

# CRYPTOCOCCAL SCREENING

A New Strategy for Saving Lives among People with HIV/AIDS



National Center for Emerging and Zoonotic Infectious Diseases  
Division of Foodborne, Waterborne, and Environmental Diseases



# Cryptococcal Meningitis: Reducing Deaths by Screening for Infection

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*Fifth Annual CUGH conference*

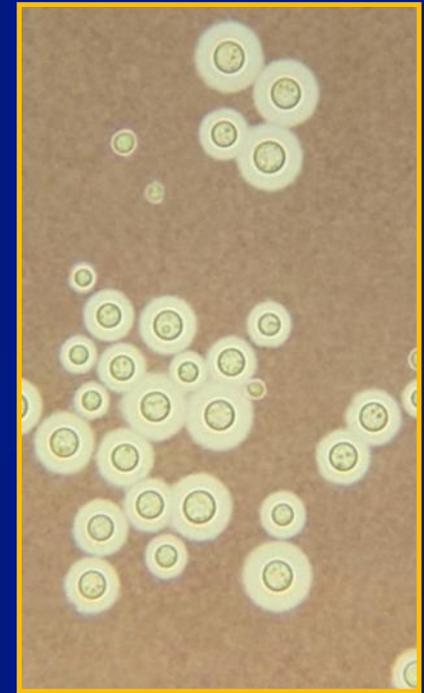
May 12, 2014

National Center for Emerging and Zoonotic Infectious Diseases



# Cryptococcus Neoformans

- ❑ Fungus found in soil, trees, bird feces
- ❑ Incubation period unknown, can be dormant for many years
- ❑ Reactivation in immunosuppressed (HIV/AIDS, especially  $CD4 < 100$ )
- ❑ No person-to-person transmission
- ❑ Usually presents as meningitis
  - Requires hospitalization and treatment with intravenous (IV) amphotericin B



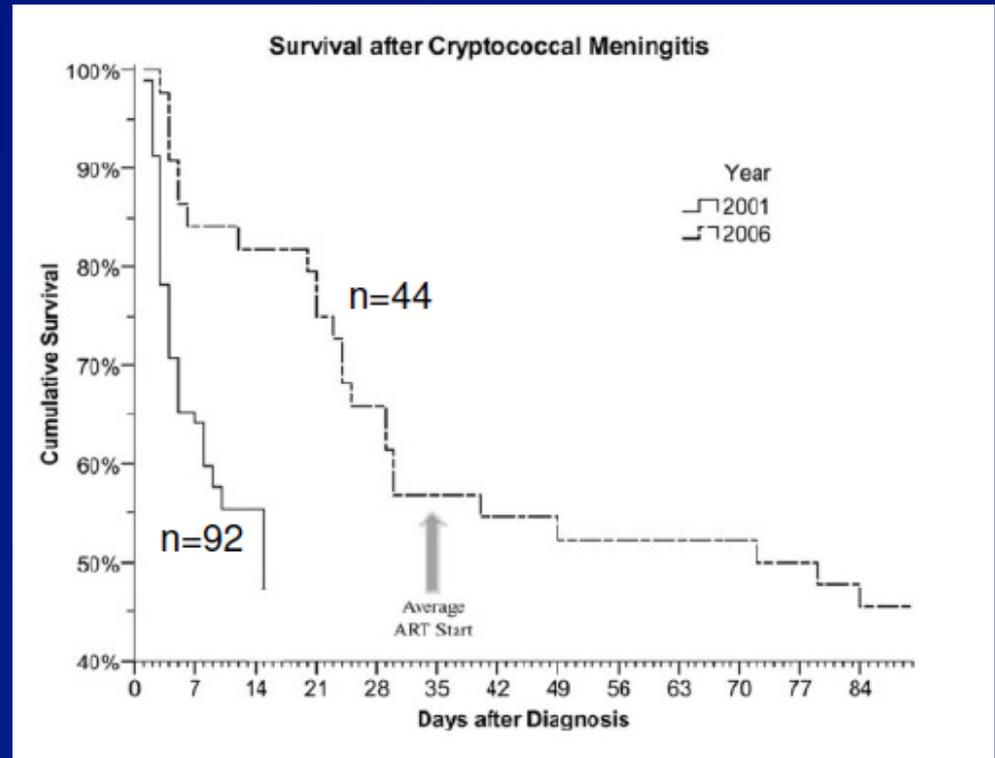
India Ink microscopy of  
*Cryptococcus*

# Cryptococcal Meningitis (CM)

- ❑ **1 million new cases per year globally**
  - Resulting in 625,000 deaths
- ❑ **Most common cause of adult meningitis in sub-Saharan Africa**
- ❑ **High mortality (>50%) due to:**
  - Late presentation to care
  - Limited access to effective medications
  - Limited access to sensitive and specific diagnostics
- ❑ **Frequent cause of IRIS (20-30% early mortality after ART)**

