

# The Common Factor

*The Voice of the Committee of Ten Thousand  
Advocate for Persons with HIV Disease*

Issue Six October 1993

## SAC Revisited Or, Throw Us a Compassionate Bone

by Corey Dubin

The last time we looked in on the NHF Special Assistance Campaign (SAC), they were groping for direction following industry's rejection of their humanitarian assistance proposal in July. To refresh your memory, NHF had proposed that the fractionation industry (manufacturers of blood concentrates) establish a \$1.5 billion humanitarian aid fund to be administered by a non-profit organization. Industry rejected that proposal as "unwarranted and unrealistic," and implied that it looked more like a damage award than a humanitarian effort by the companies.

The \$1.5 billion figure was computed by multiplying the number infected by tainted factor, 10,000 persons with hemophilia, by the amount to be paid per individual. NHF concluded that each person with hemophilia infected with HIV is worth \$150,000. However, only \$25,000 would be paid outright to each individual, while the other \$125,000 would go into a fund to be managed by the new non-profit agency.

Under this structure, those expenses and "needs" beyond the \$25,000 would have to be approved by the non-profit that is yet to be. There would be a list of "approved expenses." Anything not listed would have to be considered by the board of the non-profit. Missing from the proposal were the standards that would be applied to assess the expenses. What constitutes an acceptable need? Who makes the very loaded value judgments regarding the payments.

Meanwhile, as the National Hemophilia Foundation and the companies "talked," the legal clock continued to run regarding the statute of limitations for thousands in the community.

NHF has placed all their efforts behind the Special Assistance negotiation model while neglecting to pursue the many other available options. Not only have they failed in their responsibility to vigorously pursue all options, they have also discouraged and openly obstructed the pursuit of other legal avenues. Individuals and families were misinformed about the pros and cons of legal action against the industry. People were told that suing could cause

*(continued on page 4)*

## Deja Vu: Factor Products and Immunity

by Corey Dubin and Greg Haas

"There is no data to support that standard of care."

—Dr. Louis Aledort, Berlin 1993

"There is no proof to support immediate action."

—Dr. Joseph Bovey, Blood Products Advisory Cmte., 1983

For the second time in a decade, the hemophilia community hears that the crisis does not warrant immediate changes in treatment. In the late 1970s when hepatitis viruses were known to be in blood products, the manufacturers did not see sufficient reason to improve the viral inactivation process.

In the early 1980s, at the onset of the AIDS crisis, the manufacturers, federal regulators and medical community remained unconvinced and unwilling to act to ensure the safety of the nation's blood supply. Now we know how tragically wrong they were.

It is 1993, and two thousand persons with hemophilia have died from AIDS, and the deaths continue at a rate of 26 each month.

Since the introduction of factor concentrates in 1967, the relationship between factor purity and immune suppression has been an issue. Blood was first commercially fractionated at Hyland Laboratories, whose medical director, Dr. Ed Shanbrom, saw that technicians working with the fractionation process were contracting hepatitis. A warning that was generally ignored in the 1970s.

Numerous studies published between 1970 and 1978 show that the need for more effective purification was widely understood, yet the companies continued to underplay the danger and claimed there wasn't enough data to change the process. Another early warning not heeded by producers or government regulators.

The conclusion that the use of intermediate-purity (heat treated) products contribute to immune suppression and death in persons with hemophilia is amply supported by the facts. But, even now, intermediate-purity is the accepted "standard of care." Some physicians will not prescribe the high-purity products and some state programs will not pay for it.

It is incumbent on all advocates and care providers for persons with hemophilia to demand that high-purity factor concentrates become the standard of care.

At the AIDS Berlin Conference, the hemophilia clinician and researcher, Dr. Louis Aledort stated that current knowledge does not warrant changing the current standard of care. According to Aledort, not enough data has been collected about how impurities in factor cause immune suppression (drops in CD4 counts).

Furthermore, Aledort chastised the people in the hemophilia community who are calling for a higher standard of care. He said

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*inside:*

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BODYBUILDING & HEMOPHILIA?  
WHY THEY CALL 'EM CD4s  
COMPENSATION UPDATES

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## COTTabus

The Berlin Conference was the fourth consecutive international AIDS conference attended by representatives from the Committee of Ten Thousand. As with all such conferences, Berlin was a tremendous opportunity to indulge in (be overwhelmed by?) the tremendous breadth of AIDS-related research being done around the world and to share experiences with members of so many diverse global communities.

Coverage of the scientific information presented at the conference has been extensive in AIDS newsletters and journals, especially on the issues concerning AZT and other nucleoside analogues.

This issue of *The Common Factor* contains a reflective essay about the fallout from the Concorde trial, but we leave the in-depth analysis to those other fine publications (which are listed on our Resource Page). In this issue, we report on new developments in understanding how HIV and the immune system interact, with special attention to some studies that involved persons with hemophilia. Our Berlin coverage will continue in the next issue of *The Common Factor*. Also available from the COTT office is a footnoted article summarizing the research presented in Berlin that was done in (and on) members of the hemophilia community. Call if you'd like a copy.

COTT continues to work for justice and compensation for persons infected with HIV through factor concentrates and for their families. The recent \$4.7 billion settlement of the class-action suit against Dow Chemical for breast implants shows that it is not necessary to cuddle up to industry to achieve victory. Inside we discuss some of the issues surrounding litigation for our community.

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## Leo Murphy: Aug. 2, 1957-Aug.8 1993

### Reflections on Leo

On the morning of Sunday, August 8, 1993, my friend, brother, co-worker, and fellow fighter Leo Murphy passed into the spirit world. It was at the beginning of the new day (12-1 am) that Leo headed down the hallway and through the door. It seems so appropriate that Leo headed out under the sky of the new day.

During the last year Leo had been organizing for and articulating a new day in the hemophilia community. A day with dignity, self-respect, and control of our destiny. Leo stood for No More Business As Usual, working for a new future that fundamentally changes the business of blood as well as the power of the pharmaceuticals and the medical community.

COTT West became a strong and influential force within the California hemophilia community as well as the larger AIDS community—in part, due to Leo's tireless commitment to justice for people with hemophilia and HIV.

For Leo and me, COTT West was a labor of necessity, but it also rapidly became a labor of love. One of empowerment as well as pain; controlled rage blended simultaneously with lucid planning and implementation. A community devastated, yet in motion, struggling, fighting, and accomplishing things previously not even considered.

The loss of Leo has been personally and organizationally staggering and at times debilitating. Days before he passed out of this world, Leo looked at me and said, "I know you will continue the work; the struggle is all-important."

Leo believed our drastic and urgent situation called for principled leadership and principled action. Leo often said that the lack of principles and the corrupted national leadership in the hemophilia community is part of the reason we find ourselves experiencing this hell.

We bid farewell to Leo Murphy with the understanding that we are as committed as ever to attaining our goals and objectives, and that we must persevere so all of this death will not be in vain.

by Corey Dubin

### Autumn Recollections

by Tom Fahey

*"The blinded years, the binded years/ The desperate and divided years/ These should not be forgotten years."—Midnight Oil*

This will not be a forgotten year. The past six months have brought further reminders of the devastation being wrought on the hemophilia community by HIV. The epidemic progresses, and for the first time,



Leo Murphy on left

I've experienced the loss of several friends in a fairly short frame of time. Struggling to find some light in the darkness, I've chosen to offer reflections on each of their lives.

David Bauriedl was what is known as a "character"—just no two ways about it. He was constantly scheming for ways to defeat HIV, many of these plans seeming to hinge on nothing more than his own idiosyncratic hopes. He was proud of his 22 years of working for the same company, and even prouder of working three years straight without a sick day, "with no T-cells." He loved his horses at Saratoga. He took both hemophilia and HIV as opportunities to challenge himself.

Bill Perry lived most of his life telling nobody outside of his family that he had hemophilia, and certainly not HIV. To me, it was a great irony that the story of his life with hemophilia and death from AIDS appeared on the front page of his home-town newspaper (with his family's permission) the week he died. As his health failed, Bill took a risk and disclosed his condition to his

co-workers. They responded with unqualified support, healing many of Bill's old wounds. To make such a profound change at the end of life takes tremendous courage and strength.

Paul Tramantozzi and I would talk about how it was a shame that we hadn't met earlier. He certainly would have made a great activist. He knew Washington, having worked there as a policy writer. He was a man of letters, a voracious reader. He possessed a keen intelligence, sardonic wit, and tremendous strength of will. On a respirator, he set his goal to get home. He lived for two more months at home, letting go while watching the Red Sox. Those bastards will sap the strength from anyone.

Leo Murphy served COTT with honorable contentiousness over the past year as a board member and co-founder of COTT West. For a long time I only knew him as Matt's brother. He was a perfect big brother, larger than life. He went west to Hollywood and built a career in the film industry. He lived his dreams. Leo was Cuban cigars in the Atlanta Hyatt lobby, Amsterdam coffeehouses, and Harley-Davidson. Three of his former girlfriends (for want of a better term) came from California to eulogize him at his memorial service. What a guy!!!

As I was composing this article, it struck me how strongly "individual" these men were. Each carved a persona for himself and found his own niche in the world. They had self-created lives. I think it's true of living with hemophilia and other disabilities that certain life decisions must be made more consciously and carefully than if one is less challenged. The result is a work of art, not without flaws, but nevertheless a thoughtful rendition of the human condition.

*Remember: These shall not be forgotten years.*

COTT has struggled with how to best remember those who have died of AIDS in our community. We invite our readers to submit short memorials to celebrate the lives of those they've known and loved. Each issue, *The Common Factor* will devote space to publishing these remembrances.



## legal briefs

(continued from page one)

long-term harm to the hemophilia community, because the companies might retaliate by terminating their production of factor.

The continued failure of NHF to respond actively is not only a failure of individuals in leadership positions, but also an institutional failure based in the real nature of the organization. In reality, NHF is a trade association dressed up as an advocacy and consumer organization.

The whole approach is, in part, based on the relationship between the doctors (NHF's Medical and Scientific Advisory Committee) and the manufacturers. Conflict of interest played a central role in how the AIDS crisis played out. Key NHF medical advisors were receiving substantial grants from the fractionators during the critical early stages of the crisis. Given this, it is not too difficult to understand NHF's response to AIDS. It also provides clarity about the Special Assistance Campaign.

As a single option strategy, "Special Assistance" does not begin to address many of the legal, medical and family needs facing the community. The concept of Special Assistance is fundamentally flawed. Are economic interests and defense of the status quo driving the architects of Special Assistance?

Some points in history are worth noting. By January 1983 enough was known by the pharmaceuticals, the federal government (FDA, CDC, NIH), the blood banking industry, and the leadership of NHF to warrant

immediate action. None was taken; warnings were not timely and thousands of preventable infections occurred. The documentary evidence supporting this conclusion is available and voluminous.

Let us not forget the January 6, 1983 internal memo from Dr. Don Francis to his boss at the CDC, Dr. Jeff Koplan. In that letter, Francis warned of "post-factor VIII receipt of AIDS," lamenting that "one-third to one-half of [persons with hemophilia] might already be exposed," but added that, "We should do our utmost to prevent further exposure, and recommendations for plasma products should be made."

Individuals and families were, and are, forever impacted by what was a substantially preventable medical nightmare. Choices made in the late 1970s and early 1980s were based on economic interests rather than safety. The lives of a whole community were somehow declared expendable. That is what happened.

Special Assistance is conceptually and practically a reactive strategy designed ultimately to defend the status quo. The power of the pharmaceuticals, the medical community and the hemophilia establishment is the bottom line here. NHF's relationship to industry, then and now, illuminates the *why* of their response to AIDS.

As *The Common Factor* goes to press, industry has requested a four hour meeting on September 29 with NHF and COTT. At that meeting, executives from the four factor

## Legal Update

On the legal front, COTT continues to consider various options regarding litigation against the fractionators. We are also still looking at class-action to attain just compensation for those infected by factor.

The statute of limitations continues to be a barrier, but many lawyers believe it can be overcome by redefining the injury that was inflicted. Whether or not it is viewed as a single injury (the time of seroconversion) or as ongoing and repeated harm.

Our next issue will feature an extended piece on the class action option as well as answering some questions regarding the statute of limitations and other legal questions.

manufacturers (Armour, Baxter/Hyland, Alpha, Miles/Cutter) will present a financial aid package that was termed "substantial" by industry's representative.

The redress of this injustice cannot be dependent on the "humanitarian" inklings of the very companies that distributed and promoted tainted factor products.

The community is prepared to pursue all available options, including direct negotiations with industry. However, any process or action must be undertaken in the name of justice for persons with hemophilia and their families. The issue is not one of asking for compassionate or humanitarian aid, it is about justice—economic and social.

## Class-Action Suit Pays Off For Women with Breast Implants

On September 9, 1993, lawyers representing the manufacturers of silicone breast implants proposed creating a \$4.75 billion fund for women who have had breast implants. Women who have contracted any of eight diseases will be eligible for between \$200,000 and \$2 million, while women with implants who have not been diagnosed with any of the conditions could collect funds to have the implants removed and to receive compensation for mental anguish.

A lawyer representing the women said, "I think there is a very good probability that it will [be accepted]. It's a marvelous settlement for women."

The pharmaceutical companies involved

are Dow Corning, Baxter Healthcare (yes, *that* Baxter), and Bristol-Myers.

The proposal came out of the ten months of bitter negotiations held while a class-action suit had been filed. Thousands of women joined the class-action against the companies for harm done by the implants.

Previously, many women had filed and won individual lawsuits against the companies. A spokeswoman for Baxter said that they wanted to get the problem behind them. "We want to move this thing forward in a way that would resolve the issue for the women and for us," she said.

The manufacturers continue to insist that the implants are safe. A Bristol-Myers

statement said, "The company denies all liability and has entered into these discussions to avoid [long-lasting] litigation."

The proposed settlement includes some special legal considerations. For example, the statute of limitations on the ability of women to file claims would be waived, so that a woman could claim injuries at any time over a thirty year period. Also, any woman that is not satisfied with the settlement would be able to turn it down and sue separately for compensation and damages.

The \$4.75 billion fund would be composed of payments from the manufacturers, insurance companies, doctors and other health care providers.



## cott actions

### Potentially Historic Meeting in Madison

The unique nature of the AIDS crisis brought prominent researchers, government officials, and community activists together in a small meeting in Madison, Wisconsin in July. The meeting was organized by Project Inform and the Harvard AIDS Institute and aimed to help coordinate the future directions of AIDS research.

The participants unanimously agreed that "It is possible to develop new therapies, within a reasonable time, that are capable of providing long-term survival without clinical disease for persons infected with HIV." This is a beacon of hope in a world clouded by recent disappointments with antiretrovirals.

The meeting was chaired by Dr. June Osborne and attendees included Kristine Gebbie, the new White House AIDS Coordinator; Dr. David Kessler, Commissioner of the FDA; Dr. Anthony Fauci, Director of NIAID; Dr. Robert Gallo; Dr. Sam Broder; Dr. Robert Schooley, a representative of the new pharmaceutical consortium Intercompany Collaboration for AIDS Drug Development; and community activists from the Treatment Action Group (TAG), ACT UP New York, the National Minority AIDS Council, the Committee of Ten Thousand and others.

Dr. David Pauza of the University of Wisconsin explained the necessity of this high-level meeting: "AIDS is a rapidly moving epidemic that is constantly evolving new clinical challenges, and it will impact at catastrophic levels on our personal, social, and economic structures. The number of AIDS cases creates a reservoir for evolving infectious agents under conditions that have not previously been encountered. Furthermore, continued AIDS research benefits all biomedical research, because it continues to create insights not only into this very important area, but into other areas as well."

While no earthshaking decisions were made at the meeting, a new determination emerged to fill the gaps in AIDS research. The participants had different opinions on the best ways to coordinate research, but all agreed that better communication and more information sharing are necessary.

#### Nine consensus points were reached:

1. Insufficient resources inhibit the pace of both basic biomedical and AIDS-related research. More resources will accelerate the pace of progress.

2. Gaps or discontinuities in programs of research and in implementation of clinically relevant findings must be identified.

3. Targeted special programs should be considered for emerging, gap-filling, or risky innovative research areas. Mechanisms of prioritization are possible and will be needed.

4. Communication pathways and coordination among public and private investigators must be improved (e.g. develop high quality repositories for clinical samples).

5. The urgent challenge of AIDS highlights the problem of constituting complex drug trials using multiple proprietary compounds from distinct public and private sources. A rational and comprehensive strategy should be implemented to overcome barriers at all levels that mitigate against these novel therapeutic trials.

