The Distribution of *Schistosoma* Eggs in Human Tissues*

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In an endeavour to work out how widely *Schistosoma* eggs became distributed in the various organs of the human body, Blackie [a] began studies on organs removed at autopsy from Africans who had died from various causes in the Salisbury Native Hospital. Apart from reporting that eggs had been found in most of the organs examined, however, he published no detailed conclusions. Similar studies have been published from time to time by other workers in Southern Rhodesia, sometimes on special organs. Gilbert, for instance, claimed that the deposition of eggs in the female organs of generation had a deleterious effect on child-bearing. The most comprehensive studies carried out in recent years were by Gelfand, [b] Gelfand & Ross, [c] and Alves, Woods & Gelfand. [d]

Unfortunately the value of some of the previous work is vitiated by a failure to observe scrupulous care in the removal and transport of the organs to be examined. It was therefore decided to make some fresh studies, restricting the number of organs examined and taking as much care as possible to avoid contamination between different organs.

Technique. The following precautions were observed:

1. Several knives were used and washed thoroughly in a strong stream of water after removal of each organ.

2. Each tissue removed was also washed under running water and placed in a separate receptacle for transmission to the laboratory.

3. In the laboratory, separate knives were used to cut up the tissues and separate jars for the process of digestion.

The tissues were cut into small pieces, broken up as much as possible, and immersed in at least ten times their volume of 10% potassium hydroxide solution. After incubation at 40°C for a minimum of 48 hours (frequently a longer period was necessary for digestion) the supernatant fluid was decanted, and the remainder centrifuged and washed three times with tap-water, centrifuging after each washing. The deposit was finally examined microscopically under low power. It is perhaps of interest to note that in organs where heavy deposition of eggs had taken place, e.g. bladders, the mass of eggs remaining after the last centrifugation could be readily recognised as such by the naked eye.

Material. Specimens were taken from bodies of 200 Africans who had died in the Salisbury Native Hospital from various causes. No selection

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* Some of this work was included in a thesis submitted for the degree of Doctor of Philosophy of the University of London.

[a] Blackie, W. K. (1937) *A.R. publ. Hlth Dep. S. Rhodesia (Salisbury)*

[b] Gelfand, M. (1950) *The African schistosomiases*, Cape Town

[c] Gelfand, M. & Ross, W. F. (1953) *Trans. roy. Soc. trop. med. Hyg.*, **47**, 215

[d] Alves, W., Woods, R. W. & Gelfand, M. (1955) *Cent. Afr. J. Med.*, **1**, 166

was employed, except that new-born and very young infants were excluded. The specimens came from two sets of consecutive autopsies, and the patients were of all ages. The uterus and adnexa were removed from all the female patients, who numbered 70. For various reasons, mostly technical, it was not possible to examine all the organs from each of the 200 bodies; the first column in Table I shows the actual numbers.

TABLE I. DISTRIBUTION OF SCHISTOSOME EGGS IN VARIOUS ORGANS IN 200 BANTUS

Organ examined	Number of cases	H	H & M	H & Mt	M	M & Mt	Mt	Negative
Appendix	198	103	5	1	7	—	3	79
Bladder	198	146	8	2	5	—	2	35
Brain	150	40	2	—	4	—	—	104
Heart	30	—	—	—	—	—	—	30
Liver	200	80	25	1	20	1	2	71
Lung	193	99	7	—	7	—	—	80
Rectum	200	110	34	1	23	—	3	29
Spleen	200	52	1	—	3	—	—	144
Uterus and adnexa	70	40	4	—	1	—	—	25

H — eggs of *S. haematobium* M — eggs of *S. mansoni*
Mt — eggs of *S. mattheei* (possibly *S. bovis*)

Results. The figures for some of the organs are higher than expected (Table I), and one point which merits brief discussion is the means by which the eggs found their way to these organs. Similar studies made here on mice infected with *S. mattheei* have shown that eggs can be found in almost all the organs. Since it would be impossible for the female worm to pass through the smaller blood vessels leading to many of them, it appears certain that the eggs are carried in the circulation as emboli to the organs concerned, and are not deposited there by the worms. This may well be the case in human infections also.

The bladder. The greatest number of *S. haematobium* infections (156) were found in the urinary bladder. In the 42 cases in which no *S. haematobium* eggs were present in the bladder, infections were found in the following organs:
uterus and adnexa 3; spleen 3; rectum 5; appendix and liver 2; appendix, liver and rectum 1; appendix, liver, rectum and spleen 1; appendix, liver, rectum, spleen and brain 1; lung and rectum 1.

If these 17 cases are added to the 156 with bladder infections, a total of 173 *S. haematobium* infections in 200 Africans is reached, giving an infection rate of 86.5%.

