Reviewer's report

Title: Immuno-epidemiology of human Schistosoma haematobium infection: preferential IgG3 antibody responsiveness to a recombinant antigen dependent on age and parasite burden.

Version: 1 Date: 14 May 2006

Reviewer: Michael J. Doenhoff

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General

This study has investigated the relationship between antibody levels to a recombinant form of a 13kDa Schistosoma haematobium worm antigen (Sh13) and infection intensities in a cohort of children in Zimbabwe.

The authors found that while a positive correlation was found between specific anti-Sh13 antibodies and infection intensity in a younger age group in which infection intensities were generally rising, there was an inverse relationship between these two parameters in older children in which infection intensities were declining.

The results have been interpreted to indicate that anti-Sh13 immunity is protective against S. haematobium infection.

The study has been carefully performed and the results stringently analyzed and written up well.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Unfortunately in all studies such as this the detection of any relationship between antibody levels and infection intensities is only indirect evidence for a particular immune response being responsible for or irrelevant to protective immunity. More definitive ‘proof’ will hopefully emerge from the ‘vaccination studies’ we are told are ‘now underway’ (see end of Discussion.)

In the discussion the authors agree that there are other possible explanations for the apparent ‘uncoupling’ of schistosome infection intensity and antibody levels while a child is growing older e.g., reduced exposure to infection, changes in host physiology.

One other possibility has not however been considered: that anti-Sh13 antibodies increase with age because worms are dying or being killed by means that are completely unconnected to Sh13 (natural senescence of the parasite, immune responsiveness to one or more unrelated antigens) and that antibodies are produced against Sh13 as a result of worm decay, and thus release of this antigen, due to the unconnected causes. The different pattern of antibody responsiveness found against the crude worm antigen preparation SWAP (Figure 3c) doesn’t necessarily discount the above-mentioned possibility, as the anti-SWAP response that was measured is likely to have been extremely heterospecific, including the outcome of responses to antigens that are in other (e.g., larval) stages of the parasite, but that are cross-reactive with worm antigens. Within this extremely heterogeneous ‘anti-worm’ reactivity might there not be one or more other antibody responses that are as ‘uncoupled’ to infection intensity as the IgG3 antibody response to Sh13?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Some very minor points:

p. 14, about 2/3 down the page: Commencement of sentences with ‘In addition…’ twice in close succession.

p. 21, legend to Figure 2: the sentence beginning ‘Factor Xa cleavesâ€¦’ is irrelevant to the figure.
p. 21, legend to Figure 3 (c): text beginning “showing that unlike responses to...result...™ and not appropriate for inclusion in a figure legend.

Figures 3 (b) and (c) on my paper print our: the words “antibody level...™ (should it be “Antibody...™) adjacent to the “y...™ axis partially cover “0.15...™ and “0.2...™ on the “y...™ axis of (c)

Pages headed “Figure 3™ and “Figure 3d™ on my print-out have respective subscripts “Figure 5 and “Figure 6™.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after discretionary revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests