

CORRESPONDENCE

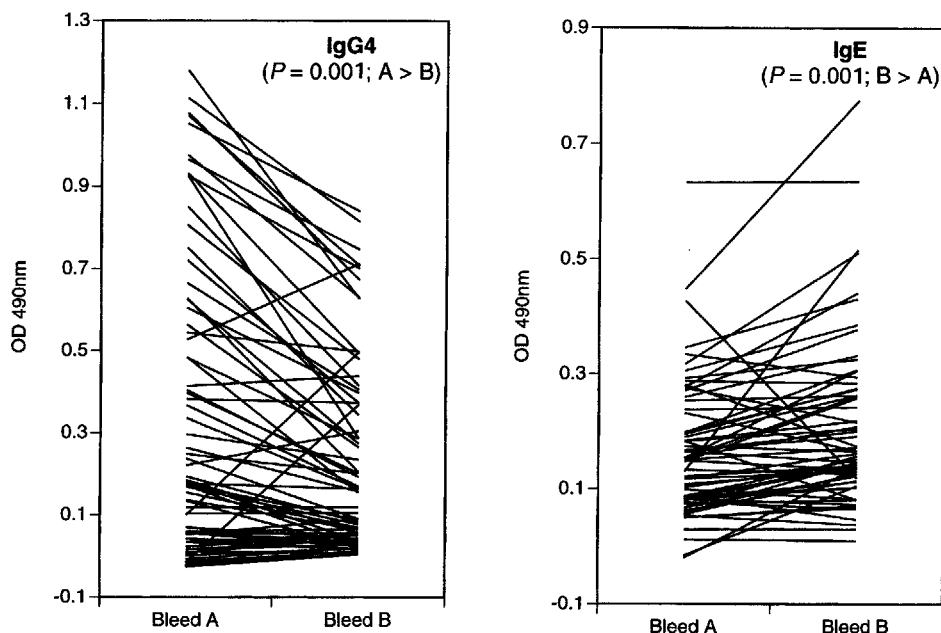
IgG4 and IgE Responses to *Schistosoma mansoni* Adult Worms after Treatment

To the Editor—Grogan et al. [1] reported that levels of *Schistosoma haematobium* adult worm-specific IgE and IgG4 both rose 5 weeks after treatment in children (5–14 years old) but remained unchanged in adults (15–48 years old). These results raise the issue of the effects of treatment on the immune response. Due to worm degeneration and death, a consequence of chemotherapy is the rapid release of adult worm antigens, some of which the host may not normally be exposed to. Butterworth et al. [2] studied immune responses to *Schistosoma mansoni* before and 5 weeks, 6 months, 12 months, and 18 months after treatment in 129 Kenyan schoolchildren 9–15 years old. Butterworth et al. [2] showed that adult worm-specific IgG antibodies and eosinophil levels peaked 5 weeks after treatment (similar to findings of Grogan et al. [1])

$P = .012$) and adults (IgG4, $P = .047$; IgE, $P = .001$). At 5 weeks after treatment, one may expect to detect a difference in immune response between adults and children, because of differing experiences of infection. Adults, for example, may have already been exposed to some of the antigens released (naturally or by drug treatment) due to worm death or damage over time.

Our observations, together with the results reported by Butterworth et al. [2], indicate that the interpretation of differences in immune responsiveness following chemotherapy for schistosomiasis depends very much on the time interval after chemotherapy at which posttreatment antibody responses are measured. We agree with Grogan et al. [1] that treatment has an effect on the immune response, but we observed contrasting effects of treatment on IgG4 levels. Moreover, we found that the effect of treatment did not differ in children and adults. More detailed temporal examination of immune responses after treatment for schistosomiasis, with

Figure 1. IgE and IgG4 ELISA responses before and 6 months after treatment (bleeds A and B, respectively) to *S. mansoni* adult worms of 68 Kenyan children and adults. Values are means of 3 assays measured at 490 nm.



but declined thereafter. Similar results were reported by Procell Wilkins et al. [3] during experimental infection in rhesus monkeys.

We have looked at pre- and posttreatment IgE and IgG4 responses to *S. mansoni* adult worm in 151 Kenyans aged 6–66 years [4]. Posttreatment responses were measured 6 months after treatment but before reinfection, which could have restimulated the host's immune response. In this population, the mean IgG4 response to *S. mansoni* adult worm was significantly lower 6 months after treatment, whereas the mean IgE response was significantly higher after treatment. Figure 1 shows the individual IgE and IgG4 responses to *S. mansoni* adult worms and illustrates the rise in IgE and the fall in IgG4. Using the same criteria to define adults and children as those of Grogan et al. [1], we observed similar effects of treatment in both children (IgG4, $P < .001$; IgE,

monitoring for reinfection, is needed to help resolve these differences.

M. Webster, P. G. Fallon, A. J. C. Fulford, A. E. Butterworth, J. H. Ouma, G. Kimani, and D. W. Dunne

Department of Pathology, University of Cambridge, Cambridge, United Kingdom; Division of Vector Borne Diseases, Ministry of Health, and Kenya Medical Research Institute, Nairobi, Kenya

References

1. Grogan JL, Kremsner PG, van Dam GJ, et al. Antischistosome IgG4 and IgE responses are affected differentially by chemotherapy in children versus adults. *J Infect Dis* 1996; 173:1242–7.

