# DIAGNOSTIC MARKERS IN SCHISTOSOMIASIS

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*In the present paper a brief overview will be given of the recent progress and trends in assaying diagnostic markers in schistosomiasis; only markers of the humoral immunological system and biochemical markers will be discussed, as markers for cellular immunological reactivity will be discussed by other authors. The following diagnostic markers will be reviewed: markers for infection, markers for immunity and markers for morbidity.*

Key words: schistosomiasis – diagnostic markers

## MARKERS FOR INFECTION

For the diagnosis of schistosome infections, parasitological diagnosis, i.e. demonstration of parasite eggs in stools or urine is still the most direct proof of an active infection. However, fluctuation in egg output and the chance of missing light infections necessitate repeated examinations. In general, techniques based on the detection of specific antibodies will be more sensitive in demonstrating light infections: a typical example of underrepresentation of positive cases by parasitological diagnosis compared to diagnosis based on antibody-detection is given by Watt et al. (1986).

Extensive research on the development of antibody-assays has resulted in the availability of a large number of tests with both a high sensitivity and specificity (cf. Mott & Dixon, 1982; Maddison, 1987). However, the presence of antibodies does not indicate an active infection and the detection of specific antibodies can therefore not easily be applied to the follow-up of chemotherapy; also, total specific antibody levels are not correlated with the intensity of the infection (egg output). Analysis of the isotype-specific response against defined antigen preparations has been shown to generate valuable additional diagnostic parameters. For example, Dunne et al. (1988) have shown that among IgG responses against egg antigen preparations the IgG4 antibody response shows the best correlation with egg output.

An important, recent approach in using antibody-detection assays is the measurement of immunity (relative risk of reinfection), as discussed below under "markers for immunity".

In contrast to antibodies, antigens excreted by the adult worms or the eggs into the circulation of the host, the so-called circulating antigens, could be expected to be present only during active infection, and antigen-levels would be correlated with the worm burden. Research on circulating antigens has primarily been focused on two genus-specific proteoglycan antigens derived from the schistosome gut: circulating anodic antigen (CAA) and circulating cathodic antigen (CCA). Using two-site enzyme-linked immunosorbent assays based on monoclonal antibodies, for both antigens sensitive assays with a lower detection level in the range of 0.1 ng antigen/ml serum have recently been developed (Deelder et al., 1989; de Jonge et al., 1990). This lower detection level corresponds with the lower detection level of a three times repeated duplicate Kato examination.

For both antigens, levels have been found to be correlated with the worm burden as measured by egg output. Antigens can be demonstrated both in serum and urine of infected patients, and after successful chemotherapy antigen levels drop rapidly.

Further studies will deal with the validation of these assays in large-scale serological studies and with the development of simple, field-applicable assays, like dipstick assays, preferably for antigen present in urine, thus allowing a non-invasive approach. Ultimately,

antigen-detection assays have the potential of offering a realistic alternative to parasitological diagnosis.

## MARKERS FOR IMMUNITY

Antibody levels can not only be used as a marker for infection, but recent research has shown that isotype-specific antibody levels may also give valuable information about the status of immunity of infected individuals. Based on reinfection studies, it was shown both for *Schistosoma haematobium* (Hagan et al., 1991) and for *S. mansoni* (Auriault et al., 1990), that high specific IgE levels are correlated with a relatively low risk of reinfection, while IgG4 levels are inversely correlated with the relative risk of reinfection. These studies have been carried out against total antigen preparations (Hagan et al., 1991) and against defined epitopes of potentially protective antigens like the glutathione-S-transferase (Auriault et al., 1990). Together with the analysis of components of the cellular immunological system, a detailed analysis of defined antibody levels as markers of immunity will provide essential data for sero-epidemiological studies and future vaccination trials.

## MARKERS FOR MORBIDITY

In schistosomiasis control programmes morbidity control is now recognized as the main objective. The availability of reliable markers for morbidity based on assays for serum or urine is thus of obvious importance.

For schistosomiasis haematobium, recent studies by Reimert et al. (1991) – who developed a sensitive assay for quantitation of the eosinophil cationic protein (ECP) – on urine samples from patients have demonstrated that ECP may be a potentially valuable marker for bladder pathology (Reimert, unpublished data).

For schistosomiasis mansoni, markers for morbidity due to liver fibrosis have been extensively studied by Zwingenberger et al. (1988a, b; 1989). Levels of procollagen-III-peptide, a cleavage product of collagen synthesis, and of peripheral blood cholylglycine, reflecting the spillover of portal blood into the systemic circulation, were found to be significantly raised in patients with hepatosplenic schistosomiasis compared to patients with the intestinal form of the disease. Levels of both markers decreased after successful treatment.

Apart from these direct markers for morbidity, several authors have described that defined antibody levels in hepatosplenic and intestinal schistosomiasis patients are different (e.g. Simpson et al., 1990), while recently De Jonge et al. (1991) showed that CCA- but not CAA-levels were significantly different in these two groups of patients.

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