Academic Alliance for AIDS Care and Prevention in Africa

ATIC News

A quarterly newsletter of The AIDS Treatment Information Centre

Dec. 2004

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Handling needlestick injuries

BY ALLAN RONALD MD FRCPC

HEALTHCARE workers around the world experience over a million "sharp" injuries annually and in some studies nurses experience two to three injuries annually. The risk of infection is estimated to be about 1:300 exposures if the source is HIV-infected. This kind of risk is similar to being hit by lightning - a low frequency but high consequence occurrence.

All patients with occupational injuries should be cared for as follows:

- The local wound should be immediately irrigated with a weak solution of sodium hypochlorite and blood drawn from the healthcare worker and the source, if possible, for baseline HIV and Hepatitis B and C serology.

Utmost precaution is necessary when handling blood samples

- Immediate assessment of the severity of the injury (What was the bore of the needle? Was blood seen on the needle? What was the depth of the penetration? Is the source known to be HIV-positive? Is the source on antiretrovirals?)
- .Depending upon the results of the assessment of the findings obtained, the patient should be offered post-exposure (PEP) if the source is HIV-positive and the injury is significant. (See additional details about choice below).
- The patient should be educated about avoiding needlestick injuries in the future and should also be counselled about the risks of transmitting HIV to sexual partners if he/she were to become infected. Although it seems quite unrealistic, in North America patients are counselled to use condoms and have only protected sex for 12 weeks after a needlestick injury.
- The percutaneous injury is documented by Infection Control and, along with other episodes of injury, is used to develop strategies to reduce "sharps" injury.
- The patient is supported throughout the course of antiretroviral (ARV) PEP therapy

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WHO modifies cotrimoxazole guidelines

THE use of the low-cost antibiotic cotrimoxazole significantly reduced the death rate among HIV-positive children participating in a clinical trial in Zambia, according to a study published in the November 20 issue of the *Lancet*. The results of the study, which was stopped early because of the drug's success, have prompted scientists to recommend that cotrimoxazole be given to all HIV-positive children in developing countries. Dr Diana Gibb of Britain's Medical Research Council and colleagues administered the drug or placebo to 541 HIV-positive children ages one to 14 in Zambia (*Reuters*, 11/19). Half of the children were given a daily oral placebo and half were given cotrimoxazole, which costs less than 10 cents per day per child. When researchers followed up with the children after 19 months, 28% of the HIV-positive children in the cotrimoxazole group had died, while 42% of the children in the placebo group had died. The findings were "so remarkable" that the study was discontinued on "ethical grounds," and all of the children were put on a regimen of co-trimoxazole.

Biomedical Research

WHO, UNAIDS and UNICEF, guided by this recent evidence, have agreed to modify as an interim the current recommendations for cotrimoxazole prophylaxis in children. These data and other new evidence will be reviewed in early 2005 by an expert committee convened to revise and update the recommendations for cotrimoxazole for adults and children.

Cotrimoxazole remains important even with increasing access to ART, as its use can improve survival independently of specific HIV treatment. Current recommendations suggest it should be used before children require ARVs because it may even postpone the time at which ART needs to be started.

Prophylactic dosing with cotrimoxazole for HIV-infected children with any sign or symptoms suggestive of HIV is a key intervention that should be offered as part of a basic package of care to reduce morbidity and mortality.

WHO

From The Editor

P. O. Box 40008, Kampala, Uganda. Tel: 256-41-542352; 542283; email: bbitangaro@iph.ac.ug

ATIC is located on 1st floor Makerere University Institute of Public Health, Mulago Hospital. ATIC acknowledges the support of Roche Pharmaceuticals, Pfizer, Makerere University, Mulago and all its partners.

A thank you to our colleagues

In this issue, *ATIC News* takes the opportunity to thank all those wonderful people and organisations that have contributed to the success of *ATIC News*.

In just one year, with the help of contributors and partners, *ATIC News* has grown in leaps and bounds and today three of our editions have been distributed to over 8,000 people in Africa, Europe and North America. This is the fourth issue of our quarterly newsletter. The first, second and third editions were distributed to 2,000, 3,500 and 2,600 colleagues respectively. *ATIC News* is distributed both electronically and in hard copy. *ATIC News* is an activity of The AIDS Treatment Information Centre which was established in July 2003 to give healthcare workers in resource-limited Africa information on HIV care and management. This is done through a website, call-in centre and newsletter.

