MPA
- October 3 - Expanded voluntary recall of all lots of MPA and all lots of sterile products intended for intrathecal injection
- October 6 - Voluntary recall of all remaining NECC products
- FDA investigates thoroughly





# CDC / Tennessee Investigation

- September 28 - investigators identified a case outside of Tennessee
- October 4
  - Total of 35 cases
  - Clinical picture consistent with fungal infection
  - Six states
    - Florida (2 cases)
    - Indiana (1 case)
    - Tennessee (25 cases, 3 deaths)
    - Maryland (2 cases, 1 death)
    - North Carolina (1 case)
    - Virginia (4 cases, 1 death)



# Early Case Definition – Oct 4

- 1: A person with meningitis<sup>1</sup> of sub-acute onset (1-4 weeks) following epidural injection after July 1, 2012.
- 2: A person, who has not received a lumbar puncture, with basilar stroke 1-4 weeks following epidural injection after July 1, 2012<sup>2</sup>.
3. A person with evidence of spinal osteomyelitis or epidural abscess at the site of an epidural injection diagnosed 1-4 weeks after epidural injection after July 1, 2012.

<sup>1</sup> Clinically diagnosed meningitis meaning 1 or more of the following symptoms: headache, fever, stiff neck, or photophobia and a CSF profile consistent with meningitis (elevated protein/low glucose/pleocytosis)

<sup>2</sup> These people, if possible, should have an LP.



# Initial Findings

- Variety of symptoms identified including: fever, new or worsening headache, nausea, and/or new symptoms consistent with a stroke.
- October 4 - CDC and FDA recommend that all healthcare personnel cease use and remove from their pharmacy inventories any product produced by the New England Compounding Center.
- Because the medical treatment for this infection is not benign, CDC does not recommend routine prophylaxis of patients who have received medication from one of these lots.



# Kentucky Engaged

- October 5 (Friday) – Tennessee notified KDPH of 3 cases who were KY residents
  - 1 deceased
  - Other KY residents exposed
- CDC initiated multi-state, daily calls that day
- DPH pushes out info to Regional Epi's
- Alerts that we may need to call upon them over weekend



# Kentucky Springs into Action

- Tennessee attempted to reach all exposed patients
- October 6 (Saturday) - Tennessee asks KY for assistance
  - Can't locate 10 patients to inform of risk
    - 10 in Barren River District
    - 3 in Pennyriple District
- Regional Epidemiologists contacted
  - Reach all patients over weekend
  - List with all facilities with NECC products distributed



# Situation Unfolds

- Regional Epi identifies another case locally – death
  - Tennessee not aware of this case
- We discover KY residents exposed in Indiana, Ohio, Virginia
- Regional Epi's asked to F/U on recalled products same weekend
  - Call all facilities
  - Verify that all NECC products are pulled
- Medical guidance sent to clinicians



# Ongoing Investigation

- October 10 - 137 patients in 10 states identified
  - No cases associated with other lots of MPA, or other NECC products
  - Twelve (9%) of the 137 patients died.
- Preliminary data are available on 70 (51%) patients.
  - 64 (91%) have meningitis (case definition 1)
  - 2 (3%) have stroke without lumbar puncture (definition 2)
  - 2 (3%) have an epidural abscess or osteomyelitis (definition 3)
  - 2 (3%) patients met more than one case definition (definitions 1 and 3)
- Tennessee asks for further assistance
  - October 24-26 – call all exposed KY residents
    - Interview about symptoms
    - Educate about risks
    - Leave follow-up contact information



# Data Collection

- Phone survey of all exposed individuals
  - Identified several with symptoms
  - Reported to respective states
- Tennessee gave access to patient tracking system
- DPH set up hotline for exposed to call for:
  - Questions
  - Report symptoms





# National Response – KY Role

- CDC attributes cases to state of exposure
- NECC products distributed to 44 facilities in KY – no implicated MPA solution
- Many KY residents exposed
  - 153 – Tennessee
  - 47 – Indiana
  - 8 – Ohio
  - 1 – Virginia
  - 1 – Florida
- Coordinated case follow-up with TN and other states