6. The government should evaluate and institute incentives to attract the pharmaceutical industry to participate in these efforts.

7. There is a need for further development of creative thinking within the AIDS research community. This should include an assessment of different management styles and structures, and an emphasis on the training of new investigators.

8. AIDS research programs must be created and expanded by infusion of money and talent from outside the NIH.

9. The president, his administration, and Congress must take a leadership role in educating the American public and world community on why these initiatives are important and urgent.

The same group will reconvene in November to further develop these points.

A lengthy transcript of the press conference that followed the meeting was printed in issue #180 of *AIDS Treatment News*.

### The Hidden Epidemic Conference

by Tim Haas

The Rural AIDS Network hosted its third conference for HIV/AIDS prevention and care in western rural areas last June in Kansas City. The conference addressed the much-ignored problem of getting services and education in less-populated areas. Much of the conference was centered on the building and maintenance of community-based organizations (CBOs). There is little funding but great need in rural areas. It was concluded that the development of regional programs might increase the potential for grant moneys.

Ideas were tossed around about how to deal with state medicaid programs and the federal social security programs. As CBOs communicate more and more, they have become very good at applying for these benefits. You should consult with a case manager before attempting to fill out those ridiculous forms.

In terms of the dissemination of information, there was much discussion of the use of computer bulletin boards. But it was mostly being considered as an opportunity for caregivers rather than PWAs.

The hemophilia community had few representatives at the conference, although it was good to see a couple folks from HTCS and one from NHF. In order to provide for the needs of our diverse and scattered population, we really need to become more involved in rural-centered programs.

For information about the Rural AIDS Network, call (505) 986-8337 or write: 1915 Rosina, Santa Fe, NM 87501.

### Flu Vaccine Time

It is generally recommended that everyone who is HIV positive receive an annual influenza vaccine. The vaccine has been distributed across the country and is ready for your arm. Flu vaccines should be taken before the onset of flu season, as it takes about two weeks for immunity to develop.



## cott actions

### Kansas City: Third National MANN Training Workshop

by Eric Howell

I had great expectations for the MANN conference to be a time of camaraderie, fellowship and discussion. Almost eighty men with hemophilia attended, as well as NHF support staff. The Embassy Suites KCI was a wonderful hotel and the cuisine most excellent. Too bad the meeting wasn't as splendid.

As a first-time attendee of the MANN "Training," I had never before realized that the CDC pays for MANN to promote "zero transmission" to our hemophilia population. While several coordinators explained to me that the role of MANN could be whatever we made it, the primary role of MANN is stopping sexual transmission of HIV. Not that I disapprove of such education, as I am an AIDS activist and educator, but I was under the impression that MANN was the acronym for "Men's Advocacy Network of NHF." My primary role as a MANN coordinator is, therefore, to disseminate sexual education materials rather than organize an advocacy network, a lobbying group, or even a support system for my hemophilia community. The CDC, through MANN, is deciding what I can tell my community. It may be their money, but it's our lives.

The workshop did provide us with a great deal of educational materials and several comprehensive presentations on treatments, clinical trials, gene therapy, and alternative therapy fraud. We were taught how to lead a MANN meeting through role-playing as we led discussions on safe sex, HIV, drug treatments, and hemophilia issues. Much of this training I found helpful, but also disconcerting as I realized we (MANN) really are not acting as true hemophilia advocates.

MANN's membership considers advocacy to be the role of the leadership of the MANN. I witnessed this hierarchy in action in Atlanta '92, but did not really understand then that MANN was designed as an oligarchy rather than a democracy. Only about ten men with hemophilia really have any major role in the direction MANN takes. The majority of MANN coordinators do not seem to realize, or they evidently trust, their leadership's decisions. After I came home

from Kansas City I realized MANN is merely a micro-NHF. I think Dana Kuhn, one of MANN's founders, probably resigned because of the duplicitous characters controlling MANN and their unwillingness to openly criticize NHF—an organization which doesn't represent me or many others with hemophilia.

I was disturbed by the complacency and cowardice I observed during the Special Assistance Campaign (SAC) Town Meeting. I never in my life expected to see men with hemophilia and HIV bow down to the leadership of MANN or NHF. It was almost unbelievable considering that the 45 minute discussion, involving dozens of men with hemophilia, had been *against* the SAC proposal. But as the assembled masses grew tired, one lackey asked for a vote of confidence for the SAC process—astoundingly, the overwhelming majority acquiesced to the pressure and voted in favor of the motion.

Under the SAC proposal, most of the money would only be granted "cafeteria-style." To get some of those funds we would have to apply, demonstrate need, and surrender any legal claim against the manufacturers. The SAC proposal would release the pharmaceuticals from liability. Originally, SAC had said that liability was not even on

the table. Now SAC has put everything on the table, and industry has laughed at them.

I also could not understand why MANN guys publicly gave the SAC chair, Don Colburn, a big congratulatory "thank you" for all of his wonderful efforts on "our" behalf, yet behind closed doors were complaining about him, discussing whether he should be involved due to his business ties—he *owns* a homecare company—and even whether he should be voted out.

I would have been extremely confused and disheartened by this meeting had I not already had a strong understanding of hemophilia, HIV, industry, medicine, and the politics intertwined in our community. For too many years, NHF had been the only national hemophilia organization (up until a year or so ago), and has traditionally kept us in the dark as to its inner-workings. Most of our population will never truly know what happened to us during the early 1980s.

With their Special Assistance Campaign, NHF and MANN appear to be asking the pharmaceuticals and government for mercy, but I think most of us would prefer justice and compensation. After attending the MANN conference I got the feeling that if NHF and MANN are our chief negotiators, we'll never see either.

### New COTT Board Members

Jan Hamilton is from Lafayette, Louisiana and is a member of Hemophilia of Acadiana, an independent hemophilia organization since its inception in 1990. She has been active as an advocate for persons with hemophilia and their families for more than thirty years. More recently, she was selected as Coordinator for The Hemophilia Federation. Jan served for seven years on the NHF Board of Directors in several capacities, including Regional Director, Secretary, Public Relations Chairperson, and Chapter Development Person.

Dana Kuhn was a member of the NHF Board of Directors from 1988-93. He is presently a HIV risk reduction counselor with the Richmond, VA Hemophilia Treatment Center. He is knowledgeable about government procedures, a member of the Surgeon General's Pediatric AIDS Campaign, and is committed to discovering the truth about HIV infection of persons with hemophilia through contaminated blood products. Dana also acts as a liaison between COTT and the Hemophilia/HIV Peer Association.



## cott actions

### The July Federation Meeting

by Jan Hamilton, Coordinator

In just a few short weeks, the excitement that permeated the air at the initial May meeting of The Federation has grown to include a wider geographic representation and a greater depth of programs and activities. The Hemophilia Federation is well on its way to becoming a major player in the world of coagulation disorders, HIV and AIDS.

At the July meeting in Chicago, final drafts of the bylaws, mission statement, memorandum of understanding, and conflict of interest document were adopted. More and more groups are "getting on board" and working to develop the programs and coordinate the activities The Federation plans to initiate.

The leadership of The Hemophilia Federation during its formative period has been entrusted to a coordinating council with people carefully chosen for their expertise.

Jan Hamilton of Hemophilia of Acadiana has been selected as the overall coordinator. Additionally, she will serve as Interim Program Coordinator helping to launch the several programs planned for the near future.

Beth Weinstein of Hemophilia Northwest will serve as Secretary in addition to giving support to all involved in the program

as Love and Compassion Coordinator.

Jonathan Wadleigh of COTT will serve as Outreach Chairperson as he helps to spread the word of The Hemophilia Federation and works toward increasing the membership.

Anna DeSimone of New Jersey is spearheading the Development Committee in search of grants.

Corey Dubin of COTT West is directing the efforts of Media coverage with assistance on the East coast from Ms. DeSimone.

Directing the efforts of The Federation in the areas of Government Relations (lobbying) and Compensation is Dana Kuhn of Virginia, who represents both The H/HIV Peer Association and COTT.

Tom Fahey of COTT is compiling an Information Bank to be a resource for treatment regimens for hemophilia and also for HIV/AIDS, and pertinent legal and historical documents about the infection of the hemophilia community with HIV.

An announcement will be made shortly concerning the initial programs which will soon be in place for member organizations and individuals. They are directed at filling voids in the arena of hemophilia support.

Many hours of thought and consideration have gone into developing the framework for this organization. It is not intended

to be an NHF clone, but to fill unmet needs of the hemophilia community. Membership in The Federation does not preclude membership in NHF. It is possible for an individual to be a member of both organizations simultaneously.

If you would like to share the excitement, contact one of our coordinating council for additional information. We will be delighted to discuss membership in The Federation with you.

Contacts are: Jan Hamilton: (318) 984-7982. Jonathan Wadleigh: (617) 731-9857. Tom Fahey: (800) 488-COTT. Dana Kuhn: (804) 739-1027. Anna DeSimone: (201) 744-5122. Corey Dubin: (805) 967-0274.

### **COTT**

**Don't forget to order your Committee of Ten Thousand t-shirts. They feature our lightning ankh logo and motto, "Action = Life," on the front, and our name on the back. Available in both extra large and large, they are a mere \$12 each.**

**To order, call (800) 488-COTT, or send in the form on the back page.**

**So join the struggle while you may  
The revolution is only a t-shirt away.**

**—Billy Bragg**

### The July ACTG CCG Retreat

In light of the recently publicized results from the Concorde study and ACTG 155 as well as the overall lack of effective drug development and definitive data from ACTG trials, many issues of clinical trials design are now the subject of widespread discussion. This discussion is a part of a larger debate about the immediate future and direction of AIDS research.

The Community Constituency Group (CCG) of the AIDS Clinical Trials Group (ACTG) met in Chicago to discuss these issues and numerous others. Two members of the COTT board participated in the discussions. The CCG made some general recommendations about the design of clinical trials. (No vote was taken on the following.)

- Phase III trials should be larger with less data collection. There is a need for reliable answers about clinically relevant questions. Intensive laboratory substudies should be minimized, follow-up should continue after the official termination of the study for survival data, as well as after an individual reaches an endpoint such as disease progression, and survival should be the primary endpoint in more trials.

- Phase IV post-marketing trials should be funded by industry, not by government.

- Clinical research should move beyond AZT, ddI, and ddC.

- Better research is needed on surrogate markers.

- The issue of using placebos in clinical

trials should be reconsidered. No consensus was reached on whether HIV-infected individuals would be willing to enter placebo-controlled trials.

- More clinical trials should be open label (when the participant knows what he or she is taking).

- Trials must be designed proactively to be accessible to women and adolescents. And effort should be made to build in statistical power to find differential effects in those groups.

There are three representatives from the hemophilia community on the ACTG CCG: Greg Haas and Jonathan Wadleigh of COTT, and Debbie Chedester of Hemophilia of Acadiana.





## berlin



### Berlin Report: Clues Found on the Path that Leads from HIV Infection to Disease

by Gregory J. Haas

Many exciting and promising leads about the process "pathogenesis," by which HIV causes AIDS, were discussed in Berlin. This topic received much more attention than it has in past years. Determining the mechanisms that the virus uses to disrupt and damage the immune system will hopefully lead to new and more effective treatment strategies.

After a person is exposed to HIV, the virus must accomplish two basic tasks in order to cause symptomatic AIDS: 1) infection must occur—the virus must get past the body's initial immune response; and 2) once infection has taken place, the virus must overcome (or destroy) the body's immune capabilities. Much of the attention in pathogenesis research was given to persons who seem to have fought off HIV at one of these stages.

#### Exposed but Not Infected

There are people who have almost certainly been exposed to HIV many times but have no detectable evidence of current infection. This phenomenon has been observed in a group of Kenyan prostitutes, sexually active gay men, babies born to HIV-positive mothers, and persons with hemophilia.

An overwhelming percentage of persons with hemophilia who were treated with factor concentrates before 1985 became HIV-positive, but a few people remain HIV-negative. A laboratory study by Dr. Tenenbaum,

of the Tulane Department of Microbiology, Immunology and Hematology, examined frozen blood samples that have been stored since the early 1980s from some such individuals. Upon using a more sensitive version of the ELISA antibody test, he found that some of the individuals actually did produce HIV antibodies after exposure, but later samples were completely negative, indicating that the individuals' bodies had seen the virus and fought it off. An important question is how they were able to do so.

The researchers removed the CD8 cells from some blood samples. The samples were then challenged with HIV. Samples that contained CD8 cells were able to resist the virus, but the samples with the CD8 cells removed were susceptible to infection. These results indicate that there is something about the CD8 cells of these individuals that protect against infection.

The research done in the other groups of people who have resisted infection also showed a strong CD8 response. In particular, investigators believe that the protection was conferred by a particular type of CD8 cell, cytotoxic lymphocytes (CTLs). (For some background on CD8 cells, see the article "Why Don't They Call 'Em T-Cells Anymore?" on page 16.)

#### Exposed, Infected, but Still Healthy

Numerous presenters reported on investigations of Long-Term Survivors—people who have been infected with HIV for

more than eight (or ten, depending on the researcher) years but have shown no clinical symptoms and still have normal CD4 counts. Dr. Jay Levy, of the University of California at San Francisco, found that long-term survivors have more of a particular type of CD4 cell (Th-1) than do those who have progressed to symptomatic disease.

The Th-1 CD4 cells encourage the growth of CTLs, while the other type of CD4 cells, Th-2, encourage the production of antibodies. The two types of CD4 cells seem to inhibit each other. Dr. Levy and others speculated that an individual's prognosis is worse when the Th-2 response becomes dominant over the Th-1 response. This change is referred to as the "Th-1/Th-2 shift."

A study supporting that conclusion divided 119 HIV-positive persons with hemophilia into three groups based on how quickly their CD4 cell counts declined: 7 non-progressors, 40 slow progressors, and 72 rapid-progressors. Rapid progressors had low levels of cytotoxic CD8 cells (CTLs), while non- and slow progressors had more HIV specific CTLs.

Researchers at the Royal Free Hospital in London examined the link between levels of CD8 and CD4 cells. The study examined the effect of a different class of CD8 cells—suppressor T8 cells. Eighty-four persons with hemophilia and HIV were followed for eight years beginning when their CD4 counts were above 300. They found that high initial levels of suppressor T8 cells were strongly correlated with faster disease progression.

These results indicate that an effective therapeutic vaccine should stimulate cytotoxic lymphocytes rather than produce neutralizing antibodies (which is what most current vaccines try to do).

#### Different Treatments for Different Disease Stages

Dr. Anthony Fauci, Director of NIAID, said in a plenary session that HIV is never truly inactive (latent), that immune suppression occurs by many dif-

#### Berlin Demonstration

On the third day of the Berlin Conference, Germans with hemophilia staged a mass demonstration for those who have died from hemophilia-related AIDS. According to one hooded marcher, "The manufacturers choose profit over human beings." Information was distributed indicating what choices were made by whom. Choices that according to Christian Vidor, "Led to the infection of over 70% of people with hemophilia in Germany." All Participants called for immediate funding for the needs of PWAs.







# berlin



ferent mechanisms and that different treatment strategies may be appropriate at different stages in the course of the disease.

For instance, he showed that in the early stages of HIV disease, the virus is mainly harbored in the lymph nodes—seemingly protected from AZT, ddI and ddC. In that stage, activation of the immune system actually leads to increased viral replication and infection of lymph tissue. Fauci suggested that it might be appropriate to treat persons in early stages of HIV disease with immunosuppressive drugs to control HIV infection. He cited retrospective data of transplant recipients (who were HIV-positive), in which persons treated with the immune suppressor cyclosporine had fewer AIDS-related infections and lived longer than those who did not take the drug.

## How Does HIV Do It?

After HIV mutates into the more cytopathic strain and moves out of the lymph nodes, depletion of CD4 cells accelerates. The way HIV disrupts immunity is still an unanswered question. The traditional explanation is that CD4 depletion can be accounted for by the direct killing of CD4s by HIV. Other theories are now becoming more accepted, one of which is that HIV can indirectly cause CD4 cells to commit suicide (apoptosis).

Apoptosis is “programmed cell death,” a natural process that the body uses to eliminate maturing T-cells that are unnecessary. Dr. Luc Montagnier of the Pasteur Institute in Paris believes that the presence of HIV can lead to inappropriate apoptotic death of CD4 cells. His theory is that the HIV envelope protein gp120 combined with the CD4 receptor of an infected CD4 cell can signal uninfected CD4 cells to commit suicide.