Information is critical if attitudes and behaviour are to be changed to suit the policies and programmes we put in place to curb the HIV epidemic. Healthcare providers must be equipped with the correct and appropriate messages at any one time for their patients, for us to expect HIV prevalence and incidence to take a fast downward trend. In this regard we would like to give special thanks to the following and encourage them to continue making *ATIC News* a newsletter worth reading: Mike Postelnick (RPh, BCPS), Tesfai Gbare-Kidan, (MD I-TECH), Kimberley Scarsi, (HIV and ID Research and Clinical Pharmacist), Peter Ssali (Drug quality analyst), Dr Sabrina Bakeera-Kitaka, (Mmed, Paed, ID Fellow), Dr Anne Merriman, Dr Charles Steinberg, (MD), Dr Richard Brown, (MD,MPH,FACCP), Dr Thomas Macharia, (MBcHB), Jennifer Cocohoba,(Assistant Clinical Prof UCSF), Rashida Ferrand (MBBS, MRCP, DTMH), Allan Ronald, (Professor of Medicine) Dr Fred Semitala, Dr Andrew Kambugu (MBcHB, M.Med) , Onie Johnson (Pharm D), counsellor Caleb Twijukye, Nurse Naomi Nantamu and our adolescent writers Brian and Godfrey. The invaluable material from UNAIDS, WHO, Population Reference Bureau and our board members who have worked tirelessly to see that the quality of the newsletter conforms to international standards cannot go unmentioned. We wish you all a good end of the the year and a prosperous new one.

Dealing with needlestick injuries

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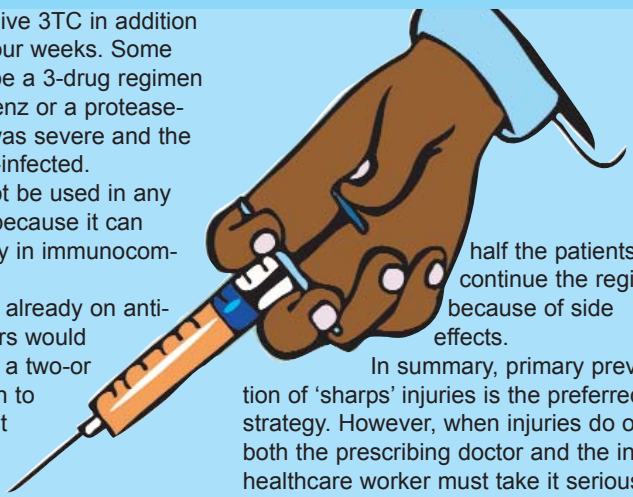
in order to ensure they complete the course of therapy and follow-up HIV and Hepatitis B and C tests are obtained at six and 12 weeks.

- If the patient is susceptible to Hepatitis B and has not been immunised, PEP for Hepatitis B is also indicated. All susceptible patients should be immunised for Hepatitis B vaccine. Currently no vaccine exists for Hepatitis C and no known precautions can reduce the chance of acquiring Hepatitis C through percutaneous injury.

The only clinical study to guide us with regard to PEP took place in the early 1990s when monotherapy with zidovudine (AZT) prescribed for 28 days, reduced the risk in a retrospective case control study by 79%. As a result, since that time all patients at risk are prescribed at least zidovudine. Should two or three drugs be prescribed? At present, there is no data, but many doctors do give 3TC in addition to AZT for the entire four weeks. Some doctors would prescribe a 3-drug regimen (AZT, 3TC, and efavirenz or a protease-inhibitor) if the injury was severe and the injury source was HIV-infected.

Nevirapine should not be used in any prophylactic regimen because it can cause fatal liver toxicity in immunocompetent patients.

If the injury source is already on antiretrovirals, most doctors would choose at least one of a two-or three-drug combination to which the virus has not been previously exposed.



Drug therapy should start within hours of the injury. If a delay occurs because of late reporting, treatment is still prescribed but it is presumably less effective. As noted earlier, it is vital that patients be supported throughout the four-week course of therapy as almost half the patients discontinue the regimen because of side effects.

In summary, primary prevention of 'sharps' injuries is the preferred strategy. However, when injuries do occur, both the prescribing doctor and the injured healthcare worker must take it seriously and proceed as listed above. Only in this way can we ensure that most patients will not acquire HIV following injury. All healthcare institutions that provide care to HIV patients should have a policy in place and should have readily available ARVs to initiate therapy immediately.

Nelfinavir, also used in PEP

Nelfinavir (NFV) is a protease inhibitor indicated for use in combination with other antiretroviral agents for the treatment of HIV 1 and HIV 2 infection, writes **Dr Mairin Ryan**

Nelfinavir is part of a second line regimen in the Ugandan National Antiretroviral Guidelines.

