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SERVICE PROVIDER NEWSLETTER
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New AfA Guidelines for Initiating HAART in Adults

AfA have updated the guidelines on when to start HAART. These changes are broadly in line with the WHO guidelines and the recently published SA HIV Clinicians Society guidelines. The major difference from the previous guidelines is the importance of clinical evidence of immune suppression (WHO clinical stage 3) without full-blown AIDS (WHO clinical stage 4). HAART can be initiated for WHO stage 3 patients provided their CD4 count is <350 (except for tuberculosis - see below).

The patient MUST be ready for treatment.

AND

The patient has a WHO stage 4 condition (For TB - see below).

OR

One CD4 count less than 350 AND a WHO stage 3 condition (For TB - see below).

OR

Stage 1 and 2 with two CD4 counts less than 350 done at least 6 weeks apart.*

*Individuals with high viral loads (> 100 000) or with rapidly declining CD4 counts or troublesome HIV-related symptoms that are not covered in the WHO staging system should have HAART commenced without delay, whilst others can wait until their CD4 count approaches 200.

It is important to note that tuberculosis by itself is not an indication for starting HAART - even with extrapulmonary or disseminated tuberculosis (both of which are WHO stage 4 conditions). The reason for this is that tuberculosis occurs with a wide spectrum of CD4 counts in endemic areas such as Southern Africa. Furthermore, there are three important problems associated with the simultaneous administration of HAART and anti-tuberculous medication: drug interactions with rifampicin (which induces the hepatic metabolism of many drugs, resulting in lower levels), shared toxicity and the immune reconstitution inflammatory syndrome (causing paradoxical deterioration of tuberculosis shortly after HAART is commenced).

AfA have adopted the WHO and South African national guidelines for commencing HAART in patients with tuberculosis:

CD4 >200	defer HAART until TB has been treated then reassess
CD4 50-200	defer HAART until 2 months of TB treatment has been completed
CD4 <50	start HAART once improving on TB therapy

WHO Clinical Stage III and IV Conditions

Clinical Stage III:
Weight loss, > 10% of body weight
Unexplained chronic diarrhoea > 1 month
Unexplained prolonged fever (intermittent or constant), > 1 month
Oral candidiasis (thrush)
Oral hairy leucoplakia
Pulmonary tuberculosis within the last year
Severe bacterial infections (i.e. pneumonia)

Clinical Stage IV (AIDS):
HIV wasting syndrome*
Pneumocystis pneumonia
Toxoplasmosis of the brain
Cryptosporidiosis with diarrhoea > 1 month
Cryptococcosis, extrapulmonary
Cytomegalovirus disease of an organ other than liver, spleen or lymph node (e.g. retinitis)
Herpes simplex virus infection, mucocutaneous (>1month) or visceral
Progressive multifocal leucoencephalopathy
Any disseminated endemic mycosis
Candidiasis of oesophagus, trachea, bronchi
Atypical mycobacteriosis, disseminated or lungs
Non-typhoid Salmonella septicaemia
Extrapulmonary tuberculosis
Lymphoma
Kaposi's sarcoma
HIV encephalopathy**

*HIV wasting syndrome: weight loss of > 10% of body weight, plus either unexplained chronic diarrhoea (> 1 month) or chronic weakness and unexplained prolonged fever (> 1 month).

** HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

Practice point OF THE MONTH

Switching from efavirenz to nevirapine

Patients who cannot tolerate efavirenz (e.g. as a result of CNS toxicity) are usually switched to nevirapine. As efavirenz is an hepatic enzyme inducer, the nevirapine should be commenced at full dose (200 mg 12 hourly) and not at the lead-in dose of 200 mg daily for the first two weeks.

Management of isolated elevated Gamma Glutamyl Transpeptidase (GGT) levels in HIV

GGT is present in many organs, including the kidney and brain, but the liver contributes most of its plasma concentration. Elevated GGT levels are a sensitive marker of liver injury and cholestasis, but have low specificity for liver disease. Low level elevations of GGT (< 5 fold upper limit of normal (ULN)) are common in HIV disease per se, and are also seen with co-administration of medications such as warfarin, phenobarbitol and phenytoin, as well as alcohol consumption. Diseases of other organs such as chronic pancreatitis, renal failure and diabetes may also be associated with elevated GGT.

