Online Only Lectures - Management of AIDS-Related Opportunistic Infections II

Speaker: Henry Masur, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

Management of AIDS-Related Opportunistic Infections II

Henry Masur, MD
Bethesda, Maryland

6/15/2022

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Question #1

A 50-year-old male has HIV (CD4=40 cells/uL and HIV viral load =600,000 copies/uL) has central nervous system toxoplasmosis documented by a compatible CT of the head and a positive CSF PCR for toxoplasma.

The patient also has cryptosporidiosis with 4 stools per day plus considerable nausea and thus has limited food intake.

The pharmacy cannot obtain sulfadiazine or pyrimethamine.

The best option for therapy of the toxoplasmosis would be:

A. Atovaquone
B. Clindamycin plus primaquine
C. Trimethoprim-Sulfamethoxazole
D. Azithromycin plus Doxycycline
E. Nitazoxanide

Answer #1

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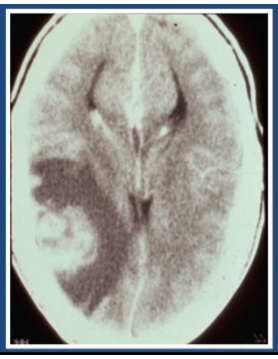
Question #2

- **A 39-year-old female from Brazil presents to an ER with a seizure.**
  - **Her CT scan is shown**
  - **Her HIV serology is positive**
  - **CD4 = 20/µL**
  - **VL = 100,000 copies/µL**
- **It is thought to be unsafe to perform an LP.**
- **She is started on sulfadiazine and pyrimethamine.**
- **ARVs are held until her acute problem is under control.**
- **After 10 days, she has not improved and a brain biopsy is performed (see image).**



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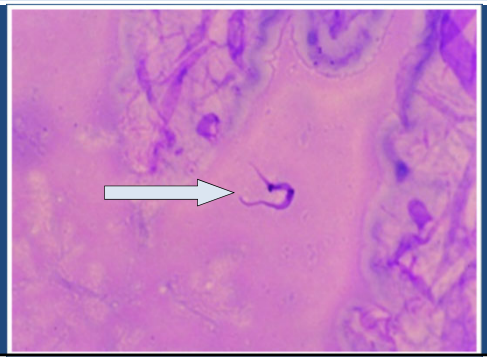

Question #2

What is the most likely diagnosis?

A. Toxoplasmosis
B. Cysticercosis
C. Leishmaniasis
D. Trypanosomiasis
E. Acanthamoeba

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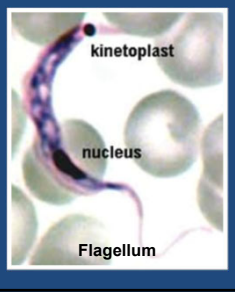
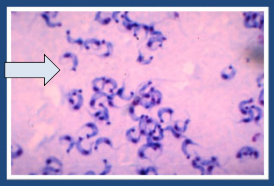
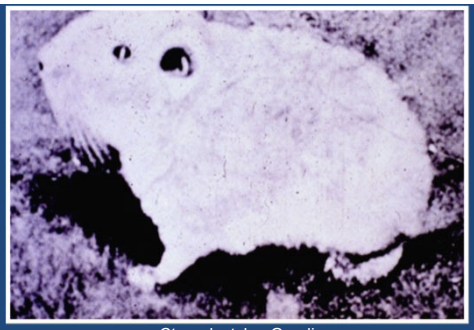
Trypanosoma cruzi Blood Smear and CSF





Badero et al, AIDS THERAPY, 4th Ed

Toxoplasmosis



Ctenodactylus Gondi

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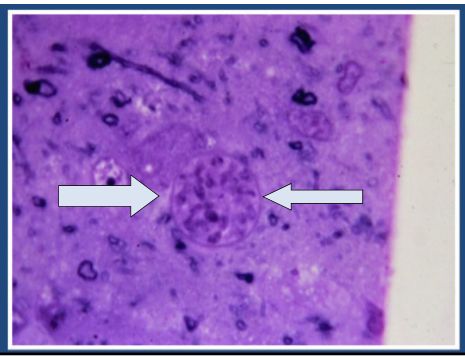


