Happy Spring!

It is pouring cats and dogs here in “sunny” Alberta today, but the good news is that the grass and trees are green (yes I am an optimist). I even had to shake off the dust from my umbrella! I won’t complain because Spring is finally here……. Hurray!

As you know, I have officially taken over the Chair from Kathy Slayter (aka “Mom”). This is my first attempt at a newsletter so please be patient with me!

Social News

Well I am sure everyone has heard the good news but I would like to officially congratulate Kathy and Mike on the birth of their little boy, Ethan James Tucker, on December 11, 1999. Congratulations Kathy!

New Members

I would like to officially welcome the following new members:

Laura Park-Wyllie who has taken over Michelle Foisy’s position as HIV Primary Care Pharmacist at the St. Michael’s Hospital, Health Centre at 410 (formerly Wellesley Health Centre).

Deborah Kelly who is as an Assistant Professor of Clinical Pharmacy at Memorial University in Newfoundland and Clinical Pharmacy Specialist at Health Care Corp of St. John’s.

Kimberly Montgomery who is a Pharmacist at the Southern Alberta Clinic (taking over from Nikola Ostrop). Unfortunately, Kim will not be with us long. She is getting married in August and then will be moving to Newfoundland. Her last day at the clinic will be June 30, 2000. Congratulations on your upcoming wedding Kim! For those of you interested, there is an opening at the SAC and you can contact Kimberly for more details…
CAHR Update

I thought the CAHR conference was excellent and the Network meeting went well (considering all of the problems we had arranging the first Network meeting of the millenium!). For those of you who were unable to attend CAHR, the minutes of the Network meeting are enclosed with this newsletter. In addition, the abstracts can be found in: March/April volume 11 supplement B issue of *The Canadian Journal of Infectious Diseases*.

Upcoming Conferences

*International AIDS Conference*
As a reminder, the XIII International AIDS Conference 2000 is in Durban, South Africa, July 9-14. I know Alice is going….anybody else? Congratulations on having a poster accepted Alice!

*ICAAC*
The 40\(^{th}\) ICAAC will be held in Toronto this year from September 17 – 20, 2000. The abstract deadline was April 26, 2000. The discounted registration deadline is July 14 and final registration August 11. Further information may be found at the following website: [http://dev.asmusa.org/mtgsrc/40icaac.htm](http://dev.asmusa.org/mtgsrc/40icaac.htm)

Drug Availability - Updates

*Ritonavir Caps*  
(Alice)  
They are here at last!!!! NOC officially kicks in Monday (January 10th). The 100 mg capsules come in bottles of 120, and should be kept in the fridge until dispensed. They are stable for 30 days at room temperature, or may be kept in the fridge by the patient until the expiry date on the bottle. The DIN is 02241480. In Ontario, a section 8 application will need to be filed for ODB patients.

*Ganciclovir Caps*  
(Christine)  
Has anyone tried getting access to the 500 mg capsules of ganciclovir in Canada? I understand that there is 500 mg caps in the US but they are not available in Canada. The drug company indicated that one may be able to access the capsules through HPB but I just wanted to know if anyone has tried this?
**Cotrimoxazole**

(Alice)

Hoffman la Roche has been out of stock for the last 3 to 4 months. No release date at this time and experiencing manufacturing issues. Due to the B/O from Roche, resulted the depletion of stock from Glaxo. Raw material is not an issue, however, Glaxo is in the process of outsourcing i.e can be quicker than manufacturing. Manufacturing takes about 1 month from raw material to finished product. If any patient being treated as PCP, Glaxo will be able to supply a small quantity by contacting the Response Centre at 416-268-0324.

**Clinical Pearls**

1. **Virologic response rate to HAART lower in community cohort**

WESTPORT, May 10 (Reuters Health) - The results of a large population-based study confirm that highly active antiretroviral therapy (HAART) and combination reverse transcriptase inhibitor therapy are effective in controlling disease progression in antiretroviral-naive HIV-infected patients. But while the rate of clinical progression was low, the rate of virologic failure in this community cohort was higher than that reported in clinical trials, according to members of the Swiss HIV Cohort Study.

Dr Peter Erb from the University of Basel and a multicenter team collected data from 755 treatment-naive patients who began antiretroviral therapy between 1995 and 1997. The patients received monotherapy with a reverse transcriptase inhibitor, combination reverse transcriptase inhibitor therapy, or HAART. Viral loads and CD4 counts were monitored at least every 6 months.

The researchers found that virologic failure occurred in 20% of the patients receiving HAART, 38% of the patients receiving combination reverse transcriptase inhibitor therapy, and in 82% of the patients receiving monotherapy.

