Leprosy and the elusive *M. leprae*: colonial and Imperial medical exchanges in the nineteenth century

A lepra e o evasivo M. leprae: *a troca de informações médicas nos períodos colonial e imperial do século XIX*

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In the 1800s, humoral understandings of leprosy successively give way to disease models based on morbid anatomy, physiopathology, and bacteriology. Linkages between these disease models were reinforced by the ubiquitous seed/soil metaphor deployed both before and after the identification of *M. leprae*. While this metaphor provided a continuous link between medical descriptions, Henry Vandyke Carter's *On leprosy* (1874) marks a convergence of different models of disease. Simultaneously, this metaphor can be traced in popular and medical debates in the late nineteenth century, accompanying fears of a resurgence of leprosy in Europe. Later the mapping of the genome ushers in a new model of disease but, ironically, while leprosy research draws its logic from a view of the world in which a seed and soil metaphor expresses many different aspects of the activity of the disease, the bacillus itself continues to be unreceptive to cultivation.

KEYWORDS: leprosy, *M. leprae*, morbid anatomy, Henry Vandyke Carter, G. Armauer Hansen.

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No século XIX, abordagens humorais da lepra deram origem a sucessivos modelos da doença baseados na anatomia patológica, na fisiopatologia e na bacteriologia. As relações entre esses modelos da doença foram reforçadas pela onipresente metáfora 'da semente e do solo', difundida tanto antes quanto depois da identificação do M. leprae. *À época em que a metáfora fornecia um elo de ligação contínuo entre as várias descrições médicas da doença, Henry Vandyke Carter publicava* On leprosy *(1874), estabelecendo uma convergência de seus diferentes modelos. Simultaneamente, a metáfora se fazia presente nos debates médicos e populares de fins do século XIX, juntamente com o medo do surgimento da lepra na Europa. Mais recentemente, o mapeamento do genoma humano determinou a formulação de um novo modelo para a doença. Mas, ironicamente, enquanto as pesquisas concernentes a ela se apóiam numa visão de mundo em que a metáfora da semente e do solo ainda expressa diferentes aspectos da ação da doença, o próprio bacilo permanece refratário a todos os esforços visando seu cultivo.*

PALAVRAS-CHAVE: lepra, M. leprae*, anatomia patológica, Henry Vandyke Carter, G. Armauer Hansen.*

> The aetiological agent of leprosy is *Mycobacterium leprae*. It is a strongly acid-fast rod-shaped organism with parallel sides and rounded ends. It occurs in large numbers in the lesions of lepromatous leprosy, chiefly in masses within the lepra cells, often grouped together like bundles of cigars or arranged in a palisade. Most striking are the intracellular and extra-cellular masses, known as globi, which consist of clumps of bacilli in capsular material. Under the electron microscope, the bacillus appears to have a great variety of forms. The commonest is a slightly curved filament, containing irregular arrangements of dense material sometimes in the shape of rods. Short rod-shaped structures can also be seen (identical with the rod-shaped inclusions within the filaments) and also dense spherical forms. Some of the groups of bacilli can be seen to have a limiting membrane. (WHO web pages http://www.who.int/lep/disease/disease.htm)

The World Health Organization (WHO) currently describes leprosy as a disease mainly affecting the skin, the peripheral nerves, the mucosa of the upper respiratory tract, and also the eyes, apart from some other structures. It is estimated that there are between one and two million people visibly and irreversibly disabled due to past and present leprosy. Treatment for leprosy only appeared in the late 1940s with the introduction of dapsone and its derivatives. Leprosy bacilli resistant to dapsone gradually appeared and became widespread, necessitating the identification and development of multi-drug therapy. In 1997, there were an estimated 1.2 million cases in the world, most of them concentrated in Southeast Asia, Africa, and the Americas. About 750,000 new cases are detected worldwide each year.

An examination of the ways in which the disease 'leprosy' is recognized and understood in any one historical moment demonstrates a dependence upon systems of medical knowledge available at the time. Interestingly, sometimes confusingly, and often imperceptibly, these systems of knowledge can be seen not to be self-contained — never hermetically sealed as discrete categories, distinct from those current in earlier or successive periods. The history of the deployment of medical categories has been well documented. They draw support from teleologies that determine an understanding of the body and also a sense of the place of the physician, and they possess their own logic. In addition, there may be an apparent eclecticism in the use of medical categories. Observation and description may draw on analogies and metaphors that seem most appropriate to the case in hand. Sometimes to do justice to the latest observation necessitates borrowing from earlier systems of understanding and combining them with more contemporary ones so that world views are brought together that are not always commensurate with each other. Other times, what needs to be said may necessitate a search for a whole new mode of expression. This

paper will examine the shifting medical categories and metaphoric continuities through which leprosy was thought of from the early 1800s in order to document the different ways in which leprosy, but most specifically the bacillus, has been thought of. As a work in progress, after the late 1800s, it will then take a very brief leap to the mapping of the genome.

Intriguingly, there is still much to be learnt about leprosy. Even after *M. leprae* was shown, by G. Armauer Hansen[1] in 1873, to be the bacillus consistently present in the nodes of leprosy patients, this entity would continue to puzzle histologists, pathologists, and clinicians. It is referred to as the aristocrat of diseases — the oldest, the most mysterious. Its effects depend more upon the reaction of the host than upon the action of the invader (Hastings, 1985, p. 32).[2] Its stages and categories have been, for a long time, subject to debate,[3] and how it enters the body and is transmitted to others is still unknown.[4] Paradoxically, although it was the first bacillus to be identified, it has still not been cultivated *in vitro*.[5]

The history of the disease is also shrouded in uncertainty that is heightened by the confusion and debate surrounding its naming. In the nineteenth century, naming and describing leprosy was a complicated and subtle process vulnerable to mistakes and misinterpretations, a trail of which had already been generated and which needed to be retraced every time attempts were made to document it comprehensively. Inevitably, at a material level, these mistakes and misinterpretations served to obscure and confuse diagnoses of leprosy, and, at the same time, they served to compound the already charged symbolic resonance of the disease and the corresponding force and power of its myriad representations. This paper will focus on a single and continuous metaphor that has resonated in many different registers and in separate, but overlapping, fields throughout the history of the disease in the English-speaking world.

The botanical metaphor

In the 1800s, humoral and environmental explanations were drawn on to explain the occurrence of disease. Michael Worboys (2000, p. 31) identifies and explicates trajectories of medical knowledge from the mid-nineteenth century. These shift from a preoccupation with morbid anatomy or the end of disease, give way to an interest in physiology and patho-physiology, by 1875, and arrive at bacteriology and experimental pathology, with its subsequent focus on the causes of disease. Disease involved "structural and functional perturbations" so that the physician's task was to intervene in positive ways which would "promote repair, … restore function, or … aid in the regeneration of damaged structures" (ibid, p. 33). Worboys (p. 193) also points out that significant continuities in the medical understanding of tuberculosis, for

example, were, in part, due to "a dominant seed and soil metaphor which allowed constitutional notions to be refashioned in terms of vulnerability of the human soil." The same dominant seed/soil metaphor can be identified in the medical categories employed to understand leprosy. This metaphor can be observed operating and being reinflected both before and after *M. leprae* was identified. The notion of 'soil' is expressive of a wide range of possibilities. The hereditary predisposition of individual bodies, the lifestyle, dietary habits, practices, such as cultural customs, and moral behavior are all encompassed by the concept of a 'soil' that is conducive to the seeds of the disease. In addition, 'racial types', and certain groups of people with their specific customs, are seen as offering a milieu in which the seeds of the disease can flourish.

