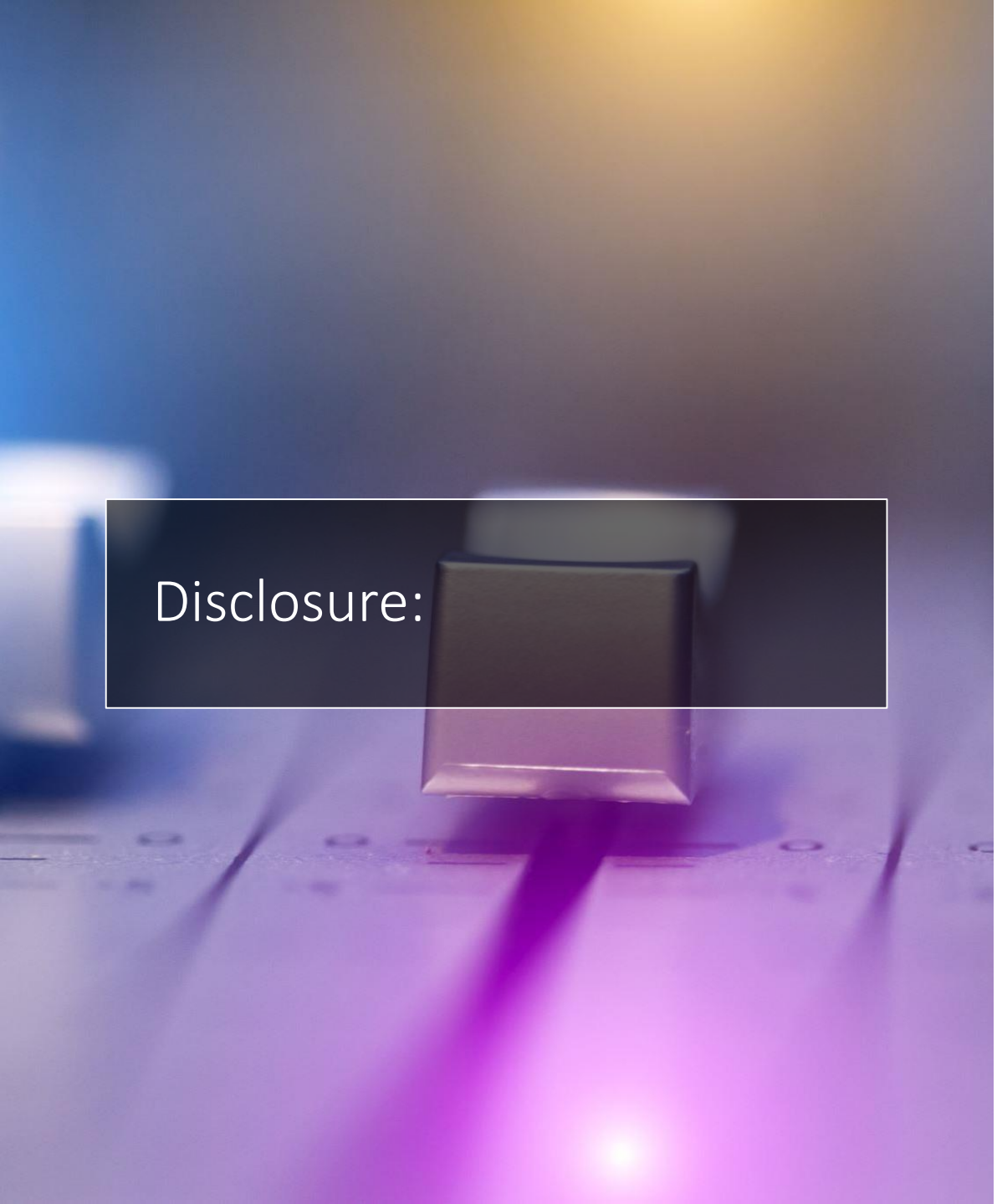
# Primary Amebic Meningo Encephaliltis


- Kevin Sherin MD
  Adjunct Professor
  Family Medicine, at UCF and FSU Colleges of Medicine, Orlando
- Founding Faculty, Orlando College of Osteopathic Medicine (Proposed)



# Disclosure:

- ***Speaker has no disclosures***

# Objectives:

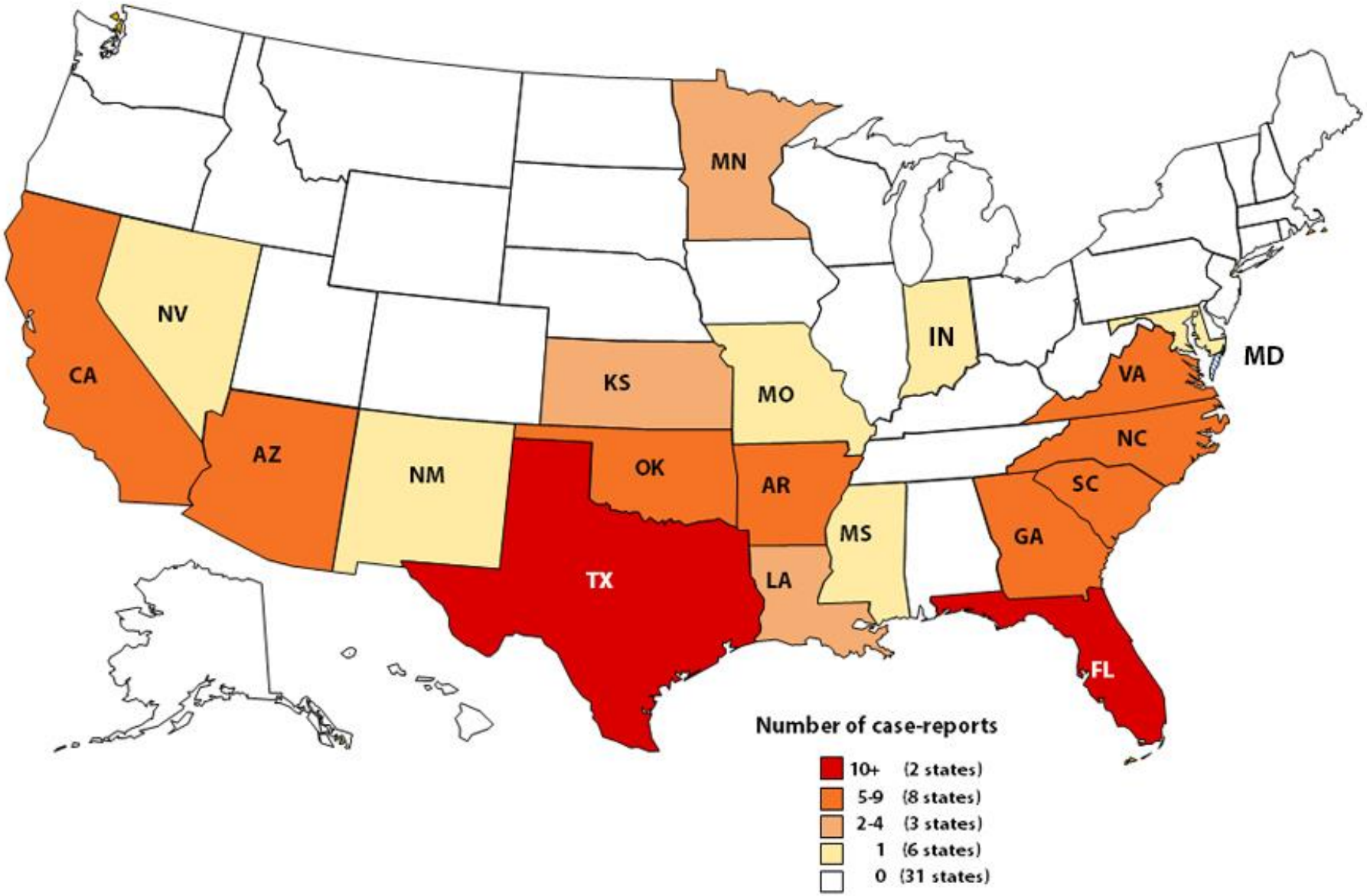
- The issue
- Clinical guidelines for rapid diagnosis
- Laboratory procedures
- Treatment
- Awareness efforts

