



#### HISTORY OF MEDICINE

### EPIDEMICS OF THE ROMAN EMPIRE, 27 BC – AD 476

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This article reviews the epidemics that struck Rome and its neighbours during the Roman Empire, starting with the reign of the emperor Augustus (27 BC) and ending with the fall of Rome in AD 476.

#### THE ROMAN EMPIRE

This era can be divided into two phases. The first was the so-called early Empire or Golden Age of Rome, which lasted approximately two centuries and was characterised by the Pax Romana. It was a time of prosperity, relative peace and cultural achievement, with countries and regions under Roman control benefiting substantially from excellent administration and the establishment of infrastructures such as roads, public safety and a reliable monetary system. The death of the philosopheremperor Marcus Aurelius in AD 180 heralded the end of this era.

The second phase or late Empire commenced at the turn of the 3rd century with a succession of so-called 'soldier emperors' appointed by the army. This led to progressive instability. Persecution of Christians intensified under Valerian (AD 253 - 260). The Empire experienced growing military aggression on its borders, in particular from Germanic tribes. Gradual decline set in, but this was temporarily halted by the efficient reforms of Diocletian (AD 284 - 305). He advocated decentralised government and divided his administration into a western and an eastern section. Constantine (324 - 337) established a new capital at Constantinople, and also proclaimed Christianity the state religion. The eastern empire now separated progressively from the western empire under Rome, and retained its autonomy until 1453. Rome could not contain the 'barbarian' invasions of the early 5th century, and was plundered by the Visigoths in 410. In 476 the Germanic commander, Odoacer, deposed the last Roman emperor, ironically called Romulus Augustulus ('little Augustus').

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Although it is difficult to establish the precise impact of epidemic disease on the Roman Empire, there can be no doubt that it contributed significantly to the multifactorial aetiology responsible for the eventual decline and fall of the Empire.

#### **EPIDEMIC DISEASE**

#### The early Empire

The first major epidemic occurred in Rome in 23 - 22 BC. It was associated with famine and soon spread to the rest of the country. Clinical features of the disease are not recorded, but Dio Cassius reported the presence of evil portents — a wolf was caught in the city, fire and storms damaged buildings, the Tiber flooded the city and carried away the wooden bridge, and thunderbolts struck statues in the pantheon, even dislocating the spear from the hand of Augustus.<sup>2</sup>

The first century AD was characterised by volcanic eruptions, earthquakes, famine and repeated epidemics, many of which were documented only vaguely. In his Natural History, Pliny the Elder mentions a communicable skin disease, mentagra, which reached Rome from Asia Minor towards the middle of the century. The disease often commenced in the chin area, for this reason the name derived from the Latin word mentum (chin). It was characterised by a scaly lesion that often affected the whole of the face (omitting the eyes), also spreading to the neck, chest and even hands. It was thought to be spread by kissing, and attacked mainly men from the noble class. It was neither painful nor dangerous, but disfiguring to such an extent that distressed patients were willing to accept treatment with caustics that left scars worse that the original lesions. Even then the lesions usually recurred unless the flesh was cauterised through to the bone.3 In AD 54 (during the reign of Nero) a severe epidemic described by Tacitus struck Rome and environs, together with a tempest that wasted Campania and wreaked agricultural havoc. All classes of citizens died in large numbers from a disease that spread by direct contact.4 Suetonius mentions 30 000 deaths in a single autumn in Libitina.5 In AD 65 while soldiers overcrowded military camps around Rome, an epidemic ensued that Tacitus put down to the unhealthy climate of the Vatican district, the drinking of unclean water from the Tiber and the soldiers' poor physical condition due to inactivity and debauchery.5 And then in 79/80, concurrent with the eruption of Vesuvius and a devastating fire

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Marcus Aurelius, during whose reign (161 - 180) the devastating Antonine epidemic occurred.

in Rome that lasted 3 days, Suetonius<sup>5</sup> and Dio Cassius<sup>7</sup> record a further epidemic of frightful proportions that caused 10 000 deaths in the Campagna alone. The disease was confined to Italy and also caused heavy livestock losses.

