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The Routes of Schistosome Egg Passage from the Human Body

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Textbooks of necessity have to be dogmatic in their statements, and in discussing bilharziasis most texts state firmly that the eggs of *Schistosoma haematobium* are passed out from the human body in the urine from the bladder and that the eggs of *S. mansoni* are passed through the wall of the lower intestinal canal mixed in the faeces and leave the body in the evacuated stool.

The very extensive literature on bilharziasis, particularly since the end of the 1939-45 War, contains many references to the finding of the eggs of both schistosome species in practically every organ and tissue of the body. In the WHO publication, *Bibliography on Bilharziasis*, 1949-1958, which contains references to 2,781 papers, over 130 deal with the subject of egg deposition in various organs of the body. Many of these papers discuss the results of the histological examination of biopsy material or of organs and tissues removed at operation. More recently there has been an increasing number of papers discussing the presence and importance of schistosome egg deposits found in the potassium hydroxide digestion of tissues removed at autopsy.

Organ Digestion Studies in Rhodesia

A number of careful studies of organ digestion have been done on biopsy and autopsy material by workers in Rhodesia, but it should be realised that much work of a similar nature has been done in bilharziasis endemic areas elsewhere in the world. Meeser *et al.* (1948) in 50 male subjects tested rectal biopsy against Weller's grooved rectal scraper for diagnostic efficiency. In 27 cases evidence of bilharziasis was found; five cases showed the presence of eggs of both species, 19 terminal spined eggs only, and three with *S. mansoni* eggs only. In only two of the cases was a diagnosis established by Weller's scraper. The authors made the point that the presence of eggs in the rectal mucosa is not in itself an indication of active infection unless it can be proved that the eggs do in fact contain active living miracidia. Gelfand (1948) examined 50 bladders removed at autopsy and compared the findings of the examination of a small snip (about 2-3 mm. in size) with the potassium hydroxide digestion of the whole viscus. He showed that bladders which had no macroscopic lesions detectable on the mucous surface still showed the presence of eggs in the digestion of the whole organ.

A urinary bladder apparently normal on cystoscopic examination cannot be claimed to be free from the disease and a biopsy snip taken through a cystoscope may well reveal the presence of eggs. Gelfand and Ross (1949a) reported a study of 150 autopsies in subjects known to have bilharziasis. Every case had a *S. haematobium* infection, 73 had *S. mansoni* in the stool and so had a double infection. It was demonstrated that bladder snips were positive in 80 per cent. of known *S. haematobium* infections diagnosed by organ digestion, and rectal snips were positive in 52 per cent. of the known *S. mansoni* cases diagnosed by organ digestion. They also demonstrated that in 60 per cent. of the series terminal spined eggs were seen in the rectal snip. The same authors, Gelfand and Ross (1949b), reported on a further series of 150 autopsies, which bore out the conclusions of their earlier paper. Despite the fact that the cases were selected at random, schistosome eggs were found in all but three instances. One case had a *S. mansoni* infection only, 71 had infections with both species and 75 had infections only of *S. haematobium*. The authors in this series compared the score as between the examination of snips taken from bladder and rectum *post-mortem* with the results of the digestion of the whole organs. Gelfand (1949a) took his studies a stage further and compared the results of rectal biopsy with the microscopic examination of urine and stool specimens for the presence of eggs. He showed that even where no eggs could be detected in the urine, they could sometimes be found in the rectal biopsy snip; and further, that in subjects in whose excreta no eggs could be found, that the eggs of both species could be seen in the rectal snip. Gel-

fand (1949b) studied the schistosome egg deposition pattern in the female genital tract at autopsy and showed that *S. haematobium* eggs were most often found. Gelfand and Ross (1953a and 1953b) went a stage further and extended their organ digestion studies to examine other groups of organs than bladder and rectum. Their first paper discussed the distribution of schistosome eggs in the alimentary tract from the stomach to the rectum, including the associated organs, liver, gall-bladder, pancreas, etc. They showed that eggs of *S. haematobium* were found in more sites and in greater numbers than the eggs of *S. mansoni*. The second paper dealt with the study of the distribution of eggs in the genito-urinary tract. *S. haematobium* eggs were again the predominant finding. In the female genital organs it would appear that eggs of *S. mansoni* are not often deposited in the ovaries and Fallopian tubes. Gelfand (1957) described three cases of *cor pulmonale*, but showed that in only one case was there evidence of egg deposition in the lungs, although all three cases had vesical bilharziasis.