Dosage /Administration[1]

Adult: For adults > 13 years NFV 1250mg twice daily or 750mg three times daily. NFV should be taken with a meal or light snack as food increases the bioavailability. For patients who have difficulty swallowing, the tablets may be crushed and mixed with milk or food.

Once crushed and mixed with food, NFV should be consumed within six hours. Mixing with acidic food (e.g. apple juice, orange juice) should be avoided due to a bitter taste. Alternatively there is a powder formulation which may be added to water, milk, soy milk or milk / soy milk based foods. Once reconstituted, powdered nelfinavir must be consumed within 6 hours.

Paediatrics[1,2]

In children 2 years and older 20-30mg/kg three times daily. Twice daily dosing at 50-55mg/kg is currently under evaluation in children older than 6 years. Children may receive the powder formulation or tablets as appropriate.

Pregnant women[1,3,4]

Nelfinavir is classed as Pregnancy Class B; no treatment related malformations were seen in animal studies. A recent study indicated that nelfinavir concentration ratios were significantly lower in pregnant women especially during the third trimester. The authors have suggested that dose adjustment to 1500mg NFV twice daily may be required in some circumstances.

Nelfinavir is distributed into breast milk. Standard guidelines recommend avoidance of breast-feeding however, due to the risk of transmission of HIV via the breast milk to the infant.

Post exposure prophylaxis[1]

Nelfinavir may be used for post exposure prophylaxis as part of a three-drug-regimen commonly containing two nucleoside analogues e.g. zidovudine and lamivudine for a period of 4 weeks.

Dosing in renal /hepatic impairment[1]

Renal clearance of NFV is negligible therefore no dose adjustment in renal impairment is recommended. NFV is principally metabolised in the liver and therefore should be used with caution in patients with impaired liver function.

Precautions and contraindications

Nelfinavir is contraindicated in patients hypersensitive to the drug or any ingredient in the formulation.

Side Effects[1]

The most frequently reported side effect is mild to moderate diarrhoea (occurring in up to 20% of patients) which may be controlled with anti-motility agents e.g. loperamide, diphenoxylate. Other gastrointestinal side effects include nausea, flatulence and abdominal pain.

Substantial increases in AST and ALT have occurred in 3% of adults receiving NFV in clinical studies. Hepatitis, increased alkaline phosphatase and gamma-glutamyl transferase have been reported in < 2% of patients.

Other side effects associated with nelfinavir and other members of the protease inhibitor class include hyperglycaemia, hyperlipidaemia and lipodystrophy (redistribution / accumulation of body fat). Spontaneous bleeding in haemophiliacs has been reported with other protease inhibitors.

Monitoring parameters[1]

Ideally liver enzymes should be monitored regularly and cholesterol and blood glucose should be monitored periodically.

Interactions[1,2,5,6]

Metabolism of nelfinavir is mediated to some extent by several cytochrome P450 isoenzymes including CYP3A and CYP2C19. Concomitant use of medications, which induce these enzymes, may result in reduced NFV concentrations and consequently increase the risk of virologic failure and the development of resistance. Therefore concomitant administration of drugs such as rifampicin, St John'sWort should be avoided.

Nelfinavir inhibits CYP3A and may result in increased blood levels of drugs metabolised by this pathway. Amiodarone, astemizole, cisapride, ergot alkaloids, halofantrine, lumefantrine, midazolam, pimozide, quinidine, terfenadine and triazolam should not be prescribed with nelfinavir as increased levels of these agents may have life threatening consequences. Co-administration with simvastatin and lovastatin is not recommended and caution is advised if used with atorvastatin. Pravastatin and fluvastatin are not metabolised by cytochrome P450 and therefore have a low propensity to interact with NFV.

Co-administration of sildenafil with nelfinavir requires caution as increased sildenafil concentrations may result in enhanced toxicity.

Recommendations on dose adjustments when nelfinavir is prescribed with other protease inhibitors may be found in the first newsletter in this series Vol 1, Issue 1 (available from ATIC on request). Dose adjustments of NFV are not required when used in combination with the non-nucleoside reverse transcriptase inhibitors efavirenz and nevirapine

Concomitant administration of NFV and oral contraceptives containing ethinyl oestradiol and norethindrone results in lowered levels of these agents. Therefore alternative means of contraception are required.

Resistance[1,5]

Resistance to nelfinavir is associated with the development of one or more of several resistance mutations, which may or may not confer or contribute to resistance against other protease inhibitors.

Generics: Not available in Uganda

Storage[1,2]

Nelfinavir tablets and powder should be stored at 15-30°C.

