Impaired warm and cold perception thresholds in leprosy skin lesions

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Summary The aim of the present study was to determine the frequency of alteration in warm perception thresholds (WPT), cold perception thresholds (CPT) and the warm and cold perception interval (WCPI) in leprosy-suspected skin lesions, and to determine if these tests could assist in the diagnosis of leprosy. Tests were conducted using a thermal sensory analyser TSA-2001 (Medoc Ltd, Israel) and the method of levels. A cross-sectional study of 112 patients presenting leprosy-suspected skin lesions ('patch'), with no clinical evidence of peripheral nerve damage, was conducted. Leprosy diagnosis was based on clinical dermato-neurological examinations and complementary tests. One hundred and eight subjects (45 males, 63 females; average age 37.7 years) completed the tests: 82 were positively diagnosed with leprosy and 26 with diseases of different etiologies. The mean values of WPT (45.63 ± 5.59), CPT (9.64 ± 11.34) and WCPI 36.01 ± 15.58) registered in leprosy-skin lesions were significantly different (P < 0.001) from lesions of diverse aetiologies and skin area without lesions. The cut-off point for WPT as determined from the ROC curve (receiver operating characteristic) was 35.10°C, with a sensitivity of 90.2% and a specificity of 100%, and the corresponding cut-off point for CPT was 28.95°C, with a sensitivity of 92.7% and a specificity of 100%. Nevertheless, all patients with leprosy presented a WCPI greater than 6.10°C (ROC curve) in skin lesions. Increase in the thermal thresholds indicated warm hypoesthesia, cold hypoesthesia or both. The WCPI, which embraces both warm and cold perception thresholds, was the best indicator of thermal sensation, a term used in literature as a non-specific expression that does not describe warm and cold stimuli explicitly in terms of units of temperature.

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Introduction

Hansen’s disease or leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, which affects the peripheral nervous system, skin, and other tissues.\(^1\)\(^-\)\(^5\)

The cardinal signs of the disease are cutaneous lesions with altered sensation, enlargement of the peripheral nerve and slit skin smears show in alcohol-acid resistant fast bacilli.\(^1\)\(^-\)\(^4\) The skin lesions, and lesions of the peripheral nerves may be associated, but they may appear separately.\(^6\)\(^-\)\(^10\) The initial cutaneous manifestations of leprosy result from direct infection of the dermal nerves, and are characterised by hypochromic lesions or erythema with reduced sensation.\(^1\)\(^-\)\(^4\)\(^,\)\(^11\) Verification of altered tactile, thermal or pain sensation of suspected skin lesions (‘patch’) confirms a diagnosis of leprosy.\(^1\)\(^-\)\(^4\)\(^,\)\(^12\) In early lesions, temperature or pain sensation may be impaired, while touch sensation is preserved.\(^12\)\(^,\)\(^13\) However, in more advanced stages of the disease, all forms of sensation are impaired.\(^12\)

In Brazil,\(^14\)\(^,\)\(^15\) sensation in leprosy (skin lesions and areas supplied by major nerve trunks) is commonly tested using Semmes–Weinstein monofilaments (SWM) to measure light-pressure thresholds, as well as standard clinical sensory tests employing cotton wool, pinpricks, and tubes containing hot (45°C) and cold (4°C) water in order to evaluate, respectively, tactile, pain and thermal sensation. The SWM kit consists of monofilaments standardised to deliver forces of 0·05 g (green), 0·2 g (blue), 2 g (purple), 4 g (red), 10 g (orange) and 300 g (magenta). Normal reference value is 0·05 g in any region of the body, except for the soles of the feet (2·0 g). The standard clinical sensory tests, however, make comparisons difficult between examinations carried out at different stages of the disease, because of the difficulties in controlling the many variables intrinsic to these tests.\(^16\) Several instruments have been developed to evaluate thermal sensation in leprosy-suspected lesions, for example, the Temperature Sensation Testing and Grading device,\(^17\)\(^,\)\(^18\) the Thermosense device,\(^19\)\(^,\)\(^20\) and the Thermal Stability Tester.\(^12\)\(^,\)\(^12\) However, according to Zaslansky and Yarnitsky,\(^21\) while altered temperature and vibration thresholds may be used as indicators of the sensory losses characteristic of leprosy, non-uniform and unconventional testing techniques render evaluation of the results obtained somewhat difficult. In 1976, Fruhstorfer and collaborators\(^22\) developed the Marstock stimulator, which employs heat and cold stimuli to evaluate routinely the small myelinated A-delta fibres and the unmyelinated C fibres. Measurement of the warm perception threshold (WPT) and the cold perception threshold (CPT), through application of heat and cold stimuli, not only allows quantification of loss of the thermo-sensitive function in the form of hypoesthesia and hypoalgnesia, but also of the hyperfunction in the form of thermal hyperalgnesia.\(^21\)\(^-\)\(^24\) While these tests are not specific for evaluating the peripheral nervous system in leprosy, they are useful for the evaluation of small fibres and their cutaneous receptors in the study of focal and generalised peripheral neuropathies of any aetiology.\(^21\)\(^,\)\(^23\)\(^,\)\(^25\) Thermal thresholds were determined for cool and warm sensation, and for heat perceived as pain,\(^26\) in leprosy skin lesions, but the detailed results were not presented. In 2005, Van Brakel *et al.* reported on thermal sensation in the skin areas supplied by major nerve trunks.\(^27\)\(^,\)\(^28\)

