Nosocomial and iatrogenic fungal infections (health care associated fungal infections)

A real increase??

- More candidates:
  - More aggressive treatment of hematological pathologies and solid tumors
  - Increase in all kinds of transplantations
  - Use of immunomodulatory agents
  - Invasive devices
  - ICU stay
- More awareness
- More diagnostic tools
- More techniques to prove causality between infection and (environmental) contamination

Nosocomial and iatrogenic fungal infections

- **Candidiasis: "medical" risk factors:**
  - Relatively minimal immunosuppression is required
  - Broad spectrum antibacterial agents
  - Surgery
  - Hemodialysis
  - TPN
  - Immunosuppression and chemotherapy
  - Transplants
  - Invasive devices
  - Hand hygiene (33% of surgical ICU and 29% of neonatal ICU HCWs with *Candida* spp. on their hands*)
  - *Candida parapsilosis* is the most common yeast isolated from the hands of HCWs

* Rangel-Fraust MS et al. National epidemiology of mycoses survey (NEMIS): variations in rates of bloodstream infections due to *Candida* species in seven surgical intensive care units and six neonatal intensive care units. Clin Infect Dis 1999; 29 (2): 253-8

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Nosocomial and iatrogenic fungal infections

- **Other yeasts:**
  - *Malassezia* fungemia in low-birth-weight neonates and in immunocompromised adults:
    - role of intravascular catheters and parenteral lipid formulations
    - colonization of the hands and pet dogs of HCWs (*Malassezia pachydermatis)*
  - *Saccharomyces cerevisiae* fungemia and Enterol® (~~*Saccharomyces boulardii*~~)

Tragiannidis A, Bisping G, Koehler G and Groll AH. Minireview: *Malassezia* infections in immunocompromised patients. Mycoses 2010; 53: 187-195

Enache-Angoulvant A and Hennequin C. Invasive *Saccharomyces* Infection: A comprehensive Review. Clin Infect Dis 2005; 41:1559-1568

Nosocomial and iatrogenic fungal infections

- **Aspergillosis**: pulmonary form
  - Most cases are sporadic and in patients with intermediate to severe immunosuppression
  - Outbreaks of environmental airborne infections within hospital settings have been reported: construction and renovation works in and around hospitals, improperly functioning ventilation systems and air filters, contaminated false ceilings and insulation material, water leaks, food, ornamental plants
  - But there is no uniform definition of what constitutes nosocomial aspergillosis. Reasons: unknown incubation period of invasive aspergillosis and frequent admissions and discharges of high-risk patients
  - Air sampling is almost always too late and is unreliable due to irregular release of spores
  - Molecular techniques reveal different strains in the environment and even in the patient (poor correlation of the spp. from the environment and species isolated from the patients)

Nosocomial and iatrogenic fungal infections

- **Aspergillosis:** cutaneous form
  - In burn units (use of dressings contaminated with *Aspergillus* spores)
  - At intravenous insertion sites because of contaminated dressings on arm boards providing support to IV lines (children)or after inserting a CVC in non-optimal conditions
- **Postoperative aspergillosis:** due to failing air handling systems

Pasqualotto AC and Denning DW. Post-operative aspergillosis. Clin Microbiol Infect 2006; 12:1060-1076

