

Happy summer, everyone! Well, even though it's usually one of the "slower" times of the year, we still have a very packed newsletter. Thanks again to all who responded to the clinical sharing session, and to those who have contributed.

1. New/Returning Network Members

I would like to welcome *Yasmin Khaliq* as an official member of our network. As we all know, Yasmin is working at the Ottawa General Hospital, Clinical Investigations Unit, and will continue to provide us perspectives on HIV research.

2. New Resources/Information/Websites, etc.

a) CATIE mailing lists (Michelle):

- Following is a list of our electronic publications and how to get them.
- 1. Our bulletin on new treatments Treatment Update, is on our web site at <http://www.catie.ca/aidsinfo.nsf/treatmentupdate>
- 2. CATIE-News is our electronic mailing list of new developments in > treatments for AIDS, HIV, and related conditions. To subscribe to CATIE-News, please send a message to the address: maiser@catie.ca with the phrase *subscribe catie.news* in the body of the message.
- 3. Journal-Scan is a weekly summary of articles from the scientific literature which we think are noteworthy, along with comments from our staff. This is presently only available by e-mail. To subscribe, send a message to the address: maiser@catie.ca with the phrase *subscribe journal-scan* in the body of the message.

b) CAHR conference, Quebec City, April 29-May 3, 1998

- Alice, Michelle, and Ann attended the CAHR conference in Quebec City.
- The abstracts of the conference have been published in a supplement of Canadian Journal of Infectious Diseases (sponsored by Merck Frosst). Abstracts are also available on disc from Glaxo Wellcome & Biochem Pharma.

c) 12th World AIDS Conference, Geneva, June 28-July 3, 1998

- Several network members, including Alice, Michelle, Nikola, Rachel, Ann, and Collette attended the conference in Geneva. Nikola has prepared an excellent summary of some of the conference highlights (document included in package). Also, the conference abstracts (yes, all >6000 of them) are available on CD-ROM through Merck.
- Some websites for the Conference proceedings:
 - www.webcast.aids98.org
 - <http://www.healthcg.com/hiv>
 - www.cmegateway.com
 - <http://www.medscape.com/Medscape/CNO/1998/AIDS/public/index-AIDS.html>
 - <http://www.hopkins-aids.edu/>
- Also find the website link to obtain the new antiretroviral and resistance guidelines which were published in JAMA on July 1, 1998.
 - <http://hivinsite.ucsf.edu/>

d) New guidelines:

- Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. MMWR April 17, 1998/Vol. 47/No. RR-4
- Report of the NIH Panel to Define Principles of Therapy of HIV Infection and Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents. MMWR April 24, 1998/Vol. 47/No. RR-5

- Also available via internet: .
 - <http://www.hivatis.org/>
 - SFGH HIVInSite (<http://hivinsite.ucsf.edu>)
- Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis. MMWR May 15, 1998/Vol. 47/No. RR-7.
- "The Hopkins HIV Report". It provides a great little review on current HIV issues and comments on guidelines. It is now available free of charge at: The Hopkins HIV Report, P.O. Box 5252, Baltimore, Maryland 21224, Attn: Distribution. Also visit the website at: <http://www.hopkins-aids.edu>
- Guidelines for the treatment of cytomegalovirus diseases in patients with AIDS in the era of potent antiretroviral therapy. Recommendations of an international panel. Arch Intern Med 1998;158:957-69. Also available on website at: www.ama-assn.org/internal.

e) Articles:

- The 4/30/98 issue of New England Journal of Medicine has an in-depth 12 page review of the Protease inhibitors.

f) Drug interaction resource:

- <http://www.projinf.org/fs/drugin.html>

g) Patient information sheets:

- New patient fact sheets on abacavir, amprenavir, efavirenz available at TTH clinic website: www.tthhivclinic.com

h) Pharmacist newsletter

- In the last newsletter, I mentioned that CommuniMed, an independent pharmacy consulting company, was producing an HIV newsletter geared at keeping community pharmacists up to date on developments in this area. CommuniMed had initially received enough funding to provide these newsletters free of charge to pharmacists in Ontario and Quebec. To date, almost 500 pharmacists have registered to receive this newsletter. CommuniMed has also indicated that they would be willing to send newsletter to pharmacists in other provinces. A copy of the first newsletter is enclosed. If anyone else is interested, they can contact CommuniMed via e-mail at: communim@total.net.

