

## Reprinted Article

# Multiple Nasal Smears in Early Lepromatous Leprosy

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Multiple smears for *Myc. leprae* were taken at various sites in the noses of 100 patients suffering from lepromatous leprosy in its earlier stages, with the object of investigating (a) the parts of the nasal cavity most intensely involved in early lepromatous leprosy, and (b) the concentration of *Myc. leprae* at sites in the nose as compared with sites in the skin. From 4 to 10 sites were tested in each patient.

The results were profoundly influenced by previous chemotherapy. Among 58 untreated cases of early lepromatous leprosy, nasal infection was very important, but was concentrated on the inferior and middle turbinates and the septum at a depth of 6 cm rather than in the anterior septal area, which in this series was an unreliable guide to the bacteriological situation in the nose.

At the same time, the Bacterial Index at sites in the nose exceeded the Bacterial Index at the most heavily infected skin site tested in 50% out of 100 patients. In this series the nose was an important site of election for *Myc. leprae*. Nasal infection was not something which developed as the lepromatous condition advanced. It was both present and severe in the early stages.

### Introduction

In earlier years, the bacteriological examination of the nasal mucosa was regarded as a necessary part of the routine assessment of patients with leprosy. A method commonly adopted was to wipe the nasal cavity with a pledget of sterile cotton wool on a probe or thin stick, and smear the result on a slide. In the 1930's this method fell into disrepute on the grounds that smears could be contaminated with saprophytic acid-fast organisms. The method was replaced by the scraping of a small area of the mucosa under direct vision, usually on the nasal septum, with the object of transferring a fragment of mucosa onto the test slide, and so observe acid-fast bacilli *in* the mucosa rather than *on* the mucosa. This method of examination also fell out of fashion at many centres, on the grounds that while positive findings were usual in lepromatous leprosy, the information revealed could more easily have been obtained by routine examination of the skin by the scraped incision technique. As a result, interest in the nose in leprosy declined, the manifestations of leprosy in the nose often being regarded as secondary to its manifestations elsewhere.

When advising the scraping, as distinct from the wiping, of the nose, Muir (1938) suggested that either the nasal septum or the inferior turbinates could be employed. Subsequently, leprologists concentrated on the nasal septum, and for the past 30 years this has been the site usually selected. The method of examining the nasal septum has been described in detail by Wade (1935), Cochrane (1964), Browne (1965), Goodwin (1967), and Dharmendra (1967), who alone mentions the inferior turbinate as an alternative site when the septum is not convenient.

In the average adult, the surface area of the nasal cavity is approximately 100 cm<sup>2</sup> on each side. The technique of scraping with a small fairly sharp instrument means that one small area of approximately 1 cm<sup>2</sup> is examined. How valid is this method of sampling? We may indeed localize the area usually chosen still further. The choice of a scalpel (Wade), a straightened paper clip (Wade), a tenotomy knife (Cochrane) and similar instruments, limits the area available for examination to a site well in the anterior segment of the nasal septum, in practice around 3 cm from the nasal orifice. Dharmendra mentions ½ in from the orifice. The selection of this site is valid only if either (a) the nasal mucosa is invaded diffusely in leprosy, and therefore any readily available site will suffice, or (b) the anterior part of the septum is the site of election of the bacillus in the nose.

Two matters here are worthy of study, (a) the intensity of bacteriological involvement of the nasal mucosa as between one area and another, and (b) the intensity of bacteriological involvement of the nasal mucosa as compared with routine skin smears undertaken on the same occasion. Both subjects lend themselves to investigation by the simple procedure of taking multiple smears of the nasal mucosa at various sites, and comparing the results both directly, and with routine skin smears taken concurrently. The results of doing this on 100 patients are reported here.

### Method

Patients were selected from among those attending for the first time at the Victoria Hospital, Dichpalli, Andhra Pradesh, between July 1972 and January 1973. Advanced, and long treated cases of lepromatous leprosy were excluded, the choice being confined to patients with lepromatous leprosy in its early stages, and patients with indeterminate, dimorphous or borderline leprosy now showing signs of degeneration to the lepromatous condition. Children with small noses were not included. Patients were chosen consecutively and no other basis of selection was employed. The 100 patients included thus represented a fair picture of these types of leprosy as encountered in central India.

Routine skin smears were carried out at at least six sites. In addition, smears were made of the nasal mucosa as follows:

- (1) 4 sites. Septum at a depth of 3 cm from the nasal orifice, right and left sides. Inferior turbinates, anterior end, right and left. 45 patients.
- (2) 8 sites. As (1), with the addition of septum and inferior turbinates at a depth of 6 cm on each side. 41 patients.
- (3) 10 sites. As (2), but with the addition of the middle turbinate on each side. 14 patients.