Causative agent of Primary Amebic: Meningoencephalitis (PAM) Naegleria Folweri

# CFR: 97%

Media: “Brain-eating disease”- very accurately described

Image: Francine
Marciano- Cabral, PhD,
Virginia Commonwealth University


MN
NV
CA
IN
MD
KS
MO
VA
AZ
NM
OK
AR
NC
SC
MS
GA
TX
LA
FL
Number of case-reports
10+ (2 states)
5-9 (8 states)
2-4 (3 states)
1 (6 states)
0 (31 states)

# GLOBAL INCIDENCE

# Environmental Factors

Warm fresh water is classic- but water temps may vary

- Municipal water supplies
- Diving and wakeboarding in lakes
- Splash pads
- Lawn hoses
- Ritual nasal ablutions
- Netti Pots
- Inadequately chlorinated pools
- Southern tier of states, but changing epi, Why?

# PAKISTAN

- KARRACHI PAKISTAN IS A KNOWN HOT SPOT
- SPECIALIZED EXPERTISE IN TREATMENT
- NETTI POTS AND RITUAL ABLUTION
- GLOBAL TRAVEL
- A DISEASE FROM ANYWHERE CAN BE 24 HOURS AWAY FROM FLAGLER HEALTH ED

# US Map of PAM 2022
# CDC

CURRENT ESTIMATE IS 16 CASES PER YEAR IN US

BASED ON RETROSPECTIVE DATA ANALYSIS OF LIKELY PROFIILE OF CASES

AN AVERAGE OF 3 CASES ARE CONFIRMED BY THE LABORATORY IN A YEAR

PAM DISTRIBUTION IS WORLDWIDE WITH MANY COUNTRIES (AND STATES) NEVER REPORTING

