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# Comparison of Dermoscopy, Skin Scraping, and the Adhesive Tape Test for the Diagnosis of Scabies in a Resource-Poor Setting

Birke Walter, MD; Jörg Heukelbach, MD, PhD; Gernot Fengler, MD; Christine Worth, MD; Ulrich Hengge, MD, MBA; Hermann Feldmeier, MD, PhD

**Background:** Scabies is a parasitic skin disease endemic in resource-poor communities in low-income countries. The best ways to diagnose scabies in this setting have not been investigated.

**Objective:** To compare the diagnostic properties of dermoscopy, the microscopic examination of a skin scraping, and the adhesive tape test in 125 patients with a presumptive diagnosis of scabies.

**Design:** A prospective evaluator-blinded study.

**Results:** The sensitivity of dermoscopy was 0.83 (95% confidence interval [CI], 0.70-0.94) and significantly higher than the sensitivity of the adhesive tape test (0.68; 95% CI, 0.52-0.81; P < .001). The sensitivity of skin scraping was low (0.46; 95% CI, 0.31-0.62). The specificity of dermoscopy was 0.46 (95% CI, 0.34-0.58); by definition, it was 1.00 for skin scraping and the adhesive tape test. The negative predictive value was identical for dermoscopy and the adhesive tape test (0.85; 95% CI, 0.69-

0.94 and 0.75-0.91, respectively) but significantly lower for skin scraping (0.77; 95% CI, 0.67-0.84; P < .001). The sensitivity of dermoscopy increased with the severity of the disease, whereas the sensitivity of the adhesive tape test did not depend on this characteristic.

**Limitations:** Because of active case finding, the duration of the infestation was short and the severity of disease was rather low in most patients. The rather short duration of the infestation might have affected the diagnostic properties of each test in different ways.

**Conclusions:** When trained personnel are available, dermoscopy is a valid tool for diagnosing scabies in a resource-poor setting. The adhesive tape test is easy to perform and, because it has high positive and negative predictive values, the test is ideal for screening purposes. Skin scraping cannot be recommended as a diagnostic tool in this setting.

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Author Affiliations: Institute of Microbiology and Hygiene, Charité Universität Berlin, Campus Benjamin Franklin, Berlin (Drs Walter, Worth, and Feldmeier), and Hautzentrum Düsseldorf, Düsseldorf (Dr Hengge), Germany; and Department of Community Health, School of Medicine, Federal University of Ceará (Dr Heukelbach), and Mandacaru Foundation, Fortaleza (Dr Fengler), Ceará, Brazil. CABIES IS A CONTAGIOUS SKIN disease caused by an infestation with female mites of *Sarcoptes scabiei* var *hominis*. With a size of  $0.3 \times 0.5$  mm, female mites are at the limit of visibility. Male mites are even smaller and are rarely detected.<sup>1,2</sup> *Sarcoptes* mites are obligate human parasites living in the upper stratum of the epidermis. They are predominantly spread by close skin-to-skin contact. Pruritis with a nocturnal exacerbation is the main symptom.

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In resource-poor urban and rural communities of the developing world, the ectoparasitosis is endemic. Prevalence may be up to 10% in the general population and up to 50% in children.<sup>3-6</sup> According to a study of an urban slum in Bangladesh, the incidence in children younger than 5 years was 952 cases per 1000 children per year, indicating that nearly all children experienced the infestation within 12 months.<sup>7</sup>

In resource-poor settings, the diagnosis of scabies is made clinically or by using a case definition.<sup>8</sup> Because scabies can mimic a variety of skin diseases of infectious or noninfectious origin, a diagnosis based on clinical criteria alone is prone to error.<sup>9-11</sup> Although a false-positive diagnosis will result in unnecessary treatment and place the patient at risk for toxic adverse effects of scabicides,<sup>12-14</sup> overlooking infested individuals likely results in the infestation of family members.<sup>15</sup>

For decades, the ex vivo microscopic examination of skin scrapings was con-

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sidered the standard procedure, although the diagnostic properties of this technique were not well known.<sup>16</sup> For the past few years, epiluminescence microscopy and dermoscopy have been suggested as alternatives for diagnosing scabies in vivo.<sup>17-19</sup> In a study in a hospital setting in Paris, France, Dupuy et al<sup>20</sup> confirmed that dermoscopy is highly sensitive when performed by an experienced dermatologist.