The appendix. The fact that over 55% of the appendices examined contained *S. haematobium* eggs is of interest because appendicitis is still relatively uncommon among the Southern Rhodesian Bantu. Indeed the few cases found are usually associated with sophisticated " Europeanised " food, and appendicitis seldom, if ever, occurs in Bantus eating the usual maize-meal, meat and vegetable diet. On the other hand " bilharzial appendicitis " is regarded by several competent Rhodesian surgeons as a clinical entity *among young Europeans*, and certainly it is to be agreed that acute inflammation of an appendix containing *S. haematobium* eggs is quite frequently seen.

In 12 cases, *S. mansoni* eggs were found in the appendix. This is contrary to the previously held opinion that they are never present in the appendix, but it is not really surprising when the findings in other organs are considered.

The brain. Neither epilepsy nor neurological symptoms in general are common in the Southern Rhodesian Bantu [e]. A study by Loveridge et al. yielded no evidence that urinary bilharziasis had any effect on the intelligence of young African school-boys, but various authors have associated brain damage and neurological symptoms with the presence of schistosome eggs. It was therefore surprising to find that 46 brains out of a total of 150 contained eggs of *S. haematobium* or *S. mansoni*. One of the patients had died from widespread burns sustained by falling into a fire during what was thought to be an epileptic fit, but none of the other cases had shown symptoms attributable to the infection.

The heart. Both auricles and ventricles were examined, but no eggs were found in any of the 30 hearts. Whether or not the rarity of " Ayerza's Disease " or *cor pulmonale* in this country is a reflection of these findings is a matter of conjecture.

The liver. Out of 200 livers examined, 106 contained *S. haematobium* eggs. There has been a marked change of thought in recent years regarding the connection between bilharziasis and liver cancer, and few pathologists today are prepared to admit a close relationship. On the other hand, many workers have seen malignant cells in proximity to—almost arising from—deposits of eggs in the liver, and it seems probable that the intense irritation and trauma produced by the presence of thousands of ova might in some cases initiate actual malignant change.

It is also of some interest that the liver was second only to the rectum as a site of *S. mansoni* eggs, since hepatomegaly has frequently been described in *S. mansoni* infections. Hepatomegaly *per se* is not common in Southern Rhodesian Bantu patients.

The lung. Here again an unexpectedly large number of specimens (106) showed *S. haematobium* eggs. Pulmonary bilharziasis has been reported in Egypt, and Turner described it many years ago in mine-labourers in South Africa. It is not regarded as important in Southern

[e] Gelfand, M. (1950) *The sick African*, Cape Town

Rhodesia, and the frequency of asthma, bronchitis, and similar diseases, is not inordinately high in the Bantu. On the other hand, pulmonary tuberculosis is increasing rapidly in the territory, and is indeed becoming the chief killing disease among Africans, but schistosome eggs are very seldom found in sputa, [f] and the present state of knowledge does not afford any evidence of a connection between pulmonary disease and schistosome eggs in the lungs.

The rectum. The presence of *S. mansoni* eggs in the rectum is presumably the most reliable index obtainable of the amount of *S. mansoni* infection in a population, and the figure of 28% is much higher than clinicians, or indeed laboratory workers examining stools, would have expected. The figure of 72% for *S. haematobium* infection in the rectum is also of very great interest for another reason: it is surpassed only by the figure for the bladder. It is hardly necessary to point out that ordinary urine examination frequently fails to reveal eggs in patients who are afterwards shown by one technique or another to be infected with *S. haematobium.* Cystoscopy would probably lead to detection of many of these cases, and bladder biopsy would reveal more. Cystoscopy is not a procedure to be taken lightly, either by the clinician or by the patient, however; sigmoidoscopy and rectal biopsy is much simpler and much less painful. Workers in South Africa and in South America have shown the reliability of rectal biopsy in the diagnosis of *S. mansoni* infections, and it is now suggested that rectal biopsy would also be an exceedingly accurate method of diagnosis in urinary bilharziasis due to *S. haematobium.* This suggestion presupposes of course that rectal snips from the living patient would reveal a high percentage of the eggs which are found when the rectum is digested, as in this study. I have figures for only 32 patients examined by rectal biopsy. All had been shown to be passing *S. haematobium* eggs in the urine, and 31 had *S. haematobium* eggs in the rectal snip. A further study is indicated in Africans who have not been shown to be passing *S. haematobium* eggs in the urine, but the rectal snip would probably be even more useful in the diagnosis of urinary bilharziasis in Europeans, who, by and large, appear to pass fewer eggs in the urine than do Africans.

The spleen. It is of course well known that Girges regarded *S. mansoni* infection as the prime cause of Egyptian splenomegaly, but he associated it with male worm infection, and not with eggs. Splenomegaly is not infrequent in Southern Rhodesian Bantus, but it is not sufficiently marked to justify the belief that bilharziasis is a common cause. Gelfand has described several cases of primary abscess of the spleen, but unfortunately the spleens were not examined for schistosome eggs. [g] It is clear from Table I that the spleen is the least frequently attacked organ of those I have examined, with the exception of the heart.

