HIV Seropositivity and Mortality in Persons with Hæmophilia - Proof that HIV causes AIDS?

The Hæmophilia Connection

Following publication in September of the Oxford Hæmophilia study attracting widespread press attention, eminent scientist Dr Eleni Papadopulos-Eleopulos and her colleagues in Perth, Western Australia respond. *Continuum* is honoured to present the paper that *Nature* refused to publish.

In a study published by a large group of epidemiologists, of British haemophiliacs *(Nature,* September 7th), it is claimed that "During 1985-92, there were 403 deaths in HIV seropositive patients, whereas 60 would have been predicted from rates in seronegatives suggesting that 85% of the deaths in seropositive patients were due to HIV infection".

In the accompanying *Nature* editorial it is said that this "thorough study", "will, for most people, be sufficient proof that the infection [HIV] leads to AIDS". However most people are not scientists and for scientists "suggesting" is not proving.

One can claim that the 85% increase in death rate amongst seropositive haemophiliacs is due to HIV if, and only if, the study had evidence which showed that:

(1) The cause of death in the 343 extra deaths in the seropositive patients was AIDS, otherwise one will have to show that in haemophiliacs HIV does not cause only AIDS but all the other diseases from which these patients died.
(2) All the patients who died from "AIDS" were infected with HIV.
(3) HIV causes AIDS.

DISEASES LEADING TO MORTALITY

A glance at table 3 [of the study] where "cause-specific mortality during 1985-92" is given, shows that of the 403 deaths in seropositive individuals, 168 died from causes other than AIDS. The other 235 died from "AIDS, HIV, etc". The statement that deaths were due to "HIV, etc" is meaningless. AIDS stands for Acquired Immune Deficiency (AID) on the one hand and the syndrome (S) on the other. Because the syndrome is constituted from more than 25 diseases and because no other single, infectious agent is posited as the cause of such a panoply of distinct and unrelated diseases including infections and neoplasms (growths), it is said that the syndrome is caused indirectly. That is, HIV causes Acquired Immune Deficiency which in its turn leads to the appearance of the Syndrome. It is accepted that in AIDS, 'AID' stands for decreased T4 (helper) cells resulting from their destruction by HIV.

AID

In the study there is no evidence that the 235 patients had a low T4 cell count due to their destruction by HIV or any other agent. In fact, at present there is no evidence that the T4 cells of haemophiliacs or for that matter, any AIDS patients, are destroyed either by HIV or any other agents, or that a causative relationship exists between a decrease in T4 cells and the appearance of the clinical syndrome.[1] In fact no agreement, or even evidence, exists that lymphocytes contain two subsets, T4 and T8 which have exclusive roles, T4 as helpers and T8 as suppressors, a fact acknowledged by immunologists from many institutions including the University of Stockholm and the Institut Pasteur.[2,3]

As far back as 1981 James Goodwin, from the University of New Mexico, wrote: "The T- and B-cell measurers - having run through the sick, the elderly, the young, the pregnant, the bereaved - had finally run out of diseases....And now it's starting all over again, this time with T-cell subsets....Why not let us unimaginative immunologists publish to our heart's content?....My strongest argument is this: Measurement of T and B cells and their subsets in disease has no clinical meaning....But most non-immunologists do not realise this....Non-immunologists have naturally assumed that any subject occupying so much Journal space must be relevant in some way - a logical but incorrect assumption".[4]

