Lepromatous Leprosy in the Nose After One Year of Dapsone Treatment: Clinical and Bacteriological Findings

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In 1972/73 a series of patients with early untreated lepromatous leprosy in South India were studied and the clinical, bacteriological and histopathological findings in the nose have been reported. The involvement of nasal tissues and the enormous numbers of viable bacilli escaping from the nose into the environment were of such clinical and epidemiological importance that it was clearly essential to repeat the studies after a period of standard out-patient chemotherapy with dapsone. This paper describes the clinical and bacteriological findings in 16 patients out of the original group of 34, who could be contacted after one year. Attention is drawn to the fact that although almost all patients showed marked improvement on clinical and nasal examination, in a significant percentage solid-staining Mycobacterium leprae could be demonstrated particularly in scrapings and biopsies of the nasal mucosa, and also in mucus of nose-blow specimens. It is considered that the findings in patients who failed to attend would almost certainly be worse and the problem of ensuring a high follow-up rate is discussed. Four patients in this series who had bacteriological evidence of persisting infectivity after a year of dapsone showed no definite abnormality on simple clinical examination of the nose, and while this is an extremely important part of the initial assessment and diagnosis in suspected lepromatous leprosy, its value is less in the follow-up of patients on treatment as it is often uninformative and may even be misleading. Careful bacteriological examination of the nasal mucus and nasal smears is of as great importance as the information obtained from routine slit-skin smears.

Introduction

During a 3 month period in the winter of 1972/73 a series of patients with early lepromatous leprosy was studied intensively at Victoria Hospital, Dichpalli in South India. The initial results of these studies were presented at the Tenth International Leprosy Congress at Bergen (Barton *et al.*, 1973) and subsequently, detailed accounts of the clinical findings (Barton, 1974), bacteriology (Davey and

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Barton, 1973; Davey and Rees, 1974) and histology (McDougall *et al.*, 1975) have been published. From these studies the nose has been confirmed both as a site of predilection for *Mycobacterium leprae* and also as the most potent source of exit of viable bacilli from the body, emphasizing the importance of patients with untreated lepromatous leprosy in the transmission of this disease within the community. Early cases are particularly dangerous in this respect as the nose may be heavily involved before the general clinical signs become obvious.

It was therefore considered essential to obtain follow-up data in order to assess the detailed response of individual patients to treatment and additionally to evaluate the continuing risk, if any, posed by these patients to the community. Therefore, although this paper is concerned primarily with the results of chemotherapy in lepromatous leprosy, the problem of persuading patients to accept adequate treatment will also be discussed.

Material

In the original series 34 patients with early lepromatous leprosy had the following investigations: clinical and nasal examination, lepromin test, routine multiple slit-skin smears, multiple nasal smears, bacteriological examination of the nasal discharge and biopsy of the nasal mucosa at several sites and of the skin. Intranasal and clinical photographs were taken in most cases although in some patients it was not possible to carry out every investigation. When the work-up on each patient was completed treatment was commenced with dapsone, rising by monthly increments from an initial dosage of 15 mg a week in divided doses to reach 300 mg in the fifth and subsequent months. Patients were normally admitted at the start of treatment and the mean length of inpatient stay was 3.3 months, ranging from nil to 12 months, as some patients refused admission while others were reluctant to leave the hospital.

One patient had died and one was a schoolboy who had stayed in the hospital's school hostel. The remaining 32 were therefore out-patients at the time of this follow-up study which took place over a period of 4 weeks in early 1974. These patients were sent letters in their own languages asking them to attend the hospital between certain dates, but when it became clear that the initial response was poor, members of staff were sent to the last known address of the non-attenders to attempt to trace them and to invite further attendance.

Sixteen patients attended for follow-up and a further 3 were known to be taking dapsone regularly but had adequate and acceptable reasons for not attending specifically for this study. Thus only 56% of the original group appeared to be in contact with the hospital between 12 and 15 months after their initial attendance.

The majority of those who attended for follow-up were prepared to stay for only 24-48 h and thus investigations had to be somewhat limited compared with those at the initial attendance. In particular, it was thought important to obtain biopsies of the nasal mucosa in preference to nasal smears. However, nasal and skin biopsies were obtained from 14 patients, nasal smears from 6, the nasal discharge was analysed in 15, and all 16 patients had routine slit-skin smears with full clinical and nasal examination.

Results

REGULARITY OF TREATMENT

Thirteen of the 16 patients (81%) appeared to have taken dapsone regularly in the prescribed dosage over the course of the year. Since discharge the other 3 had probably taken 6 months supply of dapsone in 9, 10 and 12 months respectively. Thus no patients who attended for follow-up had received less than a total of 6 months treatment subsequent to their first attendance.

SYMPTOMS

All the patients noted improvement in both general health and in nasal symptoms. General symptoms amounted to no more than occasional tingling sensations in the extremities together with some dryness of the hands and feet.

