Treatment of Cutaneous Larva Migrans

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Cutaneous larva migrans caused by the larvae of animal hookworms is the most frequent skin disease among travelers returning from tropical countries. Complications (impetigo and allergic reactions), together with the intense pruritus and the significant duration of the disease, make treatment mandatory. Freezing the leading edge of the skin track rarely works. Topical treatment of the affected area with 10%–15% thiabendazole solution or ointment has limited value for multiple lesions and hookworm folliculitis, and requires applications 3 times a day for at least 15 days. Oral thiabendazole is poorly effective when given as a single dose (cure rate, 68%–84%) and is less well tolerated than either albendazole or ivermectin. Treatment with a single 400-mg oral dose of albendazole gives cure rates of 46%–100%; a single 12-mg oral dose of ivermectin gives cure rates of 81%–100%.

Cutaneous larva migrans is the most frequent skin disease among travelers returning from tropical countries [1]. It is now easy to treat with new oral antihelmintic agents, which are both well tolerated and effective.

Cutaneous larva migrans is caused by the larvae of animal hookworms, of which *Ancylostoma braziliense* is the species most frequently found in humans [2, 3]. These hookworms generally live in the intestines of domestic pets such as dogs and cats and shed their eggs via feces to soil (usually sandy areas of beaches or under houses). Humans are infected in tropical and subtropical areas of endemicity by contact with contaminated soil. The hookworm larva burrows through intact skin but remains confined to the upper dermis, since humans are incidental hosts.

Larval migration through the skin is marked by an intensely pruritic, linear, or serpiginous track (figure 1, left) known as a creeping eruption. Note that creeping eruptions occur in many other human skin diseases. Hookworm folliculitis is an uncommon form of cutaneous larva migrans, marked by pustular folliculitis of the buttocks (figure 1, right) [4].

Cutaneous larva migrans usually heals spontaneously within weeks or months. In a series of 25 patients treated with a placebo, 12% healed by the end of the first week and 36% by the end of the fourth week; the longest period required for spontaneous healing was 11.2 weeks in this series [5], but the larvae have been known to migrate for up to 1 year [3].

Complications include impetigo and local or general allergic reactions. For example, edema and vesiculobullous reactions were reported in, respectively, 6% and 9% of 67 French patients [1] and 17% and 10% of 60 Canadians [6]. In the largest series of cutaneous larva migrans, involving 98 German patients, 20% of the 40 patients tested had hypereosinophilia (defined as an eosinophil proportion >7% of the total leukocyte count); the mean eosinophilia level was 5%, and the range was 0%–37% [7].

These potential complications, together with the intense pruritus and the duration of the disease, make treatment mandatory. However, optimal management is controversial: in 1 study, 22 German patients with cutaneous larva migrans had received 12 different treatments, including surgery and French brandy, before they were referred to a specialized center [7]. The most effective treatment is topical or oral administration of antihelmintic agents, such as albendazole, thiabendazole, and ivermectin.

Topical Treatments

*Freezing.* Freezing the leading edge of the skin track with ethylene chloride spray, solid carbon dioxide, or liquid nitrogen rarely works, as the larva is usually located several centimeters beyond the visible end of the trail. In 1 series, cryotherapy (repeated applications of liquid nitrogen) was unsuccessful for 6 patients and resulted in severe blistering or ulceration in 2 patients [7]. In another series, none of 7 patients treated with liquid nitrogen was cured [6]. Because this method is both ineffective and painful, it should be avoided.

*Thiabendazole.* Topical application of a 10%–15% thiabendazole solution/ointment to the affected area was shown decades ago to be efficacious [8, 9]. In a large study of 53 Canadian patients, in which 15% thiabendazole cream in a water-soluble base was applied to the affected area 2 or 3 times a day for 5 days, all but 1 of the patients were cured [6]. The thiabendazole cream was prepared by crushing 500-mg tablets of thiabendazole in a water-soluble base. In most patients the pruritus ceased and larval track migration halted within 48 h of treatment. In the largest such study (98 German patients), thiabendazole ointment (15% thiabendazole and 3% salicylic
acid in unguentum alcoholum lanae) was successful in 96 cases (cure rate, 98%) within 10 days. In the other 2 cases, treatment was successful after 2 weeks in 1 case and after 4 weeks in the other [7].

