AIDS: striking the happy media

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The past year has seen many controversies about AIDS research and researchers. What productive events have occurred, and what is likely to happen in the next year?

IN 1961, John F. Kennedy stood at a podium in Berlin and announced "*Ich bin ein Berliner!*" Colloquially, this can mean "I am a doughnut". Will many AIDS researchers do the same at the IX International AIDS Conference in Berlin next week? The international AIDS meeting has long since shot its bolt as a worthwhile forum for scientific debate — it is far too large, unfocused and glitzy for many scientists' tastes. But it does attract the media, on the look-out for stories. Last year's Amsterdam meeting was marred by the extraordinary focus on what transpired to be a minor issue: HIV-negative AIDS, or ICL. A premature announcement created unnecessary public anxiety about a possible new epidemic. All the ICL scare did was to attract attention away from the real issues: the plight of people infected with HIV and the attempts of science to help.

AIDS, with its combination of sex, death and celebrities, holds a strong fascination for the media. Thus there is an onus on scientists to deal responsibly with journalists. It is a common perception in the scientific community that inappropriate press coverage of AIDS issues is the fault of journalists. Except for some tabloids like the London *Sunday Times*, this is usually not the case. Journalists working for specialist science magazines and most quality newspapers are generally responsible professionals who report the field fairly and accurately. Journalists earn their corn by writing stories, but often the bread is given to them already buttered. By and large, press coverage of AIDS issues reflects what scientists say to journalists. A journalist's responsibility is to check that the facts are accurate, but not necessarily to judge their overall merit. Why should a good story be spiked just because other scientists disagree with the data interpretation? When scientists say contradictory things to the public, how can the public assess whom to believe?

Dissent and controversy

Science has a duty to inform and educate the public, but it must neither frighten people unnecessarily nor give them unjustified expectations. Claims of "AIDS cures" in the popular press need to be based on much more than just *in vitro* data. Whatever the need to attract research funding, is 15 minutes of fame for one person ever worth 15 days of fear or 15 weeks of false hopes for many? Another worrisome trend, especially in the United Kingdom, is the tendency of some AIDS researchers to whine to the press and politicians about their failure to win competitive funding, alleging a non-existent bias by funding organizations. These antics create an awful impression on the taxpayers and politicians who pay for our work, and obscure the real message: more resources need to be committed in a more effective fashion to fight against AIDS.

The consequences of dissent and controversy are now apparent, at least in the United Kingdom, where hostile press comment may have contributed to the recent change in government AIDS policies. This will be to the detriment of those infected with HIV and those yet to be infected, as well as everyone involved in AIDS research and education. The 'Murdoch' press has run a highly slanted campaign parrotting Peter Duesberg's line that HIV is not the cause of AIDS and that the risk to the heterosexual population is minimal. The subliminal message of these newspapers is that "normal" people (*Sunday Times* readers?) don't get AIDS. There is dirty politics at work, but have we scientists contributed to the current climate by our interactions with the press? Already there are signs of a backlash against AIDS issues in the US press. I believe it is the responsibility of all of us engaged in AIDS research to take a broad view when dealing with the media: hyping our own laboratories' achievements or boosting our companies' share-price may not be in the wider interest of AIDS research.

As well as the ICL fiasco, there have been several major AIDS stories since the last AIDS conference. Their significance to science has usually been a lot less than their perceived importance in the press, but can we learn any lessons from them? Duesberg's anti-HIV polemics continue to attract press attention, but to most specialists the case for HIV is proved beyond reasonable doubt and the arguments have become sterile. Duesberg reminds me of the Black Knight in "Monty Python and the Holy Grail". His limbs cut off one by one in a duel, the torso waddles towards his antagonist and threatens to bite his kneecaps! Sadly, this is no laughing matter — Duesberg's nonsense can and has hurt people.

