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Statement of Purpose:

AIDS Treatment News reports on experimental and standard treatments, especially those available now. We interview physicians, scientists, other health professionals, and persons with AIDS or HIV; we also collect information from meetings and conferences, medical journals, and computer databases. 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.

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Buenos Aires Conference on Treatment and Research: Web Reports Available

by John S. James

A new scientific conference created by the International AIDS Society (IAS) took place July 8-11 in Buenos Aires. Even before the first meeting, the 1st IAS Conference on Pathogenesis and Treatment had emerged as an important conference, with about 3,000 scientists attending and 748 scientific presentations (out of about 1,000 submitted); you can read abstracts of the presentations through the Web links below. This conference will occur every two years, during the odd numbered years when there is no international AIDS conference.

The IAS created the new meeting to focus mainly on basic and clinical science and the interaction between them -- including new treatments, vaccines, studies of pathogenesis, and how research can contribute to making good prevention, treatment and care available to the approximately 90% of persons with HIV who currently do not have access because they live in poor countries. The scheduled keynote and plenary speakers were:

David Ho: Learning Basic Science from Clinical Trials

Julio Montaner: Current Controversies in Antiretroviral Treatment

Stefano Vella: Fostering Access to HIV Treatment

Anthony Fauci: Immunopathogenesis of HIV Disease: Host Factors in Pathogenesis of HIV Disease: Implications for Therapeutic Strategies

Francoise Barre-Sinoussi: HIV: Twenty Years After the Discovery of the AIDS Epidemic

Margaret Johnston: Virologic and Immunologic Concepts in Vaccine Design

Brigitte Autran: Immune Reconstitution: Translating Immunologic Knowledge into Therapy

Eric Hunter: The Next Target in Therapy: Viral Entry

Ashley Haase: Virologic and Immunologic Concepts on HIV Transmission

David Cooper: Antiretroviral Therapy Toxicity: The Second Round, Beyond Lipodystrophy

John Mellors: Resistance: From Molecular Basis to Clinical Research

In addition, the U.S. National Institutes of Health organized a one-day meeting the day before the conference on "Formulating a Comprehensive HIV/AIDS Research Agenda in Resource-Poor Setting."

AIDS Treatment News did not attend this meeting. In future issues we may summarize some of the presentations. Meanwhile, extensive reports are available on the Web.

Web Access

The IAS has named Medscape as the official provider of online conference coverage for this meeting. The Medscape site for this conference can be reached through a link on the Medscape home page, <http://www.medscape.com>.

The official Conference site, which has background information on the conference, is: <http://www.aids2001ias.org>.

You can search and read the abstracts of the conference by reaching a search page through the IAS home page: <http://www.ias.se>. (At this time the search function is confusing. You do *not* need to log in with a user name and password in order to search or read these conference abstracts. We have not yet been able to do an 'and' search (it does an 'or' instead) -- but with fewer than a thousand abstracts, one can live with that. So far we have not found a link from the Buenos Aires conference page, only from the IAS home page -- nor have we found a link to instructions for more advanced searches. We hope these glitches will be corrected.)

Other Web sites with extensive coverage of this meeting include:

<http://www.thebody.com/confs/ias2001/ias2001.html>

<http://www.hivandhepatitis.com/2001conf/ias/main.html>

AIDS Research Today: 20 Views

by John S. James

Twenty commentaries on the current status of AIDS research, by "researchers, clinicians, and community members from varying disciplines, experience and backgrounds" appear in the Summer 2001 issue of *CRIA Update*, published by the Community Research Initiative on AIDS. These brief summaries offer diverse and informed views of what is happening today in AIDS research -- and what may happen over the next several years.

You can find these summaries at <http://www.criany.org>, or mail a request to: CRIA, 230 West 38th St., 7th floor, New York, NY 10018 (ask for the AIDS research issue).

Comment on Research

One idea largely missing from these commentaries (including our own) is the possibility of a treatment breakthrough -- and the question of how to organize research to facilitate a major, unexpected advance.