In 125 the so-called pestilence of Orosius devastated entire villages in Italy. It originated in Africa following a famine precipitated by a heavy locust invasion. The disease was said to have caused 800 000 deaths in Numidia alone and 200 000 in North Africa, but these figures may have been exaggerated by historians such as Orosius who recorded the event three centuries later. Clinical details were not recorded.8

Forty years later in AD 165 there began one of the most catastrophic epidemics ever to visit the Roman Empire. 9.10 It raged intermittently for three decades and marked the end of the Golden Age of Rome. Occurring during the reign of Marcus Aurelius Antoninus (161 - 180) it became known as the Antonine 'plague' or epidemic, and has been extensively reviewed by historians and scholars. Contemporary authors such as Lucian, 11 Aristides (who survived an attack of the

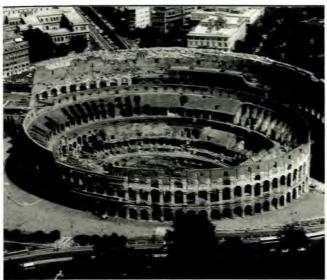
disease),<sup>12</sup>Herodian,<sup>13</sup> Dio Cassius<sup>14</sup> and others left fragmentary reports. Particularly disappointing is the unsatisfactory coverage by Galen (129-199), who as the leading physician of the 2nd century seemed to pay surprisingly little attention to the pestilence (which has also been called the 'plague'/epidemic of Galen). His references to the disease are scattered and brief. Although a cursory summary of symptoms and signs does exist, he did not compile a full description of the pestilence but gave the impression that he could manage it. He left Rome in 166 soon after the outbreak of the epidemic and quite probably because of it, later even declining an invitation from the emperor to accompany him on a military expedition on the grounds that Asclepius forbade him to go.<sup>9,10</sup>

Although the historian Crepereius Calpurnianus claimed that the epidemic was of Ethiopian origin,11 most authorities believed that it was brought to Rome by the returning army of Marcus Aurelius' son-in-law, Verus, after he defeated the Parthians and sacked Seleucia in Mesopotamia. The story was that a pestilential vapour escaped from a golden casket desecrated by soldiers in the temple of Apollo, causing the initial disease among the Roman legions in Seleucia. The epidemic ravaged the empire as far afield as Gaul and the Rhine, affecting humans and domestic animals, and causing widespread famine. 9,10 Lucian, Orosius and others recorded very high mortality figures, but reliable statistics are unavailable and recent authors suspect that death rates were probably exaggerated.9 Littman and Littman suggest a mortality of 7 - 10%,10 while Gilliam thought it could have been as low as 2%.9 From Galen's sketchy description the clinical picture comprised a pyrexial illness, with a crisis on the 9th -12th day, mild to severe respiratory infection (even haemoptysis), abdominal pathology with diarrhoea (often bloody) and vomiting, and a characteristic skin rash with blisters over the whole body.10 The first outbreak lasted 3 years (165 - 168), with major recurrences in 172 - 175 and 189. Dio Cassius described the last episode as the biggest epidemic ever, with up to 2 000 deaths per day in Rome.14 Marcus Aurelius briefly mentions the epidemic in his Meditations,15 and probably died of it himself in 180.9 However, for the next 50 years Rome was free of severe epidemic disease.16

#### The late Empire

Between AD 251 and 266 the Empire was struck by a pestilence that compared with the Antonine epidemic in severity. § 16 It significantly weakened the Roman military effort at a time when a succession of poor emperors were hard-pressed to defend the borders against Germanic and Persian invasions. In search of scapegoats, emperors such as Gallus and Valerian stepped up the persecution of Christians, who nevertheless distinguished themselves by rendering sterling service to the ill and dying. For this they were praised by the emperor, Julian. § Zosimus, § Eusebius and others wrote accounts of the epidemic, but St Cyprian, Bishop of Carthage, left the best-





The Colosseum, most famous of the Roman amphitheatres, was built by the emperors Vespasian and Titus to accommodate the tens of thousands of Romans who attended gladiatorial combats and spectacles such as fights between wild animals.