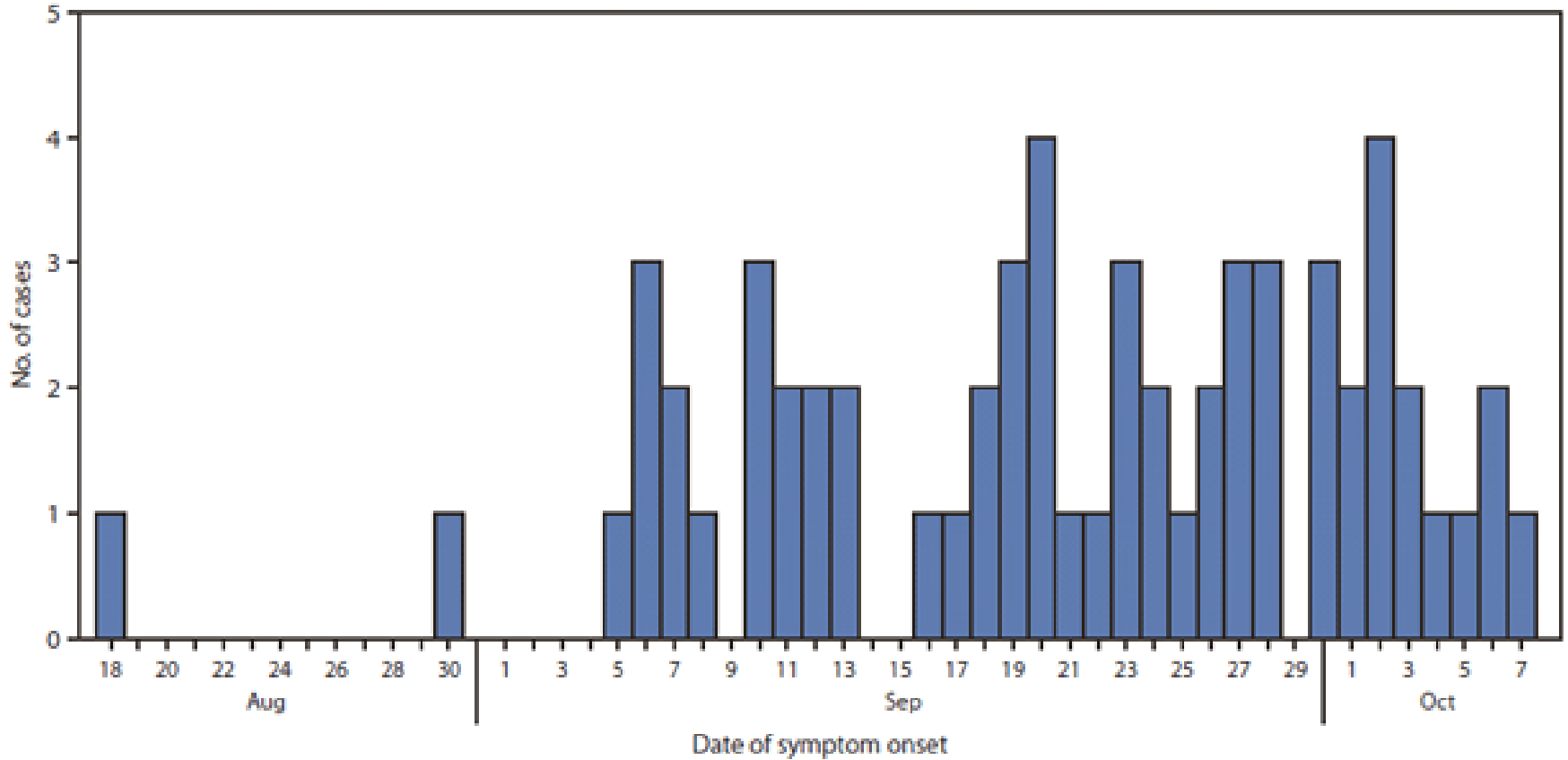


# Initial Scope

- Nearly 14,000 persons injected with solution from one of the three lots
- By October 10 - Approximately 90% of exposed patients had been contacted at least once, by telephone, voicemail, home visit, or registered mail
  - 137 patients identified
    - 12 deaths
    - Fungal meningitis (91%)
    - Basilar stroke with no cerebrospinal fluid (CSF) specimen obtained
    - Spinal osteomyelitis or epidural abscess at the site of injection
    - Septic arthritis or osteomyelitis of a peripheral joint (e.g., knee)