For example, one possible area for such a breakthrough could be a treatment to disrupt the process by which, in most patients, HIV eventually turns off the immune system's original ability to control it well (a possibility discussed in the *CRIA Update* by Sean R. Hosein of CATIE, the Canadian AIDS Treatment Information Exchange, on excessive levels of IL-10 in HIV disease, and the possibility of treatments to lower them). Such an immune-based treatment could work in both developed and developing countries (where it might not need to wait for antiretroviral combinations to become available).

Looking for a breakthrough -- a treatment good enough to be, in effect, approved by acclamation -- means we would not have to wait to solve the problem of immune-based surrogate markers, which will probably take years (and may be essentially unsolvable, if an effective immune-based treatment must first be proven by clinical endpoints before a surrogate marker can be

established). In the IL-10 example, a monoclonal antibody to reduce IL-10 might provide a proof of principle. If it clearly worked (for example, by greatly lowering viral load or reducing the need for antiretrovirals), then it would not be hard to organize a major effort to find simpler or even natural treatments to do so.

The big problem here would be the legal obstacles created by a clinical-trial system designed for big-company drug development. For example, the right kind of trial might be in one patient, looking for an efficacy result even from the first human volunteer, with no attempt to prove efficacy first in animals.

The existing rules serve two purposes -- to protect the public from unethical corporate experimentation, and to protect the same corporations from competition by making it almost impossible for anyone else to finance the whole drug-development process. Of course, if anyone could show truly convincing data, ways could be found to move fast. The problem is getting permission to do the earliest proof-of-principle human studies -- without entanglement in the gold-plated clinical trial system which already has its own mindset, investments, pipeline, and calendar in place, and naturally resists encroachment on its well-manicured turf.

So we continue to fight an epidemic with rules and procedures designed for routine, non-emergency research and development.

Africa: Interview with South African High Court Justice Edwin Cameron

by Bruce Mirken

Few moments in the history of the AIDS epidemic have been as pivotal as the speech South African High Court Justice Edwin Cameron gave one year ago at the International AIDS Conference in Durban, South Africa. In a talk that *Science* magazine writer Jon Cohen recently called "one of the most remarkable acts of activism I've seen in 12 years of covering AIDS," Cameron told of how he grew ill with AIDS in 1997, a dozen years after becoming HIV positive, and his near-miraculous return to health on combination therapy. "Amidst the poverty of Africa, I stand before you because I am able to purchase health and vigor," he told the hushed audience. "I am here because I can afford to pay for life itself."

He compared those who sit back and allow the world's poor to die for lack of access to HIV/AIDS treatment to those who passively allowed the evils of Nazi Germany and South African apartheid to unfold. The speech crystallized sentiment in favor of providing treatment in impoverished nations, leading to a variety of proposals, from drug company price cuts to U.N. Secretary General Kofi Annan's proposed international AIDS fund.

A year later Cameron is still acting as a conscience of a world that is too willing to let poor people die. *AIDS Treatment News* spoke to him during a visit to San Francisco June 19.

* * *

ATN: A year has passed since your Durban speech. How has the response been--in action, not just rhetoric?

CAMERON: There are two major changes. One is the change at the level of rhetoric, and one must never underestimate the importance of rhetoric. The Durban conference changed the discourse about drug access. Up to Durban it had been

accepted that we lived in a globalized world in which drug pricing was a given. Durban changed that irrevocably. Durban cast a moral judgment on drug companies' prices.

The rhetoric of drug company pricing was vital, and that rhetoric has changed. Supplanting it has been an international consensus that drug treatment ought to be made available in Africa--a consensus shared by almost everyone except the South African government, I might say. Our minister of health on the fifth of June reiterated that she's not providing drugs in the public sector.

The second change, of course, has been at the level of drug pricing, which has been dramatic. Some combination therapies have come down in price by 80 percent. Two nukes and one NNRTI are now available for \$100 a month--which is still out of reach of 90 percent of Africans but is no longer out of reach of 99 percent.

