TREATMENT OF SCHISTOSOMIASIS WITH LUCANTHONE
A TWO-YEAR FOLLOW-UP IN NIGERIA

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Introduction
LUCANTHONE hydrochloride (Nilodin, Miracil D) has been in use for some fifteen years as an oral treatment of schistosomiasis. Blair (1958), reviewing the pharmacological and therapeutic properties of the drug, stressed that many of the published trials were inconclusive, because of inadequate or variable dosage or of too short a follow-up period. The differences between the criteria of cure used by different workers also prevent useful comparison. Newsome (1951) deplored this situation more than ten years ago, but there is still no uniformity in assessing the results of treatment.

The special features of the group of patients described in this paper derive from the fact that nearly all were serving soldiers of the Royal Nigerian Army. They spoke English and were above a certain minimum standard of education and intelligence. Hospital accommodation was available so that they could be admitted for supervision of treatment and observation of toxic effects. In general they were exposed to re-infection only when they went home on annual leave for short periods and some were able to avoid this risk altogether. The epidemiology of the disease was explained to each patient at the time of treatment. A much longer period of follow-up was possible than can usually be employed in Africa. In addition, the soldier in Nigeria is a relatively well-off member of the community who need never go hungry. He leads a healthy outdoor life and is looked after by an efficient medical service modelled after the British Army pattern, so that his standard of general health is extremely high.

Material and Methods
The author was employed as medical specialist to the Royal Nigerian Army from May 1960 until February 1963, with a three-month leave-break in 1961. He was stationed at Kaduna in Northern Nigeria, where there is a military hospital.

The groundwork for the present study was laid by Moore (1962), who began to use lucanthone hydrochloride (Nilodin) as the standard treatment in the hospital. The dosage used was that suggested by Blair (1958), namely a total of 60 mg./kg. body weight given as two equal doses on two successive days, but a maximum of 4 g. was exceeded in only a few patients who were unusually heavy. Each dose was given in the evening one hour after sedation with amylobarbitone (3 or 4½ gr.) and promethazine theoc1ate (25 or 50 mg.) by mouth.

During the period under review 270 cases of schistosomiasis were admitted to the Military Hospital, Kaduna, for lucanthone treatment. Between September 1962 and January 1963, 107 of them were re-examined for evidence of active disease. Recruits
for the Royal Nigerian Army must show no signs of active schistosomiasis at the
initial medical examination which includes microscopic examination of urine and stool
specimens.

A standardized technique was used in each review, and the following information
was obtained for each patient. Age, and type of infection. Home, presence or absence
of childhood symptoms and length of time between first symptoms and treatment.
Previous treatment if any. Reason for diagnosis, whether routine examination or
investigation of symptoms. Length of follow-up. Presence or absence of symptoms
since treatment. Whether he had been on home leave since treatment. What water
was available at home for washing, and whether he bathed in rivers or pools. Each
patient was also asked if he knew how the disease could be contracted, and whether,
if further treatment proved necessary, he would have lucanthone again or would
prefer injections. This last question was asked in an attempt to measure the subjective
severity of toxic symptoms.

A brief clinical examination was then carried out for hepatomegaly, for spleno­
megaly and for abnormalities in the external genitals. The centrifuged deposits from
three terminal urine specimens and three stool specimens were examined under the
microscope. Three rectal snips were taken and studied by the method of Newsome
(1951). A hæmoglobin estimation was done in some of the patients.

In assessing the results of the urine tests the presence or absence of erythrocytes,
pus cells and schistosome ova was noted. The number of erythrocytes and pus cells
present was recorded as a single plus, as two pluses or as three pluses. The most
abnormal of the three results under each heading was then used in the assessment of
cure. A normal urine was taken as one which contained not more than one plus of pus
cells, no erythrocytes and no ova. The viability of ova in rectal snips was judged accord­
ing to the criteria used by Moore (1962).

Results

The group consisted of 104 males and 3 females, all Nigerians. There were 68 cases
of infection with S. hæmatobium, 22 with S. mansoni and 17 with both parasites.
Eighty-five (79 per cent) had their homes in Northern Nigeria, where the disease is
prevalent.

The age distribution is given in Table 1. There was no significant difference in age­
grouping between the different types of schistosomiasis.

Cure Rates

The results of treatment were assessed separately for each type of infection and
are shown in Fig. 1. Eighty-three per cent of hæmatobium infections were clinically
cured, i.e. had had no symptoms since treatment, but when urine tests were examined
only 38 per cent were cured, and when rectal snips were examined as well only 36 per
cent were cured. The corresponding figures for mansoni infection were 86, 81 and 67 per
cent, and for the double infections 83, 41 and 41 per cent respectively. In the rest of
the discussion “cure” means that all tests were negative.

The interval between the lucanthone treatment and the follow-up examination
varied from 3 months to 40 months, with a mean of 22 months. The average duration
of follow-up for the different types of infection was *S. haematobium* 22 months, *S. mansoni* 22 months and double infection 24 months.

