Chapter 1
Great Plagues of the Past and Remaining Questions

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Abstract Due to the difficulty of obtaining tissue samples from victims of the ancient plagues, it is not always possible to utilise palaeomicrobiology techniques to determine the etiology of ancient infection. Therefore, it is often necessary to utilise other means to arrive at a likely diagnosis. The most helpful of these is the literary description of the disease. While this is often the best evidence available, working with such documents can prove difficult. Three great plagues of the ancient world, the Plague of Athens, the Antonine Plague, and the Justiniac Plague are described in either Latin or ancient Greek. The difficulties encountered when translating any ancient foreign language are compounded by the fact that so many words in these languages have a variety of meanings. This chapter reviews the three great plagues of antiquity from a clinical perspective.

1.1 Overview

There are numerous historical accounts of epidemics in ancient times. These accounts of epidemics or plagues describe infectious diseases ravaging ancient populations. Extant accounts of ancient plagues are limited. Certainly, many epidemics and outbreaks occurred in the ancient world that were not recorded or, if they were recorded, have been lost through the ages (Martin and Martin-Granel 2006). In the accounts that have survived, there are inherent difficulties of description and interpretation (Major 1978; Procopius 1981; Thucydides 1919). The descriptive terms used by the ancients are either not those that are we are familiar with today or, more problematic, multiple interpretations of terms are used to describe the physical findings in afflicted patients, which results in various possibilities and different assumptions are made according to translator variability and interpretation. Nevertheless, until recently, the only approach with which to try to determine the etiologies of ancient plagues has been examination of the relatively few written accounts that have survived over time. These accounts

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are variable and sometimes conflicting, and are dependent upon translator interpretation of the languages in which they were first described. Using the historical approach, there are other interpretational problems. The observers or recorders of the descriptions of ancient epidemics varied in their observational and descriptive capabilities as well as in their knowledge of medical terms used at the time (Page 1953; Parry 1969). All of these confounding variables make it difficult to determine the exact cause of the various plagues that afflicted the ancients (Brothwell and Sandison 1967; Cartwright 1972; Shrewsbury 1950).

In the absence of scientific proof, the historical method remains the backbone of an analytical approach to the problem of ancient plagues. Ancient descriptions provide at least some information about locale, season, descriptions of the findings, extent of the epidemic, mortality, and clinical sequelae. Although subject to interpretational difficulties, much has been learned by applying the historical method to determine the cause of widespread pestilence in earlier epics (Bollet 1987; Cunha 2004b; Cunha and Cunha 2006). Currently, methods are available to determine the actual cause of ancient plagues, but these methods depend on intact DNA for analysis, and are methodology dependent (Gilbert et al. 2003; Drancourt and Raoult 2005).

At the present time, sophisticated analytical methods are available to analyse ancient DNA in preserved tissue samples, permitting accurate identification of microorganisms present in samples from ancient animal and human remains (Cooper and Poinar 2000). As with the historical approach, there are problems with DNA-dependent technologies. The first difficulty using the scientific approach is to find suitably preserved samples to analyse. Just as there are problems with historical interpretation, so there are also problems with palaeomicrobiology (Hofreiter et al. 2001; Pääbo 1989). Firstly, there are relatively few geographical areas that have climatic conditions suitable for the preservation of tissue specimens in a state amenable to DNA analysis (Zink et al. 2002). The most likely situations in which DNA is likely to be preserved are in the dryness of the desert, in desiccated mummies, or tissues preserved in ice/glaciers (Jackson et al. 1998). DNA of microbial organisms or parasites from such specimens is likely to be well preserved and to lend itself readily to palaeomicrobiologic analyses (Arriaza et al. 1995; Li et al. 1999, Meers 1985; Reid et al. 2000, Rollo et al 2000; Spencer and Howe 2004; Taubenberger et al. 1997; Tumpey et al. 2004; Zink et al. 2002). Unfortunately, many of the ancient plagues that we are aware of from historical records did not occur in areas with favourable climatic conditions that would lend themselves to the preservation of analysable DNA samples (Antia et al. 2003; Brothwell and Sandison 1967; Cockburn 1971; Hofreiter et al. 2001; Zink et al. 2002). The ancient plagues of Egypt occurred in dry areas, but were not preserved in mummified remains.