ATN: In recent months there has been some pulling back from that consensus, more voices saying, "Well, maybe we really can't do this, maybe prevention is more important," etc.

CAMERON: First of all, the treatment/prevention dichotomy is entirely false, because treatment offers the most persuasive way of making prevention work--at a physiological level, a psychological level, a social level. It's a false proposition to suggest that treatment is an area of concentration neglecting prevention.

With regard to your question about pulling back, I don't think one should underestimate the issues. There are real behavioral and institutional issues [in providing treatment]. Realistic approaches don't neglect those. The Harvard Declaration--despite very considerable conceptual flaws, and there are huge conceptual flaws in it--is a visionary breakthrough because it actually addresses in a hard-headed way the practicalities of treatment access.

You may be right that there's been a pulling back, but no one ever said that this was going to be easy. Every single argument that the do-nothing camp advances doesn't withstand scrutiny. In fact, the infrastructural initiatives that drug access will require will assist health care

delivery in regard to other diseases like malaria and tuberculosis. Certainly it's going to take some infrastructural initiatives in Africa, but once they're up and running they're going to alleviate other pressures.

ATN: What about the widely-quoted comments by USAID head Andrew Natsios arguing that drug treatment is impractical because most Africans "don't know what Western time is... and if you say one o'clock in the afternoon, they don't know what you are talking about"?

CAMERON: As a legitimization of inaction, it's appalling. It's almost as though it's a cheap target because he makes Africa sound like a Bongo-Bongoland, and that's an insult to Africans. The same rhetoric was used 40 years ago to justify not giving Africans the vote--the same rhetoric of incompetence and lack of sophistication. The same rhetoric was used not only by white colonialists but by black African dictators to justify denying African people fundamental rights.

The real point is that there are issues--behavioral issues of compliance, issues of infrastructure and delivery. What I want to focus on when someone says foolish things like that is how do we address the real issues, not how do we counter misdirected rhetoric.

ATN: What's your impression of the U.S. government's role?

CAMERON: I think the [Secretary of State Colin] Powell trip to Africa in May had a very productive resonance. It actively gave a sense of a Secretary of State who was concerned and was engaged. I know that he's been criticized as not following through on rhetoric, but the substantive message of the trip was the Secretary of State at least--a very highly, highly placed official in the administration--wants to be engaged. He appeared to be personally moved by the extent of AIDS. And what he said--and again, never underestimate the importance of rhetoric--he said that there is no bigger war, with thirty million lives at stake this is the biggest war on the globe at the moment

My sense is that the administration might be able to deliver more than people expect it to.

ATN: What about the U.N.?

CAMERON: Kofi Annan is the right person to head this. His global fund is a breakthrough. Again, like the Harvard statement, it creates a vision which requires implementation. But a year ago we even lacked the vision. Precedent steps to action are changing the rhetoric, creating the vision and making plans. And setting in place the preconditions, one of the preconditions being substantial reductions in pricing. We need more reductions, but at least there have been those changes since a year ago.

ATN: Is it worrisome to you that there hasn't exactly been a rush to donate billions of dollars to Kofi Annan's AIDS fund?

CAMERON: Yes, of course it worries me. I would like that pledge to be made unreservedly and immediately by the G-7 or G-8 now, today. Once the money is there, the real issues of implementation loom enormous--like democracy in Africa, like the coming of independence presented real challenges to us in how we crafted our constitutions, how we permitted freedom of association and freedom of expression.

We're going to have to start realistically. Botswana, a nation of 1.6 million, with the highest percentage prevalence of any nation in the world, over 30 percent, has undertaken to provide antiretroviral treatment in the public sector. It will offer a good model, because it's an ethnically homogeneous society with a high per capita national wealth and strong governmental commitment.

What I'm saying is the funding is essential and yes, it must be provided immediately--and then the work can begin.

ATN: How significant, in terms of day-to-day efforts to deal with AIDS in South Africa, has President Mbeki's interest in the denialists been?

