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Plague and Leprosy in the Middle Ages: A Paradoxical Cross-Immunity?

The interaction of plague and leprosy during the great epidemics of the 14th century has been the subject of considerable historical interest. It had, until recently, been an historical commonplace that the Black Death of 1347–1350 killed off huge numbers of the persons residing in leprosaria, although it was equally widely held (and still often is) that such persons did not suffer from the same disease called leprosy today.^{1–5} There have been some modifications of both aspects of this traditional view, among a few recent historians, who have countered with the view that leprosy in late medieval Europe was indeed leprosy as known today and that, whatever the effect of plague, leprosy was already on the decline

when plague struck.^{6, 7} This paper will consider the interaction of the two diseases in greater depth, relying both on historical data and modern knowledge of the two diseases. This analysis leads to a paradox. On the one hand, there is reasonable evidence to indicate that lepromatous leprosy (the type almost always diagnosed as leprosy in the late medieval period) confers an effective immunity to plague. On this basis, plague should increase the proportion of recognized leprosy patients within a given population. While the recent revisionist view that leprosy was declining independently of and before the arrival of plague is correct, it is also readily demonstrated on historical grounds that, due to the particular social and institutional situation of leprosy patients in medieval Europe, plague in fact contributed further to the decline in the incidence of leprosy in Western Europe. A situation in which one disease confers an immunity to another, while the latter still

¹ Bonser, W. *The Medical Background of Anglo-Saxon England; a Study in History, Psychology, and Folklore*. London: Wellcome Historical Medical Library, 1963, p. 371.

² Brody, S. N. *The Disease of the Soul: Leprosy in Medieval Literature*. Ithaca, New York: Cornell University Press, 1974, pp. 21–59.

³ McNeill, W. H. *Plagues and Peoples*. Garden City, New Jersey: Anchor Press, 1976, p. 175.

⁴ Innes, J. R. An approach to the history of leprosy. *Ciba Symp.* 7 (1959) 117–123.

⁵ MacArthur, W. Medieval leprosy in the British Isles. *Lepr. Rev.* 24 (1953) 8–19.

⁶ Richards, P. *The Medieval Leper and His Northern Heirs*. Totowa, New Jersey: Rowan and Littlefield, 1977, pp. 5–93.

⁷ Ell, S. R. Leprosy. In: *Dictionary of the Middle Ages*. Strayer, J. R., ed. New York: Charles Scribners' Sons, 1986, vol. 7, pp. 549–552.

hastens the disappearance of the first, may plausibly be termed a paradoxical cross-immunity. Perhaps more importantly, however, the situation to be described herein acts as a reminder of the fact that diseases do not exist as microbiological and immunological entities alone, but are part and parcel of the social circumstances of a given time and place. Certainly, this has ever been a feature of leprosy, whose social sanctions and prejudices have frequently been as onerous as the disease itself.

The traditional historiographic position.

The view that plague killed off many persons diagnosed as suffering from leprosy is based on two very compelling facts. In the first place, it is generally accepted that the single epidemic of 1347–1350 killed one third of the population of Western Europe.^{3, 8, 9} Secondly, it was noted both by contemporary commentators on the plague epidemics and by modern historians that leprosaria were often empty or nearly so in the wake of the epidemic. Many historians have further argued that leprosy patients had low immunity, being chronically ill, and they have assigned plague a Malthusian role in destroying the weaker elements of society.^{2, 10, 11} On this basis, the argument that plague was instrumental in the disappearance of leprosy seems eminently reasonable. As shall be shown, however, the historical facts taken out of context are misleading, and the concept of the interaction of the two diseases is totally incorrect.

