AIDS and HIV Management Goals:

A Treatment Primer for People Living with HIV/AIDS

Treatment Access and Research Committee

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AIDS Action Now!'s **AIDS AND HIV MANAGEMENT GOALS** describes the best practices and best guesses adopted by leading HIV physicians today. This issue incorporates findings announced at the Yokohama AIDS Conference in August 1994.

Access to treatment information and better health care is a political issue as well as a medical one. The more people living with HIV know about available treatments, the better equipped we are to redefine AIDS as a chronic, manageable disease and to transform our health care systems.

Treatment standards change and evolve as new drugs are tested and become available, and as we learn more about HIV and how it affects the immune system. Living with HIV and AIDS means having to make important treatment decisions based on incomplete information, and adjusting those decisions over time. Know the treatments that are out there, learn about your own health status and work with your health care practitioners to support you in your treatment decisions. Don't rely on any single information source for your treatment decisions. Read widely, monitor the available information sources and adjust your treatment accordingly. **Note that when this document suggests that you or your physician "consider" a treatment strategy, we are describing a standard that appears to be emerging as we put together this document.**

The following is information that does not fit into the chart that follows but is helpful in thinking about your treatment plan.

❶ **There is a broad range of anti-virals; combination therapy is an important option.** Your physician should be able to consider these anti-virals: AZT, ddI, ddC, d4T and 3TC. Currently AZT, ddI and ddC are the only licensed treatments available. None of these drugs are currently licensed for people with T4 counts over 500.

While AZT has shown benefit for people who are symptomatic and is also indicated in cases of AIDS dementia, the Concorde trial, a large European study, showed that there was no difference in survival or progression for asymptomatics on AZT and those taking a placebo after a three year period. Proper nutritional support, especially the B vitamins, is necessary in treating dementia not caused by an opportunistic infection.

The use of AZT may require supplementation. Studies have shown that AZT decreases magnesium, B_6, B_{12}, zinc and several other nutrients, all of which already tend to be low in those with HIV/AIDS.

Trials with non-nucleoside transcriptase inhibitors such as nevirapine, delavaridine and loviride are underway.

Of the twenty protease inhibitors under development, two are in Phase III study and compassionate access is likely to become available in 1995. These are Roche's Saquinavir and Merck's L-735,524.

Combination therapy is effective with other diseases and there is some preliminary evidence that it may be of benefit in AIDS. Studies are also investigating the value of **Convergent Combination Therapy,** using several agents that work at the same point in the HIV life cycle. AZT should not be combined with d4T since the anti-viral effect of the two together is less than either one alone.

❷ **Viral Load and Resistance.** Up to 10% to 20% of people who are HIV positive may have an AZT resistant strain before they start to take medication. Some of us develop resistance to anti-virals within weeks while others may take one to two years or more. Most individuals develop resistance to AZT after two to three years of therapy; some patients who have a high level of resistance do not progress clinically. Tests to more accurately measure resistance are in development and results may help you decide what anti-viral to use and when to change.

Two tests are now available to quantify the amount of HIV in your blood. Both use DNA (deoxyribonucleic acid, a fundamental molecule found in the nucleus of a cell which orchestrates the daily activities and reproduction of a cell) and calculate HIV activity by amplifying small sections of RNA, the HIV gene carrier that changes to DNA inside infected cells. These tests are based on two different testing techniques; Hoffman la Roche's **polymerase chain reaction (PCR)** and Chiron's **branched DNA testing**. In slightly different ways, both tests measure the RNA of HIV in terms of copies per millilitre of plasma.

Researchers have now shown that lowering the number of RNA copies translates to a better clinical prognosis, fewer

adverse events and less like likelihood of death. Changes in CD4 counts are also predictive but to a much lesser degree. The new test actually count pieces of virus, yielding a far more accurate assessment.

These tests may be used to help determine when to start anti-viral treatment and to measure the effectiveness of a current treatment regimen. It is not yet certain whether patients who have decreases in HIV in blood with certain drugs will do better than those who do not. The PCR test can be used to quantify other viruses, such as CMV, too. Both tests may be used to help determine the effectiveness of complementary therapies.

On average the highest viral loads are in those with low T counts. However, there is a tremendous variability in viral load in people with the same counts. Some people with low T counts may have low viral loads suggesting they may not benefit from drug therapy.

