LETTERS TO THE EDITOR

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No proof HIV antibodies are caused by a retroviral infection

Curry and his colleagues in their paper 'HIV antibody seroprevalence in the emergency department at Port Moresby General Hospital, Papua New Guinea' in the August 2005 issue of this journal reported that 18% of 300 'opportunistic' serum samples showed positive reactions with antigens present in 3/3 HIV test kits.[1] From these data HIV infection in Papua New Guinea was depicted as 'an unfolding disaster' – a conclusion requiring proof that the reactivity is due to a retroviral infection HIV.

In order to perform an antibody test for HIV infection one must first obtain the HIV antigens. That is, the proteins of a particle stated to be a unique and taxonomically distinct Lentivirus of the family Retroviridae. However, the particles that Montagnier and Gallo reported in their unpurified cell culture supernatants were not a Lentivirus but other genuses. According to Montagnier, credited as the discoverer of HIV, 'analysis of the proteins of the virus demands mass production and purification'.[2] In 1983 Montagnier and in 1984 Gallo claimed to have purified HIV particles by banding culture supernatant in a sucrose density gradient and to have proven the existence of both HIV proteins and antibodies. However, first neither Montagnier nor Gallo published electron micrographs of 'purified virus'; and second in 1997 Montagnier stated neither he nor Gallo had evidence for HIV purification and that, despite a 'Roman effort', his 'purified virus' did not even contain particles with 'the morphology typical of retroviruses', much less purified retroviral particles.[2] Instead, the reaction between some proteins in the density gradient banded material ('purified virus'), and antibodies in AIDS patient sera, was considered proof that both the proteins and antibodies were 'HIV'.

The fact that an antibody reacts with an antigen is not proof the antibody arises in response to that antigen. All antibodies including monoclonal antibodies may react ('cross-react') with non-immunizing antigens, and immunologists accept that 'Cross-reactive antibodies may have higher affinity with antigens other than the inducing antigen'.[3] Therefore, patients may possess antibodies that react with antigens to which they have neither been exposed, nor with which they have been infected. Otherwise one would have to conclude that patients with Ebstein–Barr virus infection are 'infected' with sheep and horse erythrocytes; those with group A streptococcal or *Treponema pallidum* infections are 'infected' with heart muscle proteins; and that blood group A individuals are 'infected' with group B erythrocytes and vice versa.

Cross-reactions are more prevalent in individuals with increased levels of immunoglobulins. High levels of antibodies are a feature of AIDS patients and sick individuals in general. Positive antibody tests have been reported in thousands of hospital patients at no risk of AIDS.[4] Cross-reactivity is the stated reason 'active measles infection' results in antibodies that react with the 'HIV-specific' *gag* and *pol* gene antigens.[5] There is also ample evidence that antibodies directed against the mannans (carbohydrates) present in mycobacteria and fungi, organisms responsible for 88% of AIDS diagnoses, cross-react with the same antigens.[6] Significantly, tuberculosis was highly prevalent in Curry's patients. Leading HIV experts have stated that 'ELISA and WB [Western blot] results should be interpreted with caution when screening individuals infected with *M. tuberculosis* or other mycobacterial species', and warned that 'ELISA and WB may not be sufficient for HIV diagnosis in AIDS-endemic areas of central Africa where the prevalence of mycobacterial diseases is quite high'.[7]

The only way of proving that antibody reactivity is caused by a retroviral infection is to compare the presence or absence of reactivity with the presence or absence of the retrovirus. In other words, as with other tests used in clinical practice, the test must be validated against a gold standard.[8] In a test for HIV infection, the gold standard can only be HIV itself, as proven by HIV isolation. Yet, no such data have been reported – a fact acknowledged by manufacturers of antibody tests: 'At present there is no recognized standard for establishing the presence or absence of HIV-1 antibody in human blood'.[9] Instead, specificity is determined using the clinical diagnosis of AIDS as a gold standard. However, AIDS cannot be a substitute gold standard because: (i) AIDS-indicator diseases are caused by agents other than HIV; (ii) the evidence HIV experts present that HIV is the cause of AIDS is the reaction between the antibodies in patient sera and the test kit antigens. To then

claim AIDS proves that the antibodies are HIV is a circular argument. Furthermore, if AIDS is a gold standard for HIV infection, all seropositive individuals who do not have AIDS, that is, the vast majority, must be false positives.

The World Health Organization as well as Curry *et al.* accept that patients are HIV-infected, by virtue of reactivity in three test kits. However, concordant test results do not identify antibodies any more than a pulmonary mass reveals its pathology by its presence in a series of X-ray images. One should also note that the testing algorithm used in this study by Curry *et al.* would not be used to prove HIV infection in Europe, the USA, or Australia.

Curry and his colleagues' data might have affirmed the results of many other studies. That is, patients with antibodies that react with their test kit antigens are at increased risk of developing illnesses that include AIDS indicator diseases. However, their data do not prove that the cause of the reactivity or the diseases is a retrovirus.

References

1. Curry C, Bunungam P, Annerud C, Babona D. HIV antibody seroprevalence in the emergency department at Port Moresby General Hospital, Papua New Guinea. *Emerg. Med. Australas* 2005; **17**: 359–62.

2. Tahi D. Did Luc Montagnier discover HIV? Text of video interview with Professor Luc Montagnier at the Pasteur Institute July 18th 1997. *Continuum* 1998; **5**: 30–4. Available from URL: http://www.theperthgroup.com/CONTINUUM/djamelmontagnier.html [Accessed October 2005].

3. Berzofsky JA, Berkower IJ, Epstein SL. Antigen–antibody interactions and monoclonal antibodies. In: Paul, WE (ed.). *Fundamental Immunology*, 3rd edn. New York: Raven, 1993; 421–65.

