The Significance of Schistosome Eggs in the Urine After Treatment

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Introduction

The significance of schistosome eggs seen in the urine of a patient who has been given specific treatment for bilharziasis is still a matter of dispute. There are three schools of thought: the first holds that the finding of any eggs, living or dead, at any stage after completion of treatment indicates a failure of that treatment; the second holds that the finding of eggs, even if they are viable, within the first month after initiation of treatment is unimportant, but the finding of any eggs after this time indicates failure; and the third school holds that the passage of dead eggs is a normal occurrence, even after successful therapy, and only viable eggs passed a month or more after treatment can indicate failure.

Weber *et al.* (1967) described a study of the distribution of schistosome eggs in the micturation stream of a subject whose urine was examined many times over a period of six months. The study confirmed the observations of Bennie (1949) and, more recently, of workers in East Africa that there is a well-marked diurnal variation in the egg output, which reaches its peak in the hours around midday and is at its lowest during the night hours. In addition to counts of eggs in each portion of the micturation stream, a count was made of the dead and black eggs seen in each sample. Black eggs are schistosome eggs, jet black in colour, retaining the shape and size of an egg, which have no discernible mira-

cidial structure, whereas dead eggs may contain discernible miracidia which may or may not be shrivelled, but which will not hatch nor show flame cell movement.

The occurrence of black eggs in urine and stool, but particularly in the urine, has long been recognised. They are usually found in the urine of persons who have received specific treatment, but they may be found in small numbers in urine from untreated people. Lambert *et al.* (1966) and Lambert (1969) showed that if mice were infected with *S. mansoni* and later treated with niridazole (Ambilar, Ciba), only dead eggs were to be found in liver and intestine eight weeks after treatment. These mice were killed at intervals up to 52 weeks and dead eggs of two kinds were found: black dense eggs containing dead and unidentifiable miracidia, and empty shells from which miracidia had hatched.

The importance and frequency of occurrence of black or dead eggs in untreated subjects has only been appreciated since the adoption of egg counting techniques in epidemiological surveys. Previously in such surveys, after one egg had been seen no further examination of the specimen was required and it was discarded.

In the abovementioned study (Weber *et al.*, 1967, *op. cit.*), the subject was examined over a six-month period from October, 1966, to February, 1967. From the 1st to the 6th May, 1967, the subject received specific treatment for bilharziasis. He received niridazole (Ambilar, Ciba) at a dosage level of 38.5 mg./Kg./day for six days.

Because of the comprehensive pretreatment data available, and because of his highly co-operative attitude, it was decided to follow up, in detail, the excretion of eggs in his urine after treatment.

Procedure

Commencing on 10th May, 1967, a midday terminal urine specimen was obtained from the subject, William Ndhlovu, on as many occasions as his duties as a laboratory hand permitted. Each specimen was allowed to stand for 30 minutes to allow sedimentation of eggs. Supernatant urine over and above 15 ml. was removed using a water vacuum pump. The remaining 15 ml. portion was thoroughly agitated and then decanted into a centrifuge tube. This was centrifuged for 90 seconds at 1,000 revolutions per minute and again the supernatant urine was removed to leave 0.5 ml. of urine in the tube. This sediment was re-suspended by flicking of the tip of the tube and 0.05 ml. drawn up with a pipette, placed on a slide and covered with a coverslip. The whole area of the coverslip was tracked, examined and eggs counted and the condition of the eggs noted. If no eggs were seen, a further large drop was examined. If eggs were found in the large drop, but not in the coverslip preparation, the egg count was rated as (+). One egg in the coverslip preparation was taken to represent 10 eggs in the whole sample; a (+) classification was therefore accepted as representing between one and nine eggs. If a large drop was taken for further examination it was poured back into the centrifuge tube, which was then prepared for miracidial hatching by the technique described by Meeser *et al.* (1948).

Results

The immediate follow-up results of midday terminal urine specimens were as follows:—

10th May: 500 eggs; 200 considered to be dead eggs, but many sluggish miracidia hatched.

11th May: 160 eggs; 90 of these were considered to be dead eggs, but again many miracidia hatched.

16th May: 100 eggs; no hatching.

17th May: 200 eggs, including 10 black eggs; there was no hatching.

18th May: 100 eggs; all considered to be dead.

The hatch of miracidia on 11th May was the last hatching seen in the course of the whole period of follow-up. From 19th to 31st May specimens were obtained on nine days and no eggs were seen except on 26th May, when 30 eggs, all black, were present. The presence of blood in the urine showed dramatic improvement after treatment and only occasionally were a few red blood cells found in the urine specimens.

The results of the follow-up examinations from 1st June, 1967, to 30th April, 1968, are summarised in Table I.