2. Butterworth AE, Capron M, Cordingley JS, et al. Immunity after treatment of human schistosomiasis mansoni. II. Identification of resistant individuals, and analysis of their immune responses. *Trans R Soc Trop Med Hyg* 1985; 79:393–408.
3. Procell Wilkins P, Maddison SE, Slemenda SB, Tsang VCW. Isotypic analysis of humoral immune responses in rhesus monkeys to an adult microsomal antigen of *Schistosoma mansoni*: an indicator of successful treatment. *Am J Trop Med Hyg* 1991; 45:629–35.
4. Dunne DW, Butterworth AE, Fulford AJC, et al. Immunity after treatment of human schistosomiasis: association between IgE antibodies to adult worm antigens and resistance to reinfection. *Eur J Immunol* 1992; 22: 1483–94.

Reprints or correspondence: M. Webster, Dept. of Pathology, University of Cambridge, Tennis Court Rd., Cambridge CB2 1QP, UK.
The Journal of Infectious Diseases 1997; 175:493–4
 © 1997 by The University of Chicago. All rights reserved.
 0022-1899/97/7502-0040\$01.00

Reply

To the Editor—Webster et al. [1] report that in *Schistosoma mansoni* infections IgG4 responses to adult worm antigen decrease 6 months after treatment, whereas IgE responses increase. As we reported [2], we examined the antibody isotype profiles in children infected with *Schistosoma haematobium* 5 weeks after treatment. At this early posttreatment time point, both IgG4 and IgE responses to adult worm antigen had increased significantly. We have no data for this group 6 months after chemotherapy. However, in another study from our laboratory, children in Cameroon infected with *S. haematobium* were examined 1, 3, 5, and 12 months after chemotherapy. In that study, both IgG4 and IgE responses to adult worm antigen increased in the first month after treatment but subsequently decreased to levels slightly higher than pretreatment values by 12 months after therapy (unpublished data). In the Cameroon study, the children were reexposed to infection immediately after treatment, whereas in the study reported by Webster et al., no reinfection had occurred, due to seasonal low transmission. The

difference in exposure might explain the slower decrease in IgG4 to adult worm antigen in the Cameroon population 5 and 12 months after therapy. Thus, the time after treatment is indeed important for assessing immunologic reactivities, but exposure to infection or reinfection can also play an important role.

With respect to the differences we observed between adults and children in antibody reactivity after treatment and those of Webster et al., who found that the effect of treatment was not differential in children and adults, the discrepancies between the two studies are difficult to explain and might be attributed to different sampling times after treatment and to difference in the extent of reexposure to infection. It is also possible that the level of infection in adults versus children in the two studies is different. Although Webster et al. give no indication of the egg output in their study population (children vs. adults), in our study the adults were selected by matching their egg output to that in children. We agree that it is important to study immune responses at various time points after chemotherapy and to relate these to reinfection, but it is also important to understand how schistosomes modulate the immune responses of their host to enhance their long-term survival. This can be done by comparing responses in individuals harboring high worm loads with those free of infection (or carrying very light infections).

Maria Yazdanbakhsh, Govert van Dam, and Jane Grogan

Department of Parasitology, Leiden University, Leiden, Netherlands

References

1. Webster M, Fallon PG, Fulford AJC, et al. IgG4 and IgE responses to *Schistosoma mansoni* adult worms after treatment [letter]. *J Infect Dis* 1997; 175:493–4.
2. Grogan JL, Kreamsner PG, van Dam GJ, et al. Antischistosome IgG4 and IgE responses are affected differentially by chemotherapy in children versus adults. *J Infect Dis* 1996; 173:1242–7.

Reprints or correspondence: Dr. Maria Yazdanbakhsh, Dept. of Parasitology, Leiden University, Postbus 9605, 2300 RC Leiden, Netherlands.
The Journal of Infectious Diseases 1997; 175:494
 © 1997 by The University of Chicago. All rights reserved.
 0022-1899/97/7502-0041\$01.00

NOTICES

Advanced Dermatology Update

9–10 May 1997, San Francisco. Advanced Dermatology Update will be held at the University of California, San Francisco. Credit: Category I. Information: University of California Office of Continuing Medical Education, 1855 Folsom St., MCB-630, Box 0742, San Francisco, CA 94143-0742; telephone, (415) 476-4251; fax, (415) 476-0318; web, <http://cme.ucsf.edu>; e-mail, inquire@ocme.ucsf.edu.

Posttransplant Lymphoproliferative Disorders

10–11 May 1997, Chicago. The Mayo Clinic's International Consensus Development Meeting on Epstein-Barr Virus

(EBV)-Induced Lymphoproliferative Disorders course will be held at the Sheraton Chicago Hotel and Towers. It will review current concepts regarding EBV-induced lymphoproliferation, risk factors for this disease, and available therapeutic methods. High priority will be given to an understanding of the emerging molecular techniques available for early diagnosis. Novel therapies, including preemptive strategies and cellular-based immunotherapy, will be covered. Presentations will be given by 17 internationally renowned physicians in the field of EBV-induced lymphoproliferative disorders. Registration and information: Mayo Foundation Postgraduate Course, Section of Continuing Medical Education, 200 First St. S.W., Rochester, MN 55905; telephone, (800) 323-2688 or (507) 284-2509; fax, (507) 284-0532.