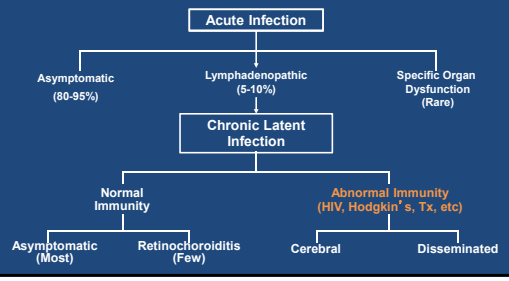
Incidence of Toxoplasmosis

- Seroprevalence in General Population
  - US-20%
  - Some areas of Europe, Africa: 80%
- Clinical disease common (30%) before ART and chemoprophylaxis
- Disease "never" occurs in seronegative patients except
  - Acute infection
  - Insensitive assay
  - Loss of ability to make antibody

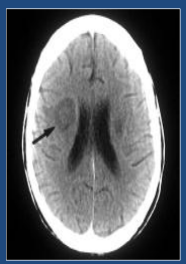
Transmission of Toxoplasma

- Feline feces (cats, but also lions etc)
  - Oocysts begin to be excreted 20 - 24 days post infection
  - Excretion persists 7 - 21 days
- Rare Meat (Lamb>Beef>Pork)
- Unusual
  - Raw shellfish, goat milk (reported 2009-2010)
  - Iatrogenic
    - Transfusion/Needle injury/transplant
- Congenital
  - Acute acquisition by mother during gestation
  - Chronic infection in immunosuppressed mother

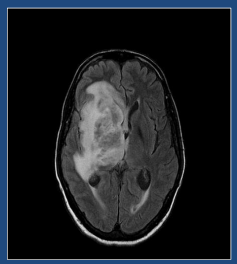
Clinical Manifestations of Toxoplasmosis when Acquired Post-Partum



CNS Toxoplasmosis



Non Contrast CT



Flair MRI

Evaluation of CNS Mass Lesions in Patients with HIV/AIDS

- Toxoplasmosis
- Lymphoma
- Tuberculosis
- Fungus
- Nocardia
- Bacterial
- Syphilis
- Kaposi
- Chagoma
- Glioblastoma

Radiologic Results

Non-specific although certain features suggestive
Look for Extra CNS lesions for biopsy

Laboratory Studies to Perform

Serology: Toxo IgG, Toxo PCR
Serum Crypt Ag and Histo ag
Blood culture - AFB, fungus
CSF - Crypt Ag
PCR (EBV, CMV, Toxo)
Urine - Histo Ag

Response to Empiric Therapy

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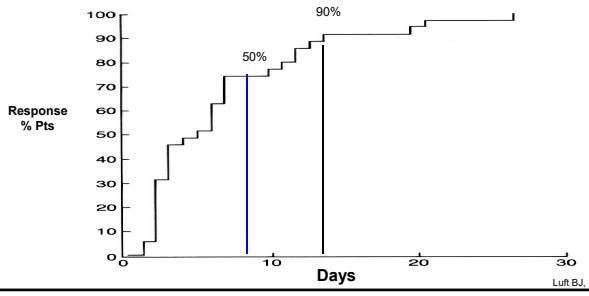
Empiric Diagnosis of CNS Toxo

- **When Initiating Therapy**
  - **Compatible CT or MR *plus***
  - **CD4 Count <100 cells/uL *plus***
  - **Toxo IgG antibody positive *plus***
  - **Not on TMP-SMX prophylaxis**
- **Post Initiation of Therapy**
  - **Radiologic and Clinical Response within 2 weeks**

Time to Neurologic Response for CNS Toxo

35 CNS Toxo Patients Treated with Clindamycin - Pyrimethamine



Luft BJ, NEJM 1993

Definitive Diagnosis of Cerebral Toxoplasmosis

- **Brain biopsy**
- **Serum PCR**
- **CSF PCR**

Therapy for Cerebral Toxoplasmosis

- **Preferred Regimen**
  - Sulfadiazine plus pyrimethamine plus leucovorin (PO only)
    - Expensive, not universally available
  - Trimethoprim-sulfamethoxazole (PO or IV)
- **Alternative Regimens**
  - Clindamycin plus pyrimethamine
  - Atovaquone +/- Pyrimethamine