INCREASED REPORTING IS A KEY TO KNOWING THE TRUE INCIDENCE OF PAM

# The Route of Infection of Naegleria fowleri

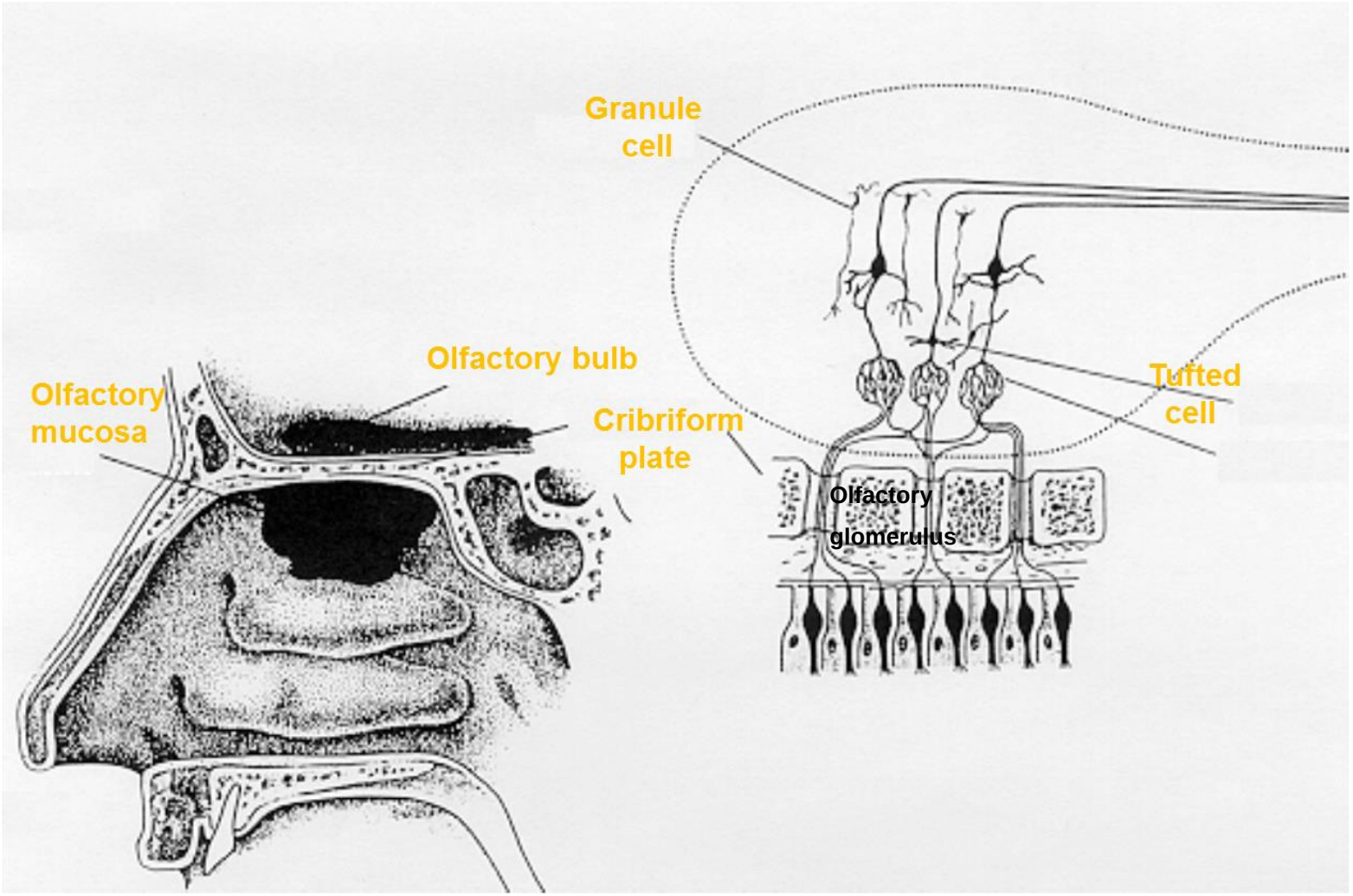
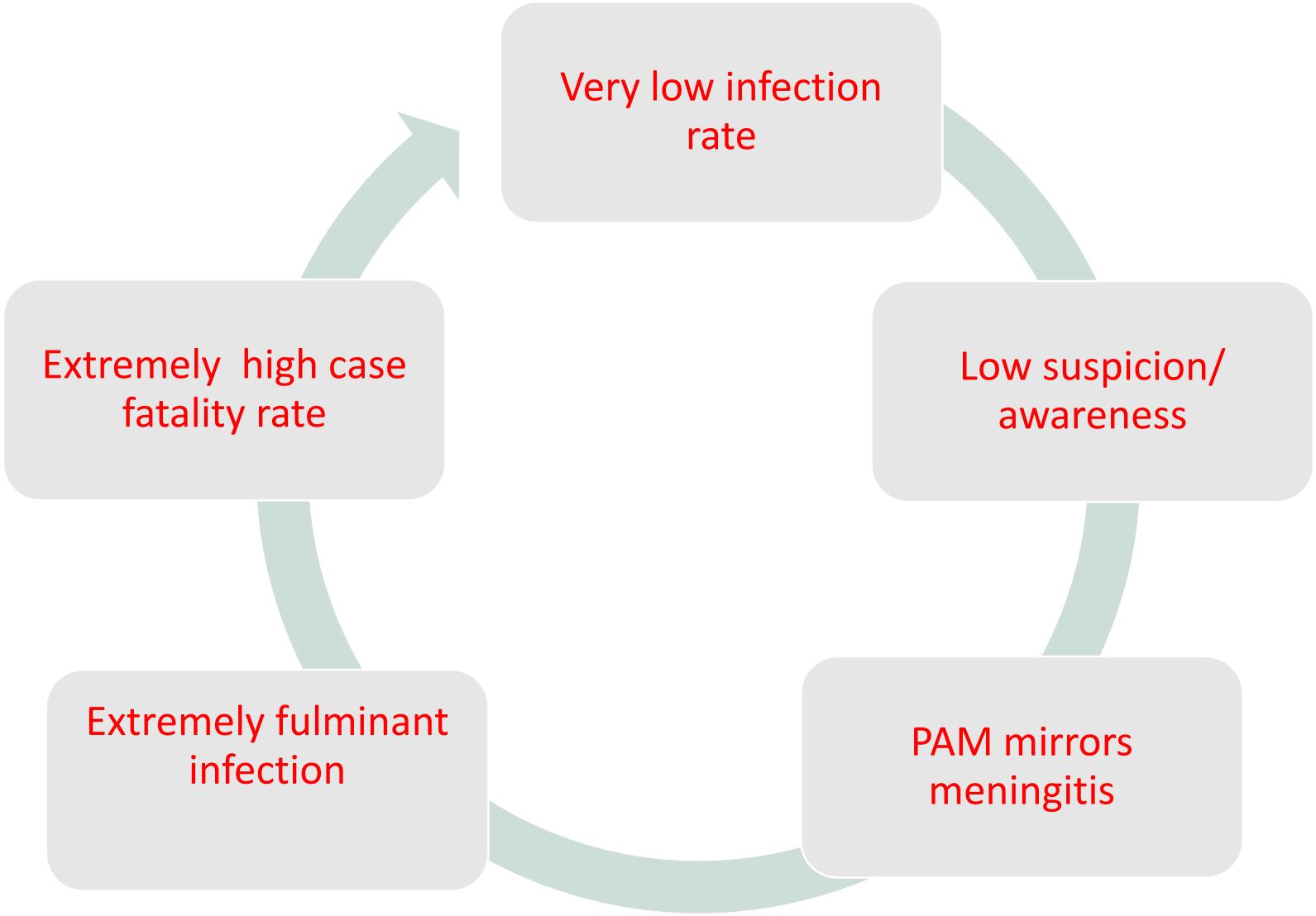



Image: Francine Marciano- Cabral, PhD, Virginia Commonwealth University

# PAM- The Issue:



# Fulminant

*Naegleria fowleri* infection (PAM) is fulminant in every sense of the word

- The median time from onset of symptoms to death is 5 days
- The median time from exposure to early symptoms is 5 days
- The early signs/symptoms last a median of 2 days
- The CNS symptoms last for a median of 3 days (range, 0-10 days)

*Diagnosis, Clinical Course, and Treatment of Primary Amoebic Meningoencephalitis in the United States*, 1937–2013 Capewell, et al J Ped Infect Dis. 2014

## Low incidence = low awareness

- Public
- Physicians
- Laboratory

## Mimics bacterial/viral meningitis

## CT, MRI – negative (“early presentation” cases)

## Laboratory

- Gram Stain: very difficult to see

# Clinical Guidelines for Rapid Diagnosis of PAM

Suspect PAM

Meningitis symptoms?

National Park Service

Nasal freshwater exposure history (especially within 2 weeks of presentation)……is the key!

