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Syphilis, HIV and AIDS: new approaches for the 21st century

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This communication, addressed to the international STD/HIV research community, follows up on my October 12, 1997 review of Bob Rolf's NEJM paper (archived on the Internet at http://www.radio.cbc.ca/programs/ideas/Aids/scimedaids.html).

I would like to share three more recent ideas about 1) where the HIV/AIDS paradigm is - or isn't - going, 2) the possible HIV/syphilis interaction, and 3) the possibility that some chronic active infectious diseases injure the immune system in a way that may be more amenable to therapy by allogeneic placental stem cell transplantation than a protracted and very costly anti-microbial approach.

Most HIV treaters are riding the wave of the success of Highly Active Anti-Retroviral Therapy (HAART), but a few sobering words are needed. Viral load does drop sharply after the initiation of therapy, but this is rarely reflected in long-term improvements in CD4 cells or quality of life. In trials comparing HAART to pre-HAART strategies (trials which are usually short, i.e. of 6 months duration), the CD4 cell count only goes up on average 100/mm^3, but at a very high price in terms of drug interactions and morbidity. Most "miracle recoveries" - the Lazarus effect - have sadly died. Viral load tends to climb back up, either due to non-compliance (usually owing to toxicity/interactions - just read the contra-indications) or inefficacy. CD4 usually sinks within a year, especially among patients who previously used nucleoside analogues before going on HAART.

As San Francisco researcher George Lemp and colleagues wrote of HAART in November 1997, "the treatment benefit is temporary and confers no long-term survival advantages" (Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology, November 1997, p. 182 - 189). Other researchers at the University of California at San Francisco, who have reported a failure rate of more than 50%, also say the cocktail "honeymoon" is over. In the course of my work, I see many men with HIV disease who are on HAART, and it's no picnic. HIV physician friends of mine use the words 'a lot of problems' to describe managing this therapy.

I would summarize HAART as follows: a marginally effective regime - better than older combinations for sure - that seems to be riding the back of the natural evolution of HIV epidemiology, which shows a strong trend away from AIDS incidence and death since 1992, long before the mass introduction of HAART. This trend is likely due to safer sex practices and therefore less exposure to co-factors or other strains of HIV. Lemp and colleagues note that "San Francisco would have experienced a significant decline in AIDS cases, due to the decrease in HIV [infections], even if combination [anti-HIV] therapy had not been developed." They added "changes in HIV sero-incidence must be factored in before attributing the decreases in AIDS incidence to the more effective combination antiretroviral treatment." Additionally, I would point out that HAART is completely unaffordable for most HIV cases worldwide.

In my respectful submission, the HIV=AIDS paradigm has been garnering the lion's share of STD research funds based on what may well be an unfounded assumption that the virus is a recent human pathogen, i.e. an HIV "Big Bang" occurring sometime shortly after World War II. As global HIV phylogeny is examined by systematists, and looking at the M-clades now identified, it becomes apparent that the virus is more like a thousand years old in close to its present form, except for the random mutations in the genes that express certain outer surface proteins, none of which have ever been correlated with disease. The Salk Institute's estimate of HIV's age was 900 years, whereas Paul

Ewald and colleagues, while not pinning down an exact date, have placed the age of the virus as vastly greater than the current AIDS crisis ("The AIDS Pandemic Is New, But is HIV New?", published in Systematic Biology, vol. 44(1), and available on line at http://www.utexas.edu/ftp/depts/systbiol/44_1/mindell/mindell.html). Indeed these authors point out that it is quite possible, looking at the well-established global HIVs, that humans may have infected the primates, rather than the other way around. One of Ewald's criticisms is that HIV systematists do not include a more "parsimonious pole approach" in their genetic analysis. There is little evidence for an African origin of HIV (other than our own Western medical prejudice).

In addition, although various experimental HIV vaccines have elicited strong anti-HIV immune responses in humans, there is no protection against AIDS itself. If the vaccinee takes AIDS risks, then there is breakthrough to AIDS despite immunization, as was the case with several gay male volunteers.