These valuable markers are known but underused. Validation and standardization should proceed at the same time as the tests are in clinical use. Some Ontario hospitals plan to introduce these tests as part of routine clinical care in the first half of 1995. **Ask your doctor.**

❸ **T4 Cells or CD4 Cells.** CD4 counts are not good markers for disease progression once you have started taking AZT. Even for patients not taking anti-virals, results may vary from time of day, lab to lab, or depending upon your immediate state of health (colds, flus, etc...). Don't make any major decisions on the strength of one test. It may take several tests to get a clear picture of your T4 cell level. You should also monitor your CD8 counts since CD8 cells are critical in controlling infections including HIV. Simultaneous drops in CD8 and CD4 cells may indicate disease progression.

❹ **Drug Trials.** AIDS Action Now! considers that the only reason to enter a drug trial is to benefit humanity with the information that can be gained through research. You should not be forced to enter a drug trial in order to get the treatment you want.

Where to find out about drug trials

There is a comprehensive directory of clinical trials available in Toronto. It can be obtained through the Ontario Region of the Canadian HIV Trials Network at (416) 978-6066, the Community Research Initiative of Toronto (CRIT) at 324-9505, the various hospitals which conduct clinical trials in HIV, or AIDS service organizations.

Alternatives to Drug Trials

If there is an experimental drug you want, ask your doctor if it can be accessed through the Emergency Drug Release Program (EDRP) phone (613) 993-3105. Activists fought very hard to open up the EDRP and therefore make it possible for individuals to request experimental drugs on a compassionate basis. Open arm and expanded access trials are also means of access for some drugs.

❺ **Bactrim is best for PCP prophylaxis** (prevention). Most doctors recommend Bactrim (Septra) at one double strength dose daily or three times a week for preventing PCP. It results in fewer breakthrough infections, fewer collapsed lungs, and its chemotherapeutic properties may protect against other opportunistic infections such as toxo. An alternative is one single strength tablet once a day, which is the same dose as a double strength tablet three times a week: this alternative causes less fluctuation in blood levels so possibly less allergic reactions. Many people who cannot tolerate full dose Bactrim can be de-sensitized through an incremental drug regimen. It is safest for everyone to begin with a de-sensitization program when your T4 cells fall below 200 or below 20%! If your count drops below 50 consider Bactrim on a daily basis as a possible prophylaxis for toxoplasmosis (if your toxo titre is positive). N-acetyl cysteine may decrease the incidence of Septra allergies. For people who cannot tolerate Bactrim, **even after de-sensitization,** other systemic prophylaxis such as dapsone, with or without trimethoprim if tolerated, are probably superior to aerosolized pentamidine. Lastly, prophylaxis with atovaquone (Mepron) may be considered (provides some prophylaxis against toxoplasmosis as well).

❻ **PCP is not the only opportunistic infection that can be prevented nowadays.** Although PCP prophylaxis is incredibly effective, with an almost 100% success rate, other diseases like cryptococcal meningitis, toxoplasmosis, CMV and MAI have prophylactic drugs. If your count drops below 100, consider prophylaxing for all opportunistic infections. (See charts for further information)

❼ **See your doctor regularly,** more frequently if your T4 cells drop or your health becomes less stable. Try to establish a relationship of trust and exchange with your doctor. Make sure that your visits to your doctor include an eye exam for CMV and a visual exam that checks your skin and mouth for things like KS lesions, thrush, etc. When you visit you doctor, ask him or her for a copy of your medical records. Study this and ask for clarification on any points that you don't understand. Be sure you understand all of you doctor's instructions and remind your doctor if he or she has overlooked something that you want information on.

❽ **Pursue the little things.** Get treatment for things like mouth sores, sinusitis, skin rashes, fevers, weight loss and diarrhea. They may not kill you, but they can be very wearing on the body and spirit. Learn about your nutritional needs and about vitamin and mineral supplementation. Regular exercise, sleep, interventions to deal with depression and substance abuse...all these areas are important in keeping a healthy immune system.

❾ **Complementary Therapies.** There is a wide range of complementary therapies available in specialized health

food stores or from "alternative" practitioners such as Chinese herbal doctors, naturopaths, homeopaths, etc. Many PLWA's report improved quality of life with such treatments. Unfortunately many of these options are not adequately researched and it is not known with scientific certainty if they are beneficial. Generally such treatments should be seen as something additional to your mainstream doctor's advice. It can be dangerous to abandon standard prophylaxis and treatments.

AIDS ACTION NOW! is an activist organization committed to fighting for treatment for people living with HIV and AIDS. Our general meetings are open to all. We meet the second and fourth Tuesday of every month at the 519 Church Street Community Centre in Toronto at 8:00pm. The Treatment, Access and Research Committee of AIDS Action Now! looks specifically at issues of drug access and federal initiatives around HIV and AIDS. For information about our next meeting call (416) 928-2206.