Typical of early- to mid-nineteenth century descriptions of leprosy, Joseph Adams (1807), James Maxwell (1839), and Alexander Fiddes (1857) all demonstrate understandings of leprosy that seek to place it within a constitutional model of disease that depends upon the seed/soil metaphor for expression of its complexities and variations.

Joseph Adams wrote his account from his experiences as a physician on Madeira, and his work was read before the London College and intended for publication in the *Transactions of the London College*. Careful observations of bodies bearing signs of what he understands as leprosy indicate that its effects produce disorders in structure, such as arresting growth to sexual maturity. Adams explains that leprosy seems to arise spontaneously, although climate, constitutional predisposition, and diet are considered responsible, either singly or in combination, for creating appropriate conditions for its appearance. If climate and diet are alone responsible, then the patient can be assisted. If there is a constitutional predisposition, then "the cure can only be permanent as long as the patient is removed from the exciting causes" (Adams, 1807, p. 269). The body acts as a predisposing soil carrying the seeds of the disease, but there is also the receptive soil of climate and/or diet in which the body as a seed, carrying a predisposition for the disease, may take root and flourish with leprosy. Body is both soil and seed. In addition, those who are predisposed to the disease usually contract it so early that they are unable to reproduce. Ironically, if a hereditary predisposition provides enabling conditions or receptive 'soil' for the seeds of the disease, then, infertility will be the result.

Thirty-two years later, for James Maxwell, writing from his experiences in Jamaica, the signs of the disease, increasing in intensity and coming to a climax, and the accompanying fever are indicators of stages in the body's attempt to eliminate the poison that arises in the blood. Initially it appears as "preliminary eruptions of blotches and scaly efflorescences" and then it shows itself as "an open ulcerated state" (Maxwell, 1839, pp. 235, 234). For some, symptoms are confined to the surface of the body, for others the nose and throat are attacked and the bones become

affected (ibid.). Its treatment should counteract and balance the natural progress of the disease: "These operations teach us to imitate nature by counter-irritants" so that suppressed symptoms are encouraged to develop and the affection is drawn from the face and throat.

In this instance, the disease is again the seed lodged in the soil of the body. It may arise spontaneously in some individuals, but it also arises in those who have a hereditary predisposition to it. Some soils are more conducive to its growth than others. It may remain latent in those who have this predisposition, and, without the occurrence of external favorable circumstances, it may skip a generation. Happily, its virulence may be mitigated by breeding with healthy stock but "when it has been confined to a long race of ancestry, it becomes possessed with powers of great inveteracy" (ibid., p. 232). Conversely, improvements in hygiene and diet will, over generations, diminish its power, as instanced in its disappearance from Europe (ibid). Once again, in a paradoxical inversion of the botanical metaphor, poor soil allows the virulence of the strain to intensify, and good soil weakens its power. Maxwell is optimistic that eventually leprosy will be "disarmed" and vanish from the Western world in the same way that it has already done "from the shores of Europe" (p. 237).

Like James Maxwell, Alexander Fiddes, publishing his observations of leprosy in Jamaica in 1857, understands the disease as typical of other blood diseases resulting from "morbid matter in the blood, and in the effusion of it on the solid textures" (Fiddes, 1857, pp. 1063, 1072, 1073). Repetitive febrile disturbances indicate natural attempts to expel poisonous matter from the system. This process of expulsion produces a disturbance and derangement in the skin and in the mucous membranes "ultimately effect[ing] a partial or complete disorganization of the texture." There is the prospect of this process actually accomplishing the expulsion of the poison. Fiddes suggests that in some rare cases, "nature has proved adequate to expel the disease, and to remove the tubercles at the same time" and he gives one instance in which "the cure was accomplished through the intervention of an inflammatory condition. … In this case, there can be no doubt that the morbid depositions were dissolved, and the poison eliminated by means of a congestive inflammation of the dermis" (ibid, pp. 1074-5). This understanding of the disease relies more on a sense of humoral balance, which, after a disturbance in the body, reasserts itself. Cultural differences, geography, latitude, and constitution are specified and rejected as immediate causes of leprosy, but they are considered as providing the soil that may modify the severity of the disease.

In the early- to mid-nineteenth century, therefore, the seed/soil metaphor was deployed flexibly to express both the vulnerability of different bodies to leprosy, as well as the predisposing influence of external circumstances.

Cross-pollination: the Royal College of Physicians, Danielssen and Boeck, Vandyke Carter, and Hansen

From the mid-nineteenth century, a significant collection of publications appeared, marking the point at which medical models of the disease, drawing upon morbid anatomy and descriptions of the effects of the disease on the structures of the body, give way to a more precise parasitic theory. With the shift from one disease model to another, it could be assumed that the soil/seed metaphor would be discarded, but as Worboys has already noted in his work on tuberculosis, the metaphor serves to bridge the transition to an understanding of the disease based on bacteriology.

Conducted and published before the identification of the bacillus, *The Report on Leprosy by the Royal College of Physicians* (1867) originated from a suggestion to the College by James Walker, Governor-in-Chief of the Windward Isles, that reports be gathered on the "character and progress of the disease of leprosy" (p. a2). This grew out of concern that leprosy was "on the increase." The survey was conducted by sending out a series of interrogatories to the colonies and related areas where leprosy may have been prevalent. There were seventeen questions. Respondents were asked if leprosy was known in their colony; to describe it as it occurred there; to enumerate its forms or outward manifestations; to give an opinion as to whether there were only varieties of the one disease or if there were distinct diseases; to describe the distinguishing characteristics of each form; to generalize about the age and the time of life at which the symptoms of the disease, its full development, and its most fatal stage became apparent; to generalize about its prevalence with respect to sex, race, and social group; to describe the topographical character of the place, and the sanitary conditions where it is prevalent; to describe the habits of the afflicted, their diet, occupations, and any conditions or circumstances of life that would seem to aggravate the disease; to suggest if they considered that it was hereditary, related to yaws, syphilis, or any other disease, and if they knew of instances where it had been communicated by contagion or by sexual intercourse; to note whether the afflicted were permitted to mix with others in the colony; to indicate what public provision was made for the reception and treatment of those with the disease who were poor; to estimate how long it had been in the colony, and if they had observed any results from hygienic, dietetic, and medical treatment, or if they had any cures to report; and, finally, to estimate the proportion of leprosy patients in the overall population of the colony.

As a counterpoint to the replies from the colonies, the definitive work of the Norwegian authorities Danielssen and Boeck (1847) is quoted as arguing that leprosy seems "to pass over one generation, and to reappear in the next" (ibid, p. lxviii). This time, the seed and soil metaphor serves to express the latent tendencies of the disease — the

longer the disease lies dormant, the greater its intensity when it re-emerges: "If it has spared the first generation, it as a general rule appears in all the individuals of the second, who transmit the germ of the disease to succeeding generations. Tolerably often, it seemed to pass over the second or third generations, and to reappear in the fourth generation, and then to spread in all directions, so to speak, with a new energy" (p. lxviii). In this instance, the 'soil' is the family, rather than the body. In addition, previously healthy soil can be altered by external influences so that it becomes receptive to the disease: "We have already said that leprosy may also be acquired. We speak of these cases where the malady declares itself in persons born of healthy parents, in whose families the disease had never resided, for a longer or shorter period, in countries where it is endemic, and who have lived under conditions liable to occasion its development" (p. lxviii). So residence in countries where the disease was endemic was considered to be conducive to its appearance in those whose family has never before shown a disposition to leprosy: colonial soil, by itself, was sufficient for the appearance of the disease in the bodies of previously untainted colonizers.

