Photo - Joan Shenton

Looking back on the Oxidative Stress theory of Aids

Eleni Papadopulos-Eleopulos

Department of Medical Physics, Royal Perth Hospital, Perth, Western

The whole purpose of a scientific theory is to explain the mechanism behind observations and make predictions. If a theory cannot explain the observations for which it was put forward, or if its predictions are not fulfiled, then it should be abandoned. In this regard, despite the lapse of 18 years, there is still no proof as to the cause(s) of AIDS. Of course, there are theories but the biggest obstacle in overcoming the problem of AIDS, and proving its cause, is that one of these theories, the HIV theory, has been uncritically accepted since 1984. However, of all the theories, the HIV is the least likely.

The observations the HIV theory was proposed to explain were threefold. The high frequency of a malignancy, Kaposi's sarcoma (KS), a few opportunistic infections (OI), principally *pneumocystis carinii pneumonia*, and a decrease in a specific cell type, T4 lymphocytes, in gay men, IV drug users and haemophiliacs. It was accepted that no single infectious agent could possibly be the direct cause of the multiple diseases seen in AIDS patients. So, it was proposed that the "hallmark" of HIV infection was the destruction of T4 cells by HIV which inevitably led to the appearance of KS and the OI. The proposition that decrease in T4 cells was the hallmark of HIV/AIDS is difficult to comprehend. At the time when the HIV theory of AIDS was put forward:

(a) there was no evidence that retroviruses kill cells, to the contrary;

(b) many factors to which patients belonging to the AIDS risk groups are exposed are immunosuppressive. This fact was known to some of the best known HIV experts. In 1985 Montagnier wrote: "This syndrome [the AIDS diseases] occurs in a minority of infected persons, who generally have in common a past of antigenic stimulation and of immune depression before LAV [HIV] infection".[1] In the same year Weiss, Ludlam and their associates wrote (concerning patients with haemophilia): "Our finding...supports our previous conclusion that the abnormal T-lymphocyte subsets are a result of the intravenous infusion of Factor VIII concentrates *per se*, not HTLV-III infection".[2] One year later researchers from CDC: "...factor concentrate [Factor VIII] itself may be immunosuppressive even when produced from a population of donors not at risk for AIDS" [3] ;

(c) evidence also existed that many factors including infections, and trivial ones, such as exposure to the sun or radiation in solaria lead to decreased T4 cells. Although some of the T4 decreases were long lasting, the patients did not develop KS and OI;[4] a significant proportion of the "AIDS" patients, including patients with KS and OI infections, had normal numbers of T4 cells.[4] In other words, T4 decrease (immune deficiency) is neither necessary nor sufficient for the development of KS and OI. Thus the proposition that KS and the OI are the result of T4 decrease and that the T4 decrease detected in the patients belonging to the AIDS risk groups was caused by HIV infection was totally inconsistent with the data available even before the hypothesis was put forward.

For some time now, all HIV/AIDS experts, including Robert Gallo, accept that HIV has no direct or indirect role in KS.[5-7]

FAILED PREDICTIONS

The HIV theory predicted that HIV was sexually transmitted and therefore AIDS would spread throughout the heterosexual population. Obviously this has not happened. The prediction by proponents of the HIV theory that a vaccine would be developed by 1986 also has not been fulfilled. In 1984 Montagnier said that the only way to prove HIV is the cause of AIDS is to have an animal model.[8] Although no effort has been spared, no model of a retrovirus causing AIDS has been forthcoming. Indeed, the only animal model that bears any resemblance to human AIDS fully supports a non-infectious *modus operandi*.[9]

WHAT LED A PHYSICIST TO STUDY AIDS

At the outbreak of AIDS, Gallo had already spent a decade in attempts to prove that the cause of some cancers was a retrovirus. This led him to put forward the retroviral theory of AIDS. From an equally biased position I put my non-infectious theory. Although trained as a nuclear physicist, with the exception of a few years, I have worked in the medical field in the Department of Medical Physics of the Royal Perth Hospital, the largest teaching hospital in Western Australia. Among its many activities it was involved in treating cancer by radiation and pioneered hyperthermia for the same purpose.