Adjunctive Therapies for CNS Toxoplasmosis

- **Corticosteroids**
  - Not routine
  - Only if increased intracranial pressure/symptoms/signs
- **Anticonvulsants**
  - Not routine
  - Only after first seizure

Primary Prevention of Toxoplasmosis in Patients with HIV

- **Indication**
  - Positive IgG and CD4<100 cells/uL
- **Drugs**
  - First Choice
    - TMP-SMX (one ds qd)
  - Alternatives
    - Dapsone-Pyrimethamine
    - Atovaquone + Pyrimethamine

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Primary Prevention of Toxoplasmosis in PLWH

- **For patients with CD4<200 who are on TMP-SMX or atovaquone for PCP prophylaxis**
  - Nothing more is needed
- **For patient on Aerosol Pentamidine or Dapsone for PCP prophylaxis**
  - If on dapsone: add pyrimethamine
  - If on Aerosol pentamidine: not protected-
    - Consider switching to atovaquone if seropositive for toxo

Mycobacteria Species

- **M. tuberculosis***
  - M. bovis
  - M. africanum
- **Mycobacteria Other Than TB (MOTT)**
  - M. avium complex*
  - M. kansasii
  - M. hemophilum
  - M. genavense
  - M. terrae
  - M. scrofulaceum
  - M. xenopi

Question #4

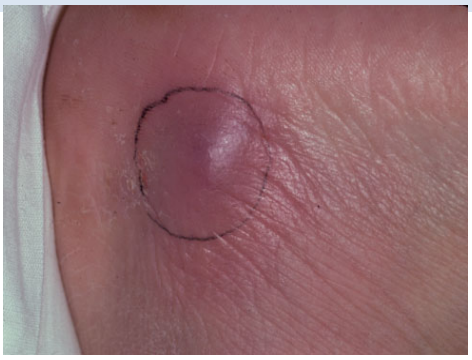
A 45-year-old male with HIV (CD4<10 cells/cc3, VL> 100k) has been taking TMP-SMX and Efavirenz-Tenofovir-Emtricitabine only intermittently.

For the past 3 weeks he has had a low grade fever, mild weight loss, and a lesion which is shown on the next slide.

Aspiration of the lesion showed many AFB rods, non branching, but after 6 weeks nothing grew.

The lesion is to be aspirated again.

See next slide



Question #4

What advice do you give the lab and hospital epi?

A. This should grow at 37°C
B. This should grow on conventional TB culture media
C. This most likely was acquired by acupuncture or some other manipulation.
D. This is treatable with trimethoprim-sulfamethoxazole
E. This can be cultured only at 32°C with iron enriched medium

Answer #4

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Tuberculosis and HIV

Susan Dorman has reviewed this in detail

- **Major Issues for Boards**
  - Most of US cases were acquired outside of US
  - Positive PPD = 5mm for PWH
  - Treat HIV infected patient with close contact for active TB regardless of PPD/IGRA result
    - (unlike HIV negative exposed person who are given prophylaxis only if IGRA or ppd pos with 5mm)

Therapy for HIV Positive Patients With Active TB

- Always start TB therapy first, and then start ART later depending on CD4 count and severity of disease
  - If CD4<50, start ART within 2 weeks
  - If CD4 >50, start within 8 weeks
- Only use regimens to treat active TB if the drugs are DAILY
- Failing Therapy?
  - Consider IRIS vs drug resistance or non adherence
- Treatment of Drug Resistant TB
  - Too complicated for exam!

Non Tuberculous Mycobacterial Infections in HIV Infected Patients

You Need Microbiologic or Epidemiologic Clue on Exam!

• Avium complex	Dissemination
• Hemophilum	Cutaneous abscesses
• Bovis	Adenitis, Dissemination
• BCG (Bovis)	Dissemination
• Genovense	Dissemination
• Scrofulaceum	Adenitis, Dissemination
• Xenopi	Lung nodules or infiltrates
• Malmoense	Cavitary lung, CNS ring lesions
• Chelonei	Skin, Soft Tissue, Joint, Bone

Mycobacterium Avium Complex

Confusing Terminology: Some Labs Are Identifying MAC Species
Not Clear If There Is Clinical Benefit in Identifying

- M. avium
- M. intracellulare
- M. chimaera
- M. colombiense
- M. arosiense
- M. marseillense
- M. timonense
- M. vulneris
- M. yongonense

Question #3

An HIV-infected patient is admitted to the hospital with three weeks of cough, fever, 25 lb weight loss, and anorexia. He is found to be HIV infected and to have a CD4 count =10 cells/uL and VL =500k

- His chest x-ray shows diffuse interstitial infiltrates
- BAL =PCP by immunofluorescence

Two weeks later while the patient is still in the hospital due to disposition issues, the lab reports
- Three blood cultures and the BAL are growing a mycobacterium
- Probe = Mycobacterium avium complex

What type of isolation is appropriate?

