The Changing Epidemiology of *Naegleria fowleri* and PAM in the United States

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Amoeba Summit – Florida Hospital for Children
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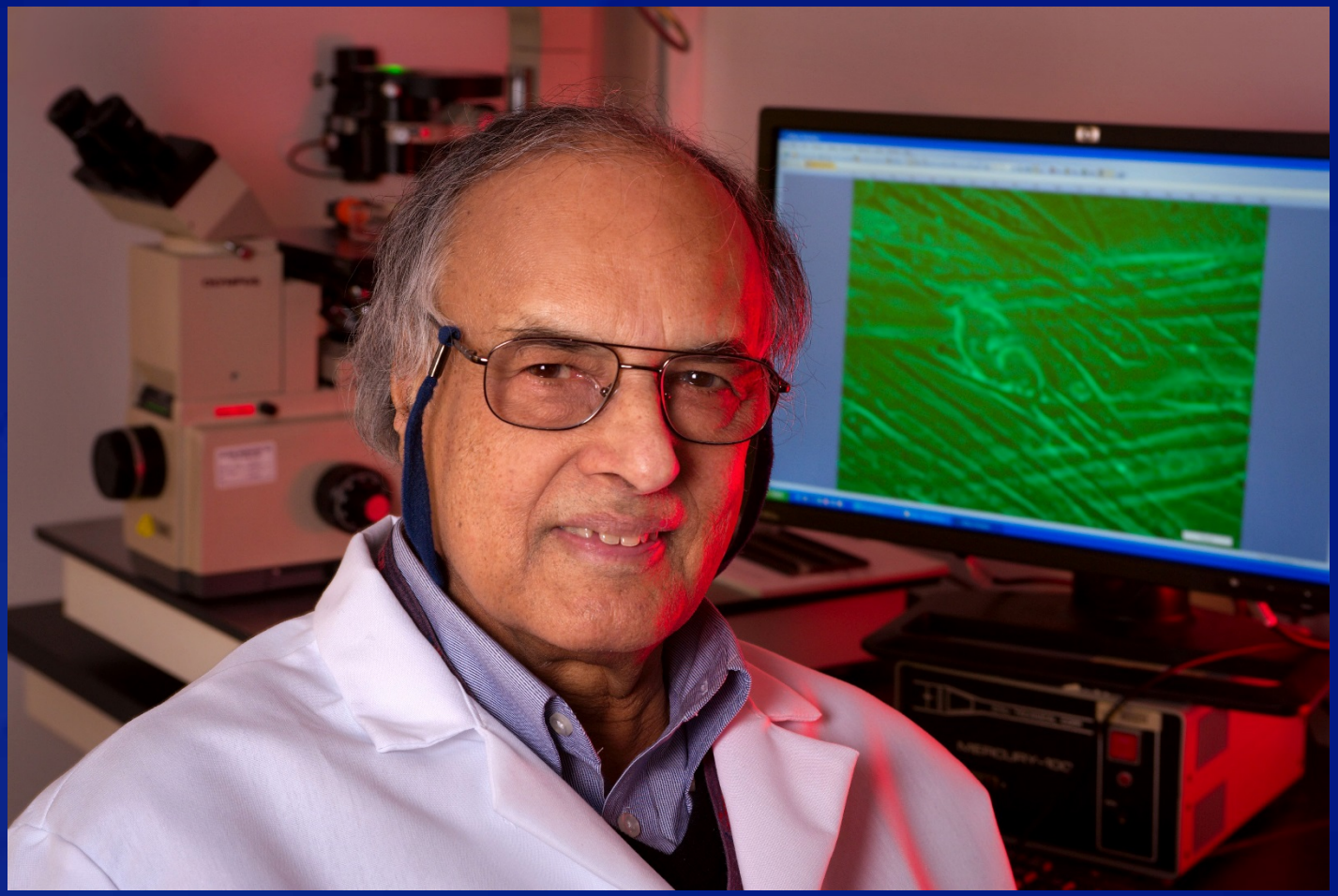
National Center for Environmental and Zoonotic Infectious Diseases
Division of Foodborne, Waterborne, and Environmental Diseases





History of Free-Living Ameba Work at CDC

Dr. Govinda Visvesvara



Dr. Michael Beach

Chief, Waterborne Disease Prevention Branch, Associate Director for Healthy Water, CDC

Why does CDC have a Free-living Ameba Program?

- Devastating impact
  - Patients and their families
  - The public – undermines confidence in activities such as swimming and using drinking water; effects on tourism
- Limited clinical, state and local public health experience
  - CDC is the front line resource for diagnostics, sampling, medical consultation, & communications
- Expanding geographic range (*Naegleria*)
- Transplant issues (*Balamuthia*)
- Eye & contact lens issues (*Acanthamoeba*)

Free-living Ameba Laboratory

- Diagnostic expertise
  - Capable of diagnosing *Naegleria*, *Balamuthia*, *Acanthamoeba*, and *Sappinia* infections
  - Most U.S. *Naegleria* and *Balamuthia* infections diagnosed as well as many international
  - CLIA certified
- Drug testing
- Environmental sampling and testing
- DNA-based detection and "typing"

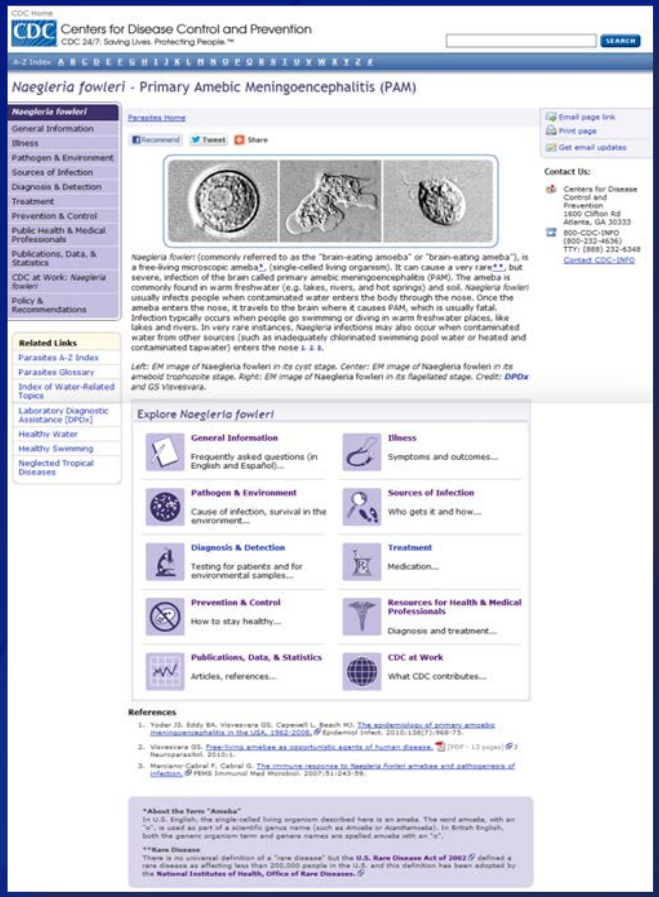
Free-living Ameba Clinical Consultations