Presentations

Nelfinavir film is available as Viracept coated tablets 250mg, 625mg and as Viracept powder: 1 level 5ml teaspoon gives 200mg NFV, 1 level scoop provided gives 50mg NFV.

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Diagnosis of cryptococcal meningitis, a challenge in resource-poor settings

By Fred Semitala

A 30-year-old woman presented to hospital on October 11, 2004 with a two-week old headache and neck pain.

She was diagnosed with HIV and got well until two weeks prior to admission when she developed progressive generalised throbbing headache associated with vomiting and photophobia but no visual disturbance. The pain was radiating to the neck making head-turning very painful.

She however reported no h/o confusion, convulsions, and loss of consciousness or focal weakness. She denied any history of fever, cough or excessive sweating.

Review of other systems was unremarkable

PMS: Index admission reported an episode of herpetic eruption on the abdomen a year prior to admission. There were no other opportunistic infection and known chronic diseases. The patient was not on ARVs, cotrimoxazole prophylaxis or any regular medications.

FSH: The patient was married. Her husband and her three children (3-7 years) were all physically well but HIV sero status was unknown.

PE: She was in severe pain and rather dehydrated. Other systems were normal except for the zoster scar along T11 left side.

CNS: The patient had photophobia but otherwise unremarkable.

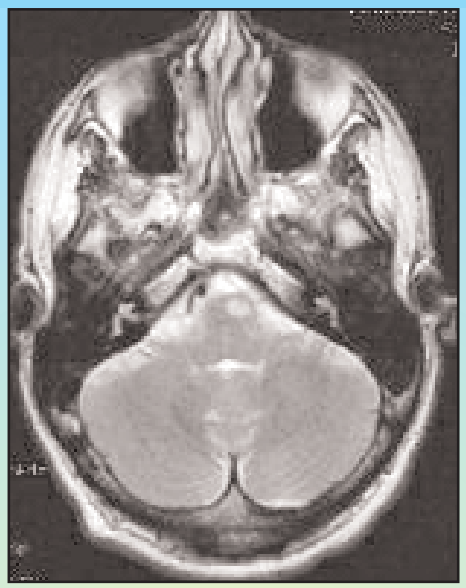
The differential diagnoses at this point were:

Cryptococcal Meningitis
R/o Bacterial meningitis
Toxoplasmosis

Investigations

CSF: Clear + colourless
Prot: 40-mg/ dl
Wbc < 5 cells/mm3
Gram stain: yeast cells
Indian ink: gram-positive capsulated yeast cells.
Toxo titers: IgM 0.95 (NR 0-.96) iu
IgG 4.64 (NR 0.5-5.01) iu
Electrolytes
CL: 86.2 mmol/l NR (98- 110)
K+: 3.7 mmol/l NR (3.5-5.5)
Na+: 121 mmol/l NR (132-145)
Crea : 92.umol/l NR (70-133)

With these results the patient was started on IV Amphotericin B. She improved fast and was on request discharged after three doses of Amphotericin B. She was at this point started on 400 mg of oral Fluconazole, which she was instructed to take for the next 10 weeks after which the Fluconazole dose would be adjusted. She was also started on Cotrimoxazole prophylaxis.



Magnetic resonance imaging showing a cryptococcoma in the medulla.

Ten days after discharge she returned to hospital with severe frontal headache, neck pain, and inability to see for two days. There was no eye pain, focal weakness, fever or any other constitutional TB symptoms. On examination she was conscious but with a stiff neck, dilated pupils that were not reacting to light and she had no perception of light. Fundoscopy showed hyperemia of the optic discs with blurred disc margins. The vessels looked normal (as reported by the ophthalmologist). Other systems were essentially unremarkable.

Tentative diagnoses at this point included:

- HIV with Cryptococco meningitis,
- Bacterial meningitis and Cytomegalo Virus retinitis to r/o cortical blindness.

The patient declined a diagnostic/therapeutic lumbar puncture but could not afford a brain CT scan at the same time. She was switched back to Amphotericin B, analgesics and empirically started on anti meningitis therapy. The patient's general condition improved over the next two weeks but she remained blind.

Discussion:

About 5-10% of people with HIV develop cryptococcosis. Cryptococcal meningitis (CCM) is the commonest manifestation in two-thirds of cases of cryptococcosis.