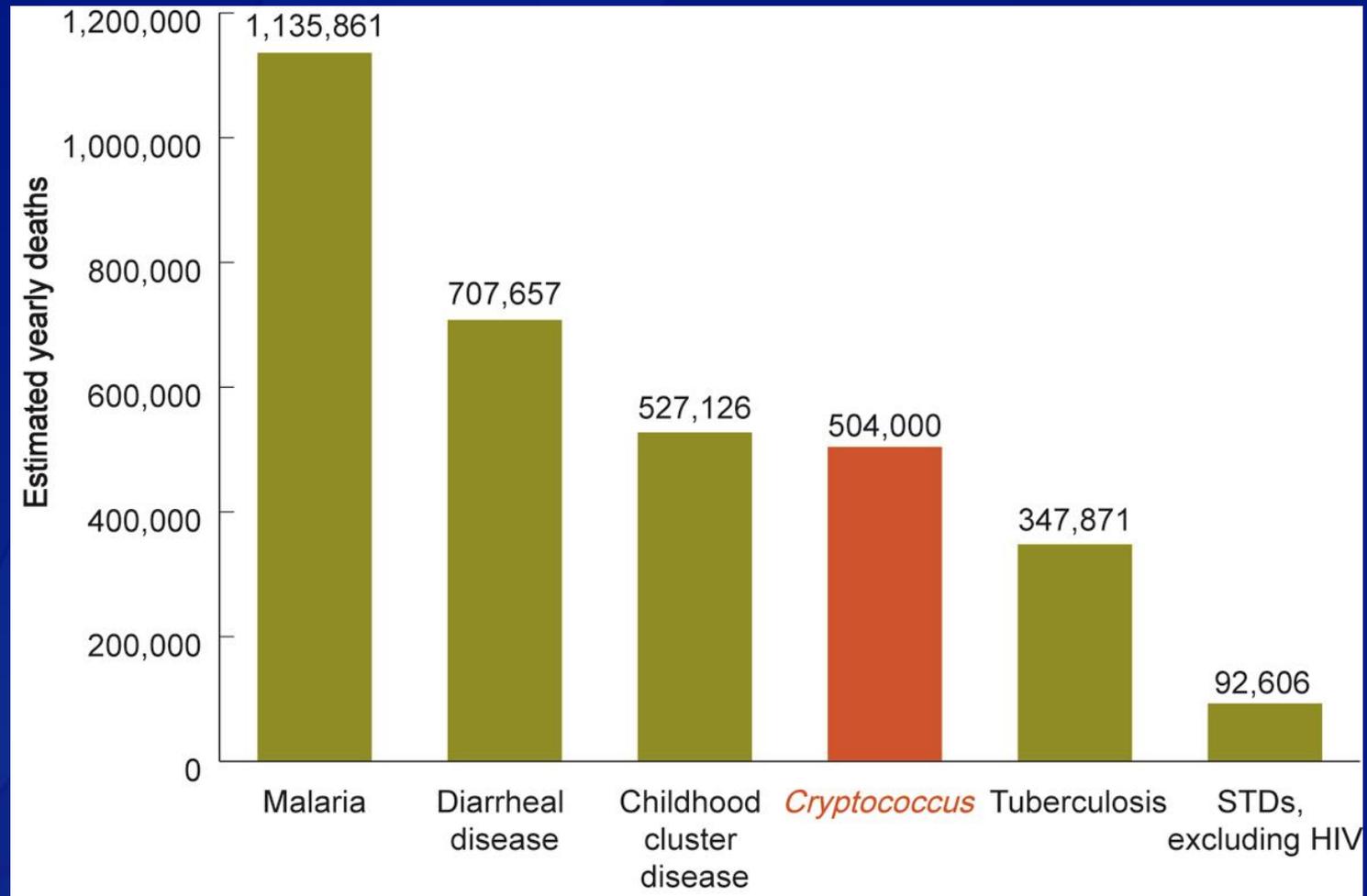
# Cryptococcal Meningitis Survival

- If untreated, case-fatality is 100%
- In sub-Saharan Africa, mortality likely 50-70%



