Hello everyone,

I had initially planned on sending this newsletter out a bit later, so that we would have time to do another Clinical Sharing Session. However, due to the upcoming registration for the Annual Retrovirus meeting, I thought that it would be best to send this out ASAP so that people could start making their arrangements. As with last year's meeting, there will be a limited registration, so I urge everyone to make their plans as soon as possible. Please see the attached letter for more details.

1. <u>New Resources/Information/Websites, etc.</u>

a) New guidelines: Updated recommendations for management of tuberculosis for HIV patients on protease inhibitors.

- Canada Communicable Disease Report, vol 24-16, 1998

b) Use of Atorvastatin and Gemfibrozil for Protease-Inhibitor-Related Lipid Abnormalities (Research Letter) Lancet (09/26/98) Vol. 352, No. 9133, P. 1031 by Henry, Keith; Melroe, Holly; Huebesch, Jacquelyn; et al.

- Scientists from Minnesota report the treatment of HIV-positive patients with both protease inhibitors and the lipid-reducing agents gemfibrozil and/or atorvastatin. Of 133 patients receiving protease inhibitors, those who took saquinavir and ritonavir were significantly more likely to have raised lipid concentrations meeting intervention criteria as outlined by the National Cholesterol Education Program (NCEP). Forty-four patients were enrolled in intervention programs. Twenty patients with lower increased lipid concentrations were started on exercise and diet programs, while the others were given gemfibrozil and/or atorvastatin. Twelve of the exercise and diet program patients were judged treatment failures and started on the lipid-lowering agents. Of those on gemfibrozil alone, 19 had sub-optimum responses and had atorvastatin added to their regimen. Patients who received both medications showed decreases in their lipid levels, with triglyceride concentration falling 60 percent over six months and mean cholesterol concentration declining 30 percent. The authors note that NCEP guidelines advise using caution in the combination of statins and gemfibrozil since there is a concern for increased risk of myopathy. There may also be increased toxicity when atorvastatin is used with cytochrome p450-interfering medications, such as protease inhibitors. However, the researchers observed no instances of myopathy, raised creatine kinase of liver enzymes, or adverse virologic effects, and they suggest that raised lipid concentrations in HIV-infected patients on protease inhibitors can be managed by following NCEP guidelines.

c) Efavirenz approved for use in children

- STUDY SHOWS EFAVIRENZ PROMISING IN TREATING PEDIATRIC HIV INFECTION: LEADS TO APPROVAL OF NEW DRUG FOR TREATING HIV-INFECTED CHILDREN
- Investigators of the Pediatric AIDS Clinical Trials Group (PACTG), a network of trial sites supported by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Child Health and Human Development (NICHD), have announced results of an interim analysis of the first pediatric study of efavirenz, a new non-nucleoside reverse transcriptase inhibitor (NNRTI) that can be taken once daily. The purpose of the study, known as PACTG 382, is to determine the safety, dosing and antiviral effect of efavirenz in combination with antiretrovirals in HIV-infected children. Efavirenz, when used in combination with nelfinavir and other antiretrovirals, suppressed HIV replication over a 20-week period in most children.
- "This study demonstrates that efavirenz used in combination with other antiretrovirals can have potent antiviral effects in children," comments Anthony S. Fauci, M.D., NIAID director. "It offers another choice for treating HIV-infected children who currently have fewer treatment options than

adults." At present, 12 drugs are approved for treating HIV disease in adults, compared to seven, including efavirenz, approved for children. Efavirenz is the second drug in the NNRTI class of antivirals to be approved for use in children. The study directly contributed to accelerated Food and Drug Administration approval earlier this month of efavirenz as a treatment option for HIV-infected children.