An alternative view. In opposition to this traditional view, I should like to offer an alternative which, hopefully, will integrate the recent advances in our knowledge of when the incidence of leprosy actually began to decline with a more accurate understanding of the predicted interaction of plague and leprosy. In the first place, it has been well demonstrated that the incidence of leprosy was sharply in decline when plague

struck, so that the latter disease cannot be a major precipitant of the former's disappearance. Further, the immune defect in lepromatous leprosy is specific and not a generalized immune-deficiency (or at least not until late in the course of that form of Hansen's disease). In fact, lepromatous leprosy in many instances represents a hyper-immune state. There is laboratory evidence indicating that lepromatous leprosy could be expected to confer some immunity to plague. Long before the laboratory evidence was available, anecdotal evidence had appeared to suggest that such an immunity in fact exists. Thus, far from killing off the population of hospitalized Hansen's disease patients, plague could be expected to increase the proportion of such persons in the general population.

Diseases, however, do not exist only as laboratory entities. As T. S. Eliot wrote,¹² "Because I know that time is always time/ And place is always and only place/ And what is actual is actual only for one time/ And only for one place." No disease can exist apart from the particular social and environmental factors of a given time and place. Such factors may profoundly affect the expression of a disease. In the case of the interaction of plague and leprosy in the Later Middle Ages, these factors acted to turn the cross-immunity between the two diseases into a circumstance which still caused plague to hasten the decline of leprosy. This situation I have termed a paradoxical cross-immunity. It is the interplay of social and microbiological factors that produces such a paradox.

The diagnosis of plague and leprosy in medieval Europe. Until quite recently, and persistently even now, many historians have considered medieval "leprosy" to be a catch-all term for a variety of skin diseases, and thus unreliably related to leprosy as known today.^{13, 14} This remains the view of such an eminent historian as William McNeill,³ as well as Saul Nathaniel Brody, one of the most influential writers on medieval leprosy.² Since 1950, a body of evidence has

⁸ Ziegler, P. *The Black Death*. New York: Harper & Row, 1971, pp. 16, 23, 43, 78, 163.

⁹ Gottfried, R. S. *The Black Death*. New York: The Free Press, 1983, pp. 1–12, 106–148.

¹⁰ Herlihy, D. Population, plague and social change in Pistoia, 1201–1430. *Econ. Hist. Rev.* (2nd series) **18** (1965) 225–244.

¹¹ Postan, M. M. Some agrarian evidence of declining population in the later Middle Ages. *Econ. Hist. Rev.* (2nd series) **2** (1950) 148–161.

¹² Eliot, T. S. *Ash Wednesday*, 1, 17–20.

¹³ Singer, C. A thirteenth century clinical description of leprosy. *J. Hist. Med.* **4** (1949) 237–239.

¹⁴ Dols, M. Leprosy in medieval Arabic medicine. *J. Hist. Med.* **34** (1979) 314–333.

accumulated which renders their viewpoint untenable.

It has long been known that Western Europe began to recover both the medical writings of Galen and the other great classical physicians along with their Islamic commentators and peers around the year 1000. By 1200 A.D., Western physicians had in their hands writings which clearly describe leprosy as we know it. Consider, for example, this passage from the Italian ecclesiastic and physician, Theodoric of Cervia: "... the face becomes puffy, the hairs of the eyelids and eyebrows thin out ... and fall out ... the voice ... finally grows hoarse ... if patients are pricked in the ankle bone [they are] unaware, they feel little."¹⁵ Clearly, there is much even in this short passage (Theodoric devotes many pages to leprosy) which unmistakably pertains to leprosy. Still, the writings of one 13th-century bishop do not represent the mean of medical practice in the Middle Ages. The fact that some men wrote of the true signs of leprosy—along with, to be sure, due to the conceptual framework of disease in use at the time, a great deal that bears no resemblance to modern leprosy—does not mean that the ordinary diagnosis was correct.