4. St. Louis ME, Rauch KJ, Peterson LR, Anderson JE, Schable CA, Dondero TJ. Seroprevalence rates of human immunodeficiency virus infection at sentinel hospitals in the United States. *N. Engl. J. Med.* 1990; **323**: 213–18.

5. Baskar PV, Collins GD, Dorsey-Cooper BA *et al.* Serum antibodies to HIV-1 are produced post-measles virus infection: evidence for cross-reactivity with HLA. *Clin. Exp. Immunol.* 1998; **111**: 251–6.

6. Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM, Causer D. HIV antibodies: further questions and a plea for clarification. *Curr. Med. Res. Opin.* 1997; **13**: 627–34. Available from URL: http://www.theperthgroup.com/SCIPAPERS/epcurmedres97.html [Accessed October 2005].

7. Kashala O, Marlink R, Ilunga M *et al.* Infection with human immunodeficiency virus type 1 (HIV-1) and human T cell lymphotropic viruses among leprosy patients and contacts: correlation between HIV-1 cross-reactivity and antibodies to lipoarabinomannan. *J. Infect. Dis* 1994; **169**: 296–304.

8. Griner PF, Mayewski RJ, Mushlin AI. Selection and interpretation of diagnostic tests and procedures. *Ann. Int. Med.* 1981; **94**: 559–63.

9. Abbott Laboratories Diagnostics Division. 100 Abbott Park Rd. Abbott Park, IL, USA. 1988, 1998. Packet Insert Axsym system (HIV-1/HIV-2). Available from URL: http://aids-kritik.de/aids/diverses/abbott-hiv-test.htm [Accessed October 2005].

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Reply

We agree that HIV antibody testing is not perfect. Even highly specific tests used in low-prevalence populations will result in a significant number of false positive results. The Western blot test, which can be performed in countries with sophisticated laboratory services, is able to distinguish the true from false positive results. In addition, the presence of virus, not just antibody, is routinely confirmed in Australian patients when clinicians check HIV viral loads. Proviral DNA, or p24 antigen assays also confirm infection with HIV in circumstances where antibody testing is unreliable (e.g. in newborn babies with maternal antibody, or in the antibody 'window period' soon after initial infection).[1]

It is an unfortunate fact of life that these sophisticated laboratory tests are not available in Papua New Guinea; however, the use of antibody testing has been well validated in similar settings in other resource-poor countries. In a high-prevalence population two rapid point of care tests in combination are highly sensitive and specific in the detection of HIV infection.[2] Use of three tests is recommended by the World Health Organization for the diagnosis of asymptomatic individuals when seroprevalence in the population being tested is less than 10%.[3] The WHO algorithm for HIV testing in resource-poor countries is a pragmatic response to inadequate resources. The dramatic increase in HIV seroprevalence in Papua New Guinea is being seen in the context of an explosive increase in the number of sick and dying patients with AIDS in hospitals around the

country. The key elements of the approach to HIV in Papua New Guinea are the prevention of transmission through education and safe sex, especially of those found HIV-positive after voluntary counselling and testing. The provision of care and support to those already infected, including the provision of antiretroviral therapy, is the necessary reassurance that those found to be infected with HIV will not be abandoned.

References

1. Dax EM, Arnott A. Advances in laboratory testing for HIV. *Pathology* 2004; **36**: 551–60.
2. Wilkinson D, Wilkinson N, Lombard C *et al*. On-site HIV testing in resource-poor settings: is one rapid test enough? *Aids* 1997; **11**: 377–81.
3. World Health Organization. HIV *Assays. Operational Characteristics Report 14/Simple/Rapid Tests*. 2004. Available from URL: http://www.who.int/entity/diagnostics_laboratory/publications/hiv_assays_rep_14.pdf [Accessed February 2006].

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Correcting the holiday roadtoll myth: Christmas and Easter holiday periods are actually safer than other times of the year

Contrary to popular belief, analysis of routine data published by the Australian Transport Safety Bureau reveals that you are less likely to die in a road crash at Easter or Christmas than you are at other times of the year.

The Australian Transport Safety Bureau defines the Christmas holiday period as the 15 day period between 00.01 hours on the Friday before 25 December, and 23:59 hours on the Friday after or including 1 January. Similarly, they define the Easter holiday period as the 5 day period from Easter Thursday to Easter Monday. Each year, they publish data documenting the road deaths that occur during these holiday periods.[1] Similarly, they publish data on total yearly road deaths.[2] From these data, I calculated the average daily number of deaths for each year from 1995 to 2004 by dividing the yearly total by 365.

The observed number of road deaths over the defined 15 day Christmas holiday period was then compared with the expected number, where the expected number was defined as 15 times the daily average number. Similarly, the observed number of road deaths over the defined 5 day Easter holiday period was compared with the expected number, where the expected number was defined as five times the daily average (Table 1).

Table 1. Observed versus expected Australian Christmas and Easter road deaths

Year	Total road deaths	Average daily road deaths	Observed versus (expected) Easter road deaths	Observed versus (expected) Christmas road deaths
1995	2017	5.5	NA	71 (82.5)
1996	1970	5.4	31 (27.0)	86 (81.0)
1997	1767	4.8	16 (24.0)	82 (72.0)
1998	1755	4.8	15 (24.0)	73 (72.0)
1999	1764	4.8	22 (24.0)	75 (72.0)
2000	1817	5.0	28 (25.0)	75 (75.0)
2001	1737	4.8	23 (24.0)	58 (72.0)
2002	1715	4.7	25 (23.5)	68 (70.5)
2003	1621	4.4	28 (22.0)	76 (66.0)
2004	1594	4.4	14 (22.0)	49 (66.0)
Total			202 (215.5)	713 (729.0)

NA, not available.