BACK

The Perth Group

November 2016

A commentary on immune deficiency and AIDS

The immune system

Broadly the immune system consists of several types of white blood cells ("immune system" cells) including the T4 and T8 subsets and antibodies and other soluble substances that circulate in blood and lymph. Immune system cells are also constituents of the lymph nodes and spleen and the collections of lymphoid tissue found in the walls of the gastrointestinal tract (gut-associated lymphoid tissue, GALT).

The HIV theory

It was accepted that no single infectious agent could directly cause the heterogeneous collection of diseases (AIDS "indicator" diseases) that constitute the clinical AID syndrome. The only credible way to link HIV to the indicator diseases, none of which were new, required an intermediary. The intermediary became the "cellular immunodeficiency" (acquired immune deficiency, the 'AID' in AIDS) that had been documented in the earliest AIDS literature[1, 2]. The cellular immunodeficiency theory of AIDS was facilitated by the prevalent belief that many different pathologies result from a "defective" or "deficient" immune system. In the case of AIDS the "defect" was specifically designated a low T4 lymphocyte count in peripheral blood. T4 lymphocytes are also called CD4, CD4+ and helper T-cells.

In his 2015 book *Knowledge Wars* the Nobel laureate immunologist Peter Doherty explains the HIV theory of AIDS as follows: "The basic problem is that HIV preferentially (though not exclusively) infects a class of white blood cell called the CD4+, or helper, T-lymphocyte that mediates both the direct control of many other infections and promotes the optimal functioning of the whole immune system. Once all the CD4+ T-cells are gone, our capacity to mount a protective immune response against a novel invading pathogen erodes as night follows day. In effect, though HIV does not kill us directly, it destroys the immune system so that bacteria like *M. tuberculosis* (the cause of TB), generally innocuous fungi and protozoa like *P. carinii* and *Cryptosporidium*, and viruses like HHV8 [human herpesvirus-8] and Epstein-Barr virus (EBV), a related herpes virus that can cause lymphomas, are released from control to cause progressive body wasting and eventual death".[3] In *Harrison's Textbook of Internal Medicine* Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, expresses the HIV theory as: "The hallmark of HIV disease is a profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as helper T cells occurring in a setting of polyclonal immune activation".[4] (Under this guise HIV is responsible for both immune activation (stimulation) and deficiency in AIDS patients).

The HIV theory was problematic even as the first cases were reported. Not all homosexual men with AIDS had cellular immunodeficiency. For example, in 1985 physicians at the St Vincent's Hospital and Medical Center New York City documented men with or dying from AIDS (*Pneumocystis carinii* pneumonia, PCP) who had normal numbers of T4 lymphocytes (17%) and "the degree of suppression did not influence mortality".[5, 6] Donald Hoover and his colleagues had reported the opposite: "Significant numbers of individuals remain free of illnesses and AIDS symptoms > or = 3 years after CD4+ cell counts drop below 200 x 10(6)/l. This occurs even in the absence of treatment",[7] that is, the "CD4 cell count is a weak surrogate endpoint".[8] As recently as 2013 Weber *et al* reported CD4 lymphocyte counts at the time of death in 459 HIV-infected patients 18 years and over enrolled in the Swiss Cohort

Study. The median duration of HIV infection was 13.5 years and 20% of all deaths occurred with T4 cell counts >= 500 cells/uL.[9] Among the latter at least 8% were due to AIDS (another 8% were "Unknown"). These facts are unheeded and to this day the HIV theory is propagated as **HIV infection → destruction of T4 cells (AID) → one or more "indicator" diseases → the clinical Syndrome = AIDS**.[10] And the greater the quantity of HIV the greater the immune suppression and the shorter the time between infection and the onset of the AIDS indicator diseases. Nonetheless, even ignoring the "weak surrogate endpoint" does not leave the HIV theory problem free.

Immune deficiency

"Immune deficiency" has virtually become a disease in its own right[11] spawning a novel pharmacopoeia with a remarkable array of products to "boost" or "support" the immune system, even for healthy children as young as two years. As a result the term has acquired a variety of meanings – from a lay nondescript panacea for many and various ills to a specific measurement, for example, a low T4 lymphocyte count. Apart from these vagaries there is the problem of the chicken and the egg: Immune deficiency leads to infections and infections are claimed to cause immune deficiency. For instance measles virus "infects CD4 lymphocytes"[12] and measles is known to "cause significant immune suppression". Hence does HIV lead to immune deficiency or immune deficiency lead to HIV?[13, 14] If there is a retrovirus HIV, is it merely another opportunistic infection like *Pneumocystis carinii* and *M. tuberculosis* that infects individuals with pre-existing "immune deficiency"?[15, 16] *The Oxford Handbook of Clinical Immunology and Allergy* lists dozens of causes of immune deficiency: "CD4 T cell numbers will be reduced…in most acute viral infections and in seriously ill patients in the ITU [intensive therapy unit] setting.[17] In the intensive care unit "Acute illness alone, in the absence of HIV infection, can be associated with profound decreases of T-lymphocyte populations".[18] According to Reinhold Schmidt, Clinic for Immunology and Rheumatology at Hanover Medical School, "The most common causes [of immune deficiency] worldwide include malnutrition, poor sanitary conditions and human immune deficiency virus (HIV) infection".[19] In other words, a low T4 lymphocyte count is not HIV-specific.[10, 20] Malnutrition, poor sanitary conditions and AIDS diseases are long prevalent in sub-Saharan Africa and associated with poverty, especially extreme poverty. According the World Health Organisation extreme poverty is "The world's biggest killer and the greatest cause of ill-health and suffering across the globe".[21] Hence why does one need a retrovirus to explain AIDS in Africa?[22-24] The principle AIDS-defining disease in Africa is tuberculosis (TB) and "In TB as well as in lepromatous leprosy, an immunosuppressive state will frequently develop in the host. This state is characterised by T lymphopenia [decreased T cell count] with a decreased number of T helper cells [T4] and an inverted T-helper/T-suppressor cell [T8] ratio...immunosuppression induced by the infection with *M. tuberculosis* can persist for life, even when TB is not progressive".[25]

Counting T4 cells and what it means

The number of T4 lymphocytes in blood is measured using antibodies which bind to a protein, the CD4 protein, situated on the cell surface. The antibodies are tagged with a fluorescent compound such as fluorescein or rhodamine and the cells counted in a machine that passes them one at a time through a laser beam. By 1980 the routine measurement of T-cell subsets was being introduced into hospital laboratories which explains how physicians were able to detect "cellular immunodeficiency" in the first AIDS cases.