Eleven patients (69%) still had some symptoms from the nose, the most common of which was crust formation. As this study was conducted in the "dry" season this finding was not altogether surprising. However, in all patients who reported persistent nasal symptoms, they were slight compared with the situation that existed prior to treatment, when in all 16 patients they had been severe and often distressing.

Table 1 summarizes the incidence of nasal symptoms.

 TABLE 1

 Summary of the nasal symptoms in 16 patients with lepromatous leprosy, initially and after one year of dapsone treatment

	Crust formation	Bleeding	Obstruction	No symptoms
Before treatment	11	10	10	0
After one year of dapsone	9	5	3	5

CLINICAL AND NASAL EXAMINATION

As might have been predicted, the patients who did return for follow-up purposes were those who had taken dapsone on a regular, or reasonably effective, basis and were likely to be doing well. This was indeed so, and all 16 patients were generally fit and healthy. Fourteen out of the 15 adults were at work and there was no medical reason preventing the one unemployed man from pursuing his trade. The 16th patient was a bright and active member of his school.

General examination showed a regression of physical signs, and no new problems were noted although one patient suffered transient ENL. Typical clinical improvement is shown in Figs 1 and 2. As the patients were all selected as having early lepromatous leprosy, the improvement in systemic signs, which were often only slight originally, was overshadowed by an impressive improvement in the nasal state. Originally the nose was involved, often heavily, in all 16 of these patients: a typical finding is illustrated in Fig. 3. After a period of 12-15 months treatment the nasal state had improved in all patients and indeed in 12 (75%) the nose was passed as normal on clinical examination. The criteria to be fulfulled before a nose could be accepted as normal, in this instance, were that there should



Fig. 1. Typical clinical finding prior to treatment.



Fig. 2. Typical clinical finding after one year of dapsone.



Fig. 3. Typical intranasal finding prior to treatment.



Fig. 4. Typical intranasal finding after one year of dapsone.

be no mucosal lesion detectable on anterior or posterior rhinoscopy, that the airways should be patent and that there should be no destruction of bone or cartilage. Slight reduction in the size of the anterior part of the inferior turbinate, provided that the mucosa was otherwise normal, was allowed, despite the fact that this physical sign is typical, though not pathognomonic, of lepromatous infiltration which has undergone resolution.

Figure 4 illustrates the effect on the nasal mucosa of one year of chemotherapy in a typical case. Four of the 16 patients, although improved, could not be passed as having a normal nose, although in only one was there thought to be definite activity clinically. These patients were:

Case B4. Possible remaining infiltration of the anterior end of the left inferior turbinate. Multiple nasal smears gave an average Bacteriological Index (BI) of 1.2 with a Morphological Index (MI) of zero. The nasal biopsies showed no evidence of solid-staining organisms.

Case B7. There appeared to be definite evidence of remaining lepromatous infiltration, and biopsies confirmed the presence of solid staining organisms in the nasal mucosa, although the nasal discharge had a zero MI (BI 2).

Case B9. An old, and previously noted, septal perforation was present, thus precluding a "normal" classification. However, the nasal mucosa was otherwise healthy and there was no bacteriological or histological evidence of active infection.

Case B21. A moderate degree of atrophic rhinitis, not otherwise encountered in this follow-up series, was present. Biopsies showed no solid-staining organisms.

BACTERIOLOGY

(a) The nasal discharge. The mucus and secretions of the nose were collected as an early morning "nose-blow" specimen and examined for acid-fast bacilli in the routine manner. One patient, who could spend only 8 h at the hospital, produced no specimen. Of the remaining 15, 10 had negative specimens. Three patients each had a BI of 2 and an MI of zero, while in 2 (patients B13 and B22) the MI was positive and the bacteriology of these patients is shown in detail in Table 2. Nasal biopsies confirmed the presence of solid-staining organisms in patient B13 but not in patient B22.

(b) Multiple nasal smears. The technique for this investigation is described in detail elsewhere (Davey and Barton, 1973). Briefly, the nasal mucosa is gently

Patient	Specimen	Before treatment		After one year of dapsone	
		BI	MI	BI	MI
B13	Skin	4.8	2.8	4.5	0.6
	Nasal discharge	5	4	2	0-2
	Nasal smear	4.1	6.5	2	0.3
B22	Skin	5.3	2.8	4.1	0.8
	Nasal discharge	1	•	3.3	0.2
	Nasal smear	4.8	8	1.2	0.1

 TABLE 2

 The bacteriology of patients B13 and B22

* No proper specimen obtained.

scraped with the sharpened, flattened end of a bicycle wheel spoke (Browne, 1965) and thus the specimen produced includes the superficial cells of the surface epithelium. Several sites in the nose should be examined and it is the anterior end of the inferior turbinate, and not the septum, which is most likely to yield a positive result. In addition to the 2 patients with potentially viable bacilli in the nasal discharge a further 2 (B.1 and B34), showed a positive MI on nasal smears. Their figures were BI 0.8/MI 0.1 and 1.5/0.1 respectively. Unfortunately these were the only patients in the follow-up series who did not have nasal biopsies taken, and thus their histological status is unknown. However, it is interesting to note that the nasal discharge in both these patients had a zero MI. The significance of this observation will be discussed below. Prior to treatment the nasal smears for the group had an average BI of 4.5 and MI of 5.9.