The aim of the present study was to determine the frequency of alteration in WPT, CPT and the warm and cold perception interval (WCPI) in leprosy-suspected skin lesions, and to determine if these tests could assist in the diagnosis of leprosy. Patients with signs and symptoms involving major nerve trunks have not been included in this study.
Patients and methods

PATIENTS

A cross-sectional study involving 112 patients from various leprosy health centres located in the metropolitan area of Belo Horizonte (MG, Brazil) was performed during the period from January 2000 to November 2004. The project was undertaken following approval by the Ethical Committee of UFMG, and an appropriate form containing the Terms of Consent was signed by each of the participants. Patients older than 7 years and with leprosy-suspected skin lesions with diameters $>18$ mm (i.e. presenting thermal stimulation areas of at least $16 \times 16$ mm) were included in the study. Potential subjects with neurological alterations and those with clinical histories of alcoholism, diabetes mellitus and other metabolic or genetic disorders, which could result in the impairment of the central and peripheral nervous system, were excluded.

For each patient, tactile sensation towards cotton wool, thermal sensation towards warm and cold water tubes, pain sensation towards pinpricks, and SWM values (at 0·05, 0·2, 2·0, 4·0, 10·0 and 300·0 g) of leprosy-suspected lesions and contralateral (opposite side of the body) and ipsilateral (same side of the body) skin area without lesion (SAWL) were determined. The areas investigated were circumscribed with a pen, and patients were redirected to the Clinical Neurophysiology Laboratory of the Orthopaedic Hospital (Belo Horizonte) for investigation of the thermal thresholds of the lesions. In patients with multiple lesions, one lesion with an appropriate area for application of the thermal stimulus and subsequent biopsy was selected. The results of the investigations carried out at the health centres were not available to the hospital laboratory technicians in order to guarantee the blind nature of the study. Following thermal studies of the areas previously selected, patients returned to their original health centres to receive a definitive diagnosis and specific treatment. Data collected at the health centres and at the hospital were correlated only after a definitive diagnosis of leprosy had been achieved.

LEPROSY DIAGNOSIS

The diagnosis of leprosy was based on clinical dermo–neurological examination together with complementary examinations including skin biopsy and histopathology, slit-skin smears, evaluation of SWM, standard clinical sensory tests (cotton, pinpricks and tubes containing hot and cold water), Mitsuda reaction, anti PGL-1 serology (ML flow), and histamine and pilocarpine tests. For some patients, a further period of observation was required before a definitive diagnosis could be reached.

CONTROLS

Subjects either with or without leprosy diagnosis have been used in the control group. The controls consisted of contralateral and ipsilateral SAWL of patients who had been diagnosed with leprosy, and of skin lesions and contralateral and ipsilateral SAWL of patients in whom leprosy was excluded.
EQUIPMENT AND PROTOCOLS

The temperature of the room in which the thermal tests were conducted varied between 23.0° and 26.2°C, and patients were allowed no visual contact with the equipment throughout the test period. Tests were conducted using a thermal sensory analyser TSA-2001 (Medoc Ltd., Israel) with a thermode of stimulation area 16 x 16 mm. The adaptation temperature (AT) of the thermode was 32°C and the temperature limits were fixed at 50 and 0°C for warm and cold perception, respectively. The rate of change of temperature during the application of a stimulus was 1°C/s, while the rate of change during the return to the baseline was 0.8°C/s. The interval between the application of each was 4–6 s. Temperatures below and above the AT (for the determination of CPT and WPT, respectively) were recorded continuously between the set limits with an accuracy of 0.1°C. For patients who did not perceive the extreme temperatures, values of 50 or 0°C were registered, as appropriate, in order to permit statistical analysis.