The utility of counting T4 cells is premised on their having a particular, well defined function[26] and their measurements being clinically useful.[10, 27] In a paper which began "This article is a diatribe against the measurement of T-cell subsets in human diseases", James Goodwin at the University of New Mexico School of Medicine wrote: "It's starting again. I had gone for 14 months without seeing an article reporting on T and B levels in one disease or another. 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. Each condition was the subject of many

reports; so that now, to give but one example, we can conclude with some assurance that T-cell numbers are up, down, or unchanged in old folks. And now it's starting all over again, this time with T-cell subsets [T4, T8 and others]…Measurement of T and B cells and their subsets in disease has no clinical meaning…There is a feeling about that T- and B-cell numbers mean something an immunologic equivalent of an SGOT level or creatinine clearance [biochemical tests of liver and renal function respectively]…Non-immunologists have naturally assumed that any subject occupying so much journal space must be relevant in some way – a logical but incorrect assumption".[26, 27] Since then (1981/83) others including researchers from the University of Stockholm have confirmed these claims arguing that T8 (suppressor) cells do not exist[28] and suggesting that the "CD4 count at AIDS diagnosis could be an insensitive indicator of association with immune deficiency".[29] So on the one hand, in 1988 Göran Möller, the foremost Scandinavian pioneer in immunology argues that T8 cells do not exist while on the other hand, in 2015 Fauci listed eleven "Major characteristics of the CD8+ cell, noncytotoxic anti-HIV response".[30] According to immunologist Victor Appay "In recent years, a subpopulation of CD4 T ["helper"] cells has also been shown to have suppressive properties".[31]

Nonetheless, a low T4 cell count as determined by antibody binding remains the defining measurement of the immune "defect" in AIDS and is claimed to be the result of HIV-induced destruction of the T4 cells ("cytopathic effect"). Under this guise the role of HIV is perceived as limiting the number of T4 cells available to play a presumptive role in the maintenance of a "healthy immune system". This is how HIV experts, infectious disease physicians, public health officials, numerous websites, NGOs and bloggers promote the belief in the existence of an immune system destroying retrovirus. Guidelines recommending lifelong monitoring of T4 cells result in patients living in constant fear of their next count. Counting continues even at the death bed despite physicians knowing that "Once the CD4 T-cell count falls below 0.05×10^9/L [50 cells/ml], further monitoring is of little clinical value (except psychologically to patients, who view cessation of monitoring as doctors giving up"[17]). Yet there is no evidence that T4 cells are killed by "HIV" or by anything else.[10]

The failure of an antibody to bind to a T4 cell does not prove the cell is missing or dead. In fact in 1985 Montagnier himself acknowledged that antibody binding to T cells is sensitive to their physiological state – "this phenomenon [antibody binding to T4 lymphocytes] could not be related to the cytopathic effect" of HIV but is "probably due to either modulation [modification, alteration] of T4 molecules at the cell membrane or steric hindrance of antibody-binding sites"[32] (steric hindrance "occurs when the large size of groups within a molecule prevents chemical reactions that are observed in related molecules with smaller groups" [Wikipedia]). That is, the T4 cells are present but the counting machine is blind to those to which the antibody cannot bind.

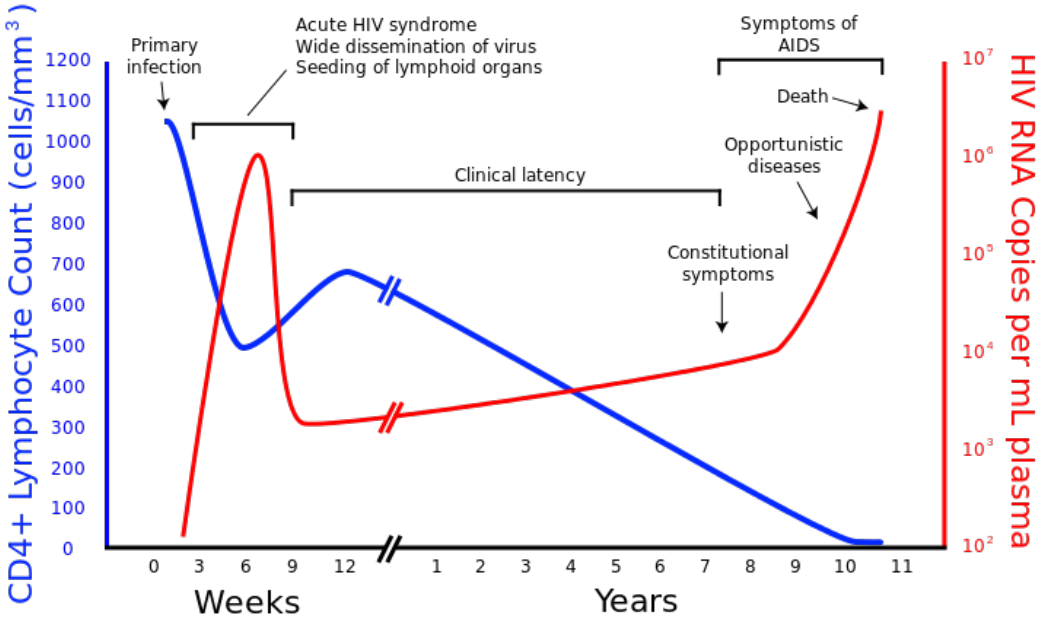
Failure to bind is not limited to modulation or steric hindrance. T4 cells can change their phenotype from one subset to another, for example, to a T8 or T10 lymphocyte.[26] As far back as 1982 it was shown that T4 cells become T8 cells following a 24 hour incubation with chemicals such as impromidine and adenosine.[33] (Adenosine is a physiological substance as well as a drug frequently used in emergency medicine to treat cardiac arrhythmias). From the beginning it was known that in AIDS patients a decrease in T4 lymphocytes is accompanied by an increase in T8 lymphocytes with their total number remaining constant, that is, normal.[34, 35] This means that T-cell markers are fluid, modulated by factors in their environment which include the physiological *milieu* of AIDS patients and those at risk of developing AIDS.[36-39]

Changing the theory

Within 16 months of publishing his discovery of HIV, Montagnier asserted "This syndrome [AIDS] occurs in a minority of [HIV] infected persons, who generally have in common a past of antigenic [immune] **stimulation** [microbial infections, drug use] and of immune depression **before** LAV [HIV] infection"[40] (emphasis added). In other words Montagnier reversed cause and effect and in doing so relegated HIV a secondary event in AIDS.