It was known that both radiation and radio-sensitisers were oxidising agents, and apart from hyperbaric oxygen the chemical radiosensitiser included compounds containing the -NO2 group, that is, nitro-compounds. To understand the interaction between the agents used to treat cancer and cancer tissue, I first needed to determine what makes a cell cancerous. I decided the best way to approach this was to attempt to fully understand the normal cell. This included the understanding of the mechanism by which sperm induced the division of the ova. In doing so I developed my own theory of biological functioning. A short version was first presented at a meeting in Colorado in 1979 and was published in Speculation in *Science and Technology* in 1980. A more detailed version was published in 1982 in the *Journal of Theoretical Biology*, after it was first rejected by *Nature*, under the title "A Mitotic Theory". Although the title suggests that it deals only with cellular division and cancer, the theory, as one of the reviewers pointed out, also proposed a "relationship between modifications in the redox state of the actin-myosin system and other key biological processes (e.g. transport, muscle function, metabolism...). Most importantly in this article, there is a clear integration of older and present data as well as "classical" and "contemporary" concepts.

The theory claimed that the cellular redox level and its oscillations, that is, the cyclic variation between oxidation and reduction, plays a pivotal role in both normal and abnormal cellular function and structure. Diseases such as cancer, cardiovascular, clotting abnormalities and ageing, for example are the result of perturbation of the cellular redox level and its oscillations.

Thus, by the time AIDS was diagnosed I was aware of the biological and pathological effects induced by many agents (semen, nitrites, recreational drugs, Factor VIII, infectious agents and the drugs used to eradicate them) to which the patients belonging to the AIDS risk groups were exposed.

More importantly all these agents showed a common property: they were oxidising agents. This led me to put forward the non-infectious theory of AIDS which claimed that the primary risk factors for AIDS were the oxidising agents to which the individuals were exposed. While the manuscript discussing this theory (in which neither HTLV-I nor Montagnier's retrovirus were mentioned) was in the hands of a few colleagues for evaluation, Gallo claimed to have proven that HTLV-III was the cause of AIDS. I was advised to re-write the manuscript to take account of these claims. The revised manuscript, which was twice rejected by *Nature* and initially by *Medical Hypotheses*, was later accepted by the latter journal.

PREDICTION OF THE OXIDATIVE STRESS THEORY OF AIDS

The predictions of my theory included:

(1) AIDS would remain restricted to the risk groups. This has been the case.

(2) The only sexual act leading to AIDS or a positive antibody test is a very high frequency of receptive anal intercourse in either sex. One of the first to publish supporting evidence of this was Gallo and his associates. In a study published in 1984 he wrote: "of eight different sex acts, seropositivity correlated only with receptive anal intercourse...and was inversely correlated with insertive anal intercourse.[10] In 1986 Gallo wrote: "Data from this and previous studies have shown that receptive rectal intercourse, for example, is an important risk factor for HTLV-III [HIV] infection. Yet, at the time of entry into this project, nearly half of the participants still practised this technique. We found no evidence that other forms of sexual activity contributed to the risk".[11] Thus Gallo was one of the first to publish evidence which contradicted his own assertion that HIV/AIDS is bi-directionally sexually transmitted.

In 1985 Montagnier and his colleagues reported that the wife of a haemophilia man who, in addition to other sexual acts, practised anal intercourse was found to have a positive antibody test and low numbers of T4 cells. "During 10 months of follow-up his wife remained clinically well, discontinued exposure to semen, and then lost the LAV antibody, and regained a normal number of T-helper cells" (T4 cells).[12]

The best and largest study, the Multicenter AIDS Cohort Study of 4995 gay men, which commenced in 1984 and is still ongoing, also confirmed this in 1987. "Receptive anal intercourse accounted for nearly all new HIV infections among the homosexual men enrolled in this study, and the hazards of this practice need to be emphasised in community educational projects".[13]

In a review of most, if not all, epidemiological studies conducted in gay men published in 1994, the authors concluded: "it can be said that the cited reports yield convincing evidence that (1) unprotected ano-genital receptive intercourse poses the highest risk for the sexual acquisition of HIV-1 infection; (2) ano-genital insertive intercourse poses the highest risk for the sexual transmission of HIV-1 infection; (3) there is mounting epidemiologic evidence for a small risk attached to oro-genital receptive sex, biologic plausibility, credible case reports and some studies show a modest risk, detectable only with powerful designs; (4) sexual practices involving the rectum and the presence of (ulcerative) STD facilitate the acquisition of HIV-1; (5) no or no consistent risk for the acquisition of HIV-1 infection has been reported regarding other sexual practices such as ano-genital insertive intercourse

and oro-anal sex...(8) the association of substance use with HIV infection is probably the result of interaction, because substance use increases the likelihood of practising ano-genital receptive intercourse".[14]

Unquestionably, to date, the best designed and executed study in heterosexuals was conducted by Nancy Padian and her associates. In a paper entitled "Male-to-Female Transmission of Human Immunodeficiency Virus" published in 1987 wrote:

"The total number of exposures to the index case (sexual contacts with ejaculation) and the specific practice of anal intercourse, also with the infected partner, were associated with transmission".[15]

The results from their long prospective study of couples, of whom only one partner of either sex was antibody positive, were published in 1997 in a paper entitled *Heterosexual Transmission of Human Immunodeficiency Virus (HIV) in Northern California; Results from a Ten-Year Study*.