Hitherto, to our knowledge, no data have been available on the diagnostic properties of skin scraping and dermoscopy in a resource-poor setting in an endemic area. As part of a research project on the epidemiology, morbidity, and control of scabies in Northeast Brazil, we assessed the diagnostic properties of dermoscopy and skin scraping in patients living in a slum and compared these procedures with the adhesive tape test, a noninvasive and easy method.

#### METHODS

## STUDY AREA AND POPULATION

The study was carried out in Morro do Sandra's, Serviluz, and Luxou, typical urban slums (*favelas*) in Fortaleza, the capital of Ceará State, Northeast Brazil. The socioeconomic characteristics of the communities have been described previously.<sup>5</sup> In brief, 94% of the population has a monthly household income of less than 2 minimum wages (1 minimum wage=415 R\$ [US \$205] per month at the time of the study). Adult illiteracy is 30%, unemployment is high, violence of all sorts is common, and hygienic conditions are precarious. In 2005, the prevalence of scabies was 8.8% in the general population.<sup>5</sup> Before the present study, no control measures for scabies had been undertaken in the area.

# STUDY DESIGN

From May 1 to December 21, 2008, all consecutive patients with a presumptive diagnosis of scabies were eligible. Patients with a presumptive diagnosis of scabies were identified through reports by family health agents, referral of patients from the Primary Health Care Center serving the communities, and patients or family members who contacted the outpatient department of the Mandacaru Foundation (a local nongovernmental organization providing education and health assistance), for whatever reason. Scabies was suspected if a patient showed a suspicious skin alteration accompanied by itching for at least 1 week. The following alterations were considered suspicious: presence of a characteristic primary lesion (papules, vesicles, or nodules) with or without secondary lesions (excoriation, eczematization, or secondary bacterial infection) that were obviously not associated with other dermatologic conditions.

To determine the topographic distribution of the lesions and the surface of the affected skin, the body surface was divided vertically into right and left. Each side was subdivided into 13 areas as follows: interdigital spaces, hand, wrist, arm, axilla, leg, foot, abdomen, thorax, mamilla/perimammilar area, back, buttock, and genital/inguinal area.<sup>21</sup> Primary lesions were differentiated into papules, crusted papules, vesicles, and nodules. Excoriations were also documented. Bacterial superinfection was diagnosed when pustules, suppuration, or an abscess were present.<sup>21</sup>

Two visual ordinal scales ranging from 0 to 4 points were used to semiquantitatively assess the degree of itching and sleep disturbance.<sup>21</sup> A severity score was calculated by adding intensity of itching (0-4 points), presence of superinfection (0-2 points), and number of topographic areas affected (1-3 areas=1 point, 4-6 areas=2 points, 7-9 areas=3 points, and  $\geq$ 10 areas=4 points). Hence, the severity score could range from 0 to 10 points.

# ORGANIZATION OF DIAGNOSTIC PROCEDURES

All patients were examined in a well-lighted room of the Mandacaru Foundation. The patient first saw a physician who recorded standard clinical and demographic data. The patient then was examined dermoscopically. After the dermoscopy, the adhesive tape test was performed and a skin scraping was obtained. Skin scrapings and adhesive tapes were transferred to a glass slide and examined in a laboratory next door. The investigator who performed the microscopic examinations was unaware of the results of dermoscopy.

Dermoscopy, skin scraping, and the adhesive tape test were performed at 3 topographic areas where mites were suspected. If the patient had more than 3 suspicious lesions, the selection of sites was left to the discretion of the investigator. If the patient had 3 or fewer lesions, all lesions were examined. For technical reasons, although conducted at the same body area, the adhesive tape test and the skin scraping were performed on different but closely located lesions.

#### DERMOSCOPY

Dermoscopy was performed using a handheld dermatoscope with  $\times$ 10magnification (Heine Alpha; Heine Optotechnik, Herrsching, Germany). The "delta wing sign" was considered to indicate the presence of a mite.<sup>20</sup>

#### ADHESIVE TAPE TEST

The adhesive tape test was performed as described by Katsumata and Katsumata.<sup>22</sup> Briefly, transparent adhesive tape (Tartan Tape; 3M Company, St Paul, Minnesota) was cut into strips of the size of a microscope slide (25 x 50 mm), firmly applied to a lesion, and then pulled off rapidly. The tape was transferred to a slide and the slide was stored at 10°C to 14°C until it was read. Slides were examined within the next 3 hours. Slides were scanned at ×40 magnification. If a mite was suspected, the magnification was increased to ×100.