The plagues of ancient Rome and ancient Athens occurred in climatic conditions that may not yield suitable specimens for palaeomicrobiologic identification (Kiple 1993; McNeill 1976). There are further problems with DNA specimen analysis, which has a corollary in contemporary clinical infectious diseases. In infectious diseases, one of the most fundamental determinations is to differentiate colonisation from infection. Similarly, in palaeomicrobiology, the mere recovery of an organism from an ancient preserved specimen does not necessarily implicate a role for this organism as the pathogen responsible for the demise of the individual whose remains

are being analysed. The recovery of *Salmonella typhi* in areas endemic for enteric fevers as well as malaria and a variety of other infectious diseases, does not necessarily imply that the organism was causally related to the patient's demise. For example, if a patient who has pulmonary tuberculosis dies of coronary artery disease, the presence of tuberculosis does not necessarily imply that tuberculosis was the cause of death. Nevertheless, the study of palaeomicrobiology has contributed greatly to our understanding of the ancient microbial milieu of humans and animals (Antia et al. 2003; Brothwell and Sandison 1967; Cockburn 1971; McNeill 1976).

The very fact that the presence of such organisms can be verified is of great scientific importance (Drancourt et al. 1998). The types of specimen that lend themselves most readily to analysis are those that are likely to survive the ravages of time, i.e. teeth, bone specimens, coproliths, etc. Palaeopathology, the study of pathological changes in ancient remains, has been very important in confirming the presence of various diseases in ancient times. Because palaeopathology depends upon observable pathological changes in ancient specimens, palaeopathology is most useful in identifying infectious diseases with observable pathological changes. Skeletal syphilis and tuberculosis are examples of infectious diseases that produce characteristic changes in bone, which are readily recognisable in palaeopathological specimens (Arriaza et al. 1995; Brothwell and Sandison 1968; Kiple 1993). Infectious diseases that kill rapidly leave no traces in teeth, bone, or coproliths, which is problematic. In the absence of permanently preserved specimens, how would scientists in the future determine the presence/lethality of severe acute respiratory syndrome (SARS) in tissue from cadaveric specimens from Asia? Palaeomicrobiology has been most successful in demonstrating bacteria, Rickettsia, and parasite ova (Drancourt and Raoult 2005).

Palaeopathology has also demonstrated non-microscopic parasites in tissue specimens. Such findings are interesting and add to our knowledge of the epidemiology of infectious diseases in the ancient world (Arriaza et al. 1995; Brothwell and Sandison 1967). Although epidemiological analyses provide the background for the endemic illnesses in ancient populations, they do not explain the causes of the various plagues described in the ancient world (Kiple 1993). Until there is incontrovertible proof based upon methodologically sound science, the best current and future approach of trying to determine the etiology of epidemics in the ancient world is to combine the epidemiological information from palaeopathology with the continuing advances made in palaeomicrobiology, and this information should be used in conjunction with historical analyses (Cunha 2004b; Cunha and Cunha 2006). This chapter will take a historical approach combined with what is currently known from palaeomicrobiological and palaeopathological information to review the likely causes of three key ancient plagues of the past.

1.2 Determination of the Cause of Ancient Plagues by Historical/Clinical Analysis

While palaeopathology is probably the best way to obtain a definitive diagnosis of an ancient disease, it is not always possible. Due to the difficulty of obtaining tissue samples from victims of the ancient plagues, it is not always possible to utilise the

technique of palaeomicrobiology to determine the etiology of ancient infection (Cooper and Poinar 2000; Drancourt and Raoult 2005; Hofreiter et al. 2001; Zink et al. 2002). Therefore, it is often necessary to utilise other means to arrive at a likely diagnosis. The most helpful of these is a primary literary description of the disease. While this is often the best evidence available, working with these sorts of documents can prove difficult. When it comes to discussing the three great plagues of the ancient world, the Plague of Athens, the Antonine Plague, and the Justiniac Plague, the descriptions are in either Latin or ancient Greek.

Therefore, The difficulties encountered when translating any ancient foreign language are compounded by the fact that so many words in these languages have a variety of meanings. Additionally, due to the precision required in medical documentation, any word or phrase that is interpreted in a way other than that intended by the original author can skew a description toward or away from the actual diagnosis (Cunha 2004b; Littman and Littman 1973; Major 1978; Procopius 1981). While Thucydides' chronicle of the plague is exquisitely detailed, variation in translation makes it impossible to definitively determine the causative agent (Page 1953; Parry 1969; Shrewsbury 1950; Thucydides 1919). Because of this, the only way to confirm a suspected diagnosis would be through the use of palaeomicrobiology (Drancourt and Raoult 2005). Indeed, a mass grave immediately outside Athens has been unearthed, but has not yet been analysed – until it is, debate will continue.