"Prospective results.
We followed 175 HIV-discordant couples over time, for a total of approximately 282 couple-years of follow-up...At last follow-up, couples were much more likely to be abstinent or to use condoms consistently, and were much less likely to practice anal intercourse ($p < 0.0005$ for all). Nevertheless, only 75% reported consistent condom use in the 6 months prior to their final follow-up visit...no seroconversions occurred among exposed partners".[16]

Thus, a positive antibody test and AIDS, like pregnancy, can be sexually acquired but not sexually transmitted. The difference is, that while pregnancy can be acquired by a single sexual intercourse, for AIDS to appear a very high frequency of receptive intercourse over a long period is absolutely necessary. AIDS is more like cervical cancer. The effect is not the result of the act itself, but its high frequency. But, as with pregnancy and cervical cancer, other factors may mitigate against the development of AIDS.

(3) Both antibody positive and antibody negative drug users will develop AIDS and that not only individuals who use dirty needles but also those who use clean needles or even non-parenteral drugs will develop positive antibody tests.

According to an interview published in the June 1986 issue of *AIDS ALERT* with Susan Neshin, Medical Director of Asbury Park (NJ) Drug Treatment Center, for clinicians to differentiate between AIDS and the health problems typically experienced by intravenous drug users, "First clinicians should interview NDUs to determine if their symptoms are related to drug abuse or AIDS. You have to talk to them and get them to tell you if their symptoms are drug-related. They can have weight loss, diarrhoea, and night sweating, but they could be having that on an ongoing basis from bad dope, withdrawal, or just poor health in general. It's very common for drug addicts to have inguinal lymphadenopathy, and maybe a few cervical or axillary nodes that are kind of shoddy. If you see oral candidiasis in an NDU, that's a real tip off". A few months later researchers from the USA wrote, "a real T- helper lymphopenia [that is, T4 cell decrease] is only consistent with and not diagnostic of AIDS; other diseases and some treatment regimens also can express a T-helper lymphopenia, such as hospitalised IV drug abusers".[17]

One year later, in an article published in the *British Medical Journal*, one reads, "Intravenous drug abusers appear to be at special risk of acquiring tuberculosis, and a high rate of infection in this group was reported well before AIDS began".[18]

In a 1994 paper published in the *Scientific American*, two researchers who studied drug abuse wrote, "Many manifestations of AIDS in drug users who inject are quite different from those in homosexual and bisexual men who do not use drugs in this manner; in drug users who inject and in their sexual partners HIV infection is associated with substantially increased morbidity and mortality from bacterial infections. In the US much of the resurgence of tuberculosis is occurring among HIV-infected users who live in crowded conditions without access to good medical care. The CDC definition of AIDS has been periodically updated to incorporate these findings".[19]

In 1994, researchers from Switzerland reported their findings from a prospective study designed "to examine differences in the incidence and spectrum of diseases comprising 314 HIV-seronegative NDU, 217 HIV-seropositive NDU, and 10 NDU with admissions registered in either group (from a total of 1011 admissions)". Narcotic drug users (NDU) were enrolled in the study if "they were hospitalised for a minimum of 24 hrs, and also presented with at least one of the following characteristics: history of either parenteral drug use or a corresponding oral substitutive medication (mainly methadone); or actual intoxication and miosis [pinpoint pupils] responding to naloxone; or opiate or cocaine metabolites in a urine sample. Individuals with exclusive oral drug use other than opiates were not included". "HIV- seropositive NDU were more frequently admitted for infectious complications or various non-infectious medical complications (including as most frequent cases, 38 admissions for ill-defined episodes, 11 for repeated seizures, nine for acute pancreatitis, and six for adverse medical drug reaction). Moreover, they also tended to have a higher admission incidence density for intoxication, whereas there was no difference in admissions for suicide tentative or withdrawal reaction". However, individuals from both groups, seropositive and seronegative were admitted for "infectious complications", including non-opportunistic pneumonia, purulent bronchitis, tuberculosis, soft tissue infection, osteoarticular infection, endocarditis, primary bacteremia and disseminated candidiasis. More importantly, of a total of 541 admissions of seropositive individuals, 187 (35%) were individuals who had an ORAL mode of drug "application" and 9 (0.5%) inhalation.[20]

That both intravenous and oral drug users develop positive "HIV" antibody tests was shown as far back as 1988 when Sterk reported that a higher percentage of prostitutes who use oral drugs (84%), than IV (46%), test positive.[21]