One could conclude from all this that HIV, in and of itself, is insufficient to cause AIDS, and therefore co-factors - be they other infectious diseases or other immunosuppressive/HIV-activating risks - are as necessary as HIV itself. Luc Montagnier has veered quite close to this position, but a consistently present co-factor continues to elude us all.

This brings me to my second point, which concerns our ability to exclude a role for chronic infection with *Treponema pallidum* in HIV activation and AIDS progression. Syphilis may play more than just a focal ulcerative role, i.e. allowing HIV amplification in activated cells. When left untreated, syphilis exerts a systemic and irreversible immunological effect, resulting in a loss of memory (E.W. Thomas, Syphilis: Its Course and Management, New York: MacMillan, 1949, p.10), a phenomenon not reversible by any amount of therapy, be it penicillin or older arsenicals (Reynolds, F., Oxford Medicine (1948), pp. 665-668).

This loss of memory is very probable in cases of long-standing infection - for example, the estimated half a million untreated syphilis cases among gay males in the early 1980s. As Konrad Wicher pointed out, "there is no natural immunity to syphilis and past infection offers no protection to the patient" (as stated on the New York State Department of Health Communicable Disease Fact Sheet, online at http://www.health.state.ny.us/nysdoh/consumer/syph.htm).

None of the pre-AIDS experiments ever consistently demonstrated protective immunity to *T. pallidum*, whether cellular or humoural in nature, in humans or animals. Authors who suggest that immunologic memory to *T. pallidum* seems non-existent - or at least very defective - include Fitzgerald, Magnuson, Beerman, Moore, Stokes, and Dattner/Thomas. Such memory failure is cytokine mediated; it is a tolerogenic and peripherally inhibitive mechanism, an active and brutal immunological process that we call latent syphilis (latent means "hidden" in Latin, as opposed to "inactive", a common misunderstanding). More than 80% of latent syphilitics had forever lost their cutaneous reaction to a diagnostic or therapeutic tuberculin, as reported for years by the University of Vienna Medical School. To the best of my knowledge, no other infectious disease has ever had such a global impact on the immune system, except perhaps late Chagas.

The follow-up question therefore is: what does re-exposure to virulent *T. pallida* do in such an unprotected host, i.e. the person with late (latent) syphilis? It's not early syphilis again - that's very clear from the literature. Only adequate treatment for early syphilis ensures reinfectability with early syphilis again. So what happens to the patient with latent syphilis, treated or not, who becomes re-exposed? Nothing - just because the VDRL is not anamnestic?

Both animal and human studies strongly suggest that silent, systemic reinfection with *T. pallidum* is the norm. Deliberate re-inoculation experiments - conducted in the pre-1950s period by investigators such

as Landsteiner, Chesney, Kemp, Arnold, Beerman, and Magnuson - usually demonstrated no Wassermann/VDRL/DTH memory in cases of re-exposure, despite a re-dissemination of the organisms. This lack of memory means to me that either *T. pallidum* is persisting despite penicillin, or it has injured the immune system as a result of delayed treatment. These experiments were designed to try and answer the question posed by Neisser: is there acquired immunity to syphilis, or is it (as he believed) an "infection immunity" disease? We simply don't know today.

After centuries of killing people, has *T. pallidum* now become a harmless pathogen? The re-inoculation experiments need to be repeated, using today's immunological tools, such as the recently available antibodies to rabbit CD4 cells, to see if re-exposure to *T. pallidum* induces AIDS in an affordable animal model. Since the rabbit is not the obligate host, there may be limitations to this approach, however. Most pathogens have narrow host ranges, as is claimed in the case of HIV.

The April 1998 Journal of Infectious Diseases paper suggesting mechanisms by which syphilis could enhance HIV activation or progression to AIDS is exciting, as we desperately need a better understanding of the molecular basis of *T. pallidum* infection. Modern tools such as the recently-sequenced genome, recombinant proteins and PCR were simply not available back in 1987, when our Toronto Hospital group first found unacceptable anomalies in syphilis serology in HIV patients, findings we presented at the WHO's Biology and Pathogenicity of Treponemes conference, held at the University of Birmingham, UK, in April 1989. We subsequently identified the mere existence of a history of syphilis as a predictor of more rapid progression to AIDS.

