

Cryptococcal Screening Program Case Studies



Image courtesy of World Health Organization

National Center for Emerging and Zoonotic Infectious Diseases
Mycotic Diseases Branch



Note to trainers

Aim of presentation

This document is intended for use as a visual aid for the Case Studies section (p.30-40) of the Cryptococcal Screening Program Training Manual for Healthcare Providers.

Intended audience

Health care workers (doctors and nurses) in health facilities in resource-limited settings (RLS) participating in clinical training in the context of cryptococcal screening and treatment programs.

Supplies needed

Cryptococcal Screening Program Training Manual for Healthcare Providers (available [online](#))

Learning objectives

Case studies reviewed in this presentation aim to improve participants' understanding of:

- The different clinical presentations among patients with cryptococcal meningitis and those with asymptomatic cryptococcal disease.
- The differences in the management and treatment of asymptomatic vs. symptomatic patients
- The side effects and importance of closely monitoring patients given amphotericin B
- The differences in management and treatment of patients with special circumstances, such as tuberculosis treatment or pregnancy

Overview

Case Study 1: Development of Symptomatic Cryptococcal Meningitis (CM)

Case Study 2: Asymptomatic Presentation of CM

Case Study 3: Previous cryptococcosis

Case Study 4: Special circumstances - Tuberculosis medication

Case Study 5: Special circumstances - Pregnancy

The trainer should present the overview of the five case studies covered in this presentation. The trainer should also highlight that all patients discussed are living with HIV.

Case Study 1

Development of Symptomatic Cryptococcal Meningitis

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The trainer leading the clinical training for Healthcare Providers should refer participants to **page 31** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 1

Development of Symptomatic Cryptococcal Meningitis

- Patient history and initial presentation
 - 49 year-old man, CD4 count of 9
 - Watery diarrhea for 1 month, has lost 10 kg in past 2 months
 - Lives alone, drinks daily
 - No symptoms of cryptococcal disease (headache, fever, confusion, neck stiffness, or light sensitivity)
 - Very wasted, mildly dehydrated, and has oral candidiasis

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 31** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 1

Development of Symptomatic Cryptococcal Meningitis

- Patient management
 - Baseline bloods ordered: full blood count, creatinine, ALT, and RPR
 - Stool sample collected and sent to lab
 - Serum cryptococcal antigen (CrAg) test: **positive**
 - Patient is told to complete readiness classes and return to the clinic in 2 weeks to begin ART

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Case Study 1

Development of Symptomatic Cryptococcal Meningitis

- Medications prescribed
 - Nystatin mouth wash
 - Bactrim 2 tabs/day
 - Vitamin B complex 2 tabs/day
 - Thiamine 200 mg/day (in view of alcohol history and possible malabsorption)

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Case Study 1

Development of Symptomatic Cryptococcal Meningitis

- Patient progress
 - Patient does not return to your clinic to start ART.
 - Unable to get in contact with patient to prompt him to return to clinic
 - Three months later, he presents to the hospital with a headache, neck stiffness, and confusion.
 - A lumbar puncture (LP) shows that his intracranial pressure is very high (45 cm), and that his spinal fluid contains *Cryptococcus* (India Ink and CrAg positive).
 - Daily therapeutic LPs are performed to reduce his intracranial pressure, and his creatinine, potassium, and magnesium are monitored.
 - He is started on amphotericin B with pre-hydration.
 - Despite appropriate management, the patient dies on day 5 of admission.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 32** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

