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Opportunistic Infection Prophylaxis in HIV

HIV Infection = Infection with HIV
AIDS = Acquired Immune Deficiency Syndrome

OI = markers of immune deficiency

CD4 <200 = marker of immune deficiency

CD4 <200 is associated with increased risk of opportunistic infections

CD4	OI
Any	TB, Lymphoma, Kaposi’s sarcoma, Zoster
<200	PJP, thrush
<100	cryptococcosis, mucosal HSV
<50	Toxoplasmosis, CMV, MAC, cryptosporidiosis

OI	Initiate primary prophylaxis	Stop primary prophylaxis	Restart primary prophylaxis	Start secondary prophylaxis	Stop secondary prophylaxis	Restart secondary prophylaxis
PJP	CD4 <200 or oral candidiasis	CD4 >200 x3mo	CD4 <200	Prior PJP	CD4 >200 on ART	CD4 <200
Toxoplasmosis	IgG+ & CD4 <100	CD4 >200 x3mo	CD4 <100	Prior Toxo encephalitis	CD4 >200 x6mo on ART + completed initial Rx + asymptomatic	CD4 <200
MAC	CD4 <50	CD4 >100 x3mo	CD4 <50	Prior disseminated MAC	CD4 >100 on ART + 12mo MAC Rx + asymptomatic	CD4 <100
Cryptococcosis	None	na	na	Prior cryptococcosis	CD4 >100 x3mo on ART + completed initial Rx + 12 mo azole	CD4 <100
Histoplasmosis	CD4 <150 + at risk	CD4 >150 x6mo	CD4 <150	Prior histoplasmosis	CD4 >150 x6mo on ART + 1 yr Rx + Neg blood fungal Cx	CD4 <150
CMV	None	na	na	Prior end organ disease	CD4 >100 x 6mo on ART + no active dz + regular exams	CD4 <100

OI	Rx
PJP	TMP/SMX DS tiw (less if CrCl <30) OR Dapsone 100mg qday OR Atovaquone 1500mg qday
Toxo	TMP/SMX DS qday (less if CrCl <30)
MAC	Azithromycin 1200mg qweek (Zpak qweek)
Cryptococcosis	Fluconazole dose dependent on ART, secondary prophylaxis only
Histoplasmosis	Itraconazole dose dependent on ART, secondary prophylaxis only
CMV	Valganciclovir 900mg qday (less if CrCl<60), secondary prophylaxis only

When to start ART during an acute opportunistic infection?

OI	ART initiation
PJP	within 2 weeks of PJP diagnosis
Disseminated MAC	2 weeks of MAC treatment
Toxoplasmosis	no data - within 2 weeks of Toxo diagnosis
Candida	no data - as soon as possible
PML	as soon as possible
Cryptococcal meningitis	controversial - 2 weeks

IRIS

Immune Reconstitution Inflammatory Syndrome

Infection	Sign/symptom
MAC	adenitis
TB	paradoxical
CMV	retinitis/uveitis
VZV	Zoster
HSV	encephalitis/mucosal
HBV/HCV	hepatitis flare
JC virus	PML
KS	new lesions/flare up of existing lesions

Reference:

1. aidsinfo.nih.gov/guidelines
2. Short WR, Opportunistic Infections (Prevention, Diagnosis, and Management) ACTHIV 2015

Metabolic Issues in HIV

- HIV infection itself as well as certain antiretrovirals have been implicated in development of metabolic disturbances

- Complications include glucose metabolism disorders, lipid abnormalities, adipose tissue disorders, abnormal bone metabolism, as well as cardiovascular implications

- Uncontrolled HIV = increase in inflammation = increased rates of CVD

- Certain ART (protease inhibitors, NRTIs - abacavir and didanosine) appear to be associated with increased CVD risk (via lipid/glycemic variables vs inherent mechanism)

HIV and glucose metabolism:

- Glucose metabolism disorders are commonly reported among HIV infected patients (with or without ART) - impaired glucose tolerance, insulin resistance, elevated fasting glucose (25-35%), & diabetes (2-7%)

- Protease inhibitors may reduce pancreatic insulin secretion and decrease glucose transport, thereby increasing serum glucose

- NRTIs associated with impaired glucose metabolism mostly via adipose tissue changes

- Increased visceral fat among HIV infected patients may play a role

HIV and lipid metabolism:

- Uncontrolled HIV is an independent risk factor for lipid abnormalities

- Low CD4 is associated with increased lipid abnormalities

- ART can increase total cholesterol, TG, LDL, and decrease HDL

- ART interruption has shown to improve lipid profile but increase CVD risk (possibly excess risk of CVD in HIV not lipid mediated?)