The relationship of apoptosis to disease can be seen in animal models. Chimpanzees infected with HIV do not exhibit programmed cell death and do not develop disease, but macaques do experience apoptosis and rapidly develop symptomatic disease. This implies that HIV itself is not sufficient to cause apoptosis and HIV might not be sufficient to cause disease, but apoptosis might

be necessary for HIV disease to progress.

Montagnier presented a case study of a person with hemophilia and HIV who was treated with AZT, NAC (n-acetyl-cysteine) and ravomycin (an antibiotic). The individual experienced a substantial increase in CD4 count and decrease in beta-2-microglobulin (an indicator of viral activity). The regimen was designed to slow HIV disease in three separate ways. AZT slows viral replication; NAC is an antioxidant which can help prevent cell damage from oxidative stress and may also inhibit apoptosis; ravomycin stops infection by mycoplasma (which Montagnier claims is a cofactor for HIV disease). He suggested that further research should be conducted on antioxidant therapies such as NAC, vitamins C and E, and SOD (superoxide dismutase).

Another indirect mechanism of CD4 cell death is cell fusion—a clustering of CD4 cells that renders them unable to do their job. Jay Levy said that symptoms tend to occur in persons after the virus switches to a more cytopathic (disease-causing) strain. Virus taken from long-term survivors grows slowly in only a few types of cells and does not

cause cell fusion (syncytia formation).

A German research team investigated the presence of syncytia-inducing (SI) strains of HIV in 51 children and adolescents with hemophilia. The virus that was isolated was graded into four categories: strong, moderate, weak, and no SI. Of the 18 adolescents with strong SI virus, five had died, and four others had symptomatic AIDS after two years of follow-up. No one in any of the other categories either died or progressed to AIDS. This reinforces previous suggestions that the presence of syncytia-inducing viral strains leads to faster disease progression.

## Conclusion

Impressive progress has been made in determining how HIV and the immune system interact. However, that interaction is extraordinarily complex. It is unlikely that any magic chemical or cytokine (chemical messenger) will be found soon that “locks-in” the Th-1 response or stops the appearance of syncytia-inducing virus. But hopefully, this developing knowledge can be used in conjunction with other therapies to devise new and better treatment strategies.

## Update: Resistance Possible In Three Drug Regimen

With much (too much) fanfare, researchers from Massachusetts General Hospital announced in February that a “new” treatment strategy (called Convergent Combination Therapy—CCT) suppressed HIV replication in the test tube and that the virus was unable to develop resistance to the treatments without losing its ability to replicate. The announcement spurred a great deal of enthusiasm among persons with AIDS and allowed NIAID to fast-track a clinical trial of the treatment strategy (ACTG 241).

In Berlin, evidence was presented that HIV could develop resistance to the three drug therapy of AZT, ddI, and nevirapine and still remain viable. This new finding does not necessarily imply that CCT will not be effective in treating HIV disease.

The treatment strategy is being studied in two NIAID clinical trials: ACTG 241 is studying CCT versus AZT plus ddI in persons with between 200 and 400 CD4 cells, and ACTG 193A is studying four different antiretroviral regimens

in persons with fewer than 50 CD4 cells.

Dr. Keith Henry, the principal investigator for ACTG 193A, said that “while development of HIV resistance to the triple drug therapy was observed in the test tube, laboratory experiments also suggest that the three drug combination of AZT, ddI, and nevirapine is more potent against HIV than the two drug combination of AZT and ddI. Thus, only clinical trials can tell us if this combination approach will work for people infected with HIV.”

This episode is a reminder that laboratory findings are often disappointing upon further research. It also shows how quickly a clinical trial can be designed and started when there is a political will to do so. We can hope this treatment strategy will show some efficacy in the current trials. We can also demand that NIAID be as responsive to other exciting leads in the future—as soon as laboratory findings are confirmed.

(Note: ACTG 241 is closed, but ACTG 193A is still accruing participants.)





## Berlin



(continued from page one)

that such demands make it very difficult to recruit people into clinical trials to study the impact of intermediate-purity products on the immune system of persons with hemophilia and HIV.

Aledort's reluctance to support the use of high-purity factor is shared by the Medical and Scientific Advisory Council (MASAC) of NHF. In MASAC's most recent treatment recommendations (May 1993), they only "recommend that physicians should *carefully consider* [the data about high-purity products] when selecting products for use in HIV-infected persons with hemophilia" (emphasis added). This position is strongly disputed by many international clinicians and researchers.

Dr. Luc Montagnier, the discoverer of HIV, stated, "On the basis of the research I've shown today (6-10-93, Berlin), I would strongly advise the use of the most highly purified products."

Numerous studies have demonstrated that large quantities of foreign antigens can adversely affect the immune system. Intermediate-purity concentrates contain substantially more foreign proteins than high-purity products. These proteins have been shown to 1) impair the body's ability to successfully develop a skin test response, an indicator of the health of cell-mediated immunity; 2) inhibit macrophages, natural killer cells (both types of white blood cells), and the ability of T-cells to secrete interleukin-2 and gamma interferon, each an important factor in cell-mediated immunity; and 3) cause the stimulation of latently HIV-infected cells—which then can begin replicating.

Foreign antigens are not removed by heat or solvent/detergent treatment. Monoclonal and recombinant products are almost completely free of such proteins.

The results presented in Berlin (see box) that showed that intermediate-purity factor is associated with decreased CD4 counts follow two other randomized clinical trials of high- versus intermediate-purity factor concentrates that have been published.

The first was published in *Blood* in 1991. Twenty HIV-positive persons with hemophilia in Italy were randomized to receive for 96 weeks either an intermediate-purity product or a monoclonal high-purity

product. Of the ten persons assigned to intermediate-purity, seven had their CD4 counts fall by more than 200, and none had CD4 count increases. In the high-purity group, only one person had a CD4 drop of more than 200, and seven actually had CD4 increases. The study found "striking immunologic differences between the patients in the two arms of the study."

The other study was also conducted in Italy and was reported in *Thrombosis and Haemostasis* in 1992. The study concluded that the higher purity product "was not clearly superior to the intermediate-purity concentrate." However, the study randomized 24 persons to either an intermediate-purity product used, or an ion exchange chromatography concentrate made by Behring, a German fractionator. The Behring product has a "purity" of only about one-tenth of the monoclonal products (but about fifty times greater than intermediate-purity products). The Behring product actually lies in between "intermediate" and "high" purity.

Even so, after two years, the average drop in CD4 counts was greater for those on the intermediate product than for those on the Behring product. This difference was

not statistically significant. Three individuals on the intermediate product progressed to AIDS, while only one on the Behring product progressed.

Other studies that were not controlled or randomized have also indicated that CD4 stabilization occurs with the use of high-purity concentrates.

In 1991, two years before the MASAC recommendations, Dr. Sam Schulman of Sweden wrote in *The Annals of Hematology*, "We have no reason to believe that ultrapure products would be more harmful than less purified concentrates. We cannot afford to wait until hard data from randomized trials are available, as many of our patients could die before that time."

Schulman added that "due to the early introduction of heat treatment of clotting factor products in the false hope of preventing hepatitis, many [persons with hemophilia] were spared the more ominous infection with HIV. By choosing factor concentrates in which the highest possible reduction in known and, probably, also unknown infectious agents has been achieved, we might prevent the occurrence of new, unforeseen disasters."

### High Purity Factor Better for CD4 Counts

by Naomi Pfeiffer

Do impurities in clotting factor hasten progression to AIDS? A new American study suggests they may suppress already compromised immune systems.

The multicenter study, presented at the Berlin AIDS Conference in June by researcher Stephanie Seremetis, MD, showed that the purer the concentrate, the slower the decline in CD4 counts in HIV+ persons with hemophilia.

In this randomized controlled prospective trial, 60 HIV+ persons with severe hemophilia received either an intermediate-purity or monoclonal antibody-purified concentrate. The trial found that of those who remained in the study, the 20 on the highly purified concentrate maintained stable CD4 counts while the 15 on intermediate-purity factor VIII experienced a significant drop. After 36 months, the individuals receiving intermediate purity factor had an average CD4 decrease of 188 (from 378 to 190). In comparison, those on high purity factor had an average decrease of only 23 (from 416 to 393). The difference was so

dramatic that Dr. Seremetis stopped the open-ended study at three years. Still, the study was the longest and largest of its kind.

"The difference was independent of the use of antiretroviral therapy," she noted. "Results indicated that repeated infusions of intermediate-purity concentrates may impair cell-mediated immunity while high-purity concentrates have a clear advantage in preserving immune function as measured by CD4 counts in HIV-infected persons with hemophilia."

The findings were a "surprise" to the researchers themselves, she said. "They should persuade the experts to rethink current treatment of these patients with standard intermediate-purity products."

Previous studies indicate that the impurities that are present in intermediate-purity concentrates can suppress lymphocyte function.

Earlier evidence convinced Great Britain to switch to the ultrapure monoclonal antibody factor VIII concentrates for their HIV+ population, Seremetis said.





## berlin



### Reflections on Antiretrovirals: There is Light Behind the Gloom

by Gregory J. Haas

Berlin—a city that for decades has conjured images of war crimes and terror. In the Summer of 1993, people with HIV and AIDS are speaking of “Berlin” as a symbol of lost hopes and impending doom. The July *Treatment Issues* called the Berlin conference “one of the bleakest moments since the AIDS crisis began.”

The news that dominated the media during and since the IX International AIDS Conference has been the Concorde study. This large clinical trial, coupled with other recent studies of antiretroviral use alone or in combinations, seems to bring us back to square one in terms of the clinical management of HIV disease. Researchers, physicians, and many of us harboring the virus admit profound confusion about what drugs to prescribe or swallow.

(The news about nucleoside analogues was frustrating, but it wasn't all that surprising. We have known that these drugs have only a limited effect for a limited time. It is important to stress that there were many other dimensions to the Berlin conference, including substantial progress in understanding the immune system. Those developments may ultimately have much greater significance than the data on AZT, etc.)

Concorde, the European clinical trial of early use of AZT, was a very large and powerful study. It showed that asymptomatic persons did not have a survival benefit after using AZT monotherapy for three years. (It also did not show that AZT kills people.) Concorde did not ask or answer any questions about the use of AZT in persons who already have symptomatic disease or those who have previously taken AZT or other antiretrovirals.

Other studies add to the confusion. A US trial, ACTG 155, investigated the use of combination antiretroviral therapy (AZT and ddC) in persons with AIDS. A working

assumption among many has been that combination therapy would prove superior than monotherapy, but the overall result of the clinical trial was that there was no difference between the combination and the drugs used alone. The Principal Investigator, Dr. Margaret Fischl, claimed that the trial showed that combination therapy was beneficial in those with CD4 counts between 150 and 300, but activists and statisticians have argued that she had to pull and tease the data like taffy to reach that conclusion.

After Berlin, the US National Institutes of Health (NIH) sponsored a conference in June to define the “State-of-the-Art” in anti-

retroviral care. Major AIDS clinicians, researchers and activists gathered to interpret the data from the many clinical tri-

als of AZT, ddI and ddC. They hammered together a hodgepodge of recommendations for twelve different disease stages (based on symptoms, previous antiretroviral usage, and CD4 counts). The NIH panel recognized that for some disease stages, continued monitoring without antiretroviral therapy is a valid option (see *Treatment Issues*, July 1993 for a more complete description of the recommendations). For many of the disease stages there is no clinical data upon which to make recommendations. They were based on extrapolation and intuition.

#### So What Do We Do?

What drugs do we take? As always that decision is one that should be made by an informed discussion with a physician (or physicians) who is knowledgeable about the current state of affairs. A general (and very non-scientific) rule-of-thumb may be, “if what you're doing seems to be working, keep doing it; if you are feeling worse, change your regimen.”

Countless people have observed, “I

knew AZT didn't work, it's killed friends of mine,” while others, equally convinced, insist that AZT has brought themselves or friends true clinical relief from AIDS. There is no reason to doubt either group. A frustrating but inevitable fact about clinical research and observation is that each of our bodies reacts differently to what we put in it. We have to try to use the available information about what has happened in other people and in our own past to find what works best.

What should we ask of future clinical research? One possibility is to conduct more clinical trials to determine more precisely who can benefit from AZT and other nucleoside analogues. Another possibility is to realize that if these drugs do have benefits, those benefits are mostly marginal and short-lived. Determining the optimal management strategy for these drugs could steer scarce federal resources away from other therapies or approaches. But at the same time, we currently do not know how to best utilize nucleosides. Should the continuing investigations of this class of antivirals be left to the pharmaceutical corporations?

After years of testing AZT and similar compounds, their value is still questionable. Is it necessary to go back to placebo-controlled trials to get definitive results about protease inhibitors, convergent combination therapy, vitamin C, or whatever else the future holds? Is this ethical? Would we want to participate in such trials?

Researchers are also asking these questions. And they are asking us. The report from the CCG Retreat on page 7 lists other major questions that are now wide-open for discussion. Talk about the issues with friends and peers. Tell your physician what you think. Tell COTT what you think.

A gloom has drifted out of Berlin. But that gloom is brightened by progress on understanding how the immune system works and is disrupted by HIV. It is brightened by the unprecedented meeting of researchers, government, and activists in Madison (reported on page 5). And it can be brightened by our taking the initiative and using our disappointments in order to more aggressively pursue meaningful answers.

*The gloom can be brightened  
by taking the initiative and  
aggressively pursuing  
meaningful answers.*



## living and loving

### Voicing Our Own Stories

by Donna Rushing

Many of the men and boys with hemophilia that I have met—those of the “treatable” generations—exclude information about their experience with hemophilia in defining who they are. While growing up, they might have avoided identifying their hemophilia as a disability; when possible they shunned the wheelchairs and avoided the crutches or slings—and the accompanying, often harsh, curiosity of classmates or anxious sympathy of adults. Even as adults, they may tend to keep that part of their lives as incidental, private.

Some people who might have been secretive about or even ashamed of their hemophilia in the past now may feel their shame compounded by the unfair stigma associated with HIV and AIDS. At the same time, we live in a world with others affected by HIV. The disclosure of one's hemophilia can play into the “innocent victim” syndrome, which can be a barrier to making connections with the diverse persons and communities struggling against AIDS.

We are the stories we tell about ourselves, some say. I like this idea; it always gives us the chance to change the stories we tell, and therefore transform both our own and others' perceptions of who we are. Coming out and declaring something that you've felt compelled to hide (perhaps for your entire life)—whether it is having hemophilia, being gay, or being HIV-positive—informs, empowers, and connects you with others, thereby allowing community to emerge, or strengthening existing community.

I consider all admissions of HIV status as educational, even political statements. How many people outside of this affected community know the depth and breadth of the hemophilia/HIV fiasco? How many know of the lurid details behind yet another under-reported, misrepresented, and misunderstood HIV/AIDS-affected population? The willingness to identify yourself as a person with HIV may, in fact, naturally free you from years of hiding your experience as a person living with another condition that most people know nothing about—hemophilia.

Ideally, people living with hemophilia and HIV will forge ties with other HIV-

affected populations and communities, and will work on obliterating any of their own personal prejudices. Finding oneself with a discriminated-against virus can create, in a fertile mind, an opportunity for working on some sticky areas concerning how we really believe and feel about things outside of our own limited experience. Finding myself immersed in the lives of people living with HIV/AIDS has created this opportunity for me.

There are uncountable places in which the lives of people with hemophilia and HIV or AIDS intersect with the lives of others living with HIV/AIDS. For instance, some people with hemophilia and some gay adults may share a common experience of having grown up feeling different; of having gained a stronger sense of self when sharing, as adults, what they “covered up” as children; of now feeling a sense of family when connecting with others who share their experience. They may be more sensitive to others' feelings, may be less likely to judge a person by outward differences.

Diseases tend to be oblivious to class and ethnic boundaries, gender differences, and sexual orientation. Ultimately, shared human experience connects us all, with or without hemophilia or HIV. Among us walk people addicted to substances and experiences, people from dysfunctional or abusive families, people who have lived through multiple tragedies, people who have always been afraid to speak up and say who they are and tell a part of their story.

It is hard enough to be affected, infinitely harder to make that choice to openly claim HIV as part of one's experience without the added burden of hiding part of that experience. Instead, I think we must ask, “What are the lessons we have to share with each other?”