In 1984 Robert Gallo and his colleagues in the USA published four papers in *Science* where they concluded "These results and those reported elsewhere in this issue suggest that HTLV-III [HIV] may be the primary cause of AIDS".[41] Nonetheless, by 1986 Gallo claimed the same papers were "clearcut evidence" that HIV is the cause of AIDS.[42] These statements were made despite none of Gallo's four *Science* papers containing the data required to prove the HIV theory of AIDS. (See Kary Mullis' account of his search for a paper that proves the HIV theory[43]). It was not until 1986 that Gallo published experimental data addressing the effects of HIV on T4 cells in culture but his results do not prove HIV destroys the T4 cells. What Gallo showed was that the addition of the material he designated "HIV", accompanied by the mitogen phytohaemagglutinin, obligatory to produce "HIV" in cell cultures, decreases the number of lymphocytes binding to the anti-CD4 fluorescent antibody.[44] This is not proof of cell destruction (see above) and even if it were, Gallo reported the same effect when the same mitogen was added to cultures in the absence of "HIV". The obvious experiment, the only experiment that mattered, testing HIV on its own without mitogens, Gallo did not report. Again in 1986 both Gallo and Montagnier published evidence showing that "viral particles, antigenic expression [the appearance of "HIV" proteins in cultures] and the cytopathic effect" cannot be detected in the absence of immune stimulation[44, 45] [mitogens added to the cultures]. But if immune stimulation is required to produce HIV then HIV cannot be the cause of the immune stimulation.[46]

Nonetheless, the theory is first there is infection, then AID as HIV kills the T4 cells, followed by a varying interval after which AIDS appears, with a direct relationship between the amount of HIV, the rate of immune system (T4 cell) decline and the time it takes for AIDS to develop.[47] As perennially illustrated in this *ersatz* graph.



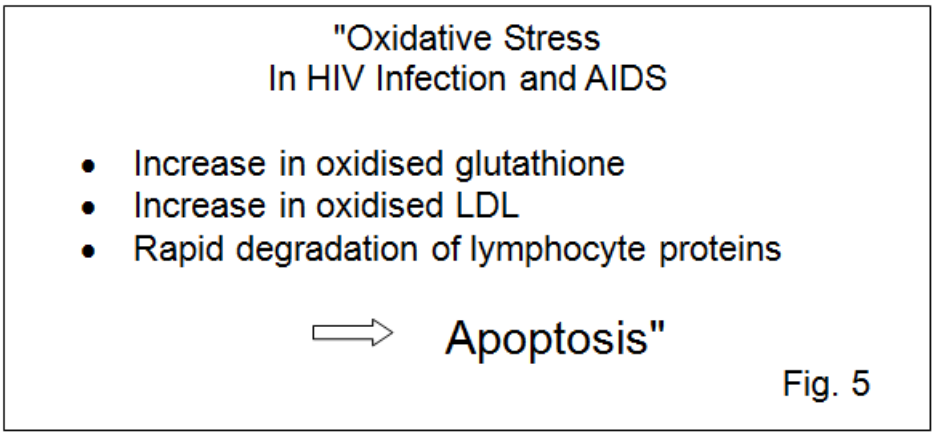
Whether one considers the "Primary infection" or the "Clinical latency" period, the graph advances an inverse relationship between the amount of virus (label of RHS ordinate) and the number of T4 cells (LHS ordinate). However in 2006 Benigno Rodriguez and fourteen

other experts from highly credentialed institutions in the USA, including the Universities of Harvard and California, published data from which they concluded that the "Presenting HIV RNA level predicts the rate of CD4 [T4] decline only minimally in untreated persons…only a small proportion of CD4 cell loss variability (4%-6%) could be explained by presenting plasma HIV RNA level…other factors, as yet undefined, likely drive CD4 cell losses in HIV infection. These findings have implications for treatment decisions in HIV infection and for understanding the pathogenesis of progressive immune deficiency".[48] The HIV expert H. Clifford-Lane, Chief of the Laboratory of Immunoregulation, Clinical and Molecular Retrovirology Section of the US National Institutes for Health, published a commentary on the Rodriguez paper entitled "Explaining, Predicting, and Treating HIV-Associated CD4 Cell Loss. After 25 Years Still a Puzzle".[49] It read "The provocative main finding from their study was that the presenting plasma HIV RNA load predicted no more than 10% of the observed CD4 cell loss in patients with chronic untreated HIV infection. What factor(s) explain the other 90%? Twenty-five years into the HIV epidemic, a complete understanding of what drives the decay of CD4 cells - the **essential event of HIV disease** - is still lacking…The findings presented by Rodriguez *et al* **provide support to those who favor nonvirological mechanisms as the predominant cause of CD4 cell loss**" (emphasis added). That is, the HIV experts accept that virtually none of the T4 cell decline is caused by HIV. According to Rodriguez and his associates the "Other factors" are immune activation (stimulation).[48] Given the preeminent scientists conceding such a minimalist role for HIV in the "essential event of HIV disease", nothing less than the fundamental axiom of the HIV theory, it is astonishing that the "support to those who favour nonvirological mechanisms as the predominant cause for CD4 cell loss" evaporated as rapidly as the ink dried. The mere suggestion that "HIV, the virus that causes AIDS" is "minimally" involved in the T4 cell destruction claimed to link HIV to 29 deadly diseases should have opened a Pandora's box and led to a major rethink of the HIV dogma. This was not to be.[50] Within a few weeks of publication Rodriguez and his colleague Michael Lederman at Case Western Reserve University posted an article at AIDSTruth.org explaining why their paper did not prove what they, their peer-reviewers and editorial commentators said their paper did prove.[51] A year after the Rodriguez *et al* paper three papers appeared in the *Journal of Immunology* with evidence equally problematic for the HIV theory.[52-54] These data led to the conclusion that "CD4 depletion by itself does not necessarily result in progression to AIDS".[55, 56]