Alves (1958) published a further series of organ digestions on an unselected series of 200 African patients dying at Salisbury hospital from various causes. In this series was included a series of organs not studied in previous work, such as lung, heart and brain. In 150 brains digested, *S. haematobium* eggs were found on 40 occasions, *S. mansoni* on four occasions and in two cases eggs of both species were seen. In 193 lung specimens *S. haematobium* eggs were found in 99 instances, *S. mansoni* in seven and a further seven cases had both infections. Alves *et al.* (1955) reported on an organ digestion study of 50 autopsies on African patients aged from 16 to 60 years, directed especially to the egg deposition pattern in the male genital tract. They showed that eggs were most likely to be deposited in the organs nearest the bladder, seminal vesicles and prostate rather than in the testes, epididymis and tunica vaginalis. From other parts of the world there have been many references to the deposition of schistosome eggs in nearly every organ and tissue in the body, from the central nervous system to the skin. It must be realised, however, that the finding of eggs in various organs at autopsy is no evidence that the subject was suffering from bilharziasis just prior to death.

The Passage of Eggs in Sputum and Spermatic Fluid

References in the literature to the finding of eggs in the body excretions, other than in stool and urine, are, however, very limited. Pfister (1922) described a case where he found schistosome eggs in the spermatic fluid and quoted Madden, a Cairo surgeon, as saying in 1911 that oospermia may be an early symptom of the disease and precede the onset of haematuria. No mention is made, however, as to the species of the eggs seen in the spermatic fluid. Ashcar and Issa (1935) described a case of bilharzial haematospermia, but again no reference is made to species. In Rhodesia there have been a number of unpublished reports of *S. mansoni* eggs found in the spermatic fluid, usually associated with a haematospermia. This is, of course, not a body excretion often examined microscopically and it is possible that eggs of both species may be present in the fluid quite frequently.

Although there are many references to the presence of schistosome eggs in lung tissue examined at autopsy or after operative removal, the presence of eggs in the sputum does not seem to have been reported often. Pijper (1934), in a symposium on bilharziasis in South Africa, reported a case with the eggs of *S. haematobium* in the sputum. Erfan (1948) states that even in advanced pulmonary bilharziasis eggs are rarely found in the sputum, but that *S. haematobium* eggs are more commonly found than those of *S. mansoni*. Alves in a discussion of Erfan's paper quoted a case from Rhodesia suffering from bronchiectasis where he found one terminal spined egg in a pint of sputum subjected to potassium hydroxide digestion, although no eggs were to be seen in specimens of urine and stool examined. Erfan (1950) found *S. haematobium* eggs in the sputum of a man who had complained of cough and dyspnoea for 18 months. In this case, too, no evidence could be found of the presence of eggs in either stool or urine. Nor-el-Din and El Bas (1954) studied 24-hour specimens of sputum from patients suspected to be suffering from pulmonary bilharziasis. They found *S. haematobium* eggs in 22 cases and *S. mansoni* eggs in two. Farid *et al.* (1959) carried out a similar study on 15 patients with *cor pulmonale*. Eggs of *S. mansoni* were found in the sputum in four cases and *S. haematobium* eggs in one instance.