- CDC staff available 24/7
- Arrange for diagnostic testing
  - DPDx telediagnosis
- Provide treatment recommendations
- Facilitate the use of investigational drug miltefosine
- Discussion of treatment and educational needs with national clinical groups

Free-living Ameba Epidemiology

- Disease tracking and investigation expertise
  - Voluntary case reporting
  - Epi-aid investigations: *Naegleria* cases, *Balamuthia* transplant clusters, *Acanthamoeba* keratitis outbreaks
- CSTE position statement to make amebic encephalitis nationally notifiable
- Assessment of organ transplant risk

Naegleria Health Communications



Naegleria website

Naegleria factsheet
(available on website)



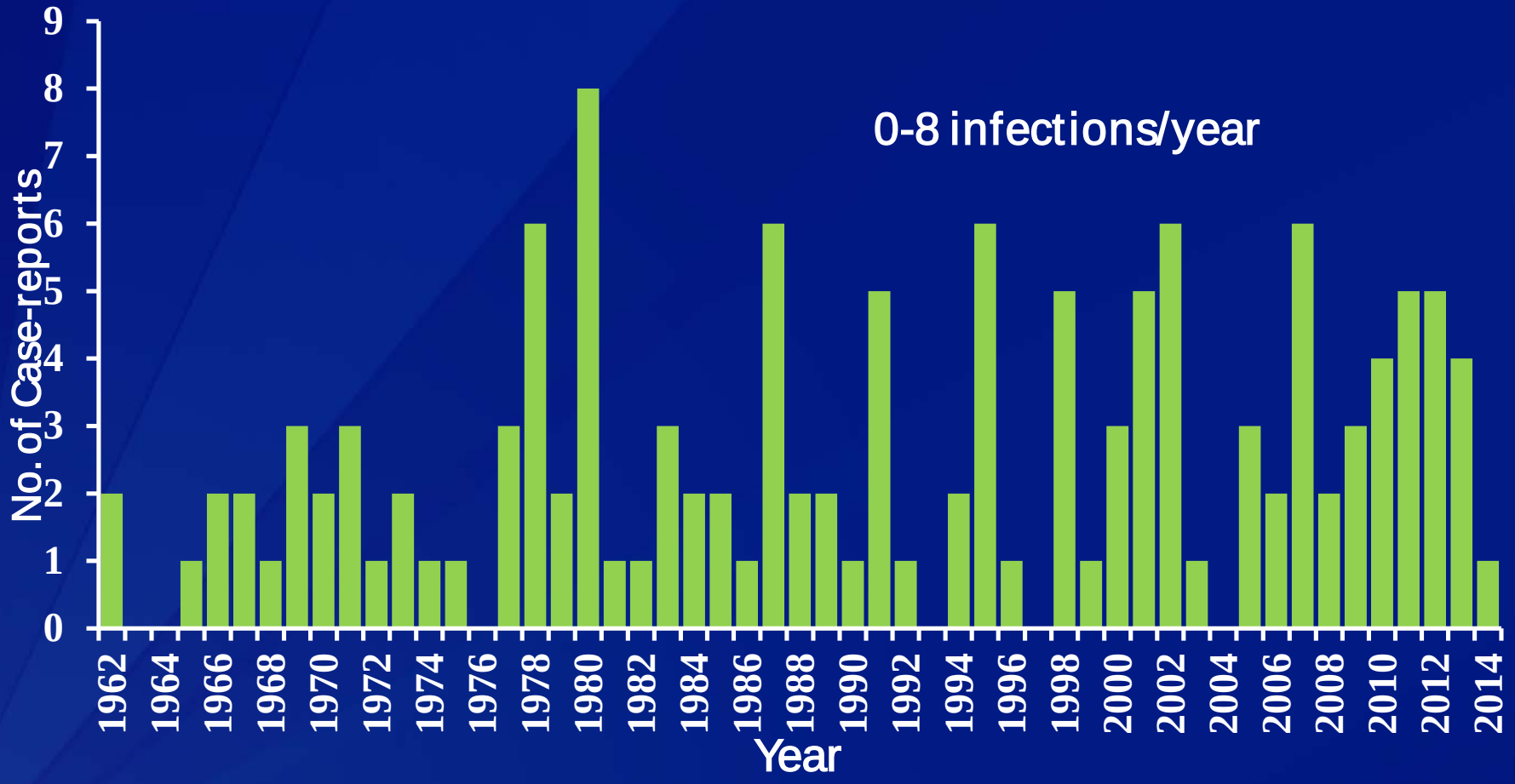


Naegleria Surveillance and Epidemiology

FLA Surveillance and Data Collection