- PACTG 382 is a Phase I/II multicentered study evaluating a combination therapy consisting of efavirenz, the protease inhibitor nelfinavir and nucleoside reverse transcriptase inhibitors (NRTIs). As a safeguard, this highly intensive study was designed to closely monitor blood levels of efavirenz and nelfinavir. Drug doses were adjusted as needed. A total of 57 children were enrolled in the study. Participants were younger than 16 years, had not been previously treated with protease inhibitors or NNRTIs, and were able to swallow capsules. The median age of the children was 8.0 years; the median CD4+ T cell count was 699 cells/mm3, and the median viral load was 10,000 copies HIV RNA/ml. NRTIs were continued or changed at entry as clinically indicated. Pharmacokinetic studies were carried out at weeks two and six. Efavirenz was given at a starting dose of 600 mg/m2 once a day in combination with nelfinavir at the currently approved dose of 20-30 mg/kg three times per day. To date, this combination has been well tolerated by most subjects.
- The most common side effects were: rash (28.1 percent), which was seen more commonly in children than in adults; diarrhea (15.8 percent); and abnormally low levels of neutrophils (8.8 percent), a type of white blood cell. The percentage of participants whose HIV RNA was less than 400 copies/ml was 3.5 percent at baseline, 51.9 percent at the second week, 60.0 percent by the fourth week, 75.0 percent by the fifth week, 78.4 percent by week 12 and 66.7 percent at week 20. This antiviral effect is comparable or superior to that observed with previously tested combinations of antiretrovirals in this patient population. Furthermore, once-a-day administration of efavirenz may make it easier for patients or caregivers to adhere to therapy. Additional follow-up through the full 48-week course of the study will be important to determine if the drop in viral load is long-lasting and if the regimen will be well tolerated in children over time.
- The study co-chair is Courtney Fletcher, Pharm..D., University of Minnesota, Minneapolis. Dr. Fletcher and Richard Brundage, Pharm.D., Ph.D., also of the University of Minnesota, are the protocol pharmacologists. Stephen Spector, M.D., University of California San Diego, is the protocol virologist. Dr. James McNamara and Dr. Lynne Mofenson are the NIAID and NICHD protocol medical officers. Pharmaceutical support for this study was provided by DuPont Pharmaceuticals Company (efavirenz) and Agouron Pharmaceuticals Inc. (nelfinavir).

2. Drug Update

i) drugs licensed in Canada

a) Nelfinavir

- Nelfinavir finally got its Notice of Compliance on August 11, 1998. It will not be available in pharmacies until September 9th. People may continue to be enrolled in the expanded access program until September 11. For people who are enrolled in the expanded access program, nelfinavir will continue to be supplied free of charge for 90 days after the September launch date, or until the drug gets accepted on provincial formularies (whichever comes first). Provisions will be made for those living in provinces where formulary status may be delayed.
- Agouron is applying to ODB to get full Formulary status in the future, but Section 8 needs to be done after Sept 9th until we hear otherwise. The drug base cost is $491.40/month at a dose of 750mg TID. If anyone has questions about drug acquisition and payment, a national patient support line has set-up 1-888-545-5314.

b) Retrovir 300mg (AZT 300mg tabs):

- The Retrovir 300 mg tablets are now available in Canada.
- In Ontario, it will NOT be available via the Sunnybrook HIV Project Centre. Glaxo Wellcome is currently applying to ODB for LUP status (which most HIV drugs are under). In the meantime, section 8 applications will need to be filled out. Expect the same for Combivir when it becomes available.

c) Delavirdine (Rescriptor®) 100mg tabs

- Delavirdine is on the market. You can still access them via the currently existing expanded access program. Alternately, an ODB Section 8 request could be completed, since the drug can be ordered in regular pharmacies now. The base cost is $260/month at the regular dose of 400mg TID.

d) Nevirapine (Viramune®) 200 mg tablets

- Nevirapine was licensed in Canada on September 4, 1998. This agent is being co-marketed by Boerhinger-Ingelheim and Glaxo Wellcome. For pricing information, contact B.I. at 1-800-263-2425. For product inquiries or to request a product monograph, contact G.W. at 1-800-268-0324.

e) Caelyx (pegylated liposomal doxorubicin) by Schering

- Indicated for the treatment of Kaposi Sarcoma. It is more effective and less toxic than the standard systemic chemotherapy agents used to treat KS (bleomycin, doxorubicin, vincristine). The dose is 20mg/m2 IV given every 14-21 days for 6 cycles. The cost is $683.00 for a 20mg vial. Generally, the cost of therapy is about $10,000. The drug is not covered by ODB at this time, therefore it would fall under the Section 8 program.

ii) drugs licensed in U.S.

f) Efavirenz (Sustiva®)

