

# Indian Journal of Dermatology, Venereology & Leprology

## CONTENTS

<p><b>Editor</b> Uday Khopkar</p> <p><b>Associate Editors</b> Ameet Valia Sangeeta Amladi</p> <p><b>EDITORIAL BOARD MEMBERS</b> Sandipan Dhar Sanjeev Handa H. R. Jerajani Sharad Mutalik C. M. Oberai M. Ramam D. A. Satish Rajeev Sharma Shruthakirti Sheno C. R. Srinivas D. M. Thappa S. L. Wadhwa</p> <p><b>Ex-officio Members</b> A. K. Bajaj S. Sacchidanand</p> <p><b>EDITORIAL OFFICE</b> <b>Dr. Uday Khopkar</b> Editor, IJDVL 2/7, Govt. Colony, Haji Ali, Mumbai-400034. E-mail: editor@ijdv.com</p> <p><b>PUBLISHED BY</b> <b>Medknow Publications</b> 12, Manisha Plaza, M. N. Road, Kurla (W), Mumbai-400070, India. Phone: 91-22-25032970 Fax: 91-22-25032398 E-mail: publishing@medknow.com Website: www.medknow.com</p> <p><b>Manuscript submission</b> www.journalonweb.com/ijdv</p> <p><b>Cover design courtesy</b> Sudler &amp; Hennessey</p>	<p><b>EDITORIAL</b></p> <p><b>PRESIDENTIAL ADDRESS</b></p> <p><b>REVIEW ARTICLE</b></p> <p><b>STUDIES</b></p> <p><b>CASE REPORTS</b></p>	<p><b>IJDVL at the crossroads</b></p> <p><b>A. K. Bajaj</b></p> <p><b>Serious cutaneous adverse drug reactions: Pathomechanisms and their implications to treatment</b> Arun C. Inamdar, Aparna Palit</p> <p><b>Diltiazem vs. nifedipine in chilblains: A clinical trial</b> A. K. Patra, A. L. Das, P. Ramadasan</p> <p><b>A comparative study of PUVASOL therapy in lichen planus</b> Lata Sharma, M. K. Mishra</p> <p><b>Utility of polymerase chain reaction as a diagnostic tool in cutaneous tuberculosis</b> Padmavathy L., Lakshmana Rao L., Veliath A. J.</p> <p><b>Therapeutic efficacy of intralesional triamcinolone acetonide versus intralesional triamcinolone acetonide plus lincomycin in the treatment of nodulocystic acne</b> B. B. Mahajan, Geeta Garg</p> <p><b>Ichthyosiform sarcoidosis following chemotherapy of Hodgkin's disease</b> M. P. S. Sawhney, Y. K. Sharma, V. Gera, S. Jetley</p> <p><b>Urticarial vasculitis in infancy</b> Sukhjot Kaur, Gurvinder P. Thami</p> <p><b>Koebner phenomenon in PLEVA</b> Arun C. Inamdar, Aparna Palit</p> <p><b>Familial acrogeria in a brother and sister</b> Shaikh Manzoor Ahmad, Imran Majeed</p> <p><b>Cornelia de Lange syndrome</b> K. Muhammed, B. Safia</p>	<p>_____ 203</p> <p>_____ 204</p> <p>_____ 205</p> <p>_____ 209</p> <p>_____ 212</p> <p>_____ 214</p> <p>_____ 217</p> <p>_____ 220</p> <p>_____ 223</p> <p>_____ 225</p> <p>_____ 227</p> <p>_____ 229</p>
----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

# Indian Journal of Dermatology, Venereology & Leprology

## CONTENTS (CONTD.)

The Indian Journal of Dermatology, Venereology and Leprology is a bimonthly publication of the Indian Association of Dermatologists, Venereologists and Leprologists and published by Medknow Publications.

The Journal is indexed/listed with Health and Wellness Research Center, Health Reference Center Academic, InfoTrac One File, Expanded Academic ASAP, NIWI, INIST, Uncover, JADE (Journal Article Database), IndMed, Indian Science Abstract's and PubList.

All the rights are reserved. Apart from any fair dealing for the purposes of research or private study, or criticism or review, no part of the publication can be reproduced, stored, or transmitted, in any form or by any means, without the prior permission of the Editor, Indian Journal of Dermatology, Venereology and Leprology.