At that time we asked ourselves: how might we best measure the persistence of long-standing syphilis in an HIV population? Antibodies seemed the best way - or so the literature implied. From 1987 until 1994, owing to my association with the Toronto Hospital's Western Division HIV clinic and the Ontario Laboratory Services Branch, I was able to participate in research designed to try to estimate the incidence of syphilis in an HIV population of approximately 500 consecutive patients. We ran into various difficulties with the tests, as many patients had a history of syphilis but negative treponemal tests, while others had no history but reactive treponemal tests, and these latter patients may or may not have received adequate happenstance therapy. The stage of syphilis didn't predict who lost antibody. We never saw late syphilis - as we currently understand it, at least.

What raised the most concern was our growing recognition of the fact that reactive treponemal tests, sometimes at high titer, were reverting to negative, often over a period of a few weeks or months, and not as a result of treatment. After a careful literature review, and discussions with Anton Luger about the Oslo study and his final 1954 follow-up with Trygve Gjestland, I can only conclude that such a loss of treponemal antibody is unprecedented in the reporting of syphilis serology. This means we cannot at present exclude syphilis from HIV cases. The principles of syphilis serology, as I learned them, must be reconsidered.

Other centers also discovered this loss of antibody (Haas J.S., *et al.*, Journal of Infectious Diseases, vol. 162 (1990), p. 862-866; Evans, B. *et al.*, British Medical Journal, vol. 298 (Jan. 28, 1989) p. 215-18). Jennifer Haas' work was significant for us, not only because she had greater numbers of patients (being in the San Francisco AIDS epicenter), but also because she reported the mean CD4 cell count when the loss of response to *T. pallidum* occurred. The Toronto group went further and tried to see whether this loss was selective, i.e. independent of other titered antibody responses, and furthermore whether the presence of a history of syphilis, and/or a loss of serologic response to it, was associated with HIV infection and/or a more rapid progression to AIDS. Several dozen HIV out-patients were involved (mostly not AIDS cases), and either reverted to negative or had sustained selectively falling titers in

antibodies directed against *T. pallidum*. All these Toronto patients were VDRL negative, which was not the case in some U.S. centers studying the HIV/syphilis interaction.

It may be that an up-regulation of treponemal antigens (different strains?), in a way that was not recognized by earlier investigators, is responsible for this disappearance of treponemal antibody, a phenomenon exclusively associated with HIV infection today (Notenboom, R.H., MacFadden, D.K., Abstract #3044, 8th International Conference on AIDS/3rd STD World Congress in Amsterdam, 1992).

In Toronto, all the patients who lost treponemal antibody are now dead. Massive penicillin therapy sometimes slowed down the process, but could not stop it. An unusually severe Jarisch-Herxheimer reaction often occurred. At least six Toronto HIV patients I knew were treated experimentally with a number of regimes for presumed late latent syphilis and carefully followed serologically, some with weekly bleedings. Many others were likewise treated by the Clinic and other HIV physicians.

HIV clinician Richard Fralick and I then went to the 1993 ISSTDR in Helsinki and presented a further summary of immune suppression associated with positive treponemal serology, and the even greater immune suppression associated with outright loss of treponemal antibody in this HIV cohort (Sexually Transmitted Diseases, March-April 1994, vol. 21, no. 2 Supplement, Abstracts of Papers from the 10th International Meeting of the International Society for STD Research, p. S183, abstract 271). My colleagues at the Semmelweis University of Medicine in Budapest have also found a strong correlation between past syphilis and HIV infection/AIDS, findings we presented at the 1997 Seville ISSTDR and 1998 Goteborg IUSTI meetings. There are other retrospective reviews suggesting syphilis is between 20 to 50 times more prevalent than any other STD or risk behaviour in the history of HIV-infected multi-partner gay men compared to their HIV-uninfected controls (Veugelers, P.J. 8th International Conference on AIDS/3rd STD World Congress in Amsterdam, 1992, abstract #4486; Renzullo, P.O. *et al.*, American Journal of Public Health, October 1991, vol. 81, no. 10, pp. 1280-1284; Horváth, I. . *et al.*, Sexually Transmitted Diseases, March-April 1994, vol. 21, no. 2 Supplement, Abstracts of Papers from the 10th International Meeting of the International Society for STD Research, p. S199, abstract 321).