- HIV and ART increase the risk of lipodystrophy (peripheral lipoatrophy and visceral lipohypertrophy)

HIV and bone metabolism:

- associated with increased risk of avascular necrosis (femur and humerus) and osteopenia/osteoporosis

- Increased risk of fractures in HIV infected patients

- HIV itself appears to contribute to low bone mineral density

- HIV infected patients on ART may have lower Vitamin D levels

- ART - protease inhibitors and tenofovir may increase the risk of low BMD

HIV and cardiovascular risk:

- independent risk factor for CVD

- HIV associated with endothelial dysfunction and increased atherosclerosis

- chronic immune activation - increased inflammation

- presence of comorbid opportunistic organisms (ex: CMV) also damage endothelium

- traditional risk factors (diabetes/HTN/dyslipidemia) contribute to more CVD among HIV infected patients compared to HIV uninfected

- Comorbid conditions like smoking is higher among HIV infected patients, raising CVD risk

- HIV infected patients are living longer = better screened for metabolic disturbances

- pertinent to assess cardiovascular risk of a patient thoroughly prior to starting ART

- ongoing counseling regarding residual risk reduction for CVD

- management of metabolic complications, active monitoring of metabolic status on ART using assessment tools that are relevant

Reference:
1. Martin A, Emery S, Expert Review Clinical Pharmacology. 2009;2(4):381
2. Mall SA, Nolan DA, Metabolic Complications of HIV Infection and its Therapy. medscape.org

Immunizations in HIV infected patients

Guidelines:

1. Infectious Diseases Society of America
2. CDC
3. NIH
4. HIV Medical Association (of IDSA)
5. DHHS
6. ACIP

- Data on vaccinations in HIV infected patients look at immunogenicity rather than clinical efficacy

- Vaccines tend to be less immunogenic and antibody responses are shorter lived compared to non HIV infected patients

- Administer vaccines early in the infection, prior to CD4 decay, or after immune reconstitution with virologic suppression

- Inactivated vaccines are generally safe

- Live vaccines (varicella/MMR) should NOT be given if CD4 <200

Same as general population:
1. Inactivated seasonal influenza vaccine
2. Td or TdaP
3. HPV (up to age 26)

Vaccines for which HIV is an indication:
1. Pneumococcal vaccines
2. Hepatitis B vaccine (if not already immune)
3. Meningococcal vaccine

Special indication in HIV:
1. Hepatitis A vaccine (if indicated)
2. Hemophilus influenza b vaccine
3. MMR (if not already immune and CD4 >200)
4. Varicella vaccine (if not already immune and CD4 >200)

Pneumococcal vaccines:
- at least one dose of PCV13, followed by PPSV23 at least 8 weeks later (prime boost strategy)
- Revaccinate with PPSV23 after 5 years of initial PPSV23
- PCV13 can be given at any CD4 count
- defer PPSV23 until CD4 >200

Influenza vaccine:
- Annual seasonal flu shot
- Live, intranasal flu vaccine should NOT be used in HIV

Hepatitis B vaccine:
- All HIV infected patients are at high risk for Hepatitis B due to shared mode of transmission
- If infected, HIV infected patients are at higher risk to develop chronic Hepatitis B infection
- Routinely screen and immunize HIV infected patients. Many need revaccination (booster shots)

Meningococcal vaccine:
- Immunize with meningococcal conjugate ACWY (Menveo or Menactra)
- 2 doses 8 weeks apart (if previously not vaccinated), booster every 5 years
- Menactra should be given at least 4 weeks after pneumonia vaccine

Reference:

1. uptodate.com
2. ACIP

HIV Associated Neurocognitive Disorders (HAND)

- Neurocognitive deficits in HIV infected patients without alternative explanation

Frascati criteria (UCSD) - 3 levels of impairment
1. ANI - Asymptomatic Neurocognitive impairment
2. MND - Mild Neurocognitive Disorder
3. HAD - HIV Associated Dementia

- Definitions applied only when impairment cannot be explained by other conditions

1. Asymptomatic Neurocognitive Impairment = score of 1SD+ below the mean in at least 2 cognitive domains in a standardized test + without symptomatic impairment

2. Mild Neurocognitive Disorder = same as above + symptomatic functional impairment

3. HIV Associated Dementia = 2SD+ below the mean in at least 2 cognitive domains + impairment of ADLs

ANI and MND should not be used in clinical setting without a formal neuropsychological testing

