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CD4 COUNTS FOR DUMMIES

The most common misconception regarding the "CD4" count, is that it is a measurement of the individual's HIV status. In effect, the CD4 count is a fairly crude measurement of a group of the cells in the immune system known as T-Helper cells, and is affected by any and all the other infections, vaccinations, and other insults suffered by the immune system on a daily basis. In addition, the CD4 count has a diurnal variation, being highest late at night, and lowest first thing in the morning. The degree of variation diminishes as the HIV disease progresses.

The T-Cells of the immune system can be considered a principal line of cellular defence, and are significantly affected in HIV disease. They all carry a common protein marker, CD3, and are further differentiated by proteins such as CD4 (T Helper cells - responsible for instructing the immune system in appropriate response to insult), and CD8 (T Cytotoxic cells, responsible for carrying out the instructions issued by the CD4 cells).

In HIV, CD4 cells are primarily infected, causing a diminishing in the quantity and quality of these cells over time. Typically, in the absence of intercurrent infections, the rate of decline of the CD4 count is between 40 and 80 cells per year. When the count falls below 200, the patient is considered at high risk for opportunistic infections such as pneumocystis carinii pneumonia. When the count falls below 100, the risk of death rises exponentially.

The use of the CD4 count :

- Single counts have limited value, with sequential assessments providing the most useful information.
- Initial staging of the illness and degree of immune suppression
- Over time (6 monthly assessments) giving an assessment of disease progression
- Making decisions regarding starting and stopping opportunistic infection prophylaxis
- With new guidelines, utilising CD4 count decline between counts of 200 and 350 to decide on optimal initiation of therapy

How to do a CD4 count :

- Take one EDTA (purple top) tube, invert 5 times gently after venesection. It is often helpful to do a concurrent full blood count in the unlikely event of having a laboratory error. In certain laboratories, the CD4 count is calculated as a percentage of the total lymphocyte count, making a full blood count mandatory. This requirement should be checked with your local laboratory.
- Cost : approximately R90 - R100/ protein marker (ie R200 - R300). A new technology being assessed in South Africa may allow reduction in this cost to approximately R90/test.

Drug interaction OF THE MONTH

HMG Co - A Reductase Inhibitors (statins)

The generalised problems of elevated cholesterol which are prevalent in Southern Africa, in addition to the cholesterol elevations which may be induced by certain of the antiretroviral agents used in treating HIV, make the use of the statin class of agents a consideration in many patients.

These agents (with the exception of pravastatin which is primarily renally metabolised) are primarily hepatically metabolised, through the Cytochrome P450 system. This may interact with antiretroviral agents which induce or inhibit this system, particularly the Protease Inhibitors (PIs)

Use of simvastatin is considered contraindicated with indinavir, saquinavir, ritonavir and amprenavir. These combinations can induce musculoskeletal problems such as:

- **Myopathy** (Elevated CPK, muscle pain, weakness +/- fever and malaise) Rhabdomyolysis with renal failure have been reported.
- **Hepatic problems** such as elevated transaminases (1-2%)
- **Miscellaneous problems** such as diarrhoea, constipation, nausea, heartburn, stomach pain, dizziness, headache, skin rash, insomnia

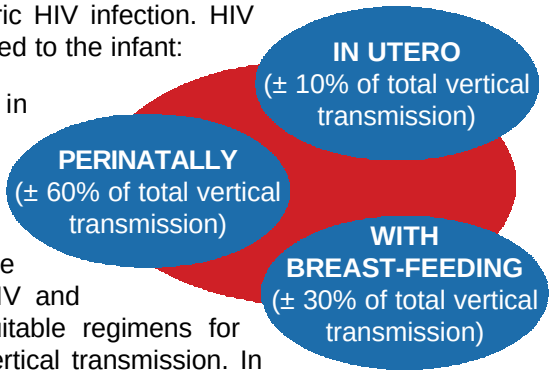
Levels of atorvastatin are elevated by the PIs listed above, so this combination should be used with caution, titrating doses from very much lower levels than those conventionally used e.g. 5 mg daily.

Practice point OF THE MONTH

Breastfeeding increases the risk of HIV transmission from an HIV positive mother to her baby and should therefore be discouraged. Some HIV positive mothers may, however elect to breastfeed. The risk of transmission can be reduced if the mother is encouraged to breastfeed exclusively (without the addition of water, formula milk, juices, cereals or solids) for a maximum of 4-6 months, with rapid weaning thereafter.

MOTHER-TO-CHILD TRANSMISSION PROPHYLAXIS

Mother-to-Child transmission accounts for 95% of paediatric HIV infection. HIV can be transmitted to the infant:



HIV infection in children can almost be eliminated if all pregnant women are screened for HIV and then offered suitable regimens for prevention of vertical transmission. In the absence of intervention, transmission rates may be as high as 30% with an additional 14% occurring through non-exclusive breast-feeding. It is therefore both a social and ethical responsibility that we as health care providers and funders, are able to reduce the risk of MTCT with the interventions available to us. All pregnant females should be offered counselling and testing for HIV.