Danielssen and Boeck (1847) appear again, with the work of Hansen, in Carter's *On leprosy and elephantiasis* in 1874. In addition, Hansen's 'Preliminary contribution respecting the characteristics of leprosy' in 1869 and his 'Further contributions towards a knowledge of the characteristic features of leprosy (spedalskhed)' (1870) were translated and published in the appendices. It is questionable what sort of circulation and direct impact Hansen's early papers may have had with the British medical fraternity, until they appeared in Vandyke Carter's 1874 publication. In addition to this intermeshing of research, Vandyke Carter visited Danielssen and Boeck in Norway in 1873. Without doubt, Vandyke Carter served to assimilate and disseminate knowledge about leprosy, from India to Europe and back again in this period.

At this point, different models of disease converge, and morbid anatomy can be seen giving way to pathology. Carter marvels in the introduction that even what little is known of the pathology of the disease indicates how adaptable it is to a theory of chronic infection. He sets up opposing views for understanding the disease and accomplishes the succession of one view over the other. There is the earlier view in which "the local deposition of leprous matter in the shape of nodules or tubercles" was considered caused by a 'dyscrasia' of the blood. Danielssen and Boeck supported this, as did "standard English works." Since then almost every observer of leprosy, has, it must be said, conformed in principle to the opinion so definitely put forth in Norway in 1848 (Carter, 1874, pp. 72-3). The opposing view promises to "reconcile the pre-existing and non-concordant opinions" in which "the implication of the system … is a secondary consequence of the primary local implantation of the malady." Here Carter is heralding Hansen's opinion, which he is careful to distinguish from "earlier and more crude hypotheses

of the extraneous origin of leprosy." At the same time, he calls for "renewed investigation, to be pursued in accordance with modern means and attainments" (ibid, p. 72). The shift to observations and conclusions based on experimental evidence accompanies Carter's introduction of Hansen's work.

Hansen's 1869 paper, excerpted and translated as an appendix in Vandyke Carter's (1874), would appear to demonstrate Carter's ideal researcher. Hansen's observations identify structural elements which he suggests are characteristic of leprous productions. In this description, minute observation, aided by the microscope, combines with a descriptive repertoire that is still within the trajectories of morbid anatomy and attention to structural detail that I have been tracing.

In describing the commencement of the softening of the tubercles, he notes "round, oblong, and spindle-shaped cells" containing nuclei and, in addition, "one or more large and small, round, yellow, granular masses" (Hansen, cited in Carter, 1874, Appendix A, p. i). The nucleus and clear part of the cell can be colored with carmine; the yellow masses remain unchanged. These masses lie in the cavity of the cell. When a cell contains a single mass, it looks like a signet ring, with the tinted mass in the middle. In some cells, these masses seem quite distinct from the rest of the cell, but in other cells they seem to be amalgamated with the rest of the cell.

There are also other cells, similar in form, containing protoplasm that is partly clear and partly finely granular, and which is mostly filled with fat-granules. As the softening of the tubercle progresses, these cells change. Their color becomes a more intense yellowish brown. Amidst these changes in the cells, rounded masses or corpuscles are found which vary in size from a quarter of the size of white blood cells to six or eight times as large. These seem to have been set free from the cells. Large collections of these masses can be detected. These may be found adhering to each other and, more often, they can be found enclosed in a colorless envelope.

Like the signet-ring-like cells, he identifies large orange masses surrounded by an extremely thin enveloping material raised on one side. The centers have a space like a vacuole with clear contents. This space is sometimes so large that there is no other space around it, except for a very narrow brownish ring. There is always a sharp boundary. The interior is minutely granular and deep-tinted and more or less translucent.

He observes that across the most clouded and dark-tinted specimens, "other underlying elements may be clearly enough perceived; and this is most apparent in the more monstrous forms" (Hansen, ibid).

He has not come to any conclusion about the history and mode of origin of these bodies. He does not know if they have been produced by the enlargement of the smaller elements that he has just described or by amalgamation of them. He describes them as large and, in their

simplest shape, appearing as a homogenous mass, indented at the middle like a dumb-bell, or further indented as a trefoil. They are tough and elastic. As seen either in motion or at rest, the outlines of the projecting hemispheres on their under surface are clearly visible. These same elements were, Hansen comments, described, but less correctly, in Danielssen's work in 1862 as pigmented clusters of fatty granules and were identified by him as characteristic results of the leprous products. This conclusion was also confirmed by Virchow (cited in Carter, 1874, p. ii). Hansen (ibid, p. iv) comments that during his earliest examination of the morbid products in leprosy, he "almost constantly" and to his astonishment "met with these peculiar structural elements." He locates these rounded masses of leprous character in the lymph glands, liver, and spleen, and in a section taken from the ulnar nerve.

Hansen (p. iv) is confident that what he is observing is the result of a "necrobiotic process," and that there is "some peculiar property in them, which is connected with such process." But he adds: "I am not acquainted with any either described, or conceivable, structures or properties, which quite correspond with the forms in question, and with their constant peculiar tinting." The anatomical changes that he has noted are completely different to anything he or anyone else has observed "in preparations taken from cases of necrosis and chronic ulcerations." Therefore, the changes that he observes are, he concludes, evidence of a specific leprous affection. Hansen (p. iv) writes:

> If one next turns to the affections of the liver and spleen, one cannot but suppose — even without paying regard to the appearance of the brown elements — from the fact of their connection with the small round cells, from the many-nucleated cells with their degeneration into fat granule masses, and from the conjoined state of the lymphatic glands, that these affections are of leprous character. When, besides all these, one finds certain peculiar looking structures — brown-tinted masses — the conclusion seems inevitable, that here are altogether specific leprous products.

In *Leprosy: in its clinical and pathological aspects*, Hansen is more certain of what he is looking at. Examination by microscope of a section of fresh nodules reveals little else but cells, with distinct nuclei, usually the size of white corpuscles, or larger. With an even higher power, "one sees in the fluid of the preparation small straight rods, which are not destroyed by the addition of potash. These are the lepra bacilli, and thus were they first discovered in the year 1871" (Hansen *et al.*, 1895, p. 31). After preparation, the rods are colored faint brown, and they can be found lying mostly in the cells. In a fresh preparation, they can be seen moving actively.

Building on his previous descriptions of the softening nodule, with its central part, with its distinct brown color, which when examined

under a microscope reveals larger or smaller clumps of a brownish color that are very granular and that lie in the cells and can be located in all the other organs affected with leprosy, he writes that they may very well serve as diagnostic indication for leprous affections because, in his experience, they can always present, except in very young nodules. Subsequent investigations have shown that these brown clumps are "nothing else but collections of lepra bacilli broken down into granules." Neisse has called them "globi" (ibid, p. 40). He is certain that the bacilli therefore occur in the cells.

Additional observations lead him to conclude that the bacilli must increase very, very slowly and that they probably produce a toxin in very small quantities which "causes no particular injury to the organism, since patients, in spite of numerous nodules with millions or milliards of bacilli, may remain in pretty good health for years" (ibid). This toxin only acts immediately around the bacilli. As a result, the blood vessels are dilated and white corpuscles migrate to the site. The bacilli multiply in the cells. In some cells the bacilli lie in separate collections; in others they fill the whole cell body but never penetrate into the nucleus. He also identifies bacilli that break down into granules as ones that have degenerated. In his numerous attempts to cultivate the bacilli, he has managed only to attain granules.

> As the bacilli at first multiply in the cells, and the breaking down appears most definitely and freely when the cells are crammed full of bacilli, it is equally possible that it is the result of diminished nutrition, and as they break down more rapidly in the internal organs, it is also possible, indeed probable, that the higher temperature in these organs favors disintegration. As we have unfortunately not been able to cultivate the bacilli, it is at present impossible to form a conclusion. At all events, we regard the transformation into granules as a degeneration, and believe that the bacilli this altered are dead (Hansen *et al.*, 1895, pp. 42-3).