The symptoms of CCM that tend to gradually get worse over a period of several weeks include headache, fever, neck stiffness and discomfort in bright light (photophobia). These are highly suggestive of the disease in advanced HIV but non-specific and so other diseases such as HIV aseptic meningitis, cerebral toxoplasmosis, lymphoma, Cerebral CMV and sinusitis should be considered and excluded where possible. This is a big challenge in resource-limited settings (RLS) where many of the lab tests as well as the money to pay for the tests are usually not available.

Amphotericin B, the drug of choice for CCM is a toxic drug which has to be given by a central line into a big vein and can cause shivering attacks with fevers, kidney toxicity (hence the need to hydrate the patient prior to the dose of Ampho B) and bone marrow suppression leading to anaemia. Routine CBC and RFTs in all patients on Ampho B is important to monitor toxicity and taking paracetamol or Aspirin at the same time can reduce drug-associated fevers. Treatment of CCM with oral Fluconazole 400mg/day, which may be adequate for mild disease, is said to be less effective than Ampho B. Although initial response rates appeared similar in a comparative study, relapse occurred more often in the fluconazole group. However during secondary prophylaxis the use of Fluconazole 200mg /day was shown to be more effective than Ampho B or Itraconazole.

There is a question on when to stop secondary fluconazole prophylaxis when on ARV. It is thought to be safe when CD4 count is sustained above 200 cells/mm3 for more than six months although some relapses have been reported.

The cause of visual loss in our patient was not clear but it might have been due to involvement of the optic tracts by cryptococcal organisms.

Resident Dept of Medicine
Makerere University
Mulago Hospital

The safety of ARVs in pregnancy

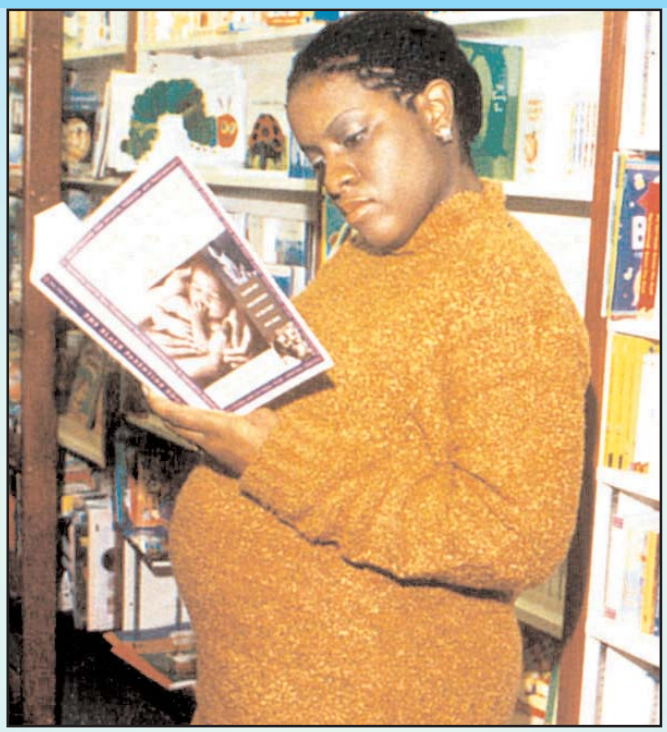
QUESTIONS
with
Robinah Nganwa

Which ARVs are safe during pregnancy?

D.C Namibia

THE WHO recommends the use of ZDV, 3TC, NVP, NFV and SQV combined with low dose ritonavir, as these have been the most widely used ARVs in pregnant women. EFZ is not recommended for use in women who could become pregnant due to its potential teratogenic effect on the foetus in the first trimester.

The choice of ART in women with the potential to become pregnant must include consideration of the possibility that the ARV drugs may be received during the early first trimester, prior to recognition of pregnancy and during the primary period of fetal organ development. Women receiving ART should be availed of effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy.



It may be desirable to initiate ART after the first trimester

It is important to note that some antiretroviral drugs (the NNRTIs NVP and EFZ and all the RTV boosted PIs as well as NFV) can lower blood concentrations of oral contraceptives and additional or alternative contraception needs to be used to avoid pregnancy in women receiving these drugs.

For pregnant women, it may be desirable to initiate ART after the first trimester, although for pregnant women who are severely ill, the benefit of early therapy outweighs any potential risks on the foetus.

Additionally, the dual NRTI combination of d4T/ddI should only be used during pregnancy when no other alternatives exist, due to the potential increased risk of lactic acidosis with this combination in pregnant women.

The use of AZT and 3TC in the first trimester of pregnancy has not been shown to be teratogenic. It is not possible, however, to guarantee the safety of ARVs regarding the foetus in the first trimester of pregnancy.

Women who are less than 12 weeks pregnant should be informed of this and be allowed to make a choice as to whether they are prepared to use the drug or not.