The information and opinions presented in the Journal reflect the views of the authors and not of the Indian Journal of Dermatology, Venereology and Leprology or the Editorial Board or the Indian Association of Dermatologists, Venereologists and Leprologists. Publication does not constitute endorsement by the journal.

The Indian Journal of Dermatology, Venereology and Leprology and/or its publisher cannot be held responsible for errors or for any consequences arising from the use of the information contained in this journal. The appearance of advertising or product information in the various sections in the journal does not constitute an endorsement or approval by the journal and/or its publisher of the quality or value of the said product or of claims made for it by its manufacturer.

For advertisements, please contact the Editor

	<b>Intralesional steroid induced histological changes in the skin</b>	
	Sukhjot Kaur, Amanjeet, Gurvinder P. Thami, Harsh Mohan	232
	<b>Sparfloxacin induced toxic epidermal necrolysis</b>	
	M. Ramesh, G. Parthasarathi, B. Mohan, A. B. Harugeri	235
	<b>Fever due to levamisole</b>	
	Ramji Gupta, Sameer Gupta	237
	<b>Localized cutaneous sporotrichosis lasting for 10 years</b>	
	Sanjay K. Rathi, M. Ramam, C. Rajendran	239
<b>QUIZ</b>	S. V. Rakesh, D. M. Thappa	241
<b>RESIDENT'S PAGE</b>	<b>Sign of Nikolskiy &amp; related signs</b>	
	Deepa Sachdev	243
<b>RESEARCH METHODOLOGY</b>	<b>Declaration of Helsinki: The ethical cornerstone of human clinical research</b>	
	Gulrez Tyebkhan	245
<b>MEDICOLEGAL WINDOW</b>	<b>Drug eruptions and drug reactions</b>	
	Subodh P. Sirur	248
<b>LETTERS TO EDITOR</b>	<b>Aggravation of preexisting dermatosis with <i>Aloe vera</i></b>	250
	<b>Familial woolly hair in three generations</b>	250
	<b>Chronic pelvic inflammatory disease and melasma in women</b>	251
	<b>Comments on "Serological study for sexually transmitted diseases in patients attending STD clinics in Calcutta"</b>	252
<b>BOOK REVIEW</b>	<b>Colour atlas and synopsis of paediatric dermatology</b>	
	Sandipan Dhar	255
<b>ANNOUNCEMENTS</b>		255, 256,
<b>INSTRUCTIONS TO AUTHORS</b>		258

## Utility of polymerase chain reaction as a diagnostic tool in cutaneous tuberculosis

Padmavathy L.,\* Lakshmana Rao L.,\*\* Veliath A. J.\*\*

\*Division of Dermatology and STD, RMMC&H; and \*\*Division of Pathology, RMMC, Annamalai University, Annamalai Nagar-608002. Tamil Nadu, India.

Address for correspondence: Dr. L. Padmavathy, B3, RSA Complex, Annamalai University, Annamalai Nagar-608002. Tamil Nadu, India. E-mail: drellellar@yahoo.com

---

### ABSTRACT

**Background:** Differentiation of cutaneous tuberculosis from other infective granulomas of the skin is difficult due to paucity of the organisms in tissue biopsies. Polymerase chain reaction (PCR) is a newer technique to identify the DNA of *Mycobacterium tuberculosis* in the tissues. **Aim:** We examined the utility of PCR as a tool for rapid diagnosis of cutaneous tuberculosis especially in cases negative by ZN staining and culture. **Material and Methods:** Twenty five random skin biopsies from patients with various types of cutaneous tuberculosis were subjected to PCR. **Results:** An overall positivity of 64% was observed, which is comparable to other series. Seventy five percent of lupus vulgaris cases, 62.2% of tuberculosis verrucosa cutis and 50% of scrofuloderma cases showed PCR positivity. **Conclusion:** Though useful, the cost and the technique involved limit the use of PCR in developing countries like ours.

**KEY WORDS:** Cutaneous tuberculosis, PCR, Rapid diagnosis

### INTRODUCTION

Tuberculosis is common in India. Demonstration of organisms in skin biopsy specimens is often difficult due to the minimal bacillary load and also due to the attenuated state of the organisms. A variety of diagnostic tools are available for the study of these cases. Cultures have a higher sensitivity (about 80 to 90%) and may detect as few as 10-100 bacilli/ml. However, the delay of 3 to 6 weeks required for culture results currently limits their use in the diagnosis of tuberculosis. The powers of newer molecular diagnostic techniques like PCR permit detection of as little as one organism in a sample.<sup>1</sup>

DNA amplification by PCR is a rapid and sensitive method for detection of *M. tuberculosis* organisms in samples. Fewer than 10 microorganisms could be detected. Though precise estimation of the sensitivity is difficult, the primer directed amplification system

used is both highly sensitive (98%) and specific (100%) in the detection of *M. tuberculosis* complex DNA from clinical specimens.<sup>2-4</sup>

The study was done to find out the utility PCR in the diagnosis of cutaneous tuberculosis among the patients attending the dermatology department of RMMC hospital, located in Chidambaram, a taluka headquarters in South Arcot district, Tamil Nadu, catering to the needs of predominantly a rural population.