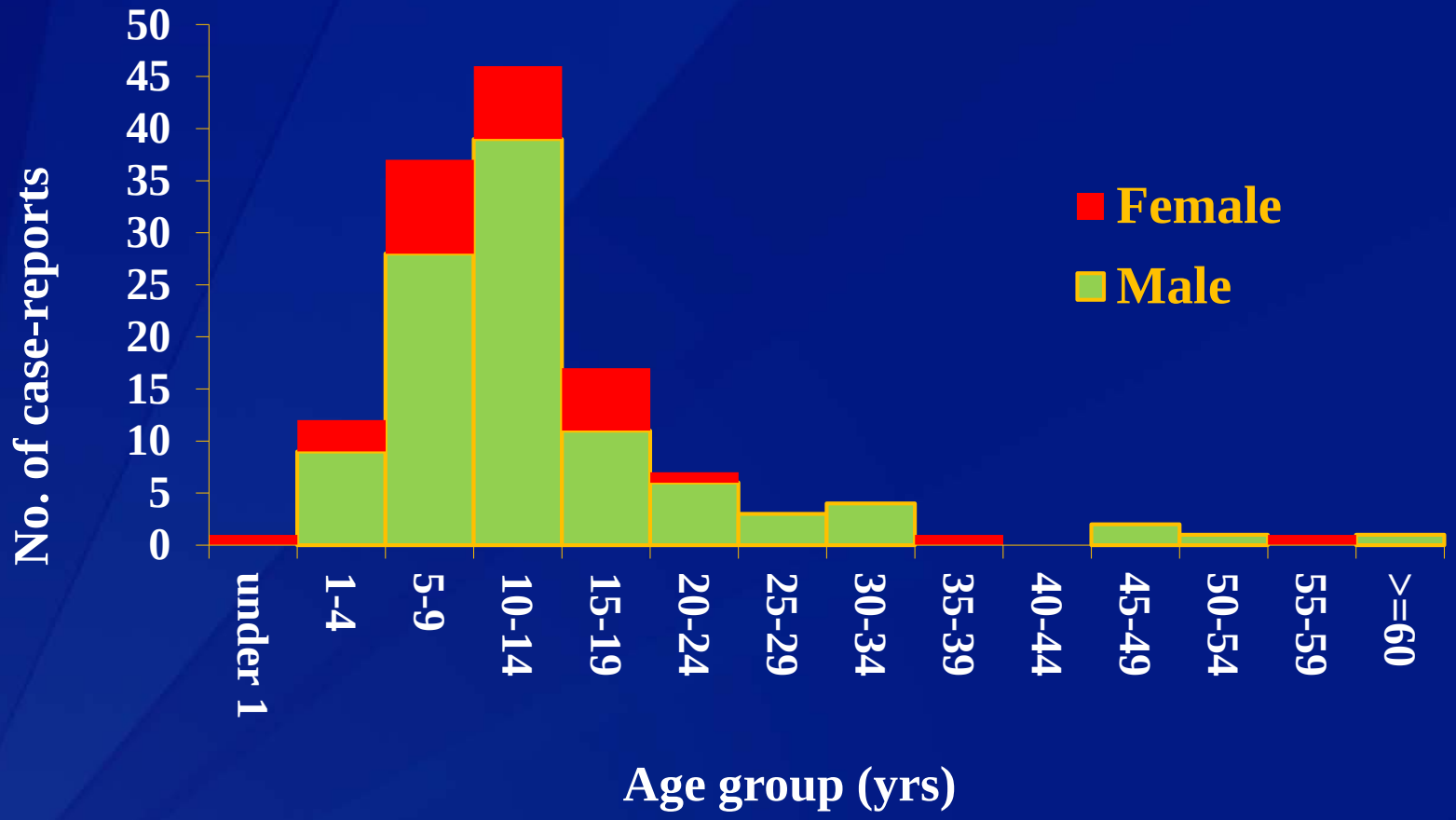
- Not nationally notifiable
  - Reportable in several states (FL, TX, LA, OK)
- CDC learns of cases because of laboratory diagnostics and clinical guidance
- Case report form completed, once lab-confirmed
  - Demographics, exposure history, medical history, treatment, outcome

Number of Case-reports of Primary Amebic Meningoencephalitis , by Year: United States, 1962–2014



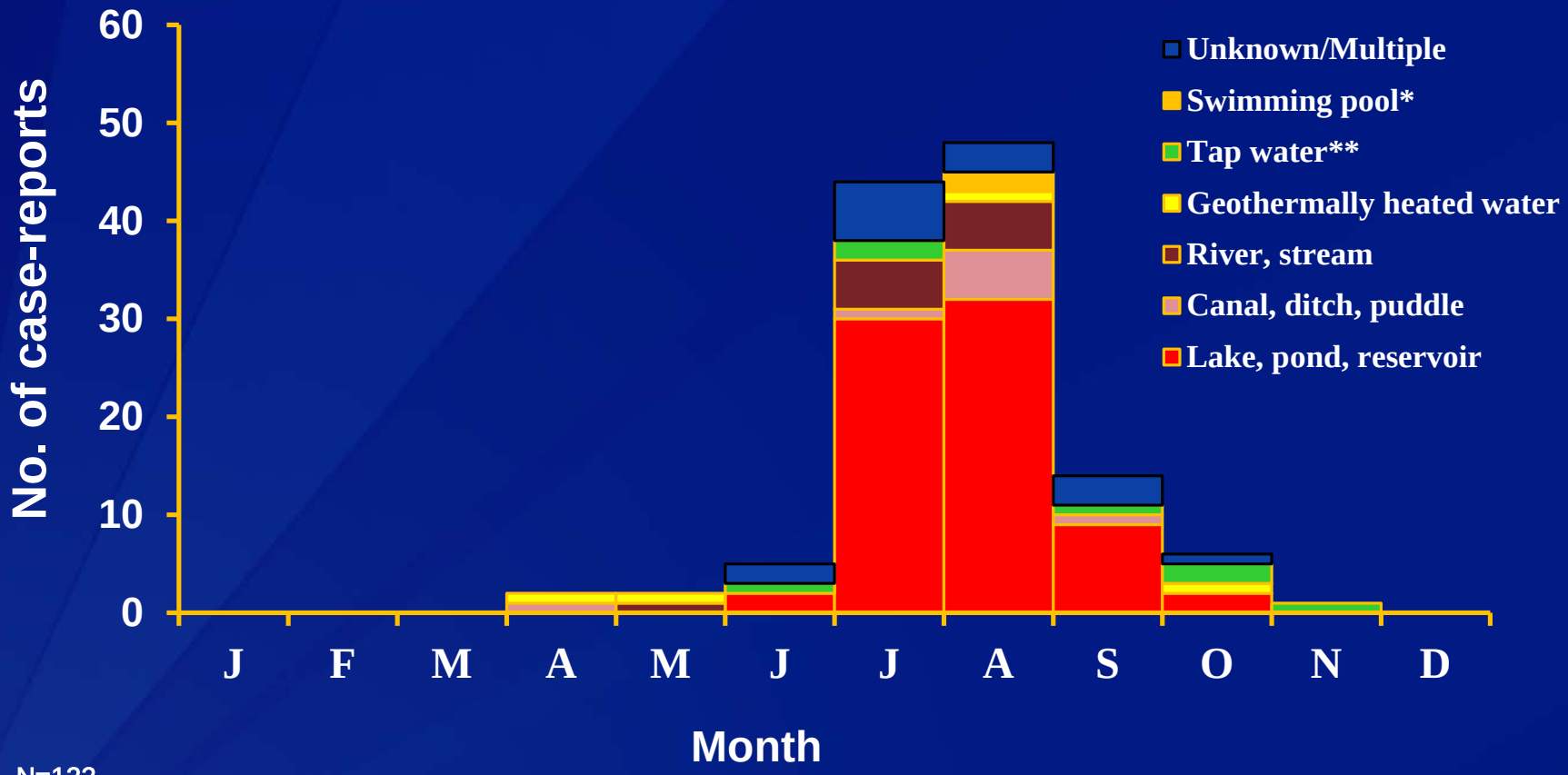
N=133; Year of exposure unknown for one case

Number of Case-reports of Primary Amebic Meningoencephalitis by Age Group and Gender—United States, 1962–2014



N=133; median age = 11; 77.4% male

Number of case-reports of Primary Amebic Meningoencephalitis, by month of illness onset and probable water exposure — United States, 1962–2014