A standard test sequence, involving the determination of CPT and WPT of the contralateral SAWL, then of the suspected lesion, and finally of the ipsilateral SAWL was applied to each subject. The thermode was placed carefully over the selected test area and fixed with adhesive tape in order to ensure good contact with the skin in the absence of excessive pressure. The skin around the area to be stimulated was surrounded with thermal insulating tape. The method of levels was used to determine perception thresholds in which a series of stimuli of fixed intensities was applied to the subject (Figure 1). After an initial temperature step of 4°C and the return to AT, subjects were questioned about their perception of the stimulus. A positive response led to a smaller subsequent stimulus, whilst a negative response was matched with a larger subsequent step. The step size was halved when the response of the subject changed from positive to negative, and vice versa. The step size remained unaltered when the response of the subject remained unchanged. The sequence of stimuli was continued until a step size of 0.1°C was attained.

STATISTICAL ANALYSIS

The mean values of the parameters measured for leprosy and control groups were compared using Student’s t-test (when the variables presented a normal distribution) and non-parametric tests (Mann–Whitney and Wilcoxon) for asymmetric distributions. Wilcoxon and paired t-tests were used to compare data obtained for suspected lesions and contralateral

![Figure 1](image-url). Schematic diagram of the method of levels employed to determine WPT showing the intensity of heat stimulus applied to the test area following a positive (Y, yes) or a negative (N, no) response by a subject concerning their perception of the previous stimulus. AT is the adaptation temperature of the thermode and dashed line is the sensory threshold finally determined.
SAWL, suspected lesions and ipsilateral SAWL, and contralateral SAWL and ipsilateral SAWL. To evaluate and validate the performance of the thermal test for the diagnosis of leprosy, a receiver operating characteristic (ROC) curve was used, which shows a graphic representation of the sensitivity and specificity of the test and allows the selection of a more appropriate cut-off point as determined by the definitive diagnosis. The statistical software used for the analysis of the data was SPSS® 11·5 (SPSS Inc, Chicago, IL, USA) values were deemed statistically significant at $P < 0·05$.

**Results**

One hundred and 12 patients presenting with leprosy-suspected skin lesions were redirected to the Clinical Neurophysiology Laboratory, from which 108 (45 males and 63 females) concluded all of the tests. Three patients abandoned the tests, and one patient did not understand the procedures involved in the thermal tests and could not complete the examination. The age of patients with leprosy-suspected lesions ranged from 9 to 73 years with an average age of $37·7 \pm 14·9$ years. The average age of patients with leprosy was $37·4 \pm 13·2$, and 93·5% of this group were younger than 60 years old. The average age of patients without leprosy was $38·7 \pm 18·7$ years. The evolution of leprosy had occurred within 30 days to 60 months, and 72·2% of patients reported that leprosy-suspected lesions developed in less than 12 months. Leprosy was diagnosed in 82 patients (75·9%) and the characteristics of the lesions were of indeterminate type (13·4%), tuberculoid type (28%), borderline tuberculoid type (51·2%) and borderline borderline type (7·3%). Leprosy lesions predominated in the lower limbs (36·6%), followed by the upper limbs (31·7%), trunk (24·4%) and face (7·3%). Twenty-six patients were diagnosed with vitiligo, pityriasis alba, granuloma annulare, atopic dermatitis, pseudo-lymphoma, post-inflammatory residual dischromia and fungal mycosis. The number of suspected skin lesions in each patient varied between one and eight: 37 patients presented with only one lesion, of whom 22 were diagnosed with other diseases.