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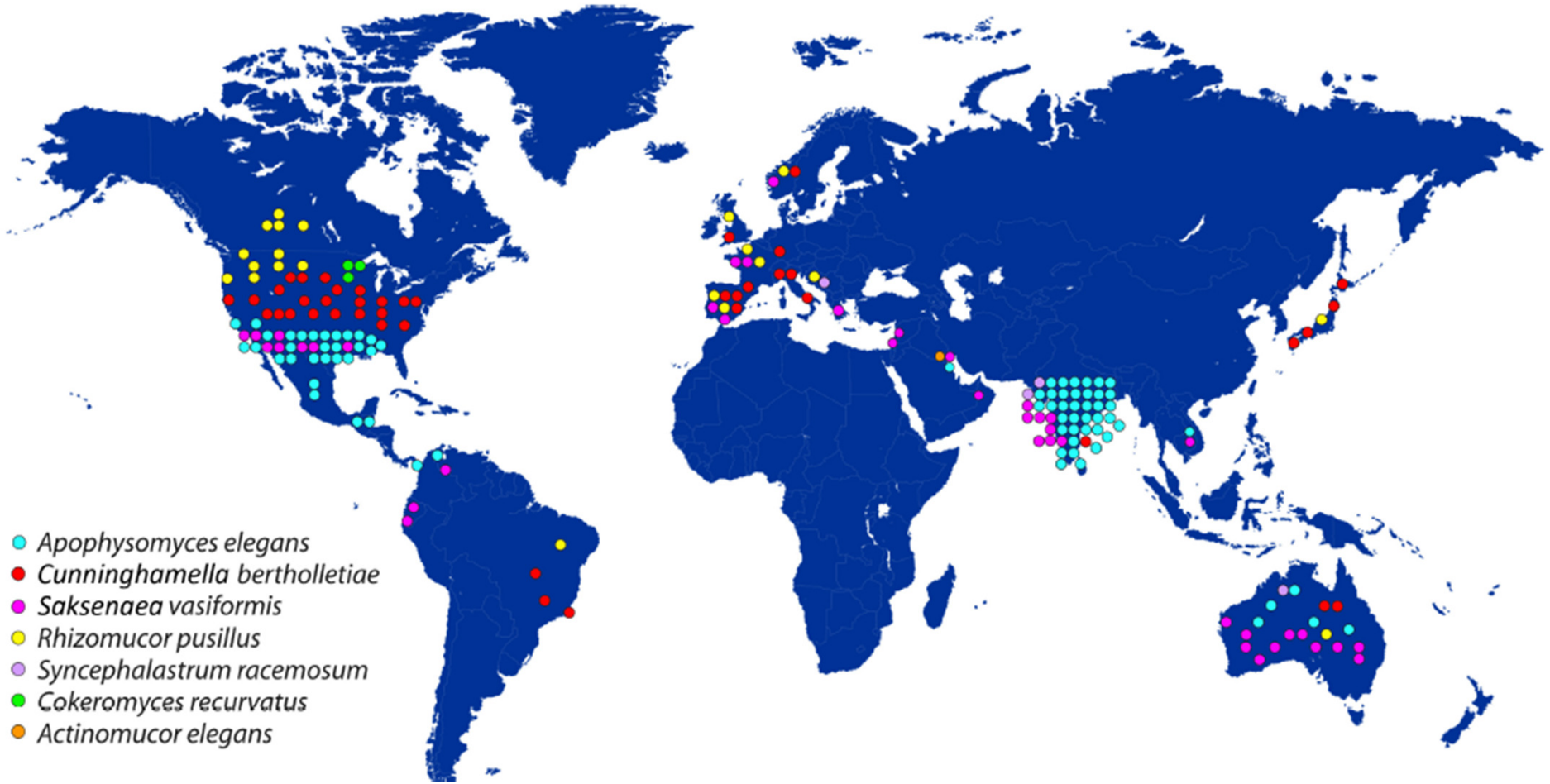
Nosocomial and iatrogenic fungal infections

- **Mucormycosis:**
  - Desferrioxamine therapy
  - Cutaneous infections associated with Elastoplast adhesive dressings
  - Airborne transmission due to contaminated ventilation systems
  - Contaminated wooden tongue depressors (gastric mucormycosis)
  - Non-sterile karaya (plant-derived adhesive) for securing ostomy bags



Gomes MZR, Lewis RE and Kontoyiannis DP. Mucormycosis Caused by Unusual Mucormycetes, Non-*Rhizopus*, -*Mucor*, and -*Lichtheimia* Species. Clin Microbiol Rev 2011; 24:411-445

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Nosocomial and iatrogenic fungal infections

- ***Fusarium* infections:**
  - Contamination of lens solutions
  - Contamination of the water system
  - Contamination of implantations??