He also remarks that: "As we do not know the manner and method of the primary infection of the organ, we must devote our attention to the search for discoveries like those described above, and to the localization of the bacilli in general, in order to form an idea of the method of action of the bacilli" (ibid, p. 39).

What sort of conceptual break do these observations indicate? Perhaps they simply indicate an intensification of the practices of observation. Hansen looked at the structure of the morbid changes in the same way as did Wilson (1867). Perhaps Hansen simply had a stronger microscope. Perhaps Hansen did not allow his looking to be so strongly influenced by the conceptual lens of earlier disease models, even though his looking is still informed by those models. He says that he was influenced by Darwin's scientific research and reasoning "to set aside every preconceived opinion and to diagnose from every approach that might

have bearing on an ultimate solution" (Hansen, 1976, p. 92). As a result, another world of observation is opened up — in finer detail.

At the same time, the familiar metaphors still have their uses. In considering the clinical variations in leprosy, Hansen (1976, pp. 79, 80) asks if these depend upon the virulence of the bacilli. He concludes that the virulence of the bacilli depend "not so much on any constant character of their own, as in the soil in which they live." In this case, the botanical metaphor serves to express climatic variations. In Hansen's experience, maculo-anaesthetic cases are more numerous where the climate is dry, and nodular cases can be found where the climate is moist. He reasons that the exposure of the skin to the influence of the weather may affect the disease. Against this hypothesis, he also argues that "it is also possible that the bacilli always possess the same virulence, and that it is solely dependant on the soil in which they live, whether they multiply freely or no." Here the 'soil' may be responsible for modifying the virulence of the bacillus or it may actually be more or less receptive to an unvarying bacillus.

A virulent metaphor

While Hansen identifies the bacillus and Carter emphasizes a modern scientific approach to research based on observation, the soil/seed metaphor serves to express an intensification of concern about the disease that was not only medical but also circulated in heated public debates. This represented a revivification of the metaphor so that it carried both new understandings of the disease, gestured towards the still unknown aspects of leprosy, and conveyed underlying fears and anxieties.

The final section of the *Report on Leprosy by the Royal College of Physicians* includes an article by Erasmus Wilson (1867), 'Observations on the true leprosy or elephantiasis, with cases.' Erasmus Wilson's case studies create a powerful impression of the dangers of transplantation in the colonies. The vivid images that they present may have fuelled the debates that followed. For Wilson, the predisposing cause of leprosy is "long residence in countries in which the disease is endemic' or, alternatively, "birth in an infected country takes the place of long residence." The period of latency may be months and even years.

His case studies describe eighteen Europeans (and one native of Hindustan) who had all lived in either India, Ceylon, Mauritius, or the West Indies. Each emerges as a narrative of diseased bodies charted over time and categorized according to race, gender, age, pursuit, and predecessors. These cases (along with a number of others) were circulated and recirculated in the debates about the disease which took place after the release of the report and up until the turn of the century. All are Europeans, except one, and all from the colonies: a sixteen-year-old

boy, born in Ceylon and vaccinated, for smallpox, with attenuated bacteria from a native child; his older brother; a young man of seventeen years, born in Bombay; a 21-year-old male, born in Jamaica; a young woman who had been living in Mauritius; a 43-year-old captain in the Indian army; a sixty-year-old man "in the judicial service of India," who had lived in the East for nearly twenty years; a captain in the Indian army; a sixty-year-old colonel who had lived in the West Indies; a 26-year-old wife of an officer in the Indian army; a 19-year-old Hindustani woman; a young medical officer in the Indian army who had originally contracted syphilis; "one of the chiefs of the Bengal medical establishment" (Wilson, 1867, p. 242), who had lived in India for forty years; and a merchant in Mauritius for 29 years.

The collective effect of the descriptions of the symptoms of these cases is of a metamorphosis in disposition as well as physical appearance — a degenerative descent in which they are poised on the boundary between what constitutes a human being and something else. A mother notes alterations in "the appearance of [a child's] countenance" and a change in behavior: "He shunned amusements; was fond of sitting alone and secluding himself" (Wilson, 1867, pp. 235, 237, 238); the features of another developed changes which "gave an occasional gleam of savageness to his countenance;" another's vital functions seem to slow down to the extent that she experienced "coldness of extremities … and a certain listlessness, heaviness, sleepiness, and indisposition for exertion of every kind." Another was "dejected, listless, and melancholy," unable to sleep at night and sitting for hours during the day "without occupation and without attempting to make any exertion."

Their faces and their skin were altered. The features were "spread out," "enlarged and flattened." The skin became covered in spots that changed from "beautiful pink" to "purple" and finally "dirty brown." It thickened around the eyebrows, nose, lips, chin, and ears, giving the face "a frowning and dejected expression" (Wilson, 1867, p. 237). Facial hair fell out. In one case, the skin was "yellowish brown with a purplish almost livid blush" and "the brow was heavy and frowning, the eye sunken, anemic, and glistening, and the general expression of features listless and melancholic." Another looked like a Satyr:

> His features were large and of a deep red-brown or copper color; the forehead was deeply wrinkled and studded with tubercles; two of the tubercles at the upper angles of the forehead resembling young horns; the brow was thickened, heavy, frowning and deprived of hair; the eyes suffused with redness. … The voice was hoarse and sonorous (p. 239).

Another begins to look like "a native": "in his infancy he was somewhat darker in complexion than his brother and sister … but

during the last few years, and especially the last twelve months, has become swarthy, and at present is darker than a native of India" (p. 240).

The ability to speak deteriorated. The hands and feet altered, the bones retracting so that the shape was lost. For example: "[He] had lost a phalanx from the little finger of one of his hands, the rest of the fingers were bent in different directions and the hands distorted. He was unable to use his hands and was incapable of walking" (p. 244).

Evidently all Europeans, particularly those with a constitutional predisposition, at the outskirts of Empire were potentially in peril. Children, young men, young women, and old and distinguished men were not safe from becoming animal, becoming native, becoming afflicted with leprosy — and such threats of atavistic reversion and racial degeneration were embodied in the figure of the leper. By implication, the price to be paid for venturing away from 'home' was loss of the defining characteristics that gave one entry into society and established one's social, racial, and imperial identity. The marks of leprosy heralded a lingering process of dying in which one's vitality was lessened in agonizingly incremental degrees. Leprosy's representation, as bringing about a metamorphosis in the bodies of colonizers, dramatically externalized anxieties about living in tropical climates and mixing with peoples of other races. Previously healthy families or those with a constitutional predisposition, upon exposure to the soil of the colonies, ran the risk of developing leprosy. Transplanted seed could 'grow' in unpredictable ways.

Dissemination

In 1887, a case study by W. T. Gairdner, Professor of Medicine in the University of Glasgow, produced a sensation in medical circles, and seemed to contribute an irrefutable instance of the contagion of leprosy by inoculation (specifically vaccination) in a chain of infection which originated with "a native child" (Gairdner, 1887b, p. 1269). The story concerns a child brought to England by his parents with a referral from a doctor who had been one of Gairdner's pupils. In consultation with another expert, it was concluded that the child had leprosy, and Gairdner was surprised that the referring doctor had not recognized it, knowing that the child had come from a region where the disease was endemic. Gairdner let the referring doctor know the diagnosis, and eventually received a reply from him indicating that he had already known that it was leprosy but had deliberately chosen not to tell the parents or Gairdner. Out of a reluctance to "have the credit of having discovered for the first time what a gentleman so much more familiar with the disease might

have been supposed to have overlooked," Gairdner informed the parents that the referring doctor had known it to be leprosy all the time.