In higher level elevations, (grade 3 : 5-10 > ULN; grade 4 : > 10 fold ULN)

1. Chronic alcohol abuse must be considered, and the patient queried about alcohol consumption, counseled appropriately, and, if necessary, referred for appropriate investigation and intervention.

2. If alcohol abuse is excluded, an abdominal ultrasound should be performed, along with a full liver function test (LFT) battery. If the ultrasound is normal, and the LFTs suggest no other pathology, the patient should be carefully observed, with repeat LFTs performed after 1 month. If the patient is on NRTIs, particularly stavudine, or a combination of stavudine and didanosine, and has other symptoms / signs of mitochondrial toxicity - peripheral neuropathy, lipodystrophy syndrome, mildly elevated transaminases (grades 1-2) and/or loss of weight, and abdominal symptomatology, a serum lactate should be performed to exclude symptomatic hyperlactataemia. If lactate level is > 5, an acid / base assessment should be considered.

3. If the abdominal ultrasound is suggestive of extrahepatic obstruction (dilated bile ducts) refer to a surgeon or physician for investigation (ERCP or MRCP).

4. If the abdominal ultrasound shows features of fatty liver, and the patient is on NRTI containing HAART, the patient should be queried regarding signs and symptoms of mitochondrial toxicity (as above), and, if deemed necessary, a serum lactate performed. HIV itself can also cause a fatty liver, but if the diagnosis is not apparent, and derangement of LFTs is worsening, a liver biopsy should be considered.

Follow-Up Results for AfA Patients

Please ensure that the results of follow-up CD4 counts, viral loads and other investigations are sent to AfA timeously. This is important to enable us to assist you in monitoring your patients. You can fax results to us on 0800 600 773.

If you write CC Aid for AIDS on the lab request form the laboratory will automatically send us a copy of the result.

NB: Most schemes are now including the HIV related out of hospital pathology costs in the AfA benefit. There are limitations on the number of tests allowed per year. This is advantageous for patients as they shouldn't run out of benefits for HIV pathology (provided that they don't exceed the number of tests allowed per year). If additional tests are clinically indicated they can be motivated for and approved by AfA. HIV resistance testing will only be paid for if approved by AfA.

Treating PCP in Patients who are Allergic to Co-trimoxazole

There are limited options available in South Africa for patients with co-trimoxazole intolerance. Pentamidine and primaquine (the latter is given with clindamycin) are no longer available in South Africa, so the only available alternative therapies are dapsone 100mg daily plus trimethoprim 300mg tds OR atovaquone 750 mg BD - these are only suitable for mild to moderate PCP. Atovaquone is extremely expensive.

Co-trimoxazole desensitisation should be considered for patients with severe PCP. The rapid desesitisation regimen listed below was successful in 19/22 patients with no significant problems in the 3 who failed. However, a further 3 patients had to subsequently discontinue due to the development of a rash (Clin Infect Dis 1995;20:849).

Use co-trimoxazole suspension 240mg/5ml. Co-trimoxazole suspension will need to be diluted appropriately. Please consult your pharmacist or contact AfA. Desensitisation must be conducted in hospital and should be done WITHOUT antihistamine or steroid cover.

Time (hours)	Dose (mls of undiluted co-trimoxazole susp)
0	0.0005
1	0.005
2	0.05
3	0.5
4	5
5	two single strength tablets

Followed by full dose.

AfA Clinical Guidelines - 5th Edition

The 5th edition of the AfA Clinical Guidelines will be available shortly. If you would like to receive an electronic copy (pdf file) of the guidelines via email please send a request to afa@afadm.co.za (enter Clinical Guidelines in the subject of the email). The guidelines will also be available on the AfA website - www.aidforaids.co.za.

The 5th edition of the guidelines have been extensively revised in consultation with experienced colleagues throughout South Africa and neighbouring countries and continue to reflect national as well as international best practice.

Drug interaction OF THE MONTH

African potato (Hypoxis hemerocallidea) and Sutherlandia with antiretroviral drugs

Latest information available shows that these two products could have a significant interaction with antiretroviral medicines. In a laboratory study African potato showed a significant inhibition of CYP3A4 activity. Sutherlandia also inhibited CYP3A4.

Extreme caution should be taken if using herbal medicines in the treatment of HIV.

Reference: Mills E et al. Impact of African herbal medicines on antiretroviral metabolism. AIDS 19: 95 - 97, 2005.