- WILMINGTON, DE (September 18, 1998) DuPont Pharmaceuticals, a component of DuPont's Life Sciences Enterprise, announced today that its anti-HIV drug, Sustiva (efavirenz), was approved by the U.S. Food and Drug Administration (FDA). Sustiva is a once-daily non-nucleoside reverse transcriptase inhibitor (NNRTI) for the treatment of HIV-1 infected individuals. The New Drug Application was submitted in June and met the FDA's fast-track criteria. Sustiva is the first anti-HIV drug to be approved by the FDA for once-daily dosing and will be used in combination with other anti-HIV drugs in both adult and pediatric patients.
- Results from more than a dozen clinical trials involving more than 2,000 patients demonstrate the efficacy, safety and flexibility of Sustiva. These results indicate that Sustiva reduces plasma viral RNA to below quantifiable levels (less than 400 copies/mL using the standard Amplicor assay) in a majority of HIV-1 infected naive and treatment-experienced individuals in two-, three-, and four-drug combinations. Studies have shown that efavirenz penetrates into the cerebrospinal fluid, a common viral sanctuary. Finally, Sustiva (efavirenz) can be taken only once a day with or without food; however, a high fat meal may increase the absorption of Sustiva and should be avoided.
- Sustiva is priced in the mid-range of the antiretroviral class at $3,942 per year ($10.95 per day). When used in triple-combination therapy, as it was studied, Sustiva will be less expensive than the current standard of care including protease inhibitors. Sustiva will be available at pharmacies within the next few days. The company has worked with pharmacies and drug wholesalers to ensure the most rapid availability. Sustiva will be available in 200 mg capsules for adult dosing of 600 mg per day, and in 100 mg capsules and 50 mg capsules for pediatric dosing.
- DuPont Pharmaceuticals conducted one of the largest and fastest enrolling antiviral Expanded Access Programs to make Sustiva available to patients who needed it while the drug was awaiting approval. To date, more than 13,000 individuals worldwide have benefited from this program. DuPont

Pharmaceuticals is committed to helping patients seek reimbursement for Sustiva. The company will offer both reimbursement counseling and a comprehensive patient assistance program to ensure access to the drug for eligible patients.

- The accelerated approval of Sustiva is based on analysis of plasma HIV-RNA levels and CD4 cell counts in controlled studies of up to 24 weeks in duration. At present, there are no results from controlled trials evaluating long-term suppression of HIV-RNA with Sustiva. In one study, Sustiva in combination with two nucleoside analogues (AZT and 3TC) suppressed HIV-RNA to below quantifiable levels in a greater proportion of patients than did the control arm consisting of a current standard of care regimen containing indinavir, AZT and 3TC. More subjects from the indinavir, AZT and 3TC control arm discontinued therapy because of adverse events, and this accounted for a substantial fraction of the difference between the treatment regimens. The open label design of the study makes it difficult to assess the relative efficacy of the treatment arms.
- In a second study of patients with extensive prior use of nucleoside analogues, the combination of Sustiva (efavirenz), the protease inhibitor nelfinavir and nucleoside analogues suppressed HIV-RNA to below quantifiable levels in a higher percentage of patients than did a control arm consisting of nelfinavir and nucleoside analogues.
- Resistant virus emerges rapidly when NNRTIs are administered as monotherapy. Therefore, Sustiva must not be used as a single agent to treat HIV or added on as a sole agent to a failing regimen. Sustiva therapy should always be initiated in combination with at least one other antiretroviral agent to which the patient has not been previously exposed.
- Safety data from clinical trials show Sustiva is generally well tolerated. The most significant adverse events associated with Sustiva therapy are nervous system symptoms, which are reported in approximately half of patients (e.g., dizziness, insomnia, somnolence, impaired concentration and abnormal dreaming). The discontinuation rate for nervous system symptoms was 2.6 percent. These symptoms occur early in treatment and generally resolve within a few weeks. Rarely, patients have more serious side effects that may affect mood or ability to think clearly. Mild to moderate skin rash was reported in approximately one out of four patients. The incidence of severe rash was less than 1 percent. The discontinuation rate for rash in clinical trials was 1.7 percent. Women should not become pregnant while taking Sustiva (efavirenz) because birth defects have been seen in animals given Sustiva.
- For questions about Sustiva, physicians and patients may call 1-800- 4PHARMA (1-800-474-2762), or visit the company's website at www.sustiva.com. DuPont Pharmaceuticals is currently seeking regulatory approval in Europe, having submitted an application for marketing clearance in June. Submission for approval has also been made to Canadian regulatory authorities.