One must not forget that originally the destruction of T4 cells was proposed as the link between HIV and the appearance of PCP and KS in a restricted cohort of homosexual men. But after a quarter of a century the theory has been revised to such an extent that the original is difficult to recognise. In 2003 Mette Hazenberg and her colleagues published a study of 102 homosexual men enrolled in the Amsterdam Cohort Studies. Noting that "elevated immune activation is related to the outcome of HIV-1 infection" they "postulated that persistent hyperactivation of the immune system may cause depletion of CD4 T cells because it leads to erosion of the naive T cell pool" and that this may act even before HIV infection. To test this hypothesis they measured preseroconversion (pre-HIV infection) T4 cell numbers and activation in patients whose T4 cell counts were <500 per ml (500 per ml is the lower limit of normal). They found that the median time to AIDS for these patients was 7.6 years compared with more than 14.0 years for patients who had > 500 cells/ml before seroconversion. They concluded "This study demonstrated for the first time that low **preseroconversion** numbers of CD4 T [T4] cells and increased levels of immune activation [stimulation] were associated with an increased risk to develop AIDS after seroconversion…our data show that chronic immune activation and the size of the CD4 T cell pool are critical factors in HIV-1 pathogenesis, **even when measured before seroconversion**. These data support the hypothesis that persistent hyperactivation of the immune system may lead to erosion of the naïve T cell pool and CD4 T cell depletion"[57] (emphasis added).

This is not surprising. From the beginning both Gallo and Montagnier knew that the obligatory *in vitro* stimulation required to detect the phenomena interpreted as HIV is also present *in vivo*. This physiological state[36, 39, 58, 59] is present in AIDS patients and those at risk because such individuals are exposed to many immune stimulating agents[4] before HIV infection and may have low T4 cells in the absence of HIV infection.[57, 60-66] As long ago as 1986 Gallo himself documented a list of immune stimulating factors in homosexual men. "Our results also suggest that multiple rounds of antigenic [immune] stimulation in vivo, as a result of infection with various microorganisms or exposure to allogeneic cells such as semen or blood, may promote HTLV-III [HIV] expression, T4 cell death, further spread of the virus, and ultimately an immunodeficiency syndrome".[44] Montagnier was obviously aware of these difficulties because in 1984 he wrote "Definite evidence [that HIV is the cause of AIDS] will require an animal model in which such viruses [HIV] could induce a disease similar to AIDS".[67] When it comes to Africa the HIV experts accept that immunodeficiencies have long been endemic in that continent.[22-24] In other words, all along the HIV experts have known that for T4 cell decrease in patients with AIDS, HIV is neither necessary nor sufficient. It is immune stimulation not immune suppression that has "predictive value for HIV-1 disease progression", that is, the development of the AIDS indicator diseases. The change in the HIV theory from "immune deficiency" to "immune stimulation" is not well known.

Again in regard to Africa, in the same year the Hazenberg study was published, several HIV/AIDS dissidents organised a meeting "Sida en Afrique - Quelles priorités pour l'aide sanitaire?" The meeting was held at the European Parliament and Montagnier was one of the speakers.[68] Montagnier stated: "Finally, one of the main problems still not totally resolved in the pathogenesis of AIDS, is the explanation for the massive killing of the T4 lymphocytes". According to him the T4 lymphocytes die by a physiological process known as apoptosis[69, 70] (also known as programmed cell suicide[71]) and the cause of the apoptosis is oxidation (see Montagnier's Fig. 5).



"These anomalies do not disappear completely after antiretroviral treatment, suggesting they merit correction by taking the appropriate antioxidants. Preliminary studies indicate that oxidative stress is higher in African patients and exists even among uninfected individuals, as a result of malnutrition" (our translation).

If:

(a) T4 decrease is the cause of the AIDS diseases;
(b) the decrease is due to cellular oxidation;
(c) oxidation in Africa is due to malnutrition;

it follows that HIV cannot be the cause of AIDS in Africa. AIDS in Africa is due to cellular oxidation which is the result of poverty and its many consequences including malnutrition. As former President of South Africa Thabo Mbeki pointed out in March 2016, "The world's

biggest killer and the greatest cause of ill-health and suffering across the globe is listed almost at the end of the International Classification of Diseases. It is given the code Z59.5 - extreme poverty".[72] Hence Montagnier is reiterating our cellular oxidative theory of AIDS published 15 years before the European Parliament meeting under the title "Reappraisal of AIDS: Is the oxidation caused by the risk factors the primary cause?[36-39] Indeed our 1988 paper is the first publication linking oxidation to AIDS, and questioning the evidence said to prove the existence of HIV and proposes the oxidative theory of AIDS.[73]