- "Early" Signs and Symptoms

  - <u>Vague, "flu-like" (28%)</u>

    - Headache (92%)
    - Fever (84%)
    - Nausea/Vomiting (65%)
    - Fatigue (16%)
    - Earache (2%)

*Diagnosis, Clinical Course, and Treatment of Primary Amoebic Meningoencephalitis in the United States*, 1937–2013 Capewell, et al J Ped Infect Dis. 2014

# Clinical Guidelines, continued
## "Late" Signs and Symptoms

CNS (72%)

- Nuchal rigidity (37%)
- Lethargy (29%)
- Confusion/ disorientation (25%)
- Anorexia (17%)
- Irritation/ combativeness (12%)
- Photophobia (10%)

*Diagnosis, Clinical Course, and Treatment of Primary Amoebic Meningoencephalitis in the United States*, 1937–2013 Capewell, et al J Ped Infect Dis. 2014

# Clinical Guidelines, continued

(1) Suspect PAM (signs and symptoms with history of nasal freshwater nasal exposure within past 14 days)

(2) Collect CSF - Order specific lab tests STAT



(3) Call CDC at 770-488-7100 for 24/7 consultation

(4) Report suspected case to Local Health Department

CDC: https://www.cdc.gov/parasites/naegleria/diagnosis.html

# Laboratory Procedures

Direct visualization: CSF

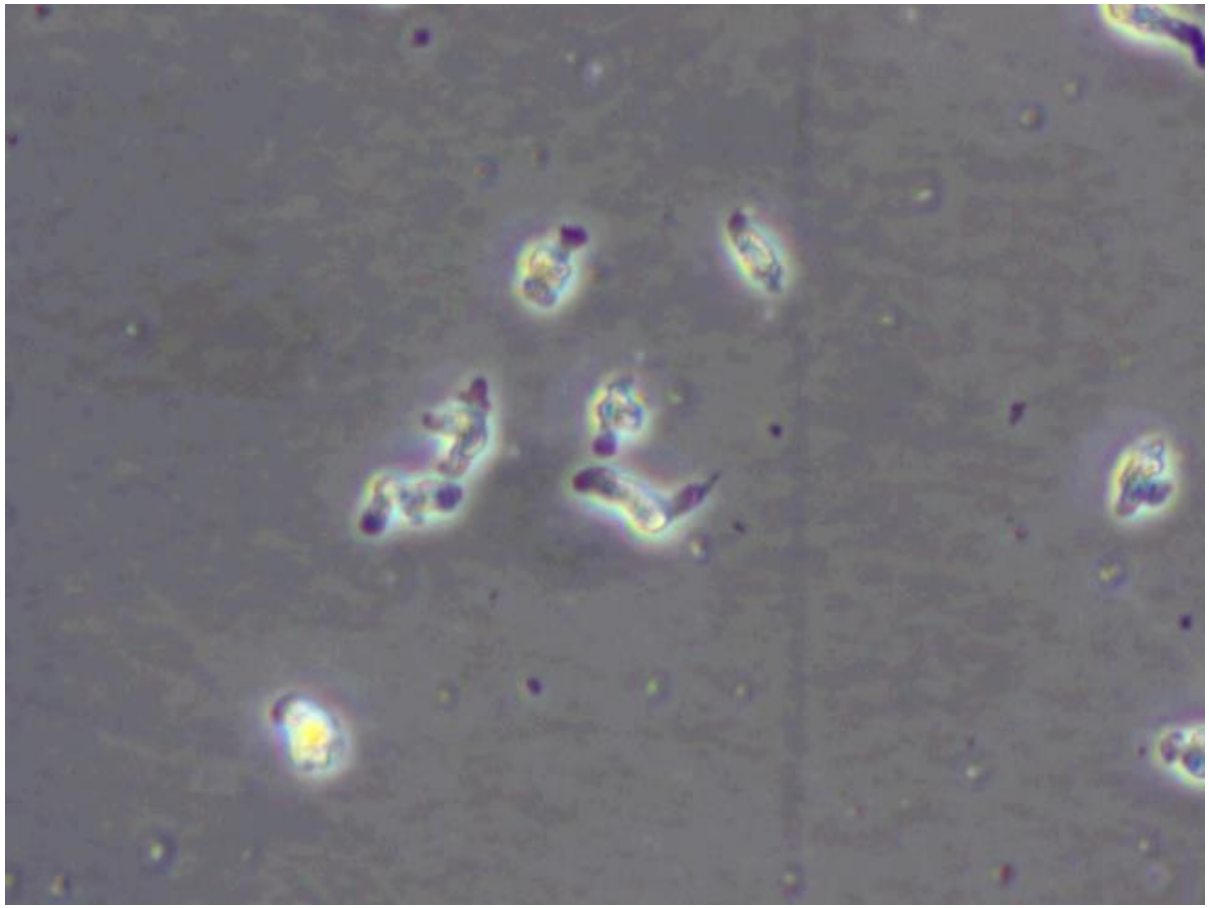
Microscopic (Local lab) (preferably, phase contrast)

(1) motility on CSF wet mount
(usually identified in wet prep
in counting chamber)
(2) Wright-Giemsa stain, Trichrome