The Passage of Schistosome Eggs Through the Principal Portals of Exit

The two principal and practically only important routes of exit of schistosome eggs from a human being are of course in the urine and stool. Textbooks and teachers alike stress that the terminal spined eggs of *S. haematobium* are found in the urine and the lateral spined eggs

of *S. mansoni* in the stool. Some of the texts give the reader the impression that the respective portals of exit are clear-cut and exclusive to a particular species. Girges (1934) is a most valuable source of information on the early discoveries on bilharziasis and much use has been made of the information so clearly set out in this important work. Theodor Bilharz in 1851, when studying the disease in Cairo, found that the bladder and lower digestive tract were equally affected and also noted that the eggs to be seen in the faeces may be either terminal or lateral spined in the same patient and found these eggs in the tissues of abdominal organs. This must be the first record of the eggs of *S. haematobium* being reported in the stool. Bilharz claimed that he had seen both terminal and lateral spined eggs lying in the oviduct of a single female worm. This observation is obviously an error, but was the root and source of the bitter argument and controversy which raged for the second half of the nineteenth century. Looss and his supporters, who carried great authority, strongly maintained that there was only one schistosome species infecting man, but that some of these laying eggs in the wall of the bowel had lateral spines. Harley in Natal in 1864 was struck by the fact that in that area he was able to find only terminal-spined eggs and considered he was dealing with a different species of worm from that seen in Egypt, which was said to lay two kinds of eggs, some with terminal and others with lateral-spined eggs. He therefore claimed that the southern African parasite was different and named it *Bilharzia capense*. There are many observers to-day who believe that Harley was nearer to the truth than was thought by his contemporaries.

In 1902 Castellani, working in Uganda, observed lateral-spined eggs in certain patients who were not suffering from haematuria and in whom no eggs could be found in the urine. Egyptian workers had not previously reported the occurrence of lateral-spined eggs in the faeces of patients who were not suffering from haematuria and were not passing terminal-spined eggs in the urine. Patrick Manson in London in 1903 examined a patient from Antigua, in the West Indies, who had never been to Africa. He could find only lateral-spined eggs in the faeces, the patient had never suffered from haematuria and the urine was examined repeatedly with negative results for schistosome eggs. Manson considered it was a significant fact that there had been no record of a urinary bilharziasis in South America and in the same year wrote: "Possibly there are two species of bilharzia, one with lateral-spined ova, depositing the eggs in the rectum only, the other haunting the rectum or bladder indifferently." It is clear, therefore, that from the earliest days of the modern history of the disease just over a century ago it has been realised that terminal-spined eggs are found in the stool. This fact is only now being re-discovered in the light of the knowledge gained from the *post-mortem* digestion of organs and the increased use of rectal biopsy methods.

Brumpt (1930) collected the references in the literature since 1884 in which *S. mansoni* eggs had been found in the urine and since 1914 in which *S. haematobium* eggs had been found in the stool. It has not been possible to study this paper in the original, but the fact that the paper contained 42 references seems to show that unusual portals of exit of schistosome eggs have for long been recognised. Khalil (1926) described a survey of over 7,000 people in whom were found 56 persons passing *S. mansoni* eggs in the urine, 48 with them in association with *S. haematobium* eggs in the urine. Eight persons were found to be excreting only *S. mansoni* eggs in the urine. Scaduto (1937) in Tripoli described eight cases passing *S. haematobium* in the urine, two of which were also passing these eggs in the stool. Cicchito (1938) recorded two cases, in one of which eggs of both species were found in the stool, and in the second case eggs of both species were after repeated examination found in the urine. Cowan (1953) described a case seen in Kenya, an African suffering from haematuria who passed a single *S. mansoni* egg in the urine and no eggs could be found in the stool. Repeated examinations of the case revealed a month later eggs of both *S. haematobium* and *S. mansoni* in the urine. De Morais (1956), describing a survey he carried out in the Zambesia district of Portuguese East Africa, found *S. haematobium* alone in 81.9 per cent., *S. mansoni* alone in 9.7 per cent. and both parasites in 7.9 per cent. of persons examined. He found *S. haematobium* eggs in the stool in 1.94 per cent. and *S. mansoni* eggs in the urine on only one occasion. Gopsill, quoted in the Annual Medical Report for Nyasaland for 1929, examined 500 stool specimens and found *S. mansoni* eggs in 20 per cent. and *S. haematobium* in 1 per cent. On the other hand, there have been analyses of urine and stool examination in which there is no reference to unusual portals of exit. Roberts (1949) at Nairobi examined the findings in 79,078 stool specimens and makes no mention of finding any *S. haematobium* eggs. Similarly, Okpala (1957) studied the laboratory records at Lagos from