Fortunately, four examinations of the skeletal remains of persons buried in the cemeteries of medieval leprosaria have uniformly shown bone changes of leprosy in approximately 80% of cases.^{16–21} The characteristic destruction of the alveolar process of the maxilla with consequent loss of the central incisors and canine teeth, erosion of the hard palate, and destruction of the nasal bone are all part of the so-called *facies*

leprosa. Wilhelm Møller-Christensen's pioneering work on the excavation at Naestved in Denmark began the recognition that persons in medieval leprosaria suffered from lepromatous leprosy. With subsequent duplication of these results in England and then Germany, the medieval diagnosis of leprosy has been completely vindicated. If anything, the disease was under-diagnosed, as influential figures such as John of Gaddesden in the 14th century counselled that no man be judged a "leper" until his face had been destroyed by the disease.²² In general, such conservative advice was followed, for the diagnosis brought severe legal and religious sanctions. Persons formally diagnosed as having leprosy were forbidden burial with other Christians and could not share daily life with them either. Seen as the outward figure of an unclean soul, leprosy evoked a special church ceremony in which the "leper" was enjoined to be "dead unto the world, but alive unto Christ." Nor was the death just a matter of words. A person with leprosy was legally dead and his heirs, in many parts of Europe, could inherit his property. After some wavering, the Church decreed, however, that leprosy was not grounds for divorce or dissolution of marriage, and that the spouse of a person afflicted with leprosy could not remarry until the infected person died.⁶

Oddly, although the evidence is much more secure with regard to the diagnosis of leprosy, there has been little question that plague, in the sense of infection of humans by *Yersinia pestis*, was the disease which produced the catastrophic mortality of 1347–1350, as well as hundreds of other epidemics. Recent painstaking studies have shown that plague was indeed responsible for most "plague" deaths, although the term was also used generically and sometimes covered simultaneous epidemics of plague and such diseases as smallpox, typhoid, and other infections.^{23, 24}

¹⁵ Theodoric of Cervia. *The Surgery of Theodoric*. Campbell, E. and Colton, J., trans. New York: Appleton Century Crofts, 2 vols., 1955–1960, vol. 2, pp. 167–182.

¹⁶ Møller-Christensen, V. *Bone Changes in Leprosy*. Copenhagen: Munksgaard, 1961.

¹⁷ Møller-Christensen, V. Skeletetfund fra St. Jorgens Kirke i Svendborg. *Fynski Minder* 5 (1963) 35–49.

¹⁸ Anderson, J. E. *Studies in the medieval diagnosis of leprosy in Denmark*, M.D. thesis, Copenhagen, 1969.

¹⁹ Schmitz-Cliever, E. Zur Osteo-archäologie der mittelalterlichen Lepra. *Med. Hist.* 6 (1971) 249–263 and 8 (1973) 182–200.

²⁰ Schmitz-Cliever, E. Das mittelalterliche Leprosarium Melatin bei Aachen. *Clio Med.* 7 (1972) 13–34.

²¹ Bayliss, J. Domus leprosa—community care in medieval England. *Nurs. Times* 75 (1979) 62–67.

²² John of Gaddesden. *Rosa Anglica* (Venice, 1507), folios 102R–104V.

²³ Carmichael, A. *Plague and the Poor in Renaissance Florence*. London: Cambridge University Press, 1968, pp. 21–38.

²⁴ Shrewsbury, J. F. D. *A History of Bubonic Plague in the British Isles*. London: Cambridge University Press, 1979, pp. 17–36.

Lepromatous leprosy and plague: Cross-immunity. There are two main bases for the claim that lepromatous leprosy confers at least some immunity to plague. First, there are anecdotal accounts of those situations in which plague has broken out in places where leprosy is prevalent. It has been observed that leprosy patients rarely succumb. The most famous such situation is that described by Girard, who spent over 30 years in association with leprosy in Madagascar, and noted the extreme paucity of cases among the hospitalized patients, even when the disease was manifest among the hospital staff and among nonleprosy family members living in the hospitals.^{25, 26} This observation led to a primitive animal model employing *Mycobacterium lepraemurium* in rats, many of which showed immunity to plague, when a control group exhibited almost 100% mortality in the face of the same inoculum of plague bacilli.²⁷