Twelve percent of patients receiving monotherapy reached undetectable plasma levels of HIV RNA compared with 41% of the patients receiving combination reverse transcriptase inhibitors and 63% of the patients receiving HAART.

"The rate of virological failure...was high in this population," they report in the April 24th issue of the Archives of Internal Medicine. "Clinical progression rates were, however, low in patients treated with reverse transcriptase inhibitor combination therapy and HAART." The preliminary findings of this study were presented at the 12th World AIDS Conference in Geneva.

While they point out that the patients receiving HAART began treatment late "by today's standards," viral load reduction and clinical benefits were still observed.
"Our findings indicate that virological and immunologic responses should be examined before antiretroviral treatment is considered a failure and the regimen is modified."


2. **Structured drug interruption may induce HIV-specific immunity**

One cycle of structured treatment interruption (STI) may result in some degree of immune stimulation in patients with chronic HIV infection, according to researchers in Spain.

Antiretroviral treatment was halted in 12 HIV-positive subjects after 2 years of successful virus suppression. Dr Lidia Ruiz and colleagues from the University Hospital Germans Trias i Pujol, in Barcelona, observed no adverse events during the interruption period, and only transient effects when treatment was restarted after 30 days.

Viral load became detectable after a median of 14 days after treatment interruption in 10 patients, after which viral load increased exponentially. The remaining 2 patients exhibited no viral rebound. "No resistance-conferring mutations associated with the pre-interruption antiretroviral regimen were detected," the investigators note in the March 10th issue of AIDS.

T-cell activation antigen CD38 on CD8 T cells increased significantly in response to viral rebound during the STI. In addition, HIV-specific T-helper cell responses to p24 were recovered during the STI in 2 patients. The researchers note that this has not been previously described in chronically infected patients after an initial STI.

One patient developed plasma viremia levels greater than 5 log copies. The researchers speculate that the lymphoproliferative responses seen in this patient "suggest that significant increases in viral load of limited duration could be useful for priming the immune system."

These results underscore the potential usefulness of STI, which has been shown to modify viral load in other preliminary studies as well. Dr Ruiz's group cautions, however, that the findings of this pilot study need to be confirmed and further studies need to be completed before this strategy can be considered as an alternative therapeutic approach to HIV infection in a clinical setting.

AIDS 2000;14:397-403.
3. Didanosine systemic exposure in children similar with or without food

The systemic exposure of the HIV nucleoside analog didanosine is similar in children regardless of whether the drug is given with or without food, according to a study in the March 20th issue of AIDS Research and Human Retroviruses.

"From the adult literature it's been shown that when didanosine is given with food, the amount that's absorbed is substantially decreased," Dr. Robert C. Stevens of the University of Tennessee, in Memphis, told Reuters Health. "But for infants and toddlers, to adhere to schedules of taking medication either with food or without food presents logistic difficulties."

To look at the effect of food on didanosine absorption in children, Dr. Stevens and colleagues from the Pediatric AIDS Clinical Trials Group Protocol 144 Study Team randomized 106 symptomatic HIV-infected children, aged 3 months to 18 years, to one of two oral doses of didanosine every 12 hours.

The researchers measured various pharmacokinetic parameters on one visit, in which the patient fasted 2 hours before and 1 hour after didanosine administration, and on another visit, in which the patient had a normal breakfast 10 minutes before drug administration.

Seventy-seven patients were evaluable at the final analysis. Although the presence of food significantly reduced didanosine absorption, the overall systemic exposure, as illustrated by the area under the curve, was similar with recent food consumption and with fasting. This was explained by the fact that "the lower fraction absorbed with food was offset by the absorption rate becoming rate limiting for elimination," they report.

These findings were "surprising," Dr. Stevens told Reuters Health. Why the results in children were different from adults is not clear. But he pointed out that the adult studies used standardized meals to control for diet, which does not represent typical eating patterns.

"I think what this reflects is that children don't eat standardized meals all the time. Perhaps in a well-controlled regulated research environment, there may have been a different outcome," he said. But with the typical eating patterns of children, "it appears that there is no impaired bioavailability of didanosine when taken with food."

"It doesn't complicate the dosing regimen for the caretaker of the child," he pointed out. "They can give the didanosine without regard to food."

There was also more interpatient variability in the pharmacokinetics and higher clearance of the drug compared with adults, which "would suggest that children may need higher doses compared to adults," he added.

