# Editorial

## HOW DO LEPROSY BACILLI LEAVE THE BODY?

This apparently simple question, which puzzled clinicians before Hansen raised it again at the Second International Leprosy Congress in Bergen in 1909, is today being asked in the field and in the laboratory. In this issue of *Leprosy Review* McDougall and Rees remind us of some half-forgotten evidence that the discharge from proximal ulcers in the skin of patients suffering from active lepromatous leprosy—perhaps in a state of tissue hyper-sensitivity, like the erythema nodosum necrotisans of the Lucio phenomenon—may contain vast numbers of morphologically normal bacilli. And Pedley, in the immediately preceding issue (*Leprosy Review* **44**(1), 33), after further painstaking investigations, suggested that the principal portal of exit of *Myco. leprae* is the nasal mucosa of patients suffering from lepromatous or near-lepromatous leprosy. He had earlier demonstrated that the only skin surfaces on which acid-fast organisms could ordinarily be found in leprosy sufferers were those near the nose or those likely to be contaminated by inspissated nasal secretion transferred from the perinasal skin.

Many workers over the years have found, by standard procedures or by concentration techniques, acid-fast organisms on the surface of the skin and in the dermis of subjects in contact with leprosy patients. The identification of the organisms and the significance of the findings are both matters of discussion and dispute. (This is quite apart from the occasional presence of an acid-fast organism that the patient histopathologist may find deposited from tap-water on the surface of a section.)

The subject is of far more than merely academic interest.

Knowledge of the common sites of exit of viable leprosy bacilli will resolve many thorny questions of transmission. It will determine attitudes to contagion and prevention; and it will provide another important piece for the jigsaw puzzle of the spread of leprosy in the world, its persistence in some foci, and its disappearance from others.

Fashions in leprosy are as transient and inexplicable as fashions sartorial or tonsorial. Time was when "prolonged and intimate contact" with a leprosy patient was held to explain all. But there were curious and well-authenticated exceptions; and in any case, no convincing evidence was forthcoming that *Myco. leprae* is at all commonly seen in histological sections traversing the epidermis. The bacilli may be present in enormous numbers in the dermis, but they are rarely present in the sub-epidermal clear zone. In tuberculoid leprosy they may be found in the ulcerating edges of an acutely inflamed lesion. Bacilli are present in greater numbers, it is true, in the epithelial cells lining the hair follicles and in the acinar cells of sweat glands and within their lumina. However, Pedley failed to find many bacilli on hairy and sweaty skin.

In the Far East the genito-urinary tract has for many centuries been associated in popular belief with the transmission of leprosy, but *Myco. leprae* are but

infrequently found in the glomeruli or cellular lining of the kidney tubules, and studies of *Myco. leprae* in urine and semen are rare. Similarly, while acid-fast organisms are found in the intestinal wall, investigations of the intestinal contents have not been enlightening. The milk of lactating females contains enormous numbers of *Myco.leprae* when the cells lining the galactophorous ducts, replete with organisms, burst and evacuate their bacillary contents into the milk stream, to be imbibed by the suckling infant. Their subsequent fate is unknown, but calls for investigation.

The discharge from neuropathic ulcerations of the extremities has for long been considered by the laity in many lands to be highly contagious, but systematic examination of both the exudate and the wall and floor of the ulcers usually fails to reveal any *Myco. leprae*, even degenerate forms of the organism.

The mucosa of the upper respiratory tract, however, provides a more convincing picture. Ulcerations of the lepromatous granulation tissue found in the soft palate, uvula and naso-pharynx discharge acid-fast organisms in abundance; they may be found in scrapings or in the saliva. The mucosa of the trachea and larynx may be heavily infected, but curiously, not the trachea or the lungs. It is the nasal mucosa *par excellence*, however, that is severely and generally invaded in lepromatous and near-lepromatous leprosy, and it is the abundant mucoid discharge from the hyperaemic nasal mucosa that is probably the vehicle for the exit of the vast majority of *Myco. leprae* leaving the body of the infected host.

