

Bacterial Density in the Skin in Lepromatous Leprosy as Related to Temperature

ROBERT C. HASTINGS, M.D.

Deputy Chief, Clinical Branch

PAUL W. BRAND, C.B.E., F.R.C.S.

Chief, Rehabilitation Branch

RICHARD E. MANSFIELD, M.D.

Chief, Laboratory Branch

JAMES D. EBNER

Occupational Therapist—Research, Rehabilitation Branch

U.S. Public Health Service Hospital, Carville, La.

To be read before the U.S. Public Health Service Clinical Society-Commissioned
Officers' Association Joint Meeting, March 26-29, 1968

INTRODUCTION

For many years observers^{1 2 3 4 5 6 7 11 12} have noted that the tissues most heavily involved in lepromatous leprosy are those expected to be relatively cool, whereas warmer areas of the body are relatively spared. Heavily involved areas include the anterior eye, upper respiratory mucosa, external ear—particularly the earlobes, and the extensor extremities, while the posterior eye, lower respiratory mucosa, internal ear, and flexor aspects of the extremities are relatively or completely spared from clinical involvement. The so-called 'immune areas' for lepromatous involvement, namely, the midline of the lumbar back, upper eyelids, perineum, axillae, and, to some extent, the antecubital and popliteal fossae are all areas in which skin temperature would be expected to be warm.

The present paper deals with an effort to demonstrate that at least one of the 'immune areas' in lepromatous leprosy is indeed warmer and furthermore contains fewer bacilli than a more heavily involved area.

MATERIAL AND METHODS

Five patients with diffuse lepromatous leprosy, as nearly 'pure' lepromatous, or LL in type⁹, as

could be determined by clinical, bacteriological and histopathological examination, were selected for study. Each was newly admitted to the U.S. Public Health Service Hospital, Carville, Louisiana, and had been on no anti-leprosy treatment for at least 4 years prior to admission.

Each patient was exposed to an ambient temperature of 19.5°C (67.1°F) for a period of 30 minutes, following which 3 thermographs (Model M-1A, Barnes Engineering Co., Stamford, Conn.*) were taken of his lumbar back. The exact skin temperature of each of 4 sites in the lumbar back was further determined with a hand-held radiometer (Medical thermometer Model MT-3, Barnes Engineering Co., Stamford, Conn.*) as an average of 3 readings. The 4 sites measured were determined as follows and marked with ink: the 2 lateral back locations were 5 cm. (2 inches) above the iliac crests, and 10 cm. (4 inches) from the midline. The midline locations were directly over the lumbar spine, 5 cm. (2 inches) and 15 cm. (6 inches) above a line joining the iliac crests.

Following the temperature measurements, the

* Manufacturer's name is for the purpose of identification only and is not meant to imply endorsement by the U.S. Public Health Service.

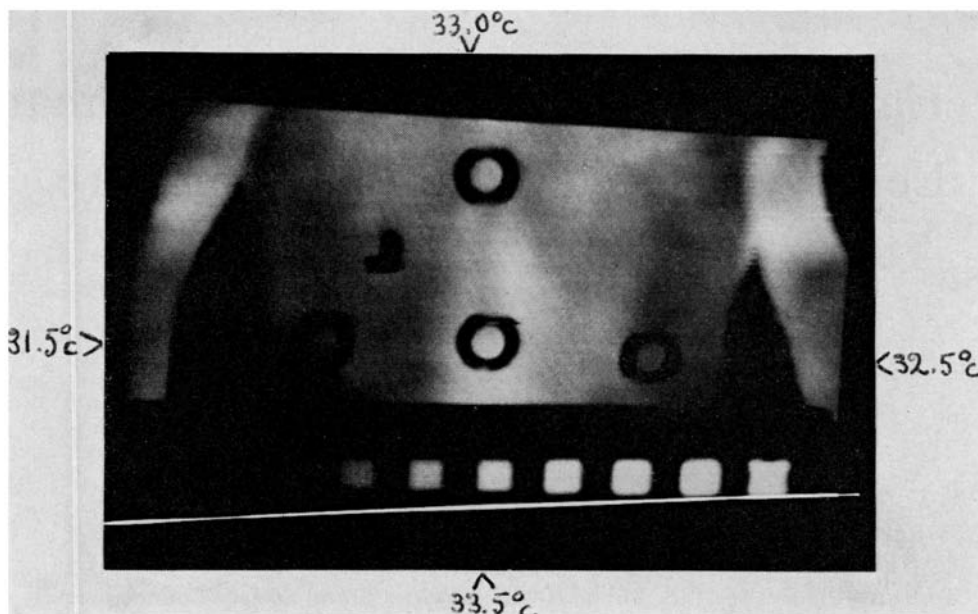


FIG. 1
 Patient 2802 — B—77.5 S—17.0
 14th April, 1967
 20.0°C 69-62

ink-marked sites were biopsied using 3 to 5 millimetre punch biopsies, taking care that each biopsy was taken perpendicular to the skin surface and extending well into the subcutaneous fat, insuring as far as possible that a full thickness of dermis was submitted.