4. **Amprenavir – labelling changes**

Volume 1, Number 1
May 1, 2000

MedWatch, the Food and Drug Administration's Medical Products Reporting Program, announced today that Glaxo Wellcome is contacting health professionals to notify them of important changes to the labeling for AGENERASE Oral Solution. These changes highlight the potential risks, associated with the large amount of the excipient propylene glycol in AGENERASE Oral Solution.

The revised warning to the labeling contains this wording:
"Because of the potential risk of toxicity from the large amount of the excipient propylene glycol, AGENERASE Oral Solution is contraindicated in infants and children below the age of 4 years, pregnant women, patients with hepatic or renal failure, and patients treated with disulfiram or metronidazole..."

5. **Abacavir – revised warning about fatal hypersensitivity reactions including respiratory symptoms**

January 2000

Glaxo Wellcome Inc., would like to bring to your attention a revised WARNING in the labeling for Ziagen (abacavir sulfate) about fatal hypersensitivity reactions to abacavir in patients presenting with respiratory symptoms. Ziagen is a nucleoside analogue reverse transcriptase inhibitor indicated for use in combination with other antiretroviral drugs for the treatment of HIV-1 infection.

Since its approval in December 1998, the labeling for Ziagen has included a WARNING and description of fatal hypersensitivity reactions to Ziagen. Although presentations vary markedly between patients, frequently occurring features of these hypersensitivity reactions are fever, rash, gastrointestinal symptoms (nausea, vomiting, diarrhea, or abdominal pain) and fatigue or malaise. While respiratory symptoms have been recognized as part of the hypersensitivity reaction in some patients, recent information underscores their importance.

Fatalities in patients treated with Ziagen who developed hypersensitivity reactions in which the initial presentation included respiratory symptoms of dyspnea, cough, or pharyngitis have been reported. Deaths have been reported in patients receiving Ziagen who were initially diagnosed with an acute
respiratory disease (pneumonia, bronchitis, or flu-like illness) who were later recognized to have had a hypersensitivity reaction to abacavir that included respiratory symptoms. A delay in diagnosis of hypersensitivity can result in Ziagen being continued or re-introduced, leading to more severe hypersensitivity reactions, including life-threatening hypotension and death.

Review of reports of hypersensitivity in patients receiving Ziagen indicates that respiratory symptoms (including cough, dyspnea, and pharyngitis) have occurred in approximately 20% of patients who have had hypersensitivity reactions. In contrast to some allergic reactions, wheezing or bronchospasm have occurred only infrequently in patients with hypersensitivity reactions to Ziagen.

The diagnosis of hypersensitivity reaction should be carefully considered for patients presenting with symptoms of acute respiratory diseases and other symptoms associated with hypersensitivity to abacavir, even if alternative respiratory diagnoses (pneumonia, bronchitis, pharyngitis, or flu-like illness) are possible. If the clinical presentation of an acute illness cannot be clearly differentiated from a hypersensitivity reaction, Ziagen must be permanently discontinued. Ziagen should not be restarted following a hypersensitivity reaction because more severe symptoms will recur within hours and may include life-threatening hypotension and death.

This updated warning about fatal hypersensitivity reactions to abacavir in patients presenting with respiratory symptoms is now included in the revised labeling for Ziagen. In addition, this revised warning is reflected in the Patient Medication Guide and Warning Card and should be discussed with patients treated with Ziagen.

6. Didanosine – revised warning about fatal and non-fatal pancreatitis

November 11, 1999

Bristol-Myers Squibb would like to advise you of a revised warning about fatal and non-fatal pancreatitis in the labeling for Videx (didanosine, ddI), a nucleoside analogue reverse transcriptase inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

Since its approval in 1991, the didanosine label has carried a warning about fatal and nonfatal pancreatitis. That warning was based on the incidence of pancreatitis found in Phase III trials in patients with very advanced HIV disease that ranged from 1% to 10% with doses higher than are currently recommended and 1% to 7% with the currently recommended dose. This letter is being provided because of deaths due to pancreatitis that have been reported from clinical trials studying the combination of didanosine plus stavudine (d4T) with and without hydroxyurea. These deaths occurred both in patients who were treatment-experienced and treatment-naive without significant immunosuppression, and at
the recommended doses of didanosine and stavudine. Use of hydroxyurea for the treatment of HIV infection is not approved by the FDA and is considered investigational.

SUMMARY OF REPORTS

Two treatment-naïve patients died of pancreatitis approximately seven months after initiation of treatment with didanosine plus stavudine and protease inhibitor in two clinical trials.