The risk is halved with the use of zidovudine monotherapy and further additive benefit is obtained by stopping breastfeeding and offering elective Caesarean section. With a combined approach using HAART rates of transmission of <5% are achieved. An undetectable viral load in the expectant mother has been associated with zero transmission in the absence of caesarean section.

Pregnant women who are found to be HIV-positive may be offered termination of pregnancy. Those who wish to continue with the pregnancy should receive comprehensive counselling. The risk of transmission should be discussed and formula feeding should be recommended wherever possible. Some mothers may elect to breast-feed. This decision should be supported and exclusive breast-feeding (without the addition of water, formula milk, juices, cereals or solids) should then be recommended for between 4 and 6 months, with rapid weaning thereafter. Milk supplements will be authorized for payment by AfA. Formula feeds will be authorized for six months (2kg a month).

Pregnant women who require treatment with antiretroviral therapy should be initiated on HAART, although drugs should be avoided in the first trimester if at all possible. Zidovudine should be used as a component of HAART in pregnancy as there is most experience with this drug. Use of zidovudine in a previous pregnancy is not associated with diminished efficacy in subsequent pregnancies. Protease inhibitors or nevirapine (liver function must be carefully monitored on nevirapine) can be used in pregnancy, although nephrolitiasis and hyperbilirubinaemia may be a problem with indinavir. Nelfinavir, ritonavir and saquinavir appear to be well tolerated and safe in pregnancy. Women who become pregnant while taking antiretrovirals, should generally continue with their drug regimen provided this has been shown to be effective. Exceptions are efavirenz or hydroxyurea as both are teratogenic - termination of pregnancy should then be offered. **(Note: women of childbearing age and on either efavirenz or hydroxyurea should be on adequate contraception and counselled to avoid pregnancy)**. While efavirenz is contraindicated in early pregnancy it may be considered in late pregnancy if no alternatives exist. Fatal lactic acidosis has been reported in pregnant women treated throughout gestation with both stavudine and didanosine. This combination should therefore be avoided.

CD4 lymphocyte counts are about 25 percent lower in pregnancy, falling to a nadir at the end of the first trimester. The CD4 percentage remains unchanged. CD4 count rises to pre-pregnant levels 3 months after delivery. If the count is less than 200/µl, daily co-trimoxazole should be given as primary prophylaxis.

Elective Caesarean section before the onset of labour has been shown to reduce the risk of transmission substantially and should be offered. If the viral load is <1000 then Caesarean section does not add further benefit. The following MTCT prophylaxis regimens are recommended:

1 Short course HAART (see above for recommended regimens) commencing at the second trimester. This is the most effective form of mother-to-child transmission prophylaxis, particularly if the viral load is greater than 1000 copies/ml before starting HAART.

2 Monotherapy with zidovudine during the last 12 weeks of pregnancy. This is a reasonable option for women with detectable virus but with levels below 1000 copies per ml.

3 Woman presenting late should be offered zidovudine during labour/delivery and the syrup to the baby. The role of nevirapine in this situation has not been fully determined. Preliminary evidence suggests additive benefit to zidovudine. What is not known is whether the zidovudine will protect the mother or infant from acquiring nevirapine resistance mutations. Nevirapine 200mg STAT to the mother and 2mg per kg to the infant may be given in addition to zidovudine, but this may jeopardise future therapy options. Women who present too late should be given nevirapine 200mg STAT together with zidovudine and lamivudine for 3 days (nevirapine has a long half life) in an attempt to prevent nevirapine resistance.

The use of dual nucleoside therapy only (e.g. zidovudine and lamivudine) as MTCT prophylaxis should be discouraged because of the risk of developing 3TC resistance.

In all cases infants should receive a short course of zidovudine suspension for 6 weeks. The dose in term infants is 2 mg/kg per dose qid, beginning 8-12 hours after birth, for up to six weeks. Where antenatal ART was commenced from 28 to 32 weeks, zidovudine need only be given to the neonate for 3 days. Beyond this period, it is preferable to give for 6 weeks. Premature infants (< 34 weeks gestation) should receive 1.5 mg/kg orally or IV every 12 hours, from 8-12 hours after birth to two weeks of age, then increase to 2 mg/kg every 8 hours up to six weeks of age. Full blood counts should be done at 3 weeks to exclude anaemia or neutrapaenia. If there is evidence of zidovudine resistance, alternative regimens should be considered for the infant - please contact the AfA programme. Zidovudine should also be given during labour and delivery (1 mg/kg/hour by constant IV infusion or 300 mg, three hourly, orally). Avoid any instruments or procedures during delivery. A qualitative HIV PCR should be performed on the infant at 4-6 weeks to determine if infection has occurred. The HIV ELISA may be positive for the first 12 months because of maternal antibodies.

After delivery women who commenced HAART with CD4 counts above 350 should discontinue antiretrovirals in order to limit toxicity and preserve future options. HAART can be recommenced when criteria for initiating therapy are fulfilled. Alternative forms of VTP may be discussed with the AfA Clinical staff.

There is overwhelming evidence that MTCT prophylaxis is safe and effective. All pregnant women should be counselled and tested for HIV!