- Prevalence of HAD is approaching that of uninfected population due to ART

- ANI and MND - 20-70% of HIV infected patients

- Risk factors = host genetic factors, HIV disease factors (low nadir CD4/AIDS, HIV duration, older age at seroconversion), comorbidities (age, vascular dz, metabolic abnormalities)

Clinical presentation:

- HAD typically occurs in advanced AIDS, untreated, high viral load
- HAD = subcortical dysfunction = attention/concentration impairment, depression, impaired psychomotor precision, apathy/ lack of motivation, irritability, anxiety, slowness of movement etc
- Subacute onset, waxing and waning (unlike Alzheimer's - progressive)

- Milder cognitive impairment = difficulty with working memory, attention, problem solving, affective disturbances
- Subtle symptoms in ANI/MND - may be overlooked or attributed to fatigue etc

CNS viral escape syndrome - Rare - Patients well controlled on ART but CSF HIV is replicating and possibly has developed resistance to current ART - symptoms could be severe

Screening for HAND:
- usually not indicated (absence of clear evidence to support change in management)
- may be considered in research setting, availability of resources, HIV specific clinics
- may indicate risk of non adherence
- baseline may be useful in case of subsequent deterioration
- Screening instruments: MoCA, HIV Dementia Scale
- Differential diagnoses are broad
- Management includes controlling HIV with ART and supportive/symptomatic care

Reference:
1. Antinori A, Arendt G, et al, Updated research nosology for HIV associated neurocognitive disorders. Neurology 2007; 69:1789
2. uptodate.com

HIV/HBV and HIV/HCV confection

HIV/HBV coinfection

- shared mode of transmission

- Chronic HBV affects 10% of HIV infected patients worldwide

- less prevalence in the US because of vaccination for HBV

- 8% of HIV infected patients in the US, not vaccinated to HBV had chronic HBV infection

- Diagnosis of chronic HBV infection is the same as in HIV uninfected patients

- All HIV infected patients should be screened for chronic HBV

-HBV dna levels and reactivation higher in HIV infected patients

- risk of reactivation may be associated with low CD4

- Reappearance og Hepatitis B has been documented in HIV infected patients with prior resolved HBV

- HIV infected patients have lower rates of spontaneous HBeAg clearance

- HIV presence can accelerate liver deterioration caused by HBV

- HCC risk is at an earlier age if HIV is present

- Drug induced liver injury risk is higher among HIV/HBV connected patients

- Hepatitis B is vaccine preventable

- Some anti HIV medications are effective against HBV (tenofovir, lamivudine) and should be used preferentially (in the absence if risk factors) when treating HIV

- Avoid treating either/or HIV/HBV - preferable to treat both (HBV is immunologically mediated)

- Treatment interruption in HIV/HBV connected patients need to be monitored very closely (risk of fulminant hepatic failure)

HIV/HCV coinfection

- 6% of HIV infected patients also have chronic Hepatitis C worldwide

- 30% of HIV infected patients in the US have chronic Hepatitis C

- Higher rates of HCV in HIV infected patients who are also IVDU

- Transmission mode based risk differs. More IVDU get infected with HCV before HIV. More MSM get infected with HIV before HCV

- HIV increases the risk of vertical transmission of HCV

- Liver fibrosis progression among patients with HCV is accelerated if they also have HIV

- Hepatitis C treatment failure rate is slightly higher if there is concomitant HIV infection

- Incidence of liver cancer up to 8 times higher in connected patients compared to HCV monoinfection

- ART for HIV may decrease the risk of liver deterioration among connected patients

- All HIV infected patients should undergo screening for HCV

- Immunocompromised patients (CD4 <100), should be screened with HCV RNA PCR if there are risk factors for HCV/elevated ALT if HCV Ab is negative

- Repeat screening for HCV among HIV infected patients should be based on ongoing risk factors

- Selection of ART may be based on possible HCV treatment options (drug interactions)

- HIV infected patients with chronic Hepatitis B or Hepatitis C should be closely monitored for liver disease progression

- HCC surveillance (ultrasound q6mo) is warranted in all patients with cirrhosis

- HCC surveillance (ultrasound q6mo) is warranted in all patients with chronic Hepatitis B regardless of cirrhosis

- Hepatitis C is curable (but not vaccine preventable)

- Hepatitis B is not curable (but vaccine preventable) and controllable

Thanks