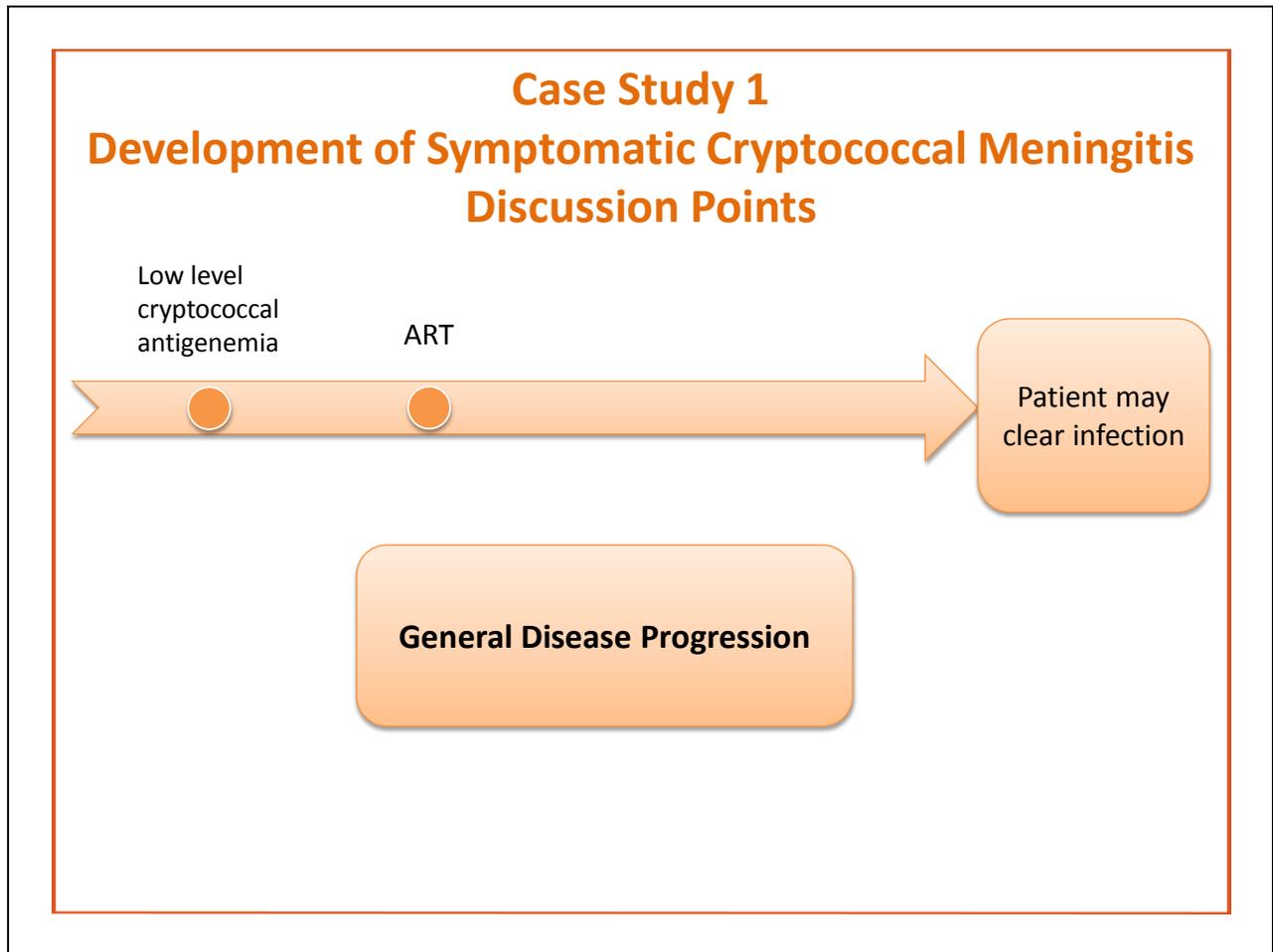
Case Study 1
Development of Symptomatic Cryptococcal Meningitis
Discussion Points

What two markers indicated the patient had cryptococcal meningitis at his return visit?