IDI training for March 2005

THE Infectious Diseases Institute (IDI) is calling for applications for the HIV/AIDS Training Programme for Healthcare providers for March 2005 at the IDI, Mulago.

The course is for both Ugandan and non-Ugandan specialists. IDI offers two types of training in collaboration with Makerere University and the Infectious Diseases Society of America, namely the HIV/AIDS Training Programme for Medical Doctors in Africa and the Multi-disciplinary Topical Training Programme.

The first, entails a comprehensive overview of HIV/AIDS related basic science, epidemiology, care and treatment, research and prevention for adult and paediatric populations. The requirements are MBChB from a recognised university and demonstrated experience in HIV/AIDS care, research and prevention activities and current registration. The multi-disciplinary Topical Training Programme entails combined cluster topical training of medical officers, senior nurses, clinical officers and medical counsellors in ARV delivery for adult and paediatric populations. The second course is only for Ugandan medical practitioners. Both courses include clinical experience and classroom teaching with instruction given by national and international HIV/AIDS experts.

Applications can be got from the IDI Training Department, Mulago or contact the Training Manager IDI on phone number 256-(0)41-307212, fax: 256-(0)41-307291, email: training@idi.co.ug; website: www.aaacp.org.

CME/CPE Corner

THE questions below provide an insight into topics on HIV/AIDS care and management useful for discussions in your continuing medical or pharmacy (CME/CPE) education sessions at work. These questions act as a guide in improving your knowledge in your interaction with HIV/AIDS patients and colleagues on a daily basis. Those who do not have these sessions can start them.

When a patient on septrin prophylaxis develops malaria, is it safe to put them on Fansidar?– E.N, Kampala.

For how long should patients on Fluconazole secondary prophylaxis be left on therapy if their CD4 count rises above 200? For life?– B.C, Arua.

Discussion Forum

ATIC News, P. O. Box 40008, Kampala, email: bbitangaro@iph.ac.ug. **ATIC News welcomes readers views**

ARVs used for PEP

By Robinah Nganwa
HIV Clinical Pharmacist

IN persons accidentally exposed to HIV through needle-stick inoculation or through contamination of mucous membranes by secretions, it has been shown that immediate administration of antiretrovirals may prevent infection. In this situation ART needs to be continued for one month. Occupational exposure to potentially infectious material may occur through an injury with a sharp object that has been used on a patient or through the contamination of mucous surfaces with patients' blood or secretions.

The following types of exposure should be considered for post-exposure prophylaxis:

- Needle-stick injury or injury with a sharp object used on a patient.
- Mucosal exposure of the mouth or eyes by splashing fluids.
- Intact skin exposed to a large volume of blood or potentially infectious secretions.
- Broken skin exposed to a small volume of blood or secretions.

Percutaneous injuries

If the exposure is not severe and the;
1. Source HIV+ and low risk-2 drug PEP
2. Source HIV+ and high risk-3drug PEP
3. HIV status unknown-usually none or 2 drug PEP

If exposure is severe (deep injury) and the;
1. Source HIV+ and low risk- 3 drug PEP
2. Source HIV+ and high risk-3drug PEP
3. HIV status unknown-usually none or 2 drug PEP

Mucous membranes

Small volumes (drops);
1. Source HIV+ and low risk- consider 2 drug PEP
2. Source HIV+ and high risk-2-drug PEP
3. HIV status unknown– usually none or two-drug PEP

Large volumes(major
1. Source HIV+ and low risk- consider 2 drug PEP
2. Source HIV+ and high risk-3 drug PEP
3. HIV status unknown-usually none or 2 drug PEP

N.B: NVP should not be used in PEP.

Antiretroviral Drugs to be used in Post-Exposure Prophylaxis

Recommended regimen: 2 drug combination
1. AZT + 3TC
2. 3TC + D4T
3. D4T +DDI
4. TDF+ 3TC

Recommended three-drug combination

1. Two NRTIs (above list) + Indinavir, Nelfinavr, Efavirenz, Abacavir or Kaletra.

Decision should be made based in part on information about the source such as ART, viral load and any data on HIV resistance testing. This regimen is continued until the results of HIV tests for patient and injured health worker are known:

- If the source is HIV-negative or the health worker is HIV-positive then drug administration should be discontinued.
- If the health worker is HIV-negative and the source is HIV positive or the source's HIV status is not determined, then continue this regimen for four weeks.