A. None
B. Droplet
C. Respiratory
D. Contact
E. Contract and droplet

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Mycobacterium Avium Intracellulare Complex

- **Epidemiology**
  - Ubiquitous in dirt, animals etc
- **Transmission**
  - Respiratory via dust
  - GI via food, water
  - Person-to-person unlikely
  - Environmental isolates correlate poorly with human isolate

Mycobacterium Avium Intracellulare

- **Risk factors**
  - CD4 < 50 or High VL
  - Colonization: GI / respiratory
- **Incidence pre ART: 20-40% (North America)**
  - Now declining with ART and probably non-ART related factors
- **Acute Disease: Clinical manifestations**
  - Fever, wasting, nodes, liver, spleen
  - Rare as cause of lung disease
  - Lab: Alk Phos, Hg, Albumen

Mycobacterium Avium Intracellulare Diagnosis

- **Source of Isolates**
  - **Blood**
    - **Bactec (7-14 days),**
  - **Sputum/Stool/Urine**
    - **Low predictive value**
- **Lab Identification**
  - **Specific DNA Probes for specimens/ cultures**
  - **MALDI-TOF**

MAC: Susceptibility Testing

Recommended for primary isolates

- **Validated CLSI** (Clinical Laboratory Standards Institute)
  - **Clarithromycin**
  - **Amikacin**
- **Other drug susceptibility results not clearly associated with clinical outcome**

Treatment for MAC

- **Antiretroviral Therapy**
  - **Start within 2 weeks of anti mac therapy**
- **Specific Therapy**
  - **Clarithro (or Azithro) + Ethambutol**
    - **Rifabutin optional 3rd drug: use if severe disease ("high burden of organisms")**
    - **Beware drug interactions with clari or rifabutin**

Treatment for MAC

- **Response:**
  - **Fever should decline within 2-4 weeks**
  - **Blood cultures should be negative in 2-4w**
  - **Repeat blood cultures only if symptoms**
- **Stop chronic suppression:**
  - **CD4 > 100 x 6M, asx and therapy >12 m**

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Salvage Therapy for MAC Not For Boards

- No evidence-based standard
- Logical to be guided by in vitro susceptibility testing
  - Not standardized for MAC other than macrolides and amikacin
  - Options
    - Amikacin, Ciproflox, Moxiflox, Mefloquine, Linezolid, Bedaquiline

~~Primary MAC Prophylaxis 2021~~

- Primary prophylaxis against disseminated MAC disease is NOT recommended if ART initiated immediately
  - Primary MAC prophylaxis, if previously initiated, should be discontinued if person is on ART

What Is This?

Immune Reconstitution Inflammatory Syndrome

- Definition
  - Worsening manifestations or abrupt /atypical presentation of infection or tumor when ART started
    - Paradoxical-exacerbation of pre-existing infection or tumor
    - Unmasking-exacerbation of previously occult infection/tumor
- Timing
  - Few days to 6 months after ART initiated
  - Viral load drop more relevant than CD4 rise
    - (better lymphocyte function>number)

Immune Reconstitution Inflammatory Syndrome

- Predictors
  - Pre therapy low CD4 or high VL
  - Prior OI or short therapy for OI
  - High pathogen load
- Outcome-Morbidity Can Be Severe
  - Obstructed bowel, biliary tract, ureter, bronchus
  - Myocarditis, meningeal inflammation/increased ICP, serositis (pleura, peritoneum, pericardium)

Pathogens Commonly Associated with IRIS

- Mycobacterium avium complex
- Mycobacterium tuberculosis
- Cryptococcus neoformans
- Many others
  - CMV retinitis, HBV
  - Mucocutaneous HSV and VZV
  - PCP, Histo
  - PML
  - KS