CAMERON: [After a long pause and a half-suppressed chuckle]: It's a question I always welcome, especially when a tape recorder's running. Let me be diplomatic. The year during which President Mbeki openly gave sustenance to denialist beliefs was a year of horror--for AIDS

prevention, for AIDS implementation, for everything. It was a year of nightmare.

In October of last year the President accepted advice that he back off on the issue publicly. In April this year he gave an interview in which he said that he wouldn't have an HIV test because it would merely be giving substance to what he called "one particular paradigm." I believe that it's a grievous tragedy that we are still approaching the matter as though these are debatable paradigms.

The underlying anxiety that everyone has is whether the President's own ambivalence on the paradigm that HIV causes AIDS is leading the government's continued dithering on drug provision. The minister of health, on the fifth of June in Parliament, on the very anniversary of the first MMWR report on AIDS, reasserted her government's refusal to provide antiretroviral treatment. She then said--very significant--I wish to assure members of parliament that our position is "not ideological."

It remains to be seen whether the President's ideological position on whether HIV causes AIDS is in fact not at the root of the government's position. If it is, the words of Professor William Makgoba, who is the President of our Medical Research Council--he gave the James Hill Memorial Lecture to the National Institutes of Health in April this year--he said that if dissident views have impeded our treatment of AIDS, "history may say we have collaborated in the greatest genocide of our time." I cannot do more than quote those words.

ATN: Is that what's behind the South African government's reluctance on treatment, even on things like mother-to-child transmission? Or is something else involved?

CAMERON: Like the free provision of nevirapine by Boehringer-Ingelheim--an offer made a year ago to South Africa, still not accepted. No, I can't think of any other issues related to that. The minister of health says, "toxicity." The birth of 200 babies with HIV every day is a toxic issue that outclasses on any scale the doubts about the toxicity of nevirapine, which could reduce those 200 births every day in South Africa to 100.

ATN: American AIDS denialists say that there is no AIDS epidemic in Africa. They admit some people are ill and even dying, but say they're dying from endemic, poverty-related diseases that have plagued Africans for generations.

CAMERON: It's demonstrable, pernicious, willful, distorted untruthfulness. What is significant about our death rate in South Africa is not just that it's increased--the dissidents, particularly [Charles] Geshekter, explain this on the basis that the figures for South Africa before 1994 excluded the bantustans. But that's not the only way that our death rate figures have changed. The shape of the figures has changed. Women in mid-life are now dying more than men are dying. Women in their 20s and 30s are dying in a way that women nowhere else in the world are dying--before men.

This is an epidemic. It is an infectious agent. It is called HIV. It leads to a syndrome of immune dysfunction that leads to a terrible and lingering death. And most importantly it is avoidable by virologically specific treatments. And to deny that there is an epidemic in South Africa is *precisely* the same as denying that five and a half million Jews died in the Holocaust in the second world war. It is a denial of the same epic and the same pernicious, ideologically loaded proportions.

ATN: How important a role have activists from the U.S. and other developed countries played in efforts to bring HIV/AIDS treatment to Africa?

CAMERON: Central. Pivotal. Critical. The change in rhetoric and the reduction in drug prices were the direct consequence of principled, strategic intervention by angry activists. The AIDS epidemic has reshaped the way we think about ourselves as humans. I don't think it's too dramatic or pretentious to say that. 20 years ago we thought that we'd conquered disease, there was a medical model of human well-being that was certainly entrenched. AIDS has shaken that.

AIDS activists in America in the 1980s changed the nature of the doctor-patient relationship, the nature of the research community's relationship to the patient community. It changed the way that the gay and lesbian community related to the larger society. And activists are still leading the

debate. They are changing the way in which people permit themselves to see other people.

ATN: What can people in the U.S. or other places outside of Africa do now?

CAMERON: Three things, which all sound quite grandiose, but we've got to start somewhere: Pressure on the drug companies to permit generic production of patented medicines. Secondly, pressure on governments to make the funds available. The question with the funds is not whether it's affordable, the question is one of will. It really is. \$7-\$9 billion a year--which is for all Kofi Annan's associated costs, not just for AIDS--is not a great amount on any metric.