In revealing our private selves, somewhere between hiding and full disclosure

lies selectivity. Perhaps in between either using the hemophilia label as a way to distance ourselves from other human beings or choosing to keep silent about hemophilia as an HIV connection, there is a realm where people can feel conscious and aware around both their choice to mention hemophilia and

their reasons behind that choice. Beyond the false, flat, two-sided coin of guilt and innocence, our real, shared, multi-dimensional humanity exists. We need to look for those places where we connect as human beings; from

the gay community we have learned the value of both personal and communal empowerment—a freedom to speak out about who we are comes with the territory.

Whatever our identity in this moment, this life, we benefit from embracing who we are right now and then trying to grow. Not everyone affected by hemophilia and HIV will be able to understand or learn from the experience of others living with HIV and AIDS. This is probably true of many people who must live with HIV and AIDS who received the virus through a transmission that society deems “innocent.” The innocent label, after all, hurts everybody.

In the case of identifying yourself as a person with HIV and hemophilia, I suppose intent is all. If you are striving to connect compassionately with others in the wider affected community; if you work to recognize commonalities among all those with HIV/AIDS; if you do not use your hemophilia connection to distance yourself—then I think you are simply allowing hemophilia, at last, to become a part of your story. Not your whole story, not your full identity—just a part of what needs to be told.

*“Some circumstantial evidence is very strong, as when you find a trout in the milk.”*

—Henry David Thoreau



## living and loving

### Berlin Report: Sexual Transmission of HIV

New data reported in Berlin confirms that consistent condom use is effective in preventing the transmission of HIV between sexual partners.

A multinational European study of HIV transmission in heterosexual couples with one HIV positive member was presented in a Berlin Conference workshop. The researchers followed 245 couples for an average of 22 months. All 245 couples reported having sexual intercourse during duration of the study. Zero HIV seroconversions occurred among the 123 couples who reported using condoms every time they had sex. By comparison, 12 seroconversions occurred among the 122 couples who used condoms some of the time. Among the irregular condom-using couples, the researchers found similar seroconversion rates no matter the frequency of condom usage.

These results were corroborated by a study done in Italy that is reported in the May 1993 issue of *The Journal of AIDS*. This study followed 305 female partners of HIV-infected men for a median of two years. Three (2%) of the 171 who used condoms consistently seroconverted, while sixteen (12%) of the 134 who never or only sometimes used condoms became HIV infected. The authors state that, "[t]he results of this study confirm in a prospective setting the protective effect of condom use."

Laboratory studies indicate that spermicides such as nonoxynol-9 can inactivate HIV. However, a study of sexual transmission of HIV in Kenyan prostitutes found that vaginal sponges containing the spermicide nonoxynol-9, used without condoms, did not reduce the rates of HIV transmission.

These studies and others underscore the importance of consistent and regular condom usage. When used correctly, condoms block HIV transmission despite occasional product failure. Data suggest that danger from inconsistent usage far outweighs the dangers of breakage or improper use.

A survey presented in Berlin of 51 HIV-positive men with hemophilia and 28 steady female partners indicated that increased communication about condoms can increase how often they are used. The men interviewed said they assumed their partners would react

negatively to talking about condoms and would be unwilling to use them. However, the women said that they wanted to talk about such issues to feel emotionally closer and did not have any unwillingness to use condoms.

**Condoms. Talk about 'em. Use 'em.**

A German study analyzed the transmission rate of HIV from infected men with hemophilia to their sexual partners. This study did not examine the use of condoms or other safe-sex practices. Between 1985 and 1992, 20 of 198 sexual partners seroconverted. Further analysis showed that the men whose partners became infected had

lower CD4 counts both in 1985 and at the end of the study in 1992, and those men were more likely to have culturable virus.

Investigators at Harvard-Deaconess Hospital in Boston presented data about the rate of leukocyte (white blood cell) infection in blood and semen. They used PCR (polymerase chain reaction) analysis to detect HIV in the blood and semen of men with hemophilia. The amount of virus in semen leukocytes varied widely among subjects, but was always less than in the blood cells. This result suggests other questions about how leukocytes are exchanged between the peripheral blood system and the male reproductive system.

### Creative Sex: Cheap Sex by Mail!

Everyone knows that HIV and hemophilia are expensive, the latter sometimes being a \$100,000+/year habit and the former varying with the amount of pills, vitamins, and medical care that you need. Even lascivious frolicking can get expensive.

Eventually, the word "cheap" almost always sounds good in our community. Of course, there is the bad type of cheap (those stupid little footballs and frisbees the pharmaceutical companies give out) and the good kind. This installment of "Creative Sex" focuses on the good kind—more specifically, 1-800 numbers for catalogs, free or inexpensive catalogs, and places you can get free information and sexy goodies.

**Condom Resource Center**  
P.O. Box 30564  
Oakland, CA 94604  
Ph.: (510) 891-0455  
**Catalogue:** free

**Gay Men's Health Crisis**  
129 West 20th Street  
New York, NY 10011-0022  
Ph.: (212) 807-7517

**Cat. of AIDS Educational Resources:** free  
These places offer a wide selection of booklets, videos, posters and buttons. *GMHC* even has comic books on HIV and AIDS.

**The Rubber Tree**  
4426 Burke Avenue North, Dept. CS  
Seattle, WA 98103  
Ph.: (206) 633-4750  
Just as it sounds—mounds o' condoms.

**Good Vibrations**  
12100 Valencia Street  
San Francisco, CA 94410  
Ph.: (415) 550-7399  
**Catalogue:** \$2

**Eve's Garden**  
119 West 57th Street, Suite 420  
New York, NY 10019  
Ph.: (800) 848-4306 (NY: (212) 757-8651)  
**Catalogue:** \$3

Both of these stores are geared toward women, and have a safe-sex orientation. *Good Vibrations* has many good videos, while *Eve's Garden* is the place to go for books.

**Adam & Eve**  
1 Apple Court  
P.O. Box 800  
Carrboro, NC 27510  
**Catalogue:** free

Nowhere as politically correct as the other catalogues, *Adam & Eve* is loaded with XXX-rated videos, but also full of sexual toys that may spark your imagination, and protect you lover.

**Xandria Collection**  
Dept. UTO 793  
P.O. Box 31039  
San Francisco, CA 94131  
**Catalogue:** \$4

Your \$4 is applied to your first order—so in effect, this a free catalogue. They guarantee discreet mailings and confidentiality, promising not to sell your name to any mailing list. This one's pretty steamy too.





## staying healthy

### My Personal Empowerment Workout

by Russ Tess

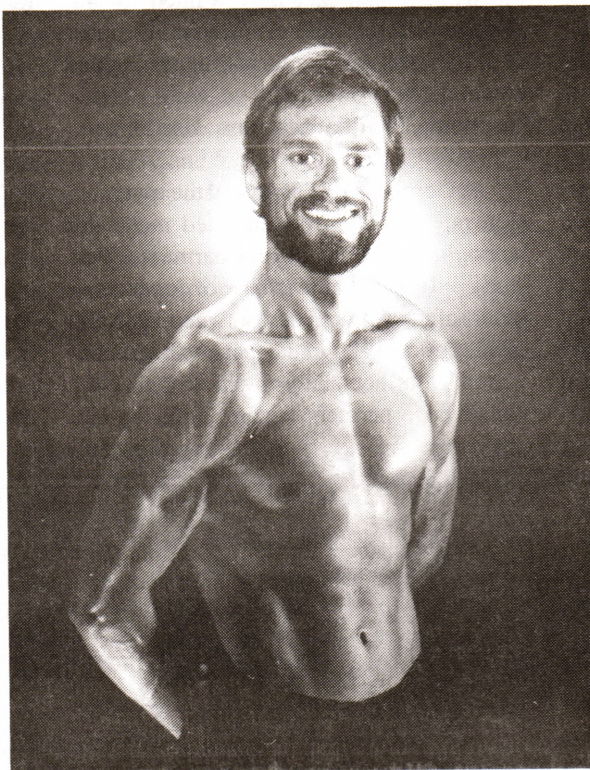
I am a thirty year-old man challenged by both severe hemophilia and AIDS. It is just within the past four years that I've been able to connect with large numbers of my peers. I can't help but notice that, as a group, most of us simply don't respect our bodies.

Growing up with hemophilia, it's easy to feel betrayed by our bodies. For no apparent reason, a joint may hemorrhage, causing us pain and denying us participation in a "normal" life. It's an attitude you frequently hear in the way some of us talk: "My right knee is my bad knee."

Certainly, HIV doesn't help matters. Most of us have learned to run to our doctors when we need what we hope will be a quick fix. It's a reactive approach to survival. By its very nature, it fosters a sense of helplessness and inevitable hopelessness.

I was fortunate enough never to have fallen into that trap for very long. I recognized early on the benefits of taking loving care of the only body I would ever have on this life's journey. It is precisely that proactive attitude that has allowed me to survive and thrive to this day and beyond.

It has been said that disease is undevel-



oped health. We are bombarded by things we *could* do in order to have a healthier lifestyle. Example: Smokers shouldn't smoke. Everyone knows that. And I know that old habits are as hard to break as good habits are

to start. But the effort does pay off.

Of the many things I do for myself, I've gotten the most benefit from weightlifting, or more correctly, bodybuilding. Early in my teens, I grew tired of my scrawny body. I hadn't taken gym class past the sixth grade, and bicycling and swimming constituted the only exercise I had ever known. That's when I started working out with weights, first at home, then at the YMCA, and finally in a gym. Progress was slow, but it was steady. As I grew stronger, my muscles grew larger. As my joints grew stronger, they resisted "bleeds." As a result, I haven't had a spontaneous hemorrhage in nearly ten years.

Despite this, the accumulated damage my ankles suffered years earlier had begun to take a toll by the time I was 22. I had developed a painful limp due to the resulting arthritis. I can remember mornings when it was so bad that I had to crawl to the bathroom. I took Indocin for the next six years, but it never seemed to help much. Neither did shoes with better support. When I began to look into obtaining a handicapped parking permit and undergoing ankle fusion surgery, I knew there had to be a better way.

### Getting Started

When I do motivational speaking at personal empowerment conferences, hemophilia camps, etc., I'm frequently told that I should write a book or make a video. I always insist that there is *nothing* unusual about what I'm doing. Many thousands of people in this country are doing the same thing. The only difference is that I have hemophilia and AIDS. It is the mind, not the body, that causes most of us to hold back our potential.

Still, here are a few tips to consider before you begin:

#### Consult a doctor:

Bodybuilding is an incredible way to

explore your physical limits and to learn how to expand those limits. But where problem joints are concerned, extra caution is needed.

#### Learn all you can:

It's vitally important to know how specific muscles and joints function, and which exercises work those muscles. There are many good books and magazines to help.

#### Exercise safely:

It's important to remember that exercises need to be performed with strict attention to proper form and in pain-free arcs. Slow, deliberate movements can make a light weight feel heavier while being safer

and equally productive when compared to heavy weightlifting.

#### Kids and exercise:

Recently, it has been determined that weightlifting is safe for prepubescent boys. However, supervision is needed, and heavy weights and overtraining should be avoided. Most bodybuilding exercises can be duplicated with a long piece of surgical tubing in place of dumbbells, which is a good place to start.

I encourage anyone wanting to know more to contact me at (414) 337-9384, or write me at 302 George St. #5, De Pere, WI 54115-2545.



## staying healthy

### Risk

Up to that time, I had been concentrating my training efforts on my chest and arms. I wanted to look good in a tank top. I trained my legs, but not with the same intensity. When I sought more balance and took leg training more seriously, wondrous things began to happen. Not only did my thigh and calf muscles increase in size, but most of my lost range of motion returned. The pain in my ankles disappeared without the use of drugs, and I was walking normally again. I would also like to add here that because of bodybuilding, I consider all my other joints to be 100% healthy. It makes sense that a strengthened joint will resist hemorrhaging.

Like far too many of us, I tested HIV antibody positive in 1985. At that time, I hadn't used blood products in almost two years and I was feeling on top of the world, so it was quite a wake-up call. Far too introspective to waste much time on denial, I knew that the challenges of my past had a purpose in preparing me for the challenges that lay ahead.

My greatest challenge to date came in 1990, when I developed a staph infection in my bloodstream. I spent two weeks in the hospital with a fever that went as high as 106.5°. I had grown so weak that I couldn't roll over in bed without help. Family and friends secretly expected me to die.

When I was sent home, I was still too weak to stand up. A few short days later, when I could get around slowly on crutches, I was back in the gym. I became my own physical therapist. Some exercises I still couldn't coordinate, but I tapped into the ones I could handle. I was forced to use much lighter weights than I had been accustomed to, yet they certainly felt heavy at the time. Two weeks after leaving the hospital, I was able to return to work full-time. It wasn't long after that I weighed more than I did before I got so sick.

I love to tell the story of my friend Digit. Digit is a hard worker, though somewhat of a loner. Digit is my T4 cell. My most recent T4 count was one, but that's okay, because it's been even lower than that. I wish I could say that bodybuilding raised my T4 count to 500, because that would impress some

people. The fact is, I was 263 when first tested in 1985, and I experienced a swift and steady decline. I credit bodybuilding for keeping me healthy, active and fit despite what I consider to be meaningless lab results. My health is what I find impressive.

I've spent a lot of time wondering specifically why bodybuilding has helped me so much in my fight against AIDS. Certainly, it helps my attitude. When I look in the mirror, I don't see an AIDS victim. When I'm working out, I feel like Superman. Even on a bad day when I have to drag myself to the gym, I always feel a lot better an hour later. And I always chuckle when some poor sap trying to work off his gut asks me how I manage to stay so lean.

That leads me to the consideration of the maintenance of lean body mass. A doctor once told me that because of HIV, my basal metabolism is probably five times greater than that of a normal person. AZT-type drugs are toxic to muscle mass. Fevers, loss of appetite, malabsorption difficulties, mouth sores, throat infections, diarrhea and bacterial infections like MAC all explain

why you don't see a lot a muscular people with AIDS. The only way I can gain or maintain weight is to intelligently eat all that I can *and* lift weights.

When you suffer a sudden and dramatic weight loss, it's mostly muscle that you lose if you're not carrying a lot of fat. It's not just skeletal muscle; it's also cardiac (heart) muscle. A major loss of cardiac muscle can easily be a contributing factor toward becoming another statistic. It makes sense for a person with HIV to increase their weight and to start when their asymptomatic.

I have dared to believe that HIV can't possibly be 100% fatal 100% of the time. I believe in maximizing my chances. Having control over the survival of my physical self has allowed me to devote energy toward the empowerment of my emotional and spiritual self. Divorced almost two years ago, I have lived to love again. I remain independent, able to work full-time, and my employer and co-workers are aware of my challenges. I have an insatiable appetite for self-improvement and living life. I thank God I've found the means.

### Update: Trial of Hepatitis B Drug Results in Deaths

Five participants in a National Institutes of Health (NIH) clinical trial have died of toxicities caused by the antiviral FIAU (Fialuridine). The clinical trial was evaluating the drug's safety in treating hepatitis B. FIAU has also been considered a potential anti-HIV agent.

The NIH trial began last Spring, and tested FIAU in fifteen individuals with hepatitis B for eleven weeks. In early June two participants developed neuropathy (nerve damage) from drug-induced liver damage and stopped taking the drug. NIH halted the trial, but since that time five more persons have been diagnosed with liver damage. Five of those seven people have died.

Early indications of potential toxicity were seen more than a year ago when a participant in a small, short study of FIAU developed severe neuropathy. His neuropathy was not definitively linked to the drug, so

NIH continued studying the drug this Spring. FIAU had previously been tested in dogs and the toxicities were not seen.

In humans, it appears that FIAU attacks the component cells of the liver, kidney and nerves, leading to liver and/or kidney failure and nerve damage. Dr. Jay Hoofnagle, the primary investigator for this clinical trial, fears that other antiviral drugs such as AZT and ddI may also be able to attack vital organs in the same way as FIAU. While AZT and ddI have demonstrable toxicities, no trial has shown such dire side effects.

These deaths are a reminder of the potential harm that can come from participating in a clinical trial of an experimental therapy. We should all recognize the risk that these five individuals, and all participants in clinical research, have taken to contribute toward finding effective treatments for HIV, hepatitis and other diseases.



## understanding hiv

### So Why Don't They Call 'Em T-Cells Anymore?

by Gregory J. Haas

Years ago, as we all awakened to the glaring dawn of the AIDS crisis, the only immunological term we had to deal with was "T-cell." As time has passed (and scientists have been more determined to confuse us with fancy terminology) the simple T-cell has "differentiated" into CD4, CD8, CTL, Th-1, Th-2 and more. What in the hell are they trying to prove?