**WARM AND COLD PERCEPTION THRESHOLDS**

The mean values of WPT ($45·63 \pm 8$) and CPT ($9·64 \pm 8$) of lesions of the leprosy group were significantly different ($P < 0·001$) from the corresponding mean values obtained from lesions of diverse etiologies (Table 1). In the group in which leprosy had not been diagnosed, there were no statistically significant differences between the corresponding mean values of WPT and CPT of skin lesions and contralateral SAWL, of suspected lesions and ipsilateral SAWL, and of contralateral SAWL and ipsilateral SAWL. Similarly, in the leprosy group there were no significant differences between the respective mean values of WPT and CPT of contralateral and ipsilateral SAWL.

Within the leprosy group, the mean value of the absolute differences between WPT of skin lesions and contralateral SAWL was $12·41 \pm 8$, while the mean value of the absolute difference between the corresponding CPT was $21·32 \pm 8$ (Table 2). These values were similar to the absolute differences between the corresponding WPT and CPT ($12·36$ and $21·31$ respectively) of leprosy lesions and ipsilateral SAWL. However, in the control group, there were no statistically significant differences between the mean values of the absolute differences between WPT or CPT of non-leprosy lesions and contralateral SAWL,
Table 1. Mean values of warm perception threshold (WPT), cold perception threshold (CPT) and warm and cold perception interval (WCPI) obtained for suspected lesions, and contralateral and ipsilateral skin areas without leprosy (SAWL) in the group diagnosed with leprosy (leprosy) and without leprosy (non-leprosy).

<table>
<thead>
<tr>
<th>Tested skin area</th>
<th>WPT (Mean ± standard deviation (°C))</th>
<th>CPT (Mean ± standard deviation (°C))</th>
<th>WCPI (Mean ± standard deviation (°C))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-leprosy</td>
<td>Leprosy</td>
<td>P-value</td>
</tr>
<tr>
<td>Suspected lesion</td>
<td>33.28 ± 0.70</td>
<td>45.63 ± 5.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contralateral SAWL</td>
<td>33.27 ± 0.60</td>
<td>33.23 ± 0.81</td>
<td>0.819</td>
</tr>
<tr>
<td>Ipsilateral SAWL</td>
<td>33.28 ± 0.67</td>
<td>33.27 ± 0.78</td>
<td>0.929</td>
</tr>
</tbody>
</table>

Thermal perception in leprosy skin lesions
non-leprosy lesions and ipsilateral SAWL, and of contralateral and ipsilateral skin area without leprosy (SAWL) in the group diagnosed with leprosy (leprosy) and without leprosy (non-leprosy).

Table 2. Mean values and ranges of the absolute differences in warm perception threshold (WPT), cold perception threshold (CPT) and warm and cold perception interval (WCPI) between suspected lesions, contralateral and ipsilateral skin area without leprosy (SAWL) in the group diagnosed with leprosy (leprosy) and without leprosy (non-leprosy)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non leprosy</th>
<th>Leprosy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differences in WPT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspected lesion and contralateral SAWL</td>
<td>0.30 ± 0.23 (0.0–0.7)</td>
<td>12.41 ± 5.68 (0.2–17.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Suspected lesion and ipsilateral SAWL</td>
<td>0.30 ± 0.29 (0.0–1.0)</td>
<td>12.36 ± 5.68 (0.1–17.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contralateral and ipsilateral SAWL</td>
<td>0.20 ± 0.16 (0.0–0.5)</td>
<td>0.17 ± 0.17 (0.0–1.2)</td>
<td></td>
</tr>
<tr>
<td>Differences in CPT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspected lesion and contralateral SAWL</td>
<td>0.28 ± 0.33 (0.1–1.4)</td>
<td>21.32 ± 11.33 (0.1–31.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Suspected lesion and ipsilateral SAWL</td>
<td>0.28 ± 0.34 (0.0–1.3)</td>
<td>21.31 ± 11.34 (0.0–31.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contralateral and ipsilateral SAWL</td>
<td>0.18 ± 0.24 (0.0–1.1)</td>
<td>0.14 ± 0.13 (0.0–0.9)</td>
<td>0.264</td>
</tr>
<tr>
<td>Differences in WCPI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspected lesion and contralateral SAWL</td>
<td>0.33 ± 0.31 (0.0–1.3)</td>
<td>33.74 ± 15.68 (4.6–49.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Suspected lesion and ipsilateral SAWL</td>
<td>0.36 ± 0.39 (0.0–1.8)</td>
<td>33.70 ± 15.68 (4.6–49.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Contralateral and ipsilateral SAWL</td>
<td>0.28 ± 0.31 (0.0–1.6)</td>
<td>0.23 ± 0.20 (0.0–1.3)</td>
<td>0.391</td>
</tr>
</tbody>
</table>

