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Cold Fingers in Leprosy[1]

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During the course of an investigation in India into the impairment of vasomotor reflex control of fingertip blood flow as a possible early indicator of peripheral neuropathy in leprosy ([5]), it was noted that many of the leprosy patients had very cold hands even though the ambient temperature was 26°C–29°C. By contrast, healthy Indian control subjects had warm hands under the same environmental conditions. This clinical finding does not seem to have been studied in detail previously, and this paper describes the results of our investigations into the relationship between cold fingers, blood flow in the fingertip skin, and sensation in the fingers.

MATERIALS AND METHODS

Patients. Twenty-two long-standing leprosy patients, all currently receiving standard WHO-recommended multidrug therapy (MDT), were admitted to the study: 13 were inpatients at the Richardson Leprosy Hospital, Miraj, India, for treatment of leg/foot ulcers and deformity and 9 were attending the outpatient clinic. The disease was classified as borderline lepromatous (BL) in 16 (mean age 35.6 years, S.D. 12.3) and as borderline tuberculoid (BT) in 6 patients (mean age 31.2 years, S.D. 14.0) ([25]). None of these patients had leprosy skin lesions on their hands, and there was no obvious reabsorption of their fingers.

Controls. Sixteen subjects (mean age 29.9 years, S.D. 6.7) were recruited in Miraj. This group consisted of 11 apparently healthy Indian leprosy control workers and five apparently healthy European subjects who were working at or visiting the Richardson Leprosy Hospital at the time of the study. All participants were volunteers and the study had been approved by the local Ethics Committee.

All subjects were allowed to equilibrate at an ambient temperature of 26°C–29°C (the daytime shade temperature at Miraj) while sitting comfortably for 15 min. The tests were always performed in the following sequence: first, assessment of sensation, then skin temperature recording and, lastly, skin blood flow measurement. At least eight fingers were examined in all subjects.

Sensory testing. Light touch was assessed first, then pressure sensation and, finally, temperature discrimination. For all tests the subject was seated comfortably with the forearms resting on a table at heart level, the eyes closed, and the head turned away from the side being tested. Care was taken to ensure that subjects—especially non-English-speaking Indian subjects—understood fully the nature of the tests at the beginning of each session. The intervals between tests and the order of testing of the fingers were deliberately varied so that a pattern would not be predicted by the patient.

Light touch was tested by the operator dabbing the skin of the fingers and fingertips lightly with cotton wool. When the subject felt the touch, he/she acknowledged sensation by pointing to the site with the index finger of the contralateral hand. At least 20 sites were tested on each subject's hands, including the palmar and dorsal aspects of all fingers.

Pressure sensation was assessed in a similar manner by use of standard, 6.1 mm, nylon von Frey hairs, one inch long. The hairs bend at a critical pressure, enabling a

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standard pressure stimulation to be applied ([19]).

Temperature sensation was assessed with a Thermal Sensibility Sensor ([26]). Both ends have identical round metal discs: one can be heated to 45°C with an internal dry battery while the other remains unheated and feels cold by comparison. The subject was asked to indicate whether each application was hot or cold.

The results of all sensation tests on each aspect of a finger were recorded on a three-point scale: 1 = absent/consistently mistaken; 2 = partial sensation (i.e., variation from area to area on the volar or dorsal aspect of the finger of positive and negative results); 3 = unimpaired sensation. For convenience of analysis the final summary of results on each subject was the mean score (out of 3) for each of the three types of sensation tested, giving a maximum total sensory score of 9.

Measurement of skin temperature. A platinum skin thermistor attached to a LCD output device was used to measure skin surface temperature. The probe (Model 4098, 9 mm diameter; Yellow Springs Instrument Co. Inc., Yellow Springs, Ohio, U.S.A.) was held in close contact with the skin with a single strip of Millipore adhesive tape. The apparatus had been calibrated against an infrared bolometer (Model KT-41; Heimann GmBH, Wiesbaden, Germany). A stable temperature was generally achieved after 5 min of contact with the skin of the pulp of the fingertip or the chest wall. The same sensor was used to measure atmospheric temperature when fully shaded from sunlight.