2. Drug Update

a) delavirdine NOC

- The 100 mg tablets of delavirdine received HPB approval in Canada on July 22, 1998 (finally!). Pharmacia is working on 200 and 300mg tablets (non-dispersable) for future use. The monthly cost is \$258.40 at a dose of 400mg TID. Pharmacia will continue to supply drug via the expanded access program to everyone on the drug, as well as those who are newly being enrolled until the drug is covered on provincial formularies.

b) ritonavir - possible shortage

- NORTH CHICAGO, July 27 (Reuters) - Abbott Laboratories Inc. said Monday that manufacturing difficulties will lead to shortages and supply interruptions of the capsule form of its HIV protease inhibitor, Norvir. The company said that capsules currently in distribution were not affected and that it will supply the liquid version of Norvir for continued patient treatment. "We have encountered an undesired formation of a Norvir crystalline structure that affects how the capsule form of Norvir dissolves," said Arthur Higgins, senior vice president, pharmaceutical operations, the company said.

“Although maximum efforts are underway, to date we do not have a solution to the capsule problem.”

- While the company cannot currently forecast the impact of this Norvir substitution on sales, Abbott remains committed to meeting its stated goal of low double-digit earnings per share growth, the company said. Recent projections estimated \$250 million of Norvir sales for the entire year of 1998, the company said.
- Abbott has contacted the U.S. Food and Drug Administration, the European Agency for the Evaluation of Medicinal Products, and other international regulatory agencies to address the problem, the company said. It will contact healthcare providers, consumers and the AIDS community through letters, the company said.
- A suggestion from Yasmin: For all studies with ritonavir, people may want to ask study participants to bring in their bottle of ritonavir and all subsequent refills so that their lot # may be recorded. There is currently a problem with the ritonavir formulation (absorption may be affected) so we need to keep track of what lots study patients are receiving.
- A copy of a letter from the company regarding this issue is enclosed.

c) adefovir

- (Michelle): Hosein S R. Adefovir: new drug, new hope. Treatment Update, 1998 March, # 85, v. 10 n. 1, pp. 1-2, Toronto: CATIE. This review summarizes information from the following trial: Deeks SG, Collier A, Lalezari J, et al. The safety and efficacy of adefovir dipivoxil, a novel anti-Human Immunodeficiency Virus (HIV) therapy, in HIV-infected adults: a randomized, double-blind, placebo-controlled trial. *Journal of Infectious Diseases* 1998;176:1517-1523.
- (Alice): A randomized, placebo-controlled trial *was* to have started up shortly in Canada. Participants with advanced HIV were to be randomized to receive adefovir or placebo as an addition to current/new antiretroviral therapy. This trial was to be in lieu of an expanded access program. We discussed this at our clinic, and while the majority of people would have preferred an expanded access/open label protocol, the company is insisting on doing this (presumably to collect data). Thus, in order to give our patients any chance of obtaining adefovir, we agreed to participate in this trial. However, the CTN has rejected this protocol, so currently, there is no compassionate access program in Canada.

d) abacavir

- There's an excellent review of the new drug "Abacavir (1592U89) in the May issue of *Drugs* (see Foster RH and Faulds D. Abacavir. *Drugs*. 1998 May, 55(5):729-736.

e) Viagra®

- Even though this agent is not yet available in Canada, it has obviously taken the U.S. by storm, and the potential for interactions with HIV medications has already been addressed by some medical/community groups. An e-mail was sent out regarding potential interactions with protease inhibitors and Viagra. Additional information has also been published in a U.S. newsletter. A hard copy of both is included in the minutes.

f) efavirenz-saquinavir interaction

- As we all know, efavirenz can act as both an inducer and inhibitor of CYP3A4. This effect is apparent with early interaction data involving saquinavir, where differing effects were seen depending on the dose used. i.e., : Preliminary data from single-dose kinetic studies show differing results: with 200 mg efavirenz, SQV [] are decreased (i.e., 39% decrease in Cmax, AUC) ; with 400 mg efavirenz:, SQV [] are increased (i.e., 30% increase in Cmax, 24% increase AUC).