g) sustained release AZT (AZTEC®)

- Here is the website address for Aztec: http://www.verex.com/amt.htm
- Apparently the company developed this with the idea that the glucuronidation pathway would not be saturated due to slower absorption and therefore less AMT toxic metabolite would be produced. Keith Gallicano believes that the AMT metabolite probably doesn't contribute that much to toxicity however based on the small percentage it contributes overall and results from a study with AZT and rifampin where the AMT was theoretically induced (although not much increase in levels was shown).
- The company: Verex Laboratories, Inc., Attn: Aztec Group, 14 Inverness Drive East, Suite D-100, Englewood, CO 80112; phone: 303-799-4499; fax: 303-799-1734; website: http://www.verex.com/index.html

iii) other news

h) ritonavir - possible shortage

- The saga on the ritonavir capsule shortage continues. Apparently, Abbot has decided to focus its efforts on finalizing product development of the soft elastic capsule (SEC) ritonavir formulation.
- However, the FDA has to be satisfied that the SEC is bioequivalent with the old capsule and that antiviral activity is equal. The FDA must also be satisfied with the SEC's bioavailability, stability and shelf-life. To satisfy the FDA, Abbott is conducting studies for bioequivalence and a phase I study in healthy volunteers. It may be at least 5-6 months before the SEC is commercially available.
- In the meantime, patients will need to continue with the liquid formulation.

i) **Indinavir - update on BID dosing data (**Project Inform's Indinavir (Crixivan) Alert!)

- 18 September, 1998 - New information from the study of indinavir (Crixivan) used in twice daily dosing has yielded important information. The information is not encouraging. The new findings are contrary to a previous, smaller study which suggested that twice daily dosing was at least equivalent to the standard 3-times daily dosing. That study, however, was quite small and ran only for about 24 weeks. A larger study, called Merck 069, was initiated to confirm these early results.
- Today, Merck Pharmaceuticals announced that it was stopping the arm of study which employed twice daily dosing because a strong trend had developed showing this arm to be inferior to the results observed among those receiving the standard thrice daily dosing regimen. The study was made up of people who had never previously taken a protease inhibitor and never previously taken 3TC (lamivudine, Epivir). The regimen being studied in the Merck 069 study included AZT (zidovudine, Retrovir), 3TC and indinavir.
- In the data summary listed below, the number of volunteers differs at week 16 and week 24 because this is an interim report and looks only at the people who have reached the 24 week endpoint.

Study arm	% below 400 copies RNA at 16 weeks (287 patients)	% below 400 copies RNA at 24 weeks (87 patients)
3 times daily	78%	91%
Twice daily	72%	64%

- Based on these findings, the company is encouraging everyone using twice daily dosing to switch back to 3-times daily.
- While this is discouraging, it's hard to interpret. Data from other studies of protease inhibitors which included similar populations with similar treatment histories have produced results no better than the twice-daily dosing regimen being rejected here (notably some saquinavir studies and some nelfinavir studies). Merck spokespeople make the point that they are essentially competing with themselves in a study like this, and that the standard 3-times daily indinavir regimen is hard to beat. In any case, it's important that health care providers and people living with HIV are aware of the superiority of the 3-times daily dosing of indinavir, as many doctors and patients have already made the switch to twice daily dosing. Having said that, it's still unclear whether a patient who simply can't adhere to a 3-times daily dosing is better off to continue struggling with that regimen (and possibly failing to adhere) or to commit to twice daily and really stick to it.
- One additional regimen under study which might still permit twice daily indinavir dosing is the combination of ritonavir and indinavir. Preliminary, short-term studies of this regimen appear to make indinavir quite suitable for twice daily dosing, while also eliminating the requirement that the drug not be taken with food. However, it's important to recognize that this is based on early data, covering a short period, in two small clinical trials.
- It's possible that more people than ever are currently employing the indinavir twice-daily dosing regimen as news from the previous smaller study, which suggested equivalence of the 2- and 3-times daily dosing schedules proceeded the announcement of a shortage in supply of another protease inhibitor, ritonavir (Norvir) capsules. When the supply problem was announced, it's likely that some people began re-thinking their anti-HIV regimens and may have been making changes in their regimens, possibly to an easier-to-use regimen employing indinavir twice daily dosing.

