Towards a Comprehensive Federal/Provincial AIDS Policy

Policy Proposals from AIDS ACTION NOW!

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I. Introduction

AIDS ACTION NOW! is a community-based organization of AIDS activists in Toronto. It has approximately 350 members and enjoys wide political support both in Toronto and across the country.

While other community-based groups carry out important public education and support work in the fight against AIDS, AIDS ACTION NOW! is concerned specifically with the provision of treatment for people living with AIDS (PLWAs) and for those living with HIV infection (PLHIV).

AIDS ACTION NOW! believes that the lack of access to AIDS treatments in Canada is primarily a political problem created by government--both federal and provincial--, the medical profession--especially medical researchers--, and international pharmaceutical corporations. Because it seeks a political solution to the lack of AIDS treatments in Canada, AIDS ACTION NOW! does not accept government funding.

In addressing treatment issues, AIDS ACTION NOW! has engaged in a number of activities in the past year and a half:

A. initiated the Pentamidine Project to support PLWAs to get Pentamidine from Buffalo, New York, at a time when aerosolized Pentamidine was only available in Canada to half the subjects enrolled in a placebo-controlled multi-centre trial of this drug;

B. led the burning in effigy of Jake Epp, former Minister of Health and Welfare, on the occasion of the fist national conference of the Canadian AIDS Society in Toronto;

C. held a press conference on Parliament Hill to denounce the complete lack of action by the Federal Centre for AIDS in making new experimental AIDS treatments available to those dying from HIV infection;

D. brought complaints to both the Royal College of Physicians and Surgeons of Ontario and the University of Toronto Board of Governors pointing out that the use of placebo-controlled trials of experimental AIDS treatments violated basic medical-ethical guidelines;

E. established a seven-point policy for the treatment of PLWAs that included a call for, among other things, a system of anonymous testing, an end to placebo controlled trials as unethical, and a treatment registry;

F. participated in the Consensus Conference hosted by the government of Ontario and argued for major changes in the way pharmaceutical products, for the treatment of HIV infection, are tested;

G. developed policy on Ribavirin trials for human subjects whereby it is unethical for individuals to enter or to be entered into clinical trials of new pharmaceutical agents for the purpose of getting treatment. Individuals who enter trial should do so only to advance the scientific effort to find treatments for HIV infection and related diseases;

H. submitted the 7-point policy to Toronto City Council. This policy was approved by the city's Board of Health and City Council in May of 1989;

I. took major responsibility for organizing the activist presence at the V International Conference on AIDS in Montréal, and on that occasion issued with ACT UP, New York, Le Manifeste de Montréal, a declaration of the universal rights and needs of people living with HIV infection;

J. held a press conference and conducted civil disobedience against the Bristol Myers' reluctance to provide DDI, a new AIDS drug, on compassionate grounds to PLWAs intolerant of AZT; and

K. published in English and French for national distribution: *Treatment AIDS*, a compendium of new experimental treatments, *Testing AIDS*, an explanation of tests presently used in monitoring and controlling HIV infection, and a monthly publication, *TreatmentUpdate* that reports on the development and testing of new, experimental treatments reported in 90 medical journals, covering a number of medical specialities, that are reviewed each month.

II. AIDS ACTION NOW!'s AIDS Policy Analysis

The development of a comprehensive federal/provincial AIDS policy requires changes in many areas of the health care system. As many observers have pointed out, the AIDS pandemic has a unique capacity to reveal, and to bring to public attention, longstanding problems with the health care delivery system. Many of the medical problems people living with AIDS and HIV infection face are not new problems. It is just that their solution has acquired a particular urgency.

As the introduction pointed out, AAN!'s community mandate is concerned specifically with the issue of treatment. While AAN! supports the concerns of other member organizations within the Canadian AIDS Society, this brief is interested specifically in how government policy affects the delivery of treatment to individuals with AIDS or HIV infection.

AIDS ACTION NOW! has used its experience, during the past year and a half, in fighting for the release of new, experimental treatments, to develop its own policy analysis. In its opinion there are five important problem areas: A.) the problem of homophobia; B.) the problem of the ineffectiveness of the Federal Centre for AIDS; C.) the enforcement of the ethical guidelines issued by the Medical Research Council of Canada dealing with using human subjects in treatment trials in Canada; D.) the complete lack of any management system, at either the federal or provincial level, for the delivery of treatments to individuals with AIDS or HIV infection; and E.) the inadequate response of the Government of Canada to the AIDS pandemic in the developing world.

A. The Problem of Homophobia

Because of the cruel hoax which epidemiologists and the media have played on heterosexuals, many people still believe that AIDS is a gay disease. For people living with AIDS or HIV infection, however, this has meant that their expectations

of the Canadian health care delivery system has been severely impacted by homophobia. The result is that not only do gay men get second class health care, so do an increasing number of heterosexuals--women, children, hemophiliacs, and so forth.

This kind of discrimination is especially evident among provincial governments. Those which come quickest to mind are British Columbia, Saskatchewan, Québec, and Nova Scotia. This form of discrimination in the case of AIDS, results not simply in someone not getting a job, or a place to live, but in their lives being cut short. Provincial governments, however, are not alone in this matter. Homophobia also infects municipal and federal government efforts to extend the lives of those living with this disease. Jake Epp's "confessions" to his cabinet colleagues at a Harrington Lake meeting in either the late spring or early summer of last year eloquently displayed his homophobia, and account for his incapacity to deal with the AIDS crisis. How many persons with AIDS have had their lives cut short by the former minister's moral incapacities?

AIDS ACTION NOW! believes that a policy framework for an effective federal AIDS program must include the passage of the long-promised amendments to the federal human rights code prohibiting discrimination of the basis of sexual orientation.

B. The Problem of the Federal Centre for AIDS

There are many problems with the FCA. Those taken up here concern the provision of treatment for people living with AIDS or HIV infection. As a public health agency, i.e., as a directorate of the Health Protection Branch of Health and Welfare Canada, it sees its mandate as a public health mandate. This mandate puts it at odds with those who are infected with HIV and who are seeking treatment. For example, the FCA is basically concerned with controlling the epidemic[1]. This means protecting people from getting infected. But this kind of public health policy, while it helps those not infected also means doing nothing for people already ill, except perhaps to quarantine them or impose some other public health remedy. Public health policy and treatment policy in these kinds of catastrophic illness are not the same. As far as AAN! can tell the FCA has done absolutely nothing, nor can it as it is presently constituted, for people with HIV infection.

Another example is its handling of new, experimental treatments for AIDS. True to its public health orientation, the FCA has seen its mandate in this area as one of testing the safety and efficacy of proposed AIDS treatments. During its existence it has done absolutely nothing to make new drugs available. Indeed, the drugs that have most recently been made available have come through the Emergency Drug Release Program (EDRP), not the FCA. The EDRP is not a public health program (better put, perhaps, an exception to a public health program), but a treatment program. Again, FCA's public health mandate has puts it on a policy collision course with PLWAs or PLHIVs who require treatment as an urgent,

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[1]The way the *Policy Framework for the Federal AIDS Program* puts this is: "It should be recognized that these policies represent established federal activities with respect to AIDS control" (our underlining)

potentially life-extending matter. The FCA has simply not taken seriously the catastrophic rights of PLWAs. The lives of hundreds of people have been cut short by this kind of policy that limits it to a purely public health role in fighting this disease.

AIDS ACTION NOW! believes that a proper federal/provincial AIDS policy must include a policy directive to the FCA to facilitate the treatment of PLWAs and PLHIVs. This will mean, as is spelled out in D. below, that a distinct piece of bureaucracy will have to be set up to provide for the "parallel tracking" of new AIDS treatments. AAN! fully realizes that the management of treatment, as such, has not historically been a responsibility of government. But, as our experience shows, the medical profession, in the person of a collection of HIV physicians, does not have the authority to manage the AIDS epidemic. The profession cannot even establish, for example, standard treatment protocols for the opportunistic infections associated with HIV infection. AIDS ACTION NOW!, consequently, believes that the Federal Centre for AIDS must have, as part of its mandate, the power to facilitate access to new treatments. This could take the form, for example, of a bureau dedicated to treatment access, backed up by something like an ombudsperson who would have the power to investigate the unavailability of a treatment on the citizen's/patient's behalf, and to recommend action to cut unnecessary bureaucracy.