The uterus and adnexa. As previously noted, bilharziasis of the reproductive organs has already been blamed in Southern Rhodesia for an adverse

[f] Alves, W. (1948) In: Erfan, M., *Trans. roy. Soc. trop. Med. Hyg.*, **42**, 114

[g] Gelfand, M. (1947) *Trans. roy. Soc. trop. Med. Hyg.*, **40**, 789

effect on child-bearing and the birth-rate. It is not proposed to go into this question at any length, but if the small series examined in this study is a reliable guide, an infection rate of 64% in the uterus and adnexa does not appear to prevent a very high birth-rate.

Male genital tract. The results of a separate study of the genital organs of 50 adult males (Table II) are included here for the sake of completeness.

TABLE II. DISTRIBUTION OF SCHISTOSOME EGGS IN THE GENITAL TRACT IN ADULT MALE BANTUS *

Site	*S. haematobium*	*S. mansoni*
Seminal vesicles	29	2
Vas deferens	9	0
Prostate	9	0
Tunica vaginalis	2	0
Scrotal skin	1	0
Epididymis	1	0
Pampiniform plexus	1	0
Testis	0	1

Eggs were found in the genital tract in 38 out of 50 bodies examined.
*** After Alves, Woods & Gelfand [d]**

The ova are far more likely to be encountered in the tissues close to the bladder (seminal vesicles, prostate, and the intra-abdominal portion of the vas deferens) than in those such as the testis, epididymis, and tunica vaginalis which are further away from its venous plexuses. Clinically, bilharzial prostatitis or vesiculitis is likely to be much more common than bilharzial orchitis, funiculitis, epididymitis or hydrocele. If one of the latter conditions is present there will probably be a co-existent vesiculitis or prostatitis.

Conclusions. When eggs of *S. haematobium* are found in 173 bodies out of a total of 200 examined, it is clear that the disease is almost universal among the population being studied. Admittedly, there was a considerable amount of selection, in that all the cases were not only hospital admissions but patients who died. Nevertheless, urine examinations carried out in surveys of apparently normal rural populations have yielded figures of 80-100% infection with *S. haematobium* in areas of Southern Rhodesia.

The studies described above do not show the tissue damage caused by schistosome eggs, but they do give an accurate picture of their wide distribution throughout the body. In Southern Rhodesia, light infections are common, and it is probable that gross damage is seldom produced by the disease. Studies by Gillet in the Belgian Congo have shown, however,

that where initial infection is heavy, as in irrigation farming, the Bantu population at risk may suffer grave illness and disability. Many parts of Africa will soon be faced with much heavier cercarial attacks and a concomitant increase in the severity of the disease in all races, because the key to the development of much of east, central and southern Africa lies in a greatly increased provision and use of water. This prospect and the present very high infection rate make it important that a combined investigation should be undertaken to arrive, if possible, at an accurate evaluation of the effect of the disease on health. Such an investigation cannot be carried out in conjunction with multifarious routine duties, and a full-time unit should include a physician, a pathologist well-versed in parasitology, a physiologist, and possibly also a psychologist. These workers should study uninfected and infected young Africans, and if a difference in health and performance can be demonstrated, they should then evaluate the effect of treatment on this difference. It is of great interest to note that accurate studies of this kind are now being carried out in the Union of South Africa under the aegis of the South African Council of Scientific and Industrial Research.

Acquired Resistance to *Schistosoma* Infection in Experimental Animals

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The question whether animals and human beings infected with *Schistosoma* can acquire resistance to reinfections or super-infections has only recently aroused general interest, although the possibility of such immunity was discussed by Fujinami in 1916,[a] and later by Ozawa,[b] Fairley, Macky & Jasudasan,[c] and Fisher.[d] The importance of the question is beyond doubt, since if it were proved that not only animals but also human beings develop effective resistance to schistosomes, current ideas on treatment might need modification. Indeed, it might even be possible to produce resistance artificially.

However, at the present time we are still far from being able to draw such conclusions. Our knowledge of acquired resistance to schistosomes, based as it is on animal experiments, is still very incomplete. As regards the resistance of human hosts, we have so far been forced to rely on conjectures based mainly on the age-distribution of cases of vesical bilhar-

[a] Fujinami, A. (1916) *Kyoto med. J.*, **13**, 176
[b] Ozawa, M. (1930) *J. exp. Med.*, **8**, 79
[c] Fairley, N. H., Macky, F. P. & Jasudasan, F. (1930) *Indian med. Res. Mem.*, **17**, 53
[d] Fisher, A. C. (1934) *Trans. Roy. Soc. trop. Med. Hyg.*, **28**, 277