- The lesson learned here is something that Project Inform has been cautioning about for some time with regard to simpler and easier regimens using the currently available therapies. When these drugs were approved, the reason they were dosed according to schedules in their label instructions (e.g. three times daily) is because studies demonstrated that these schedules were necessary in order to maintain optimal blood levels of drugs. While certainly people want, need and deserve simpler regimens, simply changing a regimen from three-times to twice daily dosing is not the solution.

j) Abacavir (1592)

- Ziagen® has recently been confirmed as the trade name for abacavir (1592U89) in the US and Canada.
- Glaxo Wellcome has prepared a letter summarizing the hypersensitivity reactions that may occur with abacavir. This was distributed via e-mail.

3. Pharmacy-Related HIV Research

- Dr. Manish Patel, the 1998-99 HIV resident (The Toronto Hospital/St. Michael's Hospital) will be doing a study to assess the utility of nelfinavir therapeutic drug monitoring in salvage therapy. This protocol has been submitted to the Ontario HIV Treatment Network and the Positive Action Fund for grant consideration. The Toronto Hospital and Ottawa General Hospital will be the primary research sites.

4. Professional News Updates

a) linkage with CPhA.

- The Ontario Pharmacy group has confirmed their affiliation with CPhA. This will be an item to discuss at our network meeting in January.

b) Update on Canadian Cardiology Pharmacy Network.

- Yasmin was a guest at the annual Cardiology Pharmacists' Network meeting in Ottawa. She was invited to give the cardiology group an update on our group's activities.
- (Yasmin): The cardio group was interesting. In terms of forming an alliance with CSHP, they mentioned that CSHP requires network members to be a CSHP member for at least 2 years! They found this a problem as do I. They don't have the good email system we have and will pursue that. They haven't done a role of the pharmacist paper but want to do a position paper on the use of ARBs. Their concern is then liability in light of the recent case about the statins and CCHOTA (sp?). The fellow who spoke on liability made most people concerned and I think mainly b/c we are practicing out of the scope of our license. I suggested to Heather that a working group be developed by network groups or others (CCCP) to address this. She will bring it up at CCCP next mtg.

5. Clinical Pearls

Part I: Novel Adverse Drug Reactions

a) If a patient develops hyperlipidemia secondary to PIs, what is your approach to managing this patient? (Alfred):

- (Alice): Depends, if the patient is on RTV/SQV, we might switch to IDV, which seems to be less of a lipemic agent. However, this if often not possible, based upon the patients antiretroviral history. We have had a lot of success with using Lipidil for treating triglycerides. I would certainly not recommend "doing nothing" as many people suggest, since we have had several people admitted and readmitted with pancreatitis due to elevated TG.

- (Michelle): What we have been doing is treating the lipid disorder. We have had a few paients with TG's in the 50's, thus we have been treating with fenofibrate or the new Lipitor (if both TG's and cholesterol are high). We have also considered using nelfinavir instead of the other PI's (nelfinavir may have a less metabolic effects). In some severe cases, we have used a non-PI containing regimen that has Sustiva in it. We do a 1 for 1 swap with the PI if the viral load is undetectable. If the viral load is up, we change at least 2 of the 3 drugs.

b) Low estrogen levels in a 31 yo female (Linda):