Kambugu et al, CID 2008

# Causes of death in sub-Saharan Africa (excluding HIV/AIDS)



# Disease progression in HIV-infected person



**Latent infection**

Disease confined to the lungs



**Subclinical infection**

Antigen is detectable in the blood; no symptoms of CM

Days to months later



**Meningitis**

Dissemination to the brain

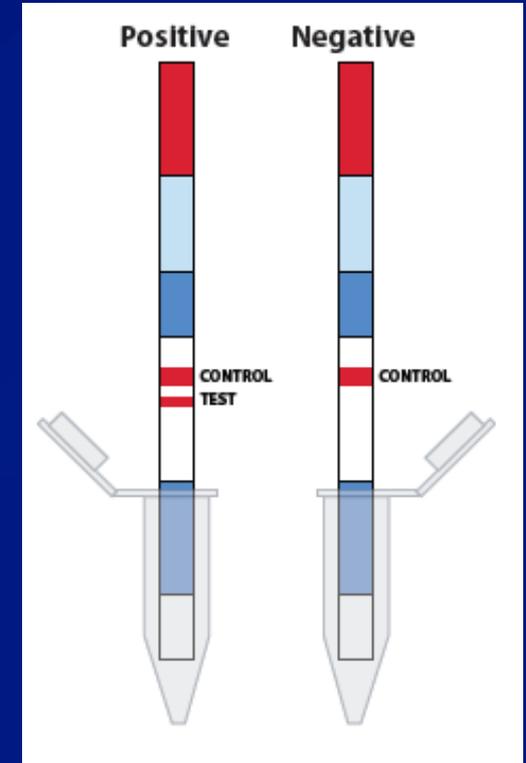
# How is *Cryptococcus* currently detected?

	MICROSCOPY	CULTURE	ANTIGEN DETECTION
Methods	India Ink staining of the fungi	Bird seed agar	Detects the fungal polysaccharide capsule
Test characteristics	Rapid diagnosis; 30-80% Sensitivity	Confirmatory test; Less sensitive than other methods	90-100% sensitivity; Excellent specificity
Specimen used	CSF	CSF, blood, any sterile fluid	CSF, blood
Picture			

# A novel POCT antigen test is available

The new dipstick test (Lateral Flow Assay, or LFA) is:

- **Simple and quick**  
*Results in 10 minutes*
- **Accurate**  
*Highly sensitive, accurate (>95%)*
- **Affordable**  
*\$2/test*
- **Easy to use**  
*Little lab infrastructure and no cold chain required*



\*FDA-approved in serum and cerebrospinal fluid (CSF).

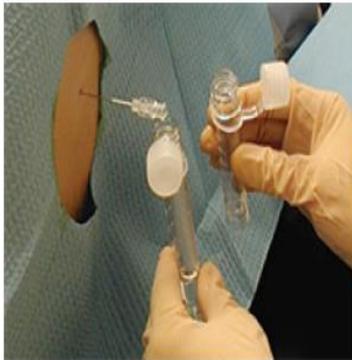
## **LFA for resource-limited settings**

- ❑ **No cold chain or laboratory infrastructure required**
- ❑ **Available in Africa at cost from manufacturer**
  - Available from manufacturer, SCMS, local distributors
- ❑ **Detects both subclinical disease and meningitis**
- ❑ **Can be used in dedicated laboratories as well as in clinics as a point of care test**
  - Useful in facilities utilizing point of care CD4 testing