- Dupont Merck has just issued a letter regarding additional information on the SQV-efavirenz interaction. Recent data from a multiple dose healthy volunteer study of efavirenz 600 mg/day and SQV-sgc (Fortovase) 1200 mg q8h shows: approx. 10% decrease in efavirenz concentrations (not clinically significant), and 60% decrease in SQV concentrations. Therefore, Dupont Merck strongly recommends that efavirenz not be used in combination regimens where SQV is the only protease inhibitor. The use of efavirenz with other SQV-containing double protease regimens is also strongly discouraged. With the combination of SQV/ RTV/EFV, clinicians should be aware of the risk of potential SQV underdosing (i.e., 400 mg SQV BID may not achieve optimal drug concentrations). Interaction data on this triple combination is now being generated.

g) nevirapine interactions

- (Alice): copy of letter from Boehringer Ingelheim summarizing nevirapine interactions is included in the minutes.

h) efavirenz

- (Alice): copy of letter from Dupont Pharma summarizing efavirenz pharmacokinetics and drug interactions is included.

3. Pharmacy-Related HIV Research

- Newsflash!!!!!! Kathy Slayter has received the Canadian Clinical Trials HIV Network Associateship Award this year. This is an especially prestigious honour, since it is the first time that the CTN has awarded this to a non-physician. CONGRATULATIONS!!!!!!

4. Professional News Updates

- CPhA linkage:
- I was finally able to speak with Bob Gadoua, Director of Corporate Affairs at CPhA about a prospective partnership. Some of the potential services they could offer us include:
 - a) communication within our own network. They could help out with photocopying, mailings etc to group members.
 - b) formulating structured policies. They have extensive experience in creating policies and by-laws, and could offer support to us if we wished to develop in that area.
 - c) advocacy at the national level.
 - d) increased exposure for our group. If we wished, people seeking expert speakers or facilitators for workshops or seminars could be referred to group members.
- Now apparently, the cardiovascular network considered the possibility of linking with CPhA and decided against it, for a number of reasons. The group wanted to remain an independent body, and they also did not want to pay membership dues for CPhA.
- I spoke with Bob Gadoua about this, and he said that since those discussions, they have decided that specialty network members who chose to link with CPhA will NOT be charged a membership fee (this may change in the far off future if our needs eventually change). The consultant pharmacists network has already gone ahead and formally developed a link with CPhA. Also, he stated that if we wished to form an affiliation with CSHP, that would not preclude forming an affiliation with them as well.
- In fact, one thing which we might want to consider is linking with both CPhA and CSHP. It appears that they would probably serve 2 very different functions (CPhA - policy, national advocacy, exposure to primarily community pharmacists; CSHP - more educational and professional development, exposure to primarily hospital or clinical practice pharmacists). We would still

maintain our own autonomy, this should not change the way we function, and there would be no additional costs involved.

- YES:
 - (Kathy): I think that this sounds phenomenal. I think in a way that it would allow us to be even more independent ie from Merck especially if CPhA would really provide all of those services to us.
 - (Yasmin): sounds good if no fees
 - (Mich): I have no problems with it. Do you think it is more trouble than it is worth??? If it helps, then great.
 -
- FURTHER DISCUSSION:
 - (Sandy): It would be nice to discuss the link when we next meet as a group...it's difficult to convey opinions or debate the pros and cons via email. The idea of a joint link with CSHP and CPhA sounds interesting...perhaps we could pursue and discuss this avenue.
 - (Tom, Christine): It's still a bit fuzzy in my mind with respect to CPhA: what additional benefits do we actually get from what we can do now ourselves; can they actually provide mailings, photocopy etc free of charge; is it worth paying another membership fee; what & how of setting the linkage.
- NO: no one.
- Bottom line: It appears as if most people are interested, but there are still many questions. Thus, we should probably discuss this at our next meeting. As a side note, the Ontario HIV Pharmacy Network has decided to go ahead with the CPhA linkage, with annual reassessment of the situation. We can update network members on this experience at the next Retrovirus Conference.