CBC: Leukocytosis

CSF: RBC's present, low glucose, high protein

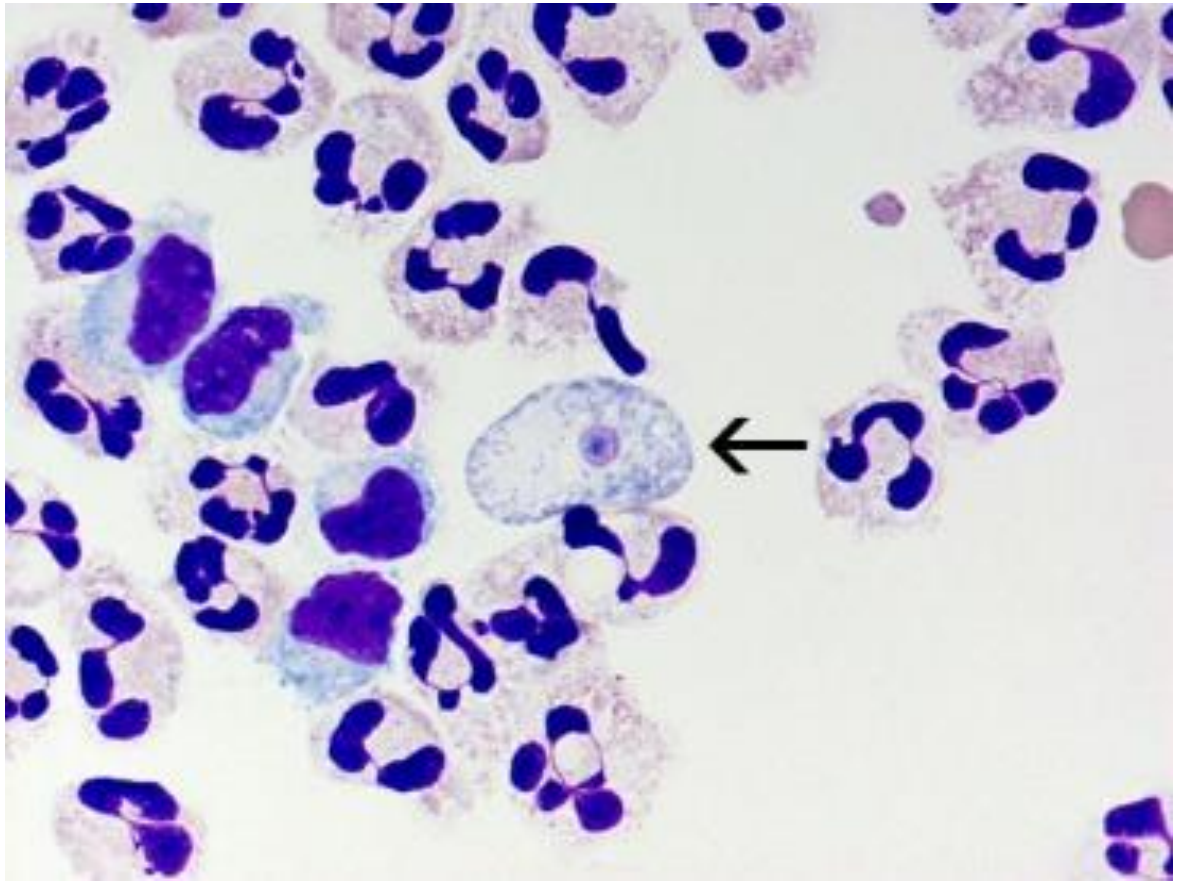
# Laboratory Procedures, continued



(from culture, not CSF)

Courtesy: CDC.gov (http://www.cdc.gov/parasites/naegleria/naegleria-fowleri-images.html)

# Laboratory Procedures, continued



Cytospin of CSF- Giemsa-Wright Stain

Courtesy: CDC.gov (http://www.cdc.gov/parasites/naegleria/naegleria-fowleri-images.html)

## Laboratory Procedures, continued

Best Practices for Rapid Laboratory Detection of *Naegleria fowleri*

- Utilize standard order code for amoeba exam

  (alerts the lab and allows for standard reporting)

- Address laboratory testing for CSF with urgency

  Delivery to the lab, workflow within the department

- Avoid use of automation for CSF cell counts

  Automation does not allow for ameba detection

  If using automation, prepare a wet prep as a “backup”

## Laboratory Procedures, continued

- SEROLOGIC TESTS FOR PAM ARE ONLY AVIALABLE FROM THE CDC
- N MULTICHANNEL ANALYZER, PCR
- HENCE IT IS WISE TO TREAT PRESUMPTIVELY UNTIL THIS NEARLY UNIVERSALLY FATAL INFECTION IS CONFIRMED
- SOUTHERN STATES SHOW A HIGHER PREVALENCE OF AMOEBA ANTIGENS IN SERUM
- HENCE SUBCLINICAL OR ASYMPTOMATIC CASES ARE POSSIBLE
- THE AVERAGE OF LABORATORY CONFIRMED CASES PER YEAR IS ONLY 3,
- HENCE 13 CASES PER YEAR ARE LIKELY MISSED ON AVERAGE

# There Are Successful Outcomes

- **1978: California**
- **2013: Little Rock , Arkansas**
- **2016: Orlando, Florida**

The key is *early recognition* and aggressive treatment:

Signs and symptoms: WITH HISTORY OF FRESHWATER EXPOSURE

Bing images

# Treatment

http://www.cdc.gov/parasites/naegleria/treatment-hcp.html

**Successful Treatment of an Adolescent With *Naegleria fowleri* Primary Amebic Meningoencephalitis**

W. Matthew Linam, Mubbasheer Ahmed, Jennifer R. Cope, Craig Chu, Govinda S. Visvesvara, Alexandre J. da Silva, Yvonne Qvarnstrom, Jerril Green