This year there has also been a debate in the press about whether HIV could have been introduced into Africa in contaminated poliovirus vaccines. The hypothesis was shown to be highly improbable, and although it would be useful to know where HIV came from, it seems to me more important to know where it is going and to stop it getting there. Similarly, the press fascination with who first isolated HIV-1 is becoming a bore, and worse. The witch-hunts just stop people from getting on their work. Now it is clear that many people played crucial roles in the isolation of HIV-1 (J. C. Gluckman, *Science* **259**, 1809; 1993), perhaps it is time to let sleeping dogs LAI!

Media manipulation

The failure of AZT to evoke long-lasting clinical benefit attracted much comment when the Concorde trial results were published recently (*Lancet* **341**, 889; 1993). These were important findings. But what was news to the public was not to most AIDS reseachers; the development of AZT-resistant variants *in vivo* is well known. The strategy for anti-retroviral drug therapy has been focused on drug combinations for some time now. A publication describing *in vitro* effects of three antiviral agents used in concert (M. Chow *et al. Nature* **361**, 650–653; 1993) attracted far more press coverage than was warranted by its scientific content. The publicity engendered by this paper seemed to me not to be in the best interests of the public or of AIDS research. If we cry wolf too often, people will stop listening when there is something really important to say.

Attempts by the MicroGeneSys company to acquire 'pork-barrel' funding from the US Congress for its gp160 'AIDS vaccine' by slick use of the lobbying system were defeated this year by a triple combination of accurate reporting in the press, scientific pressure and the efforts of AIDS activists who knew a con-trick when they saw one. In short, a triumph for science over the profit motive. The fuss originated from claims by US Army scientists at last year's Amsterdam conference that immunization of HIV-infected people with gp160 reduces viral burden and stabilizes CD4 counts, events thought to be of clinical benefit. These claims require confirmation and are still the focus of an official investigation. But the hopeful climate created enabled the manufacturers of gp160 to sneak a $20 million appropriation onto the Department of Defense finance bill. This sum could have

supported about 40 RO1 investigator grants for 5 years. A successful campaign against this mode of science funding resulted in the money being transferred to the NIH for comparative therapeutic trials of different candidate vaccines, the best outcome that could have been achieved in the circumstances. As the NIH, unlike the US Army, have refused to pay any company for their products, it appears that the MicroGeneSys' 'vaccine' will not be in the comparative trial. The company's expenditure on lobbyists could ultimately benefit only its rival companies — a truly appropriate outcome.

One important issue came out of the MicroGeneSys battle: should efficacy standards of clinical trials be lowered when considering potential AIDS therapies? This is a very tough call. An NIH/FDA advisory panel voted by 15 to 1 that there were no traditional scientific reasons to undertake a phase III trial of any therapeutic vaccine candidate, but then voted by 16 to 0 to undertake a trial essentially on compassionate grounds. The decision was understandable in the social and political climate in which it was taken, but it does set a dangerous precedent that companies with products they view as promising will no doubt exploit.

The US Army has perhaps taken this approach a step too far. Its advisory group decided that there was no "requirement for evidence of *likelihood* of efficacy" (my emphasis) for a product to get into a US Army clinical trial. Would the US Army equip its tanks with guns that had no likelihood of firing? The problem with therapeutic immunization is that while few AIDS researchers think it will work, nobody knows for sure that it won't. Thus it is hard to argue against the emotional argument that immunization might save the lives of people dying of AIDS. Ethical dilemmas abound in AIDS research, but overall a controlled trial of the concept is warranted. Yet FDA approval of a therapeutic vaccine may well require clinical endpoints of greater validity than surrogate markers.

Irrespective of how the media reports the Berlin conference, what important things might happen in selected areas of AIDS research over the next year? There is a rapidly emerging consensus that AIDS is a virus infection and not an autoimmune disease. Recent studies from several groups quantitating viraemia in both the peripheral blood and lymphoid tissues, and showing consistent changes in virus load and $CD4^+$ counts in response to antiviral treatment, should be sufficient to quiet the doubting Thomases. Although there will still be attention focused on issues such as apparent gp120 sequence homologies to MHC class II and mycoplasma adhesion sites, on cross-reactive antibodies, superantigens, and bizarre epi-phenomena in autoimmune mice, increasingly they will be seen as peripheral to the central verity that HIV is a cytopathic virus with $CD4^+$ cell tropism.