5. Clinical Pearls

Part I: Novel Adverse Drug Reactions

a) peri-oral tingling with PIs other than ritonavir (Sandy):

- We have a patient who experienced peri-oral numbness with ritonavir (on AZT, 3TC, saquinavir and ritonavir), had all his antiretrovirals D/C'd and had resolution of the peri-oral numbness. When antiretrovirals were restarted with nelfinavir (replacing ritonavir) + saquinavir + AZT + 3TC, the peri-oral numbness returned. Has anyone heard about reports of peri-oral numbness with either saquinavir or nelfinavir?
- Literature search and discussions with the companies have been negative to date. Roche has done an extensive search of their data base and have come up with no reports of peri-oral numbness with saquinavir. Agouron indicated that in their clinical trial data (1200 patients) there were a "couple" of reports of peri-oral tingling....but the physicians did not attribute them to the drug.
- Alice: We have enrolled 2 patients into an amprenavir (141W94) study, and interestingly, both have complained of perioral tingling sensations lasting approximately 1/2 hour after each dose.
- Michelle: At the Retrovirus conference in Chicago, they did some combination protease inhibitor studies with amprenavir (141W94) and found some perioral tingling when it was used in combination with indinavir, nelfinavir or saquinavir. The abstract is by Eron J et al. Preliminary assessment of 141W94 in combination with other protease inhibitors [abstract 6]. Data were presented for 16 subjects at week 4. 13/16 subjects had a decrease in viral load to less than 400 copies/mL. The most common adverse events were diarrhea, perioral tingling/numbness, nausea, rash, headache and flatulence.

b) Hallucinations, psychosis, etc. with efavirenz (Alice):

- Alice: We have heard of a couple of cases (here in the clinic as well as through the grapevine) of other CNS effects due to efavirenz, including hallucinations, psychosis, mania etc. I contacted the company, but they do not have any specific information.
 - Chris Holtzer (San Francisco): We have had a patient that developed an acute manic episode within 14 days of beginning EFV. The patient had a history of bipolar disorder so the etiology is not entirely clear, but the attending psychiatrist made the call of EFV induced mania.
- c) Severe nightmares (Christine):
- We had 2 patients this week complaining of this. The first patient has been on AZT/3TC/Indinavir for approximately 5 months and has been experiencing very frightening nightmares for about one week. He has recently stopped using intravenous drugs so given the time line I thought it was more related to this.
 - The second patient was seen by one of our physicians and he recently started on Ritonavir/Saquinavir/Delavirdine. (I am not sure if he is on a NRTI too?) He has also been having severe nightmares however he does not use intravenous drugs or any other medications.
- d) Use of Factor VIII for bleeding associated with protease inhibitors (Michelle):
- Michelle: does anyone have any experience on the use of factor VIII due to bleeding from the protease inhibitors. We have been finding that by increasing the dose of Factor VIII the response to the bleeding seems suboptimal. Any experience out there????
 - Tom: A number of our patients are Hemophiliacs & the PIs seem to cause more bleeding. So they do get Factor 8 either prevention or treatment. They are managed separately by the Hemophilia team here, so I don't have direct experience per se. Factor 8 can help some but not others. We have tried switching around PIs with variable success. I understand the Can. Hemophilia Soc. is planning a national study on this bleeding problem.
- e) Skin pigmentation with the protease, and particularly with indinavir (Michelle):
- have a patient with normal cortisol, and no other suspect drugs
 - Merck has 14 cases on file now with ? association
- f) Hemolytic anemia with indinavir (Michelle):
- 20 cases reported at Merck- we have one patient who may be experiencing this...
- g) Arthralgias with the proteases (in particular indinavir and Fortovase) (Michelle):
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- h) Cross-reactivity among NNRTI's (Michelle):
- Dupont USA has data on file reporting that of 17 patients who had rash on either delavirdine or nevirapine, 9 experienced rash when they were tried on DMP-266. There are no details about the nature/onset/severity of the rash.
 - Also, the chemical structures of all the NNRTI's differ. It seems like it is difficult to predict rash cross-reactivity in the class.
- i) Ototoxicity with azithromycin (Nikola):
- One of our patients experienced hearing loss after a single dose of azithromycin (1250mg once weekly). He took the dose in the evening, experienced sudden hearing loss within 2 hours, which had resolved by the next morning. I realize this is reported adverse reaction, but I had not come across it before.