In another study published in 1993, researchers from New York City tested 1246 seronegative drug users. "Nine had at least one CD4 cell count of <300 cells/ml or a CD4<20%" and 21 subjects "had one CD4 cell count between 300 and 500 cells/ul". They also reported that "CD4 cell counts of <500 cells/ul were, however, associated with subsequent HIV seroconversion...The relative risk for seroconversion among subjects with one or more CD4 count <500 cells/ul, compared with HIV-negative subjects with all counts >500 cells/ul was 4.53"...consistent with an Italian study showing IDU's with CD4 counts <1,000/ul were more likely to seroconvert"[22]. (The authors of the latter reported a "low number of T4 cells was the highest risk factor for HIV infection" (relative risk=8.5)[23]. In other words, in drug users, a decrease in T4 cells instead of following seroconversion is a predictor for

seroconversion, a finding completely at odds with the HIV theory of AIDS.

(4) In Africa there was neither a new disease AIDS nor a new virus HIV. When *Reappraisal of AIDS: Is the oxidation caused by the risk factors the primary cause?* as finally published was written in 1984/85, Africa was not considered an important issue. Thus, Africa is only briefly mentioned. Following the 1986 Paris AIDS conference, AIDS in Africa became the defining example of heterosexual transmission. This is the reason that my paper was initially rejected by *Medical Hypotheses*. The March 1987 letter of resubmission was accompanied by a 12 page document entitled "AIDS in Africa and its heterosexual transmission". This included the following summary:

"SUMMARY:
a. The operational definition of AIDS in Africa is different from the rest of the World. In Africa there is neither direct or indirect data which proves beyond any scientific doubt the existence of a new disease, AIDS, which affects both men and women equally and of its postulated causative virus, HTLV-III/LAV assumed to be sexually transmitted.

b. In Africa immune deficiency, opportunistic infections and KS exist and have existed for a long time in both men and women. However the pathogens could be other than HTLV-III/LAV, for e.g. poverty, infections other than HTLV-III/LAV and the drugs used for their treatment, copper, recreational drugs (if not opiates other traditional drugs), anally or orally deposited sperm itself via homosexual, bisexual or heterosexual practices.

The data from Africa used to prove heterosexual transmission will not stand up to even superficial scientific analysis".

The detail of the text included:

"IMMUNOLOGY
In 1, Piot *et al.,* [*Lancet* 1984,2:65] found that 7 out of 12 controls had low T4 /T8 ratio, 5 of which were due to a decreased T4. They state "Tuberculosis, protein caloric malnutrition and various parasitic diseases can all be associated with depression of cellular immunity".

"...Among healthy Africans resident in a non-AIDS area, the number of helper and suppressor lymphocytes were the same in HTLV-III/LAV seropositive and seronegative subjects..." (Bigger, *Lancet* 1986, 1, 79).

"Parasitic diseases and malnutrition are two possible causes of immunodepression in Africa. A wide range of prevalent protozoal and helminthic infestations have been reported to induce immunodeficiency" (Clumeck, *JAMA*, 1985, 254, 2599).

"Mild sunstroke induces immunosuppression including T4/T8 inversion" (Walker, *Lancet*, 1983, 2, 344).

"Normal volunteers (hospital and university staff) underwent a 12 half-hour exposure to a commercially available solarium on consecutive days excluding Saturday and Sunday, to acquire a suntan. Tests of immune function were carried out before, on completion and 2 weeks after exposure. A number of abnormalities were found in the exposed subjects including significant decrease in T 4 and T4/T8 which persisted 2 weeks after exposure". (Hersey, *Lancet*, 1983, 1, 545).

SEROLOGY
Very high levels of HTLV-III/LAV seropositivity has been reported from Africa.

"...25% of a sample of hospital workers in Zaire were seropositive in 1984" (Frazer, *Med. J. Aust.* 1986, 145, 525).

"65% of Ugandan children were found to have been positive in 1972" (Gallo *et al., Ann. Int. Med.* 1985, 103, 679).

"15.5% of blood donors were found to be positive at Kigali in Rwanda in 1984" (Clumeck, *JAMA*, 1985, 254, 2599).

"41 out of 410 (10%) of healthy medical personnel from Mulago Hospital Kampala were positive for HTLV-III/LAV. 5 out of 30 (17%) of controls outside the hospital were positive. 4 out of 10 (40%) of control patients deemed sexually immature were also found positive" (Serwadda, *Lancet*, 1985, 2, 849).

"Of a total of 274 patients at the Makala Tuberculosis Sanatorium in Kinshasa, half of the suspected pulmonary cases (total 56); one third of the confirmed pulmonary cases (160) and two thirds of the remaining 15 who were confirmed to have extrapulmonary disease tested positive both in the ELISA and Western blot." (Mann, Paris Conference).