Two deaths due to pancreatitis occurred among 68 previously-treated patients enrolled in an arm of the ACTG 5025 study which utilized didanosine with hydroxyurea (600 mg BID) plus stavudine and indinavir. Both patients were hospitalized for pancreatitis within three months of enrollment and died one to ten weeks after diagnosis. Although a formal causal relationship was not established, the ACTG 5025 trial was subsequently terminated due to the higher risk of several toxicities, including fatal and non-fatal pancreatitis, in this treatment group.

All of these patients had CD4>500 cells/µL and HIV RNA<200 copies/mL.

Three of the four patients who died had additional risk factors for pancreatitis, including morbid obesity, hypertriglyceridemia, and cholelithiasis.

In addition, deaths due to pancreatitis in patients treated with didanosine have been reported to the FDA MedWatch program. Since 1998, the majority of these reports have been in patients who were also receiving stavudine with and without hydroxyurea.

PATIENT MANAGEMENT

The clinical outcome of pancreatitis may be improved by early identification of the clinical and laboratory signs and symptoms of pancreatitis (abdominal pain, nausea, vomiting, elevated serum amylase and lipase levels) and prompt initiation of appropriate supportive care, including stopping all oral intake.

Didanosine, stavudine and hydroxyurea should be suspended in patients with suspected pancreatitis. Reinstitution of stavudine after a diagnosis of confirmed pancreatitis should be undertaken with caution. Didanosine should be permanently discontinued in patients with confirmed pancreatitis.

The didanosine package insert warns that individuals with risk factor for pancreatitis should use didanosine with extreme caution and only if clearly indicated.

Some of the known risk factors for pancreatitis include:
history of pancreatitis
ongoing alcohol abuse
morbid obesity
hypertriglyceridemia
cholelithiasis
endoscopic retrograde cholangiopancreatography (ERCP)
other medications known to cause pancreatitis (e.g., pentamidine)
medications known or thought to increase exposure to didanosine (e.g., hydroxyurea, allopurinol)

In addition, patients with advanced HIV infection are at increased risk for pancreatitis and should be followed closely. When treatment with life-sustaining drugs known to cause pancreatitis is required, suspension of didanosine therapy is recommended.

7. Cryptosporidium

(Kathy)
What are you guys using now to treat cryptosporidium these days?? We have a patient that we wanted to put on azithromycin & paromomycin. We only have 12 days of paromomycin and the company says that there won't be anymore available until Jan 2000. So my question is, do you know if there is any paromomycin out there that we could purchase for this patient to complete his treatment course?? There is none available in Nova Scotia.

(Deborah)
I checked with our hospitals in St.John's and they don't have any on hand at all. What's the reason for the delay from the company?

(Ann)
We went through this a month or so ago as we ran out then. The company is having to bring in stock from Europe but it takes quite awhile to go through the testing required to bring drugs into Canada. A number of years ago we went through a similar situation where all their stock expired and they had none to replace it with that had better dating. We are maintaining our current patients with antidiarrheals and hoping for the best (both had been on drug for a while so they will probably be ok). Hopefully, no new cases with come up before drug is available.
8. **Postexposure Prophylaxis**

(Natalie)
Our hospital guidelines need to be updated. Does anyone know of online references for provincial guidelines or individual hospital guidelines that are easily accessible on intranet or recently published (last year). There is a ton out there - I'm only interested in recent updated tertiary-care or provincial guidelines. I'm also interested in the same reference for street needles or sexual assault.

(Kathy)
The most recent ones that I have are found on the following site:
http://www.healthcg.com/hiv/guidelines/exposure/potential.html

(Glenda)
The BC guidelines are on the web at:
http://cfeweb.hivnet.ubc.ca/guide/open.html
in section 7

(Pierre)
What I have in my files is
Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis located at : http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00052722.htm

9. **Hair Loss and Antiretrovirals**

(Deborah)
I was wondering if anyone out there has any experience managing hair loss due to ARV therapy? I have a patient who started d4T/3TC/Sustiva just over a month ago who is now complaining of this problem. Hair loss has been reported in clinical trials with 3TC (<1%) and Sustiva (<2%), and there is also a report in Lancet (1994; 344: 1702) that describes 5 cases with 3TC use. My question is whether this is just a temporary effect, or will it continue if the patient sticks with therapy? Also, is it reversible after the drugs are stopped (as is the case with alopecia due to valproic acid)? Any thoughts?

(Alice)
I've seen a lot of alopecia especially with 3TC, and sometimes with fluconazole. With some, it persists the whole time they are on meds, but patients do often report improvement after stopping the ARV.
(Kathy)
Pretty much the same comments as Alice with regards to the 3TC and fluconazole. I have not seen it with Efavirenz. I have had patients (because of legitimate vanity) actually stop combinations that were working very very well for them because of alopecia. I have also seen it with Crixivan. In my experience the hair loss stops after the offending agent is stopped.