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Examples of IRIS

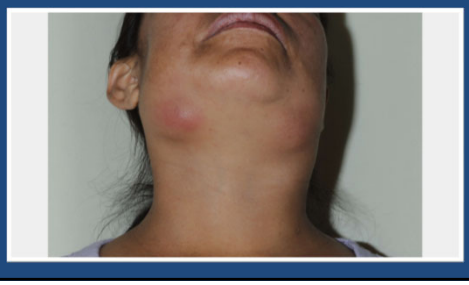
PATHOGEN	NOMENCLATURE	TYPICAL/CHARACTERISTICS OF THE DISEASE
Mycobacterium tuberculosis	TB-IRIS	Paradoxical exacerbation of TB
Nontuberculous mycobacteria (NTM)	NTM-IRIS	Mainly lymphadenitis, also pulmonary and abdominal diseases
Bacille Calmette-Guérin (BCG)	BCG-IRIS	Necrotizing regional lymphadenitis
Mycobacterium leprae	Leprosy-associated IRIS	Borderline and type 1 reactional state
Cryptococcus neoformans	C-IRIS	Mainly meningitis, also lymphadenitis
Pneumocystis jiroveci	Pneumocystosis-associated IRIS	Paradoxical exacerbation of pneumonitis
Cytomegalovirus (CMV)	CMV retinitis after ART or immune recovery uveitis	Acute retinitis after commencing ART or uveitis
JC polyomavirus	PML-IRIS	Multifocal leukoencephalopathy
Human herpesvirus 8	KS-IRIS	Rapid progression of existing and/or new KS lesions
Hepatitis B or C virus	Hepatitis B or C virus-associated IRIS (that may mimic DILI)	Hepatitis flare and/or liver enzyme elevation
Varicella-zoster virus		Dermatomal or multidermatomal zoster and rarely myelitis after ART
Herpes simplex virus		Herpes Lesions with exaggerated inflammation and rarely myelitis or encephalitis after ART
Molluscum contagiosum virus	Inflammatory molluscum contagiosum	Inflamed molluscum lesions
Malassezia spp.	Inflammatory seborrheic dermatitis	Abnormally inflamed seborrheic dermatitis

Cecil Textbook French and Meintjes)

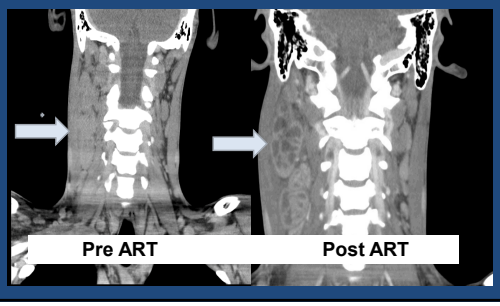
Management of IRIS

- **Reassess Diagnosis**
  - **Evaluate for concurrent, additional OIs and tumors**
- **Treat IRIS**
  - **Continue ART**
  - **Treat identified pathogen-usual practice without data**
  - **NSAIDS or Corticosteroids**
    - **Prednisone 20-40mg qd x 4-8 weeks**

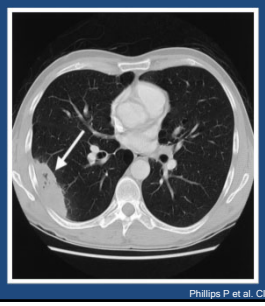
Immune Reconstitution Inflammatory Syndrome (Mycobacterium avium complex)



MAC IRIS in Patient with HIV



CT Scan: Pleural-Based MAC



Phillips P et al. Clin Infect Dis 2005;41:1483

Life Threatening IRIS –How Would They Test for These?