known description of what became known as the epidemic 'plague' of Cyprian.<sup>20</sup> Contemporaries ascribed the disease to the crimes of the Christians; in spite of their charitable work, organised by St Cyprian, hatred of them and especially of their leader increased, until he was martyred in 258. The epidemic was said to have originated in Ethiopia, from where it reached Europe through Egypt and North Africa. It lasted close on 15 years and spread intermittently over the whole known world 'from Egypt to Scotland' showing a seasonal incidence with maximal intensity in autumn and winter. The Roman province of Achaia in Greece was particularly hard hit. The disease was extremely contagious, apparently spreading by direct contact as well as by means of patients' clothing. Mortality was high, terror was extreme and phantoms were seen to hover over the houses of those who were about to fall ill.816,21 The clinical picture included redness of the eyes, fever and thirst, inflammation of the throat and pharynx, diarrhoea and vomiting, paralysis of the lower extremities, even terminal gangrene of the feet and legs. Skin lesions were not recorded.8

Lesser pestilences were recorded in Egypt, Lybia and Syria during the rest of the 3rd century, but the next major epidemic occurred early in the 4th century. The exact date is uncertain. Zinsser refers to a pestilence (without specific symptomatology) described by Cedrenius during the reign of Diocletian and Maximinian, who enforced severe persecution of Christians in North Africa between 303 and 305. Eusebius also mentions an epidemic in Syria in 302 during this period of persecution, but then describes a major epidemic at the time of religious deliverance at the hand of Constantine the Great, who was converted to Christianity in 312 and recognised the civil rights of Christians in 313. Eusebius' epidemic significant is generally accepted to have occurred in 312/313. It was

associated with drought and severe famine and caused great mortality in cities, although there were even more deaths in the countryside where entire communities were wiped out. It affected all ranks of society. Unburied corpses were devoured by dogs, which led to the pre-emptive killing of dogs lest they 'become mad and turn to devouring men'. Once again mention is made of the selfless dedication of Christians (in contrast to pagans) in looking after the ill. Eusebius described the epidemic as a new disease characterised by specific skin ulcers that covered the entire body, and a tendency towards blindness. The original Greek word used to describe the ulcers was 'anthrax'. Contrary to certain reviews, <sup>16</sup> Eusebius did not describe death of domestic animals due to the epidemic.

An interesting, brief and self-limiting epidemic occurred in the city of Amida during the reign of Constantine's son, Constantius, in 359. The overcrowded city, already containing large numbers of decomposing corpses, a populace with weakened health 'from various causes' and 'steaming heat', was now struck by an acute epidemic. People died of disease, of heat and of effects of overcrowding. However, when it started raining on the night of the 10th day 'the thick and gross exhalations were dispelled' and health returned to the city.<sup>24</sup>

For the Roman Empire in the west the 5th century brought final collapse.1 It was a time of relatively few records with war, famine and pestilence only vaguely described.8 By 406 waves of 'barbarian' tribes moved into Italy, Gaul, Spain and North Africa. They were harassed by marauding Huns displaced from China, possibly by disease, at the turn of the 2nd century.16 Rome was sacked by the Visigoths in 410 and by the Vandals in 455. The Huns, previously ravaged by an epidemic in 425, turned back from the gates of Rome in 452. This was largely attributed to the persuasive powers of Pope Leo I, but Karlen suggests that an epidemic (possibly smallpox) raging in Rome at the time also affected the Huns, and could have played a major role in their withdrawal.25 Zinsser refers to severe epidemic disease in the Roman provinces and near Orae Favianae (Vienna) in particular in 455/456; cases were characterised by inflamed eyes, reddening of the skin over the entire body, and severe pulmonary infection.16,23 In 4628 and again in 46716 Rome suffered epidemic disease with high mortality rates. Throughout this time localised epidemics ravaged the Gallic provinces and in 477 the Saxon invaders and local populace of Anjou were devastated by a pestilence. 8.16 Shortly thereafter the Vandals in North Africa were so decimated by disease that they were unable to resist later attacks by Islamic forces.8

Bede described a devastating epidemic in Britain in 444, but no clinical details were recorded. Probably as a result of this pestilence the Britons could no longer repulse the 'Redshanks' (Picts) and other invaders from the north, and took the momentous decision of inviting the Saxons from across the sea to be mercenary guards.<sup>26</sup> British history was influenced decisively by the arrival of the Saxons in 449; they soon became

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the major power in England.