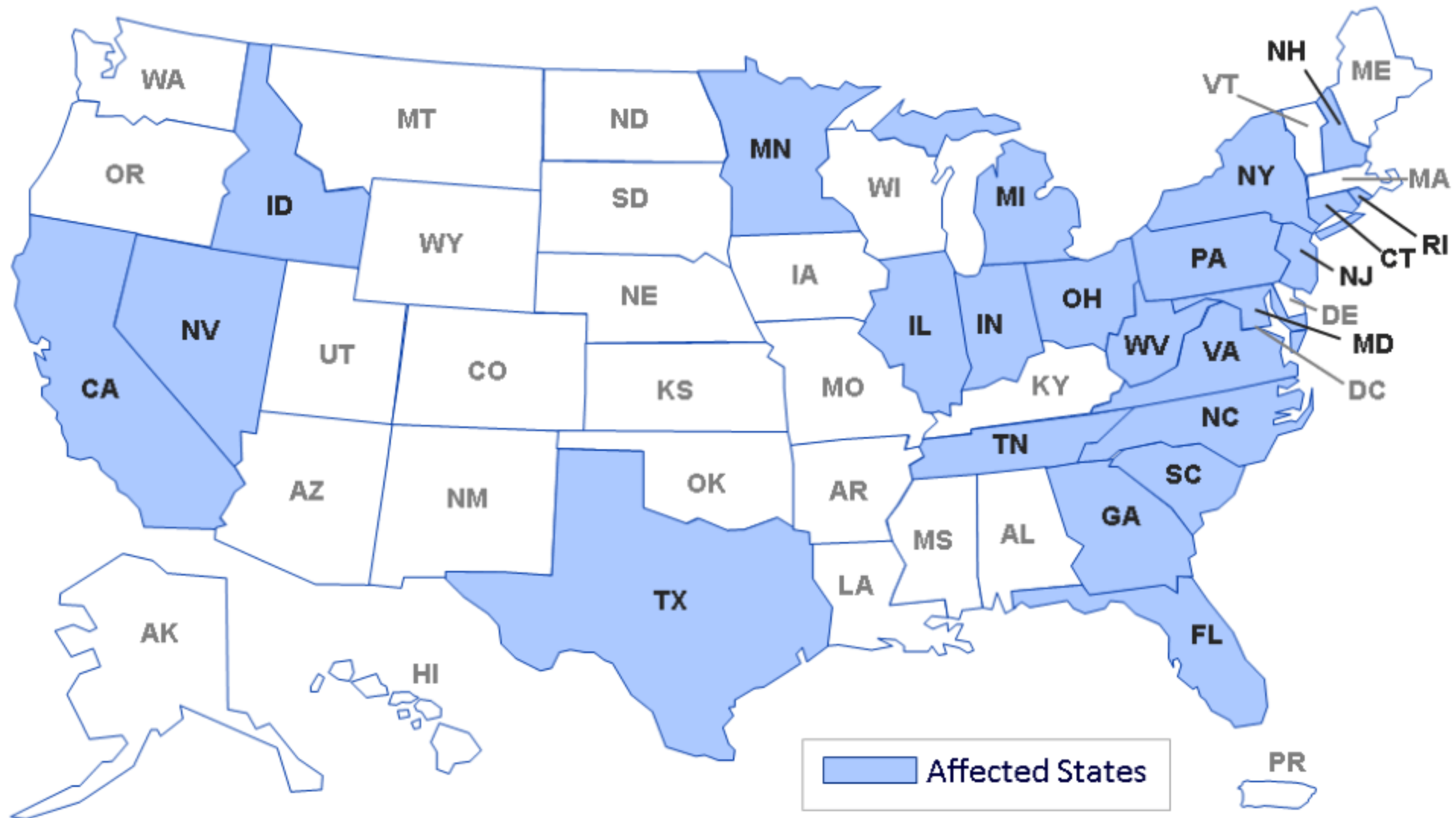
# Epi Curve – October 19



The Figure above shows the number of cases of fungal infection with known date of symptom onset, following epidural steroid injection of methylprednisolone acetate from New England Compounding Center, by date of symptom onset - United States, 2012