### MATERIAL AND METHODS

Skin biopsies of 25 randomly selected patients with clinical and histopathological diagnosis of various types of cutaneous tuberculosis, negative for AFB by culture and special stains, were included in the study. The formalin fixed skin biopsy specimens as well as tissues from the paraffin blocks were analyzed using the

standard procedure of polymerase chain reaction.<sup>5,6</sup>

## RESULTS

Out of the 25 patients with various types of cutaneous tuberculosis, 75% (6 out of 8 biopsy specimens) of lupus vulgaris, 62.2% (5 out of 9 biopsy specimens) of tuberculosis verrucosa cutis and 50% (3 out of 6 biopsy specimens) of scrofuloderma, showed PCR positivity. One case each of lichen scrofulosorum and erythema induratum submitted for PCR also tested positive, thus confirming their tuberculous etiology.

Cultures for *Mycobacterium tuberculosis* in these patients were negative. None of these patients showed any evidence of immunosuppression and all tested negative for HIV. All these patients responded well to antituberculous therapy and their lesions healed well.

## DISCUSSION

Diagnosis of tuberculosis depends on the demonstration of the organisms in the tissue or body fluids. However, the degree of bacillary load essential for this is usually seen in sputum positive cases of advanced tuberculous cavitory disease. Here the sensitivity of direct sputum examination is about 40 to 75%.

PCR results can be obtained within days, and a PCR based technique may facilitate the diagnosis of cutaneous tuberculosis.<sup>7</sup> Several anecdotal reports of the utility of PCR in the diagnosis of cutaneous tuberculosis are available. An early case of tuberculosis verrucosa cutis of only one-week duration was documented by employing PCR.<sup>1</sup> In another instance, tuberculosis complex DNA was detected in formalin fixed tissue by PCR in a PPD (tuberculin) negative patient with a chronic cutaneous lesion with histological features resembling sarcoidosis.<sup>8</sup> The lesion cleared with antituberculous therapy. *M. tuberculosis* DNA in skin biopsy specimens was demonstrated in another case of lupus vulgaris that had been followed for several years with frequent unrewarding biopsies and cultures.<sup>9</sup> The utility of PCR in the diagnosis of orificial tuberculosis with miliary spread,<sup>10</sup> erythema

induratum,<sup>11,12</sup> papulonecrotic tuberculid,<sup>13</sup> and other forms of cutaneous tuberculosis<sup>14-16</sup> has been reported from different parts of the world.

In our series, 75% of lupus vulgaris, 62.2% of tuberculosis verrucosa cutis and 50% of scrofuloderma cases, showed PCR positivity. One case each of lichen scrofulosorum and erythema induratum submitted for PCR also tested positive, thus confirming their tuberculous etiology.

All our patients responded well to standard antituberculous therapy and their lesions healed well. Since culture for AFB was negative in our patients, PCR results were correlated with histopathology and therapeutic response to standard antituberculous therapy. The overall PCR positivity of 64% (16 out of 25 cases tested) in our study is comparable to the results of other workers.

Although specific, the relatively low positivity rate of PCR in the common varieties of tuberculosis is of concern. Thus Tan et al concluded that PCR based detection of *M. tuberculosis* DNA in skin samples may extend and improve the diagnostic panel for cutaneous tuberculosis and may be also used to differentiate atypical mycobacterial infections in an immunocompromised patient with negative culture, if the technique is prudently and properly used. Moreover, PCR has not been found to be a useful complement to the clinical and histologic diagnosis of "paucibacillary" forms of cutaneous tuberculosis in their experience.<sup>17</sup>

There are other limitations to the use of PCR as well. It is a technically complex method that requires trained hands to perform the test. The inherent sensitivity of PCR amplification can lead to amplification of nonspecific sequences and contaminants. Greater care and meticulous technique are essential for a reliable PCR result.