Slight and transient nasal obstruction is frequently adduced as an early symptom of leprosy, and epistaxis may on occasion be the presenting sign. Now, after Pedley's convincing demonstration, examination of the nasal mucus will be a necessary prelude to any discussion of the infectiousness of a patient suffering from leprosy, and direct rhinoscopy of all patients with lepromatous and near-lepromatous leprosy may provide evidence, hitherto lacking, of a possible portal of entry, as well as an accepted site of exit of *Myco. leprae*. It is most unusual for the nasal mucus or the nasal mucosa to contain acid-fast organisms before they appear in the dermis in lepromatous leprosy, but systematic examination may one day conceivably reveal the site of inoculation of organisms deposited by droplet infection on the vulnerable and hospitable mucosa.

These findings and these possibilities should stimulate clinicians. It is well known that the stratified epithelium of the vestibule is rarely the site of lepromatous infiltration, although a tuberculoid lesion in the vicinity may encroach on this area. Also, the mucous membrane covering the anterior aspects of the inferior and middle turbinates, as well as the septum, may be hyperaemic and oedematous, and perhaps show small yellowish elevations of lepromatous tissue set in a thick velvety mucosa, or areas of frank ulceration. The mucosa itself, as shown by microscopical examination, is thickened and infolded; its surface area is greatly increased, and the superficial cells discharge *Myco. leprae* in enormous numbers, a high proportion of which may be morphologically normal. It is evident that, consistent with a lengthy generation time, *Myco. leprae* must be present in the cells of the mucosa in numbers many times greater (possibly 15 times greater) than the daily discharge of several hundred million bacilli.

The nasal mucus used not to be examined systematically, though in patients with lepromatous leprosy it was known to contain acid-fast organisms. These were suspected to be harmless saprophytes unless they were present in obvious *globi*. Despite the attested value of smears obtained from the nasal mucosa in patients with lepromatous leprosy, the popularity of the procedure waned somewhat. As

evidence of potential infectivity, however, and as providing evidence of bacterial relapse and persistence of morphologically normal bacilli, the nasal mucosa may be a more sensitive tissue than the dermis. Now that positive means of identifying *Myco. leprae* are available, intracellular acid-fast bacilli aggregated in *globi*—whether appearing in scrapes from the septal mucosa, or in histological sections, or in the mucoid nasal discharge—may be assumed to be *Myco. leprae*. And examination of the discharge from the nasal cavity entails no discomfort to the patient.

The epidemiological interest of these findings will not be overlooked. The important question of the duration of viability of organisms discharged from the nasal mucosa (and present in, for instance, house dust) may be answered by recourse to the established mouse-footpad technique, and the possibility of infective fomites will need to be investigated anew. When culture techniques are developed, further outstanding questions will be more readily answered, as in the case of other diseases transmitted by droplet infection. In this context, "prolonged and intimate contact" comes to mean propinquity of such a nature as to be within the range of infected particles either floating aerially or deposited on some fomites. On the practical side, the hygienic disposal of the nasal discharges assumes a new importance; and staff in contact with leprosy patients need to be warned to take precautions against droplet infection.

The clinician-*cum*-pathologist will be intrigued by these stimulating observations, and will be drawn into further inquiry and speculation. The pathology of direct bacillary invasion of the nasal cartilages, the specific bony erosion of the nasal spine, the virtual sparing of the tracheal mucosa and that of the nasal duct and conjunctival sac, the importance of temperature and oxygen availability, the existence of healthy carriers and inapparent infections—all are aspects that immediately come to mind.

The experimental microbiologist will be examining his immunologically deficient mice and his armadillos for signs of spontaneous infection of the nasal mucosa. Just as nasal washings from untreated cases of lepromatous (and borderline) leprosy have provided material for animal experimentation, so animal infections may shed light on the pathogenesis of leprosy lesions of the upper respiratory tract in human beings, and the portal of entry of the organisms.

From droplet infection to the penetration of deposited organisms through a protective epithelial barrier is a very big step. It may be that some inapparent clinical infections, or some tell-tale immunological modification of lymphocytes, may register a transient exposure to *Myco. leprae* in the inhaled air. It is easier to demonstrate the flooding of the circulation by thousands of *Myco. leprae* derived from endothelial cells lining the smaller arterioles and literally bursting with organisms, than to show convincingly the genesis of an implantation lesion in the respiratory tract or elsewhere.

Once again, as in other portions of the growing edge of leprosy research, co-operation between the observant clinician, the epidemiologist, and the laboratory research worker is needed. The question "How does *Myco. leprae* leave the body?" is now in the process of being answered. How it gets *in* is quite another matter.