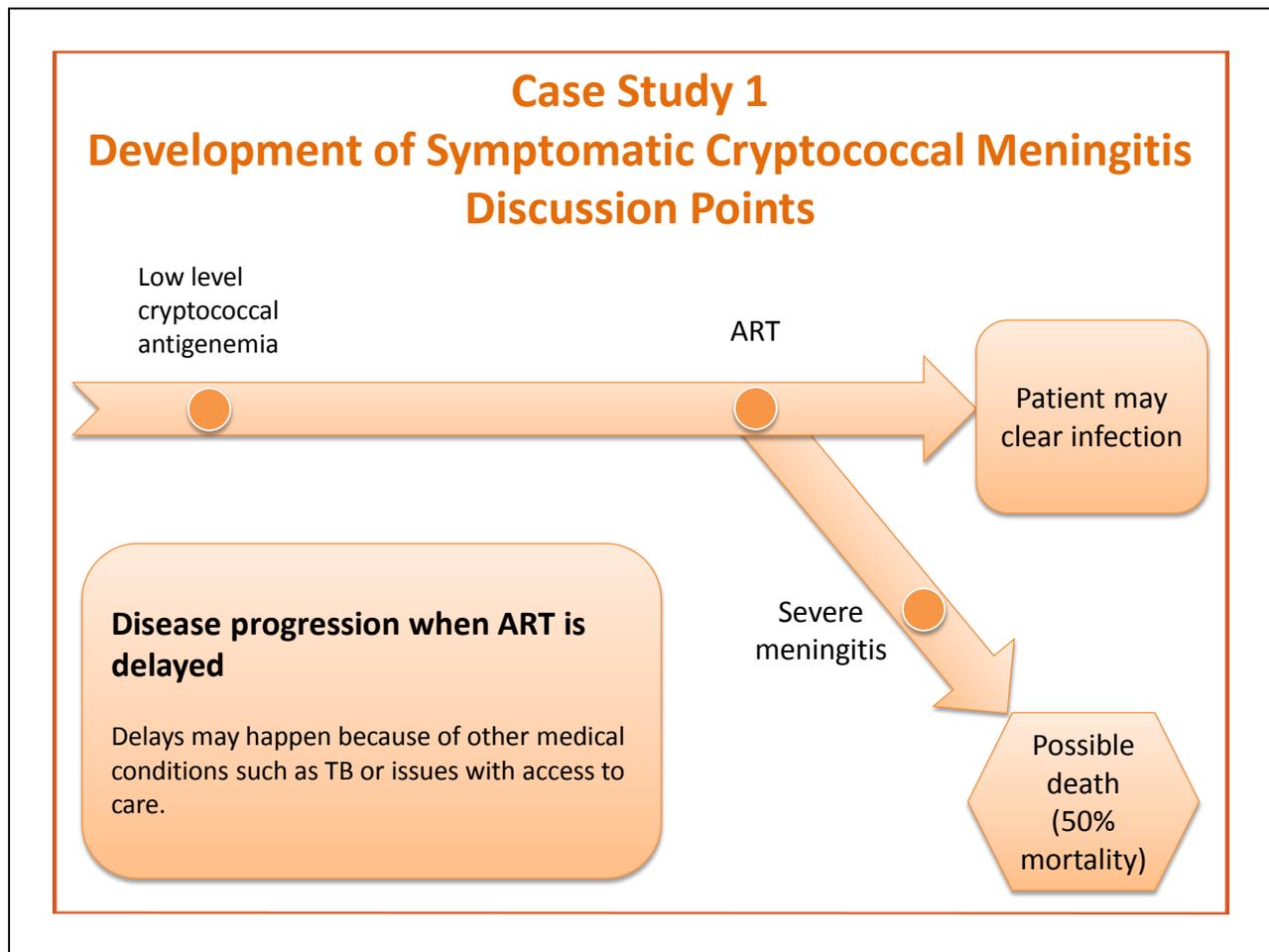
Upon his return to the clinic 3 months later, the patient had two markers for cryptococcal meningitis:

1. Altered mental status
2. Raised opening CSF pressure

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Case Study 1
Development of Symptomatic Cryptococcal Meningitis
Discussion Points

What could have prevented patient from developing cryptococcal meningitis?