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Final responsibility for this document is that of AAN!

NOTE: Most research on HIV disease in North America has been done on gay men. Women, children and hemophiliacs may require a different minimum standard, and much more work needs to be done to determine what this standard of care would look like. There are a number of treatments to reduce transmission of HIV from mother to fetus/infant. Women need to thoroughly explore all available treatment regimens. Women who are HIV+ and pregnant should be aware that pregnancy is associated with general lymphocyte and T4 decreases.

WHEN YOU TEST HIV POSITIVE (any level of T4 cell)

Consider immediate intervention with anti-viral therapy. While evidence for early intervention is strong, existing anti-virals are so weak that their usefulness is in doubt for asymptomatics. There is good evidence of benefit in symptomatics. Combination therapy should be more effective in halting viral replication than monotherapy, but we still need further results. Get a flu shot once a year, a Pneumovax, and make sure that your tetanus, diptheria and polio vaccinations are up to date. Consider immune modulators such as cimetidine or naltrexone. An immune modulator is a substance that boosts or rebuilds the immune system. To date, no substances have been conclusively proven to accomplish this. Obtain a nutrition inventory/profile and modify your dietary intake as appropriate.

Nutritional deficiencies begin early in HIV infection. There are many nutritional protocols available including; one produced by Project Inform (1-800-822-7422) and a nutritional protocol authored by Lark Land's (which is available through many ASO's (aids service organizations).

TEST TO BE PERFORMED	ACTION
T4,T8 counts and percentage, (also called CD4 and CD8)	Repeat at least every six months if over 500 baseline. Always do tests at the same time of day and at the same lab. Be aware that when samples are transported to another site for analysis, results are less reliable.
Syphilis test (use Confirmatory test)	Treat with penicillin G benzathine as for latent/tertiary syphilis. Appropriate follow-up by your M.D. to assess whether treatment was successful is of particular importance - not all pharmaceutical agents in use are successful in eradicating syphilis.
Hepatitis B	If negative, consider hepatitis B vaccine, which is free in Ontario to people determined to be at risk. Double dosing is recommended. Ensure immunity by having your M.D. ordering a hepatitis B surface antibody titre one month after vaccination. Hepatitis A vaccine is now available. Hepatitis A immune globulin is recommended as post-exposure prophylaxis for asymptomatic and symptomatic HIV-infected.
Baseline Chemscreen (includes serum electrolytes such as sodium, potassium, chloride, blood sugar, and waste products like blood urea nitrogen and creatinine)	Intervention as required including nutritional supplementation and blood transfer.

Baseline Toxoplasmosis Titre	If positive, follow carefully, monitor for symptoms. If negative, ask your M.D. for nutritional counselling to avoid contact and have follow-up titres performed bi-annually.
Tuberculosis PPD Test & anergy skin test	If PPD positive or if anergy tests all negative, get a chest x-ray. If PPD, anergy test and chest x-ray all negative, no treatment, however, prophylaxis may be considered if at high risk. If x-ray confirms active TB, get treatment. Active TB requires 9 to 12 months of combination therapy.
Baseline Opthalmic Exam	Treat if symptomatic for cytomegalovirus (CMV) or other.
Pap Smear (Women) and Internal Exam	Every six months. Treat for candidiasis if present with topical cream, oral drugs if persistent. If pap smear suggests human papilloma virus (HPV), have colposcopy, cryotherapy, electro-dessication or laser therapy as appropriate.
**Hemophilus influenza B (HbCV)	Immunization is recommended for those not vaccinated during childhood.

Many other tests will be performed when you test HIV positive, and at regular intervals. Some of these include: p24 antibody and antigen tests, beta-2 microglobulin, neopterin, hemoglobin, MCV, platelets, WBC, neutrophils, creatinine lab values, baseline dental exam and baseline pulmonary function (especially for smokers). Tests for viral load and resistance to anti-virals and prophylactic drugs are expected to become more available over the year.

IF YOUR T4 COUNT IS ABOVE 200

Examine your options around combination and monotherapy with anti-virals. Some doctors like to start you on monotherapy with AZT when you become symptomatic or fall below 300, then add ddI or ddC later on. Others begin with combination therapy. It's your choice. If monotherapy with AZT fails, move on to ddI or a combination of anti-virals. Current data analysing an AZT/3TC combination is promising (*note: 3TC is not an approved anti-retroviral). Review with your physician any prior history of STD's or viral infections. Don't forget your yearly flu shot. T4/T8 should be done every three months, same time of day, same lab. Continue other tests outlined on pages three and four.