Each specimen was routinely processed and submitted blindly to the pathologist (Dr. Mansfield) and read as to the (a) absolute thickness of the dermis in millimetres, (b) percentage of the dermis involved in lepromatous infiltrate, (c) bacterial index (B.I.), in terms of the Ridley logarithmic scale⁸, that is, 6+ equals to greater than 1,000 acid-fast bacilli per oil-immersion field; 5+ equals to 100 to 999 acid-fast bacilli per oil-immersion field; 4+ equals to 10 to 99 acid-fast bacilli per oil-immersion field; 3+ equals to 1 to 9 acid-fast bacilli per oil-immersion field; 2+ equals to 1 to 9 acid-fast bacilli per 10 oil-immersion fields; 1+ equals to 1 to 9 acid-fast

bacilli per 100 oil-immersion fields; 0 equals no acid-fast bacilli per 100 oil-immersion fields; and (d) morphological index (M.I.)^{13 14}, or the percentage of bacilli which stain uniformly on routine acid-fast staining. From this data a biopsy index⁸ was calculated for each biopsy as a product of the percent dermis involved and the bacterial index.

Results were analysed for significance by means of the t-test for paired measurements.

RESULTS

A characteristic thermograph was obtained in the lumbar back in each case, one of which is shown in Figure 1. The lighter coloured areas are warm, and the darker areas cool.

The exact skin temperature obtained for each of the 4 sites is given in Table 1.

The results of skin biopsies taken from each of the 4 sites are given in Table 2.

TABLE 1

Skin Temperature

<i>Left Lateral</i>		<i>Lower Midline</i>	
	31.33°C		33.83°C
	31.66		33.33
	31.50		34.41
	32.08		32.75
	33.50		33.00
Mean	32.01°C (89.62°F)	Mean	33.46°C (92.23°F)
<i>Right Lateral</i>		<i>Upper Midline</i>	
	31.66°C		34.00°C
	32.16		33.16
	32.41		33.75
	31.50		32.83
	32.66		33.50
Mean	32.08°C (89.74°F)	Mean	33.45°C (92.21°F)
<i>Mean of Left and Right Lateral Sites combined</i>		<i>Mean of Upper and Lower Midline combined</i>	
	32.05°C (89.69°F)		33.46°C (92.22°F)

DISCUSSION

The lumbar back was chosen for the present study because of the observed differences in clinical involvement between the midline and lateral aspects; and because this area represents a more or less uniform skin area, subject to similar degrees of protection by clothing, similar exposure to trauma, similar anatomical and physiological characteristics, etc. The sites selected were above the belt line to minimize any effect of habitually worn clothing.

The skin biopsies revealed a similar thickness of dermis in all sites; therefore the biopsy index⁸ is proportional to the actual number of *M. leprae* organisms present in each area. The outstanding difference in the sites is the warmer temperature of the midline sites (mean of 33.46°C.) compared with the lateral sites (mean of 32.05°C.). This difference is statistically significant with a p value of less than 0.01. As measures by the biopsy index⁸ the midline sites (mean of 0.88) have significantly fewer bacilli

TABLE 2

Results of Skin Biopsies

	<i>M.I.†</i>	<i>Thickness of Dermis</i>	<i>% Dermis Involved</i>	<i>B.I.‡</i>	<i>Biopsy Index</i>		<i>M.I.†</i>	<i>Thickness of Dermis</i>	<i>% Dermis Involved</i>	<i>B.I.‡</i>	<i>Biopsy Index</i>
<i>Left Lateral</i>						<i>Lower Midline</i>					
	0.6%	1.40 mm*	30%	4.5+	1.35		0.3%	1.79 mm	11%	4.0+	0.44
	0.4	4.16	42	5.0	2.10		0.5	2.19	9	4.5	0.41
	2.0	2.89	33	5.0	1.65		1.0	2.10	8.5	4.0	0.34
	5.0	4.81	50	4.8	2.40		3.0	3.11	30	4.6	1.38
	1.5	4.97	37	5.0	1.85		1.0	4.73	25	4.8	1.20
Mean	1.9%	3.65 mm	38.4%	4.86+	1.87		1.16%	2.78 mm	16.7%	4.38+	0.75
<i>Right Lateral</i>						<i>Upper Midline</i>					
	0.4%	1.31 mm*	33%	5.0+	1.65		0.4%	2.41 mm	23%	4.0+	0.92
	0.8	2.36	33	5.0	1.65		1.0	2.92	15	4.8	0.72
	1.5	2.54	36	5.0	1.80		0.8	2.80	13.5	4.5	0.61
	2.5	3.54	65	5.0	3.25		1.3	3.37	40	4.5	1.80
	1.5	4.29	35	4.5	1.58		2.0	4.46	22	4.5	0.99
Mean	1.34%	2.81 mm	40.4%	4.9+	1.99		1.1 %	3.19 mm	22.7%	4.46+	1.01
<i>Means of combined Lateral Sites</i>						<i>Means of combined Upper and Lower Midline Sites</i>					
	1.62%	3.23 mm	39.4%	4.88+	1.93		1.13%	2.99 mm	19.7%	4.42+	0.88