# States that Received NECC MPA



# Evolving Case Definition – March, 2013

## Probable Case

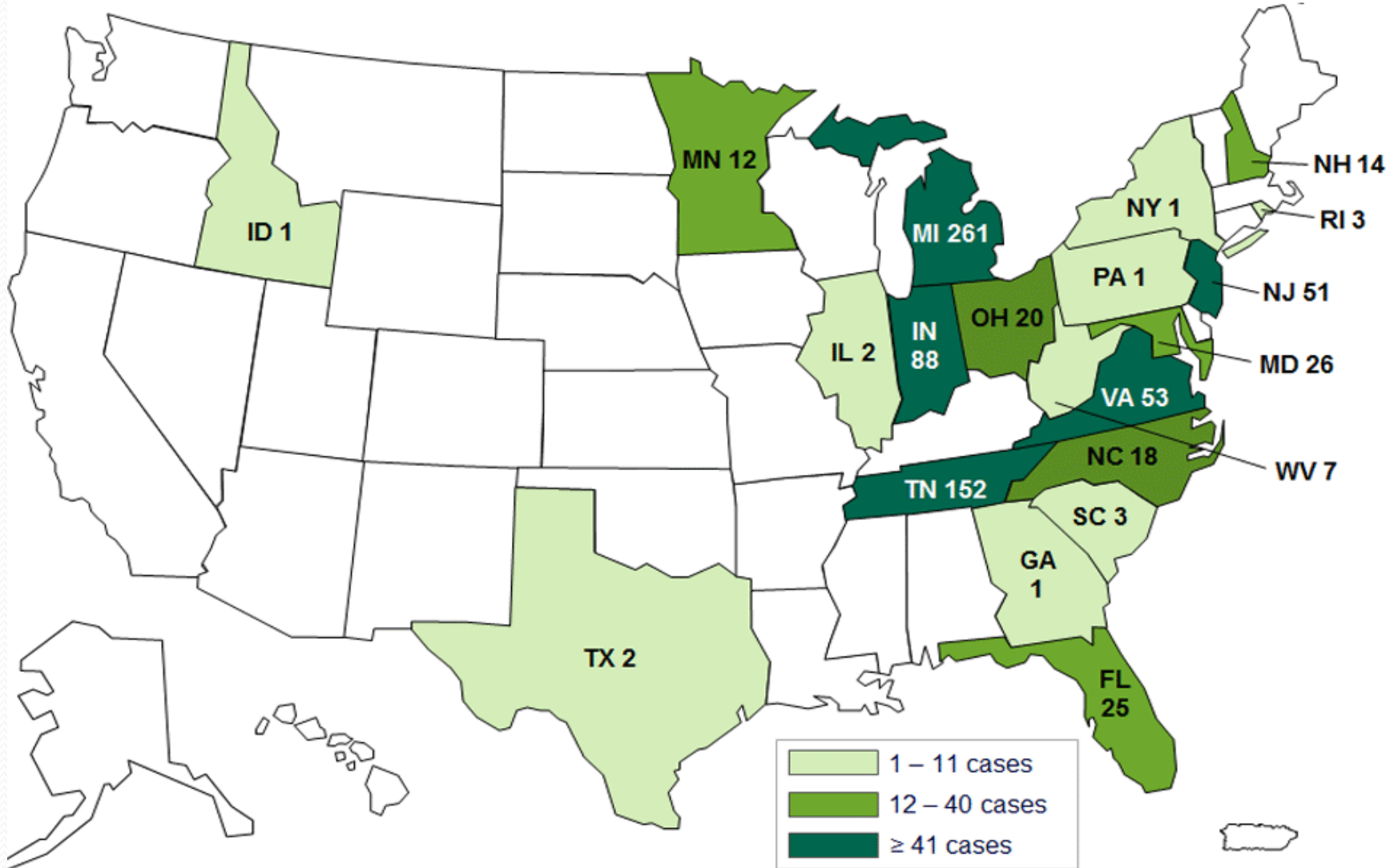
- Received a NECC preservative-free (MPA) injection from implicated lots, and developed any of the following:
  - Meningitis following epidural or paraspinal injection after May 21, 2012;
  - Posterior circulation stroke;
  - Osteomyelitis, abscess or other infection in the spinal or paraspinal structures near the site of injection; or
  - Osteomyelitis or worsening inflammatory arthritis of a peripheral joint.

## Confirmed Case

- A probable case with evidence (by culture, histopathology, or molecular assay) of a fungal pathogen associated with the clinical syndrome.