1951 to 1955 and does not mention finding *S. haematobium* eggs in the stool or those of *S. mansoni* in the urine. It is rather surprising that there appears to be no record from South America or the Caribbean of finding *S. mansoni* eggs in the urine. These are regions where the infection is very common and it would be expected that in the routine examination of urine specimens for pus cells or other cellular deposits that on occasion *S. mansoni* eggs would have been seen and recorded.

The health reports of the Federation of Rhodesia and Nyasaland, 1954-63, record the results of urine and stool examinations carried out at the laboratories in Salisbury. In the ten-year period the examination of 61,980 urine specimens from European and other non-African patients revealed 1,990 infections with *S. haematobium* and 36 with *S. mansoni*. Stool specimens from the same racial group numbering 27,428 showed 974 *S. mansoni* and 53 *S. haematobium* infections. During the same ten-year period 253,736 specimens of urine from African patients revealed 52,115 infections with *S. haematobium* and 59 with *S. mansoni*, and 180,409 stool specimens showed 11,944 infections with *S. mansoni* and 543 with *S. haematobium*. It must be conceded, however, that there is some reasonable objection to claiming unusual portals of exit of schistosome eggs from patients in hospital. In such circumstances it is sometimes difficult, particularly where female patients are concerned, to ensure that stool specimens are not contaminated with urine and *vice versa*.

A series of epidemiological surveys carried out in Rhodesia during 1964 and 1965 provided a good fund of reliable material to study the association of the two schistosome species in the same persons and to study just how egg extrusion deviates from what is generally accepted to be the normal portals. One of the advantages of using this material is that it was possible to have records of urine and stool examination obtained from each subject on one day, yet having the assurance that the way in which specimens were collected eliminated any risk of cross-contamination of urine and stool specimens.

The type of epidemiological survey conducted in Rhodesia requires egg counts to be done on one-hour specimens of urine, and the microscopic examination of at least one drop of the centrifuged deposit of the stool spread by a micro coverslip, is scanned to establish a rough estimate of the amount of egg passage and by presumption the intensity of infection. This routine ensures that diagnosis is not established on a presence or absence basis, but the observer is obliged to look at and count all the schistosome eggs in the preparation. This is very different from the more usual laboratory examination where the observer, having seen and identified one egg in a preparation of urine, would look no further and therefore not see a few eggs of, say, *S. mansoni* or *S. mattheei* which might be in the preparation.

In a series of 21 surveys a total of 7,007 persons who provided a specimen of stool and urine had their results analysed. This excluded from consideration the persons who were able

Table I

Category	Urine		Stool		Number of Cases	Percentage of Total
	S. haematobium	*S. Mansoni*	*S. haematobium*	*S. mansoni*		
1	−	−	−	−	3,450	49.24
2	+	−	−	−	1,488	21.23
3	−	+	−	−	4	0.06
4	−	−	+	−	21	0.30
5	−	−	−	+	834	11.90
6	+	+	−	−	15	0.21
7	+	−	+	−	60	0.86
8	+	−	−	+	1,013	14.46
9	−	+	+	−	0	0.00
10	−	+	−	+	2	0.03
11	−	−	+	+	12	0.17
12	+	+	+	−	2	0.03
13	+	+	−	+	43	0.61
14	+	−	+	+	61	0.87
15	−	+	+	+	0	0.00
16	+	+			2	0.03
TOTAL					7,007	100.00