non-leprosy lesions and ipsilateral SAWL, and of contralateral and ipsilateral SAWL of all patients. The mean values of the absolute differences of WPT and of CPT between leprosy lesions and contralateral SAWL, and leprosy lesions and ipsilateral SAWL, were significantly different (P < 0.001) from the corresponding values of the control group. The cut-off point for WPT as determined from the ROC curve was 35-10°C, with a sensitivity of 90.2% and a specificity of 100%, and the corresponding cut-off point for CPT was 28-95°C, with a sensitivity of 92.7% and a specificity of 100% (Table 3).

Table 3. Cut-off point, sensitivity and specificity of warm perception threshold (WPT), cold perception threshold (CPT), warm and cold perception interval (WCPI), and the absolute difference of temperature of warm and cold perception interval (Δt WCPI) obtained from the receiver operating characteristic (ROC) curve

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cut-off point (°C)</th>
<th>ROC curve</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WPT</td>
<td>35.10</td>
<td>90.2</td>
<td>100</td>
</tr>
<tr>
<td>CPT</td>
<td>28.95</td>
<td>92.7</td>
<td>100</td>
</tr>
<tr>
<td>WCPI</td>
<td>6.10</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Δt WCPI</td>
<td>2.95</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
Within the leprosy group, the mean value of WCPI of lesions was 36·01°C, while the corresponding values of contralateral SAWL and of ipsilateral SAWL were 2·27 and 2·31°C, respectively (Table 1). In the group in which leprosy had not been diagnosed, the mean values of WCPI of skin lesions, contralateral SAWL and ipsilateral SAWL were 2·43, 2·49 and 2·54°C, respectively. Patients with leprosy presented a WCPI superior than 6·10°C (the cut-off point determined from the ROC curve). As shown in Table 2, within the group presenting leprosy-diagnosed lesions, the mean value of the absolute differences between the WCPI of lesions and contralateral SAWL (33·74°C) was very similar to the mean value of the differences between the WCPI of lesions and ipsilateral SAWL (33·70°C). However, the mean values of the absolute differences of WCPI of skin lesions and contralateral SAWL, and of skin lesions and ipsilateral SAWL, between the leprosy group and the non-leprosy group were significantly different ($P < 0·001$). Patients with leprosy had presented absolute differences of WCPI between skin lesions and SAWL (contralateral and ipsilateral) equal or superior to 4·60°C (the cut-off point was 2·95°C).

**Discussion**

It is well recognised that some cutaneous and pure neural forms of leprosy are very difficult to diagnose. In spite of the acknowledged importance of thermal sensation measurements in the diagnosis of cutaneous forms of leprosy, evaluations of these modalities continues to be conducted using non-quantitative approaches including the warm and cold water tube techniques. The quantitative sensory thermodetest may be affected by various factors that reduce their reproducibility. Such factors include the equipment and methodology employed, the size of the stimulated area, the initial temperature of the stimulator, the rate of change of temperature, and the region of the body tested. Following the introduction of the Marstock stimulator, a number of different types of instruments have become commercially available. However, the results obtained using the recently-introduced technology must be compared with the thermal thresholds already established, and for this purpose it is necessary to apply the same equipment, methodology and algorithms.

In the present study, the methodology employed afforded values of WPT, CPT and WCPI of the leprosy skin lesions (Table 1) that were significantly higher than those of lesions of different aetiologies ($P < 0·001$). The observed increase in WPT indicated a warm hypoaesthesia occasioned by the involvement of the C fibres and their specific receptors, while the increase in CPT indicated a cold hypoesthesia with the involvement of A-delta fibres or their specific receptors. Pure warm hypoaesthesia is common in neuropathy. Although the study was carried out with patients with skin lesions, with no signs or symptoms of peripheral neuropathy (trunks), we expected to register a higher WPT alteration in relation to CPT.

However, on the basis of the cut-off points adopted (cf. Table 3), the sensitivities and specificities of the WPT and CPT values were similar, indicating that both parameters have the same practical importance in the diagnosis of leprosy. The observed increase in WCPI indicated the functional involvement of either C fibres, or A-delta fibres, or both.