(Pierre)
We have had several cases (between 5&10) that we believed was due to indinavir. Some of them were clearly due to PI since hair loss recovered at drug substitution.
I never thought to look at fluconazole as causal agent though!

10. Photosensitivity

(Linda)
Just wondered if there would be any additional photosensitivity concern in a patient on EFV (& Combivir) about to start ultraviolet light (PUVA) treatment for psoriasis. He will receive methoxsalen (Oxsoralen) prior. He has been on his current ARV combo since August without any apparent skin reactions. I checked the product monograph of EFV and methoxsalen without any indication of a potential concern for increased photosensitivity. I was also wondering about any interaction based on liver metabolism, but can’t find anything specific.

11. Guidelines for Lab Monitoring for Antiretrovirals

(Natalie)
I am looking for a good reference for guidelines on the frequency of lab monitoring for antiretrovirals. I was disappointed to find that the Guidelines for the Use of antiretroviral agents in HIV-infected Adults and Adolescents (may 5, 1999) did not have a paragraph on this nor even mention it.

The pharmacist covering for my maternity leave and the medical director of our clinic designed a list.
e.g., NRTIs - every 2 months
ZDV CBC, ALT
ddi ALT, amylase, lytes, uric acid

PI
IDV ALT, glucose, CBC, bilirubin, BUN, Cr, q 2 months
nonfasting TG/cholesterol q 4mos if high repeat in 2 mos as fasting (8 hr fast)
urinalysis q monthly

viral load q 4mos
CD4 q 4 mos.

So, if someone has consensus guidelines or a great reference or great guidelines (reference-based or not), I would love to know.

12. G-CSF Treatment in HIV Patients

(Linda)
I was wondering what your experience has been in using this in HIV patients (effective? Dose?, length of therapy?, etc.). We have an end-stage patient admitted to hospital 1 week ago (VL = 1.6million ,CD4=2 - it's pretty much been that way for >1year!!). She's been on several meds (& trials) & lately hasn't been very compliant - Current regimen is EFV & 3TC & d4T (stopped AZT when her RBC/Hgb dropped)

Her WBC has been around 1 (0.5neut) for quite a while, however, 1 week ago she was admitted to hospital with bacteremia (Ps aeruginosa) & started on Pip & Gent (later Gent change to Cipro). Initially she couldn't swallow so her esophageal candidiasis treatment was changed from oral fluconazole to IV ampho -

Now approx. 1 week later her platelets are 7 (down from 63 three days ago). We've stopped the Ampho & Pip & have started Itraconazole & Cipro because she can swallow, but in light of her WBC=0.6 (0.2neut), the doctor started G-CSF 300mcg sc daily. A bone marrow won't likely be done until Monday. If you have guidelines for use, I'd appreciate some help.

(Ann)
We have quite extensive experience with using Gm-CSF and G-CSF (primarily in patients who are neutropenic on ganciclovir and unable to take foscarnet but also in other situations). We used GmCSF for a long time (EDRP) as it is a multi-use vial and therefore cheaper in the long run. However, the company (Novartis I think) couldn't get it in from Europe at one point (not sure if they ever did) so we switched to G-CSF. The CFE Therapeutic Guidelines have a decision tree for the use (//cfeweb.hivnet.ubc.ca/Cfe.html). However, the summary is:

Absolute neutrophil count (ANC)<0.5g/L
- reduce dose or stop offending drug(s)
- advise patient to monitor temperature and obtain prompt evaluation plus empiric antibiotic therapy if febrile neutropenia develops

- prior history or current evidence of febrile neutropenia or neutropenia-related infection
OR
♦ balance of risks favours continuation of suspected offending drug
OR
♦ reversible cause of neutropenia not identified

If YES to above then: Consider G-CSF or GM-CSF if repeat ANC<0.5

If NO to above then: Observe and monitor ANC. If ANC remains <0.5 after 1-2 weeks, consider G-CSF or GM-CSF.

Dosing: The range is 1-5 mcg/kg Subcutaneously that we use. Generally, we start with 1 or 2 mcg/kg/day and monitor counts (including eosinophils). If patient is seriously ill, then we may start higher. You need to watch the eosinophils and back off the dose if they climb too high. We titrate the dose depending on the response of the cell counts. For ganciclovir patients, the duration is usually while the patient is on the drug. For patients with no apparent cause other than HIV, we do try to slowly back off once stable and closely monitor responses. Some never get off the drug. Patients generally do lab work weekly initially then q 2 weeks thereafter. Some patients are able to extend their dosing intervals to every 2 days or even twice a week and this seems to be enough to hold them steady.