# SKIN SCRAPING

Skin scrapings were obtained with the sharp edge of a sterile scalpel after the application of 1 drop of silicone oil onto the lesion. The scraped material was transferred to a slide and covered with a coverslip. The edges were sealed with transparent nail polish. Slides were kept in a refrigerator at 10°C to 14°C until examination. Reading was performed within 3 hours at  $\times$ 40 magnification.

#### TREATMENT

After diagnosis, the patients were treated orally with ivermectin (Revectina; Abbott Produtos para saúde Ltda, São Paulo, Brazil) at a concentration of 200 µg/kg, followed by a second dose after 7 days. Children younger than 5 years and pregnant and lactating women were treated topically with benzyl benzoate (Iquego; Goiânia, Goiás, Brazil) at a concentration of 250 mg/mL once per day for 3 days. Topical treatment was also repeated after 1 week.

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#### Table 1. Results of Diagnostic Procedures for Scabies in 113 Patients and Their Interpretation

Skin Scraping	Adhesive Tape Test	Dermoscopy	No. (%) of Patients	Interpretation	Diagnosis of Scabies
Positive	Positive	Positive	6 (5.3)	TP scraping/TP tape test/TP dermoscopy	Yes
Positive	Positive	Negative	0	TP scraping/TP tape test/FN dermoscopy	Yes
Positive	Negative	Negative	2 (1.8)	TP scraping/FN tape test/FN dermoscopy	Yes
Positive	Negative	Positive	11 (9.7)	TP scraping/FN tape test/TP dermoscopy	Yes
Negative	Positive	Positive	18 (15.9)	FN scraping/TP tape test/TP dermoscopy	Yes
Negative	Positive	Negative	4 (3.5)	FN scraping/TP tape test/FN dermoscopy	Yes
Negative	Negative	Positive	39 (34.5)	TN scraping/TN tape test/FP dermoscopy	No
Negative	Negative	Negative	33 (29.2)	TN scraping/TN tape test/TN dermoscopy	No

Abbreviations: FN, false-negative; FP, false-positive; TN, true-negative; TP, true-positive.

#### Table 2. Clinical Characteristics of 113 Patients

Characteristic	Value <sup>a</sup>
Sex	
Male	44 (38.9)
Female	69 (61.1)
Age, median (range), y	14 (2-72)
No. of topographic areas affected	
1-2	10 (8.8)
3-4	32 (28.3)
5-6	31 (27.4)
7-8	18 (15.9)
9-10	13 (11.5)
>10	7 (6.2)
Unknown	2 (1.8)
Severity score	
1-3	26 (23.0)
4-6	61 (54.0)
7-10	19 (16.8)
Unknown	7 (6.2)
Duration of lesions, wk	
≤3	47 (41.6)
4-8	25 (22.1)
>8	38 (33.6)
Unknown	3 (2.7)
Type of lesion <sup>b</sup>	
Papule	111 (98.2)
Nodule	13 (11.5)
Vesicle	5 (4.4)
Crusted papule	4 (3.5)
Excoriation	61 (54.0)
Superinfection <sup>c</sup>	30 (26.5)

<sup>a</sup>Data are given as number (percentage) of patients unless otherwise indicated.

<sup>b</sup>Multiple classifications were possible.

<sup>c</sup>Pustule, suppuration, or abscess.

## DATA ANALYSIS

Data were entered twice into a database using Epi Info, version 6.04d (Centers for Disease Control and Prevention, Atlanta, Georgia), and checked for errors that might have occurred during data entry. The primary objective was to determine the sensitivity of the 3 diagnostic procedures. Because there is no criterion standard for the diagnosis of scabies, we used the approach described by Dupuy et al,<sup>20</sup> in which the definition of true-positive, false-positive, true-negative, and false-negative findings is based on practical experience with diagnostic tests (**Table 1**). A patient was considered to have scabies if at least 1 mite was detected in a skin scraping or in the adhesive tape test. Sensitivity and other test statistics were com-

pared by the McNemar test. Sensitivity, specificity, positive predictive value, and negative predictive value are presented with their 95% confidence intervals (CIs) to acknowledge that the calculated values of the test parameters are estimates. Data analysis was conducted using Excel, version 2007 (Microsoft Corporation, Redmond, Washington).

On the basis of the assumption that the sensitivity of the adhesive tape test was not inferior to the sensitivity of dermoscopy by more than 15%, 115 patients with scabies had to be included in the study to have an  $\alpha$  of .05 and a statistical power of 0.80.