SYNDROME

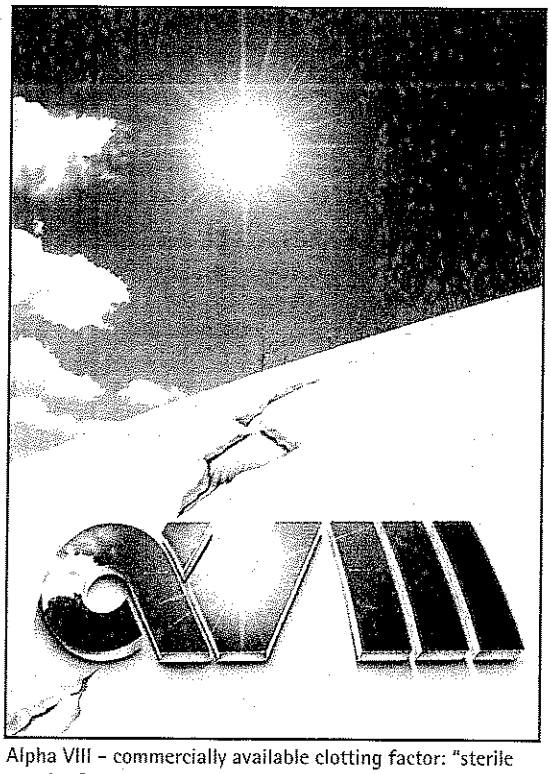
None of the diseases which constitute this syndrome is new or specific to it. The diseases which are rare in the general population and most often diagnosed in AIDS are two: Kaposi's sarcoma (KS) and

Pneumocystis carinii pneumonia (PCP). In fact these two diseases constitute the basis for the HIV hypothesis of AIDS. Although in the *Nature* studies it is not stated how many, if any, British haemophiliacs have died from KS, it is a known fact that unlike gay men, haemophiliacs rarely, if ever, die from KS. The clinical picture of PCP is not specific to this disease; both infectious and non-infectious diseases produce clinical pictures comparable with PCP. Neither can the disease be diagnosed by radiological means.

Before the AIDS era, and even in the early 1980's, the visualisation of the causative organism *P. carinii* in Gomori-methenamine salver (GMS) stained preparation of lung tissue obtained by open lung biopsy was considered the only method suitable for a definite diagnosis of PCP. Even with this method "considerable expertise is necessary to differentiate *P. carinii* from other GMS positive entities, particularly yeast".[5] In the AIDS era, the method used to diagnose PCP became less and less specific. Instead of open lung biopsy, diagnosis began to be obtained by fibreoptic bronchoscopy, a much "less dependable" procedure, or bronchoalveolar lavage (BAL). However, "one might expect to find *P. carinii* in the fluid from bronchoalveolar lavage of about 40% of patients with AIDS who present with symptomatic pneumonia caused by other organisms".[6]

Despite the very high level of false positive results obtained with BAL, this procedure is not only used to definitely diagnose PCP but, more recently, as a gold standard for other, even less specific procedures used for the "definite" diagnosis of PCP, such as testing specimens from sputum induction using GMS.[7] In turn this procedure is used as a gold standard for the "definite" diagnosis of PCP by testing sputum specimens with the use of "monoclonal antibodies" instead of GMS, although it is accepted that in sputum specimens GMS "will stain not only *P. carinii* but also host and microbial cells and amorphous debris, which make up a large part of the sputum sample; even in experienced hands, distinguishing *P. carinii* from this background can be difficult".[8]

Another method presently used for the "definite" diagnosis of PCP is the polymerase chain reaction. However, the authors themselves admit that this method, when compared to detection of *P. carinii* in BAL or sputum specimens, as gold standard, is less specific and "most falsely positive samples were from patients treated with immunosuppressive drugs or from HIV-positive patients with CD4 counts below 0.2 x 10^9/l".[9]



Alpha VIII - commercially available clotting factor: "sterile powder for reconstitution."