# CrAg LFA is the **ONLY** Point-of-Care Diagnostic



Serum



CSF



Plasma

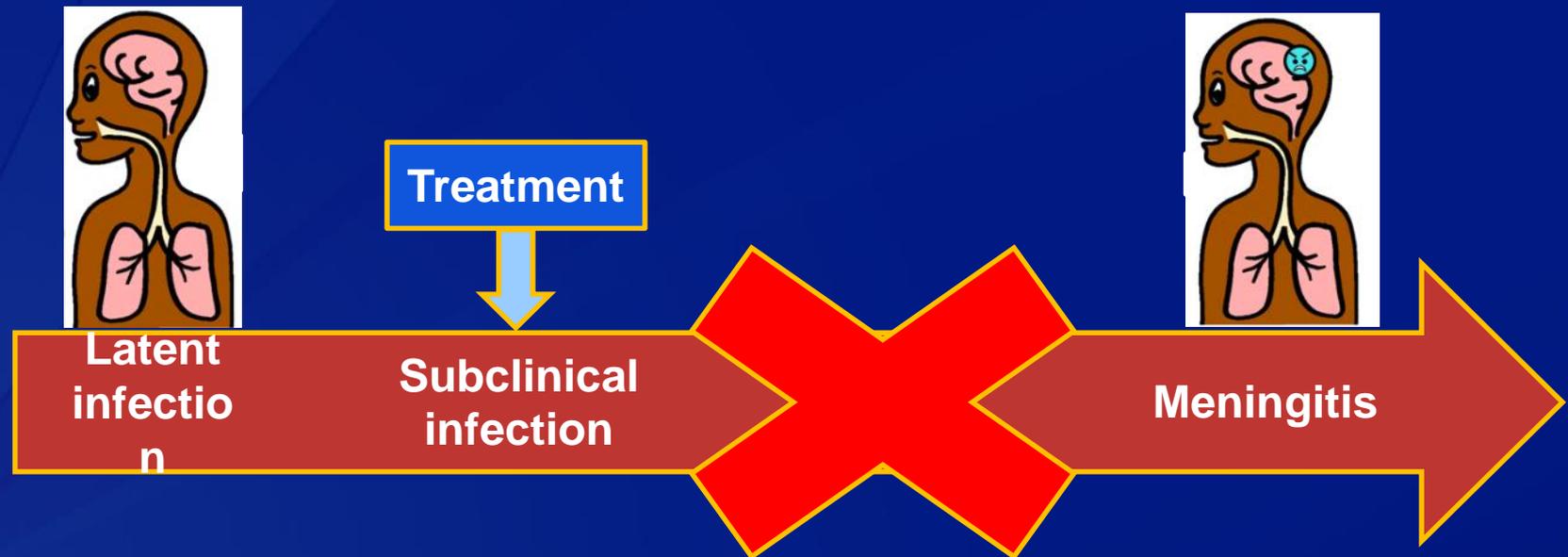


Whole Blood

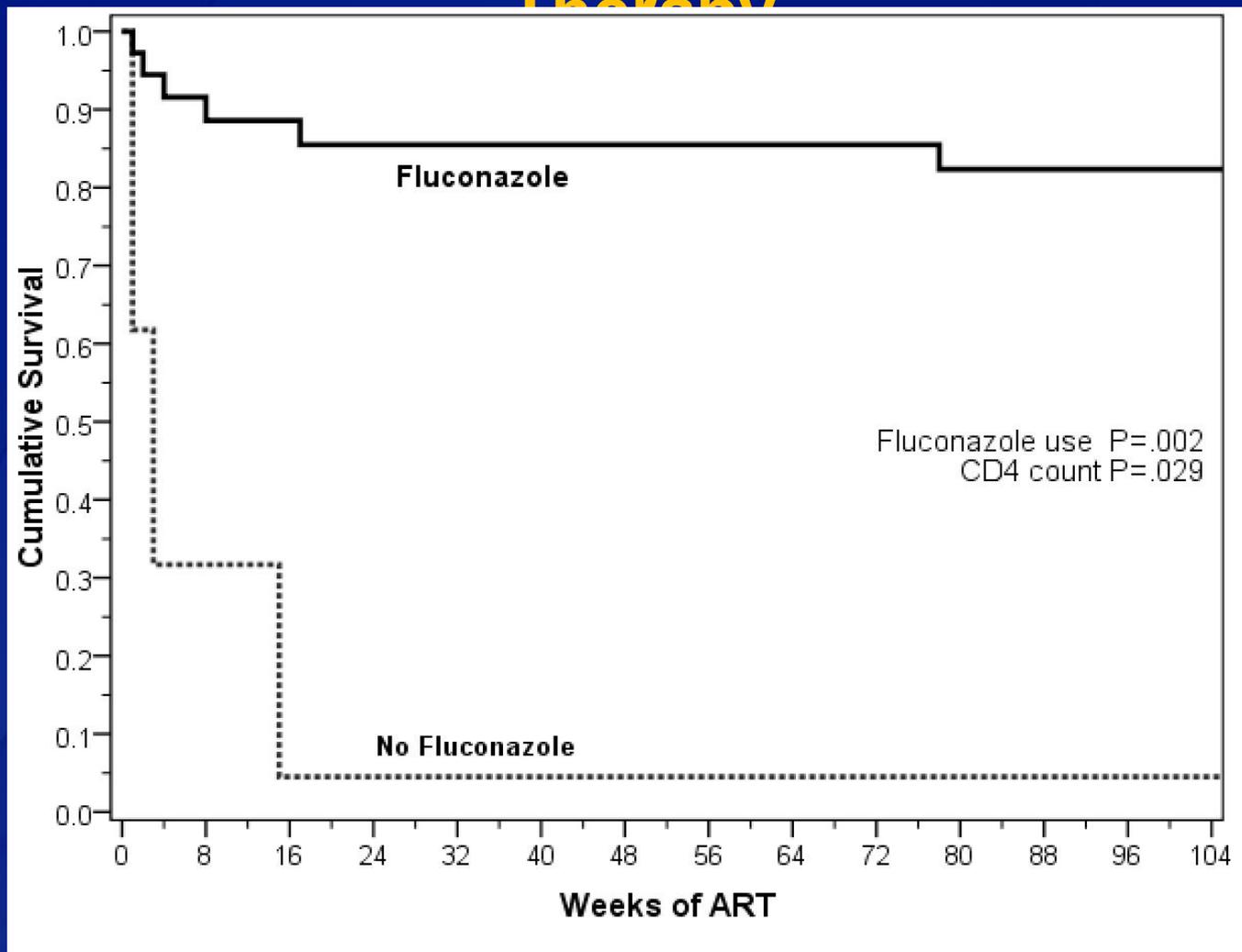
Room temperature storage  
2-year shelf life