CONDITIONS	ACTION
Pneumocystis Carini Pneumonia (PCP)	If you are symptomatic, test for active infection by inducing sputum or bronchoscopy.
Cytomegalovirus (CMV)	If changes in vision occur, eye exam immediately.
Herpes Zoster outbreak (shingles)	Treat aggressively with acyclovir (Zovirax). BV-ara-U and valaciclovir are up and coming drugs for managing shingles. Also, consider acyclovir prophylaxis if you have a history of shingles. Some investigators recommend episodic prophylaxis
Herpes (simplex)	These treatments are also effective against regular, (genital) herpes. If HSV (herpes simplex virus) titre is positive acyclovir prophylaxis may control/decrease outbreaks.
HPV/Cervical Cancer (Women) Human Papilloma Virus	Pap smear every six months. Colposcopy if smear suggests HPV, therapy if appropriate. Rectal pap smears may be useful for both men and women if you have a history of venereal warts.
Candidiasis (oral, esophageal, vaginal)	Local nystatin therapy, if persistent the azole family of drugs (fluconazole, ketoconazole, itraconazole).
Skin Problems	See dermatologist, treat topically and aggressively. Consider DNCB for molluscum contagiosim and other skin problems.

Nutrition Inventory & nutritional deficiencies	Treat through vitamin and mineral chemscreen supplementation.
Kaposi's Sarcoma	Early intervention is better when KS is rapidly progressing. Lesions can be given topical injections with vinblastine. Systemic chemotherapy is sometimes used. Radiation and excision of lesions is possible. Liquid nitrogen can be used on flat lesions. Sotradecol may be useful for oral KS as an internal therapy, possibly eliminating the need for other therapies or making them less traumatic. Emerging therapies to consider are: DNCB, CD8 expansion with interleukin II, Doxil (doxyrubicin) or DaunoXome (daunorubicin).
Inflammatory Bowel Disease/diarrhea	Early detection of gastro-intestinal problems such as colitis is extremely important. Treatment with Asacol may prolong survival. Changes in diet may be necessary.
Dental	Don't neglect your oral health; have regular dental check-ups and cleaning.

IF YOUR T4 COUNT IS BETWEEN 200 AND 100

Continue anti-viral therapy, watching for anemia if on AZT, and taking frequent amylase levels if on ddI. Treat anemia with dose reduction, transfusions, or EPO, erythropoietin injections, folic acid supplements and B_{12} injections may be helpful. Continue regular CD4/CD8 cell tests every 3 months. Also watch for peripheral neuropathy (numbness, burning and itching of feet) if using d4T, ddC or ddI.

CONDITIONS	ACTION
PCP	If asymptomatic, begin prophylaxis immediately with Bactrim/Septra, dapsone (preferably with trimethoprim) or aerosolized pentamidine as first line of defense when T4 cells reach 200 or T4% drops below 20%.
HPV/Cervical Cancer (women)	Pap smear every 6 months. Colposcopy, if smear suggests HPV. Therapy as appropriate.
Candidiasis	Treat locally with topicals or with azole drugs if systemic.
CMV	Watch for symptoms. Continue eye exams.
Toxoplasmosis	Get toxoplasmosis titre done. If negative, repeat yearly. If positive, consider prophylaxis with Bactrim, or a combination of dapsone and pyrimethamine (prophylactic effect as yet unproven).
Mycobacterium Avium Intracellulare or Avium Complex (MAI/MAC)	Watch for symptoms.
Unspecific Fevers, Night Sweats	Identify cause and treat appropriately.
Diarrhea	Eliminate milk products and alter diet. If it continues, treat with Humatin if cryptosporoidiosis is suspected and consider Acetorphan or Somastatin. Imodium may be helpful in controlling symptoms. Observe for signs of dehydration.
Peripheral Neuropathy	Acupuncture, Tegretol or Elavil, Peptide-T, Capsaicin and Zostrix topical.
Nutritional & Vitamin Deficiencies	Test and correct deficiencies with supplementation. Serum level tests for micronutrients are problematic. (For example, currently there is no reliable B_{12} test.) Similarly an apparent calcium deficiency may reflect a real magnesium deficiency.

IF YOUR T4 COUNT IS BELOW 100

Continue or modify your anti-viral therapy strategy. Boil your water to reduce possibility of getting cryptosporoidiosis and MAI/MAC. Use distilled water. Avoid salads, raw vegetables and unpeeled fruits (whenever possible). Continue regular CD4/CD8 tests every 3 months.