Ahearn DG, Zhang S, Stulting RD et al. *Fusarium* keratitis and contact lens wear: facts and speculations. Med Mycol 2008; 46:397-410

Hayette MP, Christiaens G, Mutsers J et al. Filamentous fungi recovered from the water distribution system of a Belgian university hospital. Med Mycol 2010; 48:969-974

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Nosocomial and iatrogenic fungal infections

- ***Pneumocystis jirovecii*** (PCP)
  - Person-to-person airborne transmission
  - Isolation measures, also in ambulatory care ???

De Boer MGJ, De Fijter JW and Kroon FP. Outbreaks and clustering of *Pneumocystis* pneumonia in kidney transplant recipients: a systematic review. Med Mycol 2011; 49:673-680

Siegel JD, Rhinehart E, Jackson M, Chiarello L, for the Healthcare Infection Control Practices Advisory Committee (CDC). Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. 2007. Available from: http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html

Nosocomial and iatrogenic fungal infections

- Recent “scandal”: 2012 - 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

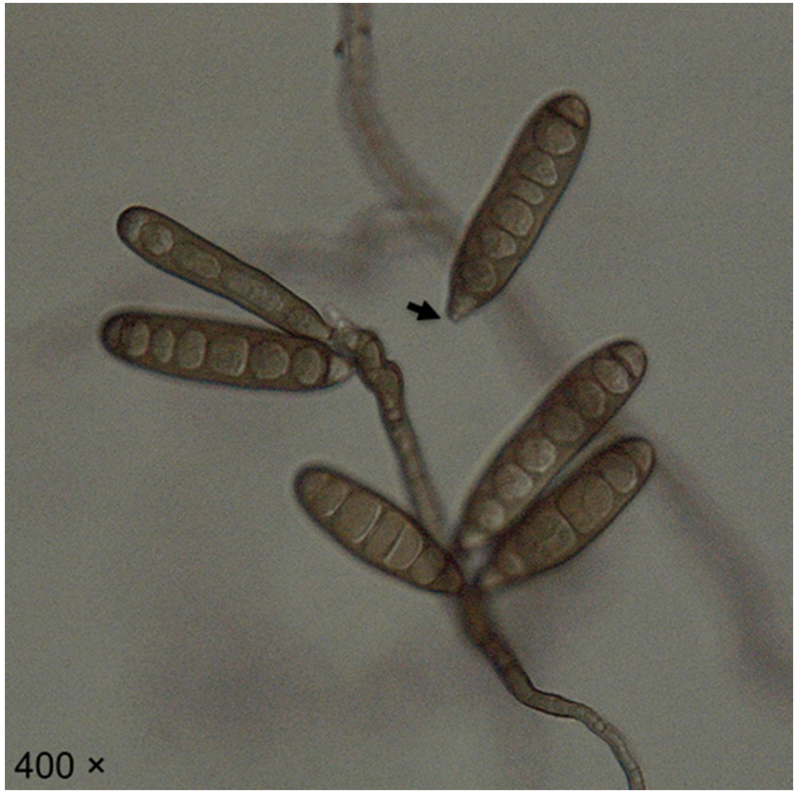
Fungal Infections Associated with Contaminated Methylprednisolone in Tennessee

Marion A. Kainer, M.B., B.S., M.P.H., David R. Reagan, M.D., Ph.D., Duc B. Nguyen, M.D., Andrew D. Wiese, M.P.H., Matthew E. Wise, Ph.D., Jennifer Ward, M.S., Benjamin J. Park, M.D., Meredith L. Kanago, M.S.P.H., Jane Baumblatt, M.D., Melissa K. Schaefer, M.D., Brynn E. Berger, M.P.H., Ellyn P. Marder, M.P.H. , Jea-Young Min, Pharm.D., M.P.H., John R. Dunn, D.V.M., Ph.D., Rachel M. Smith, M.D., John Dreyzehner, M.D., M.P.H., and Timothy F. Jones, M.D., for the Tennessee Fungal Meningitis Investigation Team*

Nosocomial and iatrogenic fungal infections

"patients who received epidural or paraspinal glucocorticoid injections of preservative-free methylprednisolone acetate prepared by a single compounding pharmacy"
not a generic drug!