References and Notes

1. Friedman-Kien A, Laubenstein L, Marmor M, Hymes K, Green J, Ragaz A, Gottleib J, Muggia F, Demopoulos R, Weintraub M. Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men--New York City and California. MMWR Morbidity and Mortality Weekly Report 1981 30:305-308.
2. Gottlieb MS, Schroff R, Schanker HM, Weisman JD, Fan PT, Wolf RA, Saxon A. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Engl J Med 1981 305:1425-1431.
3. Doherty P. The Knowledge Wars. Melbourne University Publishing, 2015.
4. Fauci AS, Lane HC. Chapter 189. Human Immunodeficiency Virus Disease: AIDS and Related Disorders. Edited by Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. New York, NY, The McGraw-Hill Companies, 2012.
5. Kales CP, Murren JR, Torres RA, Crocco JA. Early Predictors of In-Hospital Mortality for *Pneumocystis carinii* Pneumonia in the Acquired Immunodeficiency Syndrome. Archives of Internal Medicine 1987 147:1413-1417.
6. Not every patient with AIDS had immune deficiency. The 1987 Kales *et al* study at St. Vincent's Hospital and Medical Centre, New York reported 45 patients, 97% of whom were homosexuals with biopsy proven PCP. Overall 17% of AIDS patients had a T4 cell count higher than 500/mm^3, and a further 14% between 301-500/mm^3, "in addition, patients with T4-T8 ratio greater than 1.0 and those with total T4 lymphocyte counts greater than 500/mm^3 cells did not show improved survival compared with patients with abnormal values...our data did not suggest that the degree of immunosuppression affected in-hospital mortality for PCP". The fact that AIDS contravened the HIV theory in 1/6 cases of PCP passed without comment.
7. Hoover DR, Rinaldo C, He Y, Phair J, Fahey J, Graham NM. Long-term survival without clinical AIDS after CD4+ cell counts fall below 200 x 10(6)/l. AIDS 1995 9:145-152. http://www.ncbi.nlm.nih.gov/pubmed/7718184
8. Hughes MD, Daniels MJ, Fischl MA, Kim S, Schooley RT. CD4 cell count as a surrogate endpoint in HIV clinical trials: a meta-analysis of studies of the AIDS Clinical Trials Group AIDS 1998 12:1823-1832. http://www.ncbi.nlm.nih.gov/pubmed/9792383
9. Weber R, Ruppik M, Rickenbach M, Spoerri A, Furrer H, Battegay M, Cavassini M, Calmy A, Bernasconi E, Schmid P, Flepp M, Kowalska J, Ledergerber B, Swiss HIVCS. Decreasing mortality and changing patterns of causes of death in the Swiss HIV Cohort Study HIV Med 2013 14:195-207. http://www.ncbi.nlm.nih.gov/pubmed/22998068
10. Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM, Hedland-Thomas B, Causer D, Page B. A critical analysis of the HIV-T4-cell-AIDS hypothesis. Genetica 1995 95:5-24. http://www.theperthgroup.com/SCIPAPERS/HIVT4CellAIDS.pdf
11. According to the google Ngram application the term "immune deficiency" appeared in the English language around 1945, was infrequently used before 1970 and its use accelerated in the 1980s reaching a peak in 1990. "Immunodeficiency" has a similar trajectory. https://books.google.com/ngrams
12. Baskar PV, Collins GD, Dorsey-Cooper BA, Pyle RS, Nagel JE, Dwyer D, Dunston G, Johnson CE, Kendig N, Israel E, Nalin DR, Adler WH. Serum antibodies to HIV-1 are produced post-measles virus infection: evidence for cross-reactivity with HLA. Clin Exp Immunol 1998 111:251-256.

13. Chandra RK. Nutrition and immunology: from the clinic to cellular biology and back again. Proc Nutr Soc 1999 58:681-683.
14. Chandra RK, Gupta S, Singh H. Inducer and suppressor T cell subsets in protein-energy malnutrition: Analysis by monoclonal antibodies. Nutrition Research 1982 2:21-26.
15. Levy JA, Ziegler JL. Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. Lancet 1983 ii:78-81.
16. Papadopulos-Eleopulos E, Turner V, Page B, Alfonso H, Papadimitriou J, Causer D. HIV Infection—the cause or effect of acquired immune deficiency? 1989 www.theperthgroup.com/REJECTED/AIDScausesHIV3.pdf
17. Spickett G. Oxford handbook of clinical immunology and allergy. Oxford University Press, 2013.
18. Feeney C, Bryzman S, Kong L, Brazil H, Deutsch R, Fritz LC. T-lymphocyte subsets in acute illness. Crit Care Med 1995 23:1680-1685.
19. Daily S. The many causes of immune deficiency. 2009 http://www.sciencedaily.com/releases/2009/09/090914111540.htm
20. Papadopulos-Eleopulos E, Turner V, Papadimitriou J, Page B, Causer D. Montagnier, T4 cells (acquired immune deficiency) and our oxidative theory of "HIV"/AIDS. 2008. www.theperthgroup.com/Nobel/MontagnierOxidation.pdf
21. WHO. The state of world health. http://www.who.int/whr/1995/media_centre/executive_summary1/en/
22. Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM, Bialy H. AIDS in Africa: Distinguishing fact and fiction. World Journal of Microbiology and Biotechnology 1995 11:135-143. http://www.theperthgroup.com/SCIPAPERS/EPEWorldJMicro&BiotechOCR1995.pdf
23. Papadopulos-Eleopulos E, Turner VF. Deconstructing AIDS in Africa. The Independent Monthly 1994 50-51. http://theperthgroup.com/POPPAPERS/IndependentMonthly.pdf
24. Papadopulos-Eleopulos E, Turner VF. Reconstructing AIDS in Africa-Reply to Kaldor and Ashton. The Independent Monthly 1995 February: 23-24. http://theperthgroup.com/POPPAPERS/IndependentMonthly.pdf
25. Lamoureux G, Davignon L, Turcotte R, Laverière M, Mankiewicz E, Walker MC. Is Prior Mycobacterium Infection a Common Predisposing Factor to AIDS in Haitians and Africans? Annales de l'Institut Pasteur Immunologie 1987 138:521-529.
26. Zagury D, Bernard J, Morgan DA, Fouchard M, Feldman M. Phenotypic Diversity within Clones of Human Normal T Cells. Int J Cancer 1983 31:705-710.
27. Goodwin JG. OKT3, OKT4, and all that. "This article is a diatribe against the measurement of T-cell subsets in human diseases". Journal of the American Medical Association 1981 246:947-948.
28. Moller G. Do suppressor T cells exist? Scand J Immunol 1988 27:247-250.
29. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007 370:59-67.
30. Levy JA. Dispelling myths and focusing on notable concepts in HIV pathogenesis. Trends Mol Med 2015.
31. Appay V, van Lier RA, Sallusto F, Roederer M. Phenotype and function of human T lymphocyte subsets: consensus and issues. Cytometry A 2008 73:975-983.
32. Klatzmann D, Champagne E, Chamaret S, Gruest J, Guetard D, Hercend T, Gluckmann J-C, Montagnier L. T-lymphocytes T4 molecule behaves as the receptor for human retrovirus LAV. Nature 1984 312:767-768.
33. Birch RE, Rosenthal AK, Polmar SH. Pharmacological modification of immunoregulatory T lymphocytes. II. Modulation of T lymphocyte cell surface characteristics. Clin Exp Immunol 1982 48:231-238.
34. Margolick JB, Donnenbery AD, Muñoz A, Park LP, Bauer KD, Giorgi JV, Ferbas J, Saah AJ. Changes in T and Non-T Lymphocyte Subsets Following Seroconversion to HIV-1:

Stable CD3+ and Declining CD3- Populations Suggest Regulatory Responses Linked to Loss of CD4 Lymphocytes. J Acquir Immune Defic Syndr 1993 6:153-161.
35. Stanley SK, Fauci AS. T Cell Homeostasis in HIV Infection: Part of the Solution, or Part of the Problem? J Acquir Immune Defic Syndr 1993 6:142-143.
36. Papadopulos-Eleopulos E. Reappraisal of AIDS: Is the oxidation caused by the risk factors the primary cause? Med Hypotheses 1988 25:151-162.
http://www.theperthgroup.com/SCIPAPERS/EPEMedHyp1988.pdf
37. Papadopulos-Eleopulos E. Looking back on the oxidative stress theory of AIDS Continuum 1998 5:30-35.
http://theperthgroup.com/CONTINUUM/LookingBackContinuum.pdf
38. Papadopulos-Eleopulos E, Hedland-Thomas B, Causer DA, Turner VF, Papadimitriou JM. Changes in thiols and glutamate as consequence of simian immunodeficiency virus infection. Lancet 1991 338:1013-1014.
http://theperthgroup.com/SCIPAPERS/SIVMac.pdf
39. Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM. Oxidative stress, HIV and AIDS. Res Immunol 1992 143:145-148.
http://www.theperthgroup.com/SCIPAPERS/EPEOxstressHIVAIDS.pdf
40. Montagnier L. Lymphadenopathy-Associated Virus: From Molecular Biology to Pathogenicity. Ann Intern Med 1985 103:689-693.
41. Gallo RC, Salahuddin SZ, Popovic M, Shearer GM, Kaplan M, Haynes BF, Palker TJ, Redfield R, Oleske J, Safai B, White G, Foster P, Markham PD. Frequent Detection and Isolation of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and at Risk for AIDS. Science 1984 224:500-503.
42. Gallo RC. First isolation of HTLV-III. Nature 1986 321:119.
43. Dr. Kary Mullis is a US scientist who won the 1993 Nobel Prize in Chemistry for the invention of the polymerase chain reaction. In the preface to Peter Duesberg's book "Inventing the AIDS Virus" Mullis recounts how in 1988 he was employed by the US National Institutes for Health (NIH) to set up analyses for HIV testing at Specialty Labs in Santa Monica, USA. When preparing a report for his employer he asked a virologist working at the next desk, a "reliable and competent fellow", for a reference that HIV is the probable cause of AIDS. He was told he did not need one. Mullis catalogues his surprise: "I disagreed. While it's true that certain scientific discoveries or techniques are so well established that their sources are no longer referenced in the contemporary literature, that didn't seem to be the case with the HIV/AIDS connection. It was totally remarkable to me that the individual who had discovered the cause of a deadly and as-yet-uncured disease would not be continually referenced in the scientific papers until that disease was cured and forgotten. But, as I would soon learn, the name of that individual-who would surely be Nobel material-was on the tip of no one's tongue. Of course, this simple reference had to out there somewhere. Otherwise, ten of thousands of public servants and esteemed scientists of many callings, trying to solve the tragic deaths of a large number of homosexual and/or intravenous (IV) drug using men between the ages of twenty-five and forty, would not have allowed their research to settle into one narrow, channel of investigation. Everyone wouldn't fish in the same pond unless it was well established that all the other ponds were empty. There had to be a published paper, or perhaps several of them, which taken together indicated that HIV was the probable cause of AIDS, there just had to be". Mullis then spent the next two years conducting computer searches and asking scientists at the many meetings he attended for that "simple reference". The fact that no one could oblige inexorably drew him to conclude "The entire campaign against a disease increasingly regarded as the twentieth-century Black Death was based on a hypothesis whose origins no one could recall. That defied both scientific and common sense". However, after enduring several years of uncertainty, Mullis hopes were raised by a visit from Professor Luc Montagnier, who discovered HIV in 1983. Mullis again put the question and reports the reply: "With a look of condescending puzzlement, Montagnier said, "Why don't you quote the report from the Centers for Disease Control?"

I replied, “It doesn’t really address the issue of whether or not HIV is the probable cause of AIDS, does it?”
“No”, he admitted, no doubt wondering when I would go away. He looked for support to the little circle of people around him, but they were all awaiting a more definite response, like I was.
“Why don’t you quote the work on SIV [Simian Immunodeficiency Virus]?”, the good doctor offered.
“I read that too, Dr. Montagnier,” I responded. “What happened to those monkeys didn’t remind me of AIDS. Besides, that paper was just published only a couple of months ago. I’m looking for the original paper where somebody showed that HIV caused AIDS”.
This time, Dr. Montagnier’s response was to walk quickly away to greet an acquaintance across the room”.
See:
Duesberg PH. Inventing the AIDS Virus. Regnery Publishing, Inc. 1996. Washington, USA.
And https://www.youtube.com/watch?v=dL3cAS3YUKM