And thirdly, individual initiatives are also very important. This is something that is underestimated. There is an organization called AIDS Empowerment and Treatment International. AIDSETI has got 800 to 1,000 people on treatment this year who wouldn't otherwise have had treatment. It collects drugs, gets donations, makes treatment available with monitoring, with medical supervision, even in Africa.

What I'm saying is that there is something that everyone can do. Every organization ought to think of partnering with an organization in Africa. \$5,000 dollars equals the salary of one nurse for one year in South Africa. There are organizations currently that can use recyclable drugs.

We don't only have to be grandiose in what we think we can do. The problem also requires minute, person-to-person, organization-to-organization responses. If we look only at the grandiose we risk paralysis, but there's a great deal we can do at organizational and personal levels now.

ATN: Is there anything else you'd like to add?

CAMERON: I think what AIDS asks us to do is to give people on both sides of the First World/Third World divide a sense of empowerment about themselves. The people in the First World should realize that there is something they can do, not feel a sense of paralysis or helpless guilt. And the same in Africa, that this is a problem that we can confront.

Women's HIV Treatment Issues: Course for Medical Professionals, July 26-27

Johns Hopkins University will offer a 2-day update for primary care providers on HIV care for women, July 26 and 27. "This course is designed to offer support to the primary care provider in caring for HIV-positive women. Specific clinical problems, their evaluation and management, epidemiology and scope of HIV infection will be discussed. Participants can expect to become more familiar with health care issues of HIV-positive women and the management of clinical complications."

For more information, see:

http://www.hopkins-aids.edu/educational/events/womissues_2001/womissues_2001.html
(Note: Be sure to include the full Web address -- but do not include the carriage return shown here.)

HIV Resistance Meeting Web Reports

Each summer there is a small, invitation-only International Workshop on HIV Drug Resistance and Treatment Strategies; this year the 5th workshop in this series was held June 4-8, 2001 in Scottsdale, Arizona. Recently, a 9000-word detailed technical report of this meeting, written by leading HIV researcher Daniel R. Kuritzkes, M.D., was published on Medscape: <http://hiv.medscape.com>.

This report should be read by HIV-specialist physicians and other medical professionals; most patients will find it difficult, but may want to scan it to look for any information that might be relevant to their treatment.

Dr. Kuritzkes summarized the highlights "perhaps of most immediate relevance to day-to-day clinical practice":

- * Y318F is a newly recognized mutation associated with NNRTI resistance.
- * Treatment-naive patients with novel mutations

at 215 are at risk for rapid selection of resistance to zidovudine.

- * Data continue to confirm that stavudine and zidovudine are cross-resistant.

- * Presence of mutations at codons 82, 54, and 10 together with 4 additional PI resistance mutations is significantly associated with failure of lopinavir/ritonavir.

- * Ritonavir boosting of indinavir may partially overcome indinavir resistance.

- * Resistance mutations confer a loss of viral fitness relative to wild-type, but the clinical significance of this remains unclear.

- * The CCTG 575 study failed to show a benefit from phenotyping in guiding the selection of a salvage regimen, except in the subgroup of patients with virus resistant to more than 3 protease inhibitors at baseline.

- * The benefits and risks of treatment interruptions are still under investigation, but risks may include emergence of lamivudine resistance.

- * The majority of zidovudine- and abacavir-resistant viruses remain susceptible to tenofovir, although cross-resistance is observed in virus with multi-NRTI resistance.

- * New technologies to assess resistance to entry inhibitors such as T-20 and T-1249 are in development.

The abstracts and other reports from the meeting may be available through <http://www.intmedpress.com> (after a complicated registration procedure).

Other reports are can be found at:

<http://www.hivandhepatitis.com/2001conf/hivresis/main.html>
<http://www.natap.org/2001/5thresist/ndx5thresist.htm>