(c) *Skin smears.* The average figure for the group prior to treatment was BI 4.4, MI 2.4 and on follow-up these figures had fallen to 3.8 and 0.4. In 5 patients, after treatment, the MI was zero and in the remaining 11 it was 1 or less.

Discussion

Only 19 (56%) of the original 34 patients were known to be in contact with the hospital and receiving dapsone regularly between 12 and 15 months after their initial attendance. One patient had died, thus giving a total default rate of 14 out of 34 (41%). This is in line with those from several series reviewed recently by Davey (1974). A high default rate is not, incidentally, a problem peculiar to leprosy, for Booth (1972) noted default rates of 50% and 55% in 2 follow-up surveys of patients in London who had undergone elective ear surgery. However, it is a matter of great concern that so many patients with highly infectious lepromatous leprosy who have attended a hospital, well known for its sympathetic care and consideration, should fail to return for continuing treatment. Although the problem of travelling considerable distances in rural India is involved, the implication is that these patients, after initial improvement as evidenced by those who did return for follow-up, lack the understanding and motivation to return for further supplies of dapsone. Inevitably after cessation of a 3-6 month course of treatment, relapse and the capacity to infect others will recur. Further efforts to ensure the highest possible follow-up rate are thus obviously called for.*

We have reported elsewhere (Barton *et al.*, 1973) that intranasal pathology early in the disease is frequently quite out of proportion to what might be expected from a general examination of the patient. It is gratifying now to be able to report the considerable clinical regression of the nasal component of the infection after this period of treatment and also improvement in the general state of the patients. Although the nose appeared normal in 12 out of 16 patients (75%), 11 (69%) still had some symptoms, albeit mild, from the nose and the fact that 5 (31%) still had occasional bleeding suggests a potential, though possibly transient, breach in the integrity of the nasal mucosa. Under these circumstances and in the presence of persistent viable bacilli in the submucosa it is possible that a patient may retain the ability to infect others despite an apparently normal nose with satisfactory skin smears and even an MI of zero for the "nose blow", as in patients B1 and B34. Davey and Rees (1974) have demonstrated "the extraordinary sensitivity of *Myco. leprae* in the nose to even small doses of dapsone within a few weeks". However, 4 patients (25%) in this series still had solid staining bacilli in either the nasal mucus or in the superficial layers of the nasal mucosa after a minimum of 12 months regular dapsone. It would clearly be wrong to label these patients "non-infectious" despite the enormous clinical improvement. It is important to note that in none of these 4 patients was the clinical appearance of the nose pathognomonic of leprosy, nor even suggestive of persistent activity following earlier lepromatous infection. It is of interest that the one patient (B7) in this series in whom the nasal mucosa did show definite remaining infiltration clinically and who had solid-staining organisms in the nasal biopsies, had no solid-staining bacilli in the nasal mucus at the time of examination.

Three patients who had received regular dapsone for periods of 2, 5 and 8 years were investigated similarly to the main follow-up group and, though the numbers are too small to be statistically significant, it is interesting to note that no clinical, bacteriological or histological activity was detected in the noses of these patients.

From these observations it would appear that the majority of patients with early lepromatous leprosy will be clinically well, with marked regression of nasal and skin infiltration, when treated with adequate amounts of dapsone for 12-15 months. Although it has generally been thought that the majority of such cases will be no longer capable of transmitting the disease provided that treatment is continued, the present study indicates that a percentage of such patients may remain potentially infectious; this amounted to 25% in those patients who actually attended for follow-up and would surely have been greater amongst the non-attenders. Therefore, the bacteriology of the nasal smears and discharge is clearly as important as the routine skin bacteriology and should become a standard diagnostic and follow-up investigation in lepromatous leprosy. Furthermore, these tests should ideally be repeated each time that the patient is seen, as it is quite probable that the nasal discharge of a patient such as B7, mentioned above, may have been positive on another occasion. The case for routine nasal examination as a diagnostic procedure has been argued elsewhere (Barton, 1974), but as a follow-up investigation it assumes less importance, for it may well be uninformative and even be misleading; the 4 patients in this series who had bacteriological evidence of persisting infectivity showed no definite intranasal abnormality on simple clinical examination.

* The one year follow-up rate for patients outside this special research group at Victoria Hospital has been around 70%. One of us (LMH) feels that a possible reason for the low follow-up rate in the group reported here is fear of undergoing again the original extensive investigations.

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