C. The Ethical Problems in Conducting Clinical Trials

It would appear that the most serious ethical concern of the Health Protection Branch, the FCA included, is to stay a respectable distance from the pharmaceutical industry so that it can never be charged with conflict of interest, or some other such impropriety. This, no doubt, is the reason why the HPB failed to notify doctors of the release of alpha-interferon for AIDS treatment, and P24 antigen test for diagnosing viral replication. They could not be seen to be promoting the products of particular pharmaceutical firms, no matter how this might impact the lives of PLWAs.

There are, however, more serious ethical lacunae that have bedeviled the work of the Health Protection Branch, including the FCA. These are the ethical requirements for experimenting on human subjects. The HPB believes that it is perfectly alright to require individuals to enroll in a drug trial in order for these people to get the treatment they need to save their health. The way this is usually expressed is, Who will go into a drug trial if there is also an open label arm attached to the trial?

The ethical guidelines of the Medical Research Council of Canada make it clear that product testing and treatment are two different kinds of activities. Unfortunately, even the federal government's AIDS policy framework conflates these activities (see section 3.3). Trials (i.e., product testing) and treatments have to be two quite distinct policy lines in any ethically correct AIDS policy. Moreover, the overall policy must recognize that these two activities could be opposed in some instances, like the way in which the EDRP provides for overriding the usual HPB procedures.

Both ethical and practical considerations recommend to government and to pharmaceutical companies and their researchers that PLWAs and HIV positive

individuals be enrolled in drug trials simply with a view to helping science defeat the AIDS pandemic. This is the position which AIDS ACTION NOW! has recommended to its members and others. (See the Ribavirin trials policy statement in the appendix.) Unfortunately, the protocols for the trial of both aserosolized Pentamidine and Ribavirin, the only two drugs to be tested in Canada on a large scale, have been ethically flawed.

Besides the problems of ethical protocols and the proper constitution of voluntary, informed consent, there is also the problem of drug regulatory agencies using "clinical endpoints" to determine the efficacy of a experimental treatment. The notion of "clinical endpoints" makes reference to the practice of using death or the subject going on to get an opportunistic infection, especially in the placebo arm of a trial, as a way of determining whether or not the drug being tested works. A more detailed discussion of the problems associated with using "clinical endpoints" such as 1) the risk volunteers are exposed to; and 2) the resulting narrow criteria for admission to trials can be found in John S. James' article reprinted fro *AIDS Treatment News* included in the appendix.

Our experience in AAN! has made it very clear that few people are conversant with the ethical guidelines set out by the Medical Research Council of Canada in 1987. This includes: doctors, researchers, pharmaceutical companies, and even institutional review committees. We find this situation quite appalling.

AIDS ACTION NOW! believes that an essential feature of a federal/provincial AIDS policy is the implementation of the ethical guidelines for research on human subjects set out by the Medical Research Council of Canada. We also believe that the use of "clinical endpoints" in drug trials should be ended as unethical.

D. The Problem of Establishing a Treatment Delivery System

In attempting to meet the AIDS crisis, both the federal and provincial governments in Canada have reacted with various kinds of public health policies. It is important to realize, however, that public health policy does not concern itself with the delivery of treatment. In fact, in some instances, such as the licensing of new drugs, public health policy has the effect of holding back possible treatment until they are shown to be safe and efficacious. This is why the federal government is seen as not doing anything for those who are ill with HIV infection. The FCA has done nothing about treatments because this is not part of its mandate.

The management of the delivery of treatment to those who are ill has, in the past, essentially been managed by the medical profession. In the case of AIDS, however, where there are no specialists, and where the infection gives rise to a wide variety of opportunistic infections, it is clear that the medical profession does not have the capacity to manage the delivery of treatment. The epidemic goes beyond the authority of any particular doctor. It is for this reason that AAN! thinks that the government must take initiatives in this area.

In the United States, the government there has developed two innovations in this area: the treatment IND and what is now being called "parallel traking" (see the account produced by the Treatment and Data Committee of ACT UP, New York in the appendix.). In Canada, similar moves have been made by making use of the

Emergency Drug Release Program (EDRP). The problem here, however, is that the EDRP was never intended to manage something as extensive as the required flow of drugs to AIDS patients. It is especially inadequate in that it fails to provide backup for doctors in terms of how to use the treatment. It also has no provisions for systematic collection of data on the treatment of patients. What is needed is a system of providing experimental drugs that makes use of the data gathered from their effects on patients to guide the treatment of future patients. What is needed, in other words, is a federally run treatment registry. Understanding about and consensus on the use of experimental drugs would also be facilitated by the establishment, in connection with a treatment registry, of a network of computers for computer conferencing for HIV physicians, especially primary-care physicians. Lastly, there is considerable inequality across the country in the cost of AIDS drugs to those who need them to extend their lives. All AIDS drugs, including experimental treatments, should be included on provincial drug formularies.

AAN! believes, consequently, that an essential component of a federal/provincial AIDS policy must include provision for the management of treatment. This we think should encompass, for example, the development of a treatment registry; the provision of computer conferencing for HIV primary-care physicians; and particu larly at the provincial level taking care of the cost of the many expensive AIDS treatments such as AZT.

E. The Problem of Canada's Response to the World-Wide AIDS Pandemic.

Canada is one of the richer nations in the world. Its citizens have one of the highest standards of living. And yet, although we hosted the V International AIDS Conference in Montréal in June, our commitment to the fight against AIDS world wide is not impressive. We can and must do more. In June AAN! along with ACT UP, New York, issued Le Manifeste de Montréal which outlines an important list of measures to be taken, including: the treatment of AIDS as a chronic but manageable illness; an international code of rights for HIV-infected people; an international data bank to make available, world wide, information on the treatment of AIDS; a ban on placebo-controlled clinical trials as unethical; the international standardization of the licencing of AIDS treatment; a comprehensive international program of safe sex and IV-drug use information; the recognition of the rights of women in relation to HIV infection; the establishment of an international development fund to assist poor and developing countries to wage and aggressive fight ageist HIV infection; and lastly, the conversion military spending worldwide to the fight against AIDS. The details of these policies can be found in the copy of Le Manifeste de Montréal in the appendix.

AIDS ACTION NOW! believes that both federal and provincial governments should endorse Le Manifeste de Montréal as a working document in the development of their AIDS policies.

III. Policy Recommendations

Included in the appendix to this document are three major policy papers, framed by AIDS ACTION NOW! on the fight against AIDS and HIV infection. These papers are the seven-point policy, the policy paper on the Ribavirin trial, and Le Manifeste de

Montréal. AIDS ACTION NOW! welcomes the promise of new initiatives by the Minister of Health and Welfare. At the moment, Canadians with HIV infection are dying because of the lack of clear and progressive policies on the treatment of AIDS. It is past time for government to act. To facilitate this process, AIDS ACTION NOW! recommends to government that:

A. the federal government immediately pass its long-promised amendments to Canada's human rights code making discrimination on the basis of sexual orientation grounds for complaint;

B. the federal government remove the present head of the Federal Centre for AIDS, and to institute a review of its mandate for the purpose of providing a better management structure for the delivery of treatments to people living with AIDS or HIV infection;

C. the federal government, with the assistance of the Medical Research Council of Canada, institute adequate safeguards to ensure that clinical trials of pharmceuti cal products meet the ethical standards set by the Council;

D. the federal government take direct responsibility for developing a management system for the delivery of treatments to people living with AIDS or HIV infection which would include the operation of a treatment registry, and a system of com puter conferencing for HIV physicians;

E. the federal and provincial governments take direct responsibility for making sure that the treatment of AIDS or HIV infection in the corrections system be second to none in the country; and

F. the federal government exercise its leadership capacities as one of the foremost developed nations in the world by implementing Le Manifeste de Montréal helping in the fight against AIDS through the development of:

   i) an international data bank, internationally available, on the treat ment of AIDS and HIV infection;

   ii) international standards for the licencing of pharmaceutical products for the treatment of AIDS or HIV infection;

   iii) an international fund to assist poor and developing countries meet their health care responsibilities in the fight against AIDS; and

   iv) policies that will assist in the struggle to defeat poverty in the world, both in Canada and abroad, as an important co-factor in HIV dis ease, including the conversion of military spending to medical health and basic social services

AIDS ACTION NOW!

