BACK

THE PERTH GROUP

Commentary on the Mulder study: Two-year HIV-1-associated mortality in a Ugandan rural population.
Mulder *et al*. *Lancet* 1994;343:1021-3.

There are many flaws in the study by Mulder *et al*. Amongst these are:
1. The study did not randomly select individuals for inclusion or follow up and not all who were studied were healthy at the beginning of the study;
2. In both HIV^- and HIV^+ groups, mortality data did not clearly differentiate between AIDS and non-AIDS deaths;
3. In some patients the cause of death may have been determined one year prior to death;
4. The study does not mention if any patients had "known causes of immunosuppression such as cancer or severe malnutrition or other recognized etiologies", which, according to the Bangui African AIDS definition, exclude individuals as AIDS patients. (In Africa these should include exposure to sunlight since this is known to induce T4 cell depletion" [1,2]).

If one ignores the above then we would have to agree with Dondero and Curran that the study has shown in "subsistence farmers" living in rural Uganda "that the simple finding of antibodies against HIV in an individual's serum predicts a likelihood of death within the next several years far above that for a seronegative individual". However, such a finding does not prove that:
1. Death is due to a new disease;
2. The individual is infected with HIV;
3 .The death is caused by HIV.

According to HIV/AIDS researchers, including Gallo and Montagnier [3], AIDS and HIV are both new, "new disease, new agent". To substantiate that a new disease is caused by a new agent there must be:
1. Diagnostic proof for the existence of a new disease;
2. Proof that all patients with the new disease have evidence of exposure to the new agent;
3. Proof that the new agent causes the disease.

However:
1. The Bangui definition of AIDS in Africa does not include any diseases or signs which have recently appeared. Indeed, the signs and diseases in the Bangui definition are long standing and ubiquitous in Africa;
2. The presence of antibodies in an individual's serum which react with some proteins, even if there is proof that these are HIV antigens, is not sufficient proof that the patient is infected with HIV. Although this basic principle is ignored by virtually all AIDS researchers, there is at least one who has expressed some caution. According to Philip Mortimer, director

of the Virus Reference Laboratory of the Public Health Laboratory Service, London, UK, "Diagnosis of HIV infection is based almost entirely on detection of antibodies to HIV, but there can be misleading cross-reactions between HIV-1 antigens and antibodies formed against other antigens, and these may lead to false-positive reactions. *Thus, it may be impossible to relate an antibody response specifically to HIV-1 infection*. In the presence of clinical and/or epidemiological features of HIV-1 infection there is often little doubt, but anti-HIV-1 may still be due to infection with related retroviruses (e.g. HIV-2) which, though also associated with AIDS, are different viruses" [4] [italics ours]. However, although Gallo and his colleagues used the "clinical and/or epidemiological features" as a "gold standard" to determine the specificity of the HIV antibody tests, this is not scientifically valid. In fact, if this practice is adopted then the vast majority of individuals who test positive including the vast majority of individuals in the present study, will be false positive. Of the 73 HIV seropositive adults, one year prior to death, only 5 patients (8%) had "AIDS" and 44% were asymptomatic. The observed "rapid progression and high mortality rate" is not proof that these individuals died of AIDS, all known causes of death could have been operative. One would expect that at least some of these individuals died for the same reasons that the HIV seronegative individuals died. Unfortunately, the causes of death in both groups are not given and it is possible that both HIV seropositive as well as HIV seronegative individuals may have died of "AIDS". Epidemiological data shows that AIDS patients in general and Africans including healthy Africans have high levels of antibodies. For example, United States data [5] indicates that serum IgG levels are higher in HIV^+ American Blacks (mean 2234 ± 930 mg/dl) than in HIV+ Caucasians (mean 1601 ± 520 mg/dl). Serum IgG levels are also higher in Black blood donors (mean 1356± 220 mg/dl) than in Caucasians (mean 1072 ± 243 mg/dl) []. Thus, in these individuals with high level of antibodies one must expect cross-reactions with HIV antigens to be the rule rather than the exception.

Nor is it possible to determine the specificity of an HIV antibody test by repeating the test, by combination of antibody tests or by the use another antibody test as a gold standard as Mulder *et al* and others including Burke *et al* [6] have done previously. Mulder's algorithm [7] is a watered down version of Burke's algorithm, and like Burke's uses the Western blot as a gold standard. For them, the true serostatus depends on repeating two different ELISAs until they are concordant--making the same mistake twice means everything is all right! A fundamental scientific principal of antibody testing is that for a test to be valid, regardless of time of development, generation or appellation, it specificity must be authenticated by the use of an independent gold standard which, for the HIV antibody tests, can be none other than HIV itself. Comparisons between the published work on retrovirology and the presently available data on HIV reveals that no researcher has yet met the requirements for such a gold standard. Indeed, a thorough search of the HIV antibody tests literature reveals that no

such gold standard has ever been used and it may not even be possible [6]. The latter is the case because what is collectively inferred as HIV, (reverse transcriptase, virus-like particles, "HIV antigens" and "HIV PCR"), are all non-specific. The lack of a gold standard has already been adduced by one of the best known HIV/AIDS researchers, William Blattner: "One difficulty in assessing the specificity and sensitivity of retrovirus assays is the absence of a final 'gold standard'. In the absence of gold standards for both HTLV-I and HIV-1, the true sensitivity and specificity for the detection of viral antibodies remain imprecise" [8].

Even if a positive antibody test was proof of HIV infection, this would not be sufficient to claim a causal relationship between HIV and AIDS. (Most AIDS patients are also infected with CMV and HBV, but neither is claimed to be the cause of the syndrome). Proof that HIV is the cause of AIDS has not yet been presented.

Those "who will not even accept that antibody to HIV indicates infection with the virus", have no need to postulate a novel or "curious" explanation for the relationship between "a positive HIV antibody test" and AIDS or between positive HIV serology and mortality. Simple, basic scientific facts will suffice and a few easily understandable examples which may include in some cases death of the individual are:

1. Antibodies to an extract of ox heart (cardiolipin) predict the development of syphilis, but these patients are not infected with ox heart and ox heart is not the cause of syphilis;
2. Patients with infectious mononucleosis, a viral disease, develop antibodies to sheep red blood cells. However, sheep red blood cells are not present in these patients and neither is sheep blood the cause of the disorder;
3. Patients with relapsing fever, a disease caused by *Borellia recurrentis*, develop antibodies to the bacterium *Proteus* OX19, yet the latter organism is not present in these patients and neither is it the cause of relapsing fever.

Thus the most that one can conclude from the study of Mulder *et al* is that the presence of "HIV antibodies" reflects an underlying abnormality in individuals that accompanies a propensity to develop illnesses and die. "HIV antibodies" are no more than a non-specific marker for this proclivity. In this manner, rural Ugandans are no different from Western AIDS patients where all the high risk groups have high levels of antibodies directed against a plethora of antigenic determinants. Until the antibody tests are verified against a viral isolation gold standard the relationship between antibodies that react with "HIV antigens" and HIV infection will remain unknown.

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