"Forty out of 368 (11%) children admitted to Mama Yemo Hospital in Kinshasa, Zaire were positive by ELISA and 39 out of the 40, also by Western Blot. Clinically seropositivity was associated with the diagnosis of malnutrition and pneumonia" (Davachi, Paris Conference).

"21% of the staff at the Zambian Consolidated Copper Mines, and 14% of males and 44% of females at the mine hospital were found positive. Other people tested who had no connection with the mines were negative." (Buchanan, *Lancet*, 1986, 1, 155)

The diversity of these reports leads to the conclusion that, either copper mining, tuberculosis, malnutrition and pneumonia have as their aetiological factor HTLV-III/LAV or the tests are non-specific. If the tests are specific, because 10-30%. of infected cases develop AIDS within 3 years (Bigger, *Lancet*, 1986, 1, 79) then 1.5-4.6% of the Rwanda population (certainly of its blood donors) and 3.5-7.5% of the Zaireans (certainly of the medical staff at the hospital where the tests were done in 1984) should be either dead or dying by the middle of this year, not to mention prostitutes, Ugandan children, TB patients and workers in regions with copper mining. Obviously this is not the case. Even Quinn Mann, Curren and Piot admit that in developing countries, "...serodiagnosis is complicated by the need for confirmatory testing because of the presence of possible cross-reacting antibodies" (IV). [Quinn *et al., Science* 1986, 234:955]

The final section examined the evidence for heterosexual transmission of AIDS in Africa and concluded that "we are left with a sexually transmitted disease which:

(a) Has continental preferences
(b) Has racial preferences
(c) Has sexual preferences. The same bisexual men can get infected by an African woman but not by a confirmed homosexual AIDS patient with whom he practices repeatedly exclusive active intercourse".

That even today in Africa there is no such thing as a new disease AIDS, and that a positive antibody test does not prove HIV infection, it suffices to mention that: according to an editorial in the July 11th 1998 *Lancet*, the developing world "bears more than 90% of the global burden of HIV infection" and "Tuberculosis (TB) is the leading cause of death worldwide among people with HIV"; no less an authority in AIDS in Africa than de Cock admits that TB has been present in Africa in endemic proportions long before the AIDS era[24]; no less an authority on HIV/AIDS than Essex has proved that in Africa a positive antibody test does not prove HIV infection.[25]

(5) The theory also predicted that decrease in T4 cells is not the hallmark of either HIV infection or the clinical syndrome, that is, the decrease in T4 cells is not HIV specific and is neither necessary nor sufficient for the syndrome to appear, that is, the clinical syndrome is not the result of immune deficiency. In fact it was postulated that the decrease in T4 cells may not be due to their destruction by HIV or any other agent but could result from (i) the extreme sensitivity of T cells to oxidative stress; (ii) T4 cells possessing a lower negative charge than T8 cells could be the first to be destroyed by persistent oxidative stress; (iii) to be sequestrated in diseased peripheral tissues; (iv) decreased binding of the T4 antibody as a result of changes in their surface, that is, due to "down regulation" of the CD4 receptor. To illustrate that at present this is accepted even by HIV/AIDS experts it suffices to quote two papers published last year and one more recently:

"This article discusses the importance of alterations in the CD4+ and CD8+ cell migration in regulating blood lymphocyte levels and questions the extent of virus-mediated CD4+ cell destruction";[26] "Along with other recent analyses and experimental developments these considerations also suggest a need to re-evaluate current concepts about HIV pathogenesis, including the concept that a systemic depletion of CD4+ T cells is the hallmark of the disease";[27] "CD4+ T-cell lymphopenia is due to both shortened survival time and a failure to increase the production of circulating CD4+ T-cells.[28]

(6) A most important prediction was that the tissues of AIDS patients and those at risk would be oxidised, in general, and in particular they would have low sulphydryl (-SH) group levels. In recent years there have been hundreds of papers confirming this prediction. The first was published by German researchers who, for reason(s) not stated, undertook experiments to determine the level of reduced thiols (-SH) in the blood of "HIV" infected individuals. They found that: "Blood plasma samples from HIV-1 infected persons contain elevated glutamate concentrations up to 6-fold the normal level and relatively low concentrations of acid-soluble thiol (i.e. decreased cysteine concentrations). The intracellular glutathione concentration in peripheral blood-mononuclear cells (PBMC) and monocytes from HIV antibody-positive persons are also significantly decreased".[29]

Last year a book published with Luc Montagnier as principal editor further confirms the involvement of oxidative stress in AIDS.[30]

(7) The 10th of July 1986 letter of re-submission to *Nature* was accompanied by a response to the reasons given by the Journal for rejection. The response ended with the following: "If my paper does nothing other than draw attention to the oxidative nature of the risk factors and its biological importance, then it offers what is so far the only hope of treatment which will arrest and reverse the otherwise invariable fatal course of the disease. In my opinion this alone would more than justify its publication".