http://pediatrics.aappublications.org/content/135/3/e744.long

- Aggressive management of Intracerebral pressure
- Drug Regimen  CDC

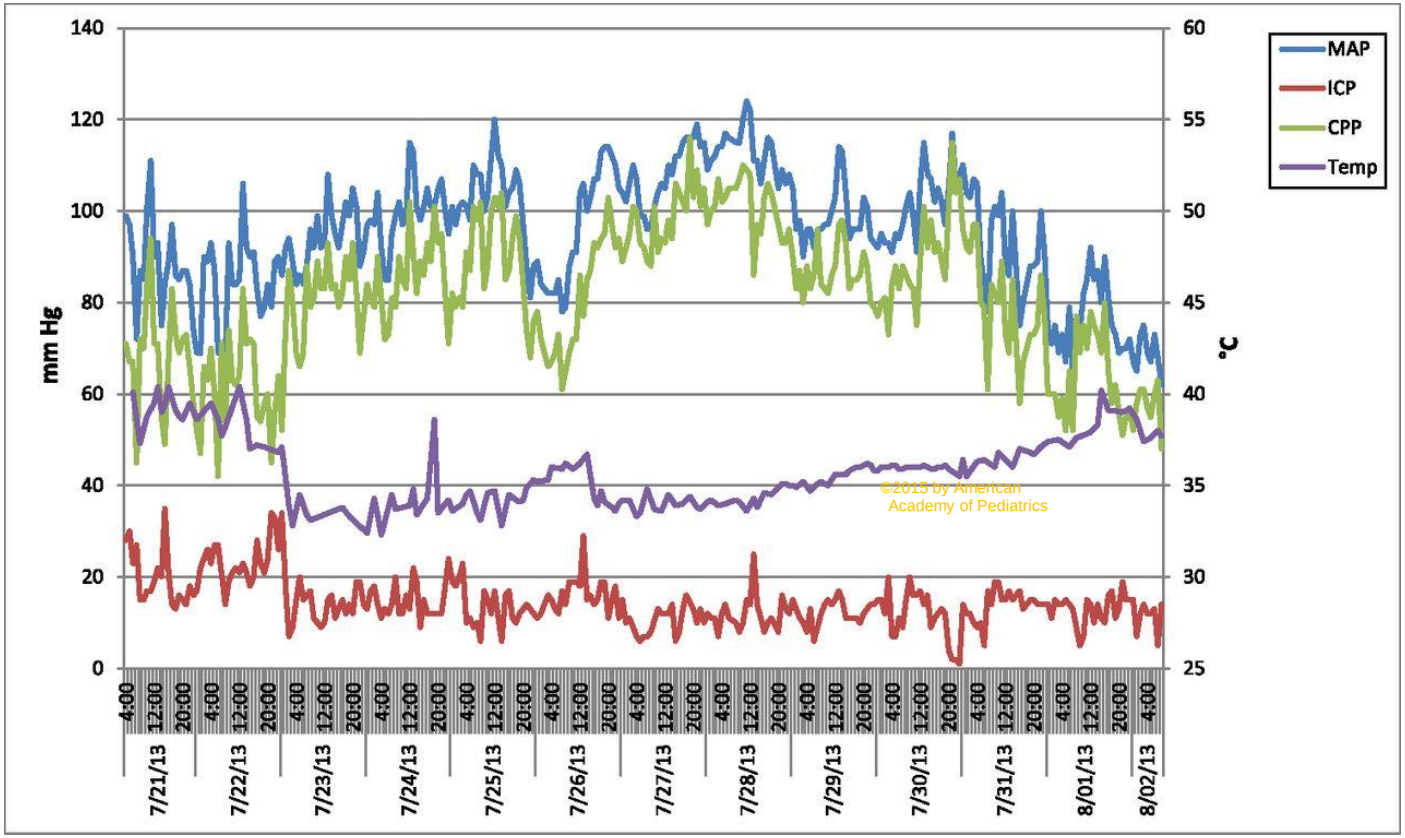
# Treatment, continued

Management of cerebral edema,  ICP

- EVD - drainage of CSF, admin of meds
- hyperosmolar therapy with mannitol and 3% saline
- moderate hyperventilation (goal $Paco_2$: 30–35 mm Hg)
- Induced coma
- induced hypothermia (32°C–34°C).

http://www.cdc.gov/parasites/naegleria/treatment-hcp.html

**The relationship between mean arterial pressure (MAP), cerebral perfusion pressure (CPP), ICP, and core body temperature (Temp) during the management of a 12-year-old girl with N fowleri PAM. The graph illustrates our management strategy for maintaining CPP...**





PEDIATRICS®

W. Matthew Linam et al. Pediatrics 2015;135:e744-e748

# Treatment, continued

| Med | Duration |
|---|---|
| Amphotericin B, IV | 14days |
| Amphotericin B, IT | 10 days |
| Azithromycin, IV or PO | 28 days |
| Fluconozole, IV or PO | 28 days |

| Med | Duration |
|---|---|
| Rifampin, IV or PO | 28 days |
| Miltefosine, PO | 28 days |
| Dexamethasone, IV | 4 days |