AIDS ACTION NOW! Seven-Point Policy Paper *

Advances in the fight against AIDS have brought us to the point where we can begin to look at AIDS as a chronic illness rather than a universally fatal illness. Unfortunately, we are still faced with a variety of problems that prevent us from adequately dealing with it as such. AIDS ACTION NOW! has come up with seven main policies that would make treating AIDS as a chronic illness a reality. We list them here and plan to fight for their adoption in the year to come.

1. CATASTROPHIC RIGHTS

People Living with AIDS and others in catastrophic life-threatening situations have an unrestricted right to treatments which they and their physicians believe to be beneficial. This includes access to and availability of all drugs and treatments that can be used to treat HIV-positive people and people living with AIDS. These drugs should be available free of charge — even when they have not been given government approval for regular distribution. People in life-threatening situations do not need to have their treatments hampered by government bureaucracies or medical researchers who work within the government's restrictive regulations. The policies that they have in place are clearly designed for situations that are not life-threatening.

When people discover that they are HIV-positive they are faced with many decisions regarding their health care. These decisions, which can be life and death decisions, are now made in a situation that does not allow for the full range of treatment possibilities. Our government continues to deny us treatments that have proven successful elsewhere and, in collusion with the pharmaceutical industry, is inflicting unethical placebo testing on Canadians in life-threatening situations.

2. DRUG TRIALS AND PLACEBOS

Placebos have no place in the treatment of people living with AIDS. People in life threatening situations should not have to put their lives in jeopardy by receiving no treatment at all. As it stands now, multinational pharmaceutical companies, in conjunction with governments and medical professionals, are engaging in and promoting "double blind" placebo tests. These tests stipulate that a portion of the test group (usually one-half) will receive the drug being tested and the other portion will receive a placebo — a practice that means one-half will receive something that is designed to look like medication but is in fact a substance with no medicinal qualities at all.

AIDS ACTION NOW! supports full testing of drugs — with the stipulation that they should still be available in "catastrophic" situations even while undergoing tests and that the tests should be done only using either historical controls or comparative studies where other drugs are given.

3. ANONYMOUS TESTING

All levels of government should be working together to provide sites for anonymous testing in Canada. At present seven Canadian provinces require the reporting of HIV positive people to authorities. These requirements should be altered so that people can have the tests anonymously — that is to say by being able to receive their results without the people giving them the results being required to report their status to provincial medical authorities. Anonymity should be guaranteed when wanted and at all times people should be able to expect complete confidentiality of their medical records. People should have the right to know their health status without fear that their condition will be reported to the authorities or perhaps leaked to their employer or elsewhere.

4. PLWA's ON ALL BOARDS AND COMMITTEES

Boards and committees that are dealing with the health and lives of people living with AIDS should always have PLWA's as members. This should include any body that is dealing with any aspect of AIDS — issues such as hospital care, home care, human rights or education about AIDS can only be adequately dealt with through the full involvement of PLWA's. Prerequisites for the full participation of PLWA's are anti-discrimination legislation and the guarantee of no quarantine legislation.

5. NATIONAL TREATMENT REGISTRY

A national treatment registry should be established. Such a registry will be composed of a variety of treatment protocols thought to be of use to people living with AIDS or HIV infection. Primary-care physicians would access this registry with inquiries for treatment protocols to suit the individual needs of their patients. Reports to the registry of individuals' treatments and health status would be made on a continual basis. Treatments of all types, including those that are not part of the medical mainstream, would be recorded. Both physicians and PLWA's should have access to the information in the registry so that PLWA's can be active participants in their own treatment. This registry should be established and run by a body that includes the full participation of PLWA's.

The national treatment registry will be a very important tool in bringing together the existing knowledge about AIDS and the ever-widening scope of treatment options. It is important that the registry be connected with other such registries in other countries. This will also allow the treatment of PLWA's and HIV-positive people to move away from a strictly hospital setting and more into the home and primary physician's office.

6. HOSPITAL CARE

Hospital administrations must work much harder at establishing state-of-the-art diagnostic and treatment protocols to deal with the health of PLWA's. At present there is no uniformity in care available for PLWA's in different hospital settings. PLWA's are continuing to have horrific experiences as they deal with hospitals where a "hit and miss" approach governs present attempts at AIDS care.

It is the responsibility of the provincial Ministry of Health to establish standard protocols for all hospitals so that care can be brought up to an acceptable level.

7. HOME CARE

In conjunction with the national treatment registry and better hospital care we need to establish a comprehensive approach to home care. The needs of PLWA's can often better be met at home than in the hospital with the help of their primary care physicians. In addition, it must be clear that people being released from hospitals are being released to situations where their needs are being fully met. It is nurses who will be able to do the most to make home care a viable alternative for most people. This will require more education for nurses about dealing with PLWA's and a recognition of the importance of this work by health care workers.

*** Adopted by the General Meeting of AAN! held in Toronto October 5, 1988**

Why No Antivirals: A Case History of Failed Trial Design

by John S. James

AZT provides limited benefits to persons with AIDS or HIV, and many people cannot use it at all. Many promising new antivirals have long been in the research and regulatory pipeline: for example, DDI, AZDU (CS-87), D4T, DDC, hypericin, and trichosanthin (compound Q). None has become available since AZT was released almost three years ago. And at the Montreal AIDS conference earlier this month, we learned why none will become available for years—unless certain current practices in the design of clinical trials can be changed. This article will illustrate some of the problems, and suggest solutions.

The basic problem lies not in any single agency, company, or other institution, but instead in a conventional wisdom which cuts across institutional boundaries. A professional consensus guides the design and conduct of clinical trials, and the shepherding of experimental drugs through the testing system. This consensus today includes certain assumptions which make it impossible for the existing system of clinical trials and drug approval to respond successfully to AIDS as a public-health emergency.

Note and disclaimer: Readers may notice that this issue of *AIDS Treatment News* has a call for volunteers (above) for the same trial analyzed below as an illustration of a failure of the clinical-trial system. This is not an oversight or contradiction.

This trial is no worse than other AIDS studies. It seems to be ethical in its treatment of volunteers. The problem is that it will not produce results for years.

But for now it is the trial we have, so we do support it.

For the same reason, this article is not intended as a criticism of persons conducting this trial, nor of it's sponsor. They have done well within the system of shared assumptions which controls all mainstream AIDS research. It is this system which needs reform.

A Case History: New DDC Trial

DDC (dideoxycytidine), an antiviral like AZT but with different toxicities, is not the most important new drug. But it is farthest ahead in the drug-approval pipeline among major antivirals. Because it is ahead of the others, and plans for a major new study have been revealed, it provides an excellent case study of the problems which will impede the approval of all important new antivirals, not only DDC but also more interesting drugs such as DDI.

DDC Background

DDC, like most of the new AIDS antivirals, was discovered to have anti-HIV activity by U.S. Government scientists. The United States then asserted exclusive worldwide rights, and assigned these rights to a pharmaceutical company (in this case, Hoffmann-La Roche, Inc. of Nutley, New Jersey).

Several trials have already been conducted. In early studies, some patients developed severe peripheral neuropathy, causing numbness or pain in the feet. Later human studies found that lower doses could reduce P24 antigen levels, a sign of antiviral activity, with manageable toxicity.