Animal models of leprosy and animal cross-immunities in general have not always proven reliable in studying the epidemiology of human diseases, but another line of research has suggested that lepromatous leprosy is, in many instances, a hyperimmune state. Far from being the result of a generalized immune deficit, lepromatous leprosy appears to result from a very specific defect in the immune system. In response to other antigens, persons with lepromatous leprosy often exhibit exaggerated immune responses.²⁸⁻³⁰ One case in which this response is very intriguing is that of typhoid. de Almeida and colleagues showed a markedly enhanced serologic response to typhoid antigen in persons with leproma-

tous leprosy.³¹ This is of particular interest because typhoid is a disease which is also felt, on experimental and epidemiological grounds, to confer immunity to plague.^{32, 33}

A more controversial possible contributor to relative immunity lies in the relative iron status of leprosy patients versus that of those most at risk for plague. There is some experimental evidence that available serum iron is essential to the plague bacillus, and that those persons with the most such available iron are most at risk of death. As noted, this is controversial and is based largely on animal experimentation, but it has been used to explain certain aspects of the epidemiology of human plague.³³⁻³⁶ Of equal interest is the fact that the diets used in most medieval leprosy were laid down by a limited number of religious writers and were very sparse in meat, while containing large amounts of vegetables whose phytates impair iron absorption.^{6, 37, 38} Thus, persons in leprosy would tend to have been iron-deficient, a state which may confer some protection to plague.³³

The older historiographical stereotype of the frail, leprosy patient open to all manner of other infections, succumbing in excess proportion to plague, needs to give way to one in which a hyperimmune patient witnesses an epidemic which decimates the

²⁵ Girard, G. Les lépreux sont-ils réfractaires à la peste? Bull. Acad. Natl. Med. (Paris) **136** (1952) 80-83.

²⁶ Girard, G. Quel fût le sort des lépreux au cours de la pandémie pesteuse du moyen âge (1348-1350)? Bull. Soc. Pathol. Exot. Filiales **68** (1975) 33-37.

²⁷ Girard, G. Comportement des rats lépreux (maladie à bacille de Stefansky) vis-à-vis de l'infection pesteuse expérimentale. C. R. Soc. Biol. (Paris) **145** (1951) 1627-1630.

²⁸ Navalkar, R. G. Immunology of leprosy. CRC Crit. Rev. Microbiol. **8** (1980) 25-47.

²⁹ Ostler, H. B. The immunology of Hansen's disease. Int. Ophthalmol. Clin. **25** (1985) 117-137.

³⁰ Bloom, B. R. and Mehra, V. Immunological unresponsiveness in leprosy. Immunol. Rev. **80** (1984) 5-28.

³¹ de Almeida, J. O., Brandao, H., de Lima, E. G. and Lippelt, A. Enhanced serologic response of lepromatous patients to antityphoid vaccination. Int. J. Lepr. **32** (1964) 292-296.

³² Brygoo, E. R. and Rajenison, S. Recherche d'une immunité paraspécifique pour le bacille de Yersin chez des souris inoculées avec des salmonelles. Arch. Inst. Pasteur Madagascar **41** (1972) 13-16.

³³ Ell, S. R. Immunity as a factor in the epidemiology of medieval plague. Rev. Infect. Dis. **6** (1984) 866-879.

³⁴ Ell, S. R. Iron in two seventeenth-century plague epidemics. J. Interdiscipl. Hist. **15** (1985) 445-457.

³⁵ Wake, A., Yamamoto, M. and Morita, H. Double effects of an iron drug in induction of mouse plague caused by an attenuated strain. Jpn. J. Med. Sci. Biol. **27** (1974) 229-239.