Many of our patients who still had treponemal antibody were IgM-positive in some bands, as was also seen in Daniel Musher's lab in Houston (Musher D.M., Hamill R.J., Baughn R.E., Annals of Internal Medicine, vol. 113 (1990), p. 872-881). As Professor Musher noted in that paper, "a substantial proportion of HIV-infected men may have unrecognized, latent, inadequately treated syphilis. These findings support more aggressive treatment of *T. pallidum* infection in this patient population."

This kind of warning strongly influenced our Toronto group's decision to continue pursuing this matter. Our center soon discovered that supra-maximal penicillin treatment failed to impact AIDS progression, however. Unfortunately, no effort was made to determine if anti-treponemal IgM could be made to disappear in these cases.

In Vienna, in the pre-AIDS era, when Professor Luger's lab found an IgM-positive patient, the patient got weeks of penicillin until the marker reverted to negative. These patients were almost exclusively VDRL-negative, but presumed relapsed or reinfected with syphilis because of the IgM detection. Today, amongst other newer techniques, this question of *T. pallidum* persistence needs a gene-based PCR applied to the lymph nodes in AIDS patients, or some other direct detection technique.

Dr. Robert Notenboom, formerly chief serologist at the Ontario Laboratory Services Branch for 17 years, has been funded by the American Society of Microbiology to chair a satellite symposium on syphilis diagnosis (centering mainly around new serologic tests) at the Chicago meeting in May 1999. Since leaving our Branch, he has been very busy working with colleagues in the United States and

Europe, publishing and developing better (i.e. recombinant, but very affordable) tests, so that syphilis won't have an opportunity to sneak by us again, we hope. We are concerned that non-treponemal tests are insensitive in a population at risk for re-exposure to *T. pallidum*, and this is a point I would be happy to discuss. The support for this assertion, especially from the pre-AIDS syphilis literature, is really quite solid.

This leads to the next logical question: is there syphilitic morbidity and mortality beyond the direct effects as measured by non-treponemal tests? - a very old question indeed. In my view, AIDS is a centuries-old syndrome, often associated with syphilis, historically presenting in adults as reactivation TB (consumption/TB phthisis), and in infants as PCP and CMV, because most children had not yet been exposed to TB, so the less dangerous but more ubiquitous infections usually reactivated first. Today's concerns about drug-resistant TB are by no means new: such problems were documented nearly half a century ago by many authors, such as the Pasteur Institute's Georges Canetti, using treatments almost identical to today's (The Tubercle Bacillus in the Pulmonary Lesion of Man. New York: Springer Publishing Company, Inc., 1955).

The syphilis/TB interaction was extensively discussed up until the 1950s. TB reactivation was a major killer in both the Oslo and Tuskegee natural history studies of syphilis. The excess mortality debate in both the syphilis research and actuarial fields was left unresolved with the introduction of penicillin. I think the well-documented excess mortality associated with a history of syphilis is quite enough to explain the susceptibility to HIV and opportunistic infections in homosexual males since 1980, due to the inordinate amount of latent syphilis in this population.

