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SHORT COMMUNICATION

Changes in Serum Antibodies to *Opisthorchis viverrini* in Humans and Hamsters Following Treatment of Opisthorchiasis

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The liver fluke, *Opisthorchis viverrini* infects over 9 million individuals in northeastern Thailand, producing significant morbidity and a predisposition to the development of cholangiocarcinoma.[1] Diagnosis, performed by microscopic stool examination for the detection of liver fluke eggs, is not only time-consuming, but may be false negative in the presence of biliary tract obstruction or light infections, and requires experties to distinguish liver fluke eggs from those of harmless intestinal flukes commonly found in Thailand.[2] The development of a sensitive and specific serodiagnostic test would therefore be desirable.

However, following treatment (Praziquantel, 40 mg/kg *per os*) of infected individuals who then remained stool egg-negative post-treatment, serum IgG, IgA and IgM antibodies (Ab) to crude adult worm homogenate (AWH) remained elevated, while total serum antibodies to metacercaria homogenate (MH) did not decrease significantly until 360 days post-treatment (Fig. 1). Because of persistent elevation post-treatment, serum Ab levels could not differentiate between recently treated and untreated infection. It is unclear to what degree these elevated post-treatment Ab resulted from immunological stimulation solely by infection present before treatment, or from ongoing

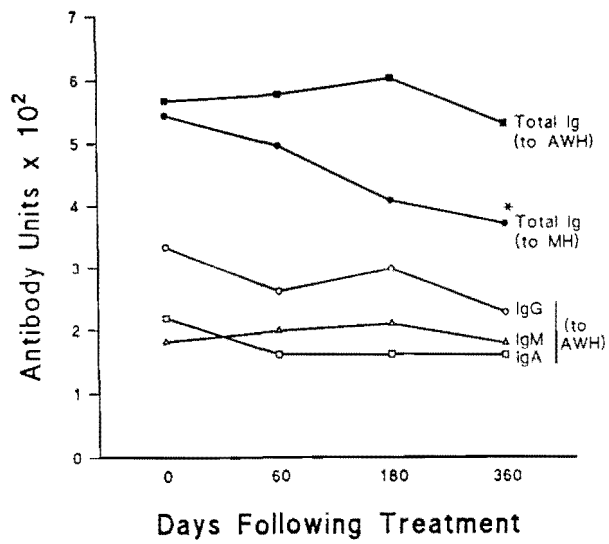

Fig. 1. Mean levels of total serum antibody (Ab) to adult worm and metacercaria homogenates in 11 individuals with opisthorchiasis, measured by enzyme-linked immunosorbent assay before (D0) and at 60 (D60), 180 (D180) and 360 (D360) days following treatment with Praziquantel. Values are in Ab units which represent Ab concentration relative to a standard dilution curve made using a pooled human infection reference serum. Ab levels were compared with matched pre-treatment values by paired *t* tests. * $p < 0.05$.

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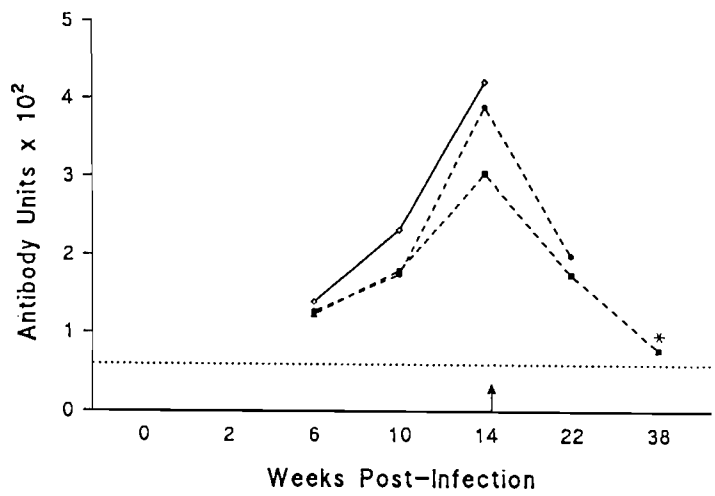

Fig. 2. Mean levels of total serum antibody to adult worm homogenate in laboratory-infected hamsters measured by enzyme-linked immunosorbent assay. Values are in Ab units which represent Ab concentration relative to a standard dilution curve made using a pooled hamster infection reference serum. All Ab levels at wk 0 and 2 were below 50 antibody units (dotted line). Sixteen animals were studies untreated until wk 14 (open diamonds). Of these, seven which were treated following serum collection at wk 14 (closed circles), while five of seven survived until wk 38 (closed squares). Post-treatment Ab levels were compared with matched wk 14 (pre-treatment) values by paired *t* tests. $^*p < 0.05$.

post-treatment stimulation by the continued presence of non-patient worms, re-exposure (eg to a sub-infective dose of metacercaria) or concomitant infection with antigenically similar parasites.

We explored some of these possibilities by studying total serum Ab to AWH in *O. viverrini*-infected hamsters (50 viable metacercaria by nasogastric tube) having no evidence of concomitant infection with other parasites and no re-exposure to *O. viverrini* following treatment with Praziquantel, 300 mg/kg *per os*. In hamsters, serum Ab to AWH rose by wk 6 post-infection and remained above pre-infection levels at wk 22 (day 60 post-treatment). However, unlike the human studies total Ab levels were significantly decreased by wk 38 post-infection (day 170 post-treatment) (Fig. 2), even though immunoblot studies revealed no qualitative changes in AWH antigen recognition by sera from these hamsters following treatment. The curative efficacy of Praziquantel in humans and hamsters is supported by previous studies[3,4] and was confirmed to be 100% by autopsies performed on treated animals at the conclusion of our study.

Thus in a re-exposure-free setting in the absence of other parasitic infections, total serum Ab levels to AWH decreased by day 170 following curative treatment of *O. viverrini*-infected hamsters. These findings therefore support further exploration of the hypotheses that prolonged elevation of serum Ab levels to AWH following curative treatment of human opisthorchiasis may be due to re-exposure or cross-reactive Ab from other parasitic infections.

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