- **Unmasking**
  - Unrecognized lymphadenitis due to TB, MAC, Fungi
  - Unrecognized cryptococcal meningitis
  - Unrecognized CMV retinitis
  - Inflammation of Kaposi sarcoma skin lesion
  - Pulmonary infiltrates due to PCP, fungi, TB
- **Exacerbation of Crypt Meningitis- Increased intracranial pressure**
  - New focal findings
- **Transaminase Flair in Patient with Untreated HBsAg or HBcoreAb**
  - Transaminase flair due to HBV
- **Exacerbation of previously treated CMV retinitis, PCP, TB**

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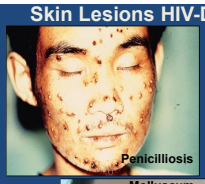
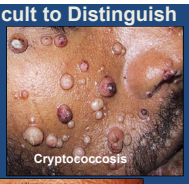
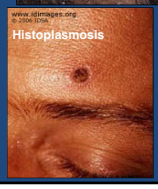
Fungal Diseases in HIV-Infected Persons

- Candidiasis
- Cryptococcosis
- Histoplasmosis
- Coccidiomycosis
- Talaromyces

Skin Lesions HIV-Difficult to Distinguish







Importance of HIV Associated Cryptococcosis

- Prevalence
  - Pre ART in United States- 5 – 8% of patients
  - More common in Sub-Saharan Africa-
    - 15% of AIDS related deaths
  - Less common in current era in US
- CD4 Count at Onset
  - <100 cells/uL in 90% of patients

HIV-Related Cryptococcal Meningitis

- Clinical Presentation
  - CNS manifestations are usually subacute (median 2 weeks)
    - Classic neck stiffness and photophobia only occur in 25%
    - Many cases are disseminated when initially diagnosed-any organ
      - e.g. May mimic PCP or present as lobar consolidation
    - Crypt IRIS is typically more acute than active infection
  - Meningeal involvement may initially be asymptomatic
    - Encephalopathic manifestations usually due to high ICP

Diagnosis of Cryptococcal Disease

- CSF
  - Often minimal abnormalities with lymphocyte pleocytosis
  - Opening pressure >20-25cm H20 in 60-80% of patients
- Crypt Antigen
  - Highly sensitive in serum and CSF
  - CSF crypt ag can be positive months before symptomatic disease
- Blood Culture positive
  - 60% of patients with clinical meningitis
  - Growth in < 7 days

Antigen Tests for Cryptococcal Disease

- Blood, Serum, Plasma, CSF:
  - Antigen Latex Agglutination or
  - Enzyme Linked Immunoassay (EIA) or
  - Cryptococcal Lateral Flow Assay (IMMY LFA)
    - Dipstick test for whole blood/serum/plasma and CSF
    - Four-fold higher titers than Latex Aggl or EIA
    - High titers suggest (1:160) or highly suggest (1:640) dissemination

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PCR Tests for Cryptococcal Disease C. neoformans and C. gatti

- **PCR for CSF**
  - **Screening test available in multiplex assays**
    - **False positives and false negatives (!!) reported**
    - **Simultaneous antigen test should be performed if cryptococcal meningitis is suspected and PCR is negative**
  - **May be useful for distinguishing**
    - **IRIS (PCR neg)**
    - **Relapse (PCR positive)**

Therapy of Cryptococcal Meningitis

Liposomal Ampho B **3-4 mg/kg qd**
plus
Flucytosine* **25 mg/kg QID**
→ 2 weeks- Induction

Fluconazole ~~400~~ **800 mg po qd** → 8 weeks- Consolidation

Fluconazole 200 mg po qd → ≥ 52 weeks-Maintenance

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→ 2 wks- Induction

Fluconazole ~~400~~ **800 mg po qd** → 8 wks- Consolidation

Fluconazole 200 mg po qd → ≥ 52 wks** Maintenance

*5FC Associated with
Earlier sterilization CSF
Fewer relapses
Improved survival

Flucon 800mg consolidation
*Cidal
*Fewer relapses 800 vs 400

** Stop after 12 m total therapy if
CD4 >100- 150 x >3m
Asymptomatic
VL <50 copies

Question #5

Patient presents with cryptococcal meningitis, severe headache, and opening pressure >25 cm H20 on day 1 of therapy

Which of the following would you initiate if the CNS symptoms persist on day 2

A. Dexamethasone
B. Acetazolamide
C. Mannitol
D. Lumbar puncture to remove fluid
E. Lumbar puncture for repeat diagnostic studies and MRI to assess for a second, concurrent infectious or neoplastic process

Answer #5

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Elevated CSF Pressure

- **75% of patients have Opening Pressure >20 cm CSF**
  - **Abnormal = >25 cm CSF**
  - **Left lateral decubitus, flat position**
- **Symptoms**
  - **Blurred vision, confusion, obtundation**
- **Management: IF symptomatic and >25cm**
  - **Remove volume to reduce pressure by half or <20cm H20**
  - **Continue LPs daily for symptomatic patients until stable for at least 2 days**
  - **Shunt if regular LPs required for "many" days**
- **Not routinely recommended**
  - **Corticosteroids, Mannitol, Acetazolamide**