My third thought centers on the suggestion that AIDS might be treated by a placental stem cell infusion. Many journals have been full of excitement recently regarding the banking of HLA-typed placental blood. It is encouraging that, for some reasons that we don't yet understand, successful grafts and mixed chimerisms occur, and control or cure many blood-borne tumours, with both less rejection (despite milder conditioning) and less GVHD than ever before. There is even a graft vs. tumour effect in adult ALL when allogeneic rather than autologous cells are used. Many of these authors are suggesting that a graft vs. tumour effect from successful lympho-poetic replacement could even extend into clinical benefit in the management of solid tumours, i.e. using grafts from younger donors. I would be willing to speculate that prophylactic grafts (from expanded placental stem cells?) will become standard practice over the next few decades, in order to extend the natural lifespan as well. Would new myeloid and erythroid lineages in an aging body improve longevity or quality of life?

More immediately, what might be the implications for AIDS treatment? Back in 1993, an unsuccessful attempt was made to xenograft baboon T-cells, or their precursors, into a human who was progressing to AIDS, the thinking being that baboon T-cells would be resistant to HIV. But what if most HIV-negative, healthy humans are also capable of resisting HIV (Immunology Today, vol. 14, no. 3 (1993), pp. 107-111; vol. 17, no. 1 (1996), p. 21-24)? As the degree of required HLA compatibility becomes better understood from all the work in the globinopathies and lymphomas/leukaemias, stem cell infusions from a suitable donor - or maybe eventually from expanded pluripotent stem cells *in vitro* - may help to revert the chronic active HIV expression (seen in AIDS) back into the HIV-resistant (surface antigen/Western blot negative) immune profile discussed by the immunologists Clerici and Shearer in the papers cited above, similar to the profile of HBV antibody responses as immunity develops in most healthy persons.

What I am trying to suggest is that the persistent immune activation disease associated with the expression of HIV surface genes and protein production - with the resulting positive HIV screening and confirmatory tests - occurs not just due to infection with HIV, but because the immune system has

been genetically switched (or injured) in the stem and precursor populations, for lack of better words. CD4-bearing cells are apoptotic and rapidly turning over, and the signaling is in disarray.

Virulent treponemes could initiate this switching, but only in the untreated and re-exposed person (who is therefore not resistant), thereby allowing HIV to be chronically active and persistent in producing its surface (and putatively AIDS-inducing) proteins. Of course, *T. pallidum* may not persist in all - or even any - AIDS cases, since such an injury to immune system genetics could easily proceed independently of its triggers, a scenario for which there are many precedents in auto-immune diseases (although we still need to explain our results showing the selective and rapid disappearance of treponemal antibody in people who then uniformly go on to develop AIDS).

This signaling injury to the immune system is likely transmissible through blood or blood products by low molecular weight signaling cytokines, quite independently of actual pathogens - viral or bacterial. These molecules are heat-resistant and go through filters, and indeed a non-native product for haemophilia is associated with much slower AIDS progression (Seremetis, S. et al., Lancet (1993) vol. 342, p. 700-703). There are a dozen other references associating clotting factor impurities with AIDS progression in HIV-positive haemophiliacs.

The larger question is: as transplantation techniques and availability seem to be making large strides, would an affordable placental stem cell transplant possibly result in the patient becoming HIV-negative, at least in the conventional HIV screening tests? They would likely remain ab-positive to core antigens, and as well retain a strong cellular response to surface proteins, a response that has already been qualified and quantified by classical blastogenesis, anti-idiotype antibody and interleukin detections. This latter profile describes thousands of persons who remain persistently HIV-negative despite documented and often repeated exposure to strains of HIV identical to those found in persons with full-blown AIDS, i.e. in HIV-discordant couples. This resistant profile is also seen in other diseases.

At least 5 possible scenarios can be imagined as a consequence of a reconstituted immune system in an HIV-case, perhaps in some combination:

1) cure of HIV disease
2) HIV reinfection of the new lineages
3) re-awakened early (and treatable) syphilis
4) no change in immune status due to untreatable chronic syphilis
5) transplantation problems (graft rejection or GVHD).

Yes, lympho-poetic replacement is a dangerous thing to do, but AIDS is dangerous too. Are we just going to keep devising more and more expensive anti-HIV drugs and vaccines of borderline efficacy, or are we going to try something new?