It was usually possible to smear the septum and inferior turbinate in the anterior positions without difficulty. In 3 cases, septal perforations impinged on this area, and then the inferior margin of the perforation was used. In 6 cases gross swelling of the inferior turbinate obliterated the cavity at that level, and made access impossible to the posterior positions. In some cases atrophy of the anterior part of the inferior turbinate made this structure difficult to see, but did not prevent the examination. The middle turbinate was often also difficult of access.

In practice, Browne's suggestion of a piece of bicycle spoke as the essential instrument proved valuable. Beaten flat for 1 cm at one end to make a blade 2-3 mm wide and sharpened on one side only, its edge parallel with the stem, this instrument in a length of 15-20 cm could be employed with balance and delicacy. Marks on the stem at 3 cm and 6 cm from the blade end gave precision to the area being examined. No patient suffered any after-effects whatever from the use of this instrument. Further reference to technique is made later.

All nasal smears were examined by one of us (TFD), who also counter-checked many skin-smears. A very experienced technician read skin smears as routine and counter-checked many nasal smears. The margin for error is small. All smears were recorded on the logarithmic international scale (Maximum B.I. = 6.0). During the second half of the trial period, sulphone estimations were done as routine on the urine of patients. Clinical classification was confirmed histologically in 27 cases, and lepromin tests undertaken on the same number were negative in all.

## Results

### DIAGNOSTIC RELEVANCE

In this series, saprophytic acid-fast bacilli presented no problems. Two features in nasal smears enable *Myc. leprae* to be identified with confidence. The presence of globi characteristic of the multiplication of bacilli in macrophage cells is a certain indication of *Myc. leprae*. The only other acid-fast bacillus likely to cause confusion is *Myc. ulcerans*, and this has never been reported from the nose. The second feature is positive evidence of the ingestion of the bacilli concerned by macrophage cells, so that they are seen intracellularly, and beginning there to multiply in a characteristic way, so that the bacilli lie parallel with one another. In exceptional circumstances *Myc. tuberculosis* could be encountered in this situation but its intracellular appearances are different.

Across this series, the whole process of globus formation was witnessed with great clarity. Globi were encountered in nasal smears in 94 out of 100 patients. In a further 3 patients the early stages of ingestion by macrophages were clearly demonstrated. These three were borderline cases in an early stage of degeneration. In no case were acid-fast bacilli encountered, morphologically resembling *Myc. leprae*, and seen only extra-cellularly.

Heavy involvement in the nose was thus a characteristic feature of patients in this series, even though the lepromatous condition was clinically mild, and in 71 patients still in its early stages.

### BACTERIAL INDEX: COMPARISON BETWEEN NOSE AND SKIN

From the standpoint of the relative level of Bacterial Index as between the nasal mucosa and the most heavily infected skin site, patients could be divided into two groups.

*Group A:* In whom the highest B.I. found in the nose was not higher than the highest B.I. found in the skin. Forty-seven patients came into this category. In 30 of them the nose and skin were at the same level of B.I., in 10 cases the B.I. in the nose was 1 point lower than in skin, and in 7 cases it was lower by more than 1 point in the scale.

*Group B:* In whom the highest B.I. found in the nose was higher by 1 or more point in the scale than the highest B.I. simultaneously recorded in the skin. Fifty patients came into this category. A further 3 were added, because although B.I. in their noses came within the same range as the most heavily infected skin site, the Morphological Index in the nose was much higher than in skin. Throughout this group the Morphological Index in the nose tended to be higher than in skin, but in these three the difference was striking (Skin M.I. 0-5, nose M.I. 20-50).

The distribution of patients between Groups A and B in relation to leprosy classification and stage and also to chemotherapy with dapsone, was as follows:

TABLE 1  
*Leprosy classification and treatment*

Leprosy type	Total patients	Group A		Group B	
		(Nose not more bacilli ferous than skin)	Dapsone taken	(Nose more bacilli ferous than skin)	Dapsone taken
Borderline	7	5	(3)	2	
Early lepromatous (LL)	20	8	(2)	12	(1)
Early lepromatous (L1, LB)	51	18	(10)	33	
Established lepromatous (LL, L1, LB)	22	16	(8)	6	(1)
	100	47		53	

Although the same pattern can be discerned in both Groups, interest centres on Group B because here the situation is not confused by sulphone treatment to an appreciable extent, and the proportion of early cases is higher. The following points arise:

(i) Group A includes 23 out of 25 patients who either admitted to having taken dapsone treatment or whose urine gave a positive reaction to sulphones. It is well-known that dapsone acts speedily on leprosy in the nose, and this was therefore a predictable finding.

(ii) Group A also includes a much higher proportion of the more advanced established lepromatous cases than Group B. This is also not surprising.