Post-sexual exposure prophylaxis

There is not enough evidence to recommend prophylaxis against infection following casual sexual exposure. However, in the event that there has been sexual abuse or rape then it is recommended that the victim be counselled and provided with the drugs recommended for post-occupational exposure prophylaxis. It is important to try and determine the HIV status of the perpetrator. If this is not possible then it may be assumed that the perpetrator is HIV positive and the victim is provided with the treatment listed in the preceding paragraph.

Johns Hopkins 2003.Medical Management of HIV Infection

IN BRIEF

Switching ARV therapy

The AIDS Treatment Information Centre is now the official national referral consultation centre for all Ministry of Health (MOH) antiretroviral therapy sites. A letter dated October 14, 2004 by Dr Elizabeth Madraa, the programme manager, STD/ACP-MOH, says there is need to promote rational drug use in view of the limited product availability and the rapidly changing clinical recommendations. “Ministry of Health is working with ATIC to ensure that the most accurate and up-to-date information is available for healthcare providers. In addition, MOH has availed guidelines to ensure optimal availability of drugs for patients,” she wrote.

Epidemic rages on

Sub-Saharan Africa has just over 10% of the world’s population but is home to more than 60% of all people living with HIV – some 25.4 million [23.4 million – 28.4 million]. In 2004, an estimated 3.1 million [2.7 million — 3.8 million] people in the region became newly infected.

UNAIDS

ATIC goes online

The AIDS Treatment Information Centre will go online next month. By logging on to ATIC-AFRICA.ORG, health workers will be exposed to vast information on HIV care and management for their day-to-day use.

Counselling informs the patient on what may happen with ARVs

By Jennifer Cocohoba, Assistant Clinical Professor University of California San Francisco (UCSF) School of Pharmacy

STARTING antiretroviral (ARV) therapy can delay complications of HIV including opportunistic infections and death. For many patients, starting antiretroviral therapy also means dealing with side effects from these powerful medicines.

The initial ARV starting period is critical to the regimen's ultimate success. Side effects and adherence are intimately tied. Lack of knowledge regarding side effects and tips on how to alleviate them can cause a patient to discontinue their ARVs. The uninformed patient may also decide to take subtherapeutic (less toxic) doses of their ARVs, creating the perfect environment for developing resistance.

When prescriptions for the first ARV medicines are written, health care providers can offer the following general information and counselling tips on common side effects in addition to offering symptomatic treatments.

Nausea: Nearly all ARVs can cause nausea but it is common with zidovudine (AZT, Retrovir®) and with protease inhibitors such as lopinavir/ritonavir (Kaletra®). Nausea is typically worst when patients first start taking their ARVs but may subside after about one month. For nausea, take the ARVs with a meal, if possible. Most ARVs can be taken with food, except for didanosine and indinavir. If a patient is nauseated it may be easier to keep food in the stomach if the patient eats smaller meals (snacks) throughout the day rather than taking fewer large meals. A cloth to cover the nose may also be helpful, since strong smells may trigger nausea.

Lastly, if the patient is nauseated and vomiting he or she should be reminded to drink plenty of fluids to avoid dehydration. For severe nausea, antinauseal agents such as prochlorperazine or metoclopramide may be helpful.

Diarrhoea: Many ARVs can also cause diarrhoea. It is common with protease inhibitors such as lopinavir/ritonavir (Kaletra®). As with nausea, diarrhoea is often worse in the beginning and may subside over the period of one month. Patients with diarrhoea should be counselled to drink plenty of fluids to avoid dehydration. Caffeinated drinks, very sugary drinks, and extremely fatty or spicy foods may worsen diarrhoea. It is probably best to follow a bland, fibrous, diet when experiencing diarrhoea. Antidiarrhoeals such as loperamide may be useful.

Headache/Fatigue: Headache and fatigue are side effects common to all ARVs. There is no better remedy for fatigue other than rest. Efavirenz is known to disturb dreaming (deep sleep), which may make a patient feel unrested. Taking efavirenz a few hours earlier, or breaking it into two doses an hour or two apart may be helpful.

Patients should avoid very high-fat meals with efavirenz as this can increase the CNS side effects. Headaches, common with zidovudine, can be treated symptomatically with rest and analgesics such as paracetamol or other non-steroidal anti-inflammatory agents.

Rash: Rash commonly occurs with non-nucleoside reverse transcriptase inhibitors (NNRTI) such as efavirenz (Sustiva®). Approximately 30% of patients starting efavirenz develop a rash. Patients should be counselled to seek medical attention if a rash develops.

A health care professional needs to evaluate whether the rash is a simple, maculo-papular drug rash or if it is a more serious drug rash such as Stevens-Johnson Syndrome.