44. Zagury D, Bernard J, Leonard R, Cheynier R, Feldman M, Sarin PS, Gallo RC. Long-term cultures of HTLV-III--infected T cells: a model of cytopathology of T-cell depletion in AIDS. Science 1986 231:850-853. http://www.ncbi.nlm.nih.gov/pubmed/2418502
45. Klatzmann D, Montagnier L. Approaches to AIDS therapy. Nature 1986 319:10-11.
46. In a 1995 *Nature* editorial John Maddox wrote “Meanwhile, one important question stands out like a sore thumb: why, after more than a decade of research, has it only now emerged that the response of the immune system to infection by HIV is hyperactivity rather than the opposite?”. See Maddox J. Duesberg and the new view of HIV. Nature 1995 373:189.
47. The delay between HIV infection and AIDS varies up to 50 fold. In untreated, HIV positive individuals the annual AIDS risk is 1-2% for haemophiliacs, 5% for drug users and homosexual men and 50% in blood transfusion recipients. Even if there is an AIDS virus it does not operate alone. As infectious disease physician Joseph Sonnabend has pointed out, with the possible exception of rabies not everyone infected with a microbe falls ill. Additional host and/or environmental factors (“co-factors”) are always part of a disease generating equation. The introduction of co-factors complicates proof of causation.
48. Rodriguez B, Sethi AK, Cheruvu VK, Mackay W, Bosch RJ, Kitahata M, Boswell SL, Mathews WC, Bangsberg DR, Martin J, Whalen CC, Sieg S, Yadavalli S, Deeks SG, Lederman MM. Predictive value of plasma HIV RNA level on rate of CD4 T-cell decline in untreated HIV infection. JAMA 2006 296:1498-1506.
49. Henry WK, Tebas P, Lane HC. Explaining, predicting, and treating HIV-associated CD4 cell loss: after 25 years still a puzzle. JAMA 2006 296:1523-1525.
50. The Failure of Viral Load Tests. 2006. http://www.thebody.com/cgi-bin/bbs/showflat.php?Board=testpos&Number=216816
51. Rodriguez B, Lederman M. What our work means. 2006.
Note: since retiring the AIDSTruth team has inexplicably removed several key postings from their website. This includes the Rodriguez/Lederman link. However, the AIDSTruth website, including the Rodriguez/Lederman link, was archived by a third party before the AIDSTruth team advised its readers “Our work is done”.
http://web.archive.org/web/20130314072102/http://www.aidstruth.org/science/rodriguez-lederman
52. Gordon SN, Klatt NR, Bosinger SE, Brenchley JM, Milush JM, Engram JC, Dunham RM, Paiardini M, Klucking S, Danesh A. Severe depletion of mucosal CD4+ T cells in AIDS-free simian immunodeficiency virus-infected sooty mangabeys. The Journal of Immunology 2007 179:3026-3034.
53. Milush JM, Reeves JD, Gordon SN, Zhou D, Muthukumar A, Kosub DA, Chacko E, Giavedoni LD, Ibegbu CC, Cole KS, Miamidian JL, Paiardini M, Barry AP, Staprans SI, Silvestri G, Sodora DL. Virally induced CD4+ T cell depletion is not sufficient to induce AIDS in a natural host. J Immunol 2007 179:3047-3056.

54. Pandrea IV, Gautam R, Ribeiro RM, Brenchley JM, Butler IF, Pattison M, Rasmussen T, Marx PA, Silvestri G, Lackner AA, Perelson AS, Douek DC, Veazey RS, Apetrei C. Acute loss of intestinal CD4+ T cells is not predictive of simian immunodeficiency virus virulence. J Immunol 2007 179:3035-3046.
55. Papadopulos E, Papadimitriou J, Turner V. Response to Jeanne Bergman “HON lies about T cells”. 2009. http://theperthgroup.com/HON/PGBergmanHONNov242009.html
56. Papadopulos E, Papadimitriou J, Turner V. Response to Jeanne Bergman “Real Answers to Fake Questions”. 2009. www.theperthgroup.com/HON/PGHONFakeQuestionsDec042009.html
57. Hazenberg MD, Otto SA, van Benthem BH, Roos MT, Coutinho RA, Lange JM, Hamann D, Prins M, Miedema F. Persistent immune activation in HIV-1 infection is associated with progression to AIDS. AIDS 2003 17:1881-1888.
58. Buhl R, Jaffe HA, Holroyd KJ, Wells FB, Mastrangeli A, Saltini C, Cantin AM, Crystal RG. Systemic glutathione deficiency in symptom-free HIV-seropositive individuals. Lancet 1989 2:1294-1298.
59. Eck HP, Gmunder H, Hartmann M, Petzoldt D, Daniel V, Droge W. Low concentrations of acid-soluble thiol (cysteine) in the blood plasma of HIV-1-infected patients. Biol Chem Hoppe Seyler 1989 370:101-108.
60. Goedert JJ, Sarngadharan MG, Biggar RJ, Weiss SH, Winn DM, Grossman RJ, Greene MH, Bodner AJ, Mann DL, Strong DM, Gallo RC, et al. Determinants of retrovirus (HTLV-III) antibody and immunodeficiency conditions in homosexual men. Lancet 1984 2:711-716.
61. Nicolosi A, Musico M, Saracco A, Molinari S, Ziliani N, Lazzarin A. Incidence and risk factors of HIV infection: A prospective study of seronegative drug users from Milan and Northern Italy, 1987-1989. Epidemiology 1990 1:453-459.
62. Moffat EH, Bloom AL, Mortimer PP. HTLV-III antibody status and immunological abnormalities in haemophilic patients. Lancet 1985 I:935.
63. Ludlam CA, Steel CM, Cheingsong-Popov R, McClelland DBL, Tucker J, Tedder RS, Weiss RA, Philip I, Prescott RJ. Human T-Lymphotropic Virus Type-III (HTLV-III) Infection in Seronegative Haemophiliacs after Transfusion of Factor VIII. Lancet 1985 II:233-236.
64. Jason JM, Evatt B, Chorba TL, Ramsey RB. Acquired immunodeficiency syndrome (AIDS) in hemophiliacs Scand J Haematol 1984 33:349-356.
65. Tsoukas C, Gervais F, Shuster J, Gold P, O’Shaughnessy M, Robert-Guroff M. Association of HTLV-III Antibodies and Cellular Immune Status of Hemophiliacs. N Engl J Med 1984 311:1514-1515.
66. Kessler CM, Schulof RS, Goldstein AL, Naylor PH, Luban NL, Kelleher JF, Reaman GH. Abnormal T-Lymphocyte Subpopulations Associated with Transfusions of Blood-Derived Products. Lancet 1983 I:991-992.
67. Vilmer E, Rouzioux C, Vezinet Brun F, Fischer A, Chermann JC, Barre-Sinoussi F, Gazengel C, Dauguet C, Manigne P, Griscelli C. Isolation of new lymphotropic retrovirus from two siblings with Haemophilia B, one with AIDS. Lancet 1984 I:753-757.
68. Montagnier L. Apports de la recherche dans la lutte contra le Sida en Afrique. Edited by Pietteur M. Belgique, Collection Resurgence, 2004, p. 224
69. Elmore S. Apoptosis: a review of programmed cell death. Toxicol Pathol 2007 35:495-516. http://www.ncbi.nlm.nih.gov/pubmed/17562483
70. “Apoptosis is a highly regulated and controlled process” leading to cell death in multicellular organisms. It occurs physiologically (naturally) as distinct from pathological cell death (necrosis) caused by external agents. The two forms differ histologically. http://en.wikipedia.org/wiki/Apoptosis
71. Wyllie AH, Kerr JFR, Currie AR. Cell Death: The Significance of Apoptosis. Int Rev Cytol 1980 68:251-306.
72. Mbeki T. 2016. A Brief Commentary on the Question of HIV and AIDS. As former President of South Africa Thabo Mbeki points out "The world's biggest killer and the greatest cause of ill-health and suffering across the globe is listed almost at the end of the International Classification of Diseases. It is given the code Z59.5 - extreme poverty".