A Couple of Notes: We have seen neutropenia with 3TC and possibly D4T. So that may be a contributor. We also look for MAC in these patients. Septra can also add to it (not sure if she is on it). Also, if using doses smaller than 300mcg, we will pull up doses in the sterile hood and use all part vials (ie draw up several doses at once to reduce wastage). BC Childrens' Hospital did a study on this and found no incidence of contamination if the prefilled syringes were kept in a container in the fridge for 1 month. I can find you the reference if you want it. So we will pull up a number of syringes for 2 weeks and the patient either takes them home or comes in when they are needed. Saves a lot of money.

13. Sperm Washing

(Deborah)
We have a discordant couple who are considering having a child (he is positive, she is not), but we have not been able to find a physician locally who does sperm washing. Does anyone know of a physician who does this procedure? Obviously it would be preferable if he/she was located on the east coast, but I believe this couple would be willing to travel further if necessary.

Or, if anyone has any other suggestions on "safer" methods, I'm all ears!
(Linda)
1 of our OBGYN docs was doing this in the past; not sure if he still is, however. If they are willing to travel here, I could check with him re: the feasibility of "helping out".

14. **New Antiretrovirals**

(Christine)
Other than lopinavir and amprenavir, has anyone heard of other antiretroviral medications that are available/will be available in the near future via expanded access? I know there are several drugs in the works (FTC, emivirine, DMP 963, T20 etc), but I was wondering if anyone has heard how close these drugs are? We have a couple of patients who have had genotypic resistance testing and are resistant to EVERYTHING! Lopinavir may be an option, but I certainly don't want to use it unless there is something to go with it. Anyhow, any suggestions you may have are greatly appreciated.

(Ann)
I have not heard of any. However, we have had a number of patients that came back resistant across the board that still responded to a mega combination of everything! There has been alot of discussion here around exactly how to interpret the genotyping etc with a big ?? still out there. Food for thought.

(Pierre)
A new protease inhibitor (apparently a second generation) is in clinical trial here in Ottawa, BMS232632. It is now used on naive patients but we might have access to that drug in one year or two. Nothing to help your patients since you have access lopinavir. I understand you are looking for agents in other classes.

15. **Hot flashes with lopinavir**

(Ann)
Has anyone seen hotflashes with ABT? We have a male patient that just started ABT (has been on all the rest of his meds before without problems) and developed "hotflashes" by day 3. Abbott, of course, was most unhelpful....

16. **Toxoplasmosis**

(Linda)
Is Sulfadiazine still available as I see it is contained in the preferred regimen? What are the usual toxo treatment regimens you use at your site? (I'm not clear why the IV dose of clinda is so much bigger than the recommended dose given orally -- 900-1200 IV q6h vs. 300-450mg po q6h??)
These are the guidelines that we use:

a) Induction therapy: (usually 4-6 weeks total)
pyrimethamine 200mg loading dose then 50-75mg/day orally with sulfadiazine 1-2g (100mg/kg/day) orally 4 times daily plus folinic acid 10mg/day with the dose adjusted according to the WCB and platelet count. OR (for patients intolerant to sulfas) pyrimethamine 200mg load then 50-75mg/day po plus Clindamycin 500-1200mg IV qid for the first 3 weeks then orally 300mg qid (or 450mg q8h) plus folinic acid 10mg/day

b) Maintenance therapy: (indefinite duration)
pyrimethamine 25-50mg/day orally plus sulfadiazine 500mg qid plus folinic acid 10mg/day orally or as required. OR (for intolerant patients) pyrimethamine 25-50mg/day plus clindamycin 300mg qid or 450mg q8h plus folinic acid 10mg/day

c) another option is atovaquone plus pyrimethamine - we only use in patients intolerant of all the other options. Dose is somewhat of a guess and no good trials have been done. However, we have used it successfully.

The reason that the clindamycin dose is high is to get BBB penetration. Clinda has very poor BBB penetration.

**Drug Interactions**

1. **Orlistat and antiretrovirals**

(Pierre)
I got a question from an internist wandering if it would be safe to administer orlistat (lipase inhibitor) with antiretrovirals. The patient uses NLV - SQV - DLV - D4T and is virologically suppressed.

I found nothing in that regard in my search but I am concern for the saquinavir absorption since F is increased by 1800% when given with a high fat meal. So if you don't absorb your fat, do you absorb SQV ????