Nonetheless, on the basis of these tests, individuals from the AIDS risk groups, including haemophiliacs are diagnosed as having PCP and are treated accordingly. Some studies recommend the use of "empiric therapy for PCP, based purely on" clinical findings. But, "The propensity of patients with PCP to present with atypical clinical finding, the ability of both infectious and non-infectious diseases to produce a clinical picture compatible with PCP, and the toxicity of anti-pneumocystis treatment regimes however, all argue against the use of empiric treatment based on clinical evaluation alone".[5] The toxic effects include "neutropenia, thrombocytopenia, or both",[6] which are of particular significance to haemophiliacs since these diseases were present in high frequency in this population long before the AIDS era, and thrombocytopenia is considered to be a contributing factor in the development of AIDS in haemophiliacs.[10]

In conclusion from the study it is not possible to say how many of the 235 hæmophiliacs died from KS and PCP, considered to be the most specific AIDS diseases; from "mild and moderate diseases", which following the 1985 CDC AIDS definition signified AIDS; from AIDS-defining conditions according to the 1987 CDC definition (according to which a patient could have been certified as dying from AIDS without a definite disease diagnosis or even with no evidence for HIV infection and even with evidence against HIV infection); or from "AIDS" in general whatever one means by it.

CAUSE

Of the 343 extra deaths in HIV seropositive hæmophiliacs between 1985-92 only 235 were due to "AIDS, HIV, etc". To account for the other 168 extra deaths one will have to assume that either:
(1) In hæmophiliacs HIV does not cause only AIDS but all the other diseases for which the 168 patients died.
(2) In the AIDS era two, or more, new pathogens appeared in hæmophiliacs, HIV which caused the 235 deaths and the other(s) which caused the other 168 diseases.
(3) The extra deaths in hæmophiliacs, including the 235 who died from "AIDS, HIV, etc." were caused by agents other than HIV.

The only evidence which one can find in the study for a causal role of HIV in hæmophilia deaths is that most of the deaths occurred in seropositive hæmophiliacs. However, as it has correctly been pointed out in the editorial, "It is well known that no amount of statistical argument can by itself prove that a disease is actually caused by the agent with which it is statistically associated". Indeed before one can claim that "85% of deaths in seropositive patients were due to HIV infection", one must satisfy two conditions:
(1) Present evidence that the "seropositive patients" were actually infected with HIV, that is, the antibody tests are HIV specific.
(2) Prove, by direct evidence, not by association, that the "85% of deaths" were caused by HIV.

There are two major problems in using "seropositivity" to diagnose HIV infection:
(i) The only way to determine the specificity of the antibody test for HIV infection is to use viral isolation as a gold standard. This has never been reported and in fact there is ample evidence that the tests are non-specific.[11] That this is the case in hæmophiliacs is acknowledged by very well known HIV/AIDS researchers.[12-14] Even the CDC accepts that a positive test in hæmophiliacs is not proof of HIV infection. "It is possible that antibody to LAV is acquired passively from immunoglobulins found in factor VIII concentrates.... Likewise, it is possible that seropositivity is caused not by infectious virus but by immunisation with noninfectious LAV or LAV proteins derived from virus disrupted during the processing of plasma into factor VIII concentrate".[15]

(ii) According to the authors of the epidemiological study, "A reliable test for HIV antibodies became available to Hæmophilia Centres early in 1985. Among those who were alive on 1st January 1985, 78% of potentially infected severe patients and 52% of moderate/mild patients had been tested by December 1985, rising to 90 and 74% respectively by January 1993. One thousand and twenty severe patients and 207 moderate/mild patients were found to be infected....The median estimated date of seroconversion was October 1982 for severe patients and December 1982 for moderate/mild patients".

Before 1987 a positive ELISA with or without a WB was considered proof of HIV infection. However, it was realised that many individuals (4000/6000) [67%] in one study[16], who had a positive ELISA did not test positive when the WB was performed. This was interpreted as evidence that the WB was more specific than the ELISA, and since 1987 many, but not all, laboratories use ELISA only as a screening test and WB as

confirmation. But in addition to the fact that the specificity of the WB has never been determined, there are many other problems associated with the use of this test to prove HIV infection, so much so, that according to Philip Mortimer, "Western blot detection of HIV antibodies began as and should have remained, a research tool".[17]

Among the many problems associated with the WB is the arbitrary introduction of criteria as to which WB pattern means HIV infection. At present these criteria vary between continents, between countries and even between laboratories in the same country. The criteria have also changed over time. It is of pivotal significance that the criteria used to define a positive WB before 1987, by which time most of the hæmophiliacs were tested and were found to be positive, would not satisfy even the "least stringent" criteria presently used to define a positive WB result.