On June 5, 1989, Hoffmann-La Roche announced new trials, designed in cooperation with the FDA (U.S. Food and Drug Administration). A major phase II trial, which could lead to marketing approval for the drug, will compare low-dose DDC head-to-head with AZT "in persons with AIDS or advanced ARC."

The problem with this trial is that because of the design chosen, it is unlikely to produce any conclusion for two and a half years.

And since DDC is ahead of all other major antivirals in the drug-approval pipeline, and the delays in this study design are generic to AIDS antivirals and not specific to DDC, it is likely that all major new AIDS drugs will face a similar delay. This fact alone strongly suggests that no major new treatment for AIDS will come out of the drug-approval pipeline for years, unless the assumptions currently guiding clinical trials can be changed.

An analysis of the design of the new DDC/AZT comparison trial, and the assumptions behind this design, will show exactly how this intolerable situation came about, and how it can be changed.

DDC Rumor: A Treatment IND?

Rumors have circulated that DDC may become more available through a "treatment IND" before the end of 1989. We hope these rumors are true.

But we are skeptical. The FDA has interpreted the treatment IND very conservatively, using it only near the end of efficacy trials, when the drug is almost sure to get full marketing approval after the final paperwork is complete. If this procedure is followed for DDC, a treatment IND will probably be more than two years away, as we will show below.

The record is full of comforting but broken promises that that things have changed and therefore AIDS research will move faster in the future. When the future arrives, the public has forgotten the promises.

Why will the trial take so long?

This new phase II trial will compare DDC with AZT, using a randomized, double-blind design. No placebo will be used; every patient will get one of the drugs. The trial is scheduled to last two years; recruiting the subjects is expected to take about six months in addition.

In theory, the study could end earlier. A team of experts will periodically monitor the results, secretly breaking the code to see if there is statistical proof that patients getting DDC are doing much better or much worse than those getting AZT. In practice, however, for reasons explained below, it is almost impossible that this study will end this way. The researchers expect it to take the whole two years.

The reason that the study will take so long must be explained in several steps:

(1) The FDA will not approve a drug based only on "surrogate markers", meaning improvement in blood work such as reduction in P24 antigen, or T-cell rises. The Agency also wants statistical proof that the drug is helping people.

(2) After rejecting surrogate markers, the FDA has insisted on the slowest measure of clinical improvement—"clinical endpoints", meaning OIs (opportunistic infections) or deaths. This means that the drug being tested is not measured by improvements in the patients who receive it, but OIs or deaths in those who do not.

The DDC trial will compare that drug with AZT. Since AZT works fairly well for the first year, the number of deaths and OIs in the control (AZT) group will be low. Therefore, even if the drug being tested were perfect and everybody taking it were cured instantly, the clinical trial design would not recognize that fact **until enough deaths and OIs had accumulated in the control group** to provide statistical proof that DDC was no worse than AZT.

(3) This study, like some others, will use a team of experts (sometimes called a "data safety monitoring board") to meet periodically and secretly break the code and examine the results so far, to see if the study should be ended early. The public is told that such reviews can end studies as soon as statistical proof of effectiveness is obtained.

But in practice it is unlikely that this or any similar study will be ended early. The reason why not involves an esoteric problem in statistical interpretation. If researchers take an early look at their data to decide whether to stop the study early and call the drug a success, but then decide that the data does not justify stopping, meaning that the study will run to its normal conclusion, then the very fact that they looked early means that they must tighten their interpretation of the final results. A drug which otherwise could have been considered a success might now need to be counted a failure—just because the researchers looked at the data and **might** have acted on that information—even though in fact they did nothing different as a result of the look.

This seemingly preposterous conclusion is hard to explain even to scientists, let alone to readers with no statistical background. We will try to do so; those who are not interested in the details can skip the next four paragraphs.

(When researchers claim statistical proof that their drug works, they are usually claiming that the drug passed a test which only a small percentage of worthless drugs could have passed by chance; the smaller the percentage, the better. For example, if a journal article claims that a result is "statistically significant at the $p<0.01$ level," this means that the probability (p) that a worthless drug could have done as well or better by chance alone is less than one percent (0.01).

What happens, then, if you look at the data early? Suppose that the researchers did not know about the problem that we are describing here, and they decided to take an early look at their data, and end the trial immediately if the drug was good enough to have reached the $p<0.01$ level already. If not, they would continue the study and see if they achieved that level later.

Clearly then the chance of accepting a worthless drug at some time in their trial would now be greater than one percent. This is because there is a full one percent chance to accept such a drug at the early look—and if the worthless drug did not pass the test at that time, there is some additional chance that it could pass later. Since the overall probability of accepting a worthless drug is now greater than one percent, the researchers cannot correctly claim that their trial showed efficacy at the $p<0.01$ level. To honestly make that claim, the researcher must use a higher standard both for the early look, and also at the normal end of the study if the early look did not result in the trial's termination.

This means that if researchers take an early look at their data but decide not to end the study as a result, they then must tighten their standard for judging a drug successful later. Drugs which would otherwise have been judged effective will therefore now be rejected. They can minimize this problem by making the early look as conservative as possible.)

The practical effect of this statistical oddity is that researchers have a strong incentive to use an extremely conservative criterion for ending a study early, or for terminating worthless or harmful treatment arms. As a result, a "data safety monitoring board" provides much less protection to the volunteers in a study than they may be led to believe. And the assurance to the public that experts are monitoring the trial and will end it early as soon as the data justifies, thereby speeding final approval of the drug, is largely empty.

(Note: The AZT trial was stopped early in September, 1986, when there were 16 deaths in the placebo group, vs. only one death in the AZT group. No one knows why this extreme difference occurred, as later experience does not support a 16 to one difference in death rate with AZT. And despite this great difference in deaths, the decision to stop the study then has been controversial.)

During the Montreal conference, Hoffmann-La Roche conducted a press conference on DDC. The speakers were Thomas Merigan, M.D., principal investigator at the AIDS Clinical Trial Group at Stanford University, and Whaijen Soo, M.D., Ph.D., director of clinical virology at Roche. Few reporters came to this meeting, which was a mile away from the main conference. Our impression from the discussions at that press conference is that nobody expected the study would end before two years.

The important question is not whether to end studies early. It is whether the best way to prove a drug is to wait for deaths and OIs in those who do not receive it. This trial design makes studies inherently slow, whether they are ended early or not.

No one at the press conference raised the issue of whether a study design which will take more than two years to get results is an acceptable public health response to the epidemic. We are concerned that all the important AIDS antivirals are behind DDC in the pipeline. If they suffer the same delay as DDC, then we can almost guarantee that no major new AIDS antiviral will be generally available for at least two years.

Recruiting Problems Likely?

One of the problems with many AIDS clinical trials is that entry criteria are designed purely for scientific reasons, without thought as to whether there will be patients available to fit them. As a result, many studies take much longer than intended, or even fail altogether, because of recruiting difficulties.

The DDC study may have this problem. Volunteers must have less than 200 T-helper cells, and also have had pneumocystis in the last four months or have certain ARC symptoms. And yet they must have never taken AZT. Most people will have already tried AZT before they have severe symptoms and under 200 T-helper cells.

Some may have never taken AZT because they chose not to. But they would be unlikely to volunteer for this study—because 50 percent of the people enrolled, chosen at random, will go into a control group and receive AZT instead of DDC.

It seems that the only volunteers left would be those who never took

AZT because they could not afford it; in the study, the drug is free. But these people face another problem. The study also **requires** use of aerosol pentamidine, **but will not pay for it.** If persons could not obtain AZT in the past, how will they obtain aerosol pentamidine for the next two years into the future?

It would seem that these conditions, taken together, systematically exclude almost everybody from the trial. A few might get through, such as those whose first contact with the medical system is pneumocystis.