Indeed the most important practical prediction of the theory was that AIDS can be prevented and treated by stopping exposure to the oxidising risk factors and by using "currently available therapeutic [antioxidants in general and SH-containing, in particular] substances". The best confirmation of this comes from researchers at Stanford University, USA. In 1997 discussing their results they wrote: "In essence, we have shown that GSH levels are lower in subjects with CD4 T cell counts below 200/ml (CD4 <200) than in subjects at earlier stages of HIV disease; that among subjects with CD4 <200, lower levels of GSB (a FACS measure of GSH in CD4 T cells) predict decreased survival; and that the probability of surviving 2-3 years increases dramatically as GSB levels approach normal range. In addition, we have presented preliminary evidence suggesting that oral administration of NAC, which supplies the cysteine required to replenish GSH, may be associated with improved survival of subjects with very low GSH levels" (GSH-reduced glutathione).[31]

Last year they stated: "We have shown that GSH depletion is associated with impaired survival; the greater the depletion, the worse the prospects for survival...By replenishing GSH, NAC or other agents we may be able to modulate such adverse effects of GSH depletion"[30]. However, although the authors are most probably aware of our work (the publications of the Perth group were sent to them a few years ago and are indexed in the Medlines under oxidative stress), for some unknown reason, they state: "HIV-infected individuals would be better served if we could identify the mechanism that underlines the GSH depletion and intervene, if possible, to prevent its occurrence". The best advice they can give in this regard is: "it may be prudent for those individuals to avoid excessive exposure to UV irradiation and unnecessary use of drugs that can deplete GSH - e.g., alcohol and prescription or over-the-counter formulations containing acetominophen [paracetamol]".

(6) Perhaps the boldest claims and predictions were made regarding the existence of HIV. I wrote HIV, "has never been isolated from fresh AIDS tissues". Furthermore, HIV "has never been isolated as an independent stable particle". That is, HIV had not been isolated from either fresh tissues or culture, which means that its existence had not been proven and this situation has not changed up to the present day. At least Montagnier in his 1997 interview to Djamel Tahi admitted that he had not isolated HIV and in his view neither had Gallo.[32] I presented evidence that the observed phenomena (particles, reverse transcriptase, antibody/antigen reactions) which were said to prove the existence of HIV were not specific to a specific retrovirus nor even to retroviruses in general. Unlike Gallo, Montagnier when interviewed by Djamel Tahi, eventually reluctantly admitted that these phenomena were not retrovirus specific.

I cited examples of evidence which, taken together, led to the conclusion that oxidising agents were causing not only AIDS but also gave rise to the phenomena which were interpreted by the Montagnier and Gallo school as indicating the presence of HIV.

As far back as 1986 Montagnier knew that the phenomena could not be obtained unless the cultures were stimulated, although he did not know that the stimulants were oxidising agents.[33] In 1991 Anthony Fauci proved that the "HIV" phenomena could be inhibited by antioxidants.[34]

CONCLUSION

It is over twenty years since I conceived the redox theory of cellular function and nearly as long since its specific application to the problem of AIDS appeared in *Medical Hypotheses*. I look back over this time with very mixed feelings. Naturally I am proud that as a scientific theory every prediction concerning AIDS has materialised. However, I am saddened that there are forces at work which have consistently prevented purposeful but friendly debate. To me and my group the problematic nature of the HIV theory was apparent from the very beginning. It is now my fervent hope that, as the HIV theory continues to fail the many patients who are diagnosed with antibodies to "HIV" and AIDS, the time is rapidly approaching when scientists and physicians will be eager to examine our contribution.