After a number of years, Gairdner was called back to the now rapidly deteriorating child, where he learnt from the parents, who had had further contact with the referring doctor, the reason for his unaccountable reluctance to disclose the disease as leprosy. The referring doctor had made a terrible blunder:

> He had vaccinated his own boy with virus derived from a native child in a leprous family, and as I understood (though perhaps not definitely so stated) that leprosy had declared itself in the native child after the vaccination; and, further, that (using his own child as a *vaccinifer*) he had vaccinated our patient directly from him (Gairdner, 1887b, p. 1269).

He had "known," not only that the child had leprosy but where it had come from — from his own child; that three children (the native child, the referring doctor's child, and the child who had been presented to Gairdner) had the disease; and that two of them had contracted it at the hand of the colonial doctor. The referring doctor was now dead, but his child, now an orphan, was attending school in Britain.[6] This presented Gairdner with 'a difficult dilemma' — should he do anything about this child, as a possible source of infection, and what would be the consequences for the child, in a foreign land? He consulted other expert medical practitioners, who reassured him that the child did not present a danger to other children, but knowing one of the medical officers at the school, he let him know of "the extraordinary circumstances" (ibid., p. 1270). As a result, the child was "sent for and privately examined" and "beyond all doubt, considered to be a case of leprosy." The medical officers then decided not to "sound the alarm" so as to avoid disturbing the boy's education. But some time later, Gairdner was called to the school by the school authorities and, because of an outbreak of contagious eczema and a deterioration in the general health of the child, "it was no longer expedient that he should remain at the school" (ibid). The child's guardian was informed, and although the child was suffering from "a mild type" of the disease, and there were no "breaches" on the surface of the skin and no discharge; and although Dr. Anderson, who supplied the other opinion, was certain that he did not represent a danger to the other children at the school, Gairdner "did not feel able to give an unqualified assent" (ibid.) to that opinion, and the child's education at that school came to an end.

The responses to this 'confession', as they appeared in the *British Medical Journal* from June to November of 1887, were instantaneous, sustained, and conflicting. The Acting Surgeon General from Trinidad wanted to know more details about the case and was rather skeptical: were the parents of the child, who was first vaccinated, European?; if they were not, then did they have any taint of leprosy?; was blood inoculated or only lymph?; was it possible to inoculate a person

with leprosy from the lymph? (Pasley, 1887, p. 270). Gairdner (1887a, p. 799) responded to Pasley's request for information with a further profession of reluctance and dutiful responsiveness, stating that he had simply reported what he had seen. But the result was that John Hillis (1887, p. 1022), the Late Medical Superintendent of the British Guiana Leper Asylums, wrote, calling for the College to reconsider their 1867 report on the basis that "much light has been thrown on the pathology of the disease." One reader commented that the whole medical profession owed a "deep debt of gratitude" to Gairdner "for his simple and clear statements concerning the communicability of leprosy by inoculation" (Jelly, 1887, p. 176). In contrast, the cautious Beaven Rake (1887a, p. 646), the Medical Superintendent of the Trinidad Leper Asylum, assembled a summary of the case for and against communicability and hereditary transmission, arguing that "no one knows what bacteriology may do for us in the future," but the matter was far from "set at rest."

This story galvanized the medical profession in Britain and in the colonies because it seemed to present evidence of transmission by inoculation, specifically by vaccination against smallpox. In addition, its power was contained in the image of double penetration that vaccination with the bacillus presented — unwitting contamination with an invading micro-organism by Western lancet. Did it encapsulate something of the compromised position that the colonizer found himself in? His penetration, by vaccination, of the black skin was responsible for the eventual transfer of an invading bacillus into the young body of his own son and heir: the sins of the fathers visited on the next generation, the very process of degeneration expressed by Nordau (1968), and, at the same time, a concrete embodiment of the supposed effects of miscegenation. The seed/soil metaphor resonated.

Colonial soil and Imperial alarm

Discussions about leprosy and its contagiousness focused implicitly and explicitly upon its potential to stage a 'return' commensurate with its activity in Europe in the past. These medical and popular debates sharpened in focus until they became debates about how to contain the contaminating agents at their point of origin: segregation in the colonies became the issue. Editorials in the *British Medical Journal* in November 1887 expressed what must have been a growing concern about the threat that the disease was coming to pose. The editorials opposed, on the one hand, the views of those who argued that any proof of infection, however isolated, was sufficient cause for alarm, to those who, in a leading article in the *Times* newspaper, supported the *Report on Leprosy by the Royal College of Physicians* that the disease was no more contagious than syphilis, and compulsory detention was unnecessary.[7]

The evidence of bacterial activity was drawn on to support what was considered to be justifiable concern: the discovery of the bacillus; the proven connection between the bacillus and the disease; the proof that, whatever part of the world the diseased body is discovered in, the bacillus is present; and the presence of the bacillus in dead bodies were all sufficient evidence to conclude that "if it is the human body which, living or dead, harbors the parasite which causes leprosy, it ought to be accepted as a matter of common prudence that healthy persons should avoid as far as possible contact with lepers living or dead" (*Brit. Med. Journ*., 1887, p. 1056). Questions of the "liberty of the subject" were considered subordinate to the importance of protecting the healthy and possibly bringing an end to the disease.[8] The editorial is thus positioned between the concern of the alarmists and the optimism of the *Times* by suggesting that the number of people with leprosy who had entered England had been underestimated. It concluded that "without sounding a note of alarm, or considering that there is any occasion at present for compulsory measures in England, we are yet unable to consider the presence of lepers … as being absolutely free from danger" *(Brit. Med. Journ*., 1887, p. 1056). Another editorial in the same month noted that the question of the contagiousness of leprosy was a question uppermost in the thoughts of those in the medical establishment and in the Government. It reassured its readers that the prevalence of the disease amongst populations that are "under the care of the British Government" was being noted.

In 1889, H. P. Wright, who had already written of his concerns in the *Times*, published *Leprosy an imperial danger*, intensifying the attack on the 1867 *Report on Leprosy*. Wright personified it, demonized it, expressed its trajectory through metaphors of invasion, and, most significantly of all, equated the individual suffering from the disease with the disease itself — the leper as a breeding ground for leprosy became the disease: "In leper lands, that which produces leprosy is not the soil, as in malaria; nor water, as with so many infectious maladies; nor decaying food; nor destitution, as in lathyrism, pellagra, &c. It is the leper" (Wright, 1889, pp. 15, 37, 31, 12, 99, 86, 116, 122, 16). He suggested that lepers might "fertilize" the soil with "their bacilli and spores," contaminating a district "for a period more or less lengthy." Consequently, if a person lived where lepers lived, even if they did not come into "close proximity," there was always the possibility that "you may be attacked by the disease, and that in a very short period." Eventually, in Wright's rhetoric, an attack from the disease leprosy becomes a "leper attack." The disease was also given demonical dimensions. It "manifests itself;" it is an evil that spreads with terrifying rapidity to be stamped out; it is a foul disease; "a frightful scourge ever threatening, and slowly advancing;" and it "threatens to become the scourge of the whole earth." Its progress throughout

history was figured as the "rapid propagation of a scourge," albeit an arbitrary one: sometimes moving slowly, sometimes with "a fearful rapidity," other times with a "primitive intensity." It invaded, attacked, abounded, prevailed, and ravaged. Most frighteningly, it was immortal: "It is ever alive, ever reviving, threatening without cessation all who approach its haunts."