Notice that the whole problem with this study, including recruitment, stems from the decision to prove DDC by counting "clinical events" (deaths and OIs) in the control group. To get clinical events, the patients must be seriously ill—although never treated with AZT. But once on the study, for ethical reasons they must receive an antiviral and pneumocystis prophylaxis, reducing the clinical events and therefore requiring more volunteers (therefore a multicenter trial) and a two-year duration. All this to get enough deaths and OIs to allow the drugs to be compared.

An alternative would be randomized, double-blind trials designed to use patients' overall clinical condition as the outcome measure, not deaths and OIs. We suggest such a design below. The problem seems to be that academic researchers do not trust physicians' evaluations in outcome measures in their experiments—even within a double-blind trial—because such evaluations involve some subjective element. A body-count outcome sounds more scientific.

The Ideology and Public Relations of Clinical Trials

Having looked at the reality of the modern phase II clinical trial for AIDS antivirals, we will now look at the image. The image is important, because it is used to calm the public, justify the existing system, and impede calls for reform.

The DDC press packet from Hoffmann-La Roche provides a convenient look at this image. Any other public relations from a mainstream clinical trial would be similar, however, as government and other controls have imposed a research monoculture. Even the public front is uniform.

From a June 5 press release we learn that "Everyone collaborating on this project at Roche, the FDA and the National Institutes of Health is intensely aware of the urgency for developing safe and effective treatments for AIDS. Awareness of that urgency constantly compels us to work together as expeditiously as possible toward definitive results." We also learn that "Initial studies suggest that DDC may have an antiviral effect at the low doses that result in manageable toxicity. The studies now being planned are essential if we are to turn suggestions into medically useful conclusions."

An undated *Dideoxycytidine (DDC) Fact Sheet* includes a question and answer section on the availability of DDC. We quote it at length because it illustrates several aspects of the currently prevailing ideology of clinical trials.

"Q: When will DDC be available?

"A: That depends largely on the results of the new trials. When dealing with human life, the adverse effects profile and optimum dosage of a drug must be carefully studied no matter how urgent the need. As soon as the clinical data warrant, Roche will file a New Drug Application (NDA).

"Meanwhile, each of the new trials has entry criteria specific to its design, and some of the studies already have their full complement of volunteer patients. People who would like to participate in, or simply learn more about, the trials should call FDA (sic) at 800/874-2572 (800/TRIALS-A) or Roche (collect) at 201/235-2355.

"Q: Will Roche provide DDC on a compassionate plea basis?

"A: The urgent need for more effective weapons against HIV weighs heavily on everyone associated with this project at Roche, the FDA, and the NIH. However, at present, we are agreed that the clinical data now available are insufficient to justify distribution or use of DDC against AIDS outside of carefully controlled clinical trials. Only new data can change this situation. Consequently, we are working closely together to expedite the next round of therapeutic trials, from which the medically necessary data will flow.

"Q: When will Roche submit an NDA for DDC?

"A: Roche will submit an NDA as soon as the data from the pivotal studies allow. A special review board will continually evaluate data from all of the trials and make appropriate recommendations to FDA."

Some points to note about the world of AIDS treatment research according to press releases:

(1) Everyone involved feels urgency, and is working well with everyone else. (During the press conference, however, this reporter could find no shred of evidence of urgency.)

(2) More studies are, of course, essential. (300 people have already been given DDC in clinical trials,.)

(3) The phrase "no matter how urgent the need", in the context of justifying withholding a drug until more studies collect still more information about "the adverse effects profile and the optimum dosage", clearly illustrates the fact that no weighing of costs and benefits (of the extra studies and their associated delays) will be considered. Instead, persons with AIDS can simply get lost until the researchers are finished. In theory they might join the study, but in practice less than one percent of persons with AIDS or related conditions will be able to do so.

Incidentally, the dose has already been determined well enough to bet this entire phase II study on it, as only one dose will be used in this study.

(4) Unless they qualify for a trial, patients and their physicians have no role in the decision of whether or not to use a drug, until someone is ready to sell it to them. This decision is made for them, by agreement between government officials and potential vendors. For AIDS, the answer is almost always no. Other diseases have been treated more liberally.

(5) The public is not told that the reason the trial will take so long is that deaths and OIs must be accumulated. Instead, the public is told that the trial might not take two years but could end any time, because experts will watch over it and pull the plug as soon as medically possible, moving the drug to the next step in the approval pipeline. As we have seen, this study will almost certainly take more than two years.

(6) The "fact sheet" also said that the first comparison trial was expected to "begin" in July and last up to two years, "depending on results". Readers might assume that the maximum delay for this trial is therefore two years and one month. This assumption would be wrong.

The six months for recruiting subjects was an informal estimate mentioned by one of the researchers at the press conference. Past experience suggests that it is probably optimistic.

Note that a trial which "begins" in one month and lasts "up to" two years may take far longer than 25 months to be finished. This is because the trial "begins" with the recruitment of the first subject, but the two-year clock starts only with the recruitment of the last. In addition, multicenter trials often have recruitment quotas for different centers, meaning that the clock starts only when the slowest center is ready.

The difference recruitment can make is illustrated by a study of

Imuthiol (DTC). Over two years ago, on April 10, 1987, *AIDS Treatment News* reported that this six-month study was underway. Most centers recruited patients promptly and completed their phase of the study. But because of stragglers, this six-month study was still running two years later, and the data from those subjects who completed the trial long ago has not been released.

The point is that press releases about clinical trials are designed to provide a comforting picture of reality. Since clinical research is a forbidding area—complex, esoteric, and involving risk to human life—few in the media or elsewhere have looked behind the image. It is much easier to trust the experts.

Because of lack of understanding of what is really going on, people are repeatedly surprised at the lack of new drugs for AIDS. Those who do look will realize that the current system of clinical trials could not possibly meet the needs of the AIDS emergency, and is very unlikely to release even a single important new AIDS drug for years—even though the drugs are there. The drugs which will provide the important treatment advances of 1992 and 1993 are already available and quite well known—we named some of them above. But DDC will take over two years for the upcoming trial alone, and all the other important antivirals are behind it in the pipeline, so they will take longer still.

The central issue

The key reason no new antivirals are available is that clinical trials have waited for deaths and OIs, instead of looking directly at clinical benefit, which with some drugs at least seems to be dramatic. Conservative trial designers have used deaths and OIs because the numbers seem more "scientific" than clinical ratings, which depend in part on judgments of physicians, and may not be identical from one doctor to the next; by contrast, everyone can agree precisely on the number of deaths in the treatment and control groups. However, "softer" kinds of data such as average ratings by panels of experts have been handled successfully in many fields of science. When we are looking for dramatic effects, as with DDI or Compound Q, these methods have more than enough precision to do the job.

The AIDS community must continue to raise the issue of whether counting deaths and OIs is truly the only legitimate way to tell whether an AIDS antiviral is working. Using "surrogate markers", such as T-helper cell count or P24 antigen level, is one approach to faster study design.

But we fear that surrogate markers alone are not enough—that to try to use blood work as the sole basis for approving new drugs would lead to a long and unproductive argument. A middle ground, which we believe will be most productive, is to use surrogate markers **and also** direct measurements of clinical benefit in persons taking the drug, such as numerical ratings based on examinations by physicians. The variability in the course of the disease, sometimes cited in arguing against this approach, can be controlled for by double-blind designs, and by well-known statistical methods. The purpose here is to find the dramatically effective drugs, the home runs, and to test them quickly; slower study designs are acceptable when researchers are looking for minor or marginal differences.

The issue of surrogate markers is already receiving serious professional attention. But the related issue of the reluctance of trial designers to use direct measures of clinical benefit as proof of efficacy of AIDS antivirals, instead of insisting on deaths and OIs in the control group as the only important measure, has been largely overlooked. The AIDS community must insist that this issue be considered on it merits, as this key reform will allow the most important new AIDS antivirals to be tested many times faster than by the methods now in use.

Statement of Purpose

AIDS Treatment News reports on experimental and complementary treatments, especially those available now. It collects information from medical journals, and from interviews with scientists physicians, and other health practitioners, and persons with AIDS or ARC.

