Parenzee Appeal – Antibody Tests for HIV

I have been asked to comment on the specificity or otherwise of antibody tests for HIV. Slide 54 quotes an old textbook of mine concerning antibody cross reactions, and related material is covered in slides 15 to 21 of a second presentation headed "The Diagnosis of HIV Infection Using Antibody Tests".

To put the matter in context, one needs to distinguish antibodies made very early after infection or immunisation from antibodies made following prolonged infection or repeated immunisation. Antibodies made early are accurate representations of the genes for antibodies carried in the B cells. They are generally of low affinity, that is they do not bind very tightly to the antigen which evoked them. However, a very specialised and elaborate machinery exists whereby the B lymphocytes can markedly "improve their performance", that is start to produce antibody of much higher affinity. This is because a structure exists in lymph tissues known as the germinal centre. The germinal centre represents an environment where antigens are stored for long periods. B lymphocytes multiply there, and over a period of time mutations occur in the antibody genes of the B cell. Only those mutations which confer a higher affinity to the antigen in question are selected for further multiplication. Mutation and selection of higher affinity variants are iterative processes so that in repeatedly immunised individuals many mutations can accumulate and the resulting antibody can bind 10,000 or 100,000 times more tightly than the original one.

The unmutated antibody of low affinity can indeed on occasion bind antigens other than the immunising antigen. On the other hand, the high affinity antibody is much more specific. For this reason, high affinity monoclonal antibodies are extensively used in research as razor-sharp and highly specific identifiers of various structures.

In the diagnostic test for HIV, only high affinity antibodies of the latter type are used. It is true that there are occasional "false positives" in such tests but these arise through the presence in serum of various sticky molecules, this rarely-encountered problem being more evident with the ELISA test than with the Western Blot technique. Rare false positives should not be used as an argument to negate a screening test which has shown itself to be very robust down the decades.

The reference to the work of Avrameus (slide 18 of the second PowerPoint presentation) relates to a special interest of his in a still somewhat mysterious subset of B cells known as B1 lymphocytes. These antibodies are the product of unmutated germ line genes. Structural studies have shown them to be rather flexible in the combining site and quite different from the bulk of antibodies namely those which carry affinity-raising mutations.

There is now a very large literature on anti-HIV antibodies, both polyclonal and monoclonal, both neutralising and non-neutralising. There are any number of studies which delineate to exactly which portion of the HIV viral surface these antibodies bind. I recently had the good fortune to chair a Technical Advisory Group to the Bill and Melinda Gates Foundation where nearly US$300 million was available for novel ideas towards an HIV vaccine, and some of the relevant monoclonal antibodies were at the centre of some of the relevant grant requests.

I should also like to comment on other tests which are performed on people who are seropositive for HIV. It is then usual to look for nucleic acid from the virus in such people's blood, representing the ultimate proof of infection. Such tests are now very sensitive – they can detect as few as 50 viral particles per millilitre of blood. Furthermore, these tests are of practical value as most HIV-infected persons exhibit relatively stable numbers of particles per millilitre, the so-called "set point". It turns out that the set point is of prognostic significance in the untreated individual – the higher the number of viral particles, the shorter the period when actual AIDS supervenes.

If one were to deny HIV as the causative agent in AIDS, it would be very difficult to explain why anti-retroviral therapy works so spectacularly well – by now life-saving in many millions of people.

I imagine it will not have escaped the Court's attention that President Mbeki's denial of the link between HIV and AIDS has been a terrible problem for the Republic of South Africa. Almost directly because of these years of neglect, South Africa now has the highest HIV prevalence among adults in the world.