Leprosy lesions can be located in diverse regions of the body and different regions of the body of healthy individuals exhibit significantly different thermal thresholds. Nevertheless, it is not practical to establish a standard reference for the diagnosis of leprosy.
for each one of the body areas. As shown above, however, suspected lesions, contralateral SAWL and ipsilateral SAWL in the control group had similar mean values of WPT, CPT and WCPI (Table 1). These results confirmed those of previous studies in which no significant differences could be established in thermal thresholds when comparing contralateral symmetric cutaneous areas, or neighbouring skin areas in the same segment of the body. A difference of more than 1°C in thermal threshold (WPT or CPT) between a suspected area and a symmetric normal area is considered as clinically valuable. In the present study, one patient in the control group presented absolute difference of this magnitude in CPT, comparing lesion (fungal mycosis) and contralateral SAWL. Another four patients presented differences of more 1°C in WPT or CPT, comparing lesions of different etiologies and ipsilateral SAWL and comparing contralateral and ipsilateral SAWL. Such differences, however, did not alter statistically the mean values of the groups in which the patients were included. In the leprosy group the absolute differences in WPT or CPT between lesions vs contralateral SAWL and lesions vs ipsilateral SAWL were less than 1°C in 13 (15.8%) patients.

For individuals of the leprosy group, the minimum absolute difference between the WCPI of lesions and the WCPI of contralateral or ipsilateral SAWL was found to be 4.6°C (cut-off point at 2.95°C). Such a temperature difference is 2.5 times larger than the greatest difference (1.8°C) recorded in the control group (Table 2). Thus, in order to ensure a more reliable comparison of thermal thresholds it is important to evaluate contralateral areas or neighbouring areas in the same segment.

None of the subjects in the present study exhibited normal thresholds for warm and cold stimulus simultaneously. The WCPI value, which embraces both WPT and CPT parameters, was the best indicator of thermal sensation, a term used in the literature as a non-specific expression that does not describe warm and cold stimuli explicitly in terms of units of temperature. Through a comparative study of the absolute differences in the values of WCPI temperatures (i.e. for lesions vs contralateral SAWL and lesions vs. ipsilateral SAWL, Tables 2 and 3) considering a cut-off point of 2.95°C or establishing a cut-off point of 6.1°C for WCPI of the lesion (Table 3), it was possible to establish a cut-off point for thermal sensation in a suspected lesion predictive of a definitive diagnosis of leprosy. The advantage in employing the absolute difference of WCPI (since SAWL had been used as control of the patient) is that it not only permits the simultaneous evaluation of warm and cold stimuli, but it also reduces the importance of various factors that interfere with the determination of thermal thresholds, such as the inclusion or not of the reaction time, the size of the thermode, the rate of temperature change, the region of the body tested, and the age of the individual.

Some studies have indicated that the thermal threshold of the feet of healthy individuals increases as a function of age, particularly in subjects older than 65 years. In the present study, only four patients were 65 years or more, but their age did not significantly affect the mean values of the thermal threshold of the group in which they were included.

The large standard deviations obtained for WPT, CPT and WCPI in leprosy-diagnosed patients (as shown in Tables 1 and 2) indicate that the lesions investigated were of a heterogeneous nature, involving not only several clinical forms of the disease, but lesions of different evolution times (30 days to 60 months), many of which may not have been accurately reported by the patients themselves. The thermal sensations across the spectrum of leprosy lesions are presented in Table 4.

Thermal receptors are very sensitive to differences between the temperature of the skin and the objects that are touched. Warmth and cold receptors are more sensitive to changes in
The temperature range was truncated at 0 and 50°C. Other devices allow the use of temperature higher than 50°C. However, warmth receptors fire most vigorously at skin temperature of 45°C. If the stimulus temperature exceeds 45°C, warmth fibres fire an intense burst of impulses and then cease firing even if the heat stimulus is maintained. Stimuli above 50°C fail to excite warmth fibres. Cold receptors fire most vigorously at skin temperature of 25°C and the nociceptive threshold is around 5°C. A clear temporal distinction between the moment of warm or cold perception and the pain caused by these stimuli have been noticed when the WPT was lower than 46°C and the CPT was higher than 6°C. Nevertheless, stimuli above 46°C or below 6°C have been, respectively, referred to as heating or cooling perception of fast installation immediately followed by pain (Villarroel et al., in preparation). Twenty-two leprosy patients (26.8%) did not report warm sensation or heat pain in the skin lesions at 50°C while thirty patients (36.5%) did not refer to cold sensation or cold pain at 0°C. Three patients (indeterminate, borderline tuberculoid and borderline borderline) reported in the lesions, paradoxical warm sensation during the measurement of cold perception thresholds (Villarroel et al., in preparation).