#### ETHICAL CONSIDERATIONS

The study was approved by the ethical review board of the Federal University of Ceará, Fortaleza, Brazil. Informed written consent was obtained from each patient after an explanation of the objectives of the study. In the case of minors, parents or guardians were asked for written consent.

# RESULTS

For 7 months, 125 consecutive patients were admitted. From 113 patients, results of the 3 diagnostic methods were available. The 12 patients without a complete data set were excluded from data analysis.

The clinical characteristics of the patients are summarized in **Table 2**. Fifty-five percent of the patients were children. Most patients (54.0%) had a moderate clinical pathology (severity score, 4-5 points). In 41.6% of the patients, the symptoms and signs had developed within the previous 3 weeks.

In total, 41 of 113 patients (36.3%) were diagnosed with scabies. The diagnostic properties of the 3 tests are shown in **Table 3**. The sensitivity of dermoscopy was significantly higher than that of skin scraping and the adhesive tape test (both P < .001). By definition, the specificity and the positive predictive value of the adhesive tape test and of skin scraping were each 1.00. The specificity of dermoscopy was low (0.46; 95% CI, 0.34-0.58) and significantly less than that of the adhesive tape test and skin scraping (both P < .001). Dermoscopy and the adhesive tape test had the same negative predictive value (0.85; 95% CI, 0.69-0.94 and 0.75-0.91, respectively).

**Table 4** shows the sensitivity of dermoscopy and the adhesive tape test according to clinical characteristics of the patients. The sensitivity of both tests decreased with increasing duration of the infestation. The sensitivity of dermoscopy increased parallel to the severity of scabies

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#### Table 3. Diagnostic Properties of 3 Tests for Scabies<sup>a</sup>

Diagnostic Property	Dermoscopy	Adhesive Tape Test	Skin Scraping
Sensitivity (TP/TP+FN)	0.83 (0.70-0.94)	0.68 (0.52-0.81)	0.46 (0.31-0.62)
Specificity (TN/TN+FP)	0.46 (0.34-0.58)	1.00 (0.94-1.00)	1.00 (0.94-1.00)
Negative predictive value (TN/TN+FN)	0.85 (0.69-0.94)	0.85 (0.75-0.91)	0.77 (0.67-0.84)
Positive predictive value (TP/TP+FP)	0.47 (0.36-0.59)	1.00 (0.85-1.00)	1.00 (0.79-1.00)
Mean accuracy $(TN+TP/TN+TP+FN+FP)$	0.60	0.88	0.81

Abbreviations: FN, false-negative; FP, false-positive; TN, true-negative; TP, true-positive. <sup>a</sup>Data are given as mean (95% confidence interval) unless otherwise indicated.

(light scabies, 0.80; moderate scabies, 0.85; and severe scabies, 0.93); however, the differences were not significant. The sensitivity of the adhesive tape test seemed to be unaffected by the severity of scabies (light scabies, 0.60; moderate scabies, 0.70; and severe scabies, 0.64).

#### COMMENT

In resource-poor settings, particularly in the developing world, scabies is one of the most common skin disorders. In Northeast Brazil, for instance, in impoverished rural and urban communities, the prevalence is up to 10% in the general population and up to 18% in children.<sup>3</sup> In these settings, scabies is diagnosed usually at the primary health care level, and the diagnosis is based on suspicious clinical findings, such as itchy papules.

Scabies can mimic a broad range of infectious and noninfectious diseases,<sup>8,10,11</sup> and the clinical picture is frequently masked by superinfection.<sup>13,23</sup> Hence, the specificity of a diagnosis based on clinical findings alone is low, and its sensitivity depends on the clinical findings considered to be diagnostic. An alternative approach is the use of a case definition. However, case definitions have to be adapted to the local epidemiologic situation, and their diagnostic accuracy is usually not known. The only pathognomonic sign, the burrow of the mite, is inconstantly present,<sup>24</sup> barely visible on pigmented skin,<sup>11</sup> and frequently obliterated or destroyed by scratching.<sup>25</sup> Moreover, Katsumata and Katsumata<sup>22</sup> showed that a burrow is not necessarily inhabited by a mite. Therefore, we decided not to include the Burrow Ink Test in the comparison of diagnostic methods.