In the beginning, scientists created names for T-cells and B-cells. Both are white blood cells called lymphocytes, which are important parts of the immune system. T-cells mature in the thymus ("T" for thymus) and B-cells mature in "gut associated lymphoid tissue." (The "B" comes from "bursa," where such cells mature in birds. The only bursas you or I have is in our joints. They don't give us B-cells—just bursitis.)

The immune system can be broken down into two distinct processes: Antibody-Mediated Immunity (also called Humoral Immunity) and Cell-Mediated Immunity. Antibody-Mediated Immunity uses antibodies to defend against foreign organisms. Cell-Mediated Immunity uses specialized cells to destroy infected cells.

B-cells play a key role in Antibody-Mediated Immunity (AMI). B-cells can turn into plasma cells, which then produce immunoglobulins (which is just a tongue-twisting way to say antibodies).

T-cells are the key to Cell-Mediated Immunity (CMI). CMI uses "killer T-cells" to destroy virally-infected cells and tumor cells. One way to measure the ability to show a successful cell-mediated response is a skin test. When a small amount of a microorganism (such as mumps or candida) is injected under the skin, a healthy body will attack it and produce a small bump under the skin surface. This is a delayed-type hypersensitivity (DTH) response.

A considerable amount of recent research is indicating that the cell-mediated arm of the immune system is more important than the antibody-mediated arm in both preventing initial HIV infection and in slowing progression to symptomatic AIDS and death.

So, let's look at these T-cells. When we first heard of them, they were broken down

into two groups: T4 "helper" cells and T8 "suppressor" cells. The terms "helper" and "suppressor" refer to the activity of those cells in terms of the antibody-mediated immune response. T4 cells help B cells develop into antibody-producing plasma cells. T8 cells suppress that antibody production.

But there's no reason to stop here. This can get much more complicated. First, stop calling them T4 and T8. The more accepted terms are now CD4 and CD8. "CD" stands for "clusters of determination." CD4 and CD8 are the names of molecules on the surface of the respective T-cells. It is impossible for a T-cell wearing CD4 to also wear CD8. Strict dress codes here in T-cell land.

Take a step back. T-cells (as well as B-cells) start out as "stem cells" in the bone marrow—buck-naked, without a cluster of determination on them. As they move through the thymus, they all get a loin cloth of CD3. So, if you ever see a CD3 count on a blood lab report, that's the same thing as your total T-cell count. In persons who are not infected with HIV, about twice as many T-cells choose CD4 molecules for apparel than CD8 molecules. In persons with HIV, that ratio is usually turned inside-out.

CD8 cells do more than suppress antibody production. They can also act as Cytotoxic Lymphocytes (CTLs). Cytotoxic lymphocytes—killer T-cells—can destroy tumors and cells that are infected by a virus. The CTL response is a major part of cell-mediated immunity. Recently there has been a lot of seemingly contradictory research on CD8 counts. Some research claims that high CD8 counts improve chances for staying healthy, while other studies indicate that low CD8 counts are better. It may be that having a lot of CTLs is good, while loads of suppressor T8 cells might be harmful.

Likewise, CD4 cells can do more than help with the production of antibodies. CD4 cells play a role in the activation of CD8 cells into cytotoxic lymphocytes. Therefore, CD4 cells can also be grouped into two classes. Those that are active in the cell-mediated immune response are called Th-1 CD4 cells. Th-1 cells produce chemical messengers (cytokines) such as Interleukin-2 (IL-2), IL-

12, and Interferon-gamma. Th-2 CD4 cells mainly produce the cytokines IL-4 and IL-5 and are active in the antibody-mediated immune response.

These two types of CD4 cells seem to be very competitive. The chemicals released by Th-1 cells inhibit Th-2 cells, and Th-2 cells return the favor. In general, the Th-1 response is dominant early in any infection, then gives way to antibodies and Th-2. Some researchers speculate that the switch from Th-1 to Th-2 in HIV disease is a warning sign for disease progression.

Interest in the cell-mediated arm of the immune system is expanding, and some experimental therapeutic approaches for HIV infection are attempting to "lock-in" the Th-1 response. A prime example of this is the Salk vaccine. Other approaches include using the cytokines that predominate in the Th-1 response including IL-2 and interferon-gamma. A third strategy is to increase the number of cytotoxic lymphocytes by transfusing HIV-specific CTLs from a healthy seropositive individual into someone who has more advanced disease.

So is this the end? Of course not. Researchers bandy about terms such as CD38 and CD56. I'd love to write about them too, but first I have to figure what they are.

**Antibody-Mediated Immunity:** AMI. *Humoral Immunity.* The part of the immune response that uses B-cells and antibodies to neutralize invading organisms.

**CD4 Cells:** T-lymphocytes that can secrete proteins to 1) assist CMI (Th-1), or 2) "help" AMI response (Th-2).

**CD8 Cells:** T-lymphocytes that can 1) act as cytotoxic lymphocytes, or 2) "suppress" the antibody response.

**Cell-Mediated Immunity:** CMI. The part of the immune response that primarily consists of T-cells. It is involved in the killing of virally infected cells.

**Cytotoxic Lymphocyte:** CTL. *Killer T-Cells.* Type of CD8 cell that can kill cells infected with a virus. They are specifically made for a particular virus.

**Helper T-Cells:** The function of CD4 cells that "helps" the production of antibodies.

**Natural Killer Cells:** NK. Lymphocytes that can destroy virally infected cells. Not specific to any virus.

**Suppressor T-Cells:** The function of CD8 cells that "suppresses" the production of antibodies.

**Th-1:** CD4 cell that makes proteins involved in CMI.

**Th-2:** CD4 cell that makes proteins involved in AMI.

**Th-1/Th-2 Switch:** When the AMI response (Th-2) becomes dominant over the CMI response (Th-1).



## updates

### Risky Drinking Water

From *Treatment Issues*, August 1993

Tap water in American cities may pose risks to PWAs, according to several recent reports. A study presented at the General Meeting of the American Society for Microbiology suggests that drinking water in Los Angeles may be a source of *Mycobacterium avium intracellulare* (MAI) as well as other mycobacteria. The study found non-tuberculous mycobacteria in all hospital water supplies sampled, 34 out of 40 home water samples, and 11 of 13 reservoir samples. MAI was found in 9 of 10 hospital water supplies, 11 of 40 home samples, and 5 of 13 reservoir samples.

*The Report of the Expert Panel on New York City's Water Supply* (1993) noted that potentially infectious levels of *Cryptosporidium* and *Giardia*, two serious intestinal parasites, were found in the city's water supply. Furthermore, the panel noted that measures to protect the city's water supply from these pathogens, such as an improved filtration system, were unlikely to be implemented within the next 10 years.

New York City officials reported July 27 that potentially infectious levels of *E. coli* bacteria were found in the water supplies of two neighborhoods. They warned people with HIV to exercise extra caution.

Larry Waites, a San Francisco physician, recommended in his regular column in *The Advocate* that PWAs with CD4 counts under 100 or those with recurrent bowel problems drink only bottled water. If bottled water is too expensive, he advises tap water be boiled and then stored in containers which have been washed in hot soapy water, rinsed, and allowed to dry completely.

*(Ed note: Boiling water in farming areas may periodically be dangerous due to nitrate contamination. A good way to assure good drinking water is to find a store that offers a reverse osmosis filter and refillable jugs. Under reverse osmosis, water is forced through a semi-permeable membrane that blocks microorganisms such as *Cryptosporidium* and *Giardia* and dissolves solids, such as heavy metals, lead, nitrates, salts, and salt-based substances.)*

### ACTG 175

ACTG 175 is a clinical trial that is being conducted by the AIDS Clinical Trials Group of NIAID. This large study started in February 1992 and involves almost 2500 participants, including about 150 with hemophilia. It is designed to compare the effectiveness of four different treatment regimens (AZT alone, ddI alone, AZT plus ddI, and AZT plus ddC) in persons with asymptomatic HIV infection and CD4 counts between 200 and 500. In ACTG 175, the group of participants taking AZT alone are considered the "standard therapy" group against which the other groups will be compared.

Recently released data from the European Concorde trial (which showed no difference in outcomes between immediate AZT use and delayed AZT use in asymptomatic persons) and from ACTG 155 (which showed no overall difference in outcomes between AZT+ddC combination therapy and either AZT or ddC alone in persons with fewer than 300 CD4 cells) call into question the design and goals of ACTG 175.

Data collected from the voluminous trials of AZT, ddI, and ddC indicate that these drugs have marginal effects at best. The

confusion about the effectiveness of AZT will make the results of this trial difficult to interpret.

In an effort to collect enough data to get significant results, the trial has been extended for another six months (so that the end of the trial will now be April 1995), and data collection (about disease progression and survival) will be extended beyond that date to get further information about the long-term effects of the therapies under study. ACTG investigators will also cooperate with the European investigators of the Delta trial, which is similar to ACTG 175 except that the participants have more advanced disease (CD4 counts less than 350). Combining the data from both trials may enable the researchers to find meaningful differences in the treatment regimens and may provide useful information about prognostic variables and surrogate markers that might help streamline future clinical trials.

As of May 1993, the last meeting of the Data and Safety Monitoring Board, no significant differences were seen among the treatment arms, and no significant toxicities were found.

### Milwaukee Saga Goes On

The contamination of the Milwaukee water system with the micro-organism *cryptosporidium* which caused thousands of cases of diarrhea continues to affect persons with AIDS in the city. Doug Nelson, the Executive Director of the Milwaukee AIDS Project, says that the contamination of the drinking water supply has led to an increased number of AIDS-related deaths in the city.

Nelson said that 67 clients have been diagnosed with *cryptosporidiosis* in the last four months. Seventeen of those have died, and another 20 are seriously ill. In the four

months prior to the outbreak, only five cases were diagnosed, one of whom died. "The conditions surrounding death have included diarrhea to the end-stage and inability to eat. There is no other reason we can see for the doubling of the death rate since mid-May."

For people who are not immune compromised, infection with *cryptosporidium* usually causes diarrhea and illness for about ten days. The epidemic in Milwaukee's general population peaked in April and is now over. "But for us," said Nelson, "it continues in a devastating way."

Amount the Health Insurance Association of America spent last spring on healthcare policy ads: \$4,000,000

Number of TV stations that have refused to air a consumer group's ad advocating a Canadian-style healthcare system: 8  
Ratio of number of Canadians who favor a U.S.-style healthcare system to those who believe Elvis is alive: 1:2

From Harper's Index, *Harper's Magazine*, July 1993



## business, politics & law

### Know Your Rights:

### Product Liability Claims for Infection with HIV Through Factor Concentrates

by Judith Kavanaugh

This article discusses in very general terms the potential claims and legal rights of persons with hemophilia, and litigation against manufacturers of HIV-contaminated Factor VIII and IX products. Persons with hemophilia have been discouraged from pursuing their claims based on misleading and erroneous information about the companies' culpability. Until recently, cases brought by HIV-infected persons with hemophilia have often not succeeded because of several factors:

- 1) an aggressive and coordinated industry defense, which has until recently "rolled over" persons with hemophilia and the smaller firms that represented them;
- 2) the inability to uncover information about the companies' conduct, including instances where sealing of the records from cases the industry lost or settled;
- 3) industry's hiring available expert witnesses, including former NHF officials such as Peter Levine, Louis Aledort, and Margaret Hilgartner to testify *against* persons with hemophilia;
- 4) dissemination of misinformation to persons with hemophilia about the merits of the claims, their legal rights, and the use of intimidation tactics, that include implied threats to stop producing concentrates; and
- 5) lack of case precedent addressing the novel legal issues these cases have presented.

These factors are changing, as events in Florida and other jurisdictions have demonstrated over the last two years. The first set of cases have paved the way for future claims by uncovering facts and establishing legal precedents. This does not mean that all cases will be successful. Children born after 1981, moderate concentrate users, and those who used product now known to have been made from contaminated plasma have the best cases. Spouses and children who were infected by association with an individual with hemophilia during the "carrier" stage or by pregnancy also have good claims. Cases involving those who have had spontaneous

brain bleeds; were heavy users of factor; or had very serious, life-threatening bleeds between 1982 and 1984 are more difficult, although also viable. Each case must be evaluated on its own merits by the counsel involved.

#### Nature of the Claims

There are essentially five categories of claims:

- 1) claims for negligent manufacture arising out of the companies' failure to use reasonably available techniques to make the product safer, or to screen out high AIDS risk donors from the pools out of which factor concentrates are made;
- 2) fraud, negligence and false advertising claims for the companies' admitted failure to warn or inform the medical or hemophilia community about the magnitude of the AIDS risk and disseminating or allowing to be disseminated misleading information which downplayed the risk and encouraged factor use;
- 3) claims for failure to recall product each company knew was made from plasma collected from high risk donors;
- 4) claims of spouses and children of persons with hemophilia who were infected as a result of sexual relationships and pregnancy; and
- 5) claims filed by surviving family members of persons who have already died from AIDS.

#### Recent Legal Rulings and Issues

##### *The Statute of Limitations Has Not Necessarily Run*

Because of the time which has passed, the major legal hurdle to overcome is the statute of limitations laws in various states. These laws establish the time frame after an injury occurs within which any legal action must be filed. These laws vary from state to state. The statute in Florida, for example, is four years from the date a person knows or reasonably should have discovered that the

injury was a result of the wrongdoing of another ("cause of action"). Most states recognize the "discovery rule," which holds that in products liability cases, the statute of limitations begins to run when a person "knew, or with due diligence, could have discovered" such knowledge.

In negligence cases, which under the Blood Shield Laws applies to factor concentrate injuries in most, but not all states, there are two elements which must be present for the statute to be triggered: 1) knowledge of an injury; and 2) knowledge of a possible negligent act by the defendant as the cause of the injury. These are usually questions of fact for the jury to resolve. In hemophilia cases, the problem has focused on knowledge of injury and when it occurred. The companies invariably argue that the statute begins to run upon knowledge of a positive HIV antibody test, which occurred mostly between 1985 and 1989.

It must be remembered, however, that the record indicates that the significance of a positive HIV antibody test was not known until later; the documented record indicates that most persons with hemophilia were told not to worry about a positive antibody test, as it was a signal only of exposure to HIV. Many persons with hemophilia still do not know if they are actually injured, because, although exposed to HIV, they have no physical symptoms of illness. At least one court has ruled that knowledge of injury does not occur until manifestation of symptoms and an AIDS diagnosis.

Similarly, because the material facts surrounding the companies' actions in 1982-1985 have only recently become discovered, and then only after arduous and expensive litigation, most persons with hemophilia had no way of knowing about the companies' negligent conduct or that a cause of action existed. The inability to discover the facts showing a "reasonable possibility" of negligence on the part of the company whose product(s) caused the infection should "toll" the statute. There also is a question of fact



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whether over the last ten years the companies have fraudulently concealed the cause of action against them by disseminating or allowing to be disseminated false or misleading information about their conduct and concealing material facts.

### *Market Share/Alternate Liability Principles Now Apply*

Courts have recently adopted new legal principles that have relaxed the traditional showing necessary to prove causation—that a specific dose of a specific company's product caused the infection. Florida courts initially applied to these HIV cases new legal principles developed in other "creeping disease" cases such as DES-related cancer and asbestosis, where the physical manifestation of the disease occurs many years after the injurious exposure. Florida has applied both the alternate liability principles used in asbestos cases, and the market share liability theories utilized in the DES cases to HIV infection from blood products. Courts in Hawaii, California, and Illinois have now also used these or related principles in cases involving hemophilia-related HIV infection.

### *Evidence of the Companies' Negligence Has Been Uncovered*

As noted above, the so-called "blood shield" laws in many states make these cases more difficult than standard products liability cases, by requiring that the plaintiff show negligence, or wrongdoing, on the part of the manufacturers as a cause of the injury. Persons with hemophilia have been led to believe that they had no recourse against the drug manufacturers, because what happened to them was an unavoidable tragedy.

That is not true. The evidence now available indicates that the companies had the technology to make the product safer in the late 1970s, but apparently not the financial incentive to use it. Had they done so, even those apparently infected before 1982 would arguably have escaped infection, since it is generally agreed that widespread HIV infection of the blood supply occurred some-

time after 1976-78.

The companies also knew by the end of 1982 that 1) all of the product on the market could transmit AIDS, 2) alternative treatments, such as the use of single donor products, posed much less risk. The companies did not disclose those facts to the hemophilia community, apparently in order to keep their market until the new, more expensive, safer product was ready to go. Since nearly half of all persons with hemophilia were infected in 1983 and 1984, many would have been saved from this tragedy if they had stopped using concentrates and managed their hemophilia through other means just for that limited period. But they were not given the chance to make that choice.