Patients should be alerted to the signs of a dangerous rash. These signs include fever, eyes, nose, or mouth (mucous membrane) involvement, other constitutional symptoms, or pain.

If it is a simple drug rash, patients should be counselled to minimise sun exposure to irritated areas and avoid harsh soaps and scrubs. If available, moisturising lotions may also be helpful.

Thorough counselling on ARV side effects informs the patient on what may happen during the weeks ahead.

By consistently offering side effect information, health care providers may prevent patients from being "surprised" and improve adherence over the crucial first four weeks of therapy.

Starting ART also means dealing with side effects of these drugs

ATIC News

Send your queries to rnganwa@ iph.ac.ug or skidde@iph.ac.ug

Clinical updates from ICAAC 2004

By Mairin Ryan

THIS report includes summary information on a number of studies presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy which took place in Washington DC in November last. Readers are referred to the conference abstract book for more detail.

Simultaneous administration of saquinavir hard gel and ritonavir is required for optimal saquinavir absorption (Boffito et al, Abstract A-453).

A small dose of ritonavir (e.g. 100mg) is used to boost blood levels of saquinavir and improve viral suppression but ritonavir boosting also increases the incidence of side effects such as nausea and vomiting, abdominal pain and diarrhoea. The authors wished to investigate the effect on saquinavir levels of reducing the frequency of ritonavir co-administration.

Eighteen HIV-positive patients taking hard gel saquinavir 1000mg /ritonavir 100mg twice daily were recruited. Saquinavir levels were taken on Day 1 for boosted saquinavir and again on Day 2 when the morning dose of ritonavir was omitted. There was a 33% [4%, 47%] lower total exposure to saquinavir and a 33% [8%, 41%] decrease in absorption half-life of saquinavir when ritonavir was omitted with no significant impact on peak concentration, trough concentration or elimination half-life.

According to the authors, these data confirm the need to administer saquinavir and ritonavir simultaneously, whether once or twice daily.

Participants during a recent HIV workshop in Kampala

Paradoxical CD4 cell count declines despite viral suppression observed in patients receiving didanosine with tenofovir (Barrios et al. Abstract H-1132).

Didanosine plus tenofovir constitutes an attractive NRTI backbone due to convenient once-daily administration, potency and a high genetic barrier to resistance.

However, tenofovir increases plasma and possibly intracellular levels of didanosine raising concerns about increased toxicity and leading to the following dosing recommendations: patients > 60 kg should receive a reduced dose of didanosine of 250mg once daily when co-administered at the same time as tenofovir 300mg once daily.

For patients < 60kg there is insufficient evidence to guide dose reductions of didanosine. Some centres recommend that patients should be prescribed didanosine 250mg once daily administered 12 hours apart from the tenofovir once-daily-dose of 300mg.

This study was a retrospective review of 570 patients who achieved viral suppression < 400 copies per ml on protease inhibitor sparing regimens. Patients receiving didanosine and tenofovir in combination as part of a protease-inhibitor sparing regimen tended to experience CD4 cell count declines despite viral suppression. The effect appeared after six months and increased thereafter. It appeared earlier and was more pronounced when tenofovir and didanosine were combined with a third nucleoside analogue than with a non-nucleoside reverse transcriptase inhibitor (NNRTI). Patients taking higher doses of didanosine had greater CD4 cell count declines than those taking lower doses.

Racial differences in response to efavirenz-containing versus lopinavir/ritonavir containing regimens (Guest at al. Abstract H-579).

Research presented earlier this year at the Conference on Retroviruses and Opportunistic Infections 2004 suggested that African-Americans may have a gene that results in slower clearance of efavirenz, implying greater drug exposure over time.

Investigators compared virologic and immunologic response to first HAART regimens containing either efavirenz or lopinavir/ritonavir in 626 African-American and Caucasian individuals. Virologic failure was defined as 2 consecutive viral load measurements > 400 copies/ml after 2 months of starting the regimen. Immunologic failure was defined as an increase of < 50 CD4 cells after two months of starting the regimen.

Multivariate analysis for each drug regimen revealed that amongst patients taking efavirenz containing regimens, race was a significant predictor of immunological failure (HR 0.63 [0.43-0.92], protective for African Americans) but there was no difference in risk of virologic failure. Race was not protective against either immunologic or virologic failure of lopinavir/ritonavir although there was a trend towards lower risk of immunologic failure.

The results suggest a better immunologic outcome amongst African-American than amongst Caucasian patients taking efavirenz.

Whether these results will be replicated amongst African counterparts has yet to be elucidated.