- She's been on SQV, RTV, AZT & 3TC since Dec/97 -- previously she was just on SQV, AZT, 3TC. Her VLs have been undetectable for over 1 year. Over the past year she has noticed occasional hot flashes and increasing irritablity, anxiety, rapid mood changes, feelings of "going crazy". To determine the cause, she recently had various types of blood work done (TSH, blood glucose, cholesterol) & found her estrogen level is very low -- her family doc wouldn't say how low, but lower limits of detection; she's been prescribed Premarin. She called me to see if the "cocktail" could cause this decrease in estrogen levels. Since RTV interacts with oral contraceptives & decreases ethinyl estradiol by 47%, it seems possible in women NOT on OCPs, that their estrogen levels could be affected/decreased as well? Have any of you found this as well? Also, I'm wondering if she may require a higher than normal Premarin dose in light of the DI with Ritonavir -- I guess we can dose it on symptom relief and repeat estrogen levels. . . ..
- (Alice): We've seen similar effects in some of our female patients. In fact, I had almost the identical conversation with the Abbott medical information pharmacist about the potential for ritonavir to decrease endogenous estrogen.
- (Glenda): We have not seen an association between PI's and low estrogen. I spoke to Dr. Money, who cautioned that interpretation of estrogen levels is very dependent on when they were taken during the menstrual cycle, and that a single level would be very difficult to interpret. If the woman is menstruating and ovulating, her estrogen levels are probably fine. In women with an intact Hypothalamic Pituitary Ovarian axis, any alterations in metabolism of estrogen should provoke increased estrogen production, not low estrogen levels. People on replacement however, such as premarin in post-menopausal women; or OCP's, which shut down the HPO axis, will have decreased estrogen levels, resulting in symptoms or lack of response. This patient should have further investigation of whether her HPO axis is functioning and if not, why not.

c) Pancrelipase for nelfinavir-associated diarrhea

- abstract from Geneva: [12383] The treatment (TX) of Nelfinavir (NFV) induced diarrhea. Kristen Razzeca Sandra Odenheimer Margaret Davis Karen Landeck. Camino Medical Group, 582 South Sunnyvale Ave Sunnyvale, CA, USA
- (Christine): We tried this in a patient who was experiencing a lot of diarrhea from nelfinavir that was not responding to other measures. I don't know exactly how soon it started working however we saw him 2 weeks after he started it and the diarrhea was much improved.
- (Alice): We have had quite a bit of anecdotal success with it as well. Here in Ontario, Ultrase MT is not on the formulary, so we have been using Cotazym ECS 20, which has the most similar components & amounts as Ultrase MT.

Part II: New dosing regimens, protocols, etc.

a) BID nelfinavir

- After the results of the Merck 069 study (where q12h indinavir did not perform as well as q8h indinavir), there has understandably been some concern over whether we are too eager to switch to

simpler dosing regimens when not enough clinical data is available. One such concern has been with the trend to using BID nelfinavir. Some network members have shared their experience:

- (Christine): We have started approximately 5 patients on BID nelfinavir in the past couple of weeks due to concerns about compliance. I think the data does look more promising than indinavir (especially since the half life of nelfinavir is longer) however we will have to wait and see. We have not had any follow up viral loads yet so I can't comment on efficacy. We should have this information very soon so I will let the group know how it turns out! I don't think we will put everyone on BID nelfinavir until there is further follow up data.
- (Kathy): We started to use 1250 mg po bid & then got scared!!! So pts are now being started on 750 mg po tid (by the way we are being told that tid is okay it doesn't have to be Q8H) I realize that it has a much longer half life but is this reasonable???
- (Alice): Yes, I think that TID dosing is very reasonable for nelfinavir. Someplace (the product monograph?) states that steady state drug levels taken 11 hours after a 750 mg dose were still well above the IC90 for nelfinavir; so even with 750 mg TID, it looks as though there is a lot of flexibility with the times. In terms of nelfinavir BID, we are using it quite often; usually if people can take 5 pills at once, and can get drug coverage (it's an extra 30 tabs/month). I think it is important to distinguish between the nelfinavir BID data and the indinavir BID data.
- Basically, with indinavir, we never did see any PK data that stated that BID gave you similar concentrations as q8h, and we know for a fact that the BID indinavir results in lower Cmin and higher Cmax (more incidence of kidney stones were actually observed in some trials). Merck initially said that indinavir Cmin were not associated with viral response, but I think these conclusions were made on a very limited and select population (i.e., small # of naive patients, using doses up to 2.4 g/day). So I for one was not really very surprised to see the results of the Merck 069 study. Incidentally, one of the reasons that Merck may have been very strict about q8h dosing of indinavir may be due to the fact that initial PK data suggested that the drug would have to be given q6h (based on plasma half-life), so they probably already thought they were stretching things with q8h dosing.
- On the other hand, nelfinavir has much more favourable PK. Similar Cmin were observed with the BID and TID regimens, with the BID having a greater AUC (not surprising, since a slightly higher dose is being used). Also, the clinical trial data has shown equivalency between the arms out to 48 weeks, so this is much more reassuring than some sketchy 12 or 16 week data. Since the case for NFV BID is much stronger, we are not hesitating to use it.
- (Marie): There seems to be a tendency for our doctors to use 1250mg am and 1000mg pm. This has been seen more since they attended the nelfinavir launch at beginning of this month. I have no follow-up yet on cd4 count and viral load. Some patients have complained of a bit more diarrhea on twice a day than tid dosing