³⁶ Tsukano, H., Yamamoto, M. and Wake, A. The effects of an iron drug on the growth of plague microorganisms *in vitro* and in guinea pig skin. Jpn. J. Med. Sci. Biol. **25** (1972) 85-93.

³⁷ Bothwell, T. H. and Charlton, R. W. Definition, prevalence, and prevention of iron deficiency. Clin. Hematol. **11** (1982) 309-325.

³⁸ Bothwell, T. H., Charlton, R. W. and Cook, J. D., eds. *Iron Metabolism in Man*. Oxford: Oxford University Press, 1978, pp. 25-28.

"normal" population while he is spared plague for reasons totally beyond his understanding.

The paradox. Although the plague epidemic has been seen as the culmination of a Malthusian crisis,^{10, 11} there is little about plague to support such a view. Plague is not a disease of the malnourished, and contemporaries of the epidemic felt that the rich were more likely than the poor to die of the disease, if infected. The rich were notorious for fleeing to their country homes in time of plague (the role of plague in the whole phenomenon of the country home among the wealthy urbanites has never received the scholarly attention it deserves, but the Palladian villas along the Brenta River in Italy probably would not be there were it not for recurrent plague), so that rate of infection was clearly not equal among social classes, but the rich were seen at even greater than usual risk to die if they contracted plague.³⁹ Most modern plague epidemiology places the burden of mortality on young adults, especially males, and children past the age of five.⁴⁰⁻⁴² Some studies from the antibiotic era still indicate that an adult male is more than twice as likely to die of plague as a female with the same infection.⁴² Thus, plague tends to destroy those members of a society, like the male-dominated world of the Later Middle Ages, that such a society can least afford to lose.

In at least two ways the epidemiology of plague in medieval Europe contributed to the decline in the incidence of leprosy. Persons in leprosaria were totally dependent on the charity of others for their food and other daily necessities. In particular, religious orders often operated leprosaria. Many of these orders are known to have lost more than 50% of their membership in the great epi-

demic of 1347-1350 alone.^{43, 44} Social services, rudimentary at best in medieval times, collapsed in the face of plague. Venice, a city which represented the model for the rule of law (and the strict observance thereof), emptied its prisons to try to maintain adequate manpower.⁴⁵ Of 18 physicians employed by that city in February of 1348, only one was still alive in July.^{46, 47} In such circumstances, the fact that many leprosaria were empty in the aftermath of the epidemic may mean that the neglected patients had to flee and fend for themselves, that they died of starvation or neglect, but not necessarily or even likely that they died of plague.

With a third of the population lost, population density dropped accordingly. To the extent that leprosy is a disease associated with overcrowding, plague may again have backhandedly contributed to its demise by decreasing such density. It has been well documented that the population densities in certain portions of Tuscany were higher in 1300 than they would be again until the 19th century.¹⁰ The populations of cities, however, tended to recover rapidly—mainly through emigration from the countryside⁴⁸—so the extent of this effect was probably relatively small.

Still, plague cannot be invoked as a primary cause of the decline of European leprosy. Careful historical studies have shown that half the leprosaria beds in England, full in 1200 were empty in 1300, an interval during which the population of England increased about 100%. Similar studies have shown the same pattern elsewhere in Europe.^{6, 49} Thus, leprosy was in full decline

³⁹ Cipolla, C. M. *Fighting the Plague in Seventeenth Century Italy*. Madison, Wisconsin: University of Wisconsin Press, 1981, pp. 7-18, 51-88, 89-109.

⁴⁰ Araujo, R. dos S. and Sherlock, I. A. Aspectos clínicos, terapêuticos e profiláticos da peste no estado de Bahia; período de 1936 a 1967. *Rev. Bras. Malariol. Doenças Trop.* 23 (1971) 51-63.

⁴¹ Butler, T. A clinical study of bubonic plague: observations of the 1970 Vietnam epidemic with emphasis on coagulation studies, skin histology, and electrocardiograms. *Am. J. Med.* 23 (1972) 268-276.