It was communicated between "races," and was a threat to the "white races." Any country "which allows itself to be freely visited by a race infected with the malady" will itself be affected (Wright, 1889, pp. 5, 13, 14, 37, 39-40, 55, 92, 93); some were more ready to receive it than others: the yellow and black races were more susceptible than the white; although some races presented an "aptitude for maturing the leprous agent," none "can claim absolute immunity;" it was caught from colored men and slaves who had been given responsibility for caring for one's children. He argued that it spread "wherever an infected race" was "brought into contact under favorable conditions with a non-infected one." The invasion by leprosy and an invasion by another "race" become indistinguishable, particularly where the Chinese are concerned: "The invasion of a country by leprosy has always coincided with the introduction of lepers into that country; and races which have avoided intercourse with leprous people have remained intact." Most importantly, Wright was explicit about the potential threat that leprosy posed to England. The disease, he predicted, "will ruthlessly invade our colonies" and again become a "common scourge throughout Europe."

This concern was exacerbated in 1889 and 1890 by the unfortunate conjunction of a series of events: the death of the well-known Catholic priest, Father Damien, in the leper colony at Molokai, Hawaii; the discovery of leprosy in an Irishman who had never been out of the country (Hawtrey Benson, 1889, p. 860); an experiment upon a condemned criminal, Keanu, by Dr. Arning, in the Sandwich Isles;[9] and British and American alarm at the discovery of a leprous Swedish immigrant who had crossed the Atlantic.

A flurry of attention was concentrated on the potential for an outbreak in Great Britain. An editorial in the *British Medical Journal* (1889) at the end of March, entitled 'Leprosy in the United Kingdom,' seeking to allay alarm, conceded with some justification that the subject had come to preoccupy both medical discussion and "the public mind." It explained how the medical mind had been impressed with the discovery of the leprosy bacillus, with Arning's experiment with Keanu, and how the popular imagination had been riveted by the death of Damien: "For these and other reasons the subject of leprosy has recently cropped up from time to time in magazines and newspapers, in addition to being a subject of discussion in medical journals" (*Brit. Med. Journ.*, 1889c, p. 721).

In their attempts to reassure, the editors of the *British Medical Journal* constantly reiterated that "leprosy is rarely seen in this country;" "cases of leprosy in this country are very uncommon;" "there is no evidence that the disease spreads by contagion in England;" "we are satisfied that there is no cause for alarm;" "we are satisfied that on the part of the general public there is no reason for fear or anxiety" (ibid, p. 722). In support of this editorial, the statistics of cases presented to the Dermatological Society in the United Kingdom were published in the same issue of the *Journal* (p. 734).

These efforts must not have defused public concern because a further editorial in June suggested that "the leprosy question is becoming one of the questions of the day" (*Brit. Med. Journ.*, 1889a, p. 1364). It welcomed public discussion in the hope that attention to "this great pest" would result in convincing governments that the disease was contagious and so lead to "enforcing compulsory segregation." Subsequent concern about the disease became increasingly focused on leprosy in the colonies. It began to be monitored with increasing attention and an eye to the possibility of its "coming home." Lepers in India were reported as uncontrolled and uncontrollably spreading germs by sitting on iron railings outside a school attended by European children, selling fruit, and contaminating the wells of the city. They were depicted as interchangeable with the bacteria: "The Principal of St Xavier's College stated that the lepers rubbed their sores against the iron railings surrounding the Elphinstone High School, and that the boys afterwards sat upon them" (*Brit. Med. Journ.*, 1889b, p. 1261). There was a call for additional powers so that the Health Department could "deal effectively with the evil" (ibid.) and a suggestion made that police powers could also be increased.

A letter to the *Journal* in June summarized the spirit of the times: the 1867 Report was "dangerous and full of false conclusions" and as a result "we are now threatened with it at home," but "timely preventative measures in our Indian and Colonial possessions" will take care of the problem. "If we legislate in India and in the colonies, enough will be done; we shall check the disorder at the spring head" (Simms, 1889, p. 1491). One study presented sixteen cases which it used to develop an argument for "a system of precaution, of segregation, … regulations influenced and dictated by a spirit of Christian charity," and a "duty imperative upon England" to stamp out the disease (Donnet, 1889, pp. 301-5).

The push for legislation intensified, and South Africa and New South Wales enacted laws to detain those diagnosed with the disease. The *Journal* (1890a, p. 1047) was full of praise for the measures enacted in these colonies: "the public of England would be making a very great mistake if they supposed, because they heard of isolated cases of leprosy in distant parts of the colony, that the matter was

not being dealt with by the Government of the colony." In fact, the article maintained that in no part of the world were such responsible measures being taken. Prompted by the discovery of several Europeans with the disease, a Leprosy Bill was passed in New South Wales with "promptitude and uncompromising thoroughness" on November 20, 1890 (*Brit. Med. Journ.*, 1891, p. 779).

Attempted cultivation in India: the 1891 Leprosy Commission

In 1891, the Leprosy Commission in India set about investigating the disease, and for a brief moment of triumph thought that they had isolated the bacterium outside the body.[10] The Leprosy Commission had grown out of the National Leprosy Fund instituted on the death of Father Damien. Its first meeting was held on June 17, 1889, and the Prince of Wales was president. Its second meeting was held as a subscription dinner at the Hotel Metropole, London (Tebb, 1893, p. 295). The Prince of Wales' speech was recorded in the *Times* the next day. He described the "wide prevalence of leprosy in the Indian Empire as an undoubted fact" and also expressed the general impression that "the disease is increasing in India, as well as in many of our colonies" (*Times*, Jan. 14, 1890, p. 7). The Prince of Wales' address was followed by one from Sir Andrew Clarke, the president of the Royal College of Physicians. He described the increase in the disease in frightening terms: "The evidence was conclusive that not only did leprosy exist in larger measures than in recent years, but that new germ centers were springing up in various quarters and the old centers were widening, and before England and the civilized world there was looming a condition of affairs which might, by growth, threaten civilization" (*Times*, Jan. 14, 1890, p. 7). Colonial India was imagined as the soil in which the germ was multiplying, and as such an appropriate site for its investigation and attempted cultivation.

The Fund appointed a Commission of three (from the Royal College of Physicians, the Royal College of Surgeons, and the General Committee of the National Leprosy Fund) with two representatives from the India Auxiliary Committee to investigate the disease in India.[11] They left England on October 23, 1890, finished their research in late 1891, and prepared their report. They had been sent to do what the 1867 Report had failed to do, but their efforts were no less free from censure and controversy. According to Tebb (1893, p. 298), the publication of their report was held up on the excuse that the statistics on leprosy in India had not yet been completed, but, in reality, because their conclusions were "strongly objected to."[12]

One facet of this extremely comprehensive report involved research on the bacillus. The members of the Commission carried out a series of investigations in two separate teams. Rake, Buckmaster, and Thomson

conducted bacteriological investigations at Almora, while Barclay and Kanthack did the same at Sabathu. They converged on the laboratory at Simla. By June 6, the *Journal* reported the "Apparently successful cultivation of the *bacillus leprae*" by A.A. Kanthack and Surgeon-Major Barclay (members of the Leprosy Commission), a preliminary communication in which they triumphantly announced: "We have succeeded in isolating and cultivating from leprous tissues, removed under all aseptic precautions from patients *intra vitam*, a bacillus which may fairly claim to be the true bacillus of leprosy" (Kanthack *et al.*, 1891b, p. 1222). In this article, they describe obtaining free bacilli which they claimed were morphologically identical with the bacilli of leprosy and which could be stained by the Koch-Ehrlich method. Some qualification about the characteristics of the bacillus had to be made. It differed from the leprosy bacillus found in the tissues because it absorbed the aqueous methyl blue dye more rapidly and did not retain the fuchsine staining as tenaciously, but they were optimistic that they would be able to produce bacillus that would be equally resistant as that obtained from tissue samples, and they sent their result to several continental laboratories for criticism (ibid, p. 1223). Then, on June 20, the *Lancet* (1891, p. 1397) also announced that Rake and Buckmaster had succeeded in cultivating the leprosy bacillus in serum. In the meantime, Kanthack and Barclay (1891a, p. 331) were looking forward to a successful animal experiment in order to substantiate their claims.