to provide only a specimen of urine but no specimen of stool or *vice versa*. One can arrange the possibilities of schistosome egg passage of two species, *S. haematobium* and *S. mansoni*, from two portals of exit, urine and stool, in a scheme providing for 16 possibilities. These are set out in Table I indicating the number of times the particular combination occurred and as a percentage of the total observations. The categories range from No. 1, in which no eggs of either species were found in either stool or urine, through No. 2, urinary infections with *S. haematobium*, to No. 5, intestinal infection with *S. mansoni;* to No. 8, where *S. haematobium* eggs in the urine are associated with the passage of *S. mansoni* eggs in the stool to the ultimate; No. 16, where the the subjects were found to be passing eggs of both species in both stool and urine, a combination of events which might be termed "a full house."

In this analysis no account has been taken of findings of *S. mattheei* eggs in urine and stool, as their consideration would complicate to a considerable degree the *haematobium/mansoni* study. The analysis of the information on *S. mattheei* and the relationship with the other two schistosome species will be made the subject of a further communication.

If the series of 7,007 observations is considered from the aspect of ordinary diagnosis, *S. haematobium* infections are diagnosed only from the urine and *S. mansoni* only from stool specimens. On this basis Table I shows 2,684 cases in the urine and 1,967 in the stool. These figures do not, however, represent the total number of cases infected, as they do not include 33 (Categories 4 and 11) infections with *S. haematobium* found only in the stool and not in the urine, and 21 (Categories 3, 6 and 12) *S. mansoni* infections found only in the urine and not in the stool. The additional cases so diagnosed represent just about 1 per cent. of the cases diagnosed by finding eggs in the excreta passed out through the usual portal of exit. It is interesting to note the number of cases who showed only a *S. mansoni* infection in the stool not associated with *S. haematobium* eggs in the urine. This observation is contrary to the views of Gelfand (1964), who states that a pure infection with *S. mansoni* is rare in Africans and that the intestinal infection is almost always found with a urinary infection with *S. haematobium*. The statement may be valid when considering autopsy studies, but is certainly not correct when applied to urine and stool studies.

Table II shows the age and sex distribution of the patients who had unusual egg excretion patterns. It will be seen that there is no sex difference and such cases are to be found in all age groups, including five children under the age of four years.

Table III sets out the results by individual surveys. It will be noted that only in one survey (Trojan Mine, 1964) were no subjects found with an unusual egg excretion pattern. In this table the surveys are ranked in order of their gross infection rate, ranging from Turk Mine, where 82 per cent. of the people examined were free from infection, to Chipoli, 1965, where only 2.5 per cent. were free. The surveys have shown the surprisingly high infection rate due to *S. mansoni*, particularly in population groups living on or adjacent to irrigation areas. In the areas of highest endemicity, where less than 10 per cent. of the people examined were *not* infected, it will be noted that the number of persons with infections with both species of schistosome exceed the total number infected with either one or other parasite. The distribution of the occurrence of the rarer categories will be seen to be well spread; in the

Table II

Age Group in Years	Categories 3, 4, 6, 10, 11, 12 & 16		Category 7		Category 13		Category 14		TOTAL	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Under 4	2	2	—	—	1	—	—	—	3	2
4- 6	3	3	7	4	7	3	1	11	18	21
7- 9	14	4	8	12	3	7	10	8	35	31
10-12	5	2	4	8	8	4	3	10	20	24
13-15	3	2	3	5	1	3	5	—	12	10
16-20	1	1	3	2	1	1	2	2	7	6
21-40	8	5	1	3	2	3	2	6	13	17
Over 41	1	2	—	—	—	—	1	—	2	2
TOTAL	37	21	26	34	23	21	24	37	110	113