**Length of Follow-up**

The cure rates were correlated with the length of follow-up with an unexpected result, in that the cure rate was highest in those in whom the follow-up period was longest. The results appear in Tables 2 and 3. In the *S. haematobium* infections, when the follow-up period was short (<18 months) the cure rate was 23 per cent, when it was of medium length (18-30 months) the cure rate was 46 per cent, and when it was long (>30 months) the cure rate rose to 60 per cent. When all three types of infection were considered together the same trend was seen, the corresponding cure rate figures being 29, 45 and 67 per cent respectively. The results for the *S. haematobium* infections alone are hardly significant (0.1 > P > 0.05), but those for all the patients together are highly significant (P < 0.01).

**Duration of Symptoms**

The cure rates in the *S. haematobium* infections were then correlated with the duration of symptoms, with the results shown in Table 4.

The cure rate in patients with no history of symptoms was 17 per cent, and that in those with a long duration of symptoms (6-20 years) was 67 per cent. The standard error of the difference between these percentages is 22, and therefore the difference is probably significant, being unlikely to arise by chance more than once in 22 times. Among the smaller number of *S. mansoni* infections the cure rate was no higher in those with a long history of symptoms.

**Previous Treatment**

The total figures were examined to see the effect of previous treatment. The cure rate in patients who had had previous treatment was 50 per cent (15/30), and in those with no previous treatment 40 per cent (31/77). This is not a significant difference.

**Toxic Effects**

Twenty-seven of the 107 patients were unwilling to have lucanthone a second time. It was thought likely that these 27 had experienced more severe toxic effects, and it was wondered whether there would be a higher cure rate in this group. They, in fact, had a cure rate of 56 per cent (15/27), as against 39 per cent (31/80) in those who were willing to have lucanthone again. This difference is not significant, the standard error of the difference being 11.

**Avoidance of Reinfection**

Twenty-nine of the 107 patients were able to convince the examiner that they understood how they could become infected. Six of these washed in stream water when at home on leave because no other water was available; the other 23 washed in piped water or water from deep wells, and avoided streams and pools. The cure rate in these 23 was 57 per cent (13 patients). This is not significantly different from the cure rate in the remainder of the group, which was 39 per cent (33/84).
Clinical Abnormalities

There were very few clinical abnormalities. In 4 patients (4 per cent) the liver was palpable up to two finger-breadths in inspiration, and in 4 other patients the spleen was palpable up to two finger-breadths; 5 patients were noted to have small left testes.

Haemoglobin Levels

The haemoglobin was measured in 71 patients and the mean value was 13.3 g. per 100 ml. In 8 patients the haemoglobin value was known both before and after treatment and the average was 13.4 g. per 100 ml. in both instances.

Discussion

The clinical cure rate of about 85 per cent in both forms of the disease is encouraging on an average follow-up period of nearly two years. However, when the results of the laboratory tests are taken into account the cure rate drops to 36 per cent in S. haematobium infections, and this is disappointing, particularly in a population which was protected from reinfection for most of the year and whose members were above average health in other respects.

On the other hand two-thirds of the S. mansoni infections appeared to be cured after considering all results. This is at variance with the generally held opinion that lucanthone hydrochloride is not very effective in intestinal schistosomiasis (Gelfand, 1962), but it agrees with the previous report from Nigeria by Moore (1962), who found that all of 10 S. mansoni infections were apparently cured. Blair (1958) also quotes several authors who found as good results in S. mansoni infections as in S. haematobium infections. It may be that the strain of S. mansoni occurring in Nigeria is unusually susceptible to lucanthone, and indeed a West African strain from Liberia has been shown to be more susceptible than an Egyptian strain (Gonnert and Vogel, 1955). There is some evidence that the metabolism of lucanthone varies in different species; perhaps it also varies in different races of mankind (Gonnert, 1962).

Rectal snips did not prove a useful investigation in the assessment of cure in the S. haematobium infections, there being only 1 case out of the 69 in which the urine tests were normal and live ova were seen in the snips. They were useful, as might be expected, in the S. mansoni infections, where 3 out of 21 cases who had normal stool specimens were shown to have live ova in the rectal mucosa.

Clinical practice in Nigeria suggests that schistosomiasis is often a self-limiting disease. In the Northern region infection is almost universal in children, and yet relatively few adults present with symptoms due to the disease, and serious complications are not common. Ogunlesi (1962) reported a single case of cor pulmonale as a rarity and said that he had seen only one similar case before. The demonstration in this series of a significantly higher cure rate in the cases which were followed up for more than two years might suggest that we are observing a natural cure process going on. It is unlikely that the effect of lucanthone could still be observed after two years or more unless it is supposed that it reduces the worm load to a size at which the natural defences of the body can deal with it. The higher cure rate observed in cases which had had symptoms of infection for the longest period may also suggest that the drug was
most effective in patients in whom some immunity mechanisms had had time to develop.