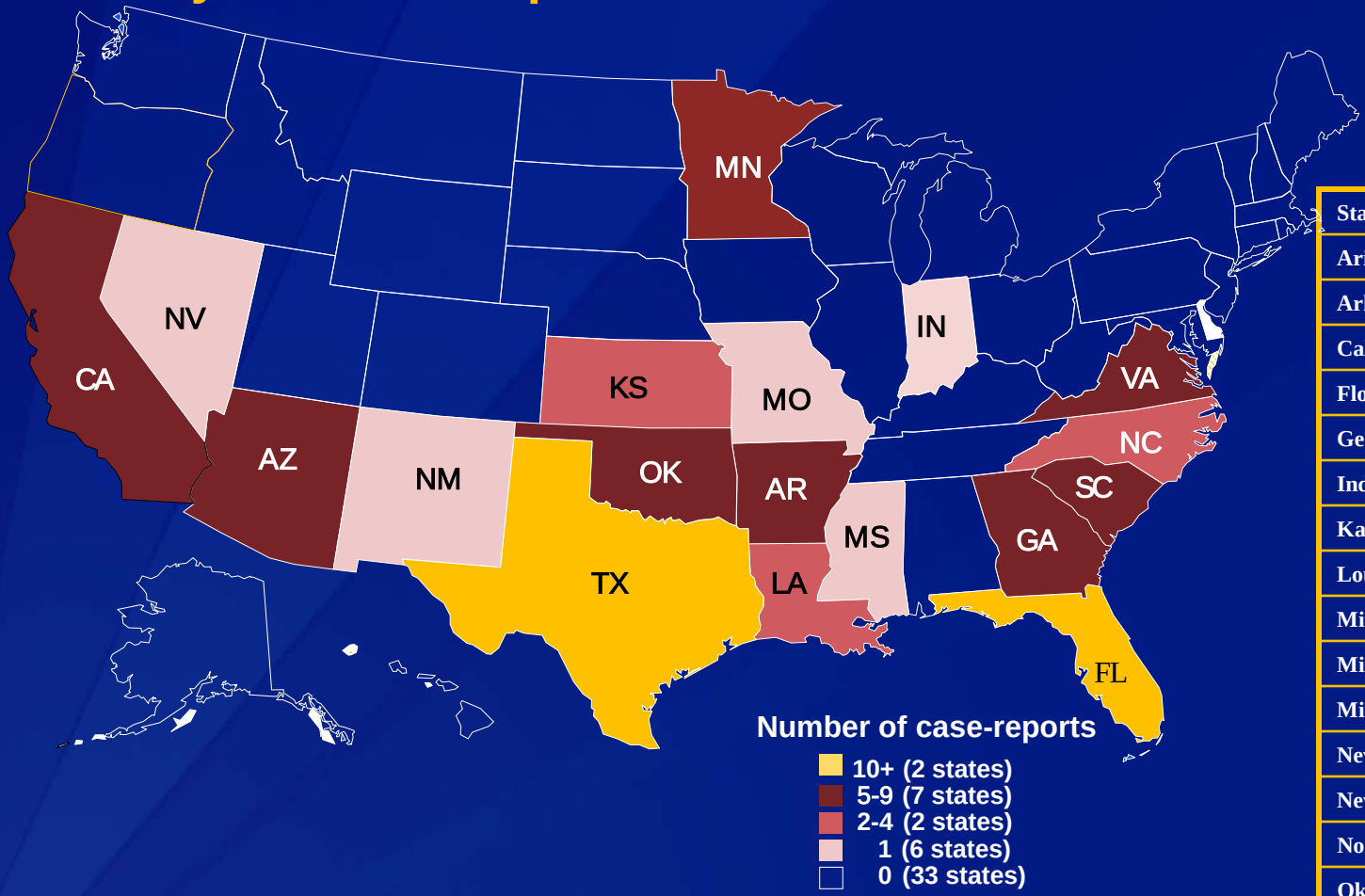


- N=122
- No information is available on the design, maintenance, or operation of these pools.

** Water was forced up the nose during use.

Month of illness onset unknown for 11 cases. Of those case-reports missing the month of exposure, probable water exposures included lake, pond, reservoir (N =5), unknown/multiple (N=5), and geothermal water (N=1)

Number of Case-reports of Primary Amebic Meningoencephalitis Caused by *Naegleria fowleri* (N=133) by State of Exposure*— United States, 1962–2014



State (Abbreviation)	# of Cases
Arizona (AZ)	7
Arkansas (AR)	6
California (CA)	7
Florida (FL)	34
Georgia (GA)	5
Indiana	1
Kansas (KS)	2
Louisiana (LA)	4
Minnesota (MN)	2
Mississippi (MS)	1
Missouri (MO)	1
Nevada (NV)	1
New Mexico (NM)	1
North Carolina (NC)	4
Oklahoma (OK)	6
South Carolina (SC)	7
Texas (TX)	32
Virginia (VA)	7