### **Conclusion**

Persons with hemophilia have not pursued their claims out of a mistaken belief that they had no cause of action. The evidence indicates that this belief has been fostered in large part by the blood products industry and those aligned with it. The purpose of this brief article is to inform persons with hemophilia of their rights so that, unlike the events of ten years ago, they can make informed choices about what they are to do about the wrong they have suffered. There is no question that some cases involve hotly contested litigation and first impression legal issues. Whether an individual elects to pursue a claim is a matter of personal choice, to be assessed in consultation with experienced counsel.

Time is running out, and now that the facts giving rise to these claims have been made public, the statute of limitations may be running. Many cases are being filed in various states, including a score of cases already filed in Florida. Individuals considering action on their claims should contact an attorney as soon as possible to evaluate their cases and avoid losing their rights altogether.

(Ed. note: A footnoted version of this article is available from The Committee of Ten Thousand.)

## FDA to Restrict Access to Vitamins and Minerals

Results from the Berlin Conference were devastating to persons with HIV who are using standard therapies (AZT, ddI...). At the same time, new studies added to the growing evidence that nutritional supplements, particularly antioxidants, are important tools in fighting disease progression.

The Food and Drug Administration (FDA) recently recommended the restriction of the sale and labeling of nutritional supplements. As it now stands, these recommendations will become law on December 31, 1993.

Many complexities surround the issue of the pending regulations that would govern dietary supplements. But at heart, the problem is simple: The FDA has concluded that many supplements are used therapeutically, not nutritionally. They are used as drugs, not as foods, and therefore, according to the FDA, they should be regulated as drugs, not as foods.

The agency has taken particular aim at amino acids and herbs, but has also expressed reservations about high-potency vitamins and about minerals for which there is no Recommended Daily Allowance (RDA). Amino acids include NAC (n-acetyl-cysteine) and lysine—supplements used by many HIV-positive persons. Nutrients that do not have an RDA include co-enzyme Q10 and selenium. Under the law, it would be impossible to buy high-dose vitamin C, or herbs such as echinacea, garlic (in pill form), and milk thistle.

What is needed is a law that establishes dietary supplements as a class of compounds separate from food and drugs and that regulates them as such, with specific standards for safety and for health claims. Such legislation, the Dietary Supplement Health and Education Act, has been introduced by Sen. Orrin Hatch in the Senate (S. 784) and by Rep. Bill Richardson in the House (H.R. 1709). These bills, although slightly different in their details, would bring fair and rational regulation to supplements.

(The FDA has extended the Public Comment Period on this until Dec. 31, 1993.)



## business, politics & law

### Pro and Cons of the Veterans' Health Care Act

by Dana Kuhn, Ph.D.

The Veterans' Health Care Act went into effect on November 4, 1992. Within this Act there was an initiative for the Hemophilia Treatment Centers (HTCs). The initiative requires the blood manufacturers to sell their factor products to hospitals and/or approved agencies at a discounted price. For example, recombinant factor would be discounted (to the distribution centers) to 66¢ per unit. The motivation and concern behind this act with regards to hemophilia is noble. The rationale is two-fold. First, factor could be sold to persons with hemophilia at a lesser price than the home care companies. This would reduce the strain on health insurance policies and their ceilings. Second, given the possible decrease of Maternal, Child and Health Bureau (MCHB) funding set aside for HTCs, there needed to be an income source to absorb those impending cutbacks. HTCs could receive factor at the discounted price, then mark-up the costs enough to cover the loss of MCHB funds while maintaining low prices for the clients. But, as with all programs and services, there needs to be quality assurance so that the benefits are not abused.

One concern with this program is that there are not adequate regulations on the size of the mark-up. The discounted price for recombinant factor (66¢) could sell to persons with hemophilia for as much as \$1.18 per unit (legal Average Wholesale Price—AWP). This mark-up would benefit the HTCs and the physicians' research programs but strain insurance policies. A balanced mark-up must be ensured to benefit both HTCs and persons with hemophilia. Unless regulations are mandated, even the most honest person can be tempted to abuse the system for gain.

A second concern is the effect of having the HTCs' funding tied directly to the use of factor. Will physicians prescribe only products for which they have contracts, or will prescriptions be written for what the patient prefers? Such a system also builds in further disincentives for HTCs and physicians to warn the hemophilia community about any potential dangers from using factor products. We know the tragedy that resulted

from less direct disincentives a decade ago.

A third concern is with HIV care. It seems that the Veterans' Health Care Plan does provide for HIV medications. But who will provide the home health care for patients who do not need to be hospitalized? Will the HIV medications be charged to the patient? Having home care companies provide the factor has advantages. For one, most HIV drugs are considered ancillary and these are often provided at cost. Second, the home care companies also sometimes provide or arrange home hospice care. It does not seem that these approved hospitals or agencies will be able to provide the hospice service needed by many HIV-positive persons with hemophilia.

How did this hemophilia initiative of the Veterans' Act materialize? The National Hemophilia Foundation, through the efforts of Alan Brownstein and MARC Associates (NHF's Washington lobbying firm) pushed for the adoption of the plasma pricing/discounting aspect of the plan. However, the NHF minutes do not give any indication that this was approved by either the NHF Executive Committee or the Board of Directors. It seems that an important issue such as this should have been brought before the Board for approval. Were any "grass roots" consumers consulted about how the Act might affect them? Once again, NHF is true to form. It decides for its constituents instead of deciding with them.

(Ed. note: The Common Factor will continue coverage of the Veteran's Health Care Act in our next issue.)

#### Corrections:

In the article in the June 1993 issue of *The Common Factor* about Managed Competition and Health Care Reform, a sentence that read, "With this plan, it might be harder to get a doctor to prescribe recombinant instead of monoclonal factor" should have been, "high-purity instead of intermediate-purity factor."

### AZT Patent Update

A federal judge has ruled Burroughs-Wellcome owns the patent on AZT. (See previous story in *Common Factor* #5.) U.S. District Court Judge Malcolm Howard rejected a challenge by two rival drug companies — Barr Laboratories of Pomona, N.Y., and Novopharm Ltd. of Canada — who want to make generic versions of AZT.

Burroughs-Wellcome President and CEO Philip Tracy quickly lauded the verdict. "We never had any doubt that Burroughs-Wellcome scientists alone discovered the use of AZT as a treatment for HIV infection and AIDS," he said.

However, Barr Laboratories vowed to appeal. "We are confident that once those issues are clearly defined, a new trial will establish the inventorship rights of the NIH scientists, and Barr will be able to bring a less expensive generic AZT to market," company President Bruce Downey said.

### Update: Foscarnet For CMV Maintenance

From *Treatment Issues*, September 1993

Foscarnet may be the drug of choice for CMV encephalitis, a research team from the National Cancer Institute reports in *Antimicrobial Agents and Chemotherapy*. Foscarnet crosses the blood brain barrier and can be detected at therapeutic levels in cerebrospinal fluid after a single dose. However, the clinical efficacy of foscarnet for CMV or herpes encephalitis is still unresolved.

In addition, a small randomized study of 32 PWAs with CMV retinitis suggests that higher maintenance doses of foscarnet may be superior to lower doses. The study, published in *The Journal of Infectious Disease*, found a daily dose of 120mg/kg significantly extended survival time and prolonged the time to retinitis progression compared with lower maintenance doses of the drug (60 or 90mg/kg/day). Median survival was 157 days for the 90mg dose compared with 336 days with the 120mg dose. Kidney toxicities, a well-known side effect of foscarnet, were slightly more common at the 120mg dose; other adverse effects did not occur more frequently.



## business, politics & law

### What's Wrong With AIDS Research

John S. James, Editor, *AIDS Treatment News*. Reprinted from *The Nation*, July 5, 1993

AIDS research is a looking glass that shows what's wrong with medical research overall. Why are there so few cures or important improvements in treatment despite an enormous financial investment—and despite the fact that we live at a time of immense advances in our knowledge of basic biology? In AIDS, at least, the answer has been obvious for years to anyone who looked. But you had to do your own investigation and analysis, because it wasn't in the general press, medical journals or government reports.

Mainstream AIDS research has been technically competent, because it is possible to hire trained statisticians, research nurses, laboratory technicians, etc. The problem has been lack of coordination to fit the pieces together. And this lack of strategy has scarcely been noticed, for two reasons.

First, much of the research is designed by people with little real-world sense. Some projects will not contribute to *any* conceivable strategy, since it is clear even before

they begin that the results—no matter what they are—will be obsolete, marginal or otherwise of no major importance.

Second, strategy isn't missed because almost all that happens in the super-expensive world of research on people happens because major pharmaceutical companies stand to benefit; this is true even when it's government money that is being spent. And those who run big companies have no incentive to make major advances, as long as no one else does. Their incentive is to push a product onto the market, not solve a public health problem. There are examples of commendable public service in the corporate pharmaceutical world, but they are rare.

So when a new drug shows promise in the laboratory, it almost always stops right there. Academics can run laboratory tests and publish papers, but they cannot afford the animal work and other preparation needed for the first human trial. Unless a company has patent rights, the capital, the interest, the right scientists available and the ability to

get the drug manufactured, and also the willingness to start down a multiyear path likely to cost many millions of dollars, the potential drug stays in limbo forever.

Since the beginning of the AIDS epidemic, only scattered activists and other individuals have argued that there is a public interest in finding a cure. There has been no institutional support. Government officials may have been prevented from giving it by the pervasive hostility of the Reagan and Bush administrations.

Even now, a disturbing pattern seems to be emerging. President Clinton proposes a correct policy, but with no public education or political groundwork to back it up. Since hate groups generate thousands of opposing telephone calls, and there is almost no one organized to generate calls on the other side, Clinton can drop the ball and walk away, claiming to be "for" the right thing, but without taking any responsibility for its implementation. (For example, the United States now has an immigration policy that openly promotes discrimination against people with HIV, creating an incentive for everyone in the world *not* to get tested, *not* to get treatment if HIV-positive and *not* to get the education that would help them avoid spreading the virus to others.) If the current trend continues, indifference may be institutionalized while entire communities around the world are written off.

The worldwide fight against AIDS cannot succeed without political support. This requires more people committed to activism, more money for advocacy, better leadership of AIDS organizations, more coalition building and more use of modern technology (such as fax broadcasts for immediate, targeted delivery of action alerts to local organizers).

### Update: Clinton Appoints AIDS Czar

From *Positively Aware*, July 1993

President Clinton appointed Kristine Gebbie as the White House Aids Coordinator on June 25, 1993. Gebbie will be responsible for creating domestic AIDS policy and for coordinating AIDS efforts among public health and social agencies. She has served as the secretary of the Washington State Department of Health and the administrator of the Oregon Division of Health. Gebbie is expected to make HIV and AIDS prevention a priority. Several other nominees before her had turned down the job.





## reader's forum

### Barry Huff

Spokane, WA

I was a naive person with hemophilia and HIV harboring half-baked views on Alan Brownstein and NHF until I read Congressman John Dingell's 1990-1 report on *Blood Supply Safety*. The testimony from Mr. Brownstein before the Subcommittee on Oversight and Investigations sent chills down my veins. Expert physicians from around the U.S. affirmed that HIV infection among people with hemophilia, and blood recipients in general, could have been avoided had the FDA, Red Cross and the American Association of Blood Banks (AABB) acted in a competent manner. However, Mr. Brownstein sidesteps accusations by these physicians as to NHF's role in encouraging factor VIII or IX usage by people with hemophilia.

In this hearing Mr. Brownstein rightly discusses the discrimination experienced by many of us in our communities. He takes the time to educate the committee on the nature of hemophilia and clotting factor. He talks about the increased cost in clotting factor over the past ten years. But it was this statement that bothered me: "NHF has been aggressive in its efforts to ensure a safe blood supply to get effective treatments that are free of viruses and to provide assistance to our community."

The above statement is not consistent with NHF action. For example, Dr. Ratnoff, a hematologist with over 40 years experience challenged Mr. Brownstein to answer why NHF continued to advocate the use of HIV contaminated blood products after this

danger was discovered. Brownstein failed to give an adequate answer to that question. Brownstein bows to MASAC, the Medical and Scientific Advisory Council, as to responsibility for NHF's policy regarding blood products at that time. Furthermore, Brownstein states that "any position of our medical leadership needs to be eventually ratified by the consumer leadership." Does he actually think that the consumer leadership was well informed about HIV during the early stages of this disease? There was not even a consensus in the scientific community as to how AIDS was spread, so why would MASAC play the role of an omnipotent scientist? There was no admission of fault by Brownstein or NHF as to Ratnoff's accusation. And there certainly was no "aggressive" action by NHF for the safety of our blood supply.

Brownstein further attempts to sidestep responsibility by saying that "we" did not know AIDS was a virus in the early 1980s. However, there were physicians who were certain that AIDS was spread by blood transfusion. One such physician was Dr. Engleman of the Stanford University Blood Center, which was the first blood bank in this country doing surrogate testing of blood such as T-cell counts as a marker for suppressed immune response, indicating the probability of HIV infection. Such surrogate testing occurred at Stanford in July of 1983, almost one and a half years before a specific test for HIV was developed. Dr. Bruce Evatt of the CDC found the same need for T-cell testing as early as November of 1982. The Stanford Blood Center was criticized by other blood banks for initiating a blood donor screening program for T-cell ratio by those who claimed there was no proof that AIDS could be transmitted by blood transfusions, and that such a test was too costly.

Brownstein's argument was that MASAC agreed with Evatt about the need for surrogate testing and the need to protect the blood supply as early as 1982. If this was true, then why were we not encouraged to be tested for low CD4 counts in 1982 or 1983? Brownstein continually contradicts himself

throughout this hearing. He wants NHF to play the role of the martyr by saying the blood banking industry did not listen to our "prestigious" MASAC medical council in recommending blood supply safety regulations. There is nothing prestigious about a council that failed to live up to its duty to inform us of potential harm in using factor VIII and factor IX concentrates.

It seems to me that Dr. Engleman and the Stanford University Blood Center has a record of a truly "aggressive" response to the AIDS crisis. In fact it was Stanford that paved the way for other blood banks to develop similar policies, not NHF. And it is Dr. Engleman who gave a balanced criticism of the American Red Cross, the AABB, and the FDA—not Brownstein or NHF. The real sin in this blood safety scandal is not the sin of commission, but rather the sin of omission. And it was NHF who omitted to inform people with hemophilia about the risks of continuing to use blood products known to be contaminated. It was Dingle's hearing on *Blood Supply Safety* that most convincingly changed me from being uninformed and uncertain toward Brownstein and NHF into being an informed, pessimistic realist.

### To the Editor,

I very much value your publication and it certainly has helped me. I was switched from aerosolized pentamidine to Dapsone recently. I first learned of ddI's interaction with Dapsone in your newsletter and changed my dosage patterns. Unfortunately, it was too late and several weeks later I was diagnosed with a mild case of PCP, but I feel it could have been worse if not for the dosage change made a few weeks earlier.

It is a shame but a reality that information seems to move faster through the consumers' media than the medical media. I do know your Editor's note in the June 1993 *Common Factor* helped trigger my doctor into notifying all patients taking those drugs to separate their administration.

Keep up the good work,

Mike Sutton, former President of NHF

#### The Question Box

This box is an opportunity for dialogue about specific topics of concern for people with hemophilia and HIV. If you have responses to these questions, please send them in.

- Has your HTC, physician or insurance company refused to provide high-purity—monoclonal or recombinant—factor? Even after you have asked?
- Does your HTC or physician restrict you in what products or brand of factor you can use?

If you have questions you'd like posted in this space in future issues, please submit them.



## reader's forum

### Mohamed Ali Shaaban

Ramsey, NJ

About six months ago my CD4 count was 350 and my platelet count was fluctuating between 75,000 and 85,000. I've been on antiretroviral therapy—I take AZT (300 mg daily), ddC (1.550 mg) and ddI (300 mg). However, I dropped the ddI because I could not tolerate it. I didn't have an appetite for food and was constantly tired. My overall health was not well at all.

I started to look into herbal extracts as an alternative therapy, even though my hematologist didn't believe in it. After reading about herbs I decided to try some and see what happened. To my surprise, my CD4 count went up to a record high of almost 500 and platelet count went up to almost 150,000. Still, I continue to have episodes of fatigue, but I'm aware of my surroundings and continue to maintain my health at a better rate.