Measurement of skin blood flow. A laser Doppler velocimeter (PF2; Perimed, Stockholm, Sweden) was used with settings "gain = 3, 12 kHz bandwidth, 0.2 sec time constant and artefact filter off." A probe holder was attached to the pulp of the fingertip with double-sided adhesive tape (Perimed). This ensured that the probe head was located close to, and orientated perpendicular to, the skin surface. The principles of measurement of cutaneous blood flow by laser Doppler methods have been described previously ([15, 21, 22]). In brief, an optical fiber directs light from a 2-mW helium-neon laser into the skin. The reflected light from the tissue is collected by other optical fibers for measurement of its intensity and wavelength shift. The relative intensity of the Doppler-shifted component of the reflected light (termed RBC flux and measured in volts) is related to the velocity of movement and the number of moving erythrocytes in the dermal blood vessels under the probe. This machine is internally standardized and it has proved reliable in clinical investigations ([3, 6]).

Statistical analysis of results. Where appropriate, *t* tests, ANOVA and discriminant analyses were performed on a microcomputer with a commercial package (Statgraphics, version 3.0; STSC, Inc., Rockville, Maryland, U.S.A.).

RESULTS

Sensory testing. The control subjects did not show impairment of any of the three sensations tested. Both borderline lepromatous (BL) and borderline tuberculoid (BT) patients' results were significantly different from the controls for each sensation and the total sensory score. Temperature sensation appeared to be the most severely affected in both BL and BT patients but the differences between these two groups in the impairment of this and the other two sensations were not statistically significant ($p < 0.08$). In the leprosy patients, the little finger showed a small, but significantly ($p < 0.05$), greater impairment of all three sensations than the thumb. The results are summarized in Table 1.

Fingertip skin temperature. There was no significant difference between the control subjects (mean + S.D. = 33.99 ± 2.19°C) and the BT patients (34.91 ± 1.53°C), but the BL patients had colder fingers (30.26 ± 3.23°C) ($p < 0.05$). Although in many patients some fingers were colder than others, there was no selective involvement of any digit.

Fingertip blood-flow velocity. The RBC flux was high in the control subjects who were showing maximal peripheral vasodilatation at the ambient temperature of 26°C–29°C (5.28 ± 1.80 V). By contrast, the BT patients had lower fingertip RBC fluxes (3.62 ± 1.59 V) and the BL patients had even lower blood-flow velocities (1.74 ± 1.49 V). Analysis of variance showed that the three groups were significantly different from each other ($p < 0.05$). There were no significant

TABLE 1. *Mean scores (±S.D.) in tests of sensory function on the front (F) and back (B) of the fingers of leprosy patients and apparently healthy controls.*[a]

Group	No. subjects	No. fingers studied	Sensory score for						Total score	
			Light touch		Pressure		Temperature		F	B
			F	B	F	B	F	B		
Control	16	158	3	3	3	3	3	3	9	9
BT	6	60	2.53 ±0.79	2.56 ±0.74	2.53 ±0.79	2.57 ±0.74	2.48 ±0.85	2.48 ±0.85	7.55 ±2.41	7.62 ±2.31
BL	16	150	2.33 ±0.92	2.25 ±0.92	2.29 ±0.94	2.33 ±0.93	2.25 ±0.88	2.27 ±0.88	6.73 ±2.41	6.76 ±2.64

[a] Tests of each sensory function, and total scores, were significantly lower in leprosy patients than in controls ($p < 10^{-5}$). The differences between BL and BT groups, and between scores on the front and back of the fingers, were not significantly different.

differences in the blood-flow velocity among the individual digits in subjects in any of the groups.

Relationship between skin temperature and RBC flux. The mean values for the measurements in the hands of each patient are shown in The Figure. With one exception, the control subjects had warm fingers and high RBC fluxes; no reason was found for this subject differing from the other control subjects. In general, the BL patients had very cold fingers and low RBC fluxes, while the small number of BT patients occupied an intermediate position.