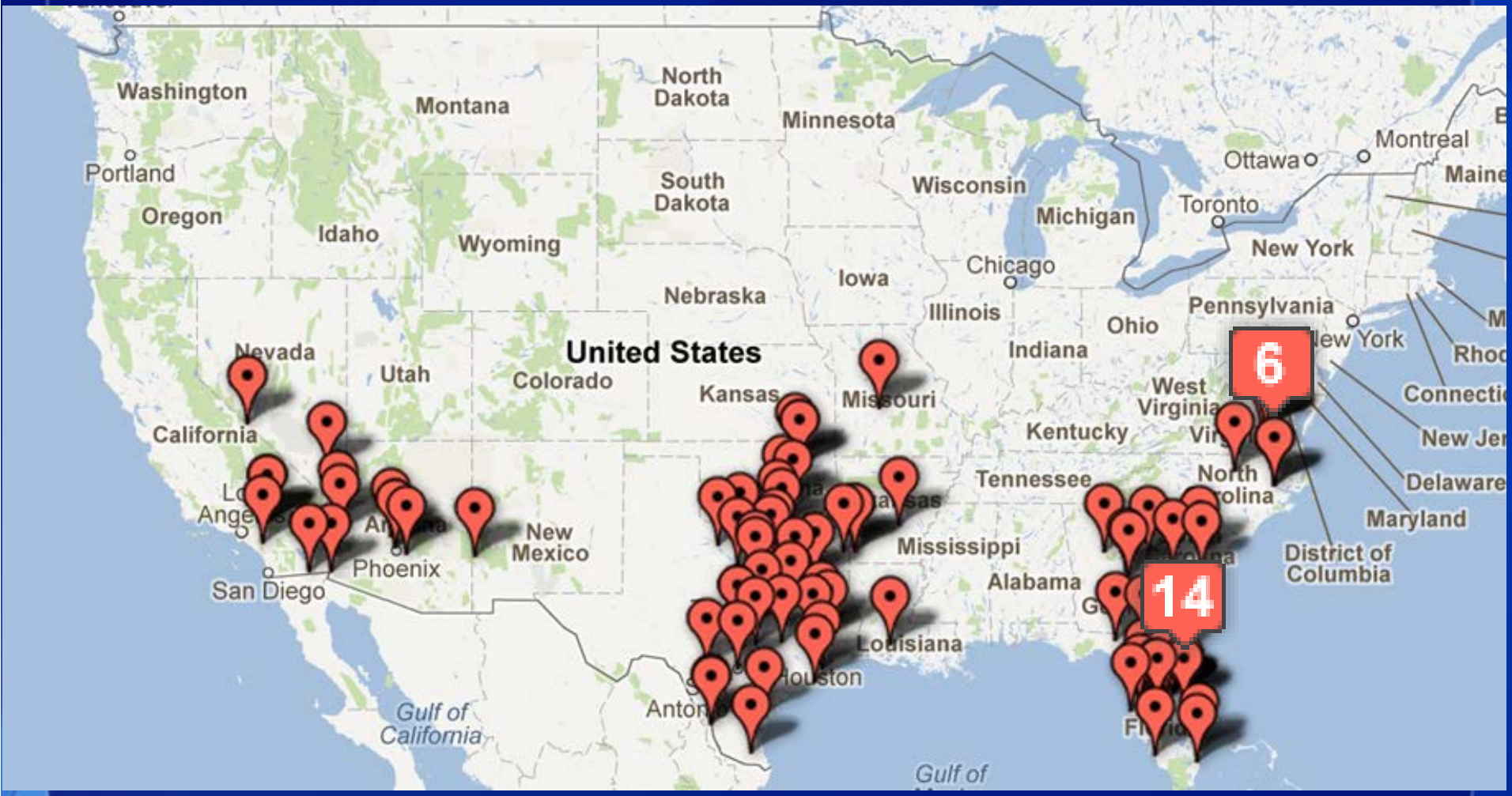
- State of exposure unknown for 4 cases.
- Does not include one case from USVI.





Geographic Distribution

Number of PAM Case-Reports by State of Exposure: United States, 1962–2009



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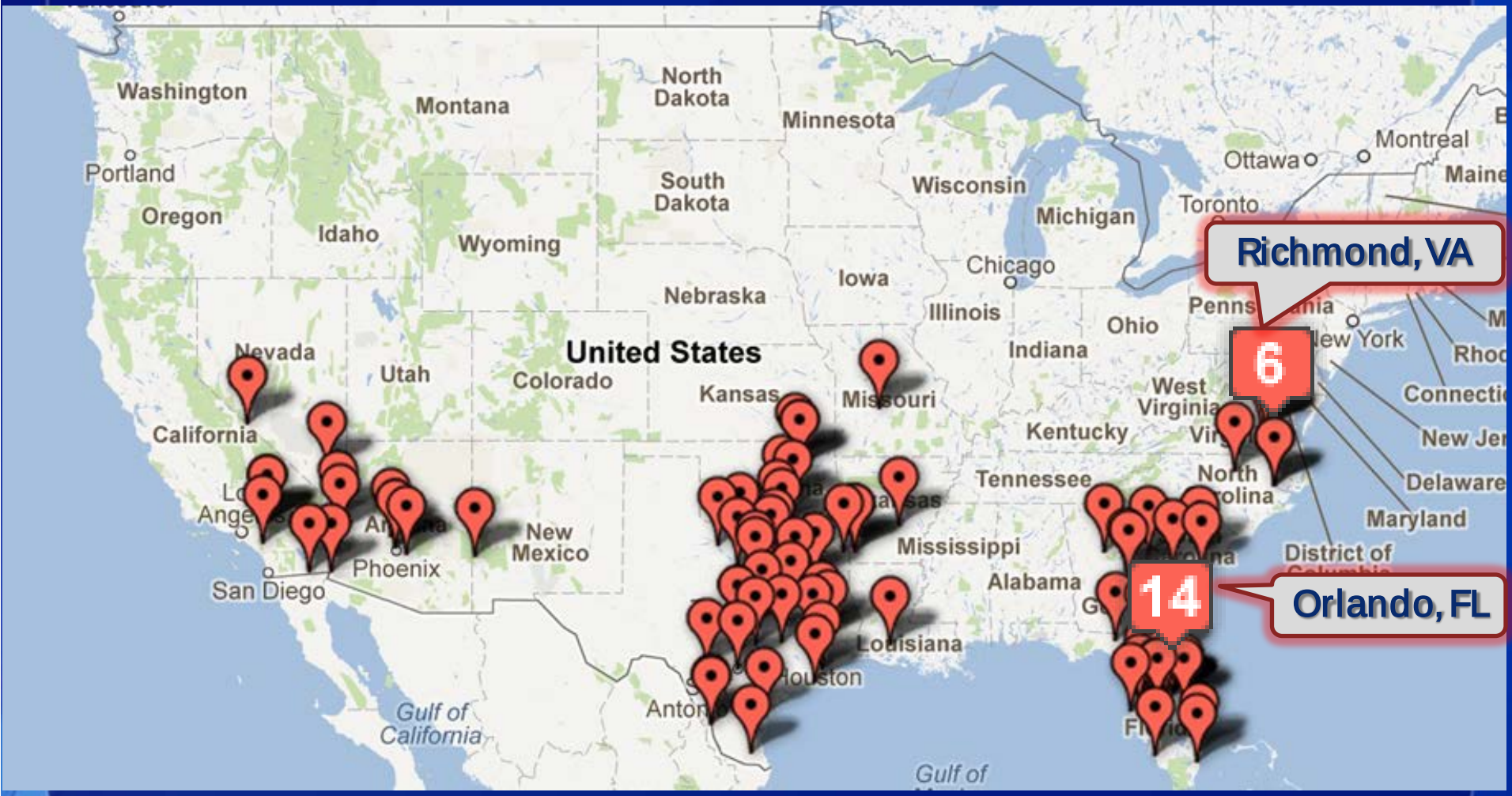

Number of PAM Case-Reports by State of Exposure: United States, 1962–2009

Number of PAM Case-Reports by State of Exposure: United States, 2010–2012

Changes in geographic range of PAM, 2010–2012?