- *Exserohilum rostratum*



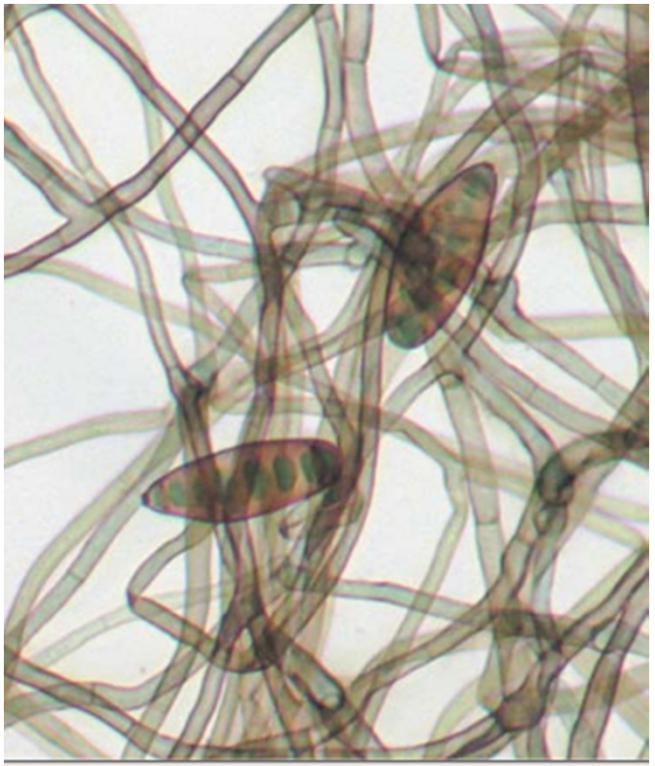


Figure 1. Photomicrograph of *Exserohilum rostratum* Isolate from Cerebrospinal Fluid Grown for 48 Hours on Potato Flakes Agar.

Courtesy of Annette W. Fothergill, Fungus Testing Laboratory, University of Texas Health Science Center at San Antonio.

Nosocomial and iatrogenic fungal infections

- More than 13 400 patients could have been exposed
- Some 750 patients have been affected
- Peak incubation period +/- 28 days
  (2,3 % more than 40 days)
- Attack rate: from 3% to 35 % depending on the lot, the delay between production and injection, and the number of injections per patient
- Clinical forms: meningitis, epidural abscesses, discitis, osteomyelitis, arthritis, bursitis
- Case fatality rate (for CNS cases): 8,9% depending on (lack of) treatment
- J. Perfect: “Iatrogenic fungal meningitis: tragedy repeated.” Ann Intern Med 2012; 157: 825-6. *Exophiala dermatitidis* in contaminated glucocorticoid injections (2002)