# “Screen and Treat” strategy

- Screen a subset of HIV infected patients with a CrAg test and treat only those with a positive test
- Detect early cryptococcal disease and prevent progression to meningitis through early treatment



# Survival of People with Asymptomatic Cryptococcal Antigenemia starting HIV Therapy



# Screening for subclinical disease

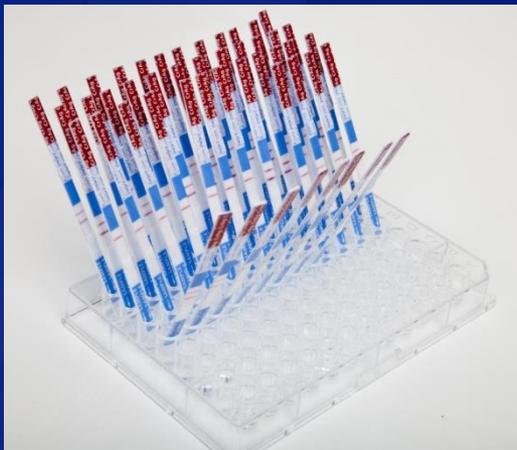
Screen those at highest risk

Laboratory

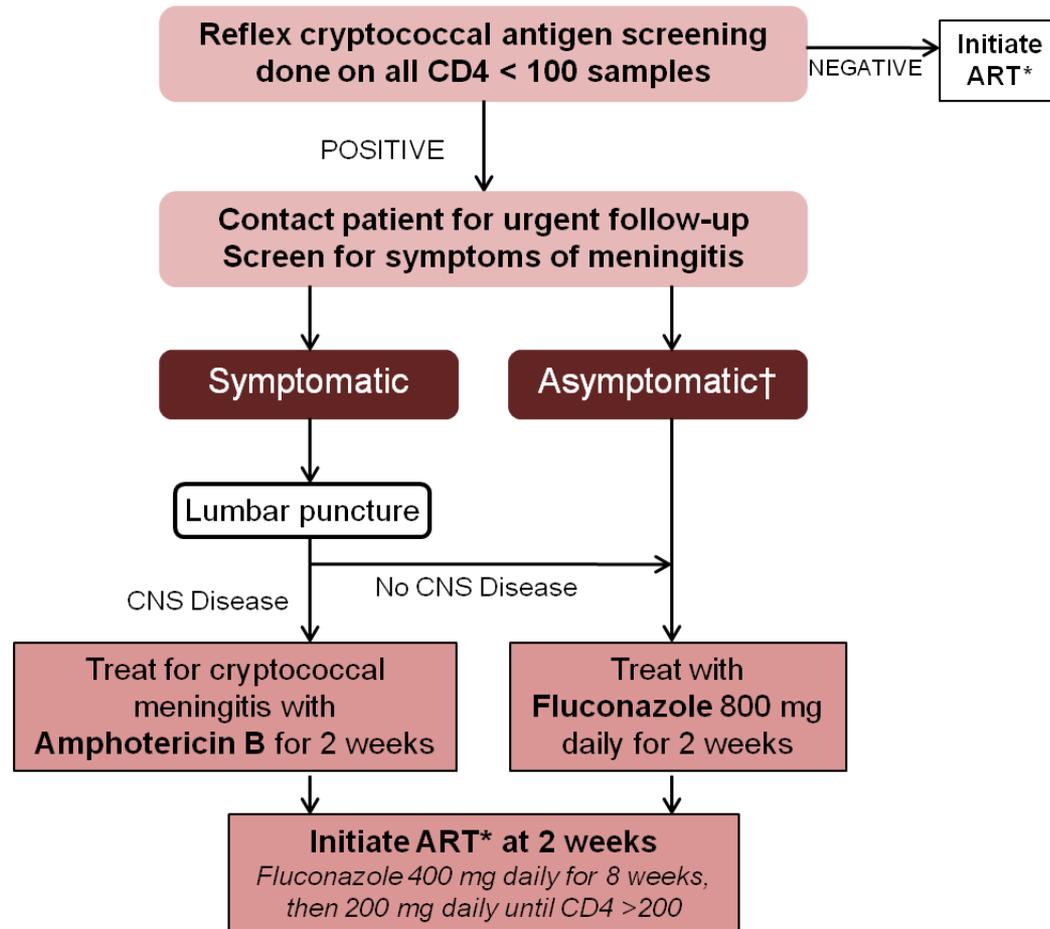
Point-of-care

Reflex

Clinician-initiated



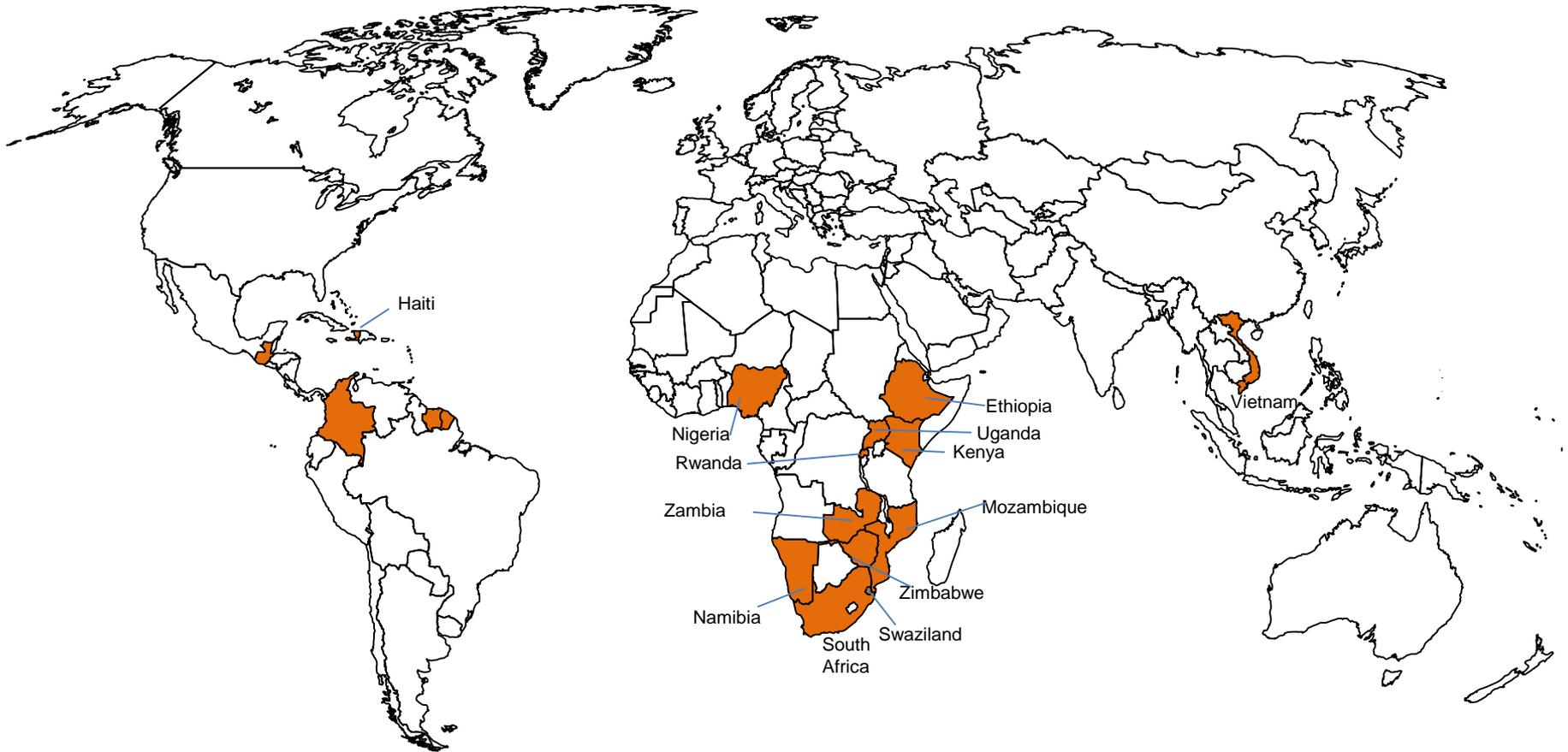
# Cryptococcal Screening Algorithm for HIV+ Patients-- South Africa



† A lumbar puncture may be considered in asymptomatic patients. Pregnant women, children, and those with liver failure may require special attention.