#### DISCUSSION

### **Epidemiological aspects**

It has been postulated that at the onset of the Christian era the Mediterranean basin probably represented a relatively stable common epidemiological pool of diseases to which the populace had become adapted.<sup>21,27</sup> By expanding its military and economic influence the Roman Empire altered the status quo through progressive contact with significant disease pools in at least three other regions, namely neighbouring Mesopotamia (Middle East), the Indian subcontinent (Ganges and Indus valleys in particular) and China in the Far East. The great lakes region of central Africa was also a significant breeding ground for diseases in antiquity, but its Mediterranean influence was less pronounced because the Roman Empire did not expand to those regions. The 'disease gradients' to new epidemiological pools were traversed by sea and particularly by land. For instance the caravan trade on the 'Silk Road' to China reached a climax in approximately AD 100. It is accepted that most of the new epidemics that ravaged the Empire were introduced by traders or soldiers. There is evidence that China was similarly visited by potent new diseases imported from the West, smallpox and/or measles arriving in 317 and bubonic plague in 610. However, historians find little evidence of increased epidemics in India. This could be due to a less helpful record system in India with its tradition of a dateless antiquity, but it could also indicate greater indigenous immunity to disease resulting from the possibility that most epidemics 'in circulation' in the known world had originated there.21,27

Epidemic disease (and viral disease in particular) needs a critical population density before it can sustain itself. Smallpox and measles need a population mass of approximately 300 000 - 500 000. It is, therefore, improbable that mankind knew epidemic disease before the 3rd millennium BC when population concentrations in Egypt and Sumeria first reached the required density. In Augustan times the Roman Empire ruled over approximately 50 million people, which suggests that there must have been a number of metropolitan areas or other population concentrations well able to sustain epidemic disease. <sup>21,27,28</sup>

In attempting to identify the epidemics of the time one may exclude certain disease entities, as most authors agree that these appeared at a later stage in world history. Bubonic plague might have occurred as a restricted disease in the 3rd century BC, but the first recognised major epidemic was in the 6th century AD (the epidemic of Justinian). Epidemic typhus appeared in the 16th century and cholera even later. 16,21

Epidemic diseases that clearly existed during the period under study include those that are recognisable in the Hippocratic writings — such as malaria, mumps and erysipelas, and possibly relapsing fever, influenza, diphtheria

and salmonellosis (including typhoid).<sup>28</sup> Smallpox is generally accepted to have appeared in the Mediterranean basin in the 5th century BC and to have caused the Athenian epidemic (430 - 426 BC) described by Thucydides.<sup>30,31</sup> Measles (with a high mortality rate) probably existed concomitantly with smallpox and was often confused with it, until Rhazes differentiated the diseases in the 10th century.<sup>21,28,32</sup> Although no clear evidence exists, scarlet fever, the arboviral diseases (e.g. Rift Valley fever and dengue), as well as a range of infectious diarrhoeas, could have been present.<sup>21,28</sup> Zoonoses such as anthrax and glanders almost certainly existed.<sup>28</sup>

#### Identification of diseases

The clinical pictures of epidemics of antiquity might well have differed from those in modern times due to factors such as changing population immunity and genetic evolution of micro-organisms across the timespan of two millennia. However, our clear recognition of diseases such as mumps, malaria, smallpox and bubonic plague from descriptions in ancient times indicates that many syndromes have retained remarkable consistency.

#### **Early Empire**

The Early Empire was struck by a number of minor or localised epidemics in addition to the widespread and catastrophic Antonine epidemic that commenced in 165 and lasted intermittently for three decades. The clinical picture as recorded by Galen is today accepted by most scholars as being that of smallpox, which originated in Mesopotamia.21,28 The pestilence of Orosius (125) that affected Italy and North Africa was the best recorded of the lesser epidemics, albeit by historians of a later era. Although the symptoms are not known to us it clearly originated in Africa (like the Athenian disease of 430 BC), and one could postulate without convincing evidence that smallpox was again responsible. The epidemic of 54 was spread by personal contact and could also have been smallpox, although measles and influenza are distinct possibilities. The epidemics of 65 and 79/80 were apparently localised to Rome and environs; contemporary historians partially blamed unhealthy climatic and living conditions. Malaria, probably the commonest cause of fever in Italy,28 could well have been a major causative factor.