CONDITIONS	ACTION
PCP	Continue prophylaxis with Bactrim. If intolerant consider Mepron, dapsone or aerosolized pentamidine.
CMV	Watch for symptoms. Continue prophylaxis. Eye exam every six months. If CMV is found, start treatment. The acyclovir pro-drug valaciclovir is being studied for oral prophylaxis of CMV in Toronto. oral ganciclovir is also being studied as prophylaxis for CMV. If CMV is found, start treatment with ganciclovir or foscarnet or combination (only if resistant). These drugs are given intravenously. A small British study suggests that a Portacath is associated with less risk of in-line infection than the Hickman line for CMV treatment. If you fail on these intravenous drugs a ganciclovir eye implant can be obtained through the EDRP (very expensive).
Toxoplasmosis	If toxo titre is positive, consider prophylaxis with Bactrim or combination of dapsone and pyrimethamine. 19% of cases of toxo occur in people who previously tested toxo negative. Watch for painful, burning, gritty eyes which may be complications associated with rifabutin.
Mycobacterium Avium Intracellulare or Avium Complex (MAI/MAC)	Consider prophylaxis with rifabutin, ethambutol or clarithromycin, azithromycin (usually with rifampin), rifabutin, or other multiple drug combination therapies. If wasting occurs, treat for MAI aggressively.
Cryptosporoidiosis	Specific testing and treatment (see diarrhea above).
Candidiasis	As prophylaxis/maintenance utilize the azole family of drugs. Treat aggressively, if systemic with ketoconazole then fluconazole.
Cryptococcal Meningitis	Treat aggressively with amphotericin B (liposomal amphotericin B is more bioavailable but expensive). Secondary prophylaxis with fluconazole and 5-flucytosine.
HPV/Cervical Cancer (women)	Pap smear every six months. Colposcopy if indicated. Aggressive therapy if HPV is confirmed.
Wasting	Consider treatment for MAI presumptively; consider steroids such as nandrolone decanoate (deca-durabolin) or growth hormones. Consider appetite stimulants. Studies on Megace show it does not increase muscle mass. If you are taking Bactrim/Septra and are experiencing wasting, check for folate deficiency and take supplements. Try a high calorie diet, the calories should derive primarily from protein and carbohydrate, and that if fat is above 3%-16% of the calories it should be from MCT (medium chain tri-glycerides) and/or fish oil. Consider oral supplements, enteral (tube) or total parenteral (TPN) intravenous nutrients.

Note: There is increasing evidence which demonstrates the drug acyclovir may be an effective anti-viral (HIV) especially for use in those with CD4 counts less than 50.

VITAMINS AND NUTRITIONAL SUPPLEMENTS

NUTRIENT	ACTIVITY	AMOUNT SUGGESTED
Essential Fatty Acids	Combat fatigue and immune dysfunction, helps skin problems.	Omega-6 fatty acids (eg. evening primrose or borage oil, gamma linolenic acid): 240 mg per day; omega 3 fatty acids: up to 300 mg per day.
Folic Acid	Helps red and white blood cell formation and synthesis of hemoglobin.	People not on anti-virals: 400 mcg; people on anti-virals: 800 mcg daily.
Magnesium	An essential element in most body processed - commonly deficient in the HIV+ population.	750-1000 mg daily.
Multi-vitamin/Mineral	Helps absorption and metabolism.	Ask for a high quality supplement at a health food store e.g."Ultimate One", many commercial brands are inadequate. 1 per day.
NAC (N-acetyl cysteine)	Anti-oxidant, provides glutathione. May decrease the incidence of Septra allergies.	500 mg 3 times per day.
Selenium	Immune system stimulation.	Up to 400 mcg daily.
Vitamin B_{12}	Involved in red blood cell production, helps brain function, helps with anemia in people not taking AZT.	500 mcg per day oral, plus nasal or under the tongue to bypass absorption problems, or get shots of vitamin B_{12}.
Other B Supplements	May help with neurological problems and anemia.	One oral supplement per day.
Vitamin C	Anti-bacterial, anti-fungal; helps thymic function and lungs.	2000-5000 mg per day - take small doses with meals. Calcium polyascorbate ester C is more bioavailable - 1000 to 2000 mg per day.
Vitamin E	Helps remove toxins from the blood, may increase AZT efficacy, may increase resistance to opportunistic infections and slow HIV progression.	400-800 i.u. per day.
Zinc	Helps skin and taste/smell disorders. Immunomodulator.	25-50 mg per day may be combined with calcium, magnesium and copper.