The main advantage of topical treatments is the absence of systemic side effects. Their main disadvantages are that they have limited value for multiple lesions and hookworm folliculitis and that they require multiple daily applications for several days.

**Oral Treatments**

**Thiabendazole.** Thiabendazole is the drug with which there has been the most experience in the oral treatment of cutaneous larva migrans [5, 9–12] (table 1). Thiabendazole is poorly effective when given as a single dose. For example, only 68% of 28 patients in 1 series were cured by a single dose of 50 mg/kg [5]. The cure rate improved to 77% after 2 consecutive days, 87% after 3–4 consecutive days, and 89% after 4 weekly doses (table 1).

Thiabendazole is less well tolerated than either albendazole or ivermectin. In a study of 138 patients treated with thiabendazole (1.25–2.5 g/d for 1–2 days) for various indications, the following adverse effects occurred: giddiness (13%–54%), nausea (49%), vomiting (2%–16%), and headache (7%) [13].

**Albendazole.** Albendazole is a third-generation heterocyclic antihelminthic drug. It has been used for about a decade to treat intestinal helminthiases, such as ascaridiasis, enterobiasis, ancylostomiasis, trichuriasis, and strongyloidiasis. Trials of albendazole in the treatment of cutaneous larva migrans have yielded conflicting results with respect to the optimal dosage. Cure rates of 100% have been obtained after treatment with a single dose of 400 mg and with the same dose given for 3 and 5 consecutive days (table 2). Albendazole has also been used with success at higher daily doses (800 mg for 3 consecutive days). However, in the largest trial of albendazole in cutaneous larva migrans (involving 26 Italian tourists), treatment with 400 mg for 5 consecutive days failed for 2 patients [18]. In addition, in a study of 11 French tourists, a single 400-mg dose failed in 6 cases [19].

Differences in the study populations may account for the different cure rates (46%–100%) observed in these studies. It is interesting that 3 of the 4 studies with a 100% cure rate involved inhabitants of regions of endemicity, in whom it is difficult to distinguish between relapse and reinfection. In 2 of the 3 studies involving tourists, albendazole failed for 2 of 26 Italian patients [18] and 6 of 11 French patients [19], while the duration of follow-up was not given in the third study [14]. These findings suggest that for tourists with cutaneous larva migrans who are treated with albendazole, the regimen should be 400–800 mg/d for 3–5 days.

Albendazole was well tolerated in trials involving patients with cutaneous larva migrans. However, 27% of 30 patients with gastrointestinal strongyloidiasis complained of gastrointestinal pain and diarrhea after receiving 800 mg of albendazole by mouth on 3 consecutive days [20]. Other publications

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Treatment</th>
<th>Patients healed, no. (%)</th>
</tr>
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<tbody>
<tr>
<td>[11]</td>
<td>17</td>
<td>2 days</td>
<td>13 (77)</td>
</tr>
<tr>
<td>[10]</td>
<td>51</td>
<td>3–4 days</td>
<td>44 (87)</td>
</tr>
<tr>
<td>[5]</td>
<td>28</td>
<td>1st dose</td>
<td>19 (68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2d dose</td>
<td>21 (75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3d dose</td>
<td>22 (79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4th dose</td>
<td>24 (89)</td>
</tr>
<tr>
<td>[12]</td>
<td>25</td>
<td>1st dose</td>
<td>21 (84)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2d dose</td>
<td>23 (92)</td>
</tr>
</tbody>
</table>

* One dose of 50 mg/kg per week.
suggest that albendazole is well tolerated unless given at high dosages or for extended periods, such as those required for hydatid disease [21].

Ivermectin. Ivermectin, an avermectin B derivative, is active against Onchocerca volvulus and other nematodes, including gastrointestinal helminths. Its mechanism of action is poorly understood [22]. Single doses of ivermectin resulted in 100% cure rates among patients with cutaneous larva migrans in 2 open studies published in 1992, in which 8 Cameroonian patients received 150 mg/kg [23] and 12 French tourists received 200 mg/kg [24] (table 3). Since then, the efficacy of ivermectin has been confirmed in 3 larger studies. One involved 57 French tourists treated with a single oral dose of 12 mg ivermectin, of whom 56 (98%) were cured [25].