Table 2 summarizes the results of discriminant analysis of mean values of all the measurements on the fingers of the individual subjects for temperature and RBC flux. The combination of these two measurements is of potential value in discriminating between the three groups—controls, BL and BT leprosy patients. Additional analysis of the results of the individual fingers confirmed the clear discrimination among the groups, but did not improve the separation significantly.

Table 2 also summarizes a subsequent discriminant analysis on the pairs of observations to determine the extent of separation of healthy subjects from leprosy patients of either clinical type. There appears to be considerable diagnostic power in this combination of observations.

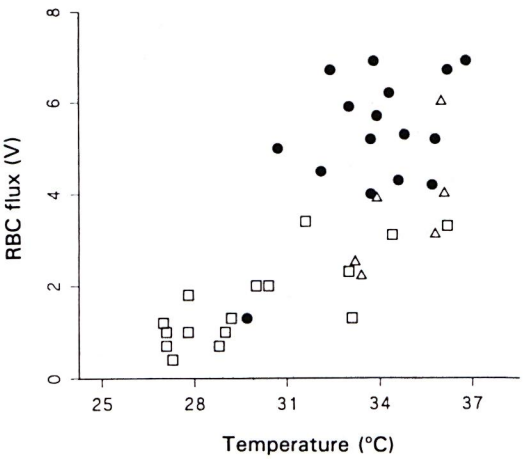
TABLE 2. *Summary of results of discriminant analysis to determine potential value of the combination of fingertip temperature and blood flow measurements in the classification of leprosy patients and for distinguishing them from apparently healthy controls.*

Separation of leprosy subgroups

Actual group	No.	Predicted group		
		Control	BT leprosy	BL leprosy
Control	16	12 (75%)	3	1
BT leprosy	6	1	5 (83%)	0
BL leprosy	16	0	4	12 (75%)

Combination of leprosy groups

Actual group	No.	Predicted group	
		Control	Leprosy
Control	16	14 (88%)	2 (12%)
Leprosy	22	1 (5%)	21 (95%)



THE FIGURE. Relationship between fingertip skin temperature and blood flow (RBC flux) in healthy controls (●), BT leprosy patients (△), and BL leprosy patients (□).

Relationship between sensory function and fingertip temperature and blood-flow measurements in leprosy patients. The patients without evidence of sensory impairment in any fingers (Group A, 3 BT and 1 BL) had high temperature and blood flow in their fingertips. Those with sensory impairment in all of their fingers (Group B, 1 BT and 5 BL) had significantly colder fingers and lower RBC flux than those in Group A ($p < 0.05$). The patients with sensory impairment in some, but not all, fingers (Group C, 2 BT and 10 BL) did not show statistically significant differences in either skin temperature or blood flow between the affected and unaffected fingers (Groups C1 and C2), but both temperature and RBC flux were significantly lower than those found in Group A ($p < 0.05$). Table 3 summarizes the results.

DISCUSSION

The skin of the fingertip has a major thermoregulatory role, and reflex adjustments of skin blood flow can have a large effect on body heat loss ([16]). Any tendency in healthy subjects toward elevation of core temperature (e.g., at high ambient temperature) promotes relaxation of sympathetic vasoconstrictor tone of the arteriovenous anastomoses in the deep dermis, inducing high blood flow in the fingertips ([7, 14]). The temperature of fingertip skin is strongly influenced by the opening and closing of these vessels although the relationship between skin surface temperature and the underlying blood flow is complex ([29]), especially when blood flow is estimated noninvasively by videophotometric methods ([23, 27]) or by laser Doppler flowmetry ([20]).