Long-term survivors have usually tried many different treatments, and found combinations which work for them. *AIDS Treatment News* does not recommend particular therapies, but seeks to increase the options available.

We also examine the ethical and public-policy issues around AIDS treatment research.

How to Subscribe to *AIDS Treatment News*

Send $100. per year for 26 issues ($150. for businesses and organizations), or $30. reduced rate for persons with AIDS or ARC who cannot afford the regular rate, to: ATN Publications, P.O. Box 411256, San Francisco, CA 94141. A six-month subscription (13 issues) is $55. ($80. for businesses or organizations), or $16. reduced rate. For subscription information and a sample issue, call (415) 255-0588.

For the complete set of over 70 back issues, send $75. ($18. for persons with AIDS or ARC) to the above address. The back issues include information on hypericin, dextran sulfate, foscarnet, passive immunotherapy, DTC (Imuthiol), naltrexone, DHEA, lentinan, propolis, coenzyme Q, monolaurin, egg lecithin lipids, fu zheng herbal therapy, DNCB, aerosol pentamidine, fluconazole, ganciclovir (DHPG) and other experimental or complementary treatments.

To protect your privacy, we mail first class without mentioning AIDS on the envelope, and we keep our subscriber list confidential.

Outside North America, add $20. per year for airmail postage, and $18. airmail for back issues. Outside U.S.A., send U.S. funds by International Postal Money Order, or by travelers checks, or by drafts or checks on U.S. banks.

A Parallel Track for Investigational AIDS Drugs: What It Is, Why It's Needed, What It Accomplishes

AIDS is a new disease. It is a disease which makes a person susceptible to a host of opportunistic infections. There is only one approved anti-AIDS drug, AZT, a drug which many people cannot tolerate. Several promising alternative anti-AIDS drugs are about to enter widespread clinical trials to determine their efficacy. These anti-AIDS drugs (antiretrovirals) have proven safe and shown some efficacy in the first phase of clinical trials, yet are far from full marketing approval by the Food & Drug Administration (FDA). In addition, many of the drugs that are used to treat AIDS-related opportunistic infections become "standard of care" long before they are fully approved by FDA. These facts make it imperative that drugs to fight AIDS or related infections are available to people with AIDS-related conditions who have no treatment alternatives long before those drugs gain the FDA's full marketing approval. People for whom the only alternative is death or the deterioration of the quality of life cannot ethically be asked to wait for a drug until all the bureaucratic niceties have been fulfilled.

Realizing the need for some sort of distribution of drugs for AIDS (and other serious or life-threatening diseases) before full marketing approval, FDA codified its Treatment IND program in June of 1987. This program was to supplement and perhaps replace the inadequate program of early drug release to individual patients under compassionate use. (Drug companies avoid compassionate use because they know they will have to pay for a drug and have no data toward final approval to show for the expense.) While of limited use, the Treatment IND program has not lived up to expectations. The reasons for this are many, and beyond the scope of this paper. The most important is that FDA has recently been interpreting its Treatment IND regulations narrowly, using the program as a bridge between the end of efficacy trials and marketing approval, not for the early release of a drug to people who need it.

ACT UP's detailed critique of Treatment IND has gained wide notoriety since its presentation to the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS. In addition, in its presentation to the Committee, ACT UP contended that clinical trials for post-AZT anti-retrovirals, because they would be measuring the new drugs against AZT, would "quarantine" people with AIDS who are AZT-intolerant, because these people would be ineligible for comparison trials. These people are the very people who need the new anti-retrovirals most desperately. The essential truth of the ACT UP critique has been accepted by Dr Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID), the federal entity responsible for most AIDS drug research. He has at times quoted this critique in his early public pronouncements on the need for a parallel track for AIDS drugs that are still investigational.

In short: there's a need for a parallel track for AIDS drugs

because people with serious or life-threatening conditions who have no treatment alternatives deserve access to a useful therapy before full FDA marketing approval. The two existing programs to deliver drugs to such people, Compassionate Use and Treatment IND, have failed.

Under a parallel track a specially-defined population could obtain an investigational AIDS drug outside a drug's primary clinical trial[s]. Such a drug would be available under a parallel track as soon as it had proven safe and shown some signs of effectiveness. Since the phase 1 trials of most AIDS antiretroviral drugs establish a drug's basic safety and look for early signs of efficacy, AIDS antiretroviral drugs should be available on a parallel track at the beginning of phase 2 efficacy trials to people with no treatment alternatives.

If, under a parallel track, the taking of a drug by a special population were carefully monitored and the data gathered, the parallel track would ideally provide adjunct data for a drug's approval. If the criteria for entering parallel track were not too narrowly drawn, parallel track could gather a wealth of information on how a drug worked in the real world (in all the community's more common drug-taking combinations). In order to gain any information from parallel track, it is not necessary that patients take no drugs other than the study drug. Such purity is what the primary trial is for. In the parallel track, it is only necessary that the investigator know what drugs a participant is taking, so the investigator can properly read the data obtained.

Today a parallel track for an antiretroviral would first of all provide drugs for the AZT-intolerant. It should, in addition, embrace everyone who can't enter the original trial because they need concurrent medication, or are too ill to fit trial criteria (even when that illness is not related to AZT toxicity), or because a trial is fully enrolled, or because the site for the trial is too far from home, or for any other valid reason. (Data on these diverse study populations could be kept separate, therefore readable, either by enrolling participants in separate tracks, or, more simply, by a retrospective stratification of a single parallel track's data.)

It's preferable that parallel track (as distinct from the primary clinical trial) not be conducted exclusively through the major medical centers. As said, a major advantage to having a parallel track is to gain knowledge of how a drug works in the real world. This would argue that the best sites for parallel track are in the settings of community-based research, in local clinics, in private physicians' offices--anywhere ~~where~~ good primary care is provided and patients trust their physicians.

A parallel track will help researchers. A trial with a parallel track will be cleaner than a trial without one. If the people who enroll in a trial are desperate to get a drug at any cost, they'll lie to get in and cheat while on protocol. If, however,

the drug is available outside the trial to those who absolutely need it, those people who enroll in a trial will more likely be those who can abide by the rigors of the trial.

The promise of cleaner data means that a parallel track will help regulators. In addition, regulators should be pleased that the data gained from the parallel track will be adjunct data, data that will give us some real-world information on a drug, very important in the world of AIDS where most people are on multiple drug regimens. (For example: even if the primary trial cannot admit people who are already on the antiviral acyclovir, the parallel track should, because it is important to know the interaction of the study drug and the commonly-used acyclovir before the study drug is approved.)

Drug companies could benefit from the parallel track. As things now stand, drug companies are fearful that any pre-marketing release of a drug will mean that trials for a drug will be impossible to conduct. This is not the case. With a parallel track, trials will in fact be easier to conduct, and the data collected "cleaner": there will (as said) be less pressure to enroll the most desperate trial participants, those least liable to comply with the rigors of the protocol. Companies would be wise to approve the widest definition of a parallel track which, unlike compassionate use, would give them data for every dollar they spend. Companies should realize that FDA will like a clean trial with lots of adjunct data. FDA's Dr Ellen Cooper herself has said that a drug with a parallel track could prove efficacy within a year. The promise of shorter efficacy trials is a major economic incentive for parallel track. Parallel track would also be a good market strategy. There is already in AZT an accepted anti-retroviral. Nothing could more quickly gain a new, effective, less toxic antiretroviral lots of word-of-mouth publicity than its acceptance by many, widely disseminated community members. FDA's permission for a drug to go on parallel track will be seen as a certification of a drug's safety and potential efficacy. Short-term economic loss due to parallel track (paying for drug) will be outweighed by long term gain (short trials, clean data, good community relations, free publicity) for any effective drug.

Unless the clinical trials establishment comes up with a workable plan to offer wide distribution of study drugs as soon in the clinical trials process as a drug has proven potential effectiveness, this establishment will have to contend with the outrage of the communities most affected by AIDS for each and every AIDS drug down the line. It is up to researchers, regulators and drug companies (and, if necessary, federal legislators) to seize the historic opportunity and make the community-generated definition of a parallel track for AIDS drugs a reality.