It will be noted that the proportion of days on which eggs were passed fell during the 12-month period of the study; in the first six months eggs were seen on 45 out of 112 days (40 per cent.) on which a midday terminal urine was examined, while in the remaining six-month period eggs were seen only on 34 out of 122 days (28 per cent.). It was also noted that there was a tendency for the eggs to be passed in brief periods of several successive days. In the six months May to October, 1967, eggs were seen on 45 days, and of these there were eight occasions when eggs were passed on two consecutive days, two occasions when eggs were passed on three consecutive days, and one occasion when eggs were passed on four consecutive days. In the six-

Table I

Summary of Examination of Midday Terminal Urine Specimens 10th May, 1967, to 30th April, 1968.

(Number of eggs counted in 0.05 ml. of centrifugal deposit adjusted to estimated number present in the deposit from the whole sample. Where eggs were found only in a large drop of deposit the number is recorded as one to nine eggs.)

Month	No. of Days Urine Examined	Estimated number of *S. haematobium* eggs				
		None	1 to 9	10-19	20-29	30 and Over
May (a)	14	8	—	—	—	6
June (b)	19	14	1	4	—	—
July (c) (d)	17	9	3	2	3	—
August	23	11	11	—	—	1
September (e)	17	8	4	1	2	2
October	22	17	3	2	—	—
November	21	14	6	1	—	—
December	18	17	1	—	—	—
January	22	16	6	—	—	—
February (f)	20	15	5	—	—	—
March	21	11	6	4	—	—
April	20	15	4	1	—	—

(a) By end of May all eggs were dead.
(b) By mid-June all eggs were not only dead, but black.
(c) Two black *S. mansoni* eggs seen on 19th July in the urine.
(d) On 14th July no eggs in coverslip preparation, but in the large drop 13 black eggs were counted in an epithelial fragment. The fragment also contained an empty unruptured shell.
(e) Patient had influenza from 7th to 10th September.
(f) On 6th February no *S. haematobium* eggs were seen. One black *S. mansoni* egg seen.

month period November, 1967, to April, 1968, eggs were detected on 34 days: on two consecutive days on three occasions, on three consecutive days on two occasions, and on four consecutive days on one occasion—this latter occurrence being in the first week of April.

At an early stage it was thought that there was a tendency towards passage of greater numbers of eggs on the early days of the week. It was thought that this might be due to changing exercise patterns or to the regular periods of bladder distension after social beer drinking. However, this tendency could not be demonstrated despite detailed investigation.

Our patient, William Ndhlovu, was known to pass occasional *S. mansoni* eggs in the urine before treatment, although eggs of this species were never discovered in his stools. From the table it can be seen that during the follow-up period he passed a few black eggs of this species on 19th July and 22nd November, 1967, and on 6th February, 1968.

The cessation of viable egg output and the decrease in output even of dead or black eggs indicate successful therapy in the treatment of the subject's schistosome infection. This success is also indicated by two further observations. The subject's weight increased from between 118 to 120 lb. pre-treatment to 126 to 130 lb. post-treatment, and his weight is now being maintained at this level. Since there has been no pronounced dietary change, this is taken as evidence of physical improvement after the treatment. The second observation, although subjective, is most important to both the physical and mental well-being of a patient. The subject reported, prior to treatment, that he was obliged to pass urine at least five times during the evening and night, including at least two which obliged him to wake up from his sleep. At the time of writing, one year after treatment, he has to wake from sleep only once to pass urine. This has contributed greatly to his happiness and his alertness.

Discussion

Some workers maintain that if a patient passes even one black or dead or unhatchable egg after specific treatment, the patient cannot have been cured of his infection. This viewpoint ignores the significance of dead or black eggs which are found in specimens of urine from persons who

have never had specific treatment. *Post-mortem* studies of bladder digests show that enormous numbers of dead and black eggs may be trapped in the mucosa and wall of the bladder. It seems likely that within a few months of initial infection eggs of *S. haematobium* begin to be held up in the bladder tissues and die. The longer an infection persists without treatment, the greater will be the number of black eggs trapped in the bladder mucosa or sloughed off into the urine. The prolonged follow-up of the subject shows that the passage of black eggs may persist for a year, and it may well be that a subject who has had his schistosome worms destroyed by treatment may continue the intermittent passage of black eggs in the urine for years.

It is difficult to assess the effects on a patient of a relatively mild *Schistosoma haematobium* infection or to assess the range of benefits to the patient after successful treatment. In the present study the subject appreciated very much the reduction of sleep-disturbing micturition episodes, and he showed a 9 per cent. weight gain and a greatly improved appetite, and he evidenced a general sense of well-being.

Summary

Probably every case of urinary bilharziasis, given time, will produce black eggs in the urine, albeit infrequently and generally in small numbers in comparison to the number of living hatchable eggs. Specific treatment, if successful, kills the worms and prevents the laying of further eggs. It does not, however, prevent the continued release of black eggs from the bladder mucosa into the urine. This process may continue for as long as a year and probably even longer.

Specific successful treatment in a case of *S. haematobium* infection improves the functional capacity of the bladder and stimulates a substantial weight gain with improved physical and mental well-being.

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