Online Only Lectures - Management of AIDS-Related Opportunistic Infections II

Speaker: Henry Masur, MD

Consolidation Therapy

- **At two weeks**
  - Perform LP and repeat CSF culture
  - Success= Substantial clinical improvement AND negative CSF culture
    - Persistent CSF crypt ag is not indicative of failure
  - If patient is not symptomatically improved
    - Continue induction regimen until CSF culture confirmed as negative
    - (or use flucytosine +fluconazole as outpatient)
- **Continue consolidation until**
  - ART started
  - CSF culture negative

Monitoring Therapy for Cryptococcal Meningitis

- **During Therapy**
  - **"Monitoring serum or CSF CrAg titers is of no value in determining initial response to therapy and is not recommended (AII)"—NIH CDC IDSA Guideline**
  - **Monitor 5FC levels after dose 3 or 5**
  - **Positive CSF culture at 2 weeks indicates need for higher dose fluconazole during consolidation**
  - **Negative serum or CSF Ag is NOT required for termination of therapy**

Commonly Asked Questions

- **Liposomal Amphotericin B Induction for < 14 days**
  - Not recommended and not for boards
- **Fluconazole based regimens in US As Initial Rx**
  - No
- **Amphotericin plus Fluconazole induction**
  - **Not for boards and not recommended in US**

When To Start ART

- **4-6 weeks after initiation of antifungal therapy for meningitis**
  - May have to defer for patients with severe disease
  - When to start for non CNS disease less clear
- **Monitor for IRIS**

Asymptomatic Cryptococcal Antigenemia

(Pre-emptive Therapy for Crypt Ag +/Low CD4)

- **Recommendation:**
  - **Screen patients with CD4< 100**
    - **Frequency: 2.9% if CD4 <100, 4.3% if CD4 < 50**
  - **Positive serum ag predicts development of active disease**
- **If Positive: Perform LP and Blood Cultures to determine Rx**
  - **If CSF positive or serum LFA is >=640**
    - **Treat like crypt meningitis/disseminated (Ampho/5FC)**
  - **If CSF negative**
    - **Treat with fluconazole 400mg or 800mg x6 months**

IDSA OI Guidelines for Crypt 2021

Flucytosine

- **Oral only form available in US**
  - 25mg/kg po q6h
- **Toxicities**
  - Marrow suppression, hepatitis, diarrhea
- **Monitoring**
  - Serum level drawn after 3-5 doses
  - Renal elimination-
    - monitor renal function
  - Maintain 2 hr peak at 30-80ug/ml

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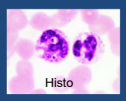
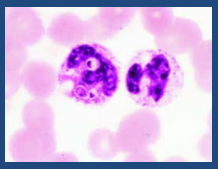
Other Fungal Diseases That Are Covered Elsewhere in IDBR

- Look for questions on patients with HIV and ….
  - Histoplasmosis
  - Coccidiomycosis
  - Talaromycosis



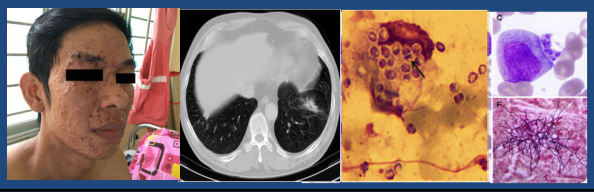
Histoplasmosis

- **Clinical Presentation**
  - CD4>200 cells/uL
    - Focal disease like immunocompetent
  - CD4<200 cells/uL
    - Disseminated disease:
      - Fever, weigh loss, fatigue, hepatosplenomegaly
      - Meningitis, Septic Shock, GI manifestations also common
- **Diagnosis**
  - Antigen detection
  - BAL antigen also useful
  - Cultures useful but….takes several weeks to grow



Talaromyces – Formerly Penicilliosis marnefii

- Rarely if Ever Seen in US
- Common in Asia transmitted by Bamboo Rat or Abiotically
- Serum antigen test (research) sensitive and specific
- Treat with Ampho or Itraconazole