http://www.theperthgroup.com/HIV/MbekiOnAIDSMarch2016.pdf
http://www.who.int/whr/1995/media_centre/executive_summary1/en/

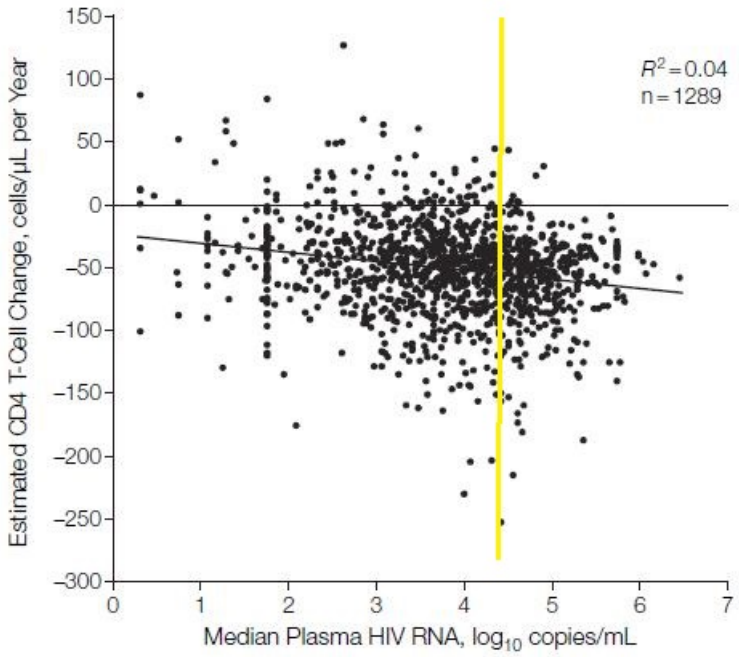
73. A Medline search conducted on Melbourne Cup Day 2016 using the keywords [HIV and redox] returned 654 publications. Our hypothesis, Reappraisal of AIDS – is the oxidation induced by the risk factors the primary cause? 25th March 1988 is number 654, that is, the first such publication on record at the *National Library of Medicine*.

Addendum

Data from Rodriguez *et al* "Predictive value of plasma HIV RNA level on rate of CD4 T-cell decline in untreated HIV infection".[1]

"Main Outcome Measures The extent to which presenting plasma HIV RNA level could explain the rate of model-derived yearly CD4 cell loss, as estimated by the coefficient of determination (R_2)".

Figure 3. Use of Multiple Measurements of HIV RNA Improves the Predictive Ability of HIV RNA Level on CD4 Cell Decline Rate Only Minimally



Scatterplot of estimated CD4 cell count change per year against presenting HIV RNA level (1 measurement per patient). The fit line and *R*2 are derived from linear regression. Although the coefficient of determination increases slightly, even using the maximum number of available measurements improves the predictive ability of plasma HIV RNA level only minimally.

Coefficient of determination

The coefficient of determination ("R squared", R^2) is a statistical technique used to calculate the error predicting one variable by a second variable. R^2 varies between 0 and 1 (0% and 100%) and the higher the value the less the error. An R^2 of 0 means the first variable cannot be predicted by the second variable.

In the Rodriguez study annual changes in a T4 cell count were plotted against the first recorded plasma HIV RNA count in order to determine how well the patient's initial "viral load" predicted the subsequent decline in cellular immunity. Their data are shown in Figure 3 in the form of a scatterplot. The R^2 result was 4% – contrary to what one would expect from the HIV theory of AIDS.

Comments

The vertical line shows for example that two individuals presenting with 4.5 log median plasma HIV RNA can lose 250 T4 cells or gain 50 T4 cells per microliter respectively over the ensuing year. Similar findings are observed at 1 log copy number (and lower). Overall the scatterplot shows there are approximately 70 patients whose T4 cell count increased 5-125/µL over the ensuing year and this occurred with initial copy numbers 0.5-5.0 log HIV RNAs.

1. Rodriguez B, Sethi AK, Cheruvu VK, Mackay W, Bosch RJ, Kitahata M, Boswell SL, Mathews WC, Bangsberg DR, Martin J, Whalen CC, Sieg S, Yadavalli S, Deeks SG, Lederman MM: Predictive value of plasma HIV RNA level on rate of CD4 T-cell decline in untreated HIV infection, JAMA 2006, 296:1498-1506.