- Alice: We had noticed a fairly high rate of ototoxicity to azithromycin in our HIV patients (17%), but the onset was much slower (mean 7.6 weeks, range 1.5-20); perhaps since our patients were taking an average of 600 mg/day (Clin Infect Dis 1997; 24:76-7.)
- j) Sudden death with delavirdine (Yasmin):
- An IND safety report was issued from Pharmacia UpJohn. Two reports of sudden cardiac death with delavirdine, that may or may not be associated. Speculated PK interaction with verapamil in one case. In both cases pts were on SQV, NFV, adefovir, L-carnitine, and delavirdine.

Part II: New dosing regimens, protocols, etc.

a) BID Indinavir (Natalie):

- I have a 15 year male (16 years in a few months) on indinavir, 3TC, and d4T who is a typical adolescent and having trouble with noncompliance right now. We are thinking of trying indinavir BID scaling his dose after 1000 mg po BID in adults. Does anyone have experience with this? I have the Chicago abstracts and my notes from the presentation given to us by Merck on Saturday in Chicago.

b) Pediatric PEP (Natalie):

- At the Children's Hospital of Eastern Ontario in Ottawa, we have developed a protocol and parent information (french/English) to deal with street needle injuries. Although this is a very emotional trial for the parents, it is important to remember that the HIV virus is only infectious for several hours after infected blood has dried on a hard surface such as a needle. An old needle covered in dirt or sand would have a very minimal if any risk of HIV. Hepatitis B and C are important risks. If you are interested in a copy of our protocol (modelled after the health care staff exposure (MMWR guidelines), please send us your mailing address. Unfortunately, there are no clinical studies to use as a basis for developing guidelines. We plan to publish our guidelines but have not rushed to do this as we do not have any clinical data to back up our modelled protocol.

c) Creatine and Anabolic Steroids in HIV:

- Alice: Medibolics has sent me an entire summary/manifesto on the use of anabolic steroids in HIV. It is quite detailed, with specific regimens for various types of patients. Not too badly written, but of course no scientific references provided. If anyone is interested, I can forward the attachment. I asked Chris Holtzer if they were using these regimens much (the PoWER regimens) in SF and he said no.
- Michelle: Here is the latest on the supplement creatine and viral load off of the following website: <http://www.medibolics.com>
- There is concern that the bodybuilding supplement creatine may increase HIV viral replication by feeding the ATP pathway. One doctor has noted a consistent trend of an increase in HIV viral load in his patients that suggests that this is true. If you have been using creatine or are using it now, please get in touch with me by e-mailing me at mmooney@ibm.net, or calling (310) 360-0654. We are in the process of collecting data on this to see if creatine use is counterproductive for people who are HIV-positive, and would like to see if there have been any detectable trends in HIV viral load related to creatine usage.

d)

6. Upcoming Events of Interest

a) Industry position:

- The headhunter from one of the leading pharmaceutical companies in HIV is looking for a bilingual person for the following position: Manager of Scientific Development and Training.
- If you have a lead or for more information please contact Donna Morohin at (416) 601-3858
- P.S. This is not the Roche job that has been advertised. That position has been filled by Sharon Yamashita, Pharm.D.

b) Another industry position (Agouron)

- A headhunter from another firm is searching for someone for a position as Head of Regulatory Affairs, Agouron Pharmaceuticals, Mississauga. The candidate should possess either a B.Sc.Pharm. or a Pharm.D. degree, and have some experience in HIV. Ability to speak French is an asset. Please contact Bob Shyley at (416) 621-4900 for more information.

c) 2nd Annual Conference on Compliance in HIV

- This conference was postponed due to low enrollment. It may be held in the fall.

d) HIV Specialty Residency

- (Michelle and Alice): We have a successful applicant for the first year of this residency program. Manish Patel, who has just completed his Pharm.D. at Wayne State University, Detroit, will be starting with us on July 27, 1998.

e)