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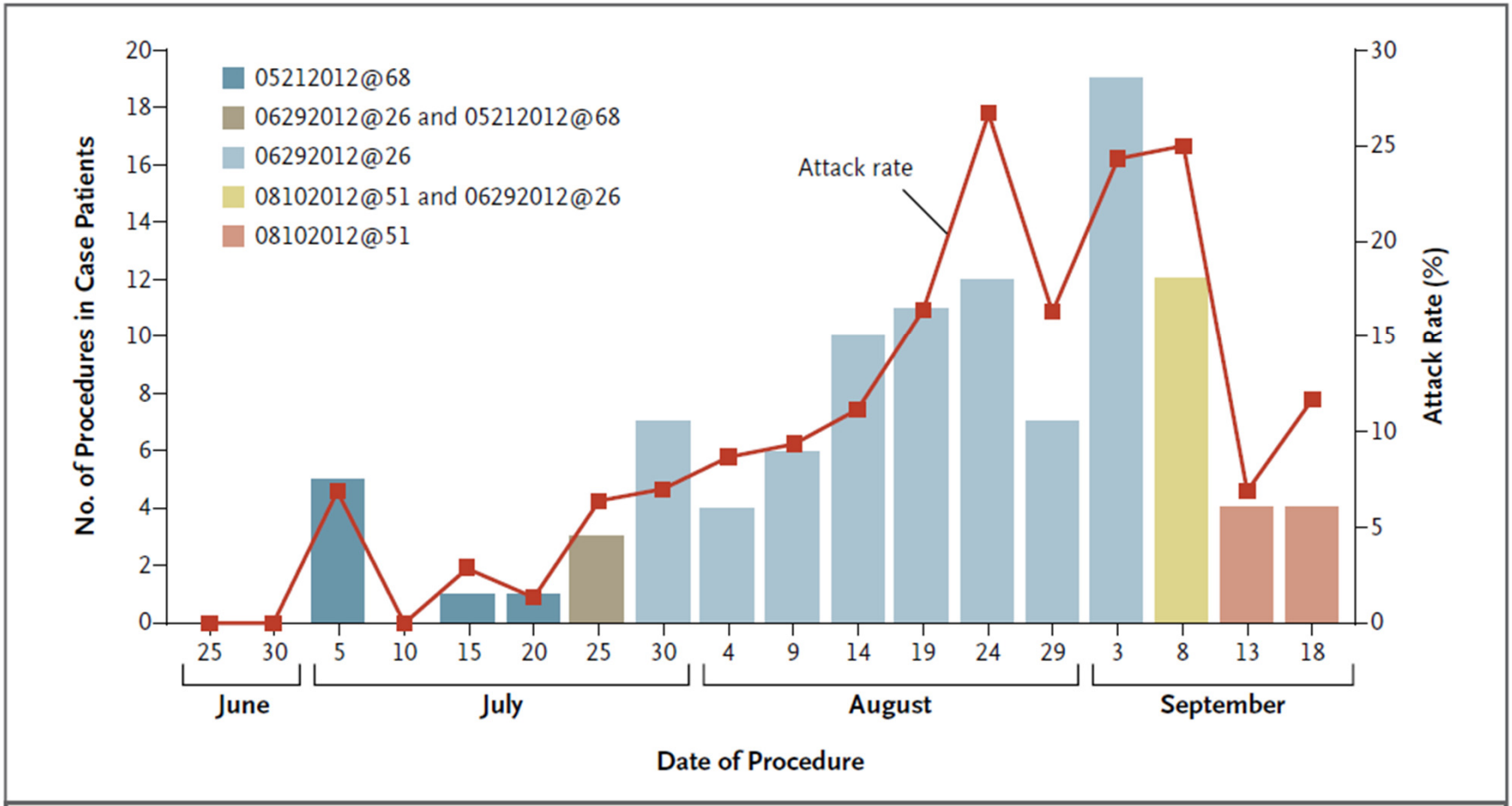
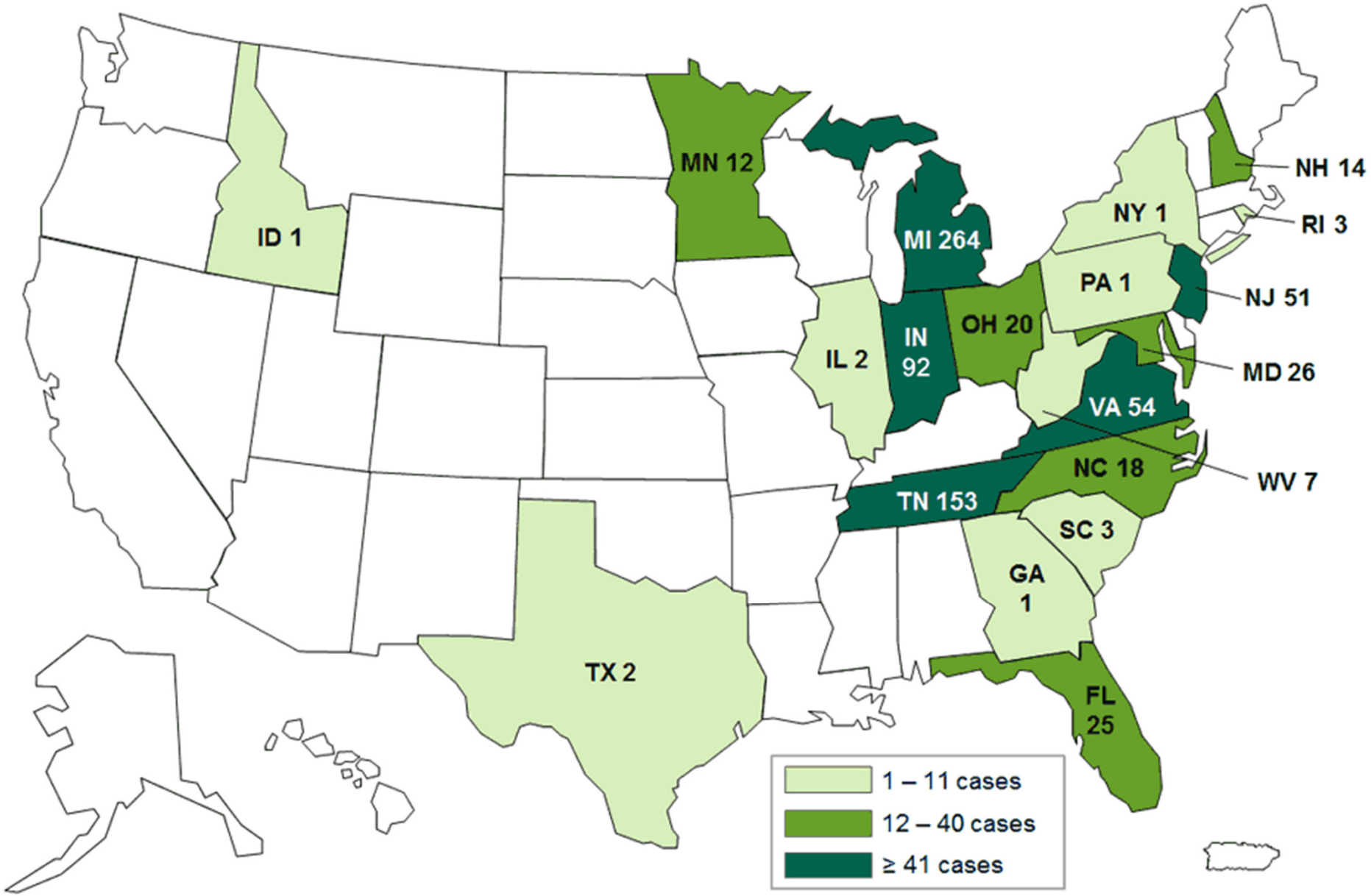