⁴² Hoepfich, P., ed. *Infectious Diseases*. 2nd ed. Hagerstown, Maryland: Harper and Row, 1972, p. 1141.

⁴³ Biraben, J.-N. *Les Hommes et la Peste en France et dans les Pays Européens et Méditerranéens*. Paris: Mouton, 1975, vol. 2, p. 138.

⁴⁴ Renouard, Y. Conséquences et intérêt démographiques de la peste noire de 1348. *Population* 3 (1948) 459-466.

⁴⁵ Archivio di Stato di Venezia, Maggior Consiglio, Spiritus, 154v.

⁴⁶ Cecchetti, B. La medicina in Venezia nel 1300. *Archivio Veneto* 25-26 (1883) 351-381 and 77-111.

⁴⁷ Ell, S. R. Maestro Francesco da Roma: portrait of a Renaissance public health officer. *Persp. Biol. Med.* 29 (1986) 539-544.

⁴⁸ Weiner, G. M. The demographic effects of the Venetian plagues of 1576-77 and 1630-31. *Genus* 26 (1970) 40-57.

⁴⁹ Cougoul, J. E. *La Lèpre dans l'Ancienne France*. Bordeaux: Delmas, 1943.

when plague struck and any plague effect would be at most additive and in no wise causative.

Of the two effects evoked as paradoxical here, the matter of neglect seems by far the more potent. We know that regular clergy (i.e., monks and friars, as opposed to parish priests) suffered devastating mortality. In every major study, it has been found that religious orders lost over 50% of their members.^{43, 44} Renouard, for example, has shown that among Dominican houses, Montpellier had 133 deaths among 140 friars, while Maguelonne lost 153 of 160.⁴⁴ The death rates in these cases are well over approximately 95%. Others fared better, but it is easy to see how a house charged with looking after leprosy patients would be unable to provide even the most basic services when barely a brother survived. Condemned by law to remain in the hospital or take to a wandering life, leprosy patients might choose the latter course and survive, but to anyone examining the hospital in the wake of the epidemic, they would almost certainly be counted among the dead. Many persons sought scapegoats for the epidemics—blaming and harming Jews is but the most famous example—so that a wandering “leper” could not expect even the usual meagre alms. We have no way of knowing which course the patients who survived in the hospitals took, but it is clear that their lot was an unenviable one in either case and led to a real or assumed death in the wake of the Black Death.

Of the real effects of changing population densities, our comments must be even more speculative. Assigning some role is reasonable. Scandinavia was one of the more sparsely settled areas of Europe, yet leprosy persisted there long after it essentially disappeared in vastly more heavily populated

areas such as Italy, leaving some questions no nearer answers than ever.

Conclusion. The traditional historiographic tendency to attribute the disappearance of leprosy from Western Europe to the wave of plague epidemics which began in 1347 requires modification. On the one hand, leprosy was already steeply declining in Western Europe (except for Scandinavia) when plague struck. The underlying cause for this earlier decline remains totally obscure. As a pure disease, plague should increase the proportion of persons with leprosy in a given population, since lepromatous leprosy (as we have noted the type essentially equated with the whole disease in late medieval Europe) appears to confer an immunity to plague. Yet no disease exists in society as a pure disease, but acts through the institutions, attitudes, and responses of that society. When the social setting is taken into account, plague hastened the decline of leprosy in other ways, especially through the neglect of hospitalized patients. This situation is a forceful reminder that no disease can be separated from its social setting. In the case of plague and leprosy in the Middle Ages, the microbiological and immunological factors, on the one hand, and the social world of leprosy, on the other hand, led to two divergent results. Lepromatous leprosy in medieval Europe protected its victims from death due to plague. Acting in the world of medieval society, however, plague killed and dispersed leprosy patients as effectively as if they had been directly infected.

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