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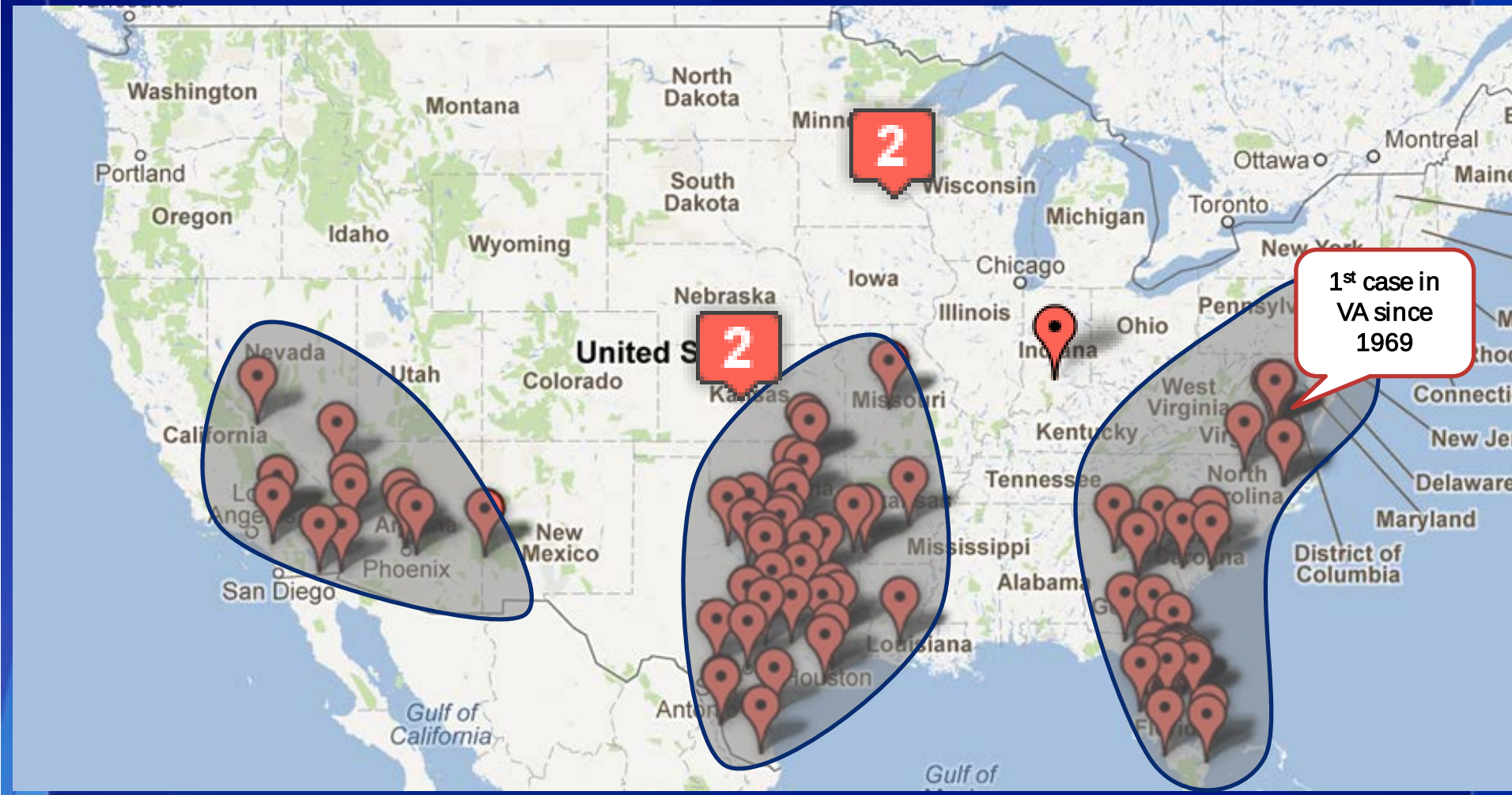
Geographic Range of PAM: 2010-2012

- First 2 cases in MN
  - 600 miles farther north than previous case in MO
  - During long, unusual heat spell
- First case reported in KS
- First case in VA reported since 1969
- First case in IN

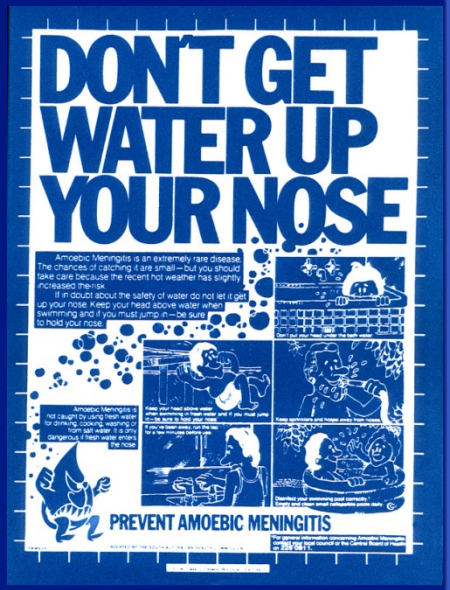
Number of PAM Case-Reports by State of Exposure: United States, 1962–2009, 2010–2014



Changing Transmission Routes of PAM

PAM Cases in Australia

- 1961–1972: 12 PAM cases in S. Australia
  - All occurred during summer
- 1972: *N. fowleri* isolated in overland pipeline
  - Chlorination instituted –0.5 ppm
  - Chlorine boosting at pumping stations throughout system
- 1972–1981: No deaths
- 1981: Single fatal PAM case in city at the end of system
  - Very warm summer
  - *N. fowleri* detected
  - Chlorination added to city at the end of system
- Continue to monitor for thermophilic amebae in drinking water

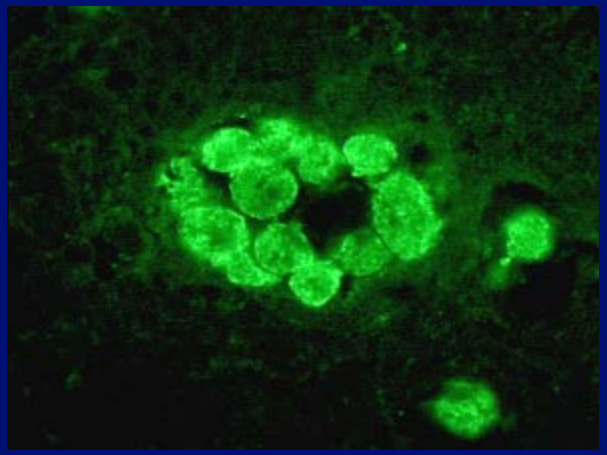


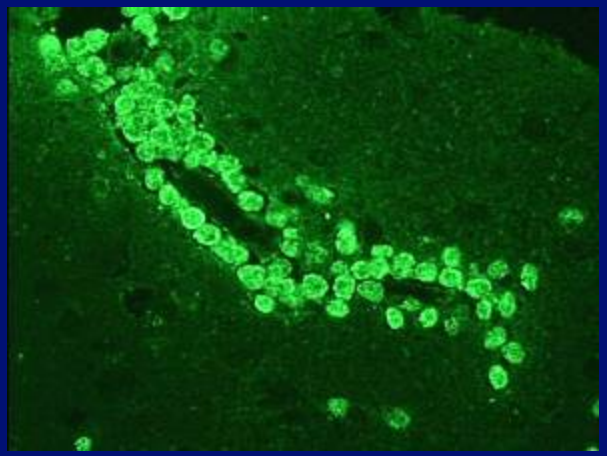
Naegleria fowleri Outbreak: Arizona, 2002

- October 2002
- Two 5-year old children died within 8 hours of each other in same town
- Suspect PAM
- First instance of simultaneous infections documented
- What was recreational water contact?