The following herbal extracts can all be bought from health food stores.

**Echinacea:** I mix 10 drops in coffee (or other beverage) two or three times a day. This herb is known to be an antiviral and may also increase CD4 counts.

**St. John's Wort:** I mix 10 drops of extract per teacup. It contains small amounts of hypericin, which is an antiviral.

**Siberian or Korean Ginseng:** I take 100 mg a day as capsules or about 10 drops a day as an extract. It increases the human body's capacity to adapt to abnormal physical, chemical and psychological factors. It also increases white blood cell counts.

**Ester C with Metabolites:** I take 275 mg a day of this special formulation of vitamin C. That dose is equivalent to 1000 mg of ordinary vitamin C. It enters the blood stream faster and shows levels four times higher in the white blood cells than conventional ascorbic acid.

**Bee Pollen:** I take 15 drops daily. It gives energy like honey.

**Kwai Garlic:** Highly concentrated garlic tablets that are odor free. I take two tablets daily. Naturally cooked garlic is much better for you and can fight HIV. Don't forget that garlic also keeps away unwanted vampires.

**Multivitamin/Multimineral Formula:** Always take vitamins and minerals after

### Congestive Cardiomyopathy in AIDS

by Angie Hendrickson

Congestive Cardiomyopathy (COCM)—heart failure—is a new issue that is being researched in AIDS, and its cause is surrounded in controversy. It is unclear whether HIV itself leads to COCM or whether drugs like AZT can cause heart failure. Although COCM is a danger to all with HIV, its primary target is children.

We had never heard of this condition until we almost lost our ten year old son Brandon to COCM in January 1993. Since that time my husband and I have been looking further into COCM—and the facts are frightening. There is a dramatically increasing incidence of COCM, and researchers are scrambling to understand what's happening. At this time I'm not quite prepared to present the different arguments surrounding the cause, but I feel that the need to inform readers of *The Common Factor* about COCM is an urgent one. If you don't recognize the signs and symptoms of heart failure, it will certainly cause death.

In the June 9, 1993 issue of *The Journal of the AMA*, Dr. Lynn Luginbuhl recom-

ended that all children who are HIV-infected should undergo routine monitoring of left ventricle function by echocardiography. She noted that the incidence of congestive heart failure in HIV-positive children is high, that it is likely to increase dramatically, and that it is currently underreported since the clinical signs are often mistakenly assumed to have other causes. It is also essential to monitor for COCM because HIV-infected

children respond well to therapy, especially if treatment is started early. Since echocardiography is not available in all geographic regions, it may be necessary to devise ways to make echocardiography accessible to all HIV-infected children.

My husband and I have found that most of our population, and health care providers know very little about Congestive Cardiomyopathy. It needs to be discussed!

Please call me if you have any questions or comments at (414) 867-4320 (W) or (414) 446-3154 (H).

*It is essential to monitor for COCM because children respond well to therapy if treatment is started early.*

### Update: IND Announced for PCP Treatment

From *Positively Aware*, July 1993

NeuTrexin (Trimetrexate Glucuronate) is now available as a therapy for pneumocystis carinii pneumonia (PCP) under a treatment IND. The drug's manufacturer, U.S. Bioscience, has received Food and Drug Administration permission to expand access of the drug for PWAs who cannot tolerate or who fail to respond to intravenous pentamidine or TMP-SMX (Bactrim). NeuTrexin penetrates normal cells and cells infected with organisms such as PCP. Physicians can enroll PWAs into the IND by calling Bioscience at (800) 537-9978.

*"I spent the afternoon musing on Life. If you come to think of it, what a queer thing Life is! So unlike anything else, don't you know, if you know what I mean."*

—P.G. Wodehouse



## resources

### Subscription List

- Action Now!**, H/HIV Peer Association, P.O. Box 931, Nevada, CA 95959. (615) 385-5425. \$15/year.
- AIDS Action Bulletin**, 2105 N. Charles St., Baltimore, MD 21218. (410) 837-2437.
- AIDS/HIV Treatment Directory**, published quarterly by AmFAR, 1515 Broadway Suite 3601, NY, NY 10036 (212) 719-0033. It is \$30/year (4 issues), but a free sample is available from the National AIDS Information Clearinghouse, (800) 458-5231.
- AIDS Treatment News**, PO Box 411256, SF, CA 94141 (415) 255-0588. \$100/year for non-profit organizations (24 issues), \$40 for HIV+ persons.
- Being Alive**, 3626 Sunset Blvd., LA, CA 90026. Subscriptions are \$20/year, but free for those who cannot afford to pay.
- Bulletin of Experimental Treatments for AIDS (BETA)**, for subscription information call (415) 863-2437.
- Critical Path AIDS Project**, 2062 Lombard St., Philadelphia, PA 19146. (215) 545-2212. Free for persons infected with HIV, \$50/year for others.
- Disability Rag**, Box 145, Louisville, KY 40201. \$17.50 per year.
- I Heard It Through The Grapevine**, Alternative Therapies. AIDS Project LA, 6721 Romaine St., LA, CA 90038. (213) 962-1600.
- Medical Alert**, published by NAPWA, 1413 K St, NW Washington DC, 20005. (202) 898-0414 free, bimonthly.
- Notes From the Underground**, by the PWA Health Group. 150 W. 26th St. Suite 201, NY, NY 10001. \$35 for individuals, or sliding scale.
- PI Perspectives**, published by Project Inform, 1965 Market St., Suite 220, SF, CA 94103. (800) 822-7422. Subscriptions are free.
- The Positive Woman**, 1959 4th St., NE, Washington, D.C. 20002. \$12 for individuals, \$40 for non-profits, \$75 for businesses.
- Positively Aware**, 1340 West Irving Park #259, Chicago, IL 60613 (312) 472-6397. \$25/year (12 issues), but free for persons with AIDS.
- PWAlive**, 2025 Nicollet Ave, Minneapolis, MN 55404.
- SIDA Ahora** (Span/Eng), 31 W. 26th St., NY, NY 10010. (212) 532-0290.
- STEP Perspectives**, 127 Broadway East Suite 200, Seattle, WA 98102. (800) 869-7837.
- Treatment and Data Digest**, ACT UP/NY, 135 W. 29th St., NY, NY 10001. (212) 564-AIDS. \$40/yr.
- Treatment Issues**, newsletter of Gay Men's Health Crisis, 129 West 20th St., NY, NY 10011. Suggested contribution for those who can afford it is \$20, \$10 for all back issues.
- Wellspring**, (617) 437-6200.
- WORLD (Women Organized to Respond to Life-threatening Diseases)**, P.O. Box 11535, Oakland, CA 94611. (510) 658-6930. \$20-50 individuals, \$50-100 businesses, free to those who can't afford it. Available in Spanish as *Mundo*.

#### Periodicals that have in-depth coverage of the Berlin Conference.

**AIDS Treatment News**: Issues 178, 179, 181  
**Medical Alert**: Good coverage of women's issues, July  
**Positively Aware**: July  
**Project Inform**: Briefing Paper, Number 3, July  
**STEP Perspectives**: July  
**Treatment Issues**: July, August, September

### Resources and Phone Numbers

- AIDS Action Committee of Boston**, Resource Library: (617) 437-6200 x432.
- AIDS Action Council** (national advocacy): (202) 986-1300.
- AIDSDRUGS, AIDSLINE, AIDSTRIALS** (databases provided by the National Library of Medicine): for free info, call (800) 638-8480.
- AIDS National Interfaith Network**: 3001 St., NE, Suite 400, Washington, DC 20002. (202) 546-5103.
- AIDS Treatment Resources** (experimental treatment & information exchange): (212) 268-4196.
- American College of Traditional Chinese Medicine**: (415) 282-9603.
- Body Positive Resource Center**: 175 NE 36th St. Miami, FL 33137. (305) 576-1111.
- Canadian HIV Trials Network**: 200-1033 Davie St. Vancouver, BC V6E 1M7. (604) 631-5210.
- Carl Vogel Foundation** (non-profit buyers' club for medications and vitamin supplements): (202) 289-4898.
- Congressional Switchboard**: (202) 224-3121.
- Connect! Friendship Service**: (310) 289-3216.
- COTT West**: Box 5338, Santa Monica, CA 90409. (310) 396-3680.
- Experimental Treatments Hotline**: (212) 239-5523.
- FAACTS** (Facts on Alternative AIDS Compounds and Treatments): 111 Gates St. San Francisco, CA 94110. (415) 648-1357.
- Gay Men's Health Crisis Medical Information**: (212) 337-3565.
- HANDI** (Hemophilia and AIDS Information): (800) 42-HANDI x3054.
- HEAL** (Health Education AIDS Liaison) (Advocates for alternative therapies; support groups): (212) 674-HOPE.
- Healing Alternatives Foundation** (non-profit buyers' club for medication and vitamin supplements): (415) 626-2316.
- Health Care Reform Task Force (Hillary Clinton)**: The White House, Washington, D.C. 20500. FAX (202) 456-6241.
- Hemophilia Foundation of Michigan**: 411 Huron View Boulevard, Suite 101, Ann Arbor, MI 48103. (313) 761-2535.
- Hemophilia Northwest**: 4309 SE 64th Ave. Portland, OR 97206. (503) 774-1238.
- H/HIV Peer Association**: (615) 385-5425.
- Home Nutrition Services HIV Network** (on-line computer data base): (800) 788-4118.
- Medication Information Services**: (310) 854-MEDS.
- National AIDS Information Clearinghouse** (provides free: educational brochures, on-line searches): (800) 458-5231.
- National Association of People with AIDS**: (202) 898-0414.
- National Pediatric HIV Resource Center**: (202) 289-5970.
- National SIDA Hotline (Spanish)**: (800) 344-7432.
- National Trials Hotline**: (800) TRIALS-A.
- New Jersey Women and AIDS Network**: 5 Elm Row #112, New Brunswick, NJ 08901. (908) 846-4462.
- NIAID Intramural Trials**: (800) AIDS-NIH.
- Positive Directions**: 140 Clarendon St. Suite 805, Boston, MA 02115. (617) 262-3456.
- Pres. Clinton, White House Public Comment Line**: (202) 456-1111.
- Project Inform Treatments Hotline**: (800) 822-7422.
- PWA Coalition Hotline** (PWA staff provides information on drugs, medical treatments, legal assistance and services): (800) 828-3280.
- PWA Health Group** (non-profit buyers' club): (212) 255-0520.
- Women's AIDS Peer Hotline** (HIV+ women only): (800) AIDS-WOMEN

"Call it intuition, call it luck/But we're right in all that we distrust."

—Tom Greehalgh (*The Mekons*)

"The master's tools will never dismantle the master's house."

—Audre Lorde



## clinical trials glossary

**Accrual:** The process of signing up participants for clinical trials.

**ACDDC:** See AIDS Clinical Drug Development Committee.

**ACTG:** See AIDS Clinical Trials Group.

**ACTU:** See AIDS Clinical Trials Unit.

**ACTU Without Walls:** The ACTU "unit" for persons with hemophilia. It is administered by NHF. ACTG trials are offered through many of the hemophilia treatment centers that are not otherwise connected with the ACTG system.

**Administration (route of):** How a drug is introduced into the body (e.g. intravenously or orally).

**Adverse Reaction:** Poisonous reactions to the experimental medicines in a clinical trial. Possible toxic reactions are usually listed in the *protocol* and the *Informed Consent*, but some may have never been reported before. A clinical trial can be stopped because of adverse reactions.

**AIDS Clinical Drug Development Committee (ACDDC):** A committee of mostly academic and government physicians who review candidate drugs submitted by researchers and drug companies. From available data they assign a research priority: high, medium, or low.

**AIDS Clinical Trials Group:** System of cooperative sites conducting NIAID's clinical AIDS trials. Participating units are academic research institutions.

**AIDS Clinical Trials Unit:** Academic institutions where NIAID's AIDS clinical trials are performed.

**American Foundation for AIDS Research:** See AmFAR.

**AmFAR:** American Foundation for AIDS Research. A private non-profit agency that raises funds for AIDS research.

**Application Pending:** Clinical trials have been completed, but the company has not yet submitted an application for marketing to the FDA.

**Baseline:** A known value with which later values can be compared (e.g. baseline CD4, baseline hemoglobin, etc.). Usually taken upon entering a clinical trial.

**Bias:** Systematic influence on the results of a clinical trial that tends to distort the results in favor of one treatment arm over another. Randomization and blinding are ways to minimize bias.

**Blinding:** Process to reduce the bias in a clinical trial. The participant and/or the physician can be blinded from knowing what treatment the participant is taking.

**CAB:** See Community Advisory Board.

**Case Control Study:** An epidemiological method in which persons with a disease condition are compared with persons who do not have the condition but share some similar characteristics (such as age, gender, etc.). Also called *retrospective studies*.

**CBCT:** See Community Based Clinical Trials.

**CBCTN:** See Community Based Clinical Trials Network.

**CCG:** See Community Constituency Group.

**Clinical:** Based on observation of symptoms and physical health as opposed to blood work or other

laboratory tests.

**Clinical Trial:** A prospective study of one or more treatments in human subjects.

**Cohort:** Group of individuals sharing a statistical factor.

**Community Advisory Board:** Every ACTU is federally mandated to have a CAB composed of consumers and community providers to oversee and advise the ACTU. Many other organizations also have CABs.

**Community Based Clinical Trial:** CBCT. A complement to traditional academic research, CBCTs are conducted by primary care physicians in close cooperation with participants and AIDS advocates.

**Community Constituency Group:** CCG. National group of AIDS activists and advocates that advises the ACTG and informs constituencies about the ACTG and clinical trials. There is also a CCG for the CPCRA.

**Community Programs for Clinical Research on AIDS:** CPCRA. An AIDS clinical trials network of NIAID that provides clinical trials in non-academic centers through primary care physicians. Its main mission is to better establish clinical guidelines for drug usage as opposed to development of new drugs.

**Community Research Initiative:** CRI. A non-profit organization started in New York in 1987 to perform scientific studies of AIDS treatments. CRIs now exist in many other cities.

**Comparison Trial:** Experimental drugs are tested against each other or against an approved drug.

**Compassionate Use:** A regulatory mechanism for releasing an *investigational new drug* when there is little established data about its *efficacy*. The drug company must be willing to give the drug free of charge to persons whose medical condition might be helped by its use.

**Concomitant Drugs:** Drugs taken together with possible adverse drug interactions.

**Concurrent Drugs:** Drugs taken together without expected adverse drug interactions.

**Confidence Interval:** Results of a clinical trial are often expressed in terms of the *mean*. But due to variation, the mean should not be considered a "true" value. A confidence interval is a range of values which is statistically likely to contain the true value. Results are often given in 95% confidence intervals.

**Confounder:** A variable whose effect is entangled with the effect of the therapy under study. For example, a study that finds that a drug is effective could be confounded by more people with high CD4 counts being on the experimental therapy. The effect of confounding variables can be reduced by *randomization* at the start of the study or by *controlling* for them in the analysis.

**Contraindication:** A symptom or condition that makes a particular treatment inadvisable.

**Control Group:** Group that receives the *standard* therapy, *placebo*, or no treatment. A standard against which the experimental treatment can be evaluated.

**Controlled Trials:** Clinical trials in which there is a control group.

**Controlling (in statistical analysis):** Method to remove possibly confounding variables. If one treatment arm has more persons with baseline CD4 counts below 200, that could distort the result. A statistician can control for CD4 by looking (for example) at only those participants with baseline CD4 under 200.

**Correlation:** If two variables (quantities) are correlated, that means they are related. A large value for one is either associated with a large value (positive correlation) or a small value (negative correlation) in the other. Correlation does not imply causation.

**CPCRA:** See Community Programs for Clinical Research on AIDS.

**CRI:** See Community Research Initiative.

**Crossover:** A procedure in a clinical trial where drug regimens are switched halfway through the trial.

**Cross-Sectional Studies:** Study to describe a population at a fixed point in time. Often used to find the prevalence of a certain condition in different populations.

**DAIDS:** See Division of AIDS.

**Data and Safety Monitoring Board:** See DSMB.

**Declaration of Helsinki:** A 1975 document that states the standards for an ethical clinical trial. 1) Clinical trials should only be carried out by properly qualified personnel; 2) Any risks involved are believed to be predictable and the level of potential risk is comparable to the foreseeable benefits; 3) The dignity, integrity, and privacy of the trial subjects are crucial and must be respected at all times; 4) Any subject may leave the trial at any time for any reason; and 5) The informed consent of each subject must be obtained.