(iii) In 11 out of 53 patients in Group B (21%) the Bacterial Index at one or more sites in the nose was at least 2 points higher in the international scale than the highest findings in skin smears, i.e. at those sites the nasal infection was around 100 times as intense as encountered in the skin. This figure is in fact a conservative one. In a further 11 patients in whom the highest B.I. recorded in the skin was 5.0, there was at least one site in the nose, where the smear revealed

huge numbers of globi, far more than were needed to give a B.I. of 6.0. The international scale has no place for such gross infections.

(iv) In two patients with negative skin smears, a bacilliferous focus with B.I. of 6.0 was found at one site in the nose, in both cases on the left inferior turbinate. Both were dimorphous cases in the earliest stages of degeneration, and thus in a very unstable condition. It is thus not true that bacteriologically positive findings cannot be obtained in the nose in the absence of positive findings in the skin. Dharmendra and Sen (1946) reported such a case with globi in the nose but negative skin smears. What matters is where one looks for the bacilli.

(v) The overall picture is given in Table 2, which relates to Group B only (53 patients).

TABLE 2  
*Bacterial Index in nasal and skin smears*

Site	Total tests	6.0	5.0	4.0	3.0	2.0	1.0	Negative
Septum anterior	104	32	31	12	3	8	4	14
Septum posterior	42	14	12	6	2	1	2	5
Inf. turbinate ant.	104	46	32	11	4	2	5	4
Inf. turbinate post.	41	12	5	3	1	1	2	6
Middle turbinate	20	6	7	3	0	1	0	3
Ear lobes	106	19	58	9	10	0	4	6
Arm/back	106	9	61	12	6	7	6	15
Thigh/buttock	86	8	58	3	0	5	1	11
Face	23	6	13	4	0	0	0	0

It is obvious from these figures that the intensity of bacilli in the nose was frequently greater than in the most heavily involved skin sites (ear lobes and face), and much higher than at other sites in the skin.

## SITES OF HEAVIEST INVOLVEMENT IN THE NOSE

### (i) *Comparison between the two sides of the nose*

Although in individual patients there was a decided difference in involvement between one side of the nose and the other, over the group as a whole these differences largely cancelled each other out, and it was impossible to detect any general tendency for one side of the nose to be involved more than the other. The left inferior turbinate was in fact involved most frequently and intensely, but this was largely compensated by the heavier involvement of the right side of the septum as compared with the left.

### (ii) *Comparison between inferior turbinates and nasal septum*

In this series the inferior turbinates were more frequently and seriously involved than the nasal septum, and this feature is particularly noticeable in the anterior positions at a depth of about 3 cm from the nasal orifice. This finding does not accord with generally accepted ideas. Its practical importance can readily be demonstrated.

If a single smear of the nasal septum had been undertaken as routine in these patients, the chances that it would have included the most heavily involved site were 8 out of 53. (In these 8 patients, both sides of the septum were equally involved with a B.I. of 6.0, also found simultaneously in the inferior turbinates.) The smearing of both sides of the septum would have yielded a true sample in 28 cases (53%), leaving 25 cases (47%) in whom smears of the anterior septum would not have given a true picture of the situation.

The inferior turbinates give a better result. A single smear of the anterior end of one inferior turbinate would have given a true picture of the whole in 15 cases (18%). The smearing of both inferior turbinates would have yielded a correct result in 41 cases (80%).

A combination of the two, i.e. the smearing of both anterior septum and inferior turbinate on both sides would have yielded a true index in 47 cases (90%).

(iii) It is also noticeable from Table 2 that at a depth of 6 cm from the nasal orifice, involvement was frequently heavy on both septum and inferior turbinate. In most cases this was part of a broader area of heavy involvement in the structure concerned, the anterior parts also being implicated, but in 6 patients (11%) the nasal infection was concentrated on these deeper levels only, and anterior smears would not have revealed it in its full intensity.

#### (iv) *Middle turbinates*

In the small group of patients tested, the middle turbinates were also an important focus of involvement by *Myco. leprae*.

## DISCUSSION

(1) The origins of this study go back to 1971, when Dr J. C. Pedley drew the attention of one of us (TFD) to the very large number of *Myco. leprae* being discharged from the noses of some of his patients in Nepal. Experience has shown that the same situation exists in central India. This study is an introduction to a much wider investigation of the role of the nose in leprosy which is now in progress.

(2) Two significant findings arose out of this study. The first is the association between early lepromatous leprosy and a very heavy involvement of the nose by *Myco. leprae*. This is not a generally recognised phenomenon. Involvement of the nose has of course been accepted as a feature of lepromatous leprosy for almost 100 years, but for a long time it has been thought that the nasal infection developed proportionately with the general advance of the lepromatous condition elsewhere in the body. In this series, 45 out of 58 untreated cases of early lepromatous leprosy were found to have concentrations of *Myco. leprae* in their nasal mucosa between 10 and 100 times as heavy as could be found at any skin site. This is a matter of importance because the bacilli do not simply remain in the nasal mucosa. Many escape in the nasal discharge.