The techniques were selected so that they could be used at the primary health care level in a resource-poor setting: dermoscopy with an illuminated, handheld dermoscope; the ex vivo examination of a skin scraping with a microscope; and the adhesive tape test, a technique derived from the collection of *Enterobius vermicularis* eggs from the perianal area with transparent tape.<sup>26</sup>

In this study, we showed that a handheld dermoscope is a valuable tool for diagnosing scabies in an endemic area. The sensitivity was 0.83 (95% CI, 0.70-0.94) and only slightly lower than determined in a hospital setting in France.<sup>20</sup> The higher sensitivity in the French study might be due to the fact that the authors continued to examine lesions at other topographic areas if the initial dermoscopy failed to identify a mite and spent up to 20 minutes for the procedure, whereas in this study,

Table 4. Sensitivity of Dermoscopy and Adhesive Tape Test
According to Duration and Severity of Scabies

Clinical Characteristic	Test	Sensitivity	
Duration of infestation			
≤3 wk	Dermoscopy	0.88	
	Adhesive tape test	0.75	
>8 wk	Dermoscopy	0.76	
	Adhesive tape test	0.65	
Severity score <sup>a</sup>			
Light (≤3 points)	Dermoscopy	0.80	
	Adhesive tape test	0.60	
Moderate (4-5 points)	Dermoscopy	0.85	
,	Adhesive tape test	0.70	
Severe ( $\geq 6$ points)	Dermoscopy	0.93	
	Adhesive tape test	0.64	

<sup>a</sup>See the "Study Design" subsection in the "Methods" section.

dermoscopy was limited to a maximum of 3 areas and to a maximum of 5 minutes.

The low specificity (0.46; 95% CI, 0.34-0.58) of dermoscopy found in this study may be explained by several factors. First, the investigators performing the dermoscopy had no previous training in mite identification and only had been shown photographs of the characteristic aspects of mites embedded in the stratum corneum. Extensive training, however, is required to not confound artifacts with mites. Correspondingly, in the study by Dupuy et al,<sup>20</sup> the accuracy of dermoscopy substantially increased for untrained observers during the study period. Second, most patients had moderately to intensely pigmented skin. The delta wing sign, which corresponds to the brownish-black anterior part of the embedded mite, is difficult to see or is completely hidden if the skin is pigmented.<sup>25</sup> Third, artifacts induced by scratching, such as crusts, point bleeding, or small particles of dirt, may be confounded with a mite. The low specificity of dermoscopy observed in this study is the reason that the positive predictive value of this method is low (Table 3). Hence, dermoscopy does not seem to be useful as a screening test in this setting.

For decades, the ex vivo examination of the scraping of a suspicious lesion has been considered the criterion standard for the diagnosis of scabies.<sup>16</sup> Although a multitude of modifications of this technique have been developed over time, its sensitivity has rarely been determined.<sup>27</sup> In our study, the sensitivity of skin scraping was significantly lower than that of dermoscopy (0.83 vs 0.46; P < .001). This seems to be a contradiction to the high

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sensitivity of this method described by Dupuy et al.<sup>20</sup> However, those authors used oriented skin scrapings in their patients; ie, when a first skin scraping was negative, another scraping was obtained exactly from the site where a mite had been identified by the dermoscopist. Obviously, such a procedure will considerably augment the sensitivity of skin scraping and will result in a falsely high performance of this method. In fact, other authors noted a rather low sensitivity of the technique when performed without the help of a dermoscopist.<sup>11,28</sup>

Palicka et al<sup>27</sup> showed that in 151 patients in whom skin scrapings were positive, only 18% of the samples contained mites. Bhutto et al<sup>29</sup> made similar observations.

We observed that mites migrated on a glass slide greased with oil, even when it was covered with a coverslip (B. Walter, MD, unpublished observation, 2009). To prevent mites from leaving the area under the coverslip or from becoming entangled at the edge of it, where they are difficult to see, the coverslip has to be sealed with nail polish and the slide has to be kept in a refrigerator, if not examined immediately.

The adhesive tape test described by Katsumata and Katsumata<sup>22</sup> is based on the rationale that Sarcoptes mites are located in the epidermis, and the upper layers of the epidermis are loosened by repeated skin scratching. Under these circumstances, residues of the stratum corneum together with mites will stick to an adhesive tape. Mites temporarily migrating on the skin also will stick to the adhesive tape. Although the sensitivity of the method was significantly lower than that of dermoscopy (0.68; 95% CI, 0.52-0.81), its negative predictive value was high (0.85; 95% CI, 0.75-0.91). Because by definition its positive predictive value is 1.00, this method is useful when screening, irrespective of the prevalence of scabies. In addition, the adhesive tape test needs no expensive equipment and is easy for untrained personnel to learn. Another practical advantage, compared with the ex vivo examination of skin scrapings, is that mites sticking to the adhesive tape cannot migrate to the edges of the coverslip and that the amount of cell debris that confounds the microscopic identification of mites and their eggs is considerably less than in a slide prepared from a skin scraping. Taken together, the properties of the adhesive tape test make it a useful diagnostic tool in resource-poor settings. Katsumata and Katsumata<sup>22</sup> used this technique in bedridden elderly patients with scabies and massive infestation. Because the texture of the epidermis is crucial for the sticking of mites to an adhesive tape, the method may perform better in patients with age-related or otherwise-caused atrophy of the skin.