There is also an underlying assumption that the description was accurate to begin with and has been preserved intact (Major 1978). In the case of the Antonine plague, mere fragments of Galen's writings describing the course of the disease remain. Enough of the text is available to develop a clinical diagnosis, but this will need to be confirmed by palaeomicrobiological testing (Drancourt and Raoult 2005).

Obviously then, the best way to determine the cause of an ancient disease would be to combine palaeopathology with a literary clinical/historical analysis. This is the case with the Justiniac plague, which not only has a clear description that leads the reader to only one obvious conclusion, but also has evidence from mass graves from the era of the plague. These have been unearthed and genetic testing has confirmed the suspected etiology (Drancourt and Raoult 2002, 2004; Drancourt et al. 2004).

1.2.1 The Plague of Athens (430–426 B.C.): Determination of Etiology by Historical/Clinical Analysis

1.2.1.1 Historical Overview

Without doubt, Athens and Sparta were the two most powerful and influential civilisations on mainland Greece in the ancient world. By 431 B.C. the Peloponnesian War between Athens and Sparta had begun in earnest. Athens had only to survive the Spartan assault in order to claim victory, while the Spartans would have to conquer the city of Athens itself. Pericles, the leader of Athens, realised this and called for the Athenians to surrender their territory in Attica and to move all people in

Athens, and in the regions immediately surrounding it, into the city itself, which was protected by the great Themistoclean walls. These walls guarded the city proper, and provided a fortified connection with the harbour of Piraeus, 9 km from the city. Taking into account the Athenian's well-established naval superiority as well as their safe access to a protected port, it seemed as though taking Athens would be next to impossible for the Spartans. However, by 404 B.C., several events occurred that resulted in the total defeat of Athens and her allies. Most significant of these is the great Plague of Athens, described so accurately by Thucydides, the Greek historian. The plague struck Athens early in the conflict, during the summer of 430 B.C., and drastically reduced the population of the city, devastating Athenian society (Bollet 1987; Brothwell and Sandison 1967; Kiple 1993).

There has been much debate by both physicians and classicists as to the exact cause of the plague and neither group has come to a consensus. Although Thucydides was not a trained physician, he was most certainly an astute observer, and was careful to utilise the medical vocabulary of his era. Thucydides himself contracted and survived the plague, thus granting modern interpreters a precise and detailed account of the disease.

1.2.1.2 Thucydides' Clinical Description

It first began, so it is said, in ***Ethiopia above Egypt****, and then descended into Egypt and Libya and into most of the King's land. Suddenly falling upon Athens, it first attacked the population at Piraeus, so that they themselves said that the Peloponnesians had thrown poison into their cisterns: for there were, as yet, no wells there. But afterwards it came to the upper city as well, and from that time the deaths became much greater. Now, anyone, either physician or layman, can, by his own opinion, speak on its origins and the causes that produced so great a departure from normal conditions; but I shall talk about its course, and explain the symptoms, by which it could be recognised in the future, having knowledge of it beforehand. For I myself was ill and saw others suffer from it.*

That year, as agreed by all, had been unprecedentedly disease-free in respect to other sicknesses; but if anyone was suffering from anything at all before, all resolved into this. In other cases, there was no apparent cause, but suddenly, healthy men were seized first with ***mighty fevers in the head****, and* ***redness, and inflamed eyes,*** *and the inside, both the* ***throat and tongue****,* ***immediately became blood-red*** *and* ***emitted an atypical, foul breath****. After which came* ***sneezing and hoarseness****, and in not much time the pain descended into the chest, and produced a* ***severe cough****; and* ***when it fixed in the stomach, it upset it****, and* ***vomiting of bile*** *of every kind named by physicians ensued, accompanied by great suffering. In most cases* ***nonproductive retching*** *followed, giving way to* ***violent spasms****, which lessened, in some sooner, in others, not until much later. Externally, the body was* ***not very hot to the touch,*** *and was not pale,* ***rather, it was reddened, livid, and flowering with small blisters and wounds****. But* ***their insides burned so hotly, that the patients could not bare garments or fine cloths being laid on them, nor be anything but***

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