7. Update on Group Projects

a) ALFRED: Communications

- I emailed Ginette about 3 weeks ago and I haven't back from her regarding funding. I've got 1/2 of the site ready but am waiting for confirmation of funding support before I go any further. If no funding is forthcoming from Merck, we may wish to consider pursuing funding from other sources.

b) GLENDA/YVONNE: Education

- Goal is to develop/conduct a survey of what educational modules are currently being done, and to identify needs (ultimate goal is to develop a national continuing education module for pharmacists, and perhaps linking with national pharmacy organizations and pharmacy faculties).
- Glenda is now in Australia for about 6 months, so Yvonne will be organizing the survey. Other members of the Education Committee may expect to be contacted in late August for their input.

c) SANDY: Publications

1. I have received submissions from the following groups for the publication: Compliance, Drug Acquisition, Research, Drug-interactions/Side Effects, Pediatric Needs, Drug Information Resources, Patient Counselling, and Alternative Therapy.
2. I am awaiting a submission from the Special Needs Populations group. Please forward this submission by email or fax as soon as possible.
3. I have only received a review of internet sites from 3 individuals (Yvonne, Yasmin, and myself). I would hate to hold up proceedings on the paper because of this section. Please forward your reviews ASAP, if you are involved with this section. If I do not receive them in the next 2 weeks....then we may drop this section of the paper, or have a much abbreviated section, or use the information as a separate publication.....I'd appreciate any input on the best course of action.
4. As a result of delays in receiving the group submissions, we are behind schedule in the progress of the paper. I am currently working with the sections that I have to come up with an initial draft....as I hope you all understand....this is a huge task.... to try and make each section flow and not read like it

was written by 20 of us and to abbreviate sections to have a paper of reasonable length! I hope to have a first draft circulated to members of the publications group by August 1st and to receive feedback from the publications group members by the end of August.

5. Circulation of the second draft will be made to the entire HIV network group and to the HIV PSG group (as discussed with Alice). I will ask for feedback from all by September 15th.
6. Hoping to get the paper submitted from publication by October 15th.
7. I thought the most appropriate journal for publication of the entire paper was CJHP, and that we could submit a notice of publication or abstract to Pharmacy Practice and Hospital Pharmacy Practice, after we received approval from CJHP to do so. I'd appreciate your comments.

8. **Clinical Sharing Session:**

Hydroxyurea - additional comments from group members

Natalie Dayneka (Children's Hospital of Eastern Ontario, Ottawa):

- We used 20 mg/kg/day in a 25 kg child 8 yr old (250 mg= ½ capsule) po bid in combo with ddI, ddC (yes - both together, nevirapine. We saw a dramatic fall in the viral load, a large weight gain, and the patient felt better. but now, 5 months later, the viral load is back up and we are stopping this regimen.
- The physicians were all for starting this regimen as the patient had failed 2 protease inhibitor regimen. The parents were very happy to have a new regimen that could be tried. The patient had no adverse effects that are monitoring revealed.

Viral load and its impact on antiretroviral management strategies.

A few things led me to think of this issue:

- a) new viral load test. In Ontario, we will soon be getting a new viral load test; our current one is the Chiron II bDNA assay, which has a lower limit of 500 copies per mL. This will soon be replaced by the Chiron III assay, which has a lower limit of 50 copies/mL. This may affect how aggressive physicians will be in trying to achieve undetectable viral loads.
- b) case reports of discordance between CD4 and viral load (e.g., AIDS 1998;12:619-624). In addition, there have been case reports of patients who have "broken through" virologically, yet continue to have rising or sustained increases in CD4. Some physicians have interpreted this as data to support not being so aggressive in their therapies.

1. What viral load test is currently being used in your province, and what is the lower limit of detection?

- (Kathy, NS): We are using Roche Amplicor LLD is also 400 copies
- (Nikola, Calgary, AB): The Southern Alberta Clinic is using the Organon-Teknika ultrasensitive viral load assay with a lower limit of detection of <40 copies/ml. This is being used routinely.
- (Christine, Edmonton, AB): We use HIV Monitor (Roche Diagnostic specimens) with a lower limit of detection of <500 copies/mL. We also use HIV Monitor Ultrasensitive (Roche Diagnostic Specimens) with a lower limit of detection of <50 copies/mL.
- (Rachel, Montreal, PQ): Chiron II, limit 500copies/mL
- (Linda, Yvonne, SK): Nuclisens Quantitative kit by Organon Technika; the provincial lab in Regina does all testing in Sask. Lower limit < 40copies per mL with a 2mL sample; less sensitivity with lower volume (400copies at 0.2mL).