REFERENCES

1. Montagnier L. (1985). Lymphadenopathy-Associated Virus: From Molecular Biology to Pathogenicity. *Ann. Int. Med*. 103:689-693.
2. Ludlam CA, Steel CM, Cheingsong-Popov R, *et al.* (1985). Human T- Lymphotropic Virus Type-III (HTLV-III) Infection in Seronegative Haemophiliacs after Transfusion of Factor VIII. *Lancet* II:233-236.
3. Jason JM, McDougal JS, Dixon G, *et al*. (1986). HTLV-III/LAV Antibody and Immune Status of Household Contacts and Sexual Partners of Persons with Haemophilia. *JAMA* 255:212-215.
4. Papadopulos-Eleopoulos E, Turner VF, Papadimitriou JM, Hedland- Thomas B, Causer D, Page B. (1995). A critical analysis of the HIV-T4- cell-AIDS hypothesis. *Genetica* 95:5-24.
5. Papadopulos-Eleopulos E. (1988). Reappraisal of AIDS: Is the oxidation caused by the risk factors the primary cause? *Med. Hypotheses* 25:151-162.
6. Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM. (1992). Kaposi's sarcoma and HIV. *Med. Hypotheses* 39:22-9.
7. Lauritsen JL. NIDA meeting calls for research into the poppers-Kaposi's sarcoma connection. (1995). p. 325-330 In: AIDS: Virus- or Drug Induced Duesberg PH, ed Kluwer Academic Publishers, London.
8. Vilmer E, Rouzioux C, Vezinet Brun F, et al. (1984). Isolation of new lymphotropic retrovirus from two siblings with Haemophilia B, one with AIDS. *Lancet* I:753-757.
9. Ter-Grigorov VS, Krifuks O, Liubashevsky E, Nyska A, Trainin Z, Toder V. (1997). A new transmissible AIDS-like disease in mice induced by alloimmune stimuli. *Nat. Med*. 3:37-41.
10. Goedert JJ, Sarngadharan MG, Biggar RJ, *et al.* (1984). Determinants of retrovirus (HTLV-III) antibody and immunodeficiency conditions in homosexual men. Lancet 2:711-6.
11. Stevens CE, Taylor PE, Zang EA, *et* al. (1986). Human T-cell lymphotropic virus type III infection in a cohort of homosexual men in New York City. *JAMA* 255:2167-2172.
12. Burger H, Weiser B, Robinson WS, *et al*. (1985). Transient antibody to lymphadenopathy-associated virus/human T-lymphotropic virus type III and T-lymphocyte abnormalities in the wife of a man who developed the acquired immunodeficiency syndrome. *Ann. Int. Med.* 103:545-7.
13. Kingsley LA, Kaslow R, Rinaldo CR, *et al.* (1987). Risk factors for seroconversion to human immunodeficiency virus among male homosexuals. *Lancet* i:345-348.
14. Caceres CF, van Griensven GJP. (1994). Male homosexual transmission of HIV-1. *AIDS* 8:1051-1061.
15. Padian N, Marquis L, Francis DP, *et al.* (1987). Male-to-female transmission of human immunodeficiency virus. *JAMA* 258:788-90.
16. Padian NS, Shiboski SC, Glass SO, Vittinghoff E. (1997). Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study. *Am. J. Epidemiol*. 146:350-357.
17. Layon J, Warzynski M, Idris A. (1986). Acquired immunodeficiency syndrome in the United States: a selective review. *Critical Care Medicine* 14:819-27.
18. Goldman KP. (1987). AIDS and tuberculosis. *Brit. Med. J*. 295:511-512.
19. Des Jarlais DC, Friedman SR. (1994). AIDS and the use of injected drugs. *Sci. Am.* 56-62.
20. Scheidegger C, Zimmerli W. (1996). Incidence and spectrum of severe medical complications among hospitalised HIV-seronegative and HIV-seropositive narcotic drug users. *AIDS* 10:1407-14.
21. Sterk C. (1988). Cocaine and HIV seropositivity. *Lancet* i:1052-1053.
22. Des Jarlais DC, Friedman SR, Marmor M, et al. (1993). CD4 lymphocytopenia among injecting drug users in New York City. *J. Acquir. Immun. Defic. Syndr*. 6:820-822.
23. Nicolosi A, Musico M, Saracco A, Molinari S, Ziliani N, Lazzarin A. (1990). Incidence and risk factors of HIV infection: A prospective study of seronegative drug users from Milan and Northern Italy, 1987-1989.*Epidemiology* 1:453-459.
24. De Cock KM, Soro B, Coulibaly IM, Lucas SB. (1992). Tuberculosis and HIV infection in sub-Saharan Africa. *JAMA* 268:1581-7.
25. Kashala O, Marlink R, Ilunga M, *et al.* (1994). Infection with human immunodeficiency virus type 1 (HIV-1) and human T cell lymphotropic viruses among leprosy patients and contacts: correlation between HIV-1cross-reactivity and antibodies to lipoarabinomannan. *J. Infect. Dis.* 169:296-304.
26. Rosenberg YJ, Anderson AO, Pabst R. (1998). HIV-induced decline in blood CD4/CD8 ratios: viral killing or altered lymphocyte trafficking? *Immunol.Today* 19:10-7.
27. Grossman Z, Herberman RB, Vatnik N, Intrator N. (1998). Conservation of total T-cell counts during HIV infection: alternative hypotheses and implications. *J. Acq. Immune Def. Syndr. Hum. Retrovirol.* 17:450-7.
28. Hellerstein M, Hanley MB, Cesar D, *et al.* (1999). Directly measured kinetics of circulating T lymphocytes in normal and HIV-1 infected humans.*Nat. Med.* 5:83-89.
29. Eck HP, Gmunder H, Hartmann M, Petzoldt D, Daniel V, Droge W. (1989).Low concentrations of acid-soluble thiol (cysteine) in the blood plasma of HIV-1-infected patients. *Biol. Chem.* Hoppe-Seyler 370:101-8.
30. Montagnier L, Olivier R, Pasquier C, eds. Oxidative stress in cancer,AIDS and neurogenerative diseases. New York: Marcel Dekker Inc, 1998.
31. Herzenberg LA, De Rosa SC, Dubs JG, *et al.* (1997). Glutathione deficiency is associated with impaired survival in HIV disease. *Proc. Natl. Acad.Sci.* U S A 94:1967-72.
32. Tahi D. (1998). Did Luc Montagnier discover HIV? Text of video interview with Prof. Luc Montagnier at the Pasteur Institute July 18th 1997. *Continuum* 5:30-34.
33. Klatzmann D, Montagnier L. (1986). Approaches to AIDS therapy. *Nature* 319:10-11.
34. Kalebic T, Kinter A, Poli G, Anderson ME, Meister A, Fauci AS. (1991). Suppression of human immunodeficieny virus expression in chronically infected monocytic cells by glutathione, glutathione ester, and N-acetylcysteine. *Proc. Natl. Acad. Sci*. U S A 88:986-990.