Does the DLV + NLV / SQV drug interaction compensate ????
2. *Didanosine and milk*

(Natalie)
BMS faxed a reply to me today. 60 ml of milk decrease the AUC of ddI by 16%. The Cmax is also decreased and the Tmax is prolonged. (in-house study) They do not recommend the administration of ddI with milk or chocolate milk. Would you like a copy of the fax?

(Deborah)
Natalie, I would really appreciate a copy of that fax. When I called BMS in October 1999 about this same issue, they gave me the following information:
- dissolve 2 tabs in 30mL H2O, then add the mixture to 60mL choc. milk
- administer orally after stirring within 1hr of preparation.
- stable at room temp for 1 hr

When I asked for a written copy of this info, the medical information associate told me that all she had was exactly as she just read to me over the phone, and there was nothing further to send (ie. no kinetic data)!

(Ann)
This is something we have asked numerous times and really never got any concrete answer - no data etc etc. We have had a few patients that could only swallow this stuff with milk- but they only used small amounts to cover the taste. To the best of my recollection, I cannot recall any patient that was doing this having therapy failure per se. The other option that we suggested to a number of patients was to use chocolate syrup, rather than chocolate milk. They added just enough syrup to the "dissolved" tablets in water to make it more palatable. This seemed to be ok with the patients.

3. *St. Johns Wart and Protease Inhibitors*

St.Johns Wart
FDA PUBLIC HEALTH ADVISORY
February 10, 2000
Subject: RISK OF DRUG INTERACTIONS WITH ST JOHN’S WORT AND INDIANAVIR AND OTHER DRUGS

Dear Health Care Professional:

The Food and Drug Administration would like to inform you about results from a study conducted by The National Institutes of Health (NIH) that showed a significant drug interaction between St John's wort (Hypericum perforatum), an herbal product sold as a dietary supplement, and indinavir, a protease inhibitor
used to treat HIV infection. In this study, concomitant administration of St. John’s wort and indinavir substantially decreased indinavir plasma concentrations, potentially due to induction of the cytochrome P450 metabolic pathway. For additional information on this study please refer to the February 12, 2000 Lancet publication (Piscitelli, et al).

RECOMMENDATIONS:

Indinavir and other antiretroviral agents
At this time, pharmacokinetic data are available only for concomitant administration of indinavir with St. John’s wort. However, based on these results, it is expected that St John’s wort may significantly decrease blood concentrations of all of the currently marketed HIV protease inhibitors (PIs) and possibly other drugs (to varying degrees) that are similarly metabolized, including the nonnucleoside reverse transcriptase inhibitors (NNRTIs). Consequently, concomitant use of St John’s wort with PIs or NNRTIs is not recommended because this may result in suboptimal antiretroviral drug concentrations, leading to loss of virologic response and development of resistance or class cross-resistance.

Because herbal products are widely used in the United States and are available in various forms such as combination products and teas, it is important that health care professionals ask patients about concomitant use of products that could contain St. John’s wort (hypericum perforatum).

In addition, FDA is working closely with drug manufacturers to ensure that product labeling of antiretrovirals is revised to highlight the potential for drug interactions with St. John’s wort.

Other drugs
Based on this study and reports in the medical literature, St. John’s wort appears to be an inducer of an important metabolic pathway, cytochrome P450. As many prescription drugs used to treat conditions such as heart disease, depression, seizures, certain cancers or to prevent conditions such as transplant rejection or pregnancy (oral contraceptives) are metabolized via this pathway, health care providers should alert patients about these potential drug interactions to prevent loss of therapeutic effect of any drug metabolized via the cytochrome P450 pathway.

All health care professionals are encouraged to report any serious adverse event associated with the concomitant use of prescription drugs and St. John’s wort products to the FDA’s MedWatch program at 1-800-FDA-1088 (fax 1-800-FDA-0178).
4. Sildenafil & Efavirenz

(Linda)
I have a patient currently on Combivir & Sustiva -- He wishes to use Viagra. Has anyone heard of a reaction between Sustiva & Viagra & if so what is the recommendation? I see that Sustiva is mixed inhibitor/inducer of 3A so may either incr or decr Viagra levels??
I suppose if the patient insists we would suggest to start with a small dose of 25mg. Any comments?

(Christine)
I am only aware of the interaction data with protease inhibitors (hence the lower starting dose of 25 mg). With efavirenz, it is more difficult to predict whether it will act as an enzyme inducer or inhibitor - if the patient wants to use Viagra, to be cautious I would start at a dose of 25 mg and take it from there.