**Diagnosis:** Evaluation of medical history. Clinical symptoms and laboratory tests confirm or establish the presence of a disease or infection.

**Division of AIDS:** DAIDS. Division within NIAID that coordinates AIDS clinical research

**Dose Escalation Study:** A drug trial in which the dose of the drug is increased with each new trial group. The intention is to find the *maximum tolerated dose*.

**Dose Ranging Study:** A drug trial in which two or more doses of a drug are being tested against each other to determine which works best and is least harmful.

**Double Blind Study:** A clinical trial in which neither the subject nor the investigator knows which treatment, if any, the subject is receiving. Traditional scientific thought is that this promotes faster and more objective results, as doctors' and subjects' biased expectations about a drug are said to be eliminated. However, truly double blinded tests may be impossible to conduct with drugs that have well known toxicities.

**DSMB:** A board that meets regularly for each Phase II or III clinical trial to review safety and efficacy data. This board may require protocol changes based on unexpected toxicities. It can also terminate a study or require that a treatment arm be discontinued if large differences are seen between the groups.

**Efficacy:** The ability to achieve a desired effect. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.



## clinical trials glossary

In the FDA-mandated procedure, *Phase II* trials gauge efficacy, *Phase III* trials confirm it.

**Endpoint:** The outcome measured by a *clinical trial*. Endpoints can be clinical, such as development of symptomatic disease (e.g. PCP) or death, or can be *surrogate markers* (e.g. CD4 count falling below 200). The occurrence of an endpoint often terminates (or alters) the *subject's* participation in the trial.

**Epidemiology:** The science concerned with the specific causes or distribution of a disease.

**Equivalence Trials:** *Clinical trials* designed to determine whether a new drug is at least as good as the *standard drug*. In AIDS, ddI was approved based on data from equivalence trials that showed it is no worse than AZT. Often used to test generic versions of drugs.

**Ethical Clinical Trial:** A clinical trial that asks a relevant question and does not violate the rights of *participants*. See Declaration of Helsinki.

**Expanded Access:** A system of distributing *experimental drugs* to persons who are unable to participate in ongoing *clinical trials*.

**Experimental Drug:** A drug that has not been approved for use as a treatment for a specific condition in a specific population.

**False Negative:** A test that shows that a condition is not present when it actually is. An example is someone who tests negative for HIV, but who is actually infected and has not yet produced HIV antibodies.

**False Positive:** A test that shows the existence of a particular condition when that condition is not actually present. An example is an infant who tests HIV seropositive because of the presence of its mother's HIV antibodies but is not truly infected itself.

**FDA:** Food and Drug Administration. An agency of the U.S. government which controls and regulates human testing of drugs before marketing.

**Follow-Up:** The period during which data is being collected in a *clinical trial*.

**Food and Drug Administration:** see FDA.

**Half-Life:** The time required for the body to eliminate half of the amount of drug administered.

**Historical Controls:** Individuals who have similar disease conditions as the group under study but were treated prior to the study group.

**Hypothesis:** Statement by which the results of the trial will be measured. Usually a trial starts with the (*null*) hypothesis that the treatments are equivalent.

**In vitro:** Latin for "in glass." When biological experiments are performed in an artificial set-up, they are "*in vitro*," such as drugs tested on human cells in a test tube.

**In vivo:** Latin for "in living tissue." When biological experiments are performed in a living organism, they are "*in vivo*." Drugs tested in mice, monkeys, or in human clinical trials are *in vivo*.

**Inclusion/Exclusion Criteria:** Conditions set out in a *protocol* for a *clinical trial* that describe who is eligible to participate.

**IND status:** See Investigational New Drug.

**Indication:** Purpose for which a drug is intended; e.g.

Bactrim is indicated for PCP.

**Induction Therapy:** Initial course of drug treatment for acute symptoms. Often followed by *maintenance therapy* after symptoms resolve.

**Informed Consent:** A mechanism to inform potential clinical study *participants* about the potential benefits and risks in entering the study. The form must be signed before starting on the study. The consent form must contain an explanation of 1) why the research is being done; 2) what researchers want to accomplish; 3) what will be done during the trial and for how long; 4) what risks and benefits can be expected in the trial; 5) other available treatments; and 6) the right to leave the trial at any time. The consent form must be understandable to the potential participant.

**Institutional Review Board:** (IRB) Every institution that conducts or supports biomedical research involving human subjects must, by federal regulation, have an IRB that initially approves and periodically reviews *clinical research* to protect the rights of the subjects.

**Intent-To-Treat Analysis:** A design of a *clinical trial* that compares the outcomes of the groups that are assigned to particular treatments, regardless of what the people in those groups actually do. It is generally considered a more "real-world" approach to analysis than *Treatment-Received analysis*.

**Investigational New Drug:** (IND) After pre-clinical trials drug companies submit IND applications, which show all the results of animal tests to the FDA. This paves the way for *phase I clinical trials*. Certain drugs are available on a case by case basis through this mechanism.

**IRB:** see Institutional Review Board.

**Kefauver Amendments:** Passed in 1962 after birth defects were discovered in children whose mothers had been prescribed thalidomide. The Amendments require *efficacy* data before a drug can be marketed.

**Longitudinal Study:** Study concerned with describing a population at several points in time. Longitudinal studies can be *prospective* or *retrospective*.

**Maintenance Therapy:** Use of a treatment regimen to maintain a desired effect that has already been achieved.

**Maximum Tolerated Dose:** (MTD) *Phase I* trials try to find the MTD—the highest dose that can be taken without significant toxicities. Many AIDS activists call for studies to determine a "minimum effective dose" instead.

**Mean:** Arithmetic average. Sum of values divided by the number of values.

**Median:** The value that splits the recorded observations. Half of the observations are greater than the median and half are less. The median is not sensitive to very large or very small values.

**Multicenter Trial:** *Clinical trial* conducted at two or more sites. Most ACTG and CPCRA studies are multicenter.

**Multiple Endpoints:** An endpoint which consists of more than one condition. Many AIDS clinical trials use development of an AIDS-defining condition as an endpoint. That endpoint contains 23 (or 26) different

conditions. This can cause confusion, as candidiasis is sometimes given the same weight as lymphoma or even death in analyzing the trial.

**National Cancer Institute:** See NCI.

**National Institute of Allergy and Infectious Diseases:** (NIAID) The most important part of NIH for AIDS research. It supports basic research, epidemiology, blood screening tests, drug discovery and development, vaccine development and testing, and treatment studies, some directly and some through contracts and cooperative agreements. NIAID administers the ACTG and CPCRA networks.

**National Institutes of Health:** NIH. Twelve constituent institutions, several research and support divisions, and the National Library of Medicine. Most basic and much applied biomedical research in the U.S. is funded by NIH, most of it at private institutions. NIH sets the nation's research agenda. AIDS research is concentrated at NIAID and NCI.

**NCI:** (National Cancer Institute) One of the NIH. Due to the prevalence of KS and lymphomas in AIDS, NCI has been closely involved in AIDS research.

**NDA:** (New Drug Application) Upon completing *Phase III* clinical trials and before the drug can be released for sale, a drug sponsor must file an NDA with the FDA. FDA review of NDA often takes 2-3 years.

**NIAID:** See National Institute of Allergy and Infectious Disease.

**NIH:** See National Institutes of Health.

**Non-Blinded Study:** *Clinical trial* in which both the *participant* and the researcher know what treatment the participant is receiving. Also called *Open Label*.

**Non-Compliance:** When a trial *participant* does not follow the assigned treatment regimen.

**Null Hypothesis:** Most *clinical trials* start by assuming that the *treatment arms* are equivalent. The trial must prove that one treatment is superior to the other.

**OAR:** See Office of AIDS Research.

**Observational Study:** Study in which the researcher observes the natural course of events without experimentally manipulating the situation.

**Off-label:** A drug prescribed for conditions other than those for which it is indicated. Medicaid, Medicare, and some insurance plans will not cover off-label drugs.

**Office of AIDS Research:** New department created by the NIH Reauthorization Act of 1993. It will centralize the budgeting and planning of AIDS research within NIH.

**Open Label Trial:** A drug trial in which both doctors and *subjects* know which drug and dose is being taken. Also called a *Non-Blinded Study*.

**Open Trial:** A clinical trial is open when it is accruing participants.

**Orphan Drug:** A drug for a rare disease or condition which affects less than 200,000 people. The patent is given to help facilitate treatment of rare disorders. It lasts for seven years and prohibits any other company from investigating the drug.

**Package Insert:** A form containing all relevant infor-



## clinical trials glossary

mation about a drug. It can be found on the inside of a prescription drug container.

**Parallel Track:** System of distributing *experimental drugs* which have completed *Phase I* testing to persons who are unable to participate in ongoing trials.

**Participant:** A participant in a *clinical trial* is considered a research subject; research is not treatment, and participants are not patients. Research trials are not designed to provide care, and the treatments being studied may or may not benefit participants.

**Pharmacokinetic:** Concerning the study of how a drug is processed by the body, the extent and rate of its absorption, its distribution and location in tissues, and how it is excreted. The information is used to find the best route of *administration* and dosage.

**Pharmacology:** The study of the activity of drugs in the body.

**Phase I:** *Toxicity* and dose-finding studies on a small group of humans. These trials investigate the *pharmacokinetics* of a drug. Usually completed within a year.

**Phase II:** The stage at which drug effectiveness is established. Designed to determine *efficacy* and *toxicities*. Usually involve 50 to 300 *subjects*.

**Phase III:** Expansion of Phase II study to hundreds or thousands of *subjects*. Designed to confirm information gathered in earlier trials. Also can compare the drug to other agents, either alone or in combination. May last several years.

**Phase IV:** *Clinical trials* done after FDA approval. These are done to more accurately determine clinical guidelines.

**Placebo:** An inactive substance that is compared to *experimental treatments* for *efficacy*.

**Placebo Controlled Trial:** *Clinical trial* in which the *control group* is given a *placebo*. The results from each group are compared.

**Placebo Effect:** A change that occurs after the initiation of a *placebo* or therapy that is due to the expectations of the individual rather than being due to the biologic activity of the therapy.

**Power (of a Clinical Trial):** The probability that the clinical trial will be able to determine a *statistically significant* difference between the treatments, if a *true* difference actually exists.

**Pre-Clinical:** First stage of drug testing, in the test tube and in animals.

**Primary Endpoint:** The event which is considered to be of primary importance in evaluating the experimental treatment.

**Prognosis:** Prediction of the future course of disease and estimation of the chance of recovery.

**Prognostic Variables:** Factors which are known to be associated with the outcome of interest (e.g. CD4 count is a prognostic variable for progression of HIV disease).

**Prospective Study:** A planned clinical study of individuals assigned to one or more drugs. *Subjects* are followed forward in time from the beginning of the study to its termination, from cause to effect.

**Protocol:** Detailed plan which states a *clinical trial's*

rationale, goal, *hypothesis*, the drugs involved, dosages as well as who may participate. Protocols must be approved by *IRBs*.

**P-Value:** Probability that a result more extreme than what occurred in a *clinical trial* could happen purely by random chance. A result is generally deemed *statistically significant* if the p-value is less than .05 (5%).

**Randomized Clinical Trial:** (RCT) *Clinical trial* in which *participants* are randomly assigned to receive one of the treatments (or *placebo*) being studied. Traditionally assumed to give better information than trials that are not *controlled* or *randomized*.

**Regression to the Mean:** The phenomenon that a measurement that is extreme (far from average) on one measurement will be closer to average for another measurement. This is caused by normal variability in measurements. This tendency can confuse *uncontrolled trials* because people with low (bad) measurements may improve simply by statistical chance, but the improvement may be interpreted to be caused by the experimental drug.

**Retrospective Study:** A clinical study in which individuals or their records are investigated after they have experienced the disease or condition. Such a study looks backward in time, from effect back to potential cause. Also called *case-control studies*.

**Salvage Therapy:** Treatment for persons who are not responsive to or cannot tolerate other available treatments for a particular condition.

**Short Form Written Consent:** A form that states that everything in the *informed consent* has been explained to the individual entering the trial. A witness to the explanation is necessary.

**Side Effects:** Actions of a drug other than those desired. The term usually refers to negative effects such as nausea, headaches, and neuropathy. *Experimental drugs* must be evaluated for both short- and long-term side effects.

**Single Blind Trial:** A *clinical trial* in which the researcher/physician knows which treatment the *participant* is on, but the participant does not know.

**Sponsor:** The people, organization, or corporation that studies a drug or pays for it to be studied.

**Standard of Care:** The treatment strategy that is considered the best available option for a particular condition. Insurance companies will often not cover a treatment that is not the Standard of Care. AZT is now considered the standard drug for treating HIV.

**Statistical Significance:** When statistical analysis determines that it is unlikely that such a result could have occurred by random chance. In general, a result is determined to be statistically significant if that probability is less than 5%.

**Stratification:** Subdividing a study population into parallel groups based on a certain factor (such as age, gender, CD4 count, etc.). Useful for comparing differences between groups.

**Subgroup:** Subset of participants that share a characteristic.

**Subgroup Analysis:** Analyzing the results of a trial in

a particular *subgroup*. This can be dangerous, because trials are usually designed to find an overall effect and may not have the *power* to find real differences in subgroups. Also, if enough subgroups are investigated, it is very likely that a *statistically significant* difference will be found in some group even if there is no *true* difference.

**Subjects:** See participant.

**Surrogate Markers:** Laboratory tests which may predict *clinical* outcomes or indicate whether a drug is effective without having to wait for *clinical endpoints*. Surrogate markers under study in HIV disease include CD4 counts, p24 antigen, Beta 2 microglobulin, plasma viremia and quantitative PCR. Sometimes surrogate markers are used instead of clinical changes as the endpoints for a *clinical trial*.

**Toxic Reaction:** See Adverse Reaction.

**Toxicity:** The extent or degree of being poisonous or harmful to the body.

**Treatment Arm:** Each arm in a *clinical trial* is a particular treatment assignment.

**Treatment IND:** Treatment Investigational New Drug. An FDA classification that allows physicians to prescribe a promising drug to persons with serious illness or immediately life-threatening diseases. It allows release of a drug prior to the end of *Phase II* testing. Drug companies may charge for the drug.

**Treatment Received Analysis:** Analysis of a clinical trial in which participants are included in the group corresponding to the treatment they actually took.

**Uncertainty Principle:** "A *clinical trial* is only *ethical* if the researchers are truly uncertain about which treatment arm is better."

**Uncontrolled Trials:** Research studies in which no participants are assigned to a *placebo* or standard therapy.

### Pres. Unveils Health Package

As we go to press, President Clinton is formally proposing his package to reform the United States Health Care system. A few points are worth mentioning.

Clinton's plan would guarantee that every American citizen be covered by a basic health insurance plan. From all indications, that plan will be at least fairly good. Also the coverage will not have yearly or lifetime maximums and will not be able to refuse payment based on any pre-existing conditions. Those would be tremendous improvements for many people with hemophilia and HIV. A problem is that, if passed, the program would not begin to be implemented until 1995, and would not be complete until 1997. Legislative struggles and attempts by some interest groups (insurance companies) might delay the enactment even longer.

The issues surrounding Health Care Reform are extremely complex. The Common Factor will include more comprehensive coverage of the President's plan in our next issue.



*The Common Factor* is dedicated to offering a forum for discussion of:

- 1) HIV treatment strategies,
- 2) Ways to stay healthy,
- 3) The science, politics and business of HIV and hemophilia,
- 4) Methods of coping with HIV infection and AIDS, and
- 5) How HIV affects love and sexuality.

The Committee of Ten Thousand believes that HIV-positive persons:

- 1) Can improve their health and extend their lives through an aggressive approach to the treatment of HIV infection,
- 2) Can lead productive and enjoyable lives,
- 3) Deserve love and support, and
- 4) Can have a healthy and positive sexuality.

These topics naturally give rise to a diversity of opinions. We strongly encourage expanding the debate about these issues and welcome Letters to the Editor, comments and submissions. Everyone's viewpoint on these difficult issues is valuable. Everything in this newsletter is solely the view of the author; COTT makes no recommendations of specific treatment strategies.

*The Common Factor* is published by the Committee of Ten Thousand, a 501c3 non-profit organization. All contributions are tax deductible. Please make your check payable to The Committee of Ten Thousand.

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*The Common Factor* is free to all people who are HIV+ and their families. For all others, we request a donation of \$20/year. Businesses and Professional Offices: \$50/year. Our mailing list is totally confidential. *The Common Factor* is mailed in a plain brown envelope.

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