* Incomplete thickness of dermis submitted † Morphological index ‡ Bacterial index

than the lateral sites (mean of 1.93) with a p value of less than 0.01. This demonstrates that at least one of the clinically 'immune' areas of the body in lepromatous leprosy actually is warmer and contains quantitatively fewer bacilli than an adjacent 'non-immune' area. These observations correlate reasonably well with Shepard's finding for the optimum temperature for the growth of *M. leprae* in mouse foot pads of from 27 to 30°C.¹⁰ and his observations on the areas most heavily involved clinically¹¹.

The present findings seem to offer additional support for the concept that in lepromatous leprosy, in which there is presumably little if any ability to localize the infection, at least one of the major factors determining the distribution of the disease process in any given patient is the optimum temperature for the growth and multiplication of the bacilli.

SUMMARY

Five untreated patients with 'pure' lepromatous leprosy were studied by determining the skin temperature at 4 sites on the lumbar back, 2 in the midline and 2 laterally, followed by a skin biopsy in each area. The midline sites were significantly warmer and contained significantly fewer organisms than the cooler, more heavily infected lateral sites. It would appear that the clinically 'immune' areas in lepromatous leprosy represent warmer skin areas in which *M. leprae* would prefer not to grow.

ACKNOWLEDGEMENTS

The authors are indebted to Mr. Fredric E. Stockwell who performed the statistical analysis of the data, and to Miss Ruth Simoneaux who typed the manuscript.

REFERENCES

1. ANTIA, N. H., DIVEKAR, S. C. and DASTUR, D. K. The facial nerve in leprosy. I. Clinical and operative aspects. *Int. J. Lepr.*, **34**, 103-117, 1966.
2. BINFORD, C. H. Comprehensive program for inoculation of human leprosy into laboratory animals. *Public Health Reports*, **71**, 995-996, 1956.
3. BRAND, P. W. Temperature variation in leprosy deformity. *Int. J. Lepr.*, **27**, 1-7, 1959.
4. BRAND, P. W. Deformity in leprosy: Orthopedic principles and practical methods of relief. In *Leprosy in Theory and Practice*. Cochrane, R. G. and Davey, T. F., ed., Williams & Wilkins Co., Baltimore, 1964, p. 451.
5. CHOYCE, D. P. The eyes in leprosy. In *Leprosy in Theory and Practice*. Cochrane, R. G. and Davey, T. F., ed., Williams & Wilkins Co., Baltimore, 1964, p. 315.
6. DOULL, J. A. (Revised by Guinto, R. S. and Binford, C. H.) *Leprosy*. Veterans Administration Medical Bulletin MB-10. May 25, 1965, 14-15.
7. FRITSCHI, ERNEST P. The pattern of sensory loss in leprosy and its significance in the pathogenesis of leprotic neuritis. *Lep. Rev.*, **27**, 151-161, 1956.
8. RIDLEY, D. S. Therapeutic trials in leprosy using serial biopsies. *Lep. Rev.*, **29**, 45-52, 1958.
9. RIDLEY, D. S. and JOPLING, W. H. Classification of leprosy according to immunity, a five-group system. *Int. J. Lepr.*, **34**, 255-273, 1966.
10. SHEPARD, C. C. Temperature optimum of *M. leprae* in mice. *J. Bacteriol.*, **90**, 1271-1275, 1965.
11. SHEPARD, C. C. Stability of *M. leprae* and temperature optimum for growth. *Int. J. Lepr.*, **33** (3, Part II), 541-550, 1965.
12. SKINSNES, O. K. II. The immunological spectrum in leprosy. In *Leprosy in Theory and Practice*, Cochrane, R. G. and Davey, T. F., ed., Williams & Wilkins Co., Baltimore, 1964, 159-160.
13. WATERS, M. F. R. and REES, R. J. W. Changes in the morphology of *M. leprae* in patients under treatment. *Int. J. Lepr.*, **30**, 266-277, 1962.
14. WATERS, M. F. R., REES, R. J. W. and SUTHERLAND, I. Chemotherapeutic trials in leprosy. 5. A study of methods used in clinical trials in lepromatous leprosy. *Int. J. Lepr.*, **35**, 311-335, 1967.