Pliny the Elder's record of an infectious skin disease brought to Rome from Asia Minor raises the interesting possibility that his mentagra was an early description of the variety of leishmaniasis known as 'oriental sore' still endemic in the Mediterranean. Pliny's illness apparently caused disfiguring skin lesions without associated systemic disease, and was probably self-limiting as an epidemic. No subsequent record of it exists. 'Oriental sore' is conveyed by the bite of a sandfly (*Phlebotamus*) vector. It characteristically causes bluish-red skin papules starting on the face and spreading to the upper body. It may heal slowly or enlarge to form ulcerated lesions that heal with scarring after many months. The patient is then immune





against further attacks.<sup>33</sup> The high incidence among men of nobility would be difficult to explain except for the interesting possibility that infection took place near the arena where nobility (and men in particular) watched gladiatorial spectacles from their reserved seats close to the sandy arena (harena means 'sand' in Latin).<sup>34</sup> Rodents and carnivores are known reservoirs of the Leishmaniasis organism,<sup>35</sup> and sandflies in the arena could have conveyed the disease from infected wild animals brought to Rome for blood sport. It is most unlikely that male kissing could have spread 'oriental sore', as was suggested by Pliny. Lupus vulgaris (skin tuberculosis) could also be considered, but it is usually more chronic and lasted a lifetime before modern therapy. It rarely occurs in epidemic form.<sup>33</sup>

#### Late Empire

The late Empire's first major epidemic (that of Cyprian) lasted 15 years (251 - 266) and devastated the whole 'known world' after originating in Africa. It spread by direct contact and showed a seasonal incidence with maximal impact in autumn



Being able to afford a ring-side seat to watch gladiators and wild animals fight to the death in a sandy arena may have put Roman noblemen at particular risk of contracting the disfiguring disease mentagra — possibly a variety of leishmaniasis transmitted by sandflies.

and winter, which is typical of epidemics spread by the respiratory route such as smallpox, measles and influenza. The absence of skin lesions suggests influenza, with gangrene of the extremities an unusual complication. It is interesting to note that peripheral gangrene also occurred in the Athenian epidemic (430 BC) ascribed to smallpox, of which it was likewise an unexpected complication.

The epidemic of 321/313 was characterised by a tendency towards blindness and skin ulceration that covered the entire body. The Greek word used by Eusebius to describe the skin lesions is 'anthrax'; in its original meaning the word refers to a

gem of dark red colour. It may also be translated as 'carbuncle'. We differ from Zinsser<sup>16</sup> in believing that this disease is unlikely to be anthrax as we know it today, namely a zoonotic affection acquired by direct and close contact with bodily products of infected animals, and characterised by a single large carbuncle-like skin ulcer and severe systemic infection in fatal cases. Pulmonary anthrax with high mortality and no skin lesions characteristically affects woolsorters and follows the inhalation of *Bacillis anthracis* spores.<sup>36</sup> Because of the need for intermediate animal reservoirs, widespread fatal anthrax epidemics are unknown in humans. Eusebius did not describe concurrent diseases of animals. It is more likely that this epidemic, characterised by widespread skin lesions, was smallpox of the virulent haemorrhagic kind, which would explain the apparent red colour of the pustules.

Descriptions of the epidemics of the 5th century are vague, and identification is therefore difficult. According to Zinsser<sup>16</sup> the epidemic of 455/456 near present-day Vienna was characterised by severe respiratory infection, inflammation of the eyes and reddening of the skin over the entire body. This would be compatible with streptococcal infection causing scarlet fever and pneumonia, while measles (even smallpox) remain possibilities. Arboviral disease, a less likely explanation, commonly manifests with systemic illness accompanied by a generalised rash of varying nature. However, the prevalence of respiratory-borne virus diseases (measles, smallpox, influenza) over the previous centuries, and their high level of infectivity, suggests that these afflictions could well have continued into the 5th century.

#### Concomitant disease of animals and humans

Historians of ancient times often described concomitant affliction of humans and animals during epidemics, as occurred during the epidemic of 79/80 as well as the Antonine epidemic (161 - 180). In earlier times the association was described *inter alia* with the Mediterranean epidemics of 463 BC, 453 BC, 433 BC, 430 - 426 BC (Athens), 428 BC and 392 BC, and usually involved domesticated animals, cattle in particular. We previously suggested that smallpox could have caused the majority of these epidemics.<sup>37</sup> Various explanations may be offered to account for this association.