There were no serious toxic effects in 270 patients treated with the dosage regime of two doses of 30 mg./kg. body weight of lucanthone hydrochloride, given one on each of two successive days. All patients were nauseated, and about 50 per cent vomited, but not usually till the morning after administration, so that the drug was presumably absorbed, the vomiting being probably due to a central mechanism, and not to gastric irritation. Many patients ran a low fever, but very few were not fully recovered 36 hours after the second dose. Toxic effects were noticeably less marked in children, as noted by Blair (1958), and it has been shown that the metabolism of lucanthone is more efficient in young people and the excretion more rapid, so that in fact children probably should be given a relatively larger dose (Halawani and Dawood, 1950). Although in this group the cure rate in those patients who experienced subjectively more severe toxic effects was slightly higher than in the others, the difference was not significant. A single large dose of 50 mg./kg. body weight has been tried in Northern Rhodesia and found to be more toxic and less effective (Gove, 1962).

A significantly higher cure rate was not found in the group of 23 patients who understood the mechanism of infection and who appeared to have avoided the danger of reinfection. However, the entire population under study ran little risk of reinfection since they were living in military camps with piped water supplies for most of the year.

Slight enlargement of the liver or spleen was present in only a few patients, and the haemoglobin levels were high. All patients were performing the ordinary duties of a Serviceman at the time of examination.

The two-day course of treatment is convenient and probably as effective as can be achieved with lucanthone. The small proportion of patients who had a recurrence of symptoms after treatment suggests that, although not often producing an outright cure, lucanthone will usually reduce the infection enough to allow the natural body defences to keep it under control or eliminate it completely.

Summary

One hundred and seven Nigerian soldiers suffering from schistosomiasis were followed up for an average of nearly two years after treatment with lucanthone. They were largely protected from reinfection.

The symptomatic cure rate in both S. haematobium and S. mansoni infections was about 85 per cent. The results of urine and stool examinations reduced the cure rate to 67 per cent in S. mansoni infections and to 36 per cent in S. haematobium infections.

Rectal snips produced no useful information in S. haematobium infection, but revealed active infection in apparently cured S. mansoni cases.

There is some evidence to suggest that in Nigeria schistosomiasis tends to be self-limiting, and that the patient may develop some resistance to the effects of infection. If so, it may not be necessary to aim at immediate and outright cure with schistosomocidal drugs.
REFERENCES


![Cure rates in each type of infection.](Image)

- **Clinical cure**, i.e., no symptoms since treatment.
- Urine (haematobium), stool (mansoni), or both (double), negative.
- Rectal snips negative in addition.
Table 1. Age distribution of cases

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>&lt;10</th>
<th>10-20</th>
<th>20-30</th>
<th>30-40</th>
<th>40-50</th>
<th>&gt;50</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>1</td>
<td>21</td>
<td>68</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td>107</td>
</tr>
<tr>
<td>Percentage</td>
<td>1</td>
<td>20</td>
<td>64</td>
<td>12</td>
<td>2</td>
<td>2</td>
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</table>

Table 2. Cure rate in *S. hematobium* infections according to length of follow-up

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Less than 18 months</th>
<th>18-30 months</th>
<th>More than 30 months</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>35</td>
<td>24</td>
<td>10</td>
<td>69</td>
</tr>
<tr>
<td>Cure rate: number</td>
<td>8</td>
<td>11</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>Percentage</td>
<td>23</td>
<td>46</td>
<td>60</td>
<td>36</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 5.15, \quad 0.1 > P > 0.05. \]

Table 3. Cure rate in all types of infection according to length of follow-up

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Less than 18 months</th>
<th>18-30 months</th>
<th>More than 30 months</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>45</td>
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<td>24</td>
<td>107</td>
</tr>
<tr>
<td>Cure rate: number</td>
<td>13</td>
<td>17</td>
<td>16</td>
<td>46</td>
</tr>
<tr>
<td>Percentage</td>
<td>29</td>
<td>45</td>
<td>67</td>
<td>43</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 10.18, \quad P = <0.01. \]

Table 4. Cure rate in *S. hematobium* infections according to duration of symptoms

<table>
<thead>
<tr>
<th>Duration of symptoms</th>
<th>Nil</th>
<th>1 month or less</th>
<th>1-12 months</th>
<th>1-6 years</th>
<th>6-20 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>6</td>
<td>17</td>
<td>20</td>
<td>14</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td>Cure rate: number</td>
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<td>7</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Percentage</td>
<td>17</td>
<td>41</td>
<td>25</td>
<td>29</td>
<td>67</td>
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ROYAL SOCIETY OF MEDICINE

MAJOR-GENERAL W. R. M. DREW, C.B., C.B.E., Q.H.P., F.R.C.P., late R.A.M.C., has been elected President of the Clinical Section, Royal Society of Medicine, for the remainder of the Session.

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As Associate Officer:
COLONEL BASIL LEVY, M.D., late R.A.M.C.