False-positive reactions in the serological diagnosis of schistosomiasis


Summary
Stool and urine samples from children living in an area in the Western Transvaal in which human schistosomiasis was not endemic were examined for parasites and the indirect fluorescent antibody test was performed on their sera. Since none of these children passed any schistosome ova in their excreta but approximately half of them had a positive serological reaction they must have been infected with either Schistosoma mattheei, which is common in snails and cattle in the area, or avian schistosomes. In view of the occurrence of such 'false-positive' results, general practitioners are advised not to rely too heavily on serological tests in the diagnosis of schistosomiasis.

At present it is more or less accepted practice for general practitioners to rely on the results of serological tests when investigating patients suspected of having schistosomiasis. Several serological techniques are available for this diagnosis and over the years they have been improved considerably, especially with regard to sensitivity. However, these techniques still have several serious disadvantages: (i) they are not specific; (ii) they do not indicate levels of infection, i.e. a high titre is not necessarily indicative of a heavy infection; (iii) most of them are time-consuming and impractical to perform on an individual basis; (iv) false-negative results sometimes occur; and (v) false-positive results caused by cross-reactions resulting from infections with non-human mammalian or avian schistosomes are known to occur.

In this paper we present the results of a recent study which demonstrate the implications of serological diagnosis without simultaneous examination of excreta.

Material and methods
Urine (total bladder contents), stool and venous blood specimens were obtained from a number of Black schoolchildren and an adult from the farm Sterkstroom 276 and its vicinity in the Ventersdorp district in the Western Transvaal. The stool and urine samples were examined for the presence of parasites and serological studies were performed on the sera by means of the indirect fluorescent antibody technique (IFAT).

Results
No schistosome ova were present in the excreta and a relatively low proportion of the stool specimens contained intestinal parasites. The only helminth ova found were those of Ascaris lumbricoides (10.6%), Hymenolepis nana (10.6%) and hookworm species (2.1%). The results of the serological studies are presented in Table I. It should be noted that no less than 20 (45.5%) of the 44 subjects had a positive reaction; 12 of these reactions were weak, 7 were moderate and 1 was strong.
TABLE 1. IFAT RESULTS IN CHILDREN AND 1 ADULT FROM STERKSTROOM

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>No. examined</th>
<th>Reaction</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-9</td>
<td>14</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>10-14</td>
<td>14</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>&gt;14</td>
<td>12</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>12</td>
<td>20</td>
</tr>
</tbody>
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**Discussion**

The Venterdorp district is a non-endemic area for human schistosomiasis, which means that all of the positive serological reactions could normally be regarded as false positives. However, if the subjects were in fact infected with Schistosoma mattheei, as appears most likely, and if there was a way of proving it, the results could obviously not be considered false positives. S. mattheei is primarily an animal parasite with a wide range of definitive hosts, including cattle, sheep, goats and various antelopes, but it also infects man. In the Komatipoort area in the Eastern Transvaal, for instance, Pitchford found a large number of Black children to be infected with this schistosome, and on one farm as many as 40% of the women and young children were infected. In man S. mattheei does not produce ova in the absence of concomitant S. haematobium or S. mansoni infections. S. mattheei also hybridizes with S. haematobium. In Natal subjects passing typical S. mattheei ova only were found on several occasions. However, when they were subsequently re-examined both S. haematobium and S. mattheei ova were invariably present in their excreta, suggesting that the eggs seen during the first observations were in fact those of S. haematobium/S. mattheei hybrids. In view of this it seems highly unlikely that the single human found to be infected with 'Bilharzia bovis' (S. mattheei?) in the Witwatersrand area by Kisner et al. in 1953 and the 4 children in the Transkei and the 1 near Uitenhage found positive for S. mattheei only by Pitchford and Geldenhuys in 1960 represented 'pure' S. mattheei infections.

The children examined during this study frequently swim in the local stream. There is a consistent Bulinus (Physopsis africana) population in this stream, and these snails have frequently been found to be infected with S. mattheei. The infection rate can in fact be as high as 80% during autumn. Faeces from a number of cattle grazing in the vicinity and drinking from the same stream were all found to contain S. mattheei ova. It therefore seems reasonable to assume that the children with a positive reaction on serological testing were in fact infected with this schistosome. Should this assumption be correct, the conclusion of Pitchford that the distribution of S. mattheei in man in South Africa '... probably follows very closely that of S. haematobium...' might not be valid in this instance; it is quite possible that S. mattheei infections in man in the Western Transvaal are more widespread in areas where man and cattle share the same water sources than is currently realized.

The possibility that avian schistosomes could have been responsible for all or some of the positive serological reactions cannot be ruled out. Appleton found eggs of avian schistosomes in the faeces of indigenous birds from several areas in the RSA; among these were eggs from bird faeces collected at Barberson (approximately 130 km from our study area) in the Western Transvaal, which he identified as belonging to the genus Tricho-bilharzia. Species of this genus are known to cause cercarial dermatitis ('swimmer's itch') in man in other countries. Unfortunately there is as yet no information on the occurrence of human infections with bird schistosomes in the Western Transvaal.

Nothing is known with regard to the morbidity caused by S. mattheei in man, but this may be negligible because: (i) S. mattheei is an unsuccessful foreign parasite in man, in whom it is self-limiting, and (ii) the schistosome eggs and not the adult worms are known to be the cause of the disease. Since S. mattheei will not lay eggs in man in the absence of the human schistosomes and since the dermatitis-producing cercariae of avian schistosomes do not penetrate further than the human skin, treatment of such infections is therefore not necessarily indicated.

False-positive serological reactions are common in areas in which schistosomiasis is endemic, where they may be (apart from the possibility of S. mattheei or avian schistosome infestation) the result of low-level S. mansoni or S. haematobium infestations, in which ova are not consistently present in the excreta.

The possible occurrence of false-positive serological reactions in humans following exposure to animal schistosomes is also referred to in a recent review by Van Wyk. There seems to be only one other report on such false-positive results in man in southern Africa, that by Pitchford and Wolstenholme, who found 62% positive serological reactions in children living in a non-endemic human schistosomiasis area in the Caprivi. They attributed this finding to the exposure of the children to the lechwe schistosomes occurring in the area.

The findings of the present study strongly support Malek's plea for more sensitive diagnostic techniques; until more specific serological tests for identifying schistosome infections and for differentiating between the species have been developed, the presence of ova in the excreta or rectal biopsy specimens will remain a sine qua non for any final diagnosis. As mentioned above, pure S. mattheei infections such as those apparently occurring in the Western Transvaal cannot be detected in this way and in these cases serological studies still remain the only available diagnostic tool, which even so should be employed with circumspection.

We are indebted to the personnel of the Senweseto Demonstration Farm for their co-operation and the facilities they provided during our survey. We are also grateful to Professor J. A. van Eeden for his interest and advice, to Mrs J. M. G. van Deventer and Miss F. Quicke for identifying the parasites and performing the serological tests respectively, to Mrs B. B. Boneschs for collecting the blood specimens from the children, and to the Medical Research Council for permission to publish.

**REFERENCES**