6. Upcoming Events of Interest

a) 9th Annual HIV/AIDS Conference "Practical Approaches for Health Care", Toronto, December 3-4, 1998

- This annual conference is organized by the Immunodeficiency Clinic, The Toronto Hospital and the Continuing Education Department, Faculty of Medicine, University of Toronto
- This year's agenda includes a number of internationally renowned speakers, such as:
    - Dr. David Cooper, Australia, will give the keynote address on lipodystrophy associated with combination antiretroviral therapy
    - Dr. Calvin Cohen, Harvard University, will discuss current antiretroviral therapies: first line and subsequent treatments

  - Dr. Spyros Kalams, Harvard University, will outline the nature and extent of current immune reconstitution strategies in HIV
  - Dr. John Baxter, Cornell University, will review implications of genotypic and phenotypic resistance testing on clinical decision making
- Other sessions include debates on first-line treatments (NRTI vs. NNRTI vs. PI combinations), complementary therapy, psychological impact of changes in body shape, medication adherence, current issues in pregnancy, HIV and severe mental illness, and management of adverse drug effects.
- The registration fee for the 2 day conference is $250, with discounted fees for students and PWAs.
- For further information, call the Continuing Education Department, University of Toronto, at (416) 978-2719.

b) 6th Conference on Retroviruses and Opportunistic Infections, Chicago, January 31-February 4, 1999

- The Retrovirus conference will be at the Sheraton Chicago, Chicago IL. The abstract deadline is October 13. Registration opens November 6 for those with accepted abstracts, and begins November 23 for everyone else.
- Additional information can be obtained via:
  a) 24-hour fax on demand service: 703-716-7348
  b) home page: www.retroconference.org
  c) Retrovirus Conference secretariat: Westover Management Group, phone (703) 684-4876; fax: (703) 684-4841, e-mail: info@retroconference.org
- Registration can be done on-line, or forms may be obtained by calling the fax-on-demand service.
- Our annual network meeting will take place on January 30, prior to the conference. Please see the attached letter for details.

c) Adherence Update

- The adherence conference that was initially scheduled for earlier this year has been rescheduled for Thursday November 5, from 8:30 am-4:00 pm, Harrisburg, PA.
- The agenda is as follows:

8:00-8:30 am:	Registration, Continental Breakfast
8:30-8:45 am:	Welcome, Introduction
8:45-9:15 am:	Overview of Adherence, Linda Frank PhD, MSN, ACRN
9:15-10:45 am:	Adherence Update from ICAAC, Chris Woodward, DO
10:45-11:45 am:	Lunch
11:45am-2:30 pm:	Adherence Update from 12th World AIDS Conference (via teleconference): Biomedical Aspects, Gerald Friedman, MD Behavioural Aspects, Margaret Chesney, Ph.D. Clinical Aspects, Calvin Cohen, MD
2:30-3:30 pm	Panel for Case Studies (Linda Frank, Chris Woodward, Stuark Fisk RN, Susanne Sites RN, MSN)
3:30-4:00 pm	Wrap-up, evaluation

- The cost for the day is $25. More information may be obtained from the Pittsburgh office at (412) 624-1895 or via fax (412) 624-4767.

Final Thoughts: For this newsletter, I thought I'd leave it to others for some words of wisdom, also affectionately known as "Quayle-isms":

SMOKING KILLS. AND IF YOU'RE KILLED, YOU'VE LOST A VERY IMPORTANT PART OF YOUR LIFE."
- Brooke Shields

"THE PRESIDENT HAS KEPT ALL OF THE PROMISES HE INTENDED TO KEEP."
- Clinton aide George Stephanopolous speaking on "Larry King Live"

"THE POLICE ARE NOT HERE TO CREATE DISORDER. THEY'RE HERE TO PRESERVE DISORDER."
- Former Chicago mayor Daley during the infamous 1968 convention

"IF YOU'VE SEEN ONE REDWOOD TREE, YOU'VE SEEN THEM ALL."
- Forestry expert Ronald Reagan