The diagnosis of leprosy based on clinical dermo-neurological examination and complementary tests was positive in 70 (85.3%) patients. SWM, cotton wool (tactile sensation) and pinpricks (pain) tests have been applied to all patients. Nevertheless, thermal tests (warm/cold water tubes) have been applied to 76 patients with leprosy (n = 82) and, in seven patients, the precise water temperature has not been reported.

Electronic thermal testing allowed the quantification of the thermal impairment in a skin lesion. The patients evaluated were referred from health centers that work with leprosy, and many of these patients were pre-selected by dermatologists in other works. It would be important to include more subjects with early multibacilary disease and those with skin lesions of different etiologies. Nonetheless, in a clinical and dermatological examination we think that electronic thermal tests may, in addition, select patients for skin biopsy.

The determination of warm and cold perception is simple, but it requires a certain level of understanding, cooperation and concentration from the patient. The method of levels is rapid to execute and does not depend on the reaction time of the individuals, hence the variability of perception thresholds determined is minimised. The tests were easily applied and only one patient could not complete the procedures. However, the application of this methodology is limited by the cost and size of the equipment, and the large surface area of lesion required for the application of the stimulus. Simpler and cheaper devices that permit the quantification of

**Table 4.** Mean values in warm perception threshold (WPT), cold perception threshold (CPT) and warm and cold perception interval (WCPT), in different forms of leprosy

<table>
<thead>
<tr>
<th>Leprosy</th>
<th>Patients</th>
<th>WPT</th>
<th>CPT</th>
<th>WCPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indeterminate</td>
<td>11</td>
<td>45.1 ± 4.7</td>
<td>15.4 ± 8.7</td>
<td>29.6 ± 12.6</td>
</tr>
<tr>
<td>Tuberculoid</td>
<td>23</td>
<td>45.9 ± 5.8</td>
<td>6.8 ± 10.3</td>
<td>39.1 ± 14.3</td>
</tr>
<tr>
<td>Borderline tuberculoid</td>
<td>42</td>
<td>46.0 ± 5.7</td>
<td>9.2 ± 11.7</td>
<td>36.9 ± 16.4</td>
</tr>
<tr>
<td>Borderline borderline</td>
<td>6</td>
<td>43.1 ± 5.8</td>
<td>13.4 ± 14.9</td>
<td>29.7 ± 18.1</td>
</tr>
</tbody>
</table>

skin temperature than constant temperatures. The temperature range was truncated at 0 and 50°C. Other devices allow the use of temperature higher than 50°C. However, warmth receptors fire most vigorously at skin temperature of 45°C. If the stimulus temperature exceeds 45°C, warmth fibres fire an intense burst of impulses and then cease firing even if the heat stimulus is maintained. Stimuli above 50°C fail to excite warmth fibres. Cold receptors fire most vigorously at skin temperature of 25°C and the nociceptive threshold is around 5°C.
temperature variation, and that consider values less than 50°C and greater than 0°C, respectively, may be very useful in the field. The use of a smaller thermode is not only important for the study of smaller lesions but also for the evaluation of potential thermal mosaic effects in larger lesions. Patients presenting necrobiosis lipoidia, in which thermal sensation may be altered, was not evaluated in the present study nor were comparisons WPT, CPT and WCPI with other diagnostic methods.

In conclusion, it has been established that cutaneous lesions in leprosy-diagnosed patients are characterized by alterations in thermosensation, functionally expressed as warm hypoaesthesia, or cold hypoaesthesia, or both, through the determination of WPT, CPT and WCPI values using the method of levels. Such tests are important mainly in refining the diagnosis of paucibacillary leprosy.

References


38 Santiago S, Ferrer T, Espinosa ML. Neurophysiological studies of thin myelinated (A delta) and unmyelinated (C) fibers: application to peripheral neuropathies. *Neurophysiol Clin*, 2000; **30**: 27–42.