- Zoonoses (human diseases derived from animal sources, e.g. anthrax and glanders) could obviously be implicated, but as argued above, they are not known to cause massive epidemics of the kind described.
- 2. Sallares<sup>28</sup> and McNeill<sup>21</sup> point out that ancient historians, accepting the viewpoints of eminent writers such as Homer and Aristotle who claimed that all pestilential disease of men originated in four-footed animals, might have included the association spuriously in their histories. This would suggest that the concomitant infection of animals should probably be ignored when studying the cause of human epidemics as described by historians of antiquity.





3. However, another perspective should be considered. It is now generally accepted that most human diseases originated from animals domesticated over the past six to eight millennia. In this regard the ancients such as Homer and Aristotle were correct. This suggests the possible existence of an evolutionary phase when the same organism could have caused illness in both animals and humans. Today we recognise that the human measles virus is related to rinderpest virus and is almost identical with canine distemper virus in dogs. Smallpox and cowpox viruses are related and influenza affects humans as well as pigs and birds. Human arboviruses also infect a variety of animals. The mumps virus is related to parainfluenza as well as to Newcastle disease of fowl, and human tuberculosis probably originated from cattle disease. It is

Could there have been a stage, two to three millennia ago, when some of the micro-organisms in evolution might indeed have caused disease both in humans and animals? The historical association of smallpox and disease of cattle (noted above) could hypothetically be a case in point. A variation of this argument would be the interesting finding that the influenza A virus is capable of 'shift', which is the genetic intermingling of human strains with animal or bird strains resulting in new pathogens capable of attacking both humans and animals. This phenomenon is indeed responsible for the recent Chinese avian influenza that also caused fatalities in humans. We therefore suggest that the simultaneous affection of humans and animals reported in epidemics of antiquity should not necessarily be regarded as fortuitous artefacts of early historiography.

#### CONCLUSIONS

Epidemics in the Roman Empire originated in various ways. In some instances indigenous reactivation of pre-existing disease was rendered endemic by a relatively high degree of population immunity in communities large enough to sustain such epidemics. Smallpox and malaria were examples. Even in such communities fresh epidemics could be precipitated by the re-introduction of the old disease once immunity levels had been lowered over time. Furthermore, traders and armies brought new epidemics to Rome as she expanded her economy and her borders to countries with new 'disease pools'. Serious epidemics started ravaging the Empire towards the end of the Pax Romana in the 2nd century, contributing to the decline and fall of the Empire.<sup>21,28</sup>

It has been suggested that the epidemics of 165 (the Antonine epidemic) and 321 (the epidemic of Eusebius) were caused by smallpox. The epidemics of 54 and 125 (the epidemic of Orosius) could also have been smallpox epidemics, but diseases such as measles and influenza, among others, are also distinct possibilities. The epidemic of Cyprian (251) likewise suggests a viral illness spread by the respiratory route, although influenza seems the likeliest cause.

The epidemics of 65 and 79 were probably malarial, and that

of 455 was most likely caused by streptococcal infection manifesting as scarlet fever and pneumonia.

We suggest leishmaniasis of the skin ('oriental sore') as a possible explanation for Pliny the Elder's 'mentagra' of the 1st century.

Too little clinical detail exists to venture diagnoses for the rest of the epidemics listed.