Naegleria fowleri Outbreak: Arizona, 2002

- Epidemiologic investigation
  - Ruled out recreational exposure to freshwater
  - Common exposure to municipal tap water system through water activities (tub and pool)
  - Groundwater wasn't required to be chlorinated or filtered
- *Naegleria* detected in household water samples





Louisiana, 2011

- **June: Adult male with PAM**
  - No recent recreational water contact based on family interviews
- **September: Adult female with PAM**
  - Different town (350 miles) than previously reported case
  - No recent recreational water contact based on family interviews

Louisiana, 2011

- Both cases regular users of neti pots for nasal irrigation
- Both residential premise plumbing systems positive for *Naegleria fowleri*
  - Hot water heaters set to low heat settings
  - FLA in premise plumbing common (~79% of 467 households in OH study)
- Municipal water system samples negative

Nasal Irrigation and Neti Pots

- At least 1 death in 1970's in Australia due to rinsing of nasal passages in shower
- Deaths in healthy young adults in Pakistan likely from Muslim ritual ablutions: putting water up nose
- Neti pots
  - Ancient yogic cleansing method
  - Used for nasal irrigation during illness and on regular basis
  - Recommended by Dr. Oz/Oprah in 2007
    - Sales apparently increased 3-4-fold
    - Millions sold per year
- Lesson: use boiled, sterile, distilled water-NOT tap water

U.S. Virgin Islands, 2012

- 47 year-old Muslim male from St. Thomas, USVI died
- Patient's cerebrospinal fluid (CSF) showed motile amebae
- No recreational water exposure and practiced ritual ablution including nasal rinsing
- Water sources
  - Home
    - Untreated groundwater from well
    - Untreated rainwater from cistern
    - Both connected to premise plumbing system
  - Mosque
    - Treated municipal water (desalinated and chlorinated)

Ritual Ablution

- Mandatory Islamic cleansing
- Preparation for prayer
- 5 times per day
- Methodical cleansing
- May include nasal rinsing

Environmental Investigation in Mosque

Sample	Chlorine (mg/L)	*N. fowleri* PCR
Ablution fountain (water)	0.02	Negative
Ablution fountain (swab)	Not tested	Negative
Mosque filter	Not tested	Negative

Environmental Investigation in Home

Sample	Chlorine (mg/L)	*N. fowleri* PCR
Shower head (water)	<0.02	Positive
Hot water heater (water)	<0.02	Positive
Shower head	Not tested	Positive

Naegleria in Pakistan

- 2008–2009: 13 fatal *N. fowleri* infections in Karachi, Pakistan
  - Limited recreational water exposure
  - All performed ritual ablution
- 2010: 1 death; exposure through nasal cleansing
- 2012: Reportedly 22 deaths
  - Very little information on exposures
  - Tap water testing
- 2013: Reportedly two deaths in May
- 2014: 10 cases reported so far

Shakoor 2011, EID

Louisiana, 2013

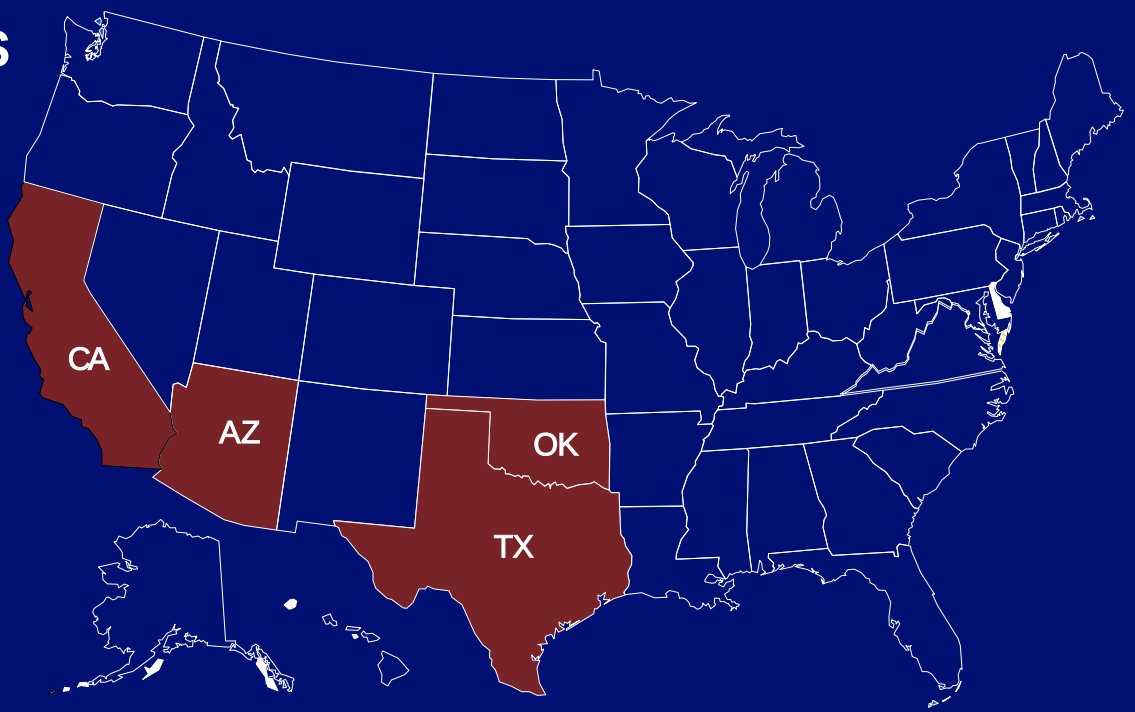
- 4 y/o child diagnosed with PAM on autopsy
- No contact with lake, pond, river, etc.
- Played all day on slip-n-slide
  - Increased risk for water going up nose
- Water samples, hoses, slip-n-slide shipped to CDC
- *Naegleria* in residential plumbing system, hot water heater, hoses supplying slip-n-slide
- Same parish as 2011neti pot-associated infection
  - Tested municipal water system (negative in 2011), positive in 2013