Table III

ANALYSIS BY SURVEYS

Survey	Number Negative	*S. haem.* in Urine	*S. mans.* in Stool	*S. haem.* in Urine; *S. mans.* in Stool	RARER CATEGORIES										TOTAL
					3	4	6	7	10	11	12	13	14	16	
Turk Mine	349	43	18	3		8		1							422
Nyamaropa Reserve	267	25	56	7			1	1			1				358
R.A.N. Mine	186	31	32	15		2	1	2		2		1	2		274
Hippo Valley, 1964	158	52	13	17				2							242
Trojan Mine	92	27	13	13											145
Chirundu	234	90	31	19				1					1		376
Premier Estate	274	83	40	35		2	1	7		1		1	2		446
Arcturus Mine	266	98	38	50		2	2	3					2		461
Bikita	191	131	14	8			1	1			1	1			348
Triangle, 1964	280	163	38	36		1						2			520
Alaska	188	79	44	30	2		1	6							350
Msasa School	107	72	10	18				4				2	1		216
Triangle, 1965	227	88	108	93	1			4		4		3	6		534
Hippo Valley, 1965	313	158	156	124		1		8		2		1	3		766
Karoi	99	112	7	43		2	2	8				1	5		279
Buffalo Range	47	25	38	20		1		1				1			133
Mazoe-Clifton	90	73	50	66		1	1	3	1	2			14		301
Iron Duke Mine	33	42	29	62			3	3				6	4		182
Mazoe School	23	35	65	98	1		2		1	1		7	2	1	236
Chipoli, 1964	23	60	22	174		1		5				7	7		299
Chipoli, 1965	3	1	12	82								10	10	1	119
TOTAL	3,450	1,488	834	1,013	4	21	15	60	2	12	2	43	61	2	7,007

Mazoe Citrus Estate school survey seven of the rarer categories are represented, in three surveys six categories and in three surveys five categories are represented.

The last survey listed in Table III was arranged to find a number of persons who were infected with both species of schistosome for a chemotherapeutic trial. Eleven of the subjects were found to be passing *S. mansoni* eggs in the urine in the three pre-treatment examinations of urine and stool. Since the drug was administered a further six examinations of stool and urine have been undertaken and it has been possible to observe how persistent has been the *S. mansoni* egg output in the urine. In one case the eggs were seen on four of the six follow-up examinations, in one case twice and in three cases only once again. In the remaining six cases in which *S. mansoni* eggs were detected in the pre-treatment examinations they were not seen again in the urine. It is interesting to note, however, that *S. mansoni* eggs appeared in the urine of a further nine cases. To sum up, 20 subjects passed *S. mansoni* eggs in the urine on at least one of the nine separate occasions on which their urine was examined. However, this species of egg was seen in the urine on only 32 occasions, in one case five times, in two cases three times and in four cases twice. The finding of *S. haematobium* eggs in the stool would seem to be more erratic. In the three pre-treatment examinations 11 patients were found to be doing this, but only two did it more than once and none of them repeated the performance in the post-treatment follow-ups. During the follow-ups a further seven patients passed *S. haematobium* eggs in the stool, each on a single occasion. It would appear, therefore, from this inadequate series of observations that a patient who is found to be passing eggs of *S. mansoni* in the urine is more likely to repeat the performance at a subsequent examination than is a patient who is found to be passing the eggs of *S. haematobium* in the stool.

CONCLUSIONS

When specimens of stool and urine are carefully examined for schistosome eggs, and particularly when egg counting or egg output estimations are being done, more and more instances of anomalous and unusual egg extrusion patterns can be expected.

In an analysis of 7,007 pairs of urine and stool observations carried out in conditions which virtually excluded the possibility of cross-contamination of stool and urine, it is shown that all but two of the possible combinations of the two species and the two portals of exit of schistosome eggs were found. It is shown that *S. mansoni* eggs in the urine and *S. haematobium* eggs in the stool in cases where these infections are not to be found in their normal sites can contribute as much as an additional 1 per cent. to the overall infection rate of the particular species concerned. The unusual combinations of egg extrusion patterns are to be found equally distributed between the sexes and occur in all age groups.

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