Treatment & Data Committee of ACT UP, July 2, 1989

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AIDS ACTION NEWS!

AIDS ACTION NOW! Statement on the Ribavirin Trial

A national trial of a proposed anti-HIV treatment, Ribavirin, has been announced in the media. Subjects are being enrolled in Toronto, and in more than a dozen other centres across the country. If you are thinking of participating in this trial there are two important things you should consider: first, the way the trial has been arranged; and second, some recent political developments around the issue of placebo-controlled trials.

The Ribavirin Trial

1. This is a placebo-controlled trial. This means that half of those participating will receive no active treatment for their HIV infection during the course of the trial which may last as long as three years. Subjects enrolled in the trial will not be allowed to take other promising treatments that might come along. Moreover, untreated HIV infection may result in damage to your immune system. Other experimental treatments are available.

2. This means that subjects who enroll in this trial should do so in the spirit of wanting to contribute to scientific research, not because they hope to get the treatment benefits of Ribavirin. There is an important distinction here between research and treatment. For this reason it is also unethical, for example, for researchers to offer any kind of treatments to you as an inducement to enroll in the trial (e.g., better monitoring of your health, or access to new, experimental treatments after the trial is over).

3. The choice of Ribavirin from the range of drugs awaiting testing, and the planning of this trial did not involve people representing HIV-positive individuals or their physicians. AAN! believes that these people should be included in the planning stages of a trial, and that drugs should be selected based on probable effectiveness rather than on commercial considerations. Ribavirin is being tested primarily because the firm that manufactures it wants it tested, not because it shows great promise as a treatment. The AIDS Resource Centre at ACT (AIDS Committee of Toronto, 464 Yonge St.) has more medical-scientific information on Ribavirin if you are interested in reading more on this issue.

Placebo-controlled Trials

AAN! agrees with the Medical Research Council of Canada that placebo-controlled trials are only ethical when treatment and research are completely divorced. The use of placebo-controlled trials to provide treatment to people who have HIV illness, consequently, is unethical. This means, first, that it is also unethical to deny a person treatment because he will not enroll in a placebo-controlled trial. And secondly, that placebo-controlled trials are only for those people who are simply interested in contributing to medical research.

At both the recent conference in London, Ontario and the Consensus Conference held in Scarborough, government officials, representatives from the pharmaceutical industry, medical researchers, and representatives of HIV-positive individuals and PLWAs agreed that the basic protocols for drug trials have to be redesigned because of the ethical problems of placebo-controlled trials. At both conferences, there was also a proposal to add a third arm to treatment trials where patients could get the treatment, if they needed it, without enrolling in the placebo-controlled branch of the trial. As far as can be determined, nothing has been done to implement these suggestions. AAN! believes that if the government, the industry, and the researchers are serious about this proposal that current and imminent treatment trials should be temporarily withdrawn and redesigned to include an open treatment arm.

Lastly, one argument being put forward for using a placebo-controlled trial with HIV-positive individuals is that you are not sick. There is an important difficulty with this argument. Just because a person does not have an opportunistic infection does not mean that he is not sick—especially when he is HIV-positive and his T4 count is below normal. There is a strong current of medical opinion in the United States that supports early intervention in cases of HIV infection. This means beginning the management of your HIV infection as early as possible, long before you come down with an opportunistic infection like PCP.

AIDS ACTION NOW, Toronto, Ontario, Canada
ACT UP, New York, New York, U.S.A.
jointly issue:

Le Manifeste de Montréal

The Declaration of the Universal Rights and Needs of People Living with HIV Disease

Preamble:

HIV disease (infection with HIV with or without symptoms) is a worldwide epidemic affecting every country. People are infected, sick and struggling to stay alive. Their voices must be heard and their special needs met. This declaration sets forth the responsibilities of all peoples, governments, international bodies, multinational corporations, and health care providers to ensure the rights of all people living with HIV disease.

Demands:

I. All governments and all international and national health organizations must treat HIV disease positively and aggressively as a chronic, manageable condition. Ensuring access and availability of treatment must be part of the social and moral obligations of governments to their citizens.

II. Governments must recognize that HIV disease is not highly infectious. Casual contact presents no threat of infection, and irrational fears of transmission must be fought.

III. An international code of rights must acknowledge and preserve the humanity of people with HIV disease. This code must include:

a) anti-discrimination legislation protecting the jobs, housing and access to services of people with HIV disease;

b) active involvement of the affected communities of people with HIV disease in decision-making that may affect them;

c) guaranteed access to approved and experimental drugs and treatments, and quality medical care;

d) the right to anonymous and absolutely confidential HIV antibody testing. Pre-and post-test counselling must be available;

e) the right to medically appropriate housing;

f) no restriction on the international movement and/or immigration of people with HIV disease;

g) full legal recognition of lesbian and gay relationships;

h) no mandatory testing under any circumstances;

i) no quarantine under any circumstances;

j) protection of the reproductive rights of women with HIV disease, including their right to freely choose the birth and spacing of their children and have the information and means to do so;

k) special attention to the unique problems and needs of intravenous drug users, including provision of substance-abuse treatment on demand;

l) special attention to the unique problems and needs of prisoners with HIV disease and guarantees that they receive the same standard of care and treatment as the general population;

m) the right to communication and all services concerning HIV disease in the language (written, signed or spoken) of his/her choice, through an interpreter if necessary;

n) the provision of reasonable accommodation, services and facilities for disable people;

o) catastrophic/immunity rights — the guaranteed right of people faced with a life-threatening illness to choose treatments they deem beneficial for themselves.

IV. A multi-national, international data bank to make available all medical information related to HIV disease must be created. This includes all data concerning drugs and treatments, especially basic bio-medical research and the initiation of any progress of clinical trials.

V. Placebo trials must be recognized as inherently unethical when they are the only means of access to particular treatments.

VI. Criteria for the approval of drugs and treatments should be standardized on an international basis so as to facilitate worldwide access to new drugs and treatments.

VII. International education programs outlining comprehensive sex information supportive of all sexual orientations in culturally sensitive ways and describing safer sex and needle use practices and other means of preventing HIV transmission must be made available.

VIII.The unequal social position of women affecting their access to information about HIV transmission must be recognized and also their rights to programs redressing this inequality, including respects for women's right to control their own bodies.

IX. Industrialized nations must establish an international development fund to assist poor and developing countries to meet their health care responsibilities including the provision of condoms, facilities for clean blood supply and adequate supplies of sterile needles.

X. It must be recognized that in most parts of the world, poverty is a critical co-factor in HIV disease. Therefore, conversion of military spending worldwide to medical health and basic social services is essential.

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June 4, 1989

AIDS Treatment Deficits: An ethnographic study of the management of the AIDS epidemic, the Ontario case

George W. Smith

The Ontario Institute for Studies in Education
and AIDS ACTION NOW!

Poster prensentation at the V International Conference on AIDS

Montreal, June 1989

AIDS Treatment News has long criticized the treatment-research establishment for having written off those now ill with AIDS or HIV, and for the remarkable lack of urgency about saving lives. Recently we have had more contact than previously with this establishment, and we have found the situation even worse than we had realized. So entrenched and near-universal is the commitment to unworkable viewpoints, approaches, and programs, that in meetings and conversations we must temporarily suspend our own view of what is happening, and operate from the prevailing mindset in order to allow any communication to take place.

John S. James
AIDS Treatment News
Issue Number 77
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Introduction

This study has been conducted for individuals in Ontario who are either HIV positive or people living with AIDS (PLWAs). A major problem for these individuals is getting access to the treatments they need within a setting of accelerated care. This difficulty has been particularly acute for PLWAs living in Ontario. From the standpoint of these people, the lack of adequate treatment is at best a problem of government "red tape", or systemic homophobia; at worst, it is a depressing enigma. One thing is certain: It is a problem that is created, not locally, but arises from somewhere beyond the scope of their everyday world, that comes to shape the kind of treatment they receive for their disease. The purpose of this research is to try to discover the social relations which shape and determine the quality of treatment they get. It is, in this respect, an investigation into the management of the AIDS pandemic in Ontario.