With a single exception, the healthy subjects in this investigation had skin temperatures greater than 31°C and high blood flow rates (4.0 V–7.0 V) at an ambient temperature of 26°C–29°C. These values were very similar to those obtained by laser Doppler flowmetry on healthy European subjects with centrally induced maximal vasodilatation ([17]). The exception was an apparently healthy leprosy control worker; no clinical explanation was found for the failure to demonstrate the usual heat adaptation response, but we have shown that healthy individuals frequently exposed to patients with

TABLE 3. *Relationship between extent of sensory impairment in the fingers of the leprosy patients and fingertip blood flow measurements.*

Group	No. subjects	No. fingers	Total sensory score (mean ± S.D.)	Temperature °C (mean ± S.D.)	RBC flux (mean ± S.D.)	No. (and %) fingers with sensory abnormality					
						Absent sensation			Impaired sensation		
						Temp.	Touch	Pressure	Temp.	Touch	Pressure
A Patients with no fingers impaired	4 (3BT, 1BL)	40	9	35.68[a] ±1.15	4.13[a] ±1.68	–	–	–	–	–	–
B Patients with all fingers impaired	6 (1BT, 5BL)	52	3.90[a] ±1.61	29.64[a] ±3.13	1.87 ±1.65	41 (78.8)	38 (73.1)	42 (80.8)	11 (21.2)	6 (11.5)	6 (11.5)
C Patients with some fingers impaired	12 (2BT, 10BL)	37 Impaired	5.16[b] ±2.05	30.24 ±2.52	1.52 ±0.98	16 (43.2)	20 (54.1)	19 (51.4)	18 (48.6)	6 (16.2)	5 (13.5)
		81 Unimpaired	9	31.43 ±3.36	1.96 ±1.47	–	–	–	–	–	–

[a] Significantly different from all other categories ($p < 0.05$).
[b] Mean sensory score for impaired fingers was significantly different from that of unimpaired fingers ($p < 0.05$).

active leprosy have a higher prevalence of impairment of the cold-induced vasomotor reflex than the unexposed population ([1]).

All six BT patients had fingertip skin temperatures appropriate to their environment (greater than 31°C), but five of these patients showed lower blood-flow velocities than the control subjects. Eleven of the BL patients had skin temperatures less than 31°C and all had slow fingertip blood flow; the remaining five BL patients had skin temperatures appropriate to their environment but their blood flow was low (1.5 V to 3.5 V). The leprosy patients reported in this study were all Indians, but we (Cree, Abbot, Larshmipati and Beck, unpublished observations) have recently shown that a Caucasian patient with long-standing BL leprosy living in Scotland had substantial reduction in fingertip blood flow when equilibrated in an environment-controlled room with an air temperature of 27°C. Accordingly, the phenomenon of cold fingers/low blood flow in leprosy patients is likely to be related to their disease and not to their race or living conditions.

There is strong histopathological evidence that, in some patients, leprosy can cause substantial damage to the larger blood vessels ([8, 11, 13]) and arteriographic studies have confirmed that there are important functional changes, such as impairment of blood flow in the terminal vascular loops ([24]), narrowing and constriction of the arteries of the lower limb ([9, 12]), and tapering tortuosity of the arteries of the hands ([2, 10, 30]). Venous involvement has also been reported ([4, 18]). These changes are most severe in patients with obvious clinical involvement of the fingers, especially progressing reabsorption, but they can be detected in some patients without clinical evidence of arterial disease or noticeable physical deformity ([28]).

The occurrence of slow blood flow and cold fingers could, therefore, be the result of an arteriopathy but since these features are strongly related to sensory impairment in individual leprosy patients, it is likely that such patients have substantial peripheral neuropathy. In a previous study of a large group of leprosy patients, the lowest fingertip blood-flow measurements were recorded in those with substantial neuropathy and/or orthopedic complications, but low flow was also observed in some newly registered patients with impairment of the vasomotor autonomic reflexes ([1]). It was also found that some patients with early leprosy had focal and selective impairment of vasomotor autonomic reflexes but relatively normal fingertip blood flow. This led us to infer that such impairment of the reflexes was the result of damage to the autonomic conduction pathways in the peripheral nerves rather than to the loss of vascular wall responses due to arteriopathy. Nevertheless, there is little doubt that arteriopathy plays a major role in the pathogenesis of cold fingers in patients with advanced disease. It is also possible that denervation hypersensitivity to catecholamines contributes to the peripheral circulatory abnormalities in leprosy patients.

Although cold fingers in environmental conditions requiring maximal vasodilatation for thermoregulation do not always occur in leprosy, the clinical sign is sufficiently frequent in the disease to suggest that there may be considerable value in feeling the patient's hands as a preliminary to clinical examination in any leprosy control clinic in the tropics.