CMV

Non ARS Question

In an HIV positive patient (CD4 count = 50 cells/uL), a positive CMV PCR test of which of the following specimens would be MOST suggestive that CMV is the cause of end organ disease:

A. Esophageal biopsy to diagnose CMV esophagitis
B. Colonic biopsy to diagnose CMV colitis
C. Bronchoalveolar lavage to diagnose CMV pneumonia
D. Blood to diagnose CMV retinitis
E. CSF to diagnose CMV encephalitis

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In an HIV positive patient (CD4 count = 500 cells/uL), a positive CMV PCR test of which of the following specimens would be MOST suggestive that CMV is the cause of end organ disease:

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B. Colonic biopsy to diagnose CMV colitis
C. Bronchoalveolar lavage to diagnose CMV pneumonia
D. Blood to diagnose CMV retinitis
E. CSF to diagnose CMV encephalitis
F. None of the above (ABIM never uses this option!!)

CMV Syndromes
CD4<50 and VL Positive In Almost All Cases

- **Retinitis (30% of Patients Before ART)**
- **Colitis**
  - Can lead to perforation
- **Ventriculitis**
  - Rapid cognitive decline with cranial nerve involvement
- Radiculopathy, Myelitis, Mononeuritis Multiplex, Guillain-Barre
- Esophagitis (uncommon)
- Adrenalitis (rare)
- Pneumonia (rare)

Diagnosis of HIV Related CMV Disease

- **Serology**
  - Disease unlikely if IgG seronegative
  - Rarely done
- **Cytology**
  - Rarely useful
- **Biopsy**
  - Helpful if many inclusions and substantial inflammation
- **PCR**
  - Correlates with CD4 Count
  - "Less than ideal" sensitivity and specificity for clinical disease

Diagnosis of HIV Related CMV Disease

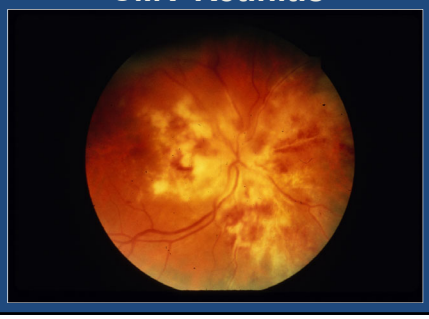
- **Serology**
  - Dise
  - Rare
- **Cytol**
  - Rare
- **Biopsy**
  - Helpful if many inclusions and substantial inflammation
- **PCR**
  - Correlates with CD4 Count
  - "Less than ideal" sensitivity and specificity for clinical disease

- **Clinical Presentation**
- **Rule Out Other Causes When Appropriate**

Diagnosis of CMV Retinitis

- **Funduscopic exam**
- **Bilateral in 30% of untreated patients**
- **Mustard and Ketchup**
- **Necrosis of retina**
- **Little vitreal inflammation**
- **PCR of blood not useful: 70% sensitive, very non specific**
- **Vitreal taps for diagnosis with PCR rarely necessary**
  - **Tap positive in 80% of cases**

CMV Retinitis



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Therapy for CMV Retinitis

(Ganciclovir intraocular implant no longer available)

- Immediate sight-threatening lesions
  - ART
  - IV Ganciclovir or Valganciclovir 900 mg PO (bid x 14–21 days), then qd for at least 3-6 months plus
  - Intravitreal ganciclovir weekly over several weeks until lesion inactivity
    - Injections can be associated with infections or retinal detachment and hemorrhage
- Small peripheral lesions
  - ART
  - Oral valganciclovir for at least 3-6 months and immune reconstitution
  - +/- intravitreal ganciclovir

Salvage Therapy for CMV Retinitis

(Hard to Ask on Exam)

- Systemic Options
  - Ganciclovir higher dose
  - Foscarnet IV
  - Foscarnet IV plus Ganciclovir IV
  - Cidofovir IV
- Intraocular
  - Ganciclovir or Foscarnet

Treatment of Other CMV Syndromes

- IV or Oral Ganciclovir or Foscarnet
- Duration hard to test
  - Colitis or Esophagitis
    - 21-42 days or until clinical resolution
  - Ventriculitis
    - Not certain: some would use ganciclovir plus foscarnet

Thank You