# Case Counts by State



# Burden of Disease in KY

- KY currently has 20 cases among residents
  - Tennessee – 18 cases
  - Ohio – 1 case
  - Indiana – 1 case
- 5 deaths – all treated in Tennessee
- High mortality rate among cases – 5/20 (25%)
  - KY accounts for 33% of TN deaths
  - KY only accounts for 12% of TN cases



# State Case Counts – 5/6/13

Cases and Deaths with Fungal Infections Linked to Steroid Injections

State	Total Case Count	Meningitis Only	Meningitis + Paraspinal/Spinal Infection	Stroke w/out Lumbar Puncture Only	Paraspinal/Spinal Infection only	Peripheral Joint Infection Only	Paraspinal/Spinal Infection + Peripheral Joint Infection	Deaths
Florida (FL)	25	22	1	1	1	0	0	5
Georgia (GA)	1	1	0	0	0	0	0	0
Idaho (ID)	1	1	0	0	0	0	0	0
Illinois (IL)	2	2	0	0	0	0	0	0
Indiana (IN)	88	31	16	1	40	0	0	11
Maryland (MD)	26	25	0	0	1	0	0	3
Michigan (MI)	261	22	43	2	167	25	2	16
Minnesota (MN)	12	10	0	0	2	0	0	1
North Carolina (NC)	18	1	3	0	14	0	0	1
New Hampshire (NH)	14	9	0	0	0	5	0	0
New Jersey (NJ)	51	31	10	0	9	1	0	0
New York (NY)	1	0	0	0	1	0	0	0
Ohio (OH)	20	12	3	0	5	0	0	1
Pennsylvania (PA)	1	1	0	0	0	0	0	0
Rhode Island (RI)	3	1	1	0	1	0	0	0
South Carolina (SC)	3	2	0	0	1	0	0	0
Tennessee (TN)	152	21	58	3	68	2	0	15
Texas (TX)	2	2	0	0	0	0	0	0
Virginia (VA)	53	40	8	0	4	0	0	2
West Virginia (WV)	7	0	2	0	5	0	0	0
<b>TOTAL</b>	<b>741</b>	<b>234</b>	<b>146</b>	<b>7</b>	<b>319</b>	<b>33</b>	<b>2</b>	<b>55*</b>

\*Deaths reported are from all causes among persons who meet the case definition and may not be directly attributed to a fungal infection.

Case counts by state are based on the state where the procedure was performed, not the state of residence.



# Epidemiologic Analysis

Tennessee did extensive epi analysis

- Found source and implicated lot numbers
- Identified NECC as only source
- Examined dose response
  - Vials on shelf for > 50 days increased risk
  - Patients receiving higher dose at increased risk
  - Patients who received high dose of older vials:
    - 50% attack rate
- Identified ongoing spinal and paraspinal infections



# NECC Investigation

- 17,000 doses of MPA distributed
- ≈14,000 doses administered
- FDA inspection of facility “deplorable”
  - Facility not sterile in key locations
  - Matter visible in compound vials on site
- Compounding pharmacies not regulated by FDA
- Operating outside licensure
  - Mass production rather than individual dose production
  - Selling large quantities nationally





# NECC - Front



# NECC - Back



(Bryce Vickmark for The New York Times)

# NECC – From the Air



(60 Minutes)

# NECC – Air Intake



(60 Minutes)



60  
MINUTES



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# The Result . . .



(Barry Chin/AP (npr.org))