PCR remains positive for periods far greater than the bacterial cultures. An important limiting factor is the inability of PCR to differentiate between the live and dead organisms which are likely to persist in inactive or treated cases. In view of this, PCR positivity does not necessarily indicate active disease.

The quality control, reproducibility of results and variations from laboratory to laboratory are still important issues to be sorted out. The cost of the PCR technique is another important limiting factor in employing this method in routine diagnosis.

#### ACKNOWLEDGEMENTS

The authors acknowledge Dr. K. Jagadeesan, Director, Dr. Sitha Lakshmi, Professor of Pathology, and the technical staff, K.J. Hospital, Chennai for extending the PCR facility, at concessional rate.

The authors thank all the colleagues for referring the cases, Medical Superintendent, RMMC&H, Annamalai University and Dean, Faculty of Medicine, Annamalai University for giving permission to carry out the work and to publish the article.

#### REFERENCES

1. Penney's NS, Leonardi CL, Cook S, et al. Identification of *Mycobacterium tuberculosis* DNA in five different types of cutaneous lesions by the polymerase chain reaction. Arch Dermatol 1993;129:1594-8.
2. Altamarino M, Kelly MT, Wong A, et al. Characterization of a DNA probe for the detection of *Mycobacterium tuberculosis* complex in clinical samples by polymerase chain reaction. J Clin Microbiol 1992;30:2173-6.
3. Hance Ad, Granchamp B, Levy-Fiebault V, et al. Detection and identification of mycobacteria by amplification of mycobacterial DNA. Molec Microbiol 1989;3:843-9.
4. Kox LF, Rheinthong D, Miranda AM, et al. Detection of *M. tuberculosis* in clinical samples. J Clin Microbiol 1994;32:672-8.
5. Kocagoz T, Yilmaz E, Ozkara S, et al. Detection of *Mycobacterium tuberculosis* in sputum samples by polymerase chain reaction using a simplified procedure. J Clin Microbiol 1993;31:1435-8.
6. Kadival GV, D'Souza CD, Kulkarni SP, et al. A highly specific polymerase chain reaction test for detection of *Mycobacterium tuberculosis*. Ind J Tub 1996;43:151-4.
7. Steidl M, Neubert U, Volkenandt M, et al. Lupus vulgaris confirmed by PCR. Br J Dermatol 1993;129:314-8.
8. Baselga E, Barnadas MA, Margall N, et al. Detection of *M. tuberculosis* complex DNA in a lesion resembling sarcoidosis. Clin Exp Dermatol 1996;21:235-8.
9. Serfling U, Penneys NS, Leonardi CL. Identification of *Mycobacterium tuberculosis* DNA in a case of lupus vulgaris. J Am Acad Dermatol 1993;28:318-22.
10. Nachbar F, Classen V, Nachbar T, et al. Orificial tuberculosis: detection by PCR. Br J Dermatol 1996;135:106-9.
11. Degitz K. Detection of mycobacterial DNA in the skin. Etiological insights and diagnostic perspectives. Arch Dermatol 1996;132:71-5.
12. Angela Y, Fearneyhough P, Rady P, et al. Erythema induratum of Bazin as a tuberculid: Confirmation of *Mycobacterium tuberculosis* DNA polymerase chain reaction analysis. J Am Acad Dermatol 1997;36:99-101.
13. Chuang YH, Kuo TT, Wang CM, et al. Simultaneous occurrence of papulonecrotic tuberculid and erythema induratum and the identification of *Mycobacterium tuberculosis* DNA by polymerase chain reaction. Br J Dermatol 1997;137:276-81.
14. Arora SK, Kumar B, Sehgal S. Development of polymerase chain reaction dot-blotting system for detecting cutaneous tuberculosis. Br J Dermatol 2000;142:72-6.
15. Hara K, Tazuzuki T, Takagi N, et al. Nodular granulomatous phlebitis of the skin - a fourth type of tuberculid. Histopathology 1997;30:129-34.
16. Margall N, Baselga E, Coll P, et al. Detection of *Mycobacterium tuberculosis* complex DNA by the polymerase chain reaction for the rapid diagnosis of cutaneous tuberculosis. Br J Dermatol 1996;135:231-6.
17. Tan SH, Tan BH, Goh CL, et al. Detection of *M. tuberculosis* DNA using PCR in cutaneous tuberculosis and tuberculides. Int J Dermatol 1999;38:122-7.