#### References

- Kapp PH, Moll JC, Scholtz PL, de Jongh PS, Grundlingh LWF. Geskiedenis van die Westerse Beskawing. Deel I. Pretoria: HAUM, 1988.
- Dio Cassius. History of Rome. Book LIII.33.4. Cary E, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1914-1927.
- Pliny the Elder. Natural History XXVI.3.3. Jones WHS, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1980.
- Tacitus. Annals XVI.13. Moore CH, Jackson J, trs. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1937.
- Suetonius. The Lives of the Caesars. Book VI: Nero, c. 39. Rolfe JC, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1997.
- Tacitus. Histories II.93. Moore CH, Jackson J, trs. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1937.
- Dio Cassius. History of Rome LXVI.23-24. Cary E, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1925.
- 8. Cartwright FF. Disease and History. London: Hart-Davis, MacGibbon, 1973: 12-16.
- 9. Gilliam JF. The plague under Marcus Aurelius. Am J Philology 1961; 82(3): 225-251.
- 10. Littman RJ, Littman ML. Galen and the Antonine Plague. Am J Philology 1973; 94: 243-255.
- Lucianus. Book IV Alexander c.36. Harmon AM, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1961.
- 12. Aelius Aristides. The Complete Works XXXIII.6-44. Behr E, tr. Leiden: Brill, 1981.
- Herodian. History of the Empire 1.12.1. Whittaker CR, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1969.
- Dio Cassius. History of Rome LXXII.14.3. Cary E, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1914-1927.
- Marcus Aurelius. Meditations IX.2 Haines CR, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1953.
- Zinsser H. Rats, Lice and History. Boston, Mass.: Atlantic Monthly Press, Little, Brown & Co., 1935.
- Ferngren GB, Amundsen DW. Medicine and Christianity in the Roman Empire. In: Haase W, ed. Aufstieg und Niedergang der Römischen Welt IL37.3. Berlin: W De Gruyter, 1996: 2957-2978.
- Zosimus. Historia Nova 1.23-28. Buchanan JJ, Davis HT, trs. San Antonio: Trinity University Press, 1967.
- Eusebius. Ecclesiastical History VII.21.8. Oulton JEL, tr. Loeb Classical Library, Cambridge, Mass: Harvard University Press, 1957.
- 20. Cyprian. De Mortalitate VI.1-2. In: Forster ES, ed. Orations. New York: Arno Press, 1979.
- 21. McNeill WH. Plagues and Peoples. New York: Anchor Press, 1976: 77-147.
- Wain H. History of Preventive Medicine. Springfield, Ill.: Charles C. Thomas Publishers, 1970: 168.
- Eusebius. Ecclesiastical History IX.7.15-IX.8.3. Oulton JEL, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1957.
- Scriptores Historiae Augustae. Constantius, Gallus XIX.4.1-4. Magie D, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1961.
- 25. Karlen A. Plague's Progress. London: Indigo, 1995.
- Bede. Ecclesiastical History XIII-XV. King JE, tr. Loeb Classical Library, Cambridge, Mass.: Harvard University Press, 1930.
- Horstmanshoff HFJ. Epidemieën in de antieke wereld. Hermeneus 1979; 51(1): 58-80.
  Sallares R. The Ecology of the Ancient Greek World. New York: Cornell University Pres
- Sallares R. The Ecology of the Ancient Greek World. New York: Cornell University Press, 1991: 221-293.
- 29. Lloyd GER, ed. Hippocratic Writings. London: Penguin Books, 1983.
- Littman RJ, Littman ML. The Athenian Plague: Smallpox. Trans Am Philological Assoc 1969; 100: 263-275.
- 31. Retief FP, Cilliers L. The Epidemic of Athens, 430-426 BC, 5 Afr Med J 1998; 88(1): 50-53.
- Cliff A, Haggett P, Smallman-Raynor M. Measles: An Historical Geography. Oxford: Blackwell, 1993.
- 33. Marshall J. Diseases of the Skin. Edinburgh: Livingstone, 1960: 428.
- Carcopino J. Daily Life in Ancient Rome. The People and the City at the Height of the Empire, c.8. Lorimer EO, tr. London: Penguin, 1962.
- Jawetz E, Melnick JL, Adelberg EA. Review of Medical Microbiology 16\* ed. Los Altos, Calif.: Lange Medical Publications, 1984: 503-505.
   Cluff LE. In: Beeson PB. McDermot W, eds. Textbook of Medicine. Philadelphia: WB Saunders.
- Cluff LE, In: Beeson PB, McDermot W, eds. Textbook of Medicine. Philadelphia: WB Saunders. 1975: 383-384.
- Retief FP, Cilliers L. Epidemic Disease in Ancient Rome and other Mediterranean Countries. Die Suid-Afrikaanse Tydskrif vir Natuurwetenskap en Tegnologie (in press).
- 38. Walker E, Christie P. Chinese avian influenza (Editorial). BMJ 1998; 316: 325.