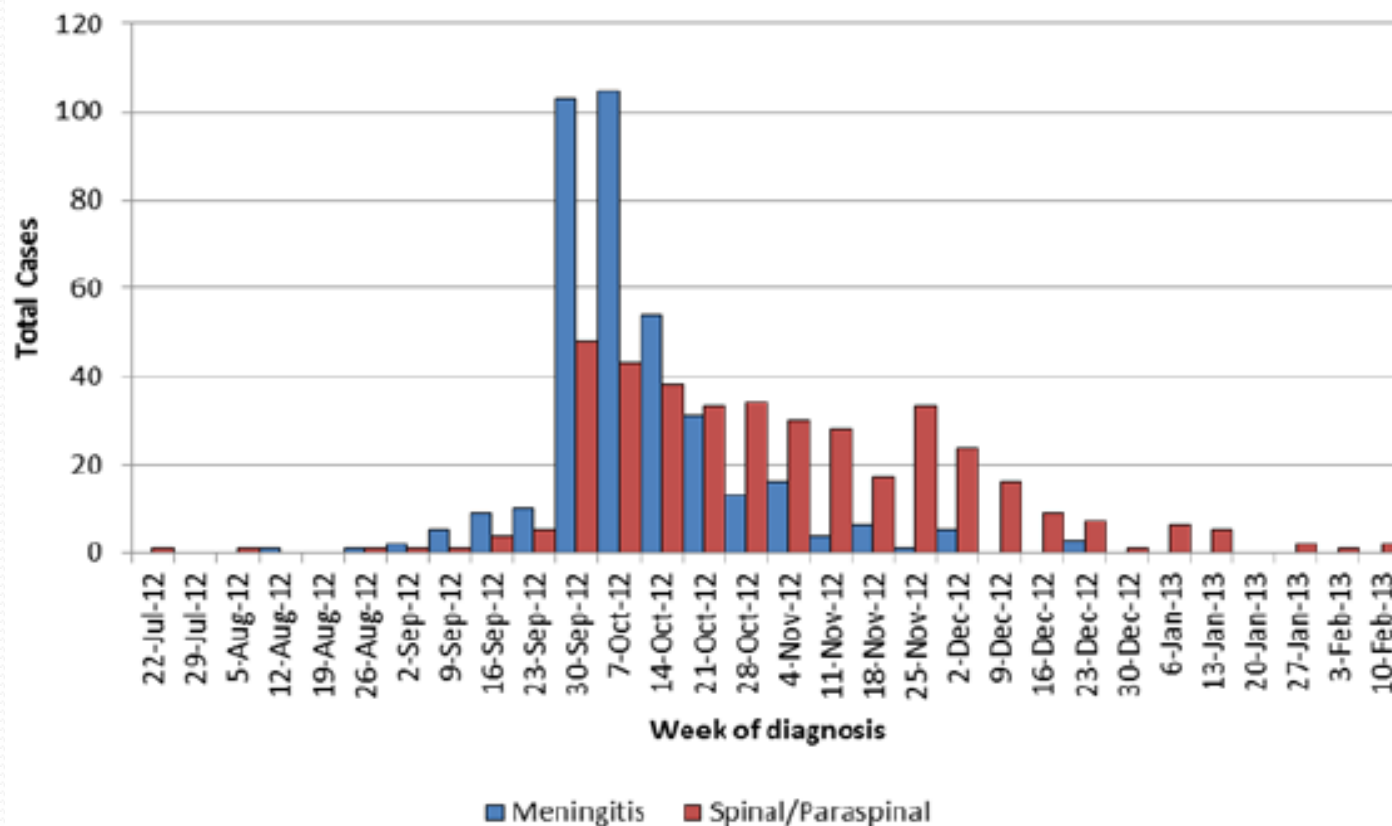
# Ongoing Case Finding - Today

- Meningitis/Stroke
- Joint infections
- Parameningeal infections
- Epidural abscesses
- Epidural abscesses with minimal symptoms
- Osteomyelitis and discitis
- Sacroiliac osteomyelitis
- Relapsing illness documented
  - Treatment ended, disease returned



# Occurrence Patterns

Week of Diagnosis of Case-Patients (n=661)  
with Meningitis or Spinal/Paraspinal Infection



# Response Partnerships

- Kentucky Dept. for Public Health
  - Division of Epidemiology and Health Planning
  - Division of Public Health Protection and Safety (Environmental Health!)
- Local Health Departments
  - Regional Epidemiologists
  - Environmental Health Specialists
- Other states
- Centers for Disease Control and Prevention
- US Food and Drug Administration (FDA)



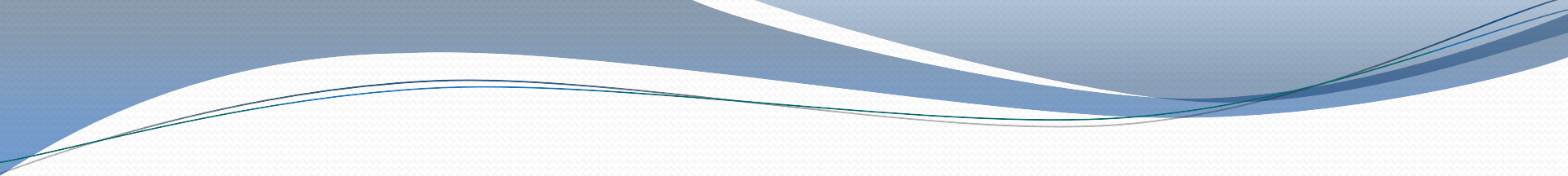
# Acknowledgements

- Local Health Departments
    - Nurses
    - Environmentalists
    - Epidemiologists
  - Kentucky Department for Public Health
    - Reportable Disease Section
    - Division of Laboratory Services
    - Food Safety Branch
    - Preparedness Branch
    - Division of Epidemiology and Health Planning
  - Indiana State Department of Health
  - Centers for Disease Control and Prevention
  - Food and Drug Administration
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