Joan Shenton
of Meditel Productions

LOSING IT

It was while we were walking down one of those long hospital corridors that the young Kenyan medical researcher paused, looked behind him, and whispered "Nine of them lost it." I had asked about the 'HIV positive' prostitutes in the long-running Nairobi study who, I'd been told, had lost HIV (or sero-reverted) - not that anyone had particularly wanted to trumpet this rather perplexing anomaly. "They can't understand it" said my companion.

That was in 1993 when "being HIV positive" meant you had it for life and your life wouldn't last much longer anyway. But why shouldn't the antibody profile of those prostitutes (who were often severely malnourished intravenous drug users), change after ten years of regular health checks and good care offered them by the Nairobi Study?

Other people around the world have been "losing it" too, and none of the orthodox AIDS scientists seem in too much of a hurry to try to understand it.

Tom (not his real name), living in London, thought he was HIV positive for 6 years. He also thought he was going to die for six years, until some further tests showed that not only was his latest blood sample negative, but so was the initial one that had been stored away in a freezer. He is suing a London teaching hospital for compensation.

Peter Nicholls was positive on three different test kits in a research project of ours, and then negative at two London teaching hospitals two months later.

A group of Miami lawyers have 80 cases of "false positive"diagnoses on their books, with one of their clients awarded $600,000 in compensation a couple of years ago.

Most of these examples of disappearing HIV relate to the commonly used ELISA and Western blot antibody tests. But now viral load tests, that check for evidence in the DNA of what are promoted as HIV related proteins, are getting in on the act.

The *Wall Street Journal* announced this week that HIV positive patients on triple therapy combination cocktails (costing $15,000 per person per year) are being allowed prolonged "drug vacations". Researchers at the University of Alabama say that a cocktail break can keep a patient's viral load in check and undetectable - more so than if they were on the ghastly 40 tablet a day regime.

And just today I read in the *Pink Paper* that a 12 year-old boy, a pregnant 40-year old woman and a 20 year old man were given a viral load test which told them they "had it" but then they "lost it" again because the tests were wrong.

These are not simply cases of laboratory error. They confirm the arguments put forward for over a decade now from the Perth Group of scientists and the Berne Study Group - namely that "HIV tests" do not identify a lethal infectious sexually transmitted virus, but instead identify raised proteins or genetic fragments in the blood which they say are specific to HIV. How they can say this when HIV has never even been isolated, as the Perth Group have long pointed out. Furthermore, these supposed HIV-specific proteins can emerge in any one of us if our bodies a specifically stressed.

It is absolutely no joke to be told you are going to die and later to be told you had a "wrong" test result. Where are the lawyers? Why hasn't the Government insisted on a national recall of all those who have tested positive? They do it with faulty cars. Why not with a faulty test based on a faulty virus-AIDS hypothesis?

With so many blatant contradictions, how much longer can the AIDS barons hold onto their argument? Sooner or later they are going to have to "lose it" too.