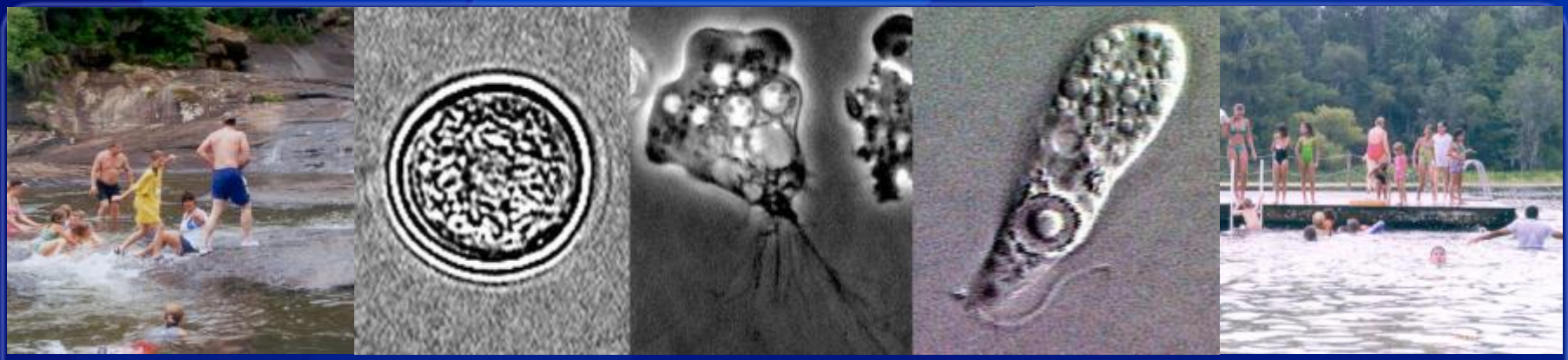
Changing Epidemiology of PAM: 2010-2013

- First cases reported in northern states (MN, KS, and IN)
- First cases associated with tap water and neti pot use
- First case associated with ritual nasal cleansing
- First death associated with water from a treated drinking water system

Summer 2015 Update

- 5 confirmed cases, 5 deaths
- 4 lake exposures, 1 untreated pool
- 3 females, 2 males
- Median age: 21





CDC Assistance

Miltefosine is available through CDC

- Promising treatment for FLA
  - *In vitro* activity
  - Successfully treated a few *Acanthamoeba* and *Balamuthia* cases
- Approved in the U.S. March 2014 for leishmaniasis treatment
- Previously only available under Emergency Investigational New Drug (IND) protocol from FDA
- Available under CDC's expanded access IND since summer 2013

Sending Miltefosine - The Logistics

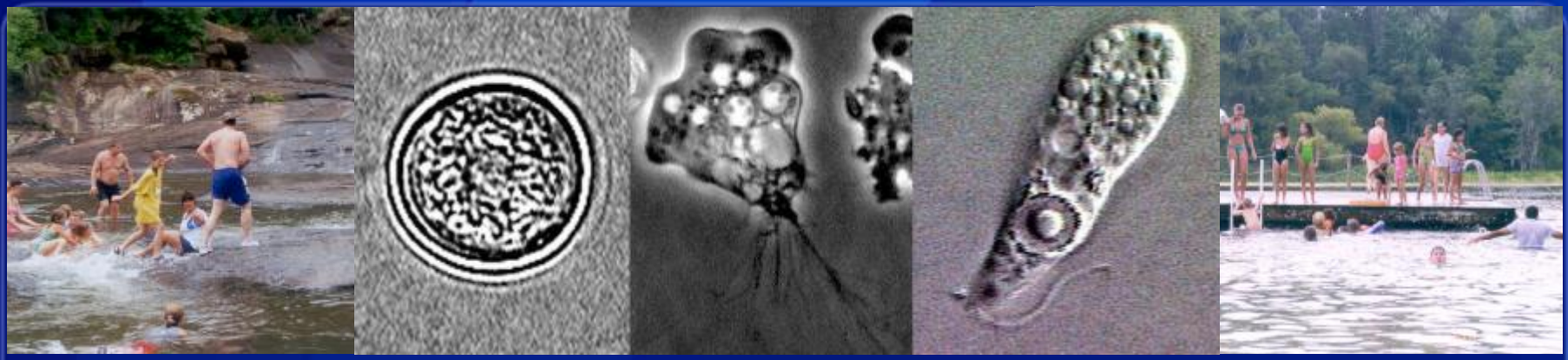
- Discuss case and determine need for drug
- Get information needed to ship and calculate dose
  - Determine how quickly drug should be shipped – FedEx overnight vs. next flight out of Atlanta
- FDA IND paperwork
  - Form 1572
  - Treating physician CV

PAM and Organ Transplantation

- Risk of transmission via organ transplant is not zero
- Evidence of *Naegleria* outside the CNS
- Seek permission to do autopsies in PAM patients
- Encourage pathologists to consult with CDC prior to performing autopsy

Next Steps and Future Directions

- Laboratory: whole genome sequencing to compare clinical to environmental *Naegleria* strains; development of point-of-care diagnostics
- Environmental: water sampling in both natural water bodies and drinking water systems, predictive modeling – what lakes put people at higher risk?
- Epi: make amebic encephalitis nationally notifiable
- Communications: online CME course, health promotion materials



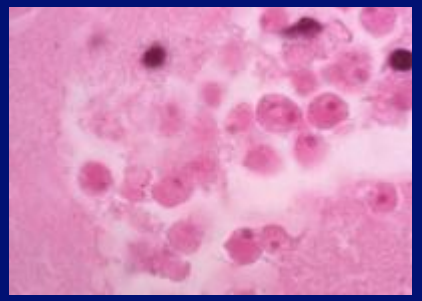
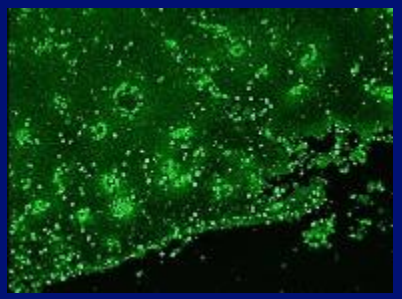
Conclusions

Conclusions

- Geographic range shifting northward
  - Also seen with other climate sensitive pathogens such as *Vibrio*, harmful algal blooms
  - Climate change indicator?
- Drinking water (via neti pots, nasal rinsing) is now playing a role in transmission
  - Ability to colonize premise plumbing, similar to other thermophilic, environmental organisms (*Legionella*, *Pseudomonas*; NTM/MAC)
  - Effect on drinking water policy?
- Miltefosine is available through CDC – please call us!

CDC Service

- 24/7 diagnostic and clinical assistance for free-living amebae
  - DPDx—telediagnosis (http://www.dpd.cdc.gov/dpdx/HTML/Contactus.htm)
  - Clinical sample testing (microscopy, PCR)
    - call EOC 770-488-7100
  - Clinical guidance and support
    - call EOC 770-488-7100

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