2. Do you have access to ultrasensitive viral load assays? If so, in what situations are these tests used?

- (Kathy, NS): We do not have access to supersensitive tests at this time
- (Christine, AB): We tend to use the ultrasensitive viral load assays in patients who have had a couple of viral loads <500 copies/mL to see if they are completely suppressed.
- (Rachel, PQ): We have access to ultrasensitive.
- (Helene, Ottawa): The ultrasensitive viral load assays are only available for clinical trials.
- (Linda, Yvonne, SK): Use Nuclisens Quantitative test (lower limit < 40copies per mL) in all HIV patients.

3. Case scenarios. What would people do/recommend for the following situations? (i.e., change therapy, intensify therapy, maintain current therapy, etc):

a) Someone whose viral load has been undetectable (<500 copies/mL) in the past, but is now starting to slowly creep up (e.g., 12 000 copies, then 20 000 copies). How high would you let the viral load go before changing therapy? What if the person's viral load had initially been below 50 copies/mL?

- (Kathy): First of all we would want two determinations. We seldom ever make a decision on one viral load. Second it would really depend on how the patient was doing clinically and immunologically. There is some thought that due to the nature of the mechanism of action of PIs that an increase in VL may really be noninfectious viral progeny??? (Wishful thinking but a theory). We would probably get antsy if the VL got over 50,000 (ie even if his T cells took a huge jump & the pt was feeling well).
- (Nikola): I would further enquire at what stage of therapy s/he is (initial vs. salvage therapy, etc.), the time line between the three tests, and about adherence. However, with this information I would likely recommend a change therapy.
- (Michelle): Usually no higher than 0.5 log increase. Of course we consider if there are any other alternatives left for the patient which would be any better.
- (Christine): This is definitely controversial at our clinic and each physician has his or her own opinion. I think it depends on the patient's previous history and prior exposure to antiretrovirals. I also would wait to get a couple of viral loads back before changing therapy. In most circumstances, I would recommend a change in therapy if the viral load increases to 20 000 copies/mL. However, if the patient has received prior therapy with many antiretrovirals, I may wait to see if it levels off. If the patient had previously been <50 copies/mL and had not received a lot of previous ARVs, I may recommend changing therapy earlier (10-15 000). I would of course assess compliance to ensure that it is not the main cause of the increase in viral load.
- (Rachel): Change therapy (but we need two viral loads).
- (Helene): physicians at the Ottawa Hospital- General site are very aggressive. The lower the viral load ----> lower risk of disease progression. They would change therapy to maintain viral load undetectable.
- (Linda, Yvonne): Would let viral load go to 10,000 copies/mL before changing therapy. If the person's viral load had initially been below 50 copies/mL, would let viral load rise to 5,000 -10,000 (depends on clinical context & patient's desires).

b) Someone who has been maintained <500 copies/mL on a 1st/2nd antiretroviral regimen, but then had an ultrasensitive viral load result between 50-500 copies/mL (i.e., no longer undetectable according to an ultrasensitive assay).

- (Kathy): AAAGGHH!!! Hard question. We would ride it out & want to see a repeat measure. Pretty much the same thing would apply as I mentioned above. If T cells were also going down there is no question switch right away!!!
- (Nikola): Again knowing more about stage of therapy and adherence might lead to a more conclusive recommendation. I probably would suggest a repeat viral load one to two months later while remaining on current treatment.
- (Michelle): At this point, we have not had many patients request (and pay for) the ultrasensitive assay. It was not available to us previously. Although we know the durability is better if <50 c/ml, once again we would have to consider what the other options are prior to switching. We would likely try to work with the regimen (ie. identify compliance issues) prior to switching, and we would repeat the Viral load, since there is variability. I still think how clinicians will interpret the ultrasensitive assay is yet to be established in a non-research setting.
- (Christine): Again this is somewhat controversial. We do have a few patients whose viral loads were <500 copies/mL and we did an ultrasensitive assay and the viral load was 300 copies/mL. In this situation, we usually do not change therapy, however I do stress compliance and review the patient's schedule to ensure they are getting maximum benefit from the medications. I think many

physicians are worried about using all of the available drugs early on and then running out of options down the road.

- (Rachel): Can be change, intensify or maintain, depending on the physician and the patient (antiretroviral still available)
- (Helene): physicians at the Ottawa Hospital- General site are very aggressive. The lower the viral load ----> lower risk of disease progression. They would change therapy to maintain viral load undetectable.
- (Linda, Yvonne): No change.

c) Someone who has been extensively treated with antiretrovirals in the past. You are able to obtain access to a few new agents for this person. What are your realistic virologic and/or immunologic goals?

- (Kathy): I think in this scenario truly immunologic and overall quality of life may be somewhat more important than chasing a viral load (like we have been used to doing in the past) esp if the pt doesn't have that many options left.
- (Nikola): I would think a significant reduction in viral load (>0.5log) and decrease in direct HIV-infection related symptoms would be a good goal to achieve.
- (Michelle): In most cases, we have been able to get them the newest agents (DMP-266, 1592U89, nelfinavir, etc...). We have few patients on amprenavir, as the study requires PI naive patients. We are hoping the expanded access for amprenavir will open up in the summer. Also having nelfinavir more widely available will be great! We have had no success in obtaining adefovir. In terms of goals.... we are at least hoping to stabilize VL and CD4 and ideally get <500, recognizing that this may not be durable. We have had a few patients who have been <500 for the past few readings, and the durability remains to be determined.
- (Christine): This is tough as some patients have taken everything out there and still have viral loads in the millions. Since there is a lot of cross-resistance, even if you do have access to a few new agents, it is not realistic to expect undetectable viral loads. Thus, I would consider a realistic goal to be a 1 log decrease in viral load and perhaps a small increase in CD4. It is really patient dependent.
- (Rachel): under 20 000 copies/mL and over 100-200 cells/mm³.
- (Helene): At least 1 log reduction in viral load.
- (Linda, Yvonne): Depends on patients goals -- would wish maximal viral suppression with best possible QOL.

Final Thoughts:

A first grade teacher collected old, well known proverbs. She gave each kid in her class the first half of a proverb, and had them come up with the rest.

- As You Shall Make Your Bed So Shall You... Mess It Up.
- Better Be Safe Than... Punch A 5th Grader.
- Strike While The... Bug Is Close.
- It's Always Darkest Before... Daylight Savings Time.
- Never Under Estimate The Power Of... Termites.
- You Can Lead A Horse To Water But.. How?
- Don't Bite The Hand That... Looks Dirty.
- No News Is... Impossible.
- A Miss Is As Good As A... Mr.
- You Can't Teach An Old Dog New... Math.
- If You Lie Down With The Dogs, You'll... Stink In The Morning.
- Love All, Trust.. Me

- The Pen Is Mightier Than The... Pigs.
- An Idle Mind Is... The Best Way To Relax.
- Where There's Smoke, There's... Pollution.
- Happy The Bride Who... Gets All The Presents!
- A Penny Saved Is... Not Much.
- Two's Company, Three's... The Musketeers.
- Don't Put Off Tomorrow What... You Put On To Go To Bed.
- Laugh And The Whole World Laughs With You, Cry And... You Have To Blow Your Nose.
- Children Should Be Seen And Not... Spanked Or Grounded.
- If At First You Don't Succeed... Get New Batteries.
- You Get Out Of Something What You... See Pictured On The Box.
- When The Blind Leadeth The Blind... Get Out Of The Way.

Encl.

- CommuniMed newsletter
- Viagra interactions newsletter
- Handbook of HIV Therapy
- Nevirapine interaction letter
- Efavirenz letters
- Protease inhibitor/NNRTI interaction chart (updated July 20, 1998)
- Geneva conference summary (Nikola)
- Ritonavir capsule letter from Abbott