It was an unexpected finding that the sensitivity of methods to diagnose scabies seems to depend on the clinical characteristics of a patient. Interestingly, the sensitivity of dermoscopy decreased with increasing duration of the infestation, but it improved parallel to the severity of scabies. Therefore, a positive dermoscopic finding would be more likely with increasing severity of the infestation. This association reflects the fact that, during the natural history of scabies, the number of mites considerably increases during the first 3 months of an infestation.<sup>30</sup> In our study, most patients were in an early stage of the disease, which would explain the lower sen-

sitivity of dermoscopy observed in our study compared with that of the French hospital study.<sup>20</sup> In contrast, the sensitivity of the adhesive tape test did not depend on the severity of scabies. An explanation could be that an alteration in the texture of the epidermis at sites where mites proliferate, together with skin abnormalities induced by scratching, increases the probability that residues of the stratum corneum along with mites stick to an adhesive tape that is firmly pressed onto the skin.

To be useful in a resource-poor setting, a test must have benefits in addition to high positive and negative predictive values. A clear disadvantage of dermoscopy is the requirement of a skilled and well-trained dermoscopist. Such expert knowledge is usually not available at the primary health care level. Because the delta wing sign is hardly visible or completely invisible on pigmented/ dark skin, this compromises the practicality of dermoscopy in many developing countries.

Skin scraping is an invasive method and requires disinfection of the skin before abrading a lesion with a scalpel. The procedure is displeasing for the patients and not well tolerated by children. Besides, the application of oil onto a lesion is disadvantageous when ambient temperature is high, and the presence of oil on the slide enables mites to move away if the slide is not sealed.

In summary, the combination of dermoscopy and the adhesive tape test is the optimal approach to diagnose scabies in resource-poor settings. If a trained dermoscopist is not available, then the adhesive tape test is the method of choice.

The following limitations of the study have to be taken into consideration. First, because of active case finding, many patients were in the early stage of the disease. This is usually not the case in patients presenting with scabies at a primary health care setting. This fact may have influenced the diagnostic performance of the 3 methods in different ways. Second, strict criteria for a presumptive diagnosis of scabies, and hence for admission to the study, led to selection of individuals with a high probability of scabies. The predictive value of a test depends not only on sensitivity and specificity but also on the prevalence of disease. Therefore, the negative predictive value of skin scraping and the adhesive tape test would be different if applied to a population with a low prevalence of scabies, such as in affluent societies. Finally, the diagnostic parameters were assessed in the absence of a criterion standard. The statistical procedure suggested by Joseph et al<sup>31</sup> to calculate diagnostic parameters in the absence of a criterion standard was not helpful in the special case of scabies. Hence, the sensitivity, specificity, and predictive values presented here are, at best, estimates for an epidemiologic situation similar to that of this study.

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**Correspondence:** Hermann Feldmeier, MD, PhD, Institute of Microbiology and Hygiene, Charité Universität Berlin, Campus Benjamin Franklin, Hindenburgdamm 27, 12207 Berlin, Germany (hermann.feldmeier@charite .de).

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the accuracy of the data analysis. *Study concept and design:* Walter, Heukelbach, Hengge, and Feldmeier. *Acquisition of data:* Fengler and Worth. *Analysis and interpretation of data:* Heukelbach, Fengler, Worth, Hengge, and Feldmeier. *Drafting of the manuscript:* Walter, Heukelbach, Worth, and Feldmeier. *Critical revision of the manuscript for important intellectual content:* Heukelbach, Fengler, Worth, Hengge, and Feldmeier. *Statistical analysis:* Heukelbach, Worth, and Feldmeier. *Funding:* Walter, Heukelbach, Hengge, and Feldmeier. *Funding:* Walter, Heukelbach, Hengge, and Feldmeier. *Study supervision:* Heukelbach, Hengge, and Feldmeier. *Study supervision:* Heukelbach, Hengge, and Feldmeier. *Financial Disclosure:* None reported.

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