\* Initiate ART if not already started

# Some Countries are Screening



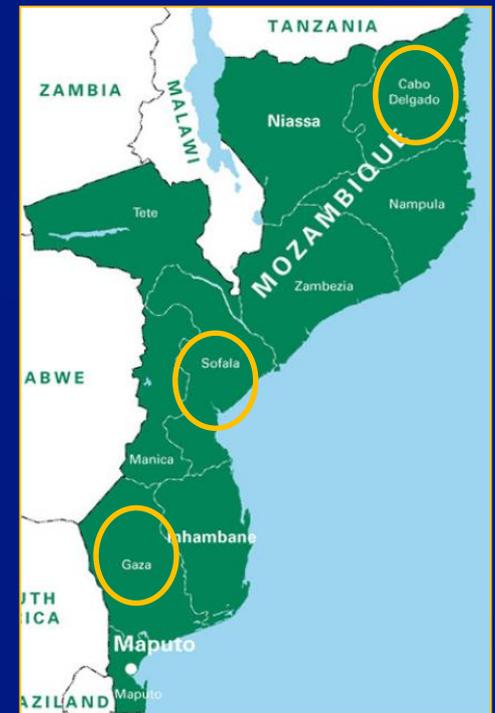
# South Africa

- ❑ **CrAg screening included in National Strategic Plan for HIV**
  - Persons with  $CD4 < 100$
- ❑ **Phased national implementation**
- ❑ **Phase 1: Sept 2012 – present**
  - Screening in two provinces
- ❑ **Phase 2**
  - National roll-out
- ❑ **19,000 people screened, 5% CrAg-positivity**



# Mozambique

- ❑ Screening among those with CD4<100
- ❑ Pilot screening in 3 provinces
  - 3 facilities in each province
- ❑ Screening in different lab settings
  - Pima POC CD4
  - FACS on-site
  - Referral laboratory reflex testing
- ❑ Phased national implementation
  - Mozambique Ministry of Health with PEPFAR support



# Key elements for successful implementation

- ❑ **Integrating screening into national guidelines**
- ❑ **Engaging key strategic partners**
  - ASLM - support lab capacity building and accreditation
  - PEPFAR – funding in-country cryptococcal activities
  - MSF/CHAI – antifungal and diagnostics access advocacy
- ❑ **Building laboratory capacity**
  - Laboratory training, test validation, LFA EQA
  - Diagnostic test procurement, distribution
- ❑ **Improving access to essential antifungal medicines**
  - Amphotericin B, Fluconazole, Flucytosine

# Previous Training - Haiti

- 1 day workshop
- POC
  - Crypto
  - Syphilis
  - Malaria



# ASLM RDT/POC Roadshow

- Combination Training on RDTs



HIV/Syphilis Duo



Malaria



CrAg LFA

# Coming Soon: African Society for Laboratory Medicine Rapid Diagnostic Test (RDT) Training Course

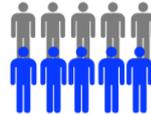
## Why Rapid Diagnostic Tests?

Rapid Diagnostic Tests (RDTs) to detect HIV and other diseases are being used more frequently because they are simple to use and can give results faster than traditional diagnostic methods. RDTs are ideal for HIV screening in Africa because many laboratories do not have access to viral load testing, which can be expensive and resource-intensive. In addition, RDTs can quickly detect other infections common among people living with HIV/AIDS, such as syphilis, malaria, and cryptococcal meningitis (a fungal infection).



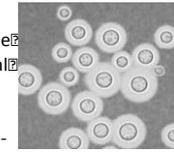
## HIV/AIDS

- 35 million people currently living with HIV/AIDS globally
- Less than half know their status



## Cryptococcal disease

- Worldwide over 500,000 people die each year from cryptococcal meningitis
- Screening and preemptive treatments both cost- and life-



## Syphilis

- Responsible for over 500,000 babies born with birth defects
- Easily treatable in childbearing-age women if detected early



## Malaria

- Misdiagnosis and treatment occurs in up to 20% of febrile patients in some settings
- RDTs provide quick and accurate diagnoses to guide treatment



ASLM plans to offer training on HIV/syphilis, malaria, and cryptococcal disease RDTs in the summer of 2015.

## Clinical Staff Training Includes:

- Use of evidence-based treatment and decision-making algorithms
- Didactic and active role play-based learning
- Case-studies based on real-world examples

## Learning objectives:

- To demonstrate competency in clinical diagnosis, treatment, and case management
- To obtain an understanding of epidemiological aspects of priority diseases
- To apply programmatic concepts for screening strategies to a local context

## Laboratory Staff Training Including:

- Hands-on experience performing and interpreting key RDTs
- Development of standard algorithms for determining and reporting low-positive test lines
- Enhanced skill-building in data recording and database management practices

## Learning objectives:

- To gain a better understanding of basic clinical aspects of each disease
- To streamline laboratory workflow
- To utilize proficiency testing and quality assurance

For more information, please contact:

Name: \_\_\_\_\_ Email: \_\_\_\_\_ Phone number: \_\_\_\_\_

Organization: \_\_\_\_\_

Address line 1: \_\_\_\_\_

Address line 2: \_\_\_\_\_

# Advocacy - CryptoMAG

## □ International, multi-organizational coalition

- Academic, International, governmental and non-governmental
  - CHAI, PEPFAR, LSHTM, MSF, NICD, WHO