What is unfortunate and hard to understand is that the very successful anti-HIV effect of HAART does not seem to endure. Neither does it translate into either HIV sero-reversion or clinically relevant and sustained CD4 increases, so that the therapy can be withdrawn. This is what we were all hoping for - three months at the most on HAART and then a rest. We can wipe out the HIV, it seems, but what if the defect is in the genes that make the CD4 molecule, or those that produce the up-regulation (or down-regulation, for that matter) and memory signaling? CD4-bearing cells would then shut down or become apoptotic and could not participate in this normal immunologic memory. Perhaps co-signaling - like the CD28 B7 ligand - is defective, as an example.

If AIDS is in the genes that make the functional G&C Type IV immune response, no amount of HAART - or any other exclusively anti-microbial strategy - will cure it, although we all sincerely wish it would. The cytokine thinking is certainly not new, but the idea that an anti-microbial approach for AIDS is too little and too late may indeed be a new way of thinking.

Such a re-assessment of the molecular basis for AIDS is surely a more logical approach and lets us better fit HIV infection into the history of infectious diseases in general. Edmund C. Tramont from Walter Reed stated in 1988 in the NEJM that HIV appears to have replaced *T. pallidum* as the "Great Masquerader" - words that may return to haunt him. History books teach us that declarations of new diseases and unprecedented pathogenic mechanisms should be made with great care.

HIV/AIDS research continues to unveil seemingly endless mysteries about the virus, and consume billions, money that I respectfully suggest would have been partly better spent trying to create a successful syphilis vaccine (which I personally think would slow AIDS faster than any HIV vaccine). We now have the entire *T. pallidum* genome generously posted on the World Wide Web and available to all researchers. The genome project should allow us to construct experimental PCRs more easily. We may even discover how to culture *T. pallidum.* and possibly identify critical targets for vaccine development. A number of recombinant *T. pallidum* proteins are presently available. The recent *B. burgdorferi* and *P. falciparum* vaccine successes suggest that poorly immunogenic treponemal proteins could be boosted adjuvantally, and a vaccine for syphilis developed. Work in this area is slowly progressing, but desperately needs funding.

I sincerely hope the points above could at least be open to discussion, and I look forward to any replies, whether public or private.

Respectfully,

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Special thanks to Colman Jones for critical review and assistance in the preparation of this paper. For more information, consult the Internet web site created to accompany Jones' 2-hour CBC Radio documentary, Déja Vu: AIDS in Historical Perspective, located at
http://www.radio.cbc.ca/programs/ideas/Aids/index.html

The above communication was mailed to several dozen individuals working in the fields of HIV/AIDS and syphilis, including:

Dr. Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases

Prof. Luc Montagnier, Director, World Federation for AIDS Research, Flushing, N.Y./Viral Oncology Department, Pasteur Institute, Paris

Dr. Alexandre Gromyko, Regional Adviser, HIV/AIDS and Sexually Transmitted Diseases, Department of Infectious Diseases, WHO Regional Office for Europe, Copenhagen

Prof. Noel Rose, Department of Molecular Microbiology and Immunology, School of Hygiene and Public Health, Johns Hopkins University

Prof. James N. Miller, Department of Microbiology and Immunology, UCLA School of Medicine

Prof. Georg Stingl, Chairman, Dept. of Dermatology, Division of Immunology, Allergy, and Infectious Diseases, University of Vienna Medical School

Dr. Bruno Schmidt, Laboratory Chief at the Ludwig Boltzmann Institute for Dermato-Venerological Sero-diagnosis, Vienna

Dr. István Horváth, Doctor of Science, Department Head for Syphilis Serology, National Institute of Dermato-Venereology, Budapest

Prof. Thomas C. Quinn, Infectious Diseases, School of Medicine, Johns Hopkins University

Prof. King K. Holmes, Director, University of Washington Center for AIDS and Sexually Transmitted Diseases

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Prof. Daniel M. Musher, Department of Microbiology and Immunology, Baylor College of Medicine, Houston, Texas