Following the positive serum CrAg result, patient should have been prescribed fluconazole at intake visit, followed by ART four weeks later.

This type of patient management may prevent his silent cryptococcal infection from progressing to symptomatic disease.

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Case Study 2

Asymptomatic Presentation of Cryptococcal Meningitis

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Case Study 2

Asymptomatic Presentation of Cryptococcal Meningitis

- Patient history and initial presentation
 - A 40-year old man is referred to your clinic after a 2-week hospital stay with pneumocystis pneumonia, where he was treated with cotrimoxazole and steroids, and made a good recovery.
 - Newly diagnosed with HIV, CD4 count of 11. Upon presentation to the clinic, he has a headache, but no fever, confusion, or neck stiffness.
 - He has severe oral candidiasis, one Kaposi's sarcoma (KS) lesion on his back, and nerve pain in his feet.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 33** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 2

Asymptomatic Presentation of Cryptococcal Meningitis

- Patient management
 - Baseline bloods ordered: full blood count, creatinine, ALT, and RPR
 - Serum cryptococcal antigen (CrAg) test: **positive**
 - Lumbar puncture performed: CSF CrAg test positive, India Ink positive
 - Patient admitted to hospital for management of cryptococcal meningitis
- Medication prescribed
 - Amphotericin B 1 mg/kg/day with pre-hydration

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 33** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 2

Asymptomatic Presentation of Cryptococcal Meningitis

- Patient progress
 - On day 4 of hospital admission, patient's creatinine is too high, which means his kidneys are failing. He is given fluids and the dose of amphotericin B is lowered.
 - On day 10, the amphotericin B causes him to develop thrombophlebitis (swelling in the veins due to blood clots) and he has become anemic.
 - He completes 14 days of amphotericin B and is discharged on fluconazole.
 - At his post-hospital discharge clinic visit, the patient is doing well and does not complain of headaches.
 - He is continued on fluconazole 800 mg/day and is started on ART (AZT, 3TC, EVZ) in view of his creatinine levels (kidney failure) and peripheral neuropathy (nerve pain).

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Case Study 2
Asymptomatic Presentation of Cryptococcal Meningitis
Discussion Points

Why is it important to look for cryptococcal meningitis in late-stage HIV patients?

Late-stage HIV patients often have other opportunistic infections such as TB, PCP, and cryptococcal meningitis.

As cryptococcal meningitis has high mortality (50%), it is important to ensure that treatment is initiated.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 34** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 2
Asymptomatic Presentation of Cryptococcal Meningitis
Discussion Points

What serious side effects are associated with amphotericin B?

- Abnormal heart rhythms
- Kidney failure
- Low potassium
- Abdominal discomfort
- Infusion reactions
- Phlebitis
- Anemia
- Low white blood cell count

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Case Study 2
Asymptomatic Presentation of Cryptococcal Meningitis
Discussion Points

Fluconazole interacts with
what medications?

Fluconazole can potentially interact with ART and TB medications; therefore, the following should be considered:

- Nevirapine may increase the risk of liver damage. Use an efavirenz-based regimen instead.
- If the patient is already on nevirapine then he or she should be monitored closely for signs of liver damage:
 - Right upper quadrant abdominal pain
 - Nausea/vomiting, or
 - Jaundice (yellowing of the skin and eyes)
- If there are signs of toxicity order liver function tests
- Rifampicin can decrease levels of fluconazole in the blood

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Case Study 3

Previous Cryptococcosis

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Case Study 3 Previous Cryptococcosis

- Patient history and initial presentation
 - 37 year-old woman, CD4 count of 19
 - She recently moved to Cape Town from Queenstown, leaving behind her medications and transfer letter
 - She reports no headache, fever, confusion, or neck stiffness, and there are no positive findings upon examination

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 35** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3 Previous Cryptococcosis