Another study involved 67 Belgian tourists treated with a single dose (12 mg) of ivermectin. Fifty-one patients were assessable and 48 (94%) were cured; 2 patients relapsed, and treatment failed in an immunodeficient patient [26]. The third study involved 59 French tourists treated with a single oral dose of 12 mg; 48 patients (81%) were cured, 9 relapsed, and treatment failed for 2. These latter 11 patients required a second (n = 9) or third (n = 2) course of ivermectin. The median intervals until disappearance of the pruritus and lesions were 3 days (range, 1–7 days) for the patients who received a second dose, and 9 days (range, 4–30 days) for those who received a third dose. Only 2 patients were not cured by ivermectin [27].

Ivermectin has been well tolerated in studies of patients with cutaneous larva migrans, and no adverse effects have been reported in indications other than filariasis [28]. Almost all the adverse effects are a result of the patient’s immune response to killed microfilariae [22].

An open study [19] compared the efficacy of single doses of oral ivermectin (12 mg) and oral albendazole (400 mg) in the treatment of cutaneous larva migrans. Twenty-one patients were randomly assigned to receive ivermectin (n = 10) or albendazole (n = 11). All the patients who received ivermectin responded, and none relapsed (cure rate, 100%). All but 1 of the patients receiving albendazole responded, but 5 relapsed after a mean of 11 days (cure rate, 46%); the difference in efficacy significantly favored ivermectin (P = .017). No major adverse effects were observed. The investigators concluded that a single 12-mg dose of ivermectin was more effective than a single 400-mg dose of albendazole for the treatment of cutaneous larva migrans [19].

Prevention

Because tourists are usually infected by walking or lying on tropical sandy beaches contaminated by dog feces, the best way to prevent cutaneous larva migrans is to ban dogs from beaches

Table 2. Treatment of cutaneous larva migrans with oral albendazole.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Daily dose, mg</th>
<th>Duration of treatment, d</th>
<th>Patients healed, no. (%)</th>
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</thead>
<tbody>
<tr>
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<td>400</td>
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<td>8 (100)</td>
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<tr>
<td>[17]</td>
<td>6</td>
<td>400</td>
<td>3</td>
<td>6 (100)</td>
</tr>
<tr>
<td>[15]</td>
<td>2</td>
<td>800</td>
<td>3</td>
<td>2 (100)</td>
</tr>
<tr>
<td>[14]</td>
<td>5</td>
<td>800</td>
<td>3</td>
<td>4 (100)</td>
</tr>
<tr>
<td>[18]</td>
<td>18</td>
<td>400</td>
<td>5</td>
<td>18 (100)</td>
</tr>
<tr>
<td>[19]</td>
<td>11</td>
<td>400</td>
<td>1</td>
<td>5 (46)</td>
</tr>
</tbody>
</table>

Table 3. Treatment of cutaneous larva migrans with a single oral 12-mg dose of ivermectin.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Patients healed, no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[23]</td>
<td>8</td>
<td>8 (100)</td>
</tr>
<tr>
<td>[24]</td>
<td>12</td>
<td>12 (100)</td>
</tr>
<tr>
<td>[19]</td>
<td>10</td>
<td>10 (100)</td>
</tr>
<tr>
<td>[25]</td>
<td>57</td>
<td>56 (98)</td>
</tr>
<tr>
<td>[26]</td>
<td>51</td>
<td>48 (94)</td>
</tr>
<tr>
<td>[27]</td>
<td>59</td>
<td>48 (81)</td>
</tr>
</tbody>
</table>
(figure 2, top) [29]. Because this is clearly impossible in developing tropical countries, where dogs are ubiquitous, it is best to wear shoes when walking in sandy areas. When on tropical beaches frequented by dogs, it is best to lie on sand washed by the tide or to use a mattress; avoid lying on dry sand, even on a towel (figure 2, bottom).

References


15. Williams HC, Monk B. Creeping eruption stopped in its tracks by alben-