http://www.cdc.gov/parasites/naegleria/treatment-hcp.html

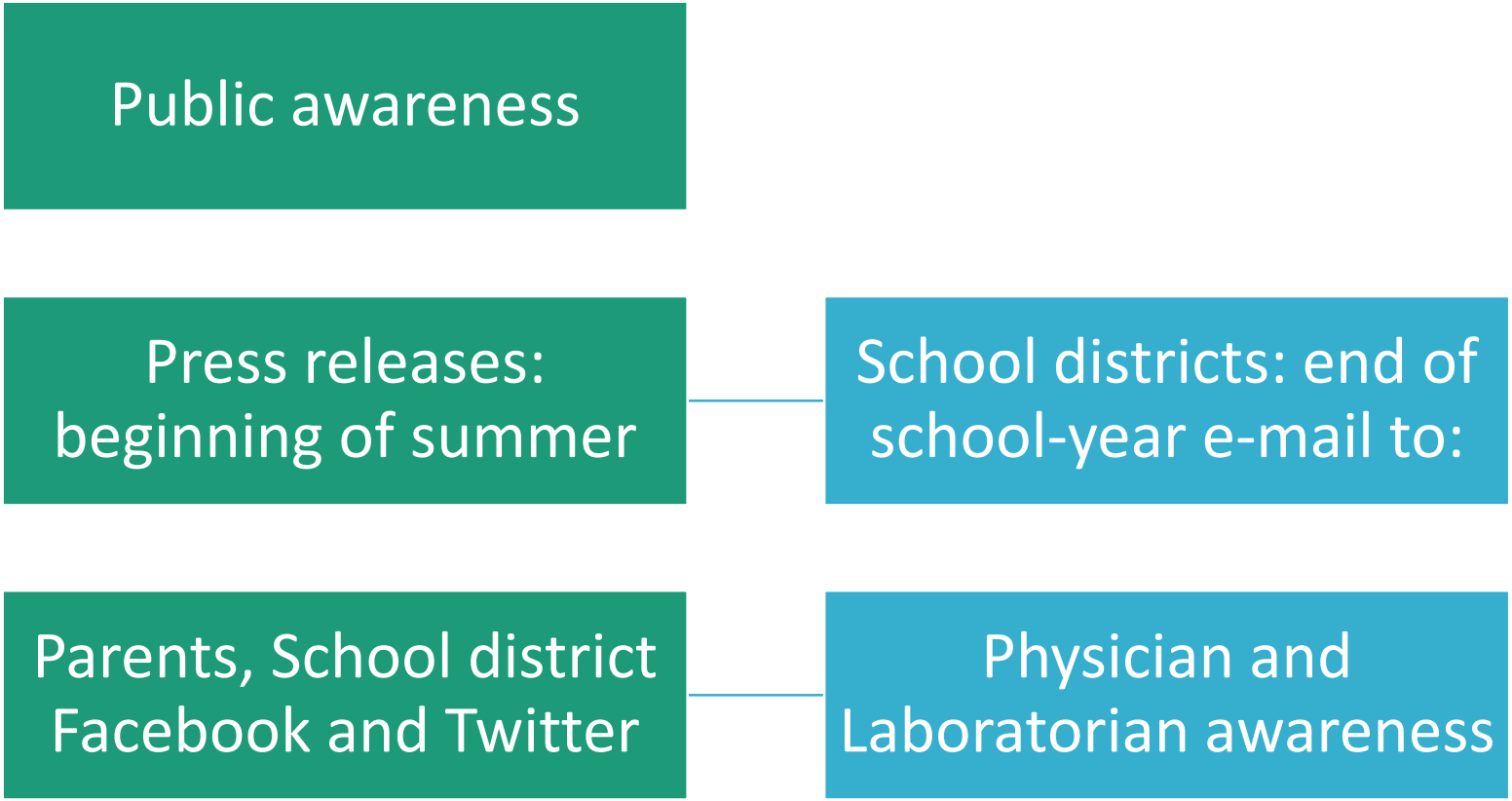
## POSACONAZOLE

STUDY FROM USF INDICATES THAT POSACONAZOLE MAY REPLACE FLUCONAZOLE FOR TREATMENT OF PAM

AZITHROMYCIN INCREASES THE EFFECTIVENESS OF POSACONAZOLE BY AN ADDITIONAL 20%

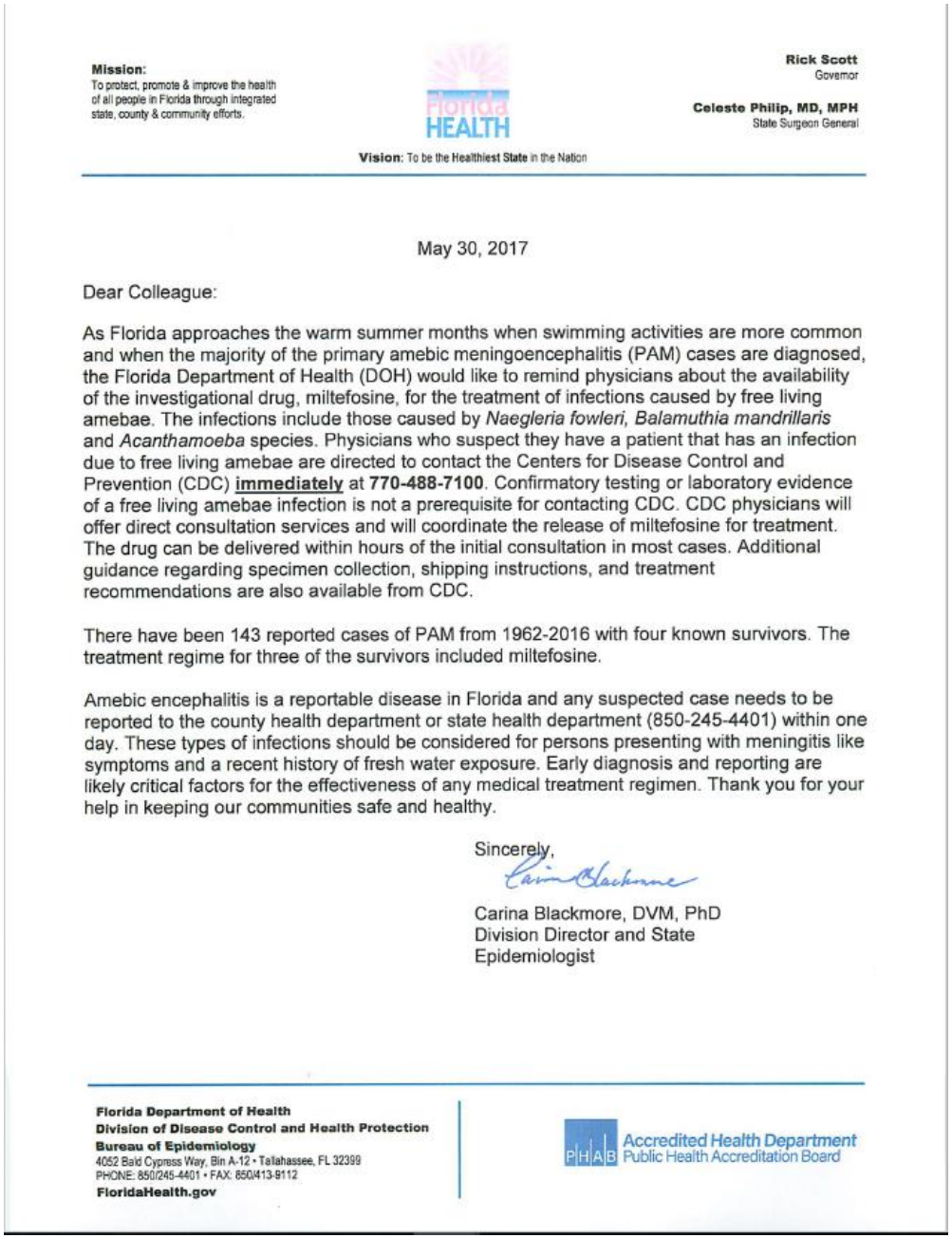
CYCLOAURINE METABOLITES ARE POTENTIAL MOLECULAR MODELS TO DEVELOP TREATEMENT.

STATINS AND ESPECIALLY FLUVISTATIN ARE SHOWING PROMISE


Public awareness
Press releases: beginning of summer
School districts: end of school-year e-mail to:
Parents, School district Facebook and Twitter
Physician and Laboratorian awareness

# PREVENTION EFFORTS

- NETTI POTS PROPER TECHNIQUE
- NOSE CLIPS
- AWARENESS CAMPAIGNS
- UNDERWATER DIVING
- SHALLOW MUDDY WATERS
- WATER PARKS
- JETSKIS
- MUNICIPAL WATER SUPPLIES
- GARDENHOSES
- OVERLAND WATER PIPES



**Mission:**
To protect, promote & improve the health of all people in Florida through integrated state, county & community efforts.

Florida HEALTH

**Rick Scott**
Governor

**Celeste Philip, MD, MPH**
State Surgeon General

**Vision:** To be the Healthiest State in the Nation

May 30, 2017

Dear Colleague:

As Florida approaches the warm summer months when swimming activities are more common and when the majority of the primary amebic meningoencephalitis (PAM) cases are diagnosed, the Florida Department of Health (DOH) would like to remind physicians about the availability of the investigational drug, miltefosine, for the treatment of infections caused by free living amebae. The infections include those caused by *Naegleria fowleri*, *Balamuthia mandrillaris* and *Acanthamoeba* species. Physicians who suspect they have a patient that has an infection due to free living amebae are directed to contact the Centers for Disease Control and Prevention (CDC) **immediately** at **770-488-7100**. Confirmatory testing or laboratory evidence of a free living amebae infection is not a prerequisite for contacting CDC. CDC physicians will offer direct consultation services and will coordinate the release of miltefosine for treatment. The drug can be delivered within hours of the initial consultation in most cases. Additional guidance regarding specimen collection, shipping instructions, and treatment recommendations are also available from CDC.