The study gave no evidence that the hæmophiliacs were even infected with HIV

IN CONCLUSION

(1) The study presented no evidence that the 235 seropositive hæmophiliacs died from AIDS, whichever definition is chosen, merely the bold assumption that they died from "AIDS, etc.".

(2) The study presented no evidence that the excess deaths in the seropositive patients were caused by HIV, or even that the hæmophiliacs were infected with HIV.

(3) The most one can claim from the evidence presented is that the finding of a positive "HIV antibody" test, whatever that signifies (but certainly not HIV infection of hæmophiliacs via factor VIII), indicates an underlying abnormal propensity to develop a number of illnesses which may prove fatal.

(4) The study, more than anything, highlights the urgent need to:

(a) Determine the meaning of a positive "HIV antibody" test in hæmophiliacs;

(b) Determine the effects which factors associated with "HIV antibodies" may have on the health of persons with hæmophilia. These include lifetime exposure to factor VIII and impurities in clotting concentrates, prophylactic and therapeutic anti-bacterial and anti-viral agents, AZT, blood transfusions, steroids and also the psychological impact of a diagnosis of HIV seropositivity.[18,19]

In any scientific debate both sides have obligations, the antagonist to question when there is indisputable evidence that contradicts the received wisdom; the protagonist to answer these questions rather than simply to suppress them. One such question rises from the following laboratory data:

1. There is unanimity that gpl20, a component of the knobs on the surface of HIV, is an absolute prerequisite for "HIV infection";[20,21]
2. Such knobs are found only in immature (budding) particles which are "very rarely observed", and are absent in cell-free HIV[22,23] thus rendering cell-free HIV non-infectious.
3. According to Professor R. Penny, Australia's leading HIV/AIDS expert, "HIV is rapidly inactivated in discarded needles and syringes";[24]
4. Levy and his colleagues have shown that the titre of HIV in plasma of HIV-infected individuals three, six or twelve hours after phlebotomy (drawing blood), "dropped from up to 500 TCID/ml to 0" [TCID=tissue culture infectious dose];
5. In January 1994, the CDC communicated the following experimental data and conclusion:

"In order to obtain data on the survival of HIV, laboratory studies have required the use of artificially high concentrations of laboratory grown virus...the amount of virus studied is not found in human specimens or anyplace else in nature,...it does not spread or maintain infectiousness outside its host. Although these unnatural concentrations of HIV can be kept alive under precisely controlled and limited laboratory conditions, CDC studies have shown that drying of even these high concentrations of HIV reduces the number of infectious viruses by 90 to 99 percent within several hours. Since the HIV concentrations used in laboratory studies are much higher than those actually found in blood or other body specimens, drying of HIV-infected human blood or other body fluids reduces the theoretical risk of environmental transmission to that which has been observed - essentially zero".[25]

Since: (a) in most instances, if not all, the time between phlebotomy and conversion of pooled plasma to factor VIII concentrate is considerably greater than 3 hours; (b) factor VIII is made from plasma which is cell-free; (c) the late 1970s factor VIII has been supplied as a dry powder which may spend weeks or months waiting use; how can one reconcile the above facts with the view that hæmophiliacs are infected with HIV via contaminated factor VIII concentrates? ■

Eleni Papadopulos-Eleopulos[1], Valendar F.Turner[2], Bruce Hedland-Thomas[1], David Causer[1], John M. Papadimitriou[3].
1-Department of Medical Physics, 2-Department of Emergency Medicine, Royal Perth Hospital, Box X2213 Perth, Western Australia 6009;
3-Department of Pathology, University of Western Australia.

Correspondence: Eleni-Papadopulos-Eleopulos.
Voice int + 61 9 2243221 Fax int + 61 0 2243511
email <vturner@uniwa.uwa.edu.au>

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