(Pierre)
To our experience, efavirenz is a mild inhibitor of CYP450 3A4. We used sildenafil 12.5 mg along with ritonavir in some patients without major toxicity. Thus, I would feel comfortable suggesting Viagra 25mg + Sustiva with proper counselling regarding side effects. I would probably not go higher than 50mg though, just because we don't know the full detail of that potential drug interaction.

(Yasmin)
Most data to my knowledge suggests the induction effect of EFV on 3A4 is most prominent. If it is indeed an inhibitor of 3A (per the monograph) it has not been demonstrated widely. The only drugs I am aware of that increase with EFV coadministration are NFV and RTV which do not increase much (20% ish) and are also 2C metabolized for which EFV is also an inhibitor. There is also conflicting evidence that suggests EFV decreases RTV.
It depends on the amount the drug is metabolized by the enzyme in question. Since Viagra is highly 3A4 metabolized I would think a decrease is actually more likely.
Reports from Working Groups

Of note, we reassigned the working groups at CAHR due to the large turnover in the Network in the past couple of years. If you could not attend CAHR, please let me know which group you would like to belong to. Here are a couple of updates…

Publication Group (Sandy)
Our paper has been published and the citation is:

Don’t forget:
♦ The next “publication” priority will be the website review. Please send your “bookmarks” to Sandy and she will divide the websites to review among the Network members.
♦ Each of the provincial reps are supposed to send a list of community pharmacies to Sandy for distribution of the paper.

Research
The new group leader for research is Laura Park-Wyllie (taking over from Nikola). Thanks Laura! Details surrounding the research group discussion at CAHR can be found in the minutes.

Communications (Alfred)
With respect to the website, I haven't done anything since Ginette first indicated that Merck would support.

Regarding hosting a web site, increased competition with web hosters have brought the costs down considerably. If you ever pick up a local computer paper, there are ads for Web Hosters eg. www.easyhost.com among many others.

There are literally hundreds of website hosters out there. Some sites such as EasyHost offer "free" website hosting by providing limited web space ie. only 1 webpage. We would probably need 5-10 meg webspace etc. at a cost of $30-35 cdn/month with access etc. and name registration. To get more features (not necessarily applicable to the group's use), the cost would vary from $40-90/month. Check out the following URL for http://www.netnation.ca/services/unixhosting.htm for examples of hosting costs.
Usually there is a one time setup fee of $50-90 (cdn) depending on the web site host. More costs if there is a need for more services (which I don't think the group needs). There is also a $70 US charge to register the domain name as eg. CHIPN.org (good for 2 years) by InterNIC (the organization that controls virtually all domain name registration.

Hence from an operation standpoint, the initial setup fee would be approx. $200 Cdn setup with monthly maintenance fees (probably $30-40 Cdn) depending on where the website hoster is. This would provide sufficient space and access to create a website.

Unfortunately, it doesn't look like I have anytime to create webpages with the current activities here. If the "look" is not important, than I could do it with FrontPage 98 using the established template if there is no alternatives.

Education (Yvonne)

? any updates
**Additional News**

(Alice)

Some of you may already be aware of an "HIV101" project that a group of us in Ontario (in conjunction with CHAMP) have been working on. This was originally designed to provide an introductory HIV workshop/seminar for primary care physicians, pharmacists, and other health care workers interested in HIV. Our first workshop was held in Ottawa last fall, and there are plans to hold similar workshops across Ontario and perhaps across Canada. Debbie, I think you've already spoken with Rob Throop about linking up and taking advantage of some of the resources that have been prepared.

As one of the next phases, we would like to prepare a set of pharmacist-specific readings that would be useful. This would be in addition to the usual sets of NIH/CDC/USPHD etc. treatment guidelines that appear on the internet regularly. Rob Throop, the project coordinator, is looking at obtaining funds to make ~200 copies available to interested pharmacists across Canada, so this is something that we could all potentially take advantage of. I already had a preliminary set of references in my files, but we wanted to get input from everyone in this group about other references that would be useful to add to this collection (see attached file).

If anyone has any comments or suggestion on additions, please let me know and I will forward them to Rob Throop.

**Updated Guidelines**


Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Non-Nucleoside Reverse Transcriptase Inhibitors. March 10, 2000. www.hivatis.org

In Print


Adherence to antiretroviral medications in an inner-city population.


*Quotes On Life (by Frank Lloyd Wright)*

"The longer I live, the more beautiful life becomes"

"Life always rides in strength to victory, not through internationalism . . . but only through the direct responsibility of the individual"

"Give me the luxuries of life and I will willingly do without the necessities"