## □ Priorities

- Improve access to accurate diagnostic tests
- Improve access to essential antifungal medicines
- Disseminate clinical practices and guidelines

## □ Accomplishments to-date

- Addition of Flucytosine and Amphotericin B on WHO core essential medicines list (EML)
- High profile publications on toxicity and access issues
- Satellite sessions at international conferences (ASLM, ICASA)



HIV/AIDS Programme

## RAPID ADVICE

DIAGNOSIS, PREVENTION AND MANAGEMENT OF CRYPTOCOCCAL DISEASE IN HIV-INFECTED ADULTS, ADOLESCENTS AND CHILDREN

December 2011



# World Health Organization



CDC Home  
**CDC** Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives. Protecting People.™

A-Z Index: A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

### C. neoformans cryptococcosis

Fungal Home > C. neoformans cryptococcosis

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#### Training Resources

CDC has developed a set of training materials which can be used to educate physicians, nurses, HIV/AIDS counselors, pharmacists, and patients about cryptococcal diagnosis, management, and prevention. These materials are intended to help healthcare providers, particularly those in resource-limited settings, implement a screen-and-treat strategy for cryptococcal infection among people living with HIV/AIDS.

- Cryptococcal Screening Program Training Manual for Healthcare Providers [PDF - 42 pages]
- Cryptococcal Screening Program Training Modules for Healthcare Workers [PDF - 44 pages]
- Cryptococcal Screening: A New Strategy for Saving Lives among People with HIV/AIDS [PDF - 42 pages]

Related Links

- All Fungal Topics
- Aspergillosis
- Blastomycosis

Contact Us:  
Centers for Disease Control and Prevention  
1600 Clifton Rd  
Atlanta, GA 30333  
800-CDC-INFO (800-232-4636)  
TTY: (888) 232-6348  
[Contact CDC-INFO](#)

PREVENTCRYPTO.ORG

HOME ABOUT CRYPTO GUIDELINES PUBLICATIONS TRAINING TREATMENT RESEARCH NEWS ABOUT US

## THIS YEAR 600,000 people WILL DIE FROM CRYPTOCOCCAL MENINGITIS

LET'S DO SOMETHING ABOUT IT

### Cryptococcosis: a deadly fungal disease

Cryptococcosis is a fungal infection that kills more than 500,000 HIV/AIDS patients every year worldwide. Many patients die because their infection is not detected until disease has progressed to a brain infection. However, many of these deaths are preventable. Patients can be screened for early cryptococcal disease and treated *before* they develop life-threatening brain infection. New inexpensive blood tests and a readily available oral medication (fluconazole) make early detection (screening) and treatment more feasible.

SEARCH WEBSITE

UPCOMING MEETING

retroconference.org  
March 3-6, 2013  
Atlanta, GA

[www.preventcrypto.org](http://www.preventcrypto.org)

## **Conclusion**

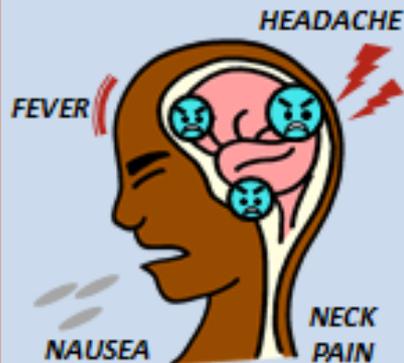
- ❑ **Cryptococcal infection is an important public health problem among people living with HIV**
- ❑ **Antigen tests can detect cryptococcal infection early before it develops into meningitis**
- ❑ **The LFA can be used in both laboratory and as a POCT**
- ❑ **Advocacy for diagnostics and essential medicines must accompany screening programs**

# Thank you!

## HIV and Brain Infection: Testing Saves Lives!

### What is the infection?

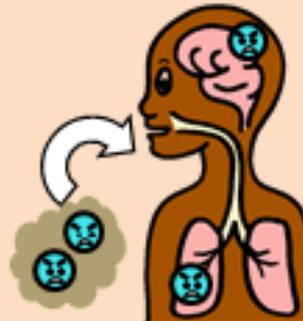
Some people with HIV can get a brain infection called *Cryptococcus* or "Crypto." If it is not treated, you could get very sick. Crypto is caused by a small germ.



### How is it spread?

This germ lives in the soil but is too small to see. It can enter our bodies through the air we breathe. Most people are strong enough not to get sick. In an HIV+ person it may start growing and can spread to the brain.

**The germ CANNOT spread from person to person!**



### What can I do?

Even if you do not feel sick now, you might already have this infection. Your doctor will test you as part of your regular visit. If you have the Crypto germ, you will need to take medicine so that you do not get sick later.