Two of the appendices of the report detail the laboratory investigations. The investigators examined the distribution of the bacillus within bodily fluids (including blood, blisters, what they termed juice from tubercles, ulcers, and nerves); secretions (such as saliva); and excreta. They looked for the bacillus in the soil, water, fish, and flies. They conducted vaccination experiments, attempts at cultivation, and experimented with animals to investigate transmission.

In order to show that their cultivated bacillus was indeed *M. leprae*, they needed to be able to demonstrate its effect, and their best chance of doing this was using animal experimentation. Frustratingly, this was not achieved. Their ultimate conclusions in the report were dramatically modified from those that had been reported in the medical journals. Attempts to determine the pathogenic character of the bacilli they had cultivated were unsuccessful and so "it was impossible to affirm with certainty that the cultivation of the bacillus had been accomplished." So they were forced to confess:

> From the numerous recorded experiments of observers in various parts of the world, and from our own attempts at inoculation, we consider it extremely doubtful whether a true leprosy, such as we recognize clinically, can be produced in animals. In absence of this step, Koch's postulates remain unfulfilled, and it is impossible to say whether the cultures we obtained from leprous tissues and fluids are growths of leprosy bacilli or not (*Leprosy in India*, 1893, p. 439).

Ironically, the colonial soil of India had not been conducive to the cultivation of the bacillus.

Twentieth century attempts at cultivation

Seventy-two years later, in 'A review of leprosy research' given by Dr. R.J.W. Rees in March, 1963, to the Medical Research Council on the contribution made by the Council (either at the National Institute for Medical Research or under the auspices of the Leprosy Committee), he states that:

> The continuing failure to culture the human leprosy bacillus *in vitro* or to transmit the infection to experimental animals as a routine procedure has seriously restricted the scope of both fundamental and applied research in leprosy. Even the simplest, though basically essential, laboratory techniques for studying an infectious disease cannot be used in leprosy. For example, it is impossible to prepare a specific vaccine against leprosy or to test *in vitro* for chemotherapeutically active drugs. As a result progress of research in leprosy has been limited.[13]

In some ways nothing much had changed. The bacillus had still not been amenable to cultivation, nor had it been transmitted to experimental animals. Fascinatingly though, the animal model for leprosy research was just beginning to take off: experiment with *M. lepraemurium* in 1958, the measured growth of bacilli in the mouse footpad in 1960, and harvesting of *M. leprae* from the nine-banded armadillo from 1971. It might be argued that while *M. leprae* continued to be as elusive as ever, analogies with the functioning of the bacillus in a few extremely specific animals enabled scientists to outwit it. How, in this era of investigation that draws on animal models, the analogies between natural growth and the mysteries of leprosy were reinvented or discarded remains to be examined.

Mapping the genome of an uncultivated bacillus

The mapping of the genome of *M. leprae* has produced another dimension for understanding *M. leprae*[14] so that the logic of the botanical metaphor may no longer be necessary in the face of the powerful rhetorical repertoire commanded by DNA. Mapping and decoding DNA enables access to the "language of life," and genomes are variously described as "the book of life," "the code of codes," and as "blueprints," "information," "lexicons," and "encyclopedias" (Bacsik, 2002, p. 2). DNA is understood as "a biochemical language that we are learning to read by learning to write" (ibid.). Its mysteries can be disentangled by identification and matching. The schematic language of the gene is written in layers and has only to be read. *M. leprae* can now be conceptualized as a series of genes that can be grouped and described,

often by analogy with those identified in another genome, such as *M. tuberculosis*. Technologies other than the microscope are available to view it. Instead of a sample of tissue in serum under a microscope, it now also exists as a genome database that can be explored via Leproma, a genome browser located on the web at http://genolist.pasteur.fr/leproma. A search of the genome can be conducted by gene name, region in the genome, gene function, by DNA or protein patterns, or by a search of the DNA sequence or protein sequence. Results are presented as a list or a drawing, and the DNA or protein sequence of a single gene can be viewed or downloaded (Jones, 2001, pp. 470-7). The whole sequence of the chromosome is available. Its density, length, number of genes, pseudogenes, and other respective genetic components are enumerated. In the era of the genome, it would seem that the botanical metaphor has given way to one in which information is revealed through processes of translation and decoding.

Firstly, it is possible to describe something of the evolutionary changes that have taken place. *M. leprae* has undergone a loss of genes and a subsequent loss of ability to respond to different environments. It is described as a decaying genome: one that has undergone considerable downsizing during its evolution. It has a trajectory and an ancestry — a former self that was more complex. Less than half of the genome contains functional genes. Its "immediate ancestor may have already undergone reductive evolution and … a single clone then expanded and … disseminated globally" (Eiglmeier *et al.*, 2001a, p. 390). As well as a history, it is imagined as having a greater degree of agency. Adaptation has been selective and self-interested. Chromosomal rearrangements and gene deletions and duplications have had a profound effect on the biology of *M. leprae* and in turn on leprosy itself (Cole *et al.*, 2001, p. 459). Yet this decay is evidence of a reduction in redundant functions so that the major repair pathways are still intact (Dawes *et al.*, 2001, p. 411).

Mapping makes it possible to answer some questions. *M. leprae* strains from different origins exhibit no obvious, important genome diversity (Eiglmeier *et al.*, 2001b, p. 465). The genome still retains its full complement of heat shock proteins, explaining why, given that its optimal growth temperature is 32°C, it multiplies in the extremities of the body. It is possible to determine the uniqueness of the metabolic pathways of the genome, as well as compare them to that of *M. tuberculosis*, indicating that the survival of *M. leprae* is dependent on a specialized niche. It has extremely reduced genes for dealing with respiration and an oxygen-rich environment, and hence exists successfully in an intracellular environment, which has relatively constant conditions. The pathogenicity of the mycobacterium depends on its ability to survive in the macrophage or in the Schwann cell (Eiglmeier *et al.*, 2001a, p. 395). As such it is characterized as "extremely specialized" and it is "irreversibly committed … to a lifestyle characterized by slow growth

and necessarily slow central metabolism" (Wheeler, 2001, pp. 402-3). The basis for resistance to dapsone and rifampicin is able to be understood (Grosset *et al*., 2001, pp. 429, 431). In addition, the susceptibility of *M. leprae* to other drugs can be determined.

Yet some questions are not answered. In considering the metabolic pathways that are retained by the mycobacterium, Wheeler (2001, pp. 405, 406) comments that "there is something unusual about this whole area of purine and pyrimidine metabolism in *M. leprae*. Why should the biosynthetic pathways have been retained in such a host-dependent pathogen?" He speculates that "maybe it is part of the mechanism that allows the leprosy bacillus to survive and grow within the rather metabolically inert Schwann cells." Wheeler also speculates about the inability to grow the bacillus *in vitro*:

> Why cannot *M. leprae* be grown axenically; do the lesions in energy metabolism only allow interrupted growth when conditions are just right in the host? Are media too toxic, at least in aerobic conditions? With a massive loss of regulatory functions have those that would allow *M. leprae* to adapt to axenic culture been lost?