We should also see an increasing awareness of the importance of cellular immunity as a limiting factor to the spread of viral infections. This was clear to some people years ago, but is only gradually sinking into the conciousness of many of us. Behind this lack of appreciation has been the absence of any consensus among immunologists about how HIV cripples the immune system. As an extreme example, most cytotoxic T lymphocytes are $CD8^+$ cells, which are seen by many as important in fighting viral infections. Yet others believe with equal passion that we should be trying to eliminate them.

Among emerging technologies that may eventually reach the clinic are vaccines based on immunization not with proteins but with DNA. Although counter-intuitive, this approach does seem promising based on animal experiments. As we understand more about AIDS pathogenesis, the human immune system and vaccine design, it is becoming more likely that the correlates of protective immunity encompass both humoral and cellular mechanisms. If that sounds like a reinvention of the wheel, that's almost a tradition in AIDS research. But it seems reasonable to assume that the success of Desrosiers' attenuated, live-virus vaccine in the SIV model is because it stimulates continuously all arms of the immune system.

The recent trend towards cooperation between companies working on antiviral drugs is both constructive and refreshing. The concept could be extended profitably to vaccine development. Subunit vaccines currently under evaluation tend to have been designed several years ago on an *ad hoc* basis but still must be tested rigorously. Even should they fail, we may learn much of help in designing the next generation of reagents. Different products have different useful features. For example, Genentech, Chiron and others have made gp120 vaccines that are effective stimulators of humoral and cellular immune responses to gp120, but which lack *gag* components against which some cellular immunity is directed. The 'Salk vaccine' was accidentally depleted of gp120 in the production process. Thus while it might be a good stimulator of cellular immunity, it lacks the ability to evoke neutralizing antibodies to the viral envelope. Current theories are sufficiently controversial for it to be uncertain whether this is a benefit or a defect. The companies could consider joining forces to compare the effects of their products in isolation and together. An analogous situation can be foreseen with therapeutic antibodies, where different companies own antibodies that might work best in combination. There are lives at stake as well as money, so would anybody be happy if several companies have half an AIDS drug or vaccine and the world has none?

A major development in AIDS research in 1993 will be organizational, with the creation of the Office of AIDS Research (OAR) as a coordinating council for US government-funded reseach programmes. It seems ironic that as the UK AIDS Directed Programme comes under pressure from the Medical Research Council, the Americans are copying its steering committee format. It is difficult to predict how the OAR will affect current trends and practices in AIDS administration, as the organization so far lacks a director(s) and an advisory board. Many scientists fear the OAR, through ignorance of its role; others feel it may merely add an unnecessary layer of bureaucracy to AIDS administration; some are concerned that funding priorities will be decided by AIDS activists, who undoubtedly wield more power under Clinton than under Reagan or Bush. I believe these fears are groundless. The role of activists in the OAR should be viewed optimistically, as its planners intended. The role of activists in the OAR is positive; the current generation of activist leaders is a responsible one with much to offer the scientists who are prepared to work with them in partnership. Nevertheless, scientists should ultimately decide about scientific issues. The OAR will estabish funding priorities and focus resources on key research areas as they emerge; it should not micro-manage research in individual research labs and it should not support administrators at the expense of scientists.

It is to be hoped that the OAR will acquire new funds for AIDS research, but equally important is to spend existing funds more wisely. There is waste and unnecessary duplication in AIDS research, and some work that is poor. All increases in scientific knowledge are incremental, but in AIDS research sorting the increment from the excrement is a real problem. Yet statistical analysis shows that AIDS literature is not much different from other areas of biomedical research (P. Brown, *New Scient.* 15 May 1993). Large sums of money have been thrown at AIDS research; merely scattering more around is not the answer. It must be well-aimed to be effective.

The younger generation of AIDS researchers tends to cooperate closely, not just to survive in a cut-throat world, but out of the realization that AIDS is bigger than all of us and that it will need a meld of all our skills to defeat it. As JFK might have put it: "Think not what AIDS research can do for you; think what you can do for AIDS research". □

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