SUMMARY

Under conditions of maximal thermoregulatory peripheral dilatation, most healthy subjects (both Indian and European) showed raised blood flow in the fingertips (measured by laser Doppler flowmetry) where the skin temperature is only slightly lower than the core body temperature. Most borderline lepromatous (BL) leprosy patients had much colder fingers and the blood flow was slow: borderline tuberculoid (BT) patients had skin temperatures similar to those seen in healthy subjects, but their fingertip blood flow was reduced relative to that in control subjects. The occurrence of cold fingers and slow blood flow was clearly associated with evidence of sensory impairment to light touch, pressure and temperature. Slower fingertip blood flow was strongly associated with impairment of vasomotor control in this anatomical region, suggesting that both may be a consequence of leprosy peripheral neuropathy, at least in patients with early leprosy, but it is likely that leprosy arteriopathy may contribute to the lowered periph-

eral perfusion in advanced cases. It is suggested that the simple clinical sign of cold fingers may be of value in the preliminary assessment of patients presenting at any leprosy control clinic in the tropics.

RESUMEN

Bajo condiciones de máxima dilatación periférica termoreguladora, la mayoría de los sujetos sanos (indúes y europeos) mostraron elevado flujo sanguíneo en la punta de los dedos (medido por flujometría laser de Doppler), donde la temperatura de la piel es sólo ligeramente más baja que la temperatura del resto del cuerpo. La mayoría de los pacientes con lepra subpolar (BL) tuvieron dedos mucho más fríos y lentas velocidades de flujo; los pacientes tuberculoides supolares (BT) tuvieron temperaturas dérmicas similares a las encontradas en los sujetos sanos pero sus velocidades de flujo sanguíneo estuvieron reducidas. La ocurrencia de dedos fríos y baja velocidad de flujo, estuvo claramente asociada con disminución sensorial al toque ligero, a la presión y a la temperatura. Las velocidades de flujo sanguíneo más lentas en las puntas de los dedos estuvieron fuertemente asociadas con alteración del control vasomotor en esta región anatómica, sugiriendo que ambas alteraciones podrían ser una consecuencia de la neuropatía leprosa periférica en los pacientes con lepra temprana, aunque es posible que la arteriopatía leprosa también pueda contribuír a la abatida perfusión periférica en los casos avanzados. Se sugiere que el simple signo clínico de dedos fríos puede ser de valor en la clasificación preliminar de los pacientes que se presentan en cualquier clínica de control de la lepra en las regiones tropicales.

RÉSUMÉ

Dans des conditions de dilatation périphérique maximale par thermorégulation, la majorité des personnes en bonne santé (aussi bien des Indiens que des Européens) a montré une augmentation du flux sanguin (mesuré par effet Doppler) dans le bout des doigts, où la température cutanée est seulement légèrement plus basse que la température interne. La majorité des patients atteints de lèpre borderline lépromateuse (BL) avait des doigts beaucoup plus froids, et la circulation sanguine était plus lente; les patients ayant une lèpre borderline tuberculoide (BT) avaient une température cutanée semblable à celle des individus en bonne santé, mais leur flux sanguin au bout des doigts était relativement réduit par rapport aux témoins. La présence de doigts plus froids et d'un flux sanguin ralenti était clairement associée à une détérioration de la sensibilité tactile légère, ainsi que de la sensibilité à la pression et à la température. Le ralentissement du flux sanguin au bout des doigts était clairement associé à une détérioration due controle vasomoteur dans cette région anatomique, suggérant que tous deux peuvent être la conséquence d'une neuropathie périphérique lépreuse, au moins chez les patients avec une lèpre débutante; il est cependant vraisemblable qu'une artériopathie lépreuse puisse contribuer à la diminution de la perfusion périphérique dans les cas avancés. La suggestion est faite que le signe clinique simple des doigts froids puisse avoir de la valeur dans l'examen préliminaire des patients se présentant à une consultation de lèpre sous les tropiques.

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