- Patient management
 - Baseline bloods ordered: full blood count, creatinine, ALT, and RPR
 - Serum cryptococcal antigen (CrAg) test: **positive**
 - The patient is told to complete readiness classes and return to the clinic in 2 weeks to begin ART
- Medications prescribed
 - Fluconazole 800 mg/day for 2 weeks
 - Bactrim 2 tablets/day
 - Vitamin B complex 2 tablets/day

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 35** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3 Previous Cryptococcosis

- Patient progress
 - At her follow-up visit, the patient is doing well.
 - Her sister brought the patient's original medications and clinic transfer letter.
 - You learn that the patient had previously been admitted to hospital with cryptococcal meningitis 2 months ago, and was prescribed fluconazole 200 mg/day, Bactrim, and Vitamin B complex.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 35** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3 Previous Cryptococcosis Discussion Points

Does a patient with previous cryptococcal disease need to be routinely screened?

No. Cryptococcal antigen can be present for up to 2 years after an episode of cryptococcosis.

A patient with previous cryptococcal disease presenting new symptoms of meningitis needs to be evaluated for disease recurrence.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 36** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3
Previous Cryptococcosis
Discussion Points

How long should a patient continue fluconazole prophylaxis?

A patient with previous cryptococcosis should remain on fluconazole prophylaxis until they have a CD4 count greater than 200 for **at least** 6 months on ART.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 36** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3
Previous Cryptococcosis
Discussion Points

What can increase a patient's risk of relapse if they have had previous cryptococcal disease?

The discontinuation of fluconazole prophylaxis.

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Case Study 3
Previous Cryptococcosis
Discussion Points

What is IRIS?

IRIS is
Immune Reconstitution
Inflammatory Syndrome.

IRIS a condition where the
immune system seems to
recover then has an
inflammatory response to a
previously acquired infection
that makes the symptoms
worse.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 36** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 3 Previous Cryptococcosis Discussion Points

Who should be
suspected of
having IRIS?

Patients starting ART who have had
previous cryptococcal disease.

These patients are at increased risk
of IRIS.

Any patient with a history of
cryptococcosis who presents with a
headache should be treated as if he
or she has recurrent disease/IRIS
until proven otherwise.

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Case Study 4

Special Circumstances: On Tuberculosis (TB) Medication

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Case Study 4

Special Circumstances: On TB Medication

- Patient history and initial presentation
 - A 35 year-old man is referred to your clinic from a TB clinic after having been diagnosed smear-positive for pulmonary TB 4 weeks ago.
 - He has started on regimen 1 (RHEZ). He is newly diagnosed with HIV, with a CD4 count of 50.
 - Upon presentation to the clinic, the patient feels well, and his respiratory symptoms are improving. He has no headache, fever, or neck stiffness. However, upon examination, the patient is wasted, has crackling in his lungs, and has a red, scaly rash.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 37** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4

Special Circumstances: On TB Medication

- Patient management
 - Baseline bloods ordered: full blood count, creatinine, ALT, and RPR
 - Serum cryptococcal antigen (CrAg) test: **positive**
 - Patient is told to complete readiness classes and return to the clinic in 2 weeks to begin ART
- Medication prescribed
 - Fluconazole 800 mg/day for 2 weeks
 - Bactrim 2 tablets/day
 - Vitamin B complex 2 tablets/day

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 37** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4

Special Circumstances: On TB Medication

- Patient progress
 - The patient telephones the clinic 2 days later, complaining of nausea and vomiting after taking the fluconazole and TB medications together.
 - The patient is asked to return to clinic for an ALT test, the results of which was normal.
 - He is advised to divide the dose of fluconazole to 400 mg two times per day and to take the fluconazole separately from the TB medications.
 - After this, the patient tolerates the medications well, and completes 6 months of TB treatment.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 37** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4
Special Circumstances: On TB Medication
Discussion Points

At what CD4 count is
TB usually seen?