Prof. Justin Radolf, Associate Professor of Internal Medicine and Microbiology, University of Texas Southwestern Medical Center at Dallas

Prof. Bob Notenboom, Phoenix Bio-Tech Corp, Mississauga, Ontario (former chief serologist, Laboratory Services Branch, Ontario Ministry of Health)

Dr. Irv Salit, Director, Toronto Hospital HIV Clinic

Dr. Robert Holzman, Hospital Epidemiologist, Bellevue Hospital, New York

Prof. Peter Duesberg, Department of Biochemistry & Molecular Biology, University of California at Berkeley

Prof. Robert Root-Bernstein, College of Natural Science, Department of Physiology, Michigan State University

Dr. Val Turner, Department of Emergency Medicine, Royal Perth Hospital, Western Australia

Neville Hodgkinson, author ("AIDS: The Failure of Contemporary Science"), Oxford, U.K.

Huw Christie, editor, Continuum Magazine, London, U.K.

Meditel, television production firm, London, U.K.

Sean Hosein, treatment editor, Community AIDS Treatment Information Exchange (CATIE)

Gabriel Rotello, author ("Sexual Ecology: AIDS and The Destiny of Gay Men"), New York

Health Education AIDS Liaison (HEAL) Toronto

This communication was also posted to AIDS/STD/HIV-related discussion groups and mailing lists worldwide, including:

Spirochete Research Discussion Group

Newsgroups: sci.med.aids, misc.health.aids, bionet.molbio.hiv, gay-net.aids, hiv.aids.dialogue, hiv.aids.data, hiv.aids.hiv, hiv.alt-treatments, hiv.aidsweekly, hiv.informal.conversations, hiv.med, hiv.med.questions, sci.med.immunology, bionet.immunology, sci.bio.microbiology, bionet.microbiology, it.medicina.aids, fj.sci.medical, de.sci.medezin.misc, medlux.medsci.immunol, medlux.medsci.talk, medlux.fido.su.medic, francom.medical, tnn.medical, misc.health.alternative, alt.health.virus.cure.alternatives

Worldwide Healthcare Forums: AIDS

AIDSTalk.com (AIDS/HIV Treatment Issues conference)

AIDS Educational Global Information System (ÆGIS) Forum (AIDS-HIV conference)

CDC National Prevention Information Network's HIV/AIDS, STD and Connections bulletin boards

The Body: Community Center Treatment (and Alternatives)

AIDS Partnership of Michigan BBS

Health DEV Community-research forum

Links2Go discussion groups: AIDS, AIDS and HIV, Biology and Virology, Bone Marrow Transplants, Clinical Practice, European Molecular Biological Laboratories, Immunology, Infectious Diseases, Medical History, Medical Research, Microorganisms, Molecular Biology, Tuberculosis

Lycos message board: Syphilis, HIV and AIDS: New approaches

National Public Radio: Health & Science: Science Friday Discussions: AIDS Update

New York Times on the Web Forums: News Forums: In the News: The AIDS Epidemic

Your Health Daily (New York Times Syndicate) AIDS Discussion group

CNN Interactive Discussion: Fight Against AIDS Message Board

MSNBC AIDS BBS

Philadelphia Online: Talk Show: AIDS

C-Health Talk: AIDS & Sexual Health

Rethinking AIDS WebBoard

Does HIV Cause AIDS? Discussion Board

Stanford Center for Tuberculosis Research Message Board

Salon Table Talk: Science and Health: Syphilis, HIV and AIDS: new approaches

Delphi AIDS Forum Message Board

Doctor on Board BBS (requires prior registration): IN- AIDS/HIV Echo (conference 191)

Cafe Utne (requires prior registration) Science conf. #48 : Numerous Flaws of the Highly Deceptive "AIDS Science"

ProCAARE (Program for Collaboration Against AIDS and Related Epidemics)

South East Asia AIDS (SEA-AIDS)

HIV-DOCS (requires approval by list moderator)

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Reappraising AIDS

AIDS Rethink