One of the most troubling questions associated with *M. leprae* in the nineteenth and twentieth centuries, arising out of the newly developed sciences of microbiology and bacteriology, has given rise to many other questions in the twenty-first century. The question of *in vitro* cultivation is now a question about the metabolism of energy, appropriate media, and evolutionary adaptation. Interestingly, the rhetoric of the genome, that of writing and reading, of decoding, translation, and making all clear, is being used to explain the bacillus as it was understood and continues to be understood in botanical terms. The 'new' questions are still as much about the right 'soil' or appropriate conditions to facilitate growth. Ironically, while leprosy research has for such a long time drawn its logic from a view of the world in which a seed and soil metaphor expressed many different aspects of the activity of the disease, in spite of the newly available technology of elucidation, the bacillus itself continues to be unreceptive to cultivation.

NOTES

[1] Hansen published his findings 'Causes of leprosy' as part of his annual report for 1873 to the *Norwegian Medical Society*. He says that he identified the bacillus in 1871 (Hansen *et al*., 1895, p. 31).

[2] "The various clinical manifestations in leprosy are the results of the variations in the tissue response of the host to the presence of leprosy bacilli in the body. In other words, they are determined by the host-parasite relationship" (Dharmendra, cited in Hastings, 1985, p. 88).

[3] A chapter in Hastings (1985) is devoted to shifts in classification, highlighting a struggle between the need for both clinical and histological classifications. The extent of this ongoing reclassification process can only be appreciated by tracing some of its mutations.

[4] In leprosy, both the reference points for measuring the incubation period — the time of infection and the time of onset of disease — are difficult to define; the former because of the lack of adequate immunological tools and the latter because of the insidious nature of the onset of leprosy (WHO web pages http://www.who.int/lep/disease/disease.htm).

[5] A history of attempts to cultivate the bacillus is outlined in Ryan and McDougall (1988).

[6] The copy of the *Brit. Med. Journ.* from which I am summarizing this story has the name of the public school that the child was attending pencilled in the margin.

[7] The editorial indicated that M. Besnier, the physician of the Hopital Saint-Louis, had delivered an address at the Academie de Medecine on October 11 on the 'Nature, origin, and propagation of leprosy,' and Archdeacon Wright had addressed a letter to the *Times* on November 8 entitled 'The spread of leprosy.' Both expressed concern and alarm that the disease was contagious.

[8] A number of studies of leprosy in the Middle Ages in Europe and Great Britain were produced that supported this argument. The waning of the disease in the Middle Ages was attributed to the natural horror with which the general population responded to the disease, so that the afflicted were inevitably shunned: for example, James Y. Simpson (1842, 1841); in 1895, as part of a collection of Prize Winning Essays published by the Sydenham Society, George Newman wrote *On the history of the decline and final extinction of leprosy as an endemic disease in the British Isles*; and, demonstrating the longstanding concern with the disease, Charles A. Mercier wrote *Leper houses and medieval hospitals*, in 1915.

[9] Dr. Arning presented a paper at the First Dermatological Congress in Prague, June 10-12, 1889, describing how he had obtained permission to suggest to a condemned criminal, Keanu, a choice between death by execution or becoming a subject in a medical experiment. Keanu cooperated with the latter option in September 1884 and was injected with leprous tissue. In December 1887, he showed unmistakable symptoms of the disease. In September 1888, he was diagnosed with fully developed leprosy. Arning concluded that the disease could be conveyed by inoculation, specifically vaccination ('The inoculation of leprosy,' in *Brit. Med. Journ*., pp. 90-1, Jan. 11, 1890). Subsequent medical reports in the *Brit. Med. Journ.* on April 19, 1890, p. 909 and pp. 917-8, revealed that members of his immediate family had already been exposed to the disease, and the case sank into oblivion. Most of the literature of the time that argued the case for contagion referred to this ethically suspect experiment for support.

[10] Articles in the *Brit. Med. Journ.* trace the journey taken by the Commission. The *Journal* recorded this in the following articles: 'The Leprosy Commission in India,' Feb. 7, 1891, p. 296; 'The Leprosy Commission in India,' Feb. 28, 1891, p. 475; 'The Leprosy Commission in India,' May 9, 1891, p. 1031; 'Leprosy Commission,' May 23, 1891, p. 1137; 'Apparently successful cultivation of the *Bacillus Leprae*,' by A.A. Kanthack and Surgeon-Major Barclay (Members of the Leprosy Commission), Jun. 6, 1891, p. 1222; 'Pure cultivation of the leprosy bacillus,' Jun. 20, 1891, p. 1330; and 'Cultivation of the leprosy bacillus in serum,' Jun. 27, 1891, p. 1395.
The *Lancet* also traced the journey and experiments of the Commission in the following: 'The Leprosy Commission,' Feb. 7, 1891, p. 324; 'The Leprosy Commission,' Feb. 28, 1891, p. 500; 'The bacillus of leprosy,' Jun. 20, 1891, p. 1397; 'The Leprosy Commission,' Jun. 27, 1891, p. 1440; 'The Leprosy Commission in India,' Aug. 8, 1891, p. 303; 'The Leprosy Commission,' Aug. 29, 1891, p. 498; 'The Leprosy Commission,' Oct. 10, 1891, p. 827.

[11] Beaven Rake, George Buckmaster, and Alfred Kanthack were appointed from the College, the General Committee, and the Surgeons, respectively. The appointees from India were Surgeon-General Barclay and Deputy Sanitary Commissioner Surgeon-General S. J. Thompson.

[12] The reasons that the recommendations of the Leprosy Investigation Commission were objected to by the executive committee of the National Leprosy Fund are explained in Tebb, but also in Buckinghams (2002, pp. 174-8).

[13] Public Record Office: FD7/1190. *Medical Research Council: Tropical Medicine Research Board: special subject 'nvitation to Dr. R.J.W. Rees to address noon session 8th March 1963.*' Rees then goes on to summarize the leprosy program at the institute. One facet of this was the use of murine leprosy as a model for human leprosy. This work is conducted on the basis of an extended analogy between murine leprosy and human leprosy. Both were chronic infections caused by acid-fast bacilli existing predominantly as intra-cellular parasites and causing surprisingly little damage to the host cell. Projects included attempts to measure the viability of murine leprosy bacilli, its rate of multiplication in tissue culture, and the application of the results of studies on murine leprosy to human leprosy in collaboration with the Research Unit (MRC/Malayan Government), Sungei Buloh leprosarium, Malaya.

[14] The analysis of the first complete *M. leprae* cosmid sequence was conducted in 1993. The genome sequencing project was coordinated by Stewart Cole and Bart Barrell, and supported by the Association Française Raoul Follereau, ILEP, the Heiser Program for Research in Leprosy and Tuberculosis of The New York Community Trust, the World Health Organization, and the Institut Pasteur. Additional funding was provided by the Wellcome Trust: The complete genome sequence of the TN strain of *Mycobacterium leprae* comprises 3,268,203 bp, with a G+C content of 57.79%. The start of the sequence is the first base of the *dnaA* gene, close to the origin of replication. The TN strain was initially isolated from a patient in Tamil Nadu, India, then subsequently passaged in a nine-banded armadillo at the National Institute for Medical Research, at Mill Hill in London. DNA was prepared from bacteria isolated from the liver and used either to construct a cosmid library in Lorist6 or a whole-genome shotgun library in pUC18. For details of the cosmid library see K. Eiglmeier; N. Honoré; S.A.,Woods; B. Caudron; S.T., Cole. 'Use of an ordered cosmid library to deduce the genomic organization of *Mycobacterium leprae*,' *Molecular Microbiology*, 7:2, 1993, pp. 197-206.
Information about, and data from, previously sequenced cosmids is still available (http://www.sanger.ac.uk/Projects/M_leprae/cosmids.shtml and http://genolist.pasteur.fr/Leproma/help/project.html).

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