There have been 143 reported cases of PAM from 1962-2016 with four known survivors. The treatment regime for three of the survivors included miltefosine.

Amebic encephalitis is a reportable disease in Florida and any suspected case needs to be reported to the county health department or state health department (850-245-4401) within one day. These types of infections should be considered for persons presenting with meningitis like symptoms and a recent history of fresh water exposure. Early diagnosis and reporting are likely critical factors for the effectiveness of any medical treatment regimen. Thank you for your help in keeping our communities safe and healthy.

Sincerely,

Carina Blackmore, DVM, PhD
Division Director and State
Epidemiologist

**Florida Department of Health**
**Division of Disease Control and Health Protection**
**Bureau of Epidemiology**
4052 Bald Cypress Way, Bin A-12 • Tallahassee, FL 32399
PHONE: 850/245-4401 • FAX: 850/413-9112
**FloridaHealth.gov**

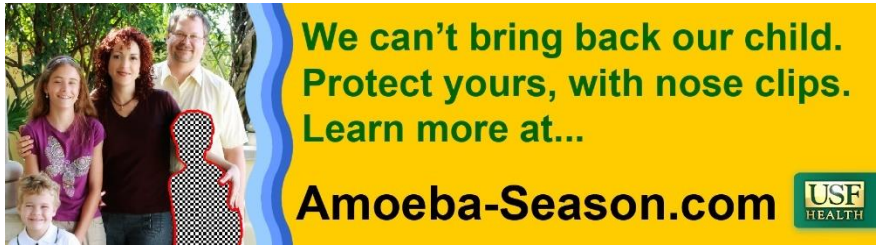
PHAB Accredited Health Department
Public Health Accreditation Board

Florida HEALTH

Physician Notification Letters: each Spring

Division of Disease Control and Health Protection

# Amoeba-season.com
# Philip Thomas Gompf









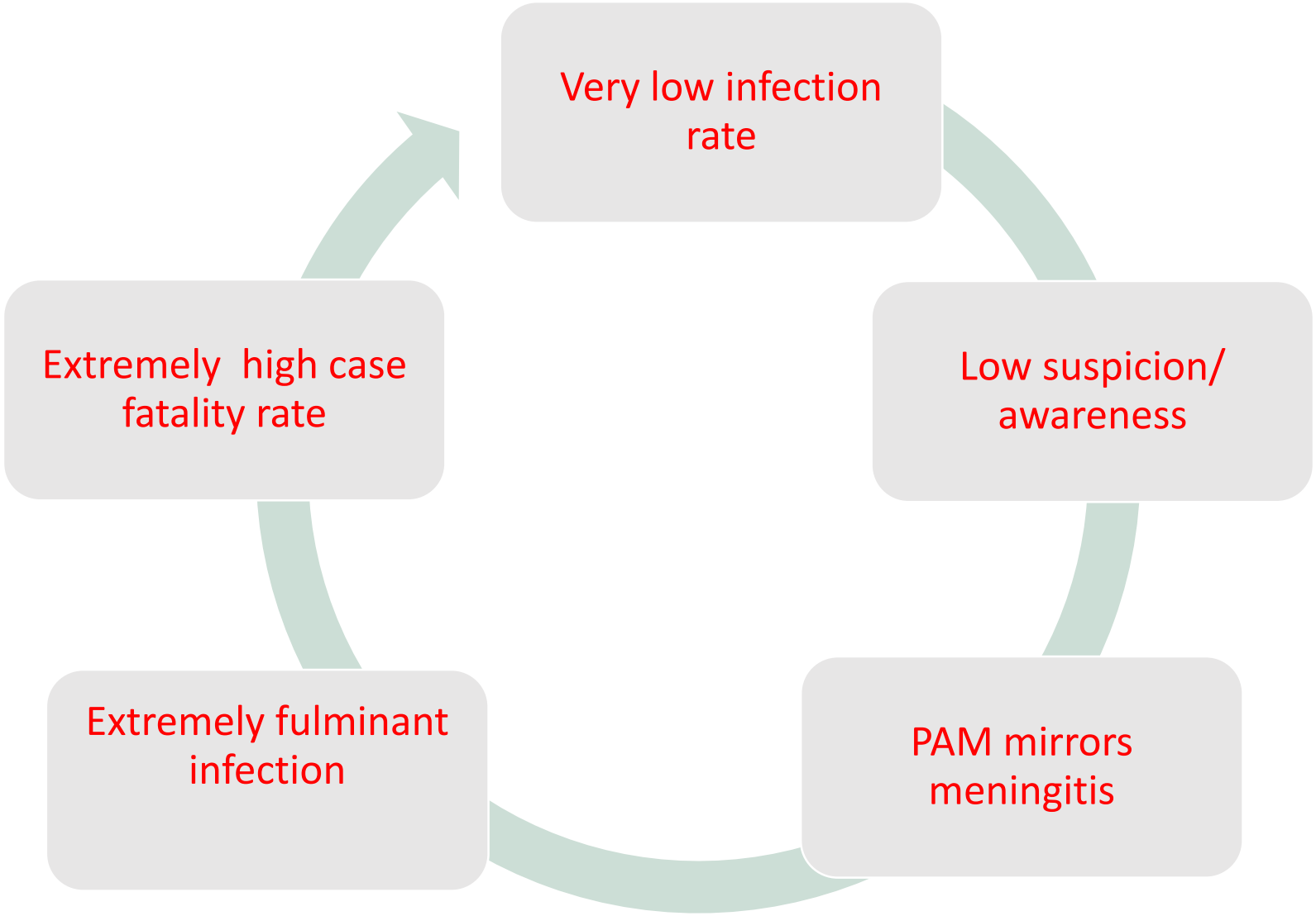
I-4 East and Westbound: Thonotosassa, near exit 14

May through August

# Video Project for CEU for Laboratorians

https://jordansmelskifoundation.org/lab-detection-naegleria-fowleri

# PAM- The Issue:



# Thank You

KEVIN SHERIN MD, MPH

**SHERINKMJ@GMAIL.COM**