Figure 1. Number of Epidural and Paraspinal Glucocorticoid Injections and Attack Rate.

Shown are the number of epidural and paraspinal glucocorticoid injection procedures performed in case patients, as well as the attack rates among persons who received methylprednisolone acetate from the implicated lots during these procedures. Data are shown according to 5-day time periods.

Kainer MA, Reagan DR, Nguyen DB et al. Fungal Infections Associated with Contaminated Methylprednisolone in Tennessee. N Engl J Med 2012;367:2194-2203



http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html

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	7
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)	92	30	17	1	44	0	0	11
Maryland (MD)	26	23	1	0	2	0	0	3
Michigan (MI)	264	23	46	2	166	25	2	19
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	30	11	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)	153	22	57	3	69	2	0	16
Texas (TX)	2	2	0	0	0	0	0	0
Virginia (VA)	54	41	9	0	4	0	0	5
West Virginia (WV)	7	0	2	0	5	0	0	0
TOTAL	**750**	**233**	**151**	**7**	**324**	**33**	**2**	**64**

http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html

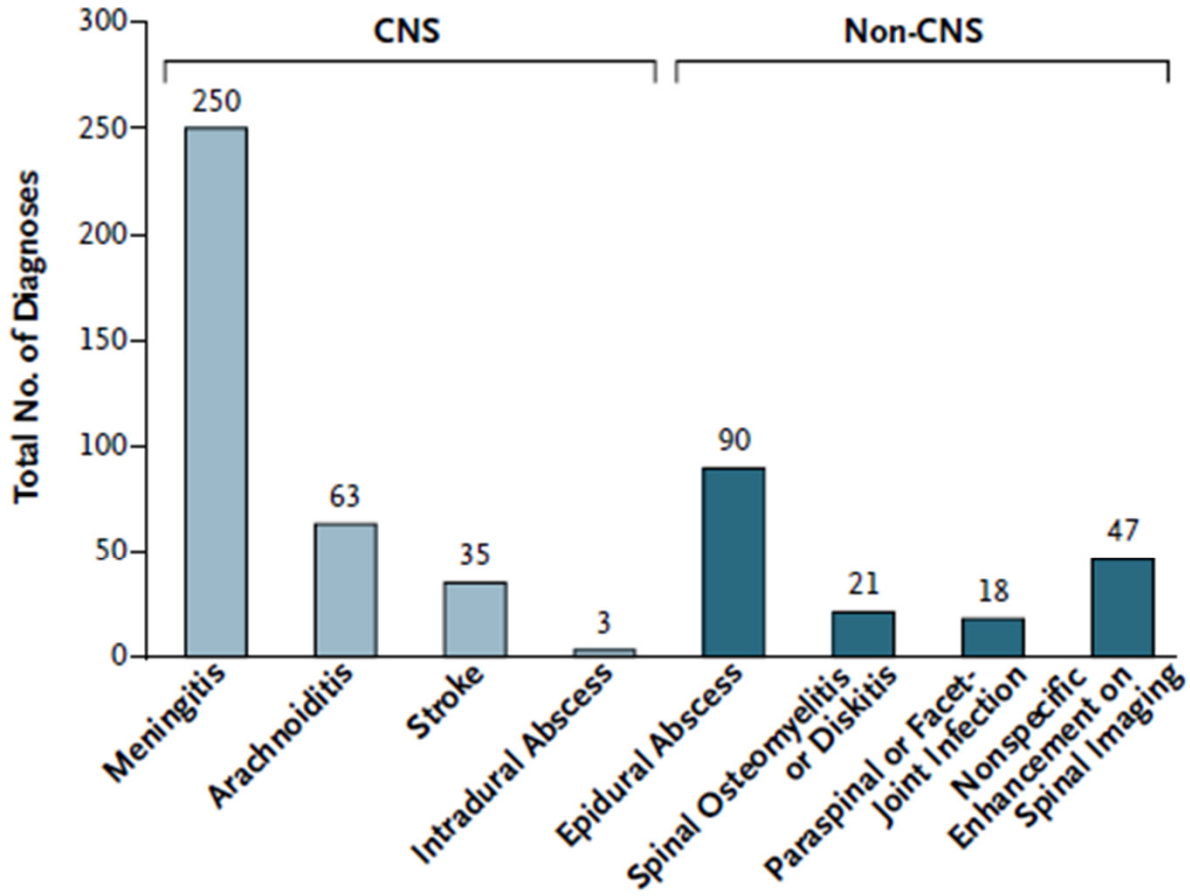


Figure 1. Distribution of Disease Types in the Clinical Cohort.

Shown are data for 328 patients, according to the total number of diagnoses. Patients with multiple diagnoses were included in more than one category.

Chiller TM, Roy M, Nguyen D et al. Clinical Findings for Fungal Infections Caused by Methylprednisolone Injections. N Engl J Med 2013; 369:1610-1619