TB can be seen at any CD4 count, but extrapulmonary and miliary TB is more common in patients with CD4 counts of less than 100.

Because cryptococcal meningitis has high mortality (50%), it is important to ensure that treatment is initiated.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 38** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4
Special Circumstances: On TB Medication
Discussion Points

Why should an efavirenz-based ART regimen be used when prescribing fluconazole for someone with TB?

Efavirenz has less risk of causing liver damage than nevirapine.

As both fluconazole and TB medications can cause liver damage, an efavirenz-based regimen may be safer.

It is important to check for symptoms of liver damage with these patients.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 38** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4
Special Circumstances: On TB Medication
Discussion Points

What are signs of liver damage?

Signs of liver damage are:

- Abdominal pains
- Nausea/vomiting
- Yellowing of the skin and eyes

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 38** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 4

Special Circumstances: On TB Medication

Discussion Points

What complications may prevent a patient from taking fluconazole and TB medications together?

Fluconazole can cause nausea/gastrointestinal problems, as can TB medications. It may help to split the fluconazole dose to two times per day.

If severe nausea occurs, give an anti-emetic 30 minutes before.

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Case Study 5

Special Circumstances: Pregnancy

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Case Study 5

Special Circumstances: Pregnancy

- Patient history and initial presentation
 - 23 year-old woman, 20 weeks pregnant, referred to your clinic
 - Newly-diagnosed HIV-positive with a CD4 count of 42
 - She reports no headache, fever, neck stiffness, or sensitivity to light, and there are no positive findings upon examination of the patient
- Patient management
 - Baseline bloods ordered: full blood count, creatinine, ALT, and RPR
 - Serum cryptococcal antigen (CrAg) test: **positive**

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 39** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 5
Special Circumstances: Pregnancy
Discussion Points

Why is treating latent cryptococcal antigenemia different for a pregnant patient than other patients?

The medication used to treat latent cryptococcal antigenemia, fluconazole, can damage the fetus, especially in the first trimester.

The potential risks and benefits must be considered carefully when managing a pregnant patient.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 39** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 5 Special Circumstances: Pregnancy Discussion Points

What factors need consideration with a pregnant patient with latent cryptococcal antigenemia?

- Gestation of fetus
- Symptoms
- Timing of ART
- Type of ART

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 39** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 5
Special Circumstances: Pregnancy
Discussion Points

How can the gestation of fetus influence treatment of latent cryptococcal antigenemia?

Fluconazole can cause birth defects, especially in 1st trimester.

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Case Study 5
Special Circumstances: Pregnancy
Discussion Points

How can symptoms help guide therapy in a pregnant patient?

Symptomatic patients need a lumbar puncture and if positive, they will need to be treated for cryptococcal meningitis (Amphotericin B-based treatment where available).

Asymptomatic patients should be counseled on risks and benefits of fluconazole therapy.

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Case Study 5
Special Circumstances: Pregnancy
Discussion Points

When should ART be started in a pregnant patient?

ART should not be delayed in pregnant patients, regardless of them starting fluconazole.

When starting ART, watch for cryptococcal IRIS.

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 39-40** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

Case Study 5
Special Circumstances: Pregnancy
Discussion Points

What kind of ART
should be prescribed
to a pregnant
patient?

ART should be initiated in
accordance with national
guidelines for HIV care in
pregnant women

If treatment for latent
antigenemia is initiated, care
must be taken as fluconazole
may compound toxicities
seen with some ART (e.g.
liver toxicity with nevirapine)

The trainer leading the clinical training for Healthcare Providers should refer participants to **page 39-40** of the *Cryptococcal Screening Program Training Manual for Healthcare Providers*.

For more information please contact Centers for Disease Control and Prevention

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Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: <http://www.cdc.gov>

The views expressed in these materials are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The materials are for training and informational purposes only, and do not preplace national guidelines for the treatment of HIV and related conditions in the respective countries where the materials will be used.

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