(3) Is this a peculiarity of leprosy in central India, or has it a wider relevance? Certainly in the experience of one of us (TFD) in Nigeria, nothing comparable was found, though the type of study here described was never undertaken there. If the relative prevalence of the different types of leprosy is any guide, there certainly is a difference in genetic and immunological background between Nigeria and central India. Here, the dominant presentation of leprosy is the

unstable, indeterminate, dimorphous or borderline forms of the disease, the degeneration of which to the lepromatous form is a frequent occurrence, and often manifests itself first in the ears and face. The nose too may be important at this stage. Twelve patients in this series, all of whom had recently experienced a downgrading exacerbation of their disease, firmly related the onset of this to their noses, in the shape of blocking of the nostril and bleeding. This opinion was volunteered, not elicited by direct questioning.

(4) The second interesting finding was the variation between one part of the nasal cavity and another in the frequency and intensity of invasion by *Mycobacterium leprae*. The anterior portion of the nasal septum was the area least likely to offer a fair sample of the bacteriological situation in the nose. The inferior turbinates gave a decidedly better picture. At a depth of 6 cm from the nasal orifice, both septum and inferior turbinates were also frequently and heavily involved, while the middle turbinates were also important in the small group of patients in whom they were tested. In this part of India, nasal smears from the anterior septal area could give rise to highly misleading judgments regarding the role of the nose in leprosy.

(5) Is this another finding of local interest only, or are we here too confronted with something of wider importance? In the latter case, the implications are considerable. In established lepromatous leprosy, a more or less uniform involvement of the nasal mucosa is to be expected. Dutz, Chen and Wen-Hsiang (1972) have drawn attention to the continuous bacillaemia which is inseparable from established lepromatous leprosy. It means that every tissue is continuously exposed to the bacillus, and the nasal mucosa, with its rich blood supply can be no exception. The finding of intense concentrations of the bacillus in nasal smears in the early stages of the disease must have meaning. Does it signify that the infection started there, or that bacilli grow there more vigorously than in skin, or that they are selectively filtered from the blood at this site? These are pregnant questions, to which nasal smears by themselves can provide no answer. They are a pointer to underlying pathological processes which are as yet insufficiently understood. The coming together of Bacteriologists, Immunologists, Ear, Nose and Throat specialists, and Leprologists in joint studies will alone find the answers.

(6) The practical question immediately presents itself as to how far nasal smears should be undertaken by leprosy workers as routine, especially in field conditions. There can be no doubt that nasal smears, especially if both septum and inferior turbinates are included, will sometimes give an indication of the severity of an early lepromatous infection in a way that skin smears will not reveal. On the other hand, in unskilled hands, more harm than good may be done to the patient. Certainly whoever undertakes this type of examination must be conversant with the internal anatomy of the nose, and be able to recognise a pathological situation when he sees it.

A few further notes on technique may not be out of place.

All the tests in this series were undertaken by the light of a good but ordinary torch, held by an assistant standing immediately behind the examiner, himself seated close to, and on the same level as, the patient. A preliminary inspection of each nasal cavity is necessary, with the nasal orifice dilated by a speculum, and the examiner himself using the torch to illuminate the different parts of the cavity. Before undertaking the actual smears, the area of mucosa to be examined must be seen to be clear from adherent crusts. In the dry climate of central India hard adherent crusting is frequently encountered, and must be removed. Easily

the best way of doing this is for the nose to be irrigated with warm normal saline, when the patient can usually blow out the softened crusts himself. Gentleness in the examination is essential. The mucosa in many patients is very friable and liable to bleed. After a preliminary wipe with a sterile pledget of cotton wool, the instrument, sterilized by flaming immediately before use, is introduced under direct vision with its blade downwards, and then rotated through 90 degrees when the site to be examined is reached. A gentle scrape up and down a few times is quite enough to obtain the tiny fragments of mucosa and accompanying exudate needed. A faint trace of blood is a certain indication that these objectives have been achieved. A smear on a carefully labelled slide is then made immediately. This technique is easily learned, and if reserved for patients whose nasal cavities show abnormality, and whose leprosy is towards the lepromatous side of the spectrum, will have a positive usefulness.

(7) If this study induces colleagues in India and elsewhere to look once again into the noses of their patients and question the meaning of what they see there, its primary purpose will have been achieved. To our patients the nose is supremely important, for the threat of disfigurement of the nose lies behind much of the anxiety and depression to which people with lepromatous leprosy are prone. Clinical examination of the nasal cavities is an essential part of the assessment of any patient with overt or incipient lepromatous leprosy, and will often destroy any illusions the examiner may have regarding the extent of the disease in that patient. It is then and in the subsequent follow-up that nasal smears are of practical value.

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