Method

The method of investigation begins from the actual situation of PLWAs in Toronto seeking treatment for HIV infection, and explores the social relations beyond the scope of their everyday world, which create problems of access to treatments. The dominant analytic is the notion of "social relations" used as a method of orienting to (i.e., investigating) the ways in which social phenomena are organized, concerted and elaborated within and through people's activities. This method is used to think and talk about the ways in which the organization of local settings are but a moment of an extended temporal sequence of human activity.

The notion of social relations does not operate referentially to stand in for an actual thing. Rather, it serves indexically as a methodological injunction, pointing to the social character of phenomena; to their temporal production in the practices and activities of people.

Within this context, a participant/observer methodology (AIDS activist as ethnographer) was used to investigate the social relations creating treatment deficits in the management of the AIDS pandemic in Ontario. Data was collected from meetings with physicians, researchers, representatives of the pharmaceutical industry, government officials, and politicians. Throughout the research, these individuals were treated as knowledgeable informants.

Because the managerial relations governing the response to the AIDS pandemic, goes forward on paper in documents, a number of texts were also incorporated as part of the data. These included: government legislation, annual reports of departments and ministries, internal government documents and memoranda that are publicly available, press releases and media reports, along with a variety of official publications. The management of the AIDS crisis, in this respect, constitutes a textually-mediated social organization. It was this form of social organization that we set about to study.

The analysis of the data required the bracketing of whatever political explanations were proffered of why PLWAs in Ontario could not get the treatments they needed within a setting of accelerated care. These kinds of explanation merely begged the question of how the delivery of treatment is actually organized. The scientific character of the research, consequently, meant eschewing the question of why treatments were not

available in favour of an interest in how the management of the pandemic was actually put together. This investigation resulted in the production of a sketch of an actual form of organization the properties of which are public, and therefore open to verification by others.

Results

This analysis of the management of the AIDS pandemic in Ontario began when AIDS ACTION NOW, realizing that HIV infection should be treated as a chronic but manageable illness, demanded that the federal government make available experimental treatments to people with HIV disease. When access to treatments was not forthcoming, AAN! began a political campaign to obtain them. The research presented here was conducted during the course of this campaign.

1. Discovering the social relations of public health

What became clear early on was that the initial response of government to the epidemic was in terms of public health programs such as epidemiological studies and public education on the transmission of HIV disease. A large portion of federal funding went to the Canadian Public Health Association, for example. There was no funding for access to treatments.

The examination of programs at both the federal and provincial level revealed that they were located within the bureaucracy of public health administration. The Federal Centre for AIDS, for example, operated as a directorate within the Health Protection Branch of Health and Welfare Canada. Similarly, municipal departments of health functioned as creatures of provincial public-health legislation. None of these organizations or agencies as it turned out had either the mandate or the organizational capacity to manage the delivery of treatments for people living with AIDS. This simply was not what they were set up to do.

A fundamental feature of public health relations is that they focus on the protection of "the public" and produce the sick or infected as "dangerous". Consequently, within the management of the AIDS pandemic, the public health relations coordinated by this conception operated to create policies that excluded communities with high rates of infection (e.g., gay male, and IV-drug communities) as beyond the pale of "the public". Besides these "us and them" relations, public health practices also came to be elaborated by homophobic and "moralist" procedures. For example, public health educational materials, targeting heterosexuals and espousing monogamy, failed to address the needs of the gay male population, or to provide information on sex-positive, safer sex. In these circumstances the organization of public health did nothing to provide access to treatment.

2. Discovering the social relations of palliative care

The examination of government funding around the AIDS crisis in Ontario also revealed the activities and organization coordinating the social relations of palliative care. These were concerted and organized by the conception of AIDS as a fatal disease. Compassion served as a major conceptual coordinator of these activities. The social relations of

palliative care were often initiated as voluntary and philanthropic activities of community-based AIDS organizations offering psycho-social support and palliative-hospice care. These social relations, however, did not organize access to treatment for the clients of these organizations.

These organizational forms, supported by the social service departments and agencies of government, were designed to handle clients who were "beyond" treatment--the traditional conception organizing the work of palliative care. Like the social relations of public health, consequently, these arrangements provided no management structure for the delivery of the new treatments required by PLWAs to continue to survive the epidemic.

3. Discovering the social relations of AIDS research

Early on in the struggle for treatment access, AAN! faced the problem of placebo-controlled clinical trials for new, experimental AIDS drugs. In Toronto AIDS researchers were preparing to mount a placebo-controlled trial of aerosolized pentamidine. It was in studying the ethical requirements of research on human subjects that the distinction between the social relations of research and those of treatment for AIDS became concrete.

The primary organization of a drug trial is to test a pharmaceutical product, not to treat patients. Drug trials are organized by protocols that have to be uniformly enforced, for example. Treatments are organized as regimens that can be tailored to meet the patient's needs. When people are entered into the social relations of research they become subjects. When they are entered into the social relations of treatment they become patients. The primary purpose of a drug trial is to test a pharmaceutical product, not to treat patients. This distinction between the organization of research and the organization of treatment is particularly easy to see in placebo controlled trials where only half the subjects get the treatment being tested. What distinguishes treatment from research, in this context, is that in the former the physician has a clear ethical responsibility to improve the health of his or her patient. No such obligation rests with a researcher.

The examination of the social relations of AIDS research in Ontario revealed that almost all AIDS research was organized within the social relations of public health. Epidemiological studies are an obvious instance. Also the trials of new, experimental treatments were managed by agencies within the federal Health Protection Branch of Health and Welfare Canada. For all intent and purposes, then, AIDS research in Ontario--apart from some small grants for basic research--was coordinated by the social relations of public health.

4. Discovering the Social Relations of Treatment

Physicians provided the only official access to treatments within the social relations managing the AIDS pandemic. These individuals, depending on how disposed they were to out maneuvering public health authorities, more or less provided treatment that would otherwise have been impossible to access. Even when the Health Protection Branch began to release drugs on compassionate ground through the Emergency Drug Release Program, physicians were basically left to their own devices in providing treatments to their patients. There was no backup management system to facilitate this work.

The lack of a treatment management system, moreover, meant that patients had to begin to manage their own access to new experimental treatments. AIDS ACTION NOW!, for example, issued two brochures, *Treatment AIDS* and *Testing AIDS*, and began publishing *TreatmentUpdate*, a monthly news sheet on the latest in treatments for AIDS. People in Toronto with HIV infection have also sought access to promising treatments from Chinese pharmacies and health food stores. People with HIV disease have also begun to import treatments from overseas.

Conclusions

In Ontario the management of the AIDS pandemic has been the responsibility of government at three levels: federal, provincial, and municipal. At all three levels, the management of the AIDS pandemic has basically been organized within the social relations of public health. The emphasis has been on epidemiology and on efforts to control the spread of infection. Even AIDS research, basically organized in Ontario as the testing of pharmaceutical products, has been coordinated as part of public health relations.

What the results of this study reveal is that the government in Ontario--federal, provincial, municipal--do not have the mandate or the infrastructure to manage access to treatments. Moreover, given the enormous complexity of administering AIDS treatments, and public health control over access to them, physicians--unless they are prepared to circumvent the rules--have little capacity to access treatments for their patients. The fact that government ~~have~~ has failed to provide a management structure to improve access to treatments constitutes a real deficit in the provision of treatment to people who have HIV infection or disease in Ontario.

I began this report with a quote from John S. James. His complaint can now be understood as the problem of someone interested in access to treatment having to deal with institutionalized mentalities structured by the social relations of public health, AIDS research, or palliative care. What it also makes evident is that the problem of AIDS treatments deficits goes beyond the boundaries of Ontario.