"TRADITIONALLY, MOST OF AUSTRALIA'S IMPORTS COME FROM OVERSEAS."
- Former Australian cabinet minister Keppel Enderbery

"IT IS WONDERFUL TO BE HERE IN THE GREAT STATE OF CHICAGO."
- Former U.S. Vice-President Dan Quayle

"THE STREETS ARE SAFE IN PHILADELPHIA. IT'S ONLY THE PEOPLE THAT MAKE THEM UNSAFE."
- Former Philadelphia Mayor and Police Chief Frank Rizzo

"THE INTERNET IS A GREAT WAY TO GET ON THE NET."
- Republican presidential candidate Bob Dole

"IT IS BAD LUCK TO BE SUPERSTITIOUS."
- Andrew Mathis

"IT'S LIKE AN ALCATRAZ AROUND MY NECK.
- Boston mayor Menino on the shortage of city parking spaces

"I WAS RECENTLY ON A TOUR OF LATIN AMERICA, AND THE ONLY REGRET I HAVE WAS THAT I DIDN'T STUDY LATIN HARDER IN SCHOOL SO I COULD CONVERSE WITH THOSE PEOPLE."
- Former U.S. Vice-President Dan Quayle

"THEY'RE MULTIPURPOSE. NOT ONLY DO THEY PUT THE CLIPS ON, BUT THEY TAKE THEM OFF."
- Pratt & Whitney spokesperson explaining why the company charged the Air Force nearly $1,000 for an ordinary pair of pliers

"WE'RE GOING TO TURN THIS TEAM AROUND 360 DEGREES."
- Jason Kidd, upon his drafting to the Dallas Mavericks

I'M NOT GOING TO HAVE SOME REPORTERS PAWING THROUGH OUR PAPERS. WE ARE THE PRESIDENT."
- Hillary Clinton commenting on the release of subpoenaed documents

"WHEN MORE AND MORE PEOPLE ARE THROWN OUT OF WORK, UNEMPLOYMENT RESULTS."
- Former U.S. President Calvin Coolidge

"CHINA IS A BIG COUNTRY, INHABITED BY MANY CHINESE."
- Former French President Charles de Gaulle

"THAT LOWDOWN SCOUNDREL DESERVES TO BE KICKED TO DEATH BY A JACKASS, AND I'M JUST THE ONE TO DO IT."
- A congressional candidate in Texas

"THINGS ARE MORE LIKE THEY ARE NOW THAN THEY EVER WERE BEFORE."
- Former U.S. President Dwight D. Eisenhower

"A BILLION HERE, A BILLION THERE-SOONER OR LATER IT ADDS UP TO REAL MONEY."
- Everett Dirksen

"I DON'T FEEL WE DID WRONG IN TAKING THIS GREAT COUNTRY AWAY FROM THEM. THERE WERE GREAT NUMBERS OF PEOPLE WHO NEEDED NEW LAND, AND THE INDIANS WERE SELFISHLY TRYING TO KEEP IT FOR THEMSELVES."
- John Wayne

"IT ISN'T POLLUTION THAT'S HARMING THE ENVIRONMENT. IT'S THE IMPURITIES IN OUR AIR AND WATER THAT ARE DOING IT."
- Former U.S. Vice-President Dan Quayle

"WITHOUT CENSORSHIP, THINGS CAN GET TERRIBLY CONFUSED IN THE PUBLIC MIND."
- General William Westmoreland, during the war in Viet Nam

"WHAT A WASTE IT IS TO LOSE ONE'S MIND. OR NOT TO HAVE A MIND IS BEING VERY WASTEFUL. HOW TRUE THAT IS."
- Former U.S. Vice- President Dan Quayle at a fundraising event for the United Negro College Fund. He was attempting to quote the line "a mind is a terrible thing to waste."

"IF YOU LET THAT SORT OF THING GO ON, YOUR BREAD AND BUTTER WILL BE CUT RIGHT OUT FROM UNDER YOUR FEET."
- Former British foreign minister Ernest Bevin

"I LOVE CALIFORNIA. I PRACTICALLY GREW UP IN PHOENIX."
- Former